



AMERICAN COLLEGE OF  
OCCUPATIONAL AND  
ENVIRONMENTAL MEDICINE

# Knee Disorders

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## Summary of Recommendations

The Evidence-based Practice Knee Disorders Panel’s recommendations are based on critically appraised higher quality research evidence and on expert consensus observing First Principles when higher quality evidence was unavailable or inconsistent (see [Methodology](#)). The reader is cautioned to utilize the more detailed indications, specific appropriate diagnoses, temporal sequencing, preceding testing or conservative treatment, and contraindications that are elaborated in more detail for each test or treatment in the body of this Guideline in using these recommendations in clinical practice or medical management. These recommendations are not simple “yes/no” criteria.

All ACOEM guidelines include analyses of numerous interventions, whether or not FDA-approved. For non-FDA-approved interventions, recommendations are based on the available evidence; however, this is not an endorsement of their use. In addition, many of the medications recommended are utilized off-label. (For example, anti-epileptic agents have been used off-label since the 1960s to treat chronic pain.)

Recommendations are made under the following categories:

- Strongly Recommended, “A” Level
- Moderately Recommended, “B” Level
- Recommended, “C” Level
- Insufficient-Recommended (Consensus-based), “I” Level
- Insufficient-No Recommendation (Consensus-based), “I” Level
- Insufficient-Not Recommended (Consensus-based), “I” Level
- Not Recommended, “C” Level
- Moderately Not Recommended, “B” Level
- Strongly Not Recommended, “A” Level

<b>Acetaminophen</b>	Acetaminophen for Treatment of Acute, Subacute, Chronic or Post-operative Knee Pain	Recommended, Evidence (C)
	Acetaminophen or Aspirin as First-Line Therapy for Patients at Risk for Cardiovascular Adverse Effects	Strongly Recommended, Evidence (A)
<b>Activity Modification</b>	Activity Modification for Acute, Subacute, or Chronic Knee Pain	Recommended, Insufficient Evidence (I)
	Modifying Activities to Avoid Kneeling or Other Pressure Over the Knee for Bursitis	Recommended, Insufficient Evidence (I)
<b>Acupuncture</b>	Acupuncture for Acute or Subacute Knee Pain	No Recommendation, Insufficient Evidence (I)
	Acupuncture for Anterior Knee Pain	No Recommendation, Insufficient Evidence (I)
	Acupuncture for Chronic Osteoarthritis of the Knee	Moderately Recommended, Evidence (B)
<b>Antibodies</b>	Antibodies for Diagnosing Knee Pain with Suspicion of Chronic or Recurrent Rheumatological Disorder	Recommended, Insufficient Evidence (I)
	Antibodies to Confirm Specific Disorders	Strongly Recommended, Evidence (A)
<b>Antibiotics</b>	One-day Use of Systemic Antibiotics for Knee Surgery	Moderately Recommended, Evidence (B)
<b>Anticonvulsants</b>	Topiramate for Acute Knee Pain	Not Recommended, Insufficient Evidence (I)

	Topiramate for Subacute or Chronic Knee Pain	No Recommendation, Insufficient Evidence (I)
	Topiramate for Knee Osteoarthritis	No Recommendation, Insufficient Evidence (I)
<b>Antidepressants</b>	Norepinephrine Reuptake Inhibiting Anti-depressants for Acute Knee Pain	Not Recommended, Insufficient Evidence (I)
	Norepinephrine Reuptake Inhibiting Anti-depressants for Knee Osteoarthritis	No Recommendation, Insufficient Evidence (I)
	Norepinephrine Reuptake Inhibiting Anti-depressants for Subacute or Chronic Knee Pain	No Recommendation, Insufficient Evidence (I)
	Selective Serotonin Reuptake Inhibitors for Acute, Subacute, or Chronic Knee Pain	Not Recommended, Insufficient Evidence (I)
	Selective Serotonin Reuptake Inhibitors, SSRIs, or Tricyclic Anti-depressants for Chronic Knee Pain in Patients with Co-morbid Depression	Recommended, Evidence (C)
<b>Aspiration</b>	Aspiration for Infected Bursa	Recommended, Insufficient Evidence (I)
	Fluid Aspiration and Analyses for Knee Bursitis	Recommended, Insufficient Evidence (I)
<b>Aspirin</b>	Aspirin for Prevention of Venous Thromboembolic Disease	Moderately Recommended, Evidence (B)
<b>Biofeedback</b>	Biofeedback for Chronic Knee Pain	No Recommendation, Insufficient Evidence (I)
	Biofeedback for Patellofemoral Pain	Not Recommended, Evidence (C)
<b>Bone Scans</b>	Bone Scanning for Select Use in Acute, Subacute, or Chronic Knee Pain	Recommended, Insufficient Evidence (I)
	Routine Use of Bone Scanning for Knee Joint Evaluations	Not Recommended, Insufficient Evidence (I)
<b>Braces</b>	Functional Bracing for Anterior Cruciate Ligament Injuries Post-operatively	Not Recommended, Evidence (C)
	Functional Bracing for Prevention of Anterior Knee Pain	No Recommendation, Insufficient Evidence (I)
	Functional Bracing for Treatment of Non-Operative Anterior Cruciate Ligament Injuries	No Recommendation, Insufficient Evidence (I)
	Knee Braces for All Other Osteoarthritis	No Recommendation, Insufficient Evidence (I)
	Knee Braces for Knee Sprains	Recommended, Insufficient Evidence (I)
	Knee Braces for Moderate to Severe Chronic Knee Osteoarthritis	Recommended, Evidence (C)
	Off-loader Braces for Knee Osteoarthritis	Recommended, Evidence (C)
<b>Canes / Crutches</b>	Canes and Crutches for Moderate to Severe Acute, Subacute, or Chronic Knee Pain	Recommended, Insufficient Evidence (I)
<b>CT</b>	CT for Evaluating Patients with Osteonecrosis (AVN)	Recommended, Insufficient Evidence (I)
	CT for Evaluating Patients with Periprosthetic Osteolysis after Total Knee Arthroplasty	Recommended, Insufficient Evidence (I)

	Routine CT for Evaluating Acute, Subacute, or Chronic Knee Pain	Not Recommended, Insufficient Evidence (I)
<b>Education</b>	Educational Sessions for Treatment of Knee Osteoarthritis	Recommended, Insufficient Evidence (I)
	Pre-operative Educational Program Prior to Arthroplasty	Moderately Recommended, Evidence (B)
<b>Electrical Therapy</b>	Electrical Stimulation Therapies for Treatment of Acute, Subacute, or Chronic Knee Pain	No Recommendation, Insufficient Evidence (I)
	Electrical Stimulation for Anterior Knee Pain	Not Recommended, Evidence (C)
	Electrical Stimulation Therapies for Treatment of Knee Osteoarthritis	No Recommendation, Insufficient Evidence (I)
	Extracorporeal Shockwave Therapy for Patellar Tendinosis	Moderately Not Recommended, Evidence (B)
	Interferential Therapy for Post-Operative Knee Patients	Recommended, Evidence (C)
	Iontophoresis for Knee Osteoarthritis	No Recommendation, Insufficient Evidence (I)
	Iontophoresis for Acute, Subacute, or Chronic Knee Pain	
	Microcurrent Therapy for Post-Operative Total Knee Arthroplasty Patients	No Recommendation, Insufficient Evidence (I)
	Percutaneous Electric Therapy for Knee Osteoarthritis	Recommended, Evidence (C)
	Percutaneous Electric Therapy for Other Knee Pain	Recommended, Insufficient Evidence (I)
	Pulsed Electromagnetic Fields for Acute, Subacute, or Chronic Knee Pain	No Recommendation, Insufficient Evidence (I)
	Pulsed Electromagnetic Fields for Osteoarthritis	No Recommendation, Insufficient Evidence (I)
	TENS for Acute, Subacute, or Chronic Knee Pain	No Recommendation, Insufficient Evidence (I)
	TENS for Knee Osteoarthritis	No Recommendation, Insufficient Evidence (I)
	<b>EMG</b>	Electromyography for Diagnosing Subacute or Chronic Peripheral Nerve Entrapments
<b>Ergonomics</b>	Ergonomic Interventions for Knee MSDs	No Recommendation, Insufficient Evidence (I)
	Fall Protection	Recommended, Insufficient Evidence (I)
	Knee Pads for Kneeling Activities	Recommended, Insufficient Evidence (I)
<b>Exercise</b>	Aerobic Exercise for Treatment of Knee Osteoarthritis	Strongly Recommended, Evidence (A)
	Aquatic Therapy for Knee Osteoarthritis	Recommended, Insufficient Evidence (I)
	Exercise for Patellofemoral Joint Pain	Moderately Recommended, Evidence (B)
	Pre-operative Exercise Program	Recommended, Insufficient Evidence (I)
	Strengthening Exercises for Treatment of Knee Osteoarthritis	Moderately Recommended, Evidence (B)
	Stretching Exercises for Treatment of Knee Osteoarthritis	Recommended, Insufficient Evidence (I)
	Yoga for Chronic Knee Pain	No Recommendation, Insufficient Evidence (I)

<b>Gabapentin</b>	Gabapentin for Acute Knee Pain	Not Recommended, Insufficient Evidence (I)
	Gabapentin for Subacute or Chronic Knee Pain	No Recommendation, Insufficient Evidence (I)
	Gabapentin for Knee Osteoarthritis	No Recommendation, Insufficient Evidence (I)
	Gabapentin for Peri-Operative Pain	Recommended, Insufficient Evidence (I)
<b>Glucosamine</b>	Glucosamine Sulfate, Chondroitin Sulfate, or Methylsulfonylmethane for Knee Osteoarthritis	No Recommendation, Insufficient Evidence (I)
	Glucosamine Sulfate, Chondroitin Sulfate, or Methylsulfonylmethane for Osteoarthritis Prevention	No Recommendation, Insufficient Evidence (I)
<b>Heat</b>	Heat for ACL Tears	No Recommendation, Insufficient Evidence (I)
	Heat for Knee Sprains	Recommended, Insufficient Evidence (I)
	Heat for Meniscal Tears	Recommended, Insufficient Evidence (I)
	Heat for Patellofemoral Joint Pain	Recommended, Insufficient Evidence (I)
	Heat for Quadriceps, Gastrocnemius, or Soleus Strains	Recommended, Insufficient Evidence (I)
	Self-application of Heat Therapy for Acute, Subacute, or Chronic Knee Pain	Recommended, Insufficient Evidence (I)
	Self-application of Heat Therapy for Osteoarthritis	Recommended, Insufficient Evidence (I)
<b>Heparin</b>	Low-molecular Weight Heparin for Prevention of Venous Thromboembolic Disease	Strongly Recommended, Evidence (A)
	Warfarin and Heparin for Prevention of Venous Thromboembolic Disease	Moderately Recommended, Evidence (B)
<b>Ice</b>	Cryotherapy for Treatment of Knee Arthroplasty and Arthroscopy and Other Surgery Patients	Recommended, Insufficient Evidence (I)
	Home Use of Cryotherapies for Acute, Subacute, or Chronic Knee Pain	Recommended, Insufficient Evidence (I)
	Home Use of Cryotherapies for Knee Osteoarthritis	Recommended, Insufficient Evidence (I)
	Ice for ACL Tears	No Recommendation, Insufficient Evidence (I)
	Ice for Knee Sprains	Recommended, Insufficient Evidence (I)
	Ice for Meniscal Tears	Recommended, Insufficient Evidence (I)
	Ice for Patellofemoral Joint Pain	Recommended, Insufficient Evidence (I)
	Ice for Quadriceps, Gastrocnemius, or Soleus Strains	Recommended, Insufficient Evidence (I)
	Progressive Agility, Trunk Stabilization and Icing (PATS) for Quadriceps, Gastrocnemius, or Soleus Strains	Recommended, Evidence (C)
<b>Inflammatory Markers</b>	Non-specific Inflammatory Markers for Screening for Inflammatory Disorders in Subacute or Chronic Knee Pain Patients	Recommended, Insufficient Evidence (I)
<b>Injections</b>	Aprotinin Injections for Patellar Tendinopathy	Recommended, Evidence (C)
	Autologous Blood Injections for Moderate to Severe Knee Osteoarthritis	No Recommendation, Insufficient Evidence (I)

Botulinum Injections for Knee Osteoarthritis or Other Knee Disorders	No Recommendation, Insufficient Evidence (I)
Glucocorticosteroid Injections after Arthroscopy	Recommended, Evidence (C)
Glucocorticosteroid Injections for Iliotibial Band Syndrome	Recommended, Evidence (C)
Glucocorticosteroid Injections for Knee Bursitis	No Recommendation, Insufficient Evidence (I)
Glucocorticosteroid Injections for Meniscal Tears	Not Recommended, Insufficient Evidence (I)
Glucocorticosteroid Injections for Select Patients with Patellar Tendinopathy	Recommended, Insufficient Evidence (I)
Glucosamine Sulfate Intraarticular Injections for Knee Osteoarthritis	No Recommendation, Insufficient Evidence (I)
Glucosamine Sulfate Intramuscular Injections for Knee Osteoarthritis	No Recommendation, Insufficient Evidence (I)
Glycosaminoglycan Injections for Patellar Tendinosis	Not Recommended, Evidence (C)
Intraarticular Glucocorticosteroid Injections for Knee Osteoarthritis	Recommended, Evidence (C)
Intraarticular Knee Viscosupplementation Injections for Moderate to Severe Knee Osteoarthritis	No Recommendation, Insufficient Evidence (I)
Intraarticular Platelet-Rich Plasma and Plasma Rich in Growth Factor, and Injections for Moderate to Severe Knee Osteoarthritis	No Recommendation, Insufficient Evidence (I)
Local Anesthetic Injections to Diagnose Subacute or Chronic Knee Pain	Recommended, Insufficient Evidence (I)
Other Modalities/Injections for ACL Tears	No Recommendation, Insufficient Evidence (I)
Other Modalities/Injections for Meniscal Tears	No Recommendation, Insufficient Evidence (I)
Other Modalities/Injections for Knee Sprains	No Recommendation, Insufficient Evidence (I)
Other Modalities/Injections for Patellofemoral Joint Pain	No Recommendation, Insufficient Evidence (I)
Percutaneous Needle Tenotomy for Chronic Tendinosis	No Recommendation, Insufficient Evidence (I)
Periarticular Glucocorticosteroid Injections for Arthroplasty Patients	No Recommendation, Insufficient Evidence (I)
Platelet-Rich Plasma or Autologous Blood Injections for Meniscal Tears	No Recommendation, Insufficient Evidence (I)
Platelet-Rich Plasma or Autologous Blood Injections for Patellar Tendinopathy	Not Recommended, Insufficient Evidence (I)
Polidocanol Injection for Acute, Subacute, or Post-operative Patellar Tendinopathy	No Recommendation, Insufficient Evidence (I)
Prolotherapy Injections for Acute, Subacute, or Chronic Knee Pain	Not Recommended, Evidence (C)
Prolotherapy Injections for Chronic Patellar Tendinopathy	Recommended, Insufficient Evidence (I)

	Radiation Synovectomy for Knee Osteoarthritis	Not Recommended, Evidence (C)
	Stem Cell Therapy	Not Recommended, Insufficient Evidence (I)
	Tidal Knee Joint Irrigation for Knee Osteoarthritis	Not Recommended, Insufficient Evidence (I)
<b>Laser Therapy</b>	Low-level Laser Therapy for Acute, Subacute, or Chronic Knee Pain	Not Recommended, Evidence (C)
	Low-level Laser Therapy for Knee Osteoarthritis	Not Recommended, Evidence (C)
	Low-level Laser Therapy for Meniscal tears	Not Recommended, Insufficient Evidence (I)
<b>Magnets</b>	Magnets and Magnetic Stimulation for Acute, Subacute and Chronic Knee Pain	No Recommendation, Insufficient Evidence (I)
	Magnets and Magnetic Stimulation for Osteoarthritis	No Recommendation, Insufficient Evidence (I)
	Pulsed Electromagnetic Fields for Acute, Subacute, or Chronic Knee Pain	No Recommendation, Insufficient Evidence (I)
	Pulsed Electromagnetic Fields for Osteoarthritis	No Recommendation, Insufficient Evidence (I)
<b>Manipulation / Mobilization</b>	Manipulation or Mobilization for Acute Knee Pain	No Recommendation, Insufficient Evidence (I)
	Manipulation or Mobilization for Knee Osteoarthritis	No Recommendation, Insufficient Evidence (I)
	Manipulation or Mobilization for Surgical or Knee Fracture Patients	No Recommendation, Insufficient Evidence (I)
	Manipulation or Mobilization for Post-operative Patients with Significantly Reduced Range of Motion	Recommended, Insufficient Evidence (I)
	Manipulation or Mobilization for Subacute or Chronic Knee Pain	Recommended, Evidence (C)
	Manipulation under Anesthesia for Post-operative Patients with Significantly Reduced Range of Motion	Recommended, Insufficient Evidence (I)
	Manual Therapy and Manipulation for Meniscal Tears	Not Recommended, Insufficient Evidence (I)
	Mobilization and Manipulation for Anterior Knee Pain	No Recommendation, Insufficient Evidence (I)
<b>Massage</b>	Massage for Acute, Subacute, or Chronic Knee Pain	No Recommendation, Insufficient Evidence (I)
	Massage for Knee Osteoarthritis	No Recommendation, Insufficient Evidence (I)
	Reflexology for Acute, Subacute, or Chronic Knee Pain	Not Recommended, Insufficient Evidence (I)
	Reflexology for Knee Osteoarthritis	Not Recommended, Insufficient Evidence (I)
	Transverse Friction Massage for Iliotibial Band Syndrome	No Recommendation, Insufficient Evidence (I)
<b>Medications, Other</b>	Complementary or Alternative Treatments, Dietary Supplements, Etc., for Acute, Subacute, or Chronic Knee Pain	Not Recommended, Insufficient Evidence (I)
	Diacerein for Treatment of Osteoarthritis	No Recommendation, Insufficient Evidence (I)
	Factor Xa Inhibitors for Prevention of Venous Thromboembolic Disease	Strongly Recommended, Evidence (A)

	Glucosamine Sulfate, Chondroitin Sulfate, or Methylsulfonylmethane for Knee Osteoarthritis	No Recommendation, Insufficient Evidence (I)
	Glucosamine Sulfate, Chondroitin Sulfate, or Methylsulfonylmethane for Osteoarthritis Prevention	No Recommendation, Insufficient Evidence (I)
	Herbal and Other Preparations for Acute, Subacute, or Chronic Knee Pain	No Recommendation, Insufficient Evidence (I)
	Interleukin-1 Receptor Antagonists for Knee Osteoarthritis	Not Recommended, Insufficient Evidence (I)
	Low-molecular Weight Heparin for Prevention of Venous Thromboembolic Disease	Strongly Recommended, Evidence (A)
	Muscle Relaxants for Acute and Subacute Knee Pain with Significant Muscle Spasm	No Recommendation, Insufficient Evidence (I)
	One-day Use of Systemic Antibiotics for Knee Surgery	Moderately Recommended, Evidence (B)
	Routine Peri-operative Use of Bisphosphonates	No Recommendation, Insufficient Evidence (I)
	Routine Post-operative Use of Calcitonin	No Recommendation, Insufficient Evidence (I)
	Warfarin and Heparin for Prevention of Venous Thromboembolic Disease	Moderately Recommended, Evidence (B)
<b>MRA</b>	MR Arthrogram for Evaluation of Select Patients Needing Advanced Meniscal and Cartilage Imaging and Following Chondrocyte Implantation	Recommended, Insufficient Evidence (I)
<b>MRI</b>	MRI for Diagnosing Osteonecrosis (AVN)	Recommended, Insufficient Evidence (I)
	MRI for Evaluation of Knee Sprains	Recommended, Insufficient Evidence (I)
	MRI for Evaluation of Meniscal Tears	Recommended, Insufficient Evidence (I)
	MRI for Knee Joint Pathology, Including Diagnosing Meniscal Tears, Cruciate Ligament Tears, Hamstring and other Muscular Tears, and for Select Patients with Post-arthroplasty Chronic Pain or Periarticular Masses	Recommended, Insufficient Evidence (I)
	MRI for Routine Evaluation of Acute, Subacute, or Chronic Knee Joint Pathology	Not Recommended, Insufficient Evidence (I)
	MRI for Severe Quadriceps, Gastrocnemius, or Soleus Strains	Recommended, Insufficient Evidence (I)
	MRI for the Evaluation of ACL Tears	Recommended, Insufficient Evidence (I)
	MRI for the Evaluation of Patellofemoral Joint Pain	No Recommendation, Insufficient Evidence (I)
<b>NSAIDs</b>	Acetaminophen for Treatment of Acute, Subacute, Chronic or Post-operative Knee Pain	Recommended, Evidence (C)
	Acetaminophen or Aspirin as First-Line Therapy for Patients at Risk for Cardiovascular Adverse Effects	Strongly Recommended, Evidence (A)
	Aspirin for Prevention of Venous Thromboembolic Disease	Moderately Recommended, Evidence (B)

	Concomitant Prescriptions of NSAIDs and Cytoprotective Medications for Patients at Risk for GI Adverse Effects (H2 Blockers)	Recommended, Evidence (C)
	Concomitant Prescriptions of NSAIDs and Cytoprotective Medications for Patients at Risk for GI Adverse Effects (Proton Pump Inhibitors, Misoprostol)	Strongly Recommended, Evidence (A)
	Concomitant Prescriptions of NSAIDs and Cytoprotective Medications for Patients at Risk for GI Adverse Effects (Sucralfate)	Moderately Recommended, Evidence (B)
	NSAIDs Counseling for Patients at Risk for Cardiovascular Adverse Effects	Recommended, Insufficient Evidence (I)
	NSAIDs for ACL Tears	Recommended, Insufficient Evidence (I)
	NSAIDs for Iliotibial Band Syndrome	Recommended, Insufficient Evidence (I)
	NSAIDs for Knee Bursitis	No Recommendation, Insufficient Evidence (I)
	NSAIDs for Knee Sprains	Recommended, Insufficient Evidence (I)
	NSAIDs for Meniscal Tears	Recommended, Insufficient Evidence (I)
	NSAIDs for Patellofemoral Joint Pain	Recommended, Insufficient Evidence (I)
	NSAIDs for Quadriceps, Gastrocnemius, and Soleus Strains	Recommended, Insufficient Evidence (I)
	NSAIDs for Treatment of Acute Flares of Knee Pain	Recommended, Evidence (C)
	NSAIDs for Treatment of Acute, Subacute, or Post-operative Knee Pain	Recommended, Insufficient Evidence (I)
	NSAIDs for Treatment of Chronic Knee Pain	Strongly Recommended, Evidence (A)
<b>Opioids</b>	Limited Use of Opioids for Post-operative Pain	Recommended, Evidence (C)
	Opioid Dose Limits in Acute Pain	Recommended, Evidence (C)
	Opioid Dose Limits in Post-operative Pain	Recommended, Insufficient Evidence (I)
	Opioid Dose Limits in Subacute and Chronic Pain	Recommended, Evidence (C)
	Opioids for Treatment of Acute, Severe Pain	Recommended, Evidence (C)
	Opioids for Treatment of Subacute or Chronic Severe Pain	Recommended, Insufficient Evidence (I)
	Routine Use of Opioids for Subacute and Chronic Non-malignant Pain	Moderately Not Recommended, Evidence (B)
	Routine Use of Opioids for Treatment of Non-Severe Acute Pain	Strongly Not Recommended, Evidence (A)
	Screening Patients Prior to Initiation of Opioids	Recommended, Insufficient Evidence (I)
	Screening Patients Prior to Continuation of Opioids	Recommended, Insufficient Evidence (I)
	Urine Drug Screening for Patients Prescribed Opioids	Recommended, Evidence (C)
	Use of an Opioid Treatment Agreement (Opioid Contract, Doctor/Patient Agreement, Informed Consent)	Recommended, Insufficient Evidence (I)

<b>Orthoses</b>	Orthoses for Moderate to Severe Chronic Knee Osteoarthritis	Moderately Not Recommended, Evidence (B)
	Orthotics or Knee Splints for Patellofemoral Knee Pain	No Recommendation, Insufficient Evidence (I)
<b>Psychological / Behavioral</b>	Cognitive Behavioral Therapy (CBT) for Patients with Subacute or Chronic Knee Pain	Recommended, Insufficient Evidence (I)
	Psychological Evaluation for Chronic Knee Pain	Recommended, Insufficient Evidence (I)
<b>Rehabilitation</b>	Continuous Passive Motion for Knee Arthroplasty Patients	Not Recommended, Evidence (C)
	Early Post-operative Rehabilitation After ACL Reconstruction Surgery	Recommended, Evidence (C)
	Home-Based Physical Therapy for Post-ACL Operative Repair Patients	Recommended, Evidence (C)
	Interdisciplinary Pain Rehabilitation Program for Chronic Knee Pain	Recommended, Insufficient Evidence (I)
	Meniscal Tear Rehabilitation after Surgical Repair	Recommended, Insufficient Evidence (I)
	Meniscal Tear Rehabilitation without Surgical Repair	Recommended, Evidence (C)
	Perturbation Training As Part of a Rehabilitation Program for ACL Injured Patients	Recommended, Insufficient Evidence (I)
	Post ACL Injury Rehabilitation with or without Surgical Repair	Recommended, Evidence (C)
	Post-Operative Vocational or Avocational Activities	No Recommendation, Insufficient Evidence (I)
	Post-Operative Rehabilitation of Knee Arthroplasty Patients	Recommended, Insufficient Evidence (I)
	Rehabilitation Therapy for Knee Sprains	Recommended, Insufficient Evidence (I)
	Rehabilitation Therapy for Meniscal Tears	Recommended, Insufficient Evidence (I)
	Rehabilitation Therapy for Patellofemoral Joint Pain	Recommended, Insufficient Evidence (I)
	Rehabilitation Therapy for Quadriceps, Gastrocnemius, or Soleus Strains	Recommended, Insufficient Evidence (I)
	Work Conditioning, Work Hardening, or Early Intervention Programs for Chronic Knee Pain Syndromes	Recommended, Insufficient Evidence (I)
<b>Rest</b>	Bed Rest and Knee Immobilization for ACL Tears	Not Recommended, Insufficient Evidence (I)
	Bed Rest and Knee Immobilization for Knee Sprains	Not Recommended, Insufficient Evidence (I)
	Bed Rest and Knee Immobilization for Meniscal Tears	Not Recommended, Insufficient Evidence (I)
	Bed Rest and Knee Immobilization for Patellofemoral Joint Pain	Not Recommended, Insufficient Evidence (I)
	Bed Rest and Non-weight Bearing for Patients with Acute, Subacute, or Chronic Knee Pain	Not Recommended, Insufficient Evidence (I)

	Bed Rest and/or Non-weight Bearing for Unstable Fractures	Recommended, Insufficient Evidence (I)
	Bed Rest for Quadriceps, Gastrocnemius, or Soleus Strains	Not Recommended, Insufficient Evidence (I)
	Knee Immobilization for Iliotibial Band Syndrome	Not Recommended, Evidence (C)
<b>Return to Work</b>	Work Limitations for Other Cases of ACL Tears	No Recommendation, Insufficient Evidence (I)
	Work Limitations for Other Cases of Knee Sprains	No Recommendation, Insufficient Evidence (I)
	Work Limitations for Other Cases of Meniscal Tears	No Recommendation, Insufficient Evidence (I)
	Work Limitations for Other Cases of Patellofemoral Joint Pain	No Recommendation, Insufficient Evidence (I)
	Work Limitations for Other Cases of Quadriceps, Gastrocnemius, or Soleus Strains	No Recommendation, Insufficient Evidence (I)
	Work Limitations for Select Cases of ACL Tears	Recommended, Insufficient Evidence (I)
	Work Limitations for Select Cases of Meniscal Tears	Recommended, Insufficient Evidence (I)
	Work Limitations for Select Cases of Patellofemoral Joint Pain	Recommended, Insufficient Evidence (I)
	Work Limitations for Select Cases of Quadriceps, Gastrocnemius, or Soleus Strains	Recommended, Insufficient Evidence (I)
	Work Limitations for Select Knee Sprains	Recommended, Insufficient Evidence (I)
<b>Saline Load</b>	Saline Load Test for Select Knee Lacerations	Recommended, Insufficient Evidence (I)
<b>Scoters</b>	Motorized Scooters for Severe Chronic Knee Osteoarthritis	Recommended, Insufficient Evidence (I)
<b>Sleeves</b>	Ace Wraps, Supports or Sleeves for Meniscal Tears	Recommended, Insufficient Evidence (I)
	Neoprene Knee Sleeves for Moderate to Severe Chronic Knee Osteoarthritis	No Recommendation, Insufficient Evidence (I)
	Sleeves for Knee Osteoarthritis	Moderately Not Recommended, Evidence (B)
	Supports or Sleeves for Patellofemoral Joint Pain	Recommended, Insufficient Evidence (I)
<b>Splints</b>	Orthotics or Knee Splints for Patellofemoral Knee Pain	No Recommendation, Insufficient Evidence (I)
<b>Surgery</b>	Autologous Blood Re-infusion Systems	Moderately Recommended, Evidence (B)
	Cartilage Grafts, Osteochondral Autografts, and/or Transplantation	Moderately Recommended, Evidence (B)
	Chondroplasty and Debridement for Knee Osteoarthritis	Moderately Not Recommended, Evidence (B)
	Compression Stockings for Prevention of Venous Thromboembolic Disease	Moderately Recommended, Evidence (B)
	Intra-operative Autologous Blood Transfusion	Recommended, Insufficient Evidence (I)
	Knee Arthroplasty for Bilateral Disease	Recommended, Evidence (C)

	Knee Arthroplasty for Moderate to Severe Arthritides	Strongly Recommended, Evidence (A)
	Knee Arthroscopy for Diagnosing Acute Knee Pain	Not Recommended, Insufficient Evidence (I)
	Knee Arthroscopy for Diagnosing and Treating Knee Pain with Suspicion of Meniscal Tear, Intraarticular Body, or Other Subacute or Chronic Mechanical Symptoms	Recommended, Insufficient Evidence (I)
	Knee Arthroscopy for Diagnosis or Treatment in Acute, Subacute, or Chronic Osteoarthritis without Mechanical Symptoms and Other Remediable Mechanical Defect	Not Recommended, Insufficient Evidence (I)
	Knee Arthroscopy for Staging a Surgical Procedure	Recommended, Insufficient Evidence (I)
	Lower-Extremity Pumps for Prevention of Venous Thromboembolic Disease	Moderately Recommended, Evidence (B)
	Pre-operative Autologous Blood Donation	Recommended, Insufficient Evidence (I)
	Prevention of Venous Thromboembolic Disease	Strongly Recommended, Evidence (A)
	Surgery for ACL Reconstruction	Recommended, Insufficient Evidence (I)
	Surgery for Anterior Knee Pain	Recommended, Insufficient Evidence (I)
	Surgery for Grade III LCL Tears	Recommended, Insufficient Evidence (I)
	Surgery for Iliotibial Band Syndrome	No Recommendation, Insufficient Evidence (I)
	Surgery for Meniscal Tears	Recommended, Insufficient Evidence (I)
	Surgery for Select Cases of Grade III MCL Tears	Recommended, Insufficient Evidence (I)
	Surgical Drainage for Knee Bursitis	Recommended, Insufficient Evidence (I)
	Surgical Resection for Chronic Knee Bursitis	Recommended, Insufficient Evidence (I)
	Unicompartmental Knee Arthroplasty for Largely Unicompartmental Disease	Recommended, Evidence (C)
<b>Taping</b>	Taping for Anterior Knee Pain	Not Recommended, Evidence (C)
<b>TNF-a Blockers</b>	Tumor Necrosis Factor-alpha Blockers for Arthroplasty Patients with Osteolysis	Not Recommended, Insufficient Evidence (I)
	Tumor Necrosis Factor-alpha Blockers for Acute, Subacute, or Chronic Knee Pain or Other Non-inflammatory Knee Disorders	Not Recommended, Insufficient Evidence (I)
	Tumor Necrosis Factor-alpha Blockers for Osteoarthritis	Not Recommended, Insufficient Evidence (I)
<b>Ultrasound</b>	Ultrasound for Evaluation of Meniscal Tears	No Recommendation, Insufficient Evidence (I)
	Ultrasound for the Evaluation of Patellofemoral Joint Pain	No Recommendation, Insufficient Evidence (I)
	Phonophoresis for Iliotibial Band Syndrome	No Recommendation, Insufficient Evidence (I)
	Phonophoresis for Knee Osteoarthritis	Not Recommended, Evidence (C)

	Ultrasound for Evaluating Other Knee Disorders including Osteonecrosis, Osteoarthritis, Dysplasia, or Fractures	No Recommendation, Insufficient Evidence (I)
	Ultrasound for Evaluating Patellar Tendinopathy, Pes Anserine Bursitis, Hamstring Strains, Quadriceps Strains or Post-arthroplasty Chronic Pain When Peri-Articular Masses Are Suspected	Recommended, Insufficient Evidence (I)
	Ultrasound for Evaluation of Knee Sprains	No Recommendation, Insufficient Evidence (I)
	Ultrasound for the Evaluation of ACL Tears	No Recommendation, Insufficient Evidence (I)
	Ultrasound for Treatment of Knee Osteoarthritis	No Recommendation, Insufficient Evidence (I)
<b>Wedges</b>	Lateral Wedges for Medial Compartment for Knee Osteoarthritis	Moderately Not Recommended, Evidence (B)
<b>Weight Bearing</b>	Bed Rest and Non-weight Bearing for Patients with Acute, Subacute, or Chronic Knee Pain	Not Recommended, Insufficient Evidence (I)
	Bed Rest and/or Non-weight Bearing for Unstable Fractures	Recommended, Insufficient Evidence (I)
<b>Wraps</b>	Ace Wraps for Knee Sprains	Recommended, Insufficient Evidence (I)
	Ace Wraps for Quadriceps, Gastrocnemius, or Soleus Strains	Recommended, Insufficient Evidence (I)
	Ace Wraps, Supports or Sleeves for Meniscal Tears	Recommended, Insufficient Evidence (I)
	Soft Knee Padding and Ace Wraps for Knee Bursitis	Recommended, Insufficient Evidence (I)
	Wraps for Patellofemoral Joint Pain	Recommended, Insufficient Evidence (I)
<b>X-ray</b>	X-ray for Bursitis	Recommended, Insufficient Evidence (I)
	X-ray for Diagnosing Fracture	Recommended, Insufficient Evidence (I)
	X-ray for Diagnosing Osteonecrosis (aka Avascular Necrosis, AVN)	Recommended, Insufficient Evidence (I)
	X-ray for Evaluating Acute, Subacute, or Chronic Knee Pain	Recommended, Insufficient Evidence (I)
	X-ray for Evaluation of ACL Tears	Recommended, Insufficient Evidence (I)
	X-ray for Evaluation of Meniscal Tears	Recommended, Insufficient Evidence (I)
	X-ray for Evaluation of Patellofemoral Joint Pain	Recommended, Insufficient Evidence (I)
	X-ray for Severe Quadriceps, Gastrocnemius, or Soleus Strains	Recommended, Insufficient Evidence (I)
	X-rays for Evaluation of Knee Sprains	Recommended, Insufficient Evidence (I)

## Evaluation and Diagnostic Issues

The knee should be carefully evaluated with a history, physical examination, and focused diagnostic testing. A complete physical exam is recommended, since pain can be referred, particularly from the back or hip to the knee joint.

The initial knee examination or consultation should focus on the detection of conditions that are remediable and “red flags” (e.g., fractures, osteonecrosis, or septic arthritis).

Initial evaluation of knee joint symptoms may require knee x-rays depending on the presentation. The threshold for additional x-rays, particularly of the back and hip, should be low and may be indicated in certain situations.

Magnetic resonance imaging is helpful for soft tissue disorders, including meniscal and cruciate tears.

### **Patient Education Issues**

Patients should be reassured that knee pain is common. Knee arthroplasty is a major surgical procedure, but has a good prognosis. However, most knee arthrosis patients, particularly those without severe disease, do not require arthroplasty.

Osteonecrosis often requires surgery, although bisphosphonates may substantially reduce the need for surgery.

Rest and disuse of body parts are not recommended for the management of knee conditions other than fractures, as they usually cause further disability and prolong treatment and recovery.

Patients should be encouraged to maintain a high level of function, although activity modifications may be helpful in reducing stresses on the knee.

### **Occupational Issues**

Aside from knee fracture patients in whom prolonged time away from work is often required, or stress fracture patients in whom significant restrictions to limit forceful activity and weight bearing may be recommended, patients should be encouraged to return to normal activity or work as soon as possible. Some situations might require modified duty. However, the more these activities are reduced, the greater the time generally required to rehabilitate the patient.

If knee pain is present, reduced activity may be necessary if the job physical requirements exceed the patient's capabilities.

A functional capacity evaluation (FCE) can establish appropriate physical capacity for work. However, results should be interpreted with caution, as patients' efforts might be submaximal because of pain. Testing is therefore preferably conducted by someone experienced in dealing with these types of patients. Nonphysical factors, return to work programs and participatory ergonomics should be addressed as needed. Patients should be empowered to accept responsibility for managing their recovery.

### **Adaptive Equipment/Assistive Devices and Other Physical Methods**

Ambulatory assistive devices (e.g., canes and crutches) are often mandatory for severely affected patients until they can ambulate.<sup>i</sup> However, physicians should balance use against risks of accelerated muscle weakness, particularly in mildly affected patients.

Ice should be considered as a part of self-care at home, particularly in the acute pain setting, and heat or ice in the chronic setting. They can provide temporary relief of symptoms, but can also reinforce pain and illness behaviors in persons with chronic pain. Many providers believe heat is not indicated in the acute phase of strains, sprains, and some other injuries, although acute low back pain has been demonstrated to be successfully treated with heat. Quality evidence for heat and ice in knee pain is lacking.

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<sup>i</sup>Some patients require coaching to not limp, as some continue to limp as a pain behavior.

Ice, heat, ultrasound, and other similar modalities are rarely indicated for treatment of knee pain outside the self-care setting. However, they may be considered for certain cases of patellar tendinopathy and anserine bursitis.

Insoles and knee braces are modestly helpful for patients with osteoarthritis who are compliant with their use and can be considered if other therapeutic options are limited.

There is no evidence to support prolonged and repetitive use of allied health therapies (massage, electrical therapies, manipulation, and acupuncture). Long-term and repetitive treatment, particularly if there is no documentation of functional improvement, is not indicated in managing patients with chronic pain, including knee pain from DJD.

## **Exercise Issues**

Graded exercises to assist in achieving a return to normal function are indicated.

Gentle exercises are useful to regain normal range of motion (ROM) in the acute pain and post-operative settings. Aggressive stretching may be contraindicated if symptoms (e.g., pain and/or swelling) are substantially aggravated. It is also important for patients to understand that, while exercises after surgery may cause some discomfort, they should not cause significant increases in pain or new onset of increased swelling.

Aerobic and strengthening exercises appear most helpful for the rehabilitation of most chronic knee pain conditions. Consultation with a physical therapist to determine the most appropriate exercises for the patient is recommended.

## **Medications**

Initial management of most knee pain conditions should be with NSAIDs and acetaminophen.

Opioids should be avoided for most patients. Opioids may be considered for the management of selected patients with confirmed moderate to severe knee DJD.

Glucocorticoid injections are indicated for treatment of bursitis, osteoarthritis, chondromalacia patella, and as initial therapy in degenerative meniscal tears.

## **Other Issues**

Knee replacement surgery, osteotomy and other procedures are selectively recommended for symptoms of severe knee DJD that cannot be managed with other non-operative treatments (e.g. medications, injections).

Surgery is indicated for knee meniscal tears that are unresponsive to non-operative treatment.

Surgical treatment is generally recommended for anterior cruciate ligament tears, although non-operative treatment may be attempted particularly in older patients and in patients without clinically unstable knees.

Intra-articular fragments, such as cartilage, in the knee joint may require arthroscopic exploration and removal.

## Impact

Of the many knee disorders reviewed in this guideline, few have been comprehensively studied using high-quality methods. For example, while robust prevalence, incidence, and cost estimates are available for osteoarthritis and meniscal and cruciate ligament tears, robust data on the burden of other knee disorders is largely unavailable.

Meniscal and anterior cruciate ligament (ACL) injuries are the first and second most common knee injuries, respectively. There are as many as 250,000 ACL injuries per year in the U.S., (1, 2) amounting to 1 in 3,000 of the general population. (3) Of those 250,000 injured, at least one-third elect to have surgery (the actual number is estimated to be approximately 100,000 procedures per year). (4) With operative costs of \$11,768, and non-operative costs of \$2,333 per procedure, (5) the total annual costs of knee injuries is approximately \$1.4 billion per year. But unlike knee replacements, the prevalence of ACL surgery is resistant to the aging of the population. The highest incidence of those suffering from an ACL injury occurs in the 15 to 25 year old age group (2) and 70% of all ACL injuries occur in the context of sport. The incidence of meniscal injuries has been estimated at 61 per 100,000 persons in the U.S., and the prevalence is 12 to 14%, with a strong relationship to age. Meniscal surgical procedures are common, comprising 10 to 20% of all orthopaedic surgeries and an estimated total of 850,000 patients per year.

Osteoarthritis (OA) is common, increases in incidence with age, and is associated with significant morbidity and cost. OA affects 13.9% of adults aged 25 years and older and between 33.6 to 46% of adults over age 65. Nearly 66% of obese adults will develop painful knee OA over their lifetime.(6, 7) Of the arthritis-related procedures that require hospitalization, 35% are due to hip and knee replacements. Job-related costs for OA overall are \$3.4 to \$13.2 billion per year with an average patient out-of-pocket direct expense of \$2,600 per year. Twenty-five percent of those affected with OA cannot perform major activities of daily living.(7)

Non-fatal work-related knee injuries and diseases involving days away from work have been decreasing, but physician visits for knee complaints and the incidence of certain knee surgeries has been increasing. According to the U.S. Department of Labor Statistics, number of non-fatal work-related knee injuries decreased from a peak of 130,000 in 2000, to 95,000 in 2007. Yet, total physician visits for knee complaints increased from 10,790,000 in 1998, to 14,960,000 in 2006, and the number of emergency room visits for knee complaints increased from 1,039,000 in 1998, to 1,452,000 in 2006.(8) The rate of total knee replacements for persons aged 65 years and older has been increasing, with women having more surgeries than men. Data from the National Center for Health Statistics indicate that from the period of 1980 to 2002, knee replacements increased approximately 8.1 times, from 10 per 10,000 in women to just fewer than 80 per 10,000, with similar trends observed in men.

## Overview

The following knee disorders are covered in detail in this guideline. Other disorders not reviewed in this guideline in depth should be considered in the differential diagnosis of knee pain and knee symptoms. These include lumbar radiculopathy and lumbar spinal stenosis, (see Low Back Disorders guideline), osteochondritis dissecans, vascular disease, avulsion fractures, femoral mononeuritis, tumor, cancer, crystal arthropathies (e.g., gout, pseudogout, hydroxyapatite), and infections, including septic arthritis (see Basic Principles and Definitions for normal anatomy). Several of these disorders have a tenuous relationship with work, but are included for purposes of completeness (see Work-Relatedness section).

### Avascular Necrosis

See Osteonecrosis below.

### Anserine, Infra-Patellar and Pre-Patellar Bursitis

Bursitis occurs when the bursae become inflamed and irritated, although classic symptoms and signs of inflammation are not always present. Bursitis results in swelling and pain when muscles overlying the bursae are used. There are many bursae around the knee, and this discussion includes some of those more commonly affected. Infra-patellar bursitis involves the bursa between the patellar tendon and the skin. Pre-tibial bursitis involves the bursa between the tibial tuberosity below the knee and the overlying dermis. Pre-patellar bursitis involves the bursa between the patella and the overlying dermis. Anserine bursitis (also pes anserine bursitis) involves a deeper bursa located between the conjoined tendons of the sartorius, gracilis, semitendinosus, and the medial collateral ligaments. Treatment of bursitis has most commonly included avoidance of kneeling or other exposures, NSAIDs, glucocorticosteroid injections (with or without aspiration), and rehabilitation therapy.

### Fracture of the Knee

Knee fractures include frank fractures and dislocated, hairline, and “stress” fractures. All fractures involve an application of force that is beyond the strength of the bone. In the knee, fractures can occur in the tibia (commonly as the tibial plateau), fibula, or patella. These almost invariably require surgical fixation, but treatment can range from immobilization with a knee brace to casting immobilization to surgical fixation, depending on the severity of the fracture. Stress fractures typically involve repeated applications of unaccustomed force over a relatively short interval of hours to a few days. These are usually treated with elimination of the offending exposure and observation. Physical therapy assessment to address movement system impairments, such as muscle performance and motor patterns, may assist in developing management plans to reduce forces on the affected site.

### Groin Strains

See Hip and Groin Disorders guideline.

### Hamstring, Calf, and Quadricep Strains, and Tears

A strain usually consists of a disruption of a myotendinous junction. The lower extremity is particularly prone to muscle strains, and strains of certain structures are more common than others. A hamstring strain involves the hamstring muscles of the thigh and can be located either distally or proximally

depending on the strained muscle-tendon units, usually in the long head of the biceps femoris muscle. Calf strains typically involve the gastrocnemius or soleus muscles in the upper calf. Quadriceps strains involve one or more of the quadriceps muscles as they insert on the superior patella. Complete muscular tears usually occur in the same muscles prone to developing strains. Strains are most commonly treated by removal from high force activities, NSAIDs, and therapy for more severe cases. Immobilization is sometimes implemented. Complete tears/ruptures of the quadriceps tendon or patellar ligament commonly require surgical repair while other muscle-tendon units are usually managed non-operatively.

### **Iliotibial Band Syndrome**

This entity is common in runners, cyclists and participants in endurance sports. Pain is in the lateral knee. Treatment is largely empiric, as quality evidence is sparse, and may consist of NSAIDs, active physical therapy, glucocorticosteroid injections, and deep friction massage.

### **Lumbar Radiculopathy and Lumbar Stenosis**

These disorders may present as knee, thigh, and calf pain. Thus, they should be considered in the differential diagnosis of knee pain (see Low Back Disorders guideline).

### **Meniscal Tears**

Menisci are prone to degenerative changes and tears with age. Meniscal tears frequently accompany degenerative joint disease. Younger patients tend to tear with high-force discrete trauma as a result of sporting activities such as football. Older patients tend to acquire tears over time, without any inciting event or with relatively mild trauma, during performance of usual activities (e.g., stair climbing). The type of tear may help determine whether it is more likely degenerative or traumatic in nature. The medial meniscus is 2.7-fold more likely to be torn than the lateral meniscus.<sup>(9)</sup> Pain tends to be focal – e.g., at the posteromedial joint line for a medial posterior horn meniscal tear. Joint effusions tend to occur if there is an acute, large tear. Small degenerative tears may produce no effusion. Treatment of large “bucket-handle” tears involves surgical removal. Treatment of degenerative and small tears involves NSAIDs, activity modifications to avoid aggravating activities, glucocorticoid infiltration, and therapeutic exercises. Surgery may be needed in cases where non-operative results are not satisfactory.

### **Osteoarthritis Including Degenerative Joint Disease (“Osteoarthritis” and “Degenerative Arthritis”)**

Degenerative joint disease (DJD) of the knee is most commonly caused by osteoarthritis (OA). While osteoarthritis is the more common name for this entity, osteoarthritis is more technically precise since there is no classic inflammation. Other types of arthritic disorders that cause DJD include inflammatory autoimmune disorders (e.g., rheumatoid arthritis, systemic lupus erythematosus, and psoriasis) and crystal diseases (e.g., gout, pseudogout, apatites). These latter disorders are non-occupational and are not included in this discussion. Knee OA and inflammatory knee arthritis can result in destruction of the knee joint, and these conditions may therefore be indistinguishable on x-ray. Thus, a correct interpretation of an x-ray may include DJD, but not “osteoarthritis.”

Most joints in the body have a modest female preponderance of OA and the knee is no exception with an estimate of 84% higher risk in women than men for reasons that are unclear.<sup>(10)</sup> Patients who already have OA in one or two joints may be at higher risk for developing OA in other joint groups. This

is sometimes referred to as “systemic osteoarthritis.” Systemic osteoarthritis likely reflects genetic or other systemic predispositions. Several genetic risk factors have been identified.(11)

OA is more common with age and is associated with thinning of cartilage on the articular surfaces of the knee joint. Thinning of the cartilage in the knee joint may lead to pain with movement and stiffness. OA is generally characterized by stiffness (and pain) after both long periods of inactivity or in association with unaccustomed increases in activity. Most cases of OA are symmetrical and appear to arise without obvious physical exposure(s). A minority of cases occur after discrete significant trauma, most commonly fractures. The disease tends to progress irrespective of physical exposures.

### **Osteoarthritis: Initial Interventions/Role of Rehabilitation Therapy and Other Non-pharmacologic or Non-Invasive Interventions**

Many patients with knee osteoarthritis are able to control their pain adequately through avoidance of activities that significantly provoke symptoms and through the use of over-the-counter (OTC) medication. Topical agents, heat, and ice may be helpful self-treatments. Braces and orthotics/insoles are sometimes helpful. Patients may benefit from education about the natural history of knee OA. Regular participation in programs stressing aquatic or gentle aerobic (e.g., walking programs), or strengthening exercise may also be of benefit, although these modalities should be individualized to the patient’s diagnosis, prior activity levels, desired activity levels, and overall preferences. Weight loss also is thought to be strongly indicated for patients who are either overweight or obese.(12-33) A few recent trials have suggested that weight loss reduces pain and morbidity.(13, 24, 34-36)

### **Osteoarthritis: Pharmacologic Management**

Non-steroidal anti-inflammatory drugs (NSAIDs) are most commonly used for patients with OA. Chronic NSAID therapy may warrant ancillary use of proton pump inhibitors, H-2 histamine blocking agents, or misoprostol to provide prophylaxis against gastrointestinal adverse effects. The advantage of selective Cox-2 inhibitors is their lower risks of gastrointestinal side effects. Tricyclic antidepressants, dual reuptake inhibiting antidepressants (i.e., SSNRIs) and acetaminophen may be of benefit for some patients. Highly selected patients may be candidates for judicious use of low doses of opioids if this results in functional improvement. Providers should also take into consideration that many OA patients are older and have significant comorbidities, including renal impairment. Medications should therefore be carefully prescribed.

### **Osteoarthritis: Role of Invasive Procedures**

Invasive procedures are not indicated in the management of most osteoarthritis patients unless the condition is unable to be satisfactorily controlled with other non-invasive treatments. In such cases, intraarticular injections with glucocorticosteroid and viscosupplementation are sometimes utilized. In advanced cases, joint replacements and other surgical procedures are often performed.

## **Osteochondritis Dissecans**

Osteochondritis dissecans most commonly affects the knee, although the elbow, hip, and ankle are sometimes affected.(37) It is manifested by articular cartilage that dislodges or dissects from the underlying bone. Osteochondritis dissecans most commonly occurs in teenagers, although it can occur in adults. The cause of osteochondritis dissecans is unclear. However, there appears to be important genetic risks.(37, 38) Although sports activities, particularly in teenage years, also appear to be an important risk factor, there are no quality epidemiological studies of the association of osteochondritis dissecans with work. Consequently, osteochondritis dissecans will not be addressed further in this guideline.(39-51)

## **Osteonecrosis (Avascular Necrosis)**

Osteonecrosis occurs when the tenuous blood supply to the bone is interrupted. Osteonecrosis may result from traumatic or non-traumatic factors. The condition is painless at early stages, but when it advances, patients generally present with pain and limitation of motion. Pain most commonly localizes over the affected bone. This condition most commonly affects the head of the femur, but it can affect any bone. Pain in the lower extremity is usually exacerbated by weight bearing and relieved with rest. Management of knee osteonecrosis is extrapolated from quality evidence for treatment of osteonecrosis of the head of the femur (see Hip and Groin Disorders guideline).

## **Patellar Dislocation and Instability**

The patella is subject to instability from congenital or inherited tendencies to dislocate (52-55) as well as trauma. Pain from dislocation is usually severe and associated with an inability to use the limb. Individuals with a congenital or inherited tendency to dislocate have usually dislocated their patella prior to reaching an employable age. The patella may dislocate with lesser force or stress over time, and recurrences are quite common. Surgery to attempt to tighten the quadriceps mechanism is usually attempted. Other cases of patellar dislocation occur as a result of significant trauma (e.g., motor vehicle accident or fall). The patella may then be prone to recurrent dislocation after the initial dislocation, and a subjective feeling of instability may result. Strengthening exercises may be helpful. In most cases, particularly if recurrent, surgical repair is attempted.

## **Patellofemoral Joint Syndrome and Patellofemoral Joint Degenerative Arthrosis (Including Chondromalacia Patellae)**

Patellofemoral joint syndrome is a diagnostic category that includes patients with pain thought to be primarily from the patellofemoral joint or the anterior aspect of the knee. Some of these patients are thought to have degenerative joint disease that is focused on that aspect of the knee joint, although they may also have degenerative changes in other parts of the knee joint. Theoretical mechanisms are controversial. Some patients may have muscle weakness that is present in one part of the quadriceps (e.g., vastus medialis), or alternatively the whole quadriceps may be judged as demonstrating weakness. When pain arises from arthrosis in the patellofemoral joint then treatment is comparable to other arthrosis reviewed above. However, when there is evidence of quadriceps muscle weakness, specific strengthening exercises for that muscle are usually prescribed.

## **Patellar Tendinopathy**

Patellar tendinosis, which affects the patellar tendon, is sometimes referred to as “jumper’s knee.” This usually arises from high-force activities on a stereotypical basis, direct trauma, and/or as a degenerative condition. Patellar tendinosis is usually treated with NSAIDs and exercises. Knee appliances (e.g., sleeve, strap) are also sometimes used as are heat, ice, and topical treatments. Severe cases may rupture (see Patellar Tendon Tears).

## Patellar Tendon Tears

Patellar tendon tears usually occur with either a high-force event or an accident, but can result from severe patellar tendinosis. They are treated with surgical repair and rehabilitation; partial tears may be treated non-operatively.

## Sprains and Tears of the Cruciate Ligament (Anterior and Posterior)

Cruciate ligament sprains and tears are sprains or partial or complete tears of the ligaments connecting the femur to the tibial plateau that generally occur as the result of high-force injuries from sports, accidents, or falls. In some cases involving less trauma, rupture is believed to occur because of prior injury and weakness. Symptoms include pain and instability. A large effusion may occur with large ruptures. Partial tears are usually treated with NSAIDs, ice, and may involve physical or occupational therapy. Complete tears of the anterior cruciate ligament are usually surgically reconstructed, although non-surgical treatment with rehabilitation may be attempted. Complete tears of the posterior cruciate are usually treated with exercise, although sometimes they are treated surgically.

## Sprains and Tears of the Collateral Ligaments (Medial and Lateral)

Collateral ligament sprains and tears are sprains and partial or complete tears of the ligaments connecting the lateral femur to the tibia (lateral collateral ligament) or medial femur to the tibia (medial collateral ligament). By definition, these are high force injuries and may occur during sports, accidents, trips, slips or falls. Pain is localized to the affected ligament. The medial collateral ligament may be accompanied by a medial meniscal tear due to shared fibers in these two anatomical parts. Treatments usually consist of NSAIDs and ice or heat, knee support sleeves in the acute phase, and may involve physical or occupational therapy. Isolated complete tears of the medial collateral ligament are usually treated non-operatively.

## Synovitis

Synovitis refers to inflammation of a synovial membrane, although in most cases, there are no classic symptoms and signs of inflammation. Synovitis is usually painful, especially with motion. Fluctuating swelling may occur due to effusion within the synovial sac. Treatments usually consists of NSAIDs, elimination of physical exposures (especially direct pressure if thought to be problematic), and often ice or heat.

## Basic Principles and Definitions

**Acute, Subacute, and Chronic Pain:** For the purposes of identifying interventions at different stages of diseases, acute pain is defined as pain of up to 1 month, subacute is pain from 1 to 3 months, and chronic is pain of more than 3 months duration (see Chronic Pain guideline for additional information).

**Active Therapy:** The term “active therapy” is commonly used to describe treatment that requires the patient to assume an active role in rehabilitative treatment. Although there is no one specific treatment defined by this term, it most commonly includes therapeutic exercises, particularly aerobic activities and muscle reconditioning (weight lifting or resistance training).(56) Some authors include active stretching and treatment with psychological, social and/or educational components requiring active participation from the patient.(57)

**Active Exercise Therapy:** Therapy that typically consists of cardiovascular training and muscle strengthening,(58, 59) though it may also include progressive or occasionally even active stretching, especially in those with substantially reduced ranges of motion. Active exercise therapy is used as a primary treatment for chronic pain, is frequently initiated in the course of treating subacute pain, and is a primary treatment after various surgeries. The goal of active exercise therapy is to improve function.(58) The word “active” is used to differentiate individualized exercise programs designed to address and rehabilitate specific functional, anatomic or physiologic deficits from passive treatment modalities or from forms of “exercise” that require very little effort or investment on the part of the patient or provider.

**Bursae:** Fluid-filled sacs within the body which provide lubrication in areas where muscles move over bony projections. Inflammation of the bursae may occur and is referred to as bursitis (see Bursitis). Commonly affected bursae include the infra-patellar, pre-patellar, suprapatellar and anserine bursae. These bursae lie in front of the tibial tuberosity, anterior to the patella, above the patella, and between the bone and adductor tendons along the medial knee, respectively.

**Collateral Ligament:** Ligaments connecting the lateral femur to the fibula (lateral collateral ligament) or the medial femur to the tibia (medial collateral ligament).

**Cruciate Ligament:** Ligament connecting the center of the distal femur to the center of the tibial plateau. There are two cruciate ligaments per knee – the anterior and posterior.

**Delayed Recovery:** Defined as an increase in the period of time between the onset of the injury and/or illness and the patient’s return to work or usual activities relative to the expected recovery time. Expected recovery takes into account reasonable expectations, disorder severity, age, and treatments provided.

**Enthesopathy:** Disorder of the muscular or tendinous attachment to bone.

**Functional Capacity Evaluation (FCE):** A comprehensive battery of performance-based tests used to attempt to assess an individual’s ability for work and do activities of daily living.(60) An FCE may be done to identify an evaluatee’s ability to perform specific job tasks associated with a job (job-specific FCE) or his or her ability to perform physical activities associated with any job (general FCE).

**Functional Improvement:** Entails tracking and recording evidence that the patient is making progress towards increasing his or her functional state. Use of validated tool(s) to track functional improvement is preferable.

**Functional Restoration:** A term initially used for a variant of interdisciplinary pain alleviation, or at least amelioration, characterized by objective physical function measures, intensive graded exercise and multi-modal pain/disability management with both psychological and case management features.(61-67) The term has become popular as a philosophy and an approach to medical care and rehabilitation. In that sense, functional restoration refers to a blend of various techniques (physical and psychosocial) for evaluating and treating the chronic non-malignant pain patient, particularly in the workers’ compensation setting (see Chronic Pain guideline).

**Iliotibial Band:** Fibrous connection between the ilium of the pelvis to the tibia. The iliotibial band syndrome involves pain mostly in the lateral knee joint.

**Knee Joint:** The knee joint is a synovial hinge type joint based on the articulation of the distal femur and the tibia of the calf. Four ligaments hold the femur to the tibia – the medial and lateral collateral ligaments and the anterior and posterior cruciate ligaments.

**Knee Pain:** Pain originating from the knee is usually focally felt in the knee joint. However, some cases are experienced with pain primarily in the hip region. Anterior knee pain is commonly due to patellofemoral joint pain, patellar tendinopathy, and quadriceps strains. Medial joint pain is often caused by medial collateral ligament (MCL) sprains, medial meniscal tears, medial compartment OA, groin strains, and anserine bursitis. Lateral joint pain is frequently due to lateral collateral ligament (LCL) sprains, lateral meniscal tears, lateral joint OA, and iliotibial band syndrome. Posterior knee joint pain is commonly due to hamstring strains, calf strains, Baker’s cysts, hyperextension injuries, and popliteal arterial disorders. Other patients have proximally or distally radiating pain. Pain in the knee may also be due to referred pain from cardiovascular or metastatic processes, lumbar disc herniation with nerve impingement, lumbar spinal stenosis, or arterial insufficiency.

**Meniscus:** A semilunar (“C-shaped”) fibrocartilaginous structure which covers approximately 60% of the surface of the tibial plateau and helps distribute weight from the respective femoral condyle evenly. Each joint has a medial and lateral meniscus.

**Pain Behavior:** Verbal and non-verbal actions (e.g., grimacing, groaning, limping, using pain relieving or support devices, requesting pain medications, etc.) which communicate the concept of pain to others.

**Passive Modality:** Various types of provider-administered treatments in which the patient is passive. These treatments include medication, injection, surgery, allied health therapies (e.g., massage, acupuncture, and manipulation), and various physical modalities such as hydrotherapy (e.g., whirlpools, hot tubs, spas, etc.), ultrasound, TENS, other electrical therapies, heat and cryotherapies.

**Primary Prevention:** Primary prevention involves preventing the condition or risk factor from developing (e.g., physical activity programs to prevent obesity).

**Rehabilitation:** Rehabilitation is used in these guidelines to mean physical medicine, therapeutic and rehabilitative evaluations, and procedures. Rehabilitation services are delivered under the direction of trained and licensed individuals such as physicians, occupational therapists, and physical therapists. Sometimes mental health professionals are incorporated into the treatment team, particularly for select chronic pain patients. Jurisdictions may differ on qualifications for licensure to perform rehabilitative evaluations and interventions.

**Secondary Prevention:** Secondary prevention involves reduction in the exposure or risk factor after the risk factor has already developed, but before the disease has manifested (e.g., use of fall protection equipment to prevent hip fractures).

**Sprain:** Disruption of a joint’s ligaments. Examples in the knee include sprains of the medial or lateral collateral ligaments or anterior or posterior cruciate ligaments (see Cruciate and Collateral Sprain).

**Strain:** Disruption of a muscle or myotendinous junction, usually from a high force or unaccustomed exertion(s). It may also occur during an accident. This term is occasionally used to describe non-specific muscle pain in the absence of knowledge of an anatomic pathophysiological correlate. In the knee region, examples include hamstring, calf, and quadriceps strains (see Hamstring, Calf, Quadriceps Strain).

**Stress Fracture:** Fractures that occur mainly due to unaccustomed, forceful use. Treatment is generally activity modification to preclude high force use.

**Synovial Membrane:** The membrane surrounding the entire knee, including the medial, lateral, and patellofemoral joints. The synovial membrane may become inflamed, leading to synovitis (see Synovitis).

**Synovial Plicae:** Remnants of the divisions of the knee compartments. These are thought to be involved in inflammation and irritation, termed “plicae syndrome.”

**Tenosynovitis:** Tenosynovitis refers to inflammation of a tendon sheath, although in most cases, there are not classic symptoms and signs of inflammation. Classic inflammation may occur with arthropathies or infectious agents.

**Tertiary Prevention:** The amelioration of the condition after it has already developed. For example, after a patient has osteonecrosis, precluding them from diving, which may be associated with dysbaric osteonecrosis, is a method of tertiary prevention.

**Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC):** Most common knee outcome measure for osteoarthritis of the knee, other than standard and VAS pain ratings. It combines subjective ratings of pain with measures of activity levels, stiffness, physical function, social function and emotional function.(68)

## Initial Assessment

The physician performing an initial evaluation of a patient with knee symptoms should aim to develop an appropriate differential diagnosis. A careful, thorough history and focused physical examination is required (see General Approach to Initial Assessment and Documentation). A review that not only focuses on the knee, but also addresses the hip, foot, spine, abdomen, and genitourinary tract, is necessary. The examination of the patient with knee symptoms should focus on the knee joint and relevant neighboring structures. Findings of the medical history and physical examination can alert the physician to other non knee-related pathology. Certain findings, referred to as “red flags,” raise suspicion of serious underlying medical conditions (see Table 1). Potentially serious disorders include infections, tumors, and systemic rheumatological disorders.

Knee disorders may be classified into one of four somewhat arbitrary and overlapping categories (examples):

**Potentially serious knee conditions:** fractures, dislocation, infection, neurovascular compromise, tumors.

**Mechanical disorders:** derangements of the knee more commonly related to acute trauma, such as ligament sprains and tears, myotendinous strain, and some meniscus tears.

**Degenerative disorders:** mostly consequences of aging, including osteoarthritis, tendinosis, and most meniscal tears.

**Nonspecific disorders:** occurring in the knee and suggesting neither internal derangement nor referred pain.

**Table 1. Red Flags for Potentially Serious Conditions Associated with Knee Pain\***

<b>Disorder</b>	<b>Medical History</b>	<b>Physical Examination</b>
Tumor and Neoplasia	Severe localized pain, often deep-seated, unrelenting bony pain History of cancer (at any point in lifetime) Age >50 years Symptom consistent with disease in a specific organ system (e.g., cough, change in bowel habit, epigastric pain, early satiety) Constitutional symptoms, such as recent unexplained weight loss, fatigue Pain that continues at night or at rest	Pallor, reduced blood pressure, diffuse weakness New mass or tenderness, including tenderness over bony landmarks New findings at a distant site relative to the original complaints, including abnormal pulmonary examination (crackles, wheezes, rhonchi, decreased breath sounds)
Infection	Constitutional symptoms, such as recent fever, chills, or unexplained weight loss Recent bacterial infection (e.g., urinary tract infection); IV drug abuse; diabetes mellitus; or immunosuppression (due to corticosteroids, transplant, or HIV) History of recurring infections treated with antibiotics (e.g., repeated urinary tract infections) Foreign travel with potential exposure to infectious agents	Fever, tachycardia, tachypnea, hypotension Elevated white blood cell count (may be decreased in elderly or immunocompromised) Shift in the WBC differential towards immature cells ("left shift") Abnormal urinalysis Abnormal body part examination (e.g., pulmonary) Tenderness over bony landmarks Joint effusion, tenderness and difficulty moving knee joint (if knee septic arthritis)
Significant or Progressive Neurologic Deficit	Severe spine or extremity pain Progressive numbness or weakness Complaints of new gait difficulty	Significant or progressive dermatomal and/or myotomal (motor) involvement Evidence of cauda equina syndrome, including urinary retention or bowel incontinence Hyper-reflexia, or other evidence of myelopathy
Compartment Syndrome	History of fracture, crush wound or other major trauma Very painful muscular compartment History of peripheral vascular disease	Tense compartment Exquisitely tender Distal neurovascular compromise (e.g., absent or decreased pulses or pale/cold extremity) if severe and/or prolonged
Rheumatologic Disease	Diffuse arthralgias Prior arthropathies, autoimmune diseases Skin changes, lesions, or ulcers Fatigue, malaise	Polyarticular joint effusions (usually with warmth) X-ray abnormalities consistent with erosive pathology Elevated sedimentation rate (ESR) or C-reactive protein (CRP) Hematuria, proteinuria Other specific abnormalities, as appropriate (e.g., ANA, RF, anti-DNA, C3, anti-Ro, anti-La, oral ulcers, pulmonary abnormalities, ophthalmological involvement, dermal abnormalities)

\*The above list is not meant to be comprehensive but rather reviews many common historical and examination findings.

## Medical History

The initial evaluation of patients with knee pain should include a thorough medical history. Although knee symptoms are generally more accurately attributed to the knee joint than the hip joint, some cases of knee joint pathology may present with hip pain (see Hip and Groin Disorders guideline).<sup>ii</sup> A complete occupational history is also necessary to assist the patient with successful accommodation and rehabilitation, as well as to determine work-relatedness. Asking the patient open-ended questions, such as those listed below, allows the clinician to gauge the need for further discussion or specific inquiries to obtain more detailed information (see also General Approach to Initial Assessment and Documentation guideline):

1. “What may I do for you today?” (This question helps focus the discussion on what the patient feels is the main purpose of the visit. It also helps ensure that the physician is able to eventually address the main purpose of the visit, which is important for patient satisfaction.)
2. What are your symptoms? (Observing how the worker acts when describing symptoms may provide insight into the diagnosis and help the physician understand the impact of symptoms on the patient.)
  - What are your symptoms?
  - When did your symptoms begin?
  - Where are the symptoms located?
  - Do you have pain or stiffness?
  - Do you have swelling, locking, or giving way? If swollen, how long after the injury did your knee become swollen? What is the pattern to your symptoms? Are they better when first getting out of bed in the morning, during the morning, mid-day, evening or while asleep? When is it worst?
  - Do you have fever, night sweats, or weight loss?
  - Do you have pain or other symptoms elsewhere?
  - Do you have numbness, tingling, or weakness? Have you lost control of your bowel or bladder? Are your symptoms worse when climbing or going down stairs or hills? (These questions are particularly important if knee pain is felt to be associated with radicular spine pain or spinal stenosis).
  - Since these symptoms began, have your symptoms changed? How?
  - How do your symptoms affect your life?
  - Can you walk on your leg?
  - Do you have difficulty sleeping? What position is most comfortable?
3. How did the condition develop?

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<sup>ii</sup>The clinical phenomena of primary hip and pelvic region pathology referring pain to the knee is well documented (69) and appears to be particularly prevalent in the pediatric population. This may include delayed diagnoses of serious pelvic region pathology such as osteogenic sarcoma in younger soldiers. Disorders such as Legg-Calve-Perthes and slipped capital femoral epiphysis may be associated with primary complaints of knee pain. These conditions might be seen in younger workers.(70,71) Similarly many patients with a chief complaint of hip pain actually have a knee disorder that is usually osteoarthritis. Clues to the origin of symptoms can be determined with a careful patient history as primary hip pathology typically is perceived in the buttocks, anterior inguinal region, thigh and occasionally in the foot and ankle.(69) Hip pathology presents as difficulty crossing legs, laying on the hip and restricted internal rotation, while knee pathology presents as difficulty climbing stairs, kneeling onto the knee, and bending the knee to get in and out of the car. Consequently, the hip, pelvic region and lumbar spine should be examined thoroughly in any instance of thigh or knee pain that is not clearly an isolated acute knee injury. (69-71)

*Past:*

- Have you had similar episodes previously?
- Have you had previous testing or treatment? What treatment? What were the results? With whom? How long did it take to get back to work? To light duty?
- Did you receive a disability or impairment rating?
- Was recovery complete? (Did you get a disability award?)

*Cause:*

- What do you think caused the problem? When?
- Do you think it is related to work?
- Did your symptoms begin suddenly or gradually? (It is important to distinguish between symptoms associated with a specific traumatic injury and those that represent cumulative trauma over time).
- What were you doing at the time when your symptoms began? Did you have a slip, trip, fall, or twist or strike an object? (It is important to document the circumstances surrounding the injury and any biomechanical risk factors).
- For traumatic injuries: Was the area deformed? Did you lose any blood or have an open wound? When after the injury did your symptoms begin?
- For degenerative conditions: Is there a history in your family of this problem? Does anyone else have arthritis in your family?

*Job:*

- What are your specific job duties?
- What are your work hours, and what is your break schedule?
- Do you rotate duties?
- How long do you spend performing each duty on a daily basis?
- How much do you lift, push, or pull at work as a maximum? Usual lift, push, or pull?
- Do you have assistance of other people or assistive (e.g. lifting) devices?
- What previous jobs have you held, and what were your job duties?
- What is the hardest part of the job for you to do with your injury? Why?
- Is modified duty available at your workplace? What type of modified duty is available?

*Non-Occupational Activities:*

- What other activities (e.g. hobbies, sports) do you engage in at home or elsewhere? What prior activities did you engage in?
- Describe your current daily activities. Do you do any heavy lifting, pushing, or pulling? How often?
- Could these activities have contributed to the development of your symptoms?

4. Assess treatments and determine whether responses differ from expected outcomes.
  - What treatments have you had?
  - Did anything help decrease your symptoms? What, and for how long?
  - Are you doing any exercises at home? Which ones? How often?
  - Are you taking any non-prescription medications and supplements?
5. Discuss symptom limitations.
  - Do you expect to recover? How soon?
  - How do your symptoms limit you?

- Can you perform activities of daily living (e.g., dressing, bathing, grooming, etc.) or instrumental activities of daily living (e.g., shopping, food preparation, housekeeping, etc.)?
  - How long can you sit, stand, walk, and bend?
  - How much weight can you lift (use items such as gallons of milk, groceries, etc. as examples)?
  - How much can you push or pull?
  - If these symptoms limit you, how long have your activities been limited?
6. Do you have other medical problems? For example:
- Osteoarthritis, rheumatoid arthritis, gout, pseudogout, or other arthritides?
  - Fractures or lower extremity surgeries?
  - Cardiovascular disease?
  - Pulmonary disease?
  - Gastrointestinal disease?
  - Diabetes mellitus?
  - Neurological disorders (including radiculopathies, headaches)?
  - Psychophysiologic disorders (e.g. irritable bowel syndrome, chronic fatigue syndrome, or fibromyalgia)?
7. Do you have a history of mental health disorders or alcohol, tobacco, or other substance use?
- Have you ever had a substance use problem? Have you ever been charged with driving under the influence (DUI)? Have you ever been in a detoxification program? Have you ever had an alcohol problem? (CAGE or MAST screening should be performed in the case of suspected osteonecrosis, as alcohol use is associated with a higher risk of osteonecrosis)
  - Do you or have you ever used tobacco (assess pack-years)?
  - Do you or have you ever used any other drugs?
8. What do you think about your job (psychosocial context)?
- Do you like your job?
  - Do you have control over your job? Partial control?
  - Do you feel your job demands are reasonable?
  - What is your relationship with your co-workers and supervisor? How do they treat you?
9. Assess whether there are problems at home or in the social life? Is there support?
- How do you get along with your family members? Do they help and support you?
  - Does your family treat you differently now that you are in pain? Have your roles at home changed because of your injury? Do your friends treat you differently?
  - Are your symptoms worse when you are dealing with problems with your family and friends?
10. Are there advocagenic (litigious) influences?
11. Do you have a workers' compensation claim for this injury?
12. Do you have a lawsuit or other legal action involving this problem?

## Physical Examination

Objectives of the physical examination of the knee include defining physical abnormalities, narrowing diagnostic considerations, and developing and focusing an effective, specific treatment plan. In order to align an intervention strategy with deficits such as impaired strength, or movement balance, the examination should first reveal the impairments. Examination of knee includes active and passive ranges of motion and accessory movements. Muscle strength and flexibility should be revealed through valid testing. Coordination, balance, and fall risk should also be assessed. Special tests for specific pathologies are often only a small aspect of the examination and may be overall less important to nonsurgical management of the knee disorder. Special tests are more helpful when there is clear evidence that the pathology revealed is better managed by a process other than restoring normal movement, strength, flexibility, and coordination to the knee.

Physical examination data, including vital signs, should be reviewed for potential inferences about infectious or neoplastic etiologies of knee symptoms. The physical examination should begin the moment the physician sees the patient. Observing how the patient sits, walks, and moves is extremely important. It is also helpful to have the patient demonstrate what positions caused or seem to provoke the symptoms.

Guided by the medical history, the physical examination includes:

- general observation of the patient, including stance and gait, and how the patient changes positions (monitoring for pain behavior during range of motion (ROM) and posture changes often offers a clue to the origin of the problem);
- regional examination of the knee and testing for specific knee disorders;
- examination of organ systems related to appropriate differential diagnoses, including a neurological examination.

Much of the knee examination is not purely objective. There is an element of patient cooperation when determining strength or active range of motion, and most maneuvers require a subjective statement of pain to be considered positive. It is often helpful to assess patients' capabilities in the clinic to follow in subsequent clinic visits. These may include:

- walking distance and ability to climb stairs (observe, if possible, and inquire about any progress);
- repeated toe raises (number able to perform), heel walking (distance), and squats (number);
- sensory examination findings (e.g. pin prick, using monofilaments).

The use of validated functional assessment tools is recommended, if possible, to assess capabilities. Active involvement of the provider in evaluating patients' function is believed to be helpful in facilitating patients' recoveries.(72)

### Physical Examination for Specific Diagnoses

Physical examination findings vary based on the acuity and severity of the disorder. In general, conditions that arise acutely present with more pronounced physical examination findings. Patients with long-standing conditions may have less prominent physical examination findings. The most commonly used physical examination maneuvers are described below. In addition, there are other examination maneuvers and techniques, including performance of maneuvers under anesthesia.(73-91) It is suggested that the examiner become familiar with a specific set of maneuvers rather than an entire battery.

### **Pes Anserine Bursitis**

Tenderness over the pes anserine bursa is usually present.(92, 93) In contrast with other bursidities, there is usually no palpable swelling or warmth.(92, 94, 95)

### **Bursitis (Infrapatellar, Prepatellar, Suprapatellar)**

Swelling in the affected bursa(e) is present.(96-98) The affected bursa may be slightly warm, but is generally minimally tender or non-tender. Moderate or severe pain or tenderness, overlying warmth, and erythema raise the probability of septic bursitis.(98, 99) Crystal arthropathies may affect the bursae, but are rare, particularly in the infrapatellar or prepatellar bursae.

### **Collateral Ligament Sprains and Tears (MCL and LCL)**

Collateral ligament sprains present with focal tenderness over the specific ligament.(100, 101) Increased pain with stressing the ligament (i.e., valgus stressing for the medial collateral ligament and varus stressing for the lateral collateral ligament) is consistent with a ligamentous sprain.(102, 103) Patients with complete tears have tenderness over the normal location of the ligament, and valgus or varus stressing reveals widening of the joint line.(100, 102-104)

### **Cruciate Ligament Tears and Sprains**

Cruciate ligament tears generally have effusions that may be sizable, particularly if acute.(105-108) Joint tenderness may be present. Joint laxity is the major clinical finding and may be detected with Lachman's maneuver which is performed recumbent, with the knee flexed 20° and the examiner pulling the shin forward. If an ACL tear is present, there is greater movement than normal and compared with the other knee and with a soft endpoint.(85, 102, 109-112) The anterior drawer sign is performed with the knee flexed 90° and shin pulled forward, with greater movement than normal and compared with the other knee indicating an anterior cruciate ligament tear. The posterior drawer sign is performed with the knee flexed 90° and shin pushed backwards, with greater movement than normal indicating a posterior cruciate ligament tear.(111, 113, 114) Sprains without complete tears may present with some laxity in the drawer signs, but generally with hard endpoints. There is conflicting evidence on the utility of the most commonly used physical examination signs (see Table 2). For example, there is disagreement about the utility of the pivot shift test.(73, 83) This test may only be adequately performed under anesthesia.(115) However, there is general consensus that the Lachman's test is the most sensitive physical examination maneuver for detecting ACL tears.(84, 111, 115-122)

**Table 2. Operant Characteristics of Physical Examination Signs of Anterior Cruciate Ligament Tears\***

	Sensitivity (%)	Specificity (%)
Lachman	82-100	43-100
Anterior Drawer	22-80	74-100
Pivot shift	71-90	4-98

\*Data compiled from Sandberg, Kim, Liu, Torg, Jonsson, Donaldson, Zarins, Gelb, Lee, and Katz.(84, 111, 115-122)

### **Hamstring, Calf, and Quadricep Strains and Tears**

Complete ruptures are accompanied by an inability to use the knee, including an inability to walk.(123, 124) Moderate to severe strains also produce considerable difficulty using the limb and bearing weight. Moderate to severe strains and tears generally cause swelling and ecchymosis. Development of hematoma in the area of the strain or rupture is common.(123) Mild strains may present with some difficulty with knee use and focal tenderness.(123-125)

### Iliotibial (IT) Band Syndrome

Patients with IT Band Syndrome have pain in the distal lateral thigh, which is typically worse with provocative activities, including running, cycling and other endurance sports.(126-130) Tenderness may be present along the lateral fascia from the lower thigh to the knee, particularly the lateral femoral condyle,(131) and pain may be worse at 30° of flexion,(132) otherwise, the knee joint is usually normal.

### Knee Fracture

Patients with knee fractures are often unable to bear weight or walk,(133) and bony deformity and crepitus may be present. Patients with stress fractures may be able to bear weight normally but usually have focal tenderness over the fibular head, patella, or tibia.(133, 134)

### Knee Dislocation

Patellofemoral dislocations are the most common knee dislocation and may be congenital or trauma associated.(135) Patients with tibiofemoral knee dislocations tend to have a history of high-impact trauma(135) which do not spontaneously reduce are unable to bear weight or walk, have deformity, and may have signs of fractures. Tears of multiple ligaments are usually present and tenderness over sprained and/or torn ligaments is present. Effusions are usually present.

### Meniscal Tears

The extent of the meniscal tear usually determines the degree of physical examination abnormalities, which can range from marked findings to a normal examination. Patients with large, acute tears tend to have swelling, focal tenderness, difficulty walking, difficulty using the knee, locking, and giving out or buckling. Patients with mild, chronic degenerative tears that are symptomatic frequently have no effusion, but may have focal tenderness. Specific physical signs include joint line tenderness, McMurray's test (painful palpable click when moving knee from full flexion to 90°), Ege's test (audible and painful palpable click with squatting; feet turned outwards for medial meniscus and inwards for lateral), and Apley's test (pain on axial compression of the tibia with external rotation while patient prone and knee flexed).(75, 102, 114, 136-141) The sensitivity of these tests is generally higher for medial than lateral meniscal tears,(142, 143) and it has been suggested that the tests should be combined for increased accuracy.(144) However, there is conflicting data on the value of these physical examination signs (see Table 3), and they may not have the same operant characteristics depending on the anatomic location, e.g., with anterior tears less likely to be captured by McMurray's. Acutely locked knees have been reported to reflect meniscal tears (47.9%), ACL tears (14.6%), meniscal and ACL tears (22.9%), a loose body (4.2%), or an unidentifiable mechanical cause (10.4%).(145)

**Table 3. Operant Characteristics of Physical Examination Signs of Meniscal Tears\***

	Sensitivity (%)	Specificity (%)	Accuracy (%)
Joint Line Tenderness	55-92	31-97	57-96
McMurray	20-67	69-96	45-82
Apley (distraction or compression)	6-16	90	28
Ege	64-67	81-90	71-84
History of mechanical symptoms	20	94	--

\*Data compiled from Kurosaka, Konan, Corea, Wadey, Fowler, Lowery, Akseki, Anderson, and Benjaminse.(74, 75, 83, 139, 142-144, 146, 147)

### **Osteoarthrosis**

Patients with osteoarthroses usually have an antalgic or slow gait. Those with more severe disease commonly are slow to stand and initiate gait. Bony enlargement (osteophytes) develops.(148) Alignment may become abnormal. If medial joint disease is disproportionate, varus deformities can develop. Other physical signs of osteoarthrosis include crepitus on range of motion. Tenderness is usually present but poorly localized, and effusions may or may not be present. Warmth and erythema are normally absent.(149, 150)

### **Patellar Dislocation**

Patients with a dislocated patella cannot walk or bear weight on the knee.(135) Deformity with displacement of the patella is apparent. Testing for instability can include variants of a patellar apprehension test (putting a lateral force on the patella, causing a sensation that the patella may dislocate).(52, 151) The sensitivity and specificity of apprehension testing has been reported to be 39 to 100%, and 88.4%, respectively.(52, 152)

### **Patellar Tendinopathy**

The main finding of patellar tendinosis on physical examination is tenderness over the patellar tendon. The tendon is often affected at the junction with the patella, but the quadriceps insertion on the patella may also be affected. This condition is often seen in athletes and others with high loading of the tendon (“jumper’s knee”).(153-156) Unless the patellar tendon is ruptured, other associated anatomic abnormalities are infrequent.

### **Patellar Tendon Tears**

Patellar tendon tears are relatively uncommon and present with an inability to walk.(157, 158) Deformity of the anterior knee, with clinical findings of a ruptured patellar tendon, is present. Tenderness is also present, and there is usually some proximal patellar retraction proximally, also known as patella alta.

### **Patellofemoral Syndrome**

Patients with patellofemoral syndrome have anterior knee pain, usually with a normal gait.(159, 160) Patellar alignment may be normal, but is often lateral. Some measure the Q-angle ), formed by a line drawn from the anterior superior iliac spine through the center of the patella and a line drawn from the center of the patella to the center of the tibial tubercle, is too large, although the clinical applicability of this angle appears weak.(161-163) Crepitus on range of motion (ROM) of the patella and with squatting is common. Pain with patellofemoral compression during ROM constitutes a positive grind test and may be helpful in the diagnosis of patellofemoral joint syndrome.(164) Tenderness along the edges of the patella has been reported to be 78% sensitive, 37% specific, and 58% accurate for the diagnosis of patellofemoral joint syndrome,(74) although the positive likelihood ratio for this sign is under 2.5.(165)

## **Work-Relatedness**

Acute occupational knee injuries are related to a specific acute traumatic event. The location of that event determines work-relatedness, and work-relatedness in this case is usually non-controversial. Most jurisdictions also request an opinion from the physician as to whether a disease or disorder should be considered as work-related for the purpose of a workers’ compensation claim. Physicians need to remember that their role is to supply opinion, and that the “medical/scientific answer” and the “legal answer,” as determined by the regulations and case law precedents in a particular jurisdiction (workers’ compensation system), are different (see Work-relatedness guideline). However, there have few quality

epidemiological studies that address work-related knee disorders. Thus, aside from these specific circumstances (e.g., occupational fractures and other acute trauma, meniscal tears from acute trauma, osteonecrosis from barotrauma, prepatellar bursitis in a roofer), most opinions are speculative.

### **Pes Anserine Bursitis**

Anserine bursitis appears to occur both in the presence and absence of trauma. There are no quality studies of occupational factors, and one study reported the only associated factor found was a valgus knee deformity.(95) In settings where significant trauma has occurred to precipitate the bursitis, work-relatedness is not controversial. In the absence of trauma, a theory may be constructed whereby physical factors such as unaccustomed forceful use of the knee may cause the condition; however, this is speculative.

### **Bursitis (Infrapatellar, Prepatellar, Suprapatellar)**

Infrapatellar bursitis appears to occur most commonly in the setting of kneeling activities, often in workers who are unaccustomed to kneeling.(166) This diagnosis in this context is considered work-related and is not usually controversial. Similarly, prepatellar bursitis in the context of discrete trauma or kneeling is considered work-related.(167-170) However, for other cases of bursitis, including where there is no discrete trauma, there are no quality studies of occupational factors. However, a theory may be constructed whereby physical factors such as unaccustomed forceful use of the knee may cause the condition.

### **Collateral Ligament Sprains and Tears (MCL and LCL)**

Collateral ligament sprains are thought to be consequences of significant trauma. The mechanism of the trauma determines whether the condition is work-related.

### **Cruciate Ligament Tears and Sprains**

Cruciate tears and sprains are largely attributed to the consequences of significant trauma.(171-174) The mechanism of the trauma determines whether the condition is work-related.

### **Hamstring, Calf and Quadriceps Strains and Tears**

Hamstring, calf, and quadriceps strains involve myotendinous strains in the respective muscle-tendon unit. Symptoms are usually acute in onset and these injuries are considered more analogous to acute injuries than diseases, although repeated, unaccustomed use may have precipitated the event. Thus, the nature of the forceful unaccustomed use determines whether the condition is work-related.

### **Iliotibial Band Syndrome**

This entity is considered a disease, rather than an acute injury. Most case series occur in athletes, particularly in runners, weight lifters, bicyclists, and downhill skiers, and among military recruits.(127, 129, 175-197) However, quality epidemiological studies are absent and risk factors are unclear. As there are no quality epidemiological studies, the condition has not been documented as occupational.

### **Knee Fracture**

Knee fractures are consequences of significant trauma. The mechanism of the trauma determines whether the condition is work-related.

### **Meniscal Tears**

Meniscal tears are highly prevalent.(198-208) The mechanism of injury will determine whether the meniscal tear is considered work-related. Acute, large meniscal tears occurring with a discrete traumatic event are usually considered as being consequences of that trauma.(208) The mechanism of the trauma normally determines whether the condition is work-related. On the other end of the spectrum, there are cases of degenerative-appearing meniscal tears without a discrete traumatic event. In such cases,

these tears are diseases. There is little quality epidemiological evidence that they are work-related, although some have theorized a relationship.(208-212) There are many cases occurring between the two extremes noted above, and work-relatedness is often unclear.

### **Osteoarthritis**

A minority of cases of osteoarthritis appear to arise in a knee after either fracture, removal of a meniscus,(213-219) torn meniscus,(29, 220, 221) ACL surgery,(222-224) other surgery, or major trauma or injury.(220, 225-228) The mechanism of that trauma is usually believed to be responsible for the osteoarthritis particularly as the magnitude or risk is generally considerable,<sup>iii</sup> and this often determines work-relatedness. However, the majority of cases have no significant traumatic history and thus causation is often unclear. Yet, while some aspects are poorly understood or controversial, there are some aspects of the epidemiology of knee osteoarthritis that are robust. The condition has been traditionally labeled non-inflammatory in contrast with rheumatoid arthritis and other inflammatory arthritides. Yet there are many different inflammatory mediators that are detectable in joints or systemically in affected individuals, including collagenase, tissue inhibitor of metalloproteinases, proteoglycan fragments, aggrecan, stromelysin-1, decorin, biglycan, lumican, keratocan,(229-239) and hyaluronic acid, which has predicted earlier progression of OA.(240) Weight loss has been shown to reduce those same inflammatory markers among knee osteoarthritis patients.(25)

Age is a well documented risk factor for knee osteoarthritis.(10, 241-255) Obesity has been shown to be an unusually robust risk factor for osteoarthritis of the knee,(10, 31, 225, 244, 246, 250, 256-274) as it is for other joints throughout the body(244, 275-277) (see Hip and Groin Disorders and Hand, Wrist, and Forearm Disorders guidelines). That obesity is associated with osteoarthritis of the upper extremity suggests the mechanism is at least partially unrelated to weight bearing. Additionally, weight loss appears to result in lower risk for osteoarthritis,(258) reduces biomarkers,(25) and improves prognoses of patients with osteoarthritis.(25, 278, 279)

Genetic factors have been reportedly strong,(260, 280-282) and the knee joint is frequently involved in generalized osteoarthritis.(201, 203, 251, 274, 283-288) Generalized OA as well as signs of active disease including effusions predicts faster progression of OA.(289) Heberden's nodes reportedly increase risk of knee degenerative changes by 6-fold over a 12-year period,(274) hand osteoarthritis conveys a 50% increased risk for knee OA,(10) and a specific hand-knee OA subset has been proposed.(290, 291)

Muscle weakness is thought to increase risk of knee OA(292-299) and forms a basis for one of the interventions for which there is some quality evidence of efficacy (see exercise section). Leg length discrepancy is also an apparently risk factor(300) as is knee malalignment.(274) Bone marrow edema is another reported risk.(301)

Job physical factors have not been studied in a quality epidemiological study reported to date. The proper study designs have yet to be reported, particularly either cohort studies or at least a well done case-control study with measured job physical factors and adjustments for the non-occupational factors.

Purported associated factors have included kneeling, squatting and lifting. However, results are inconsistent,(256, 257, 302) concerns about biases have been noted,(303) risks are nearly always low magnitude when positive, and nearly completely based on retrospective methods without measured job factors.(170, 220, 270, 304-313) However, some studies reported interactions of risk factors, and this

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<sup>iii</sup>Pooled odds ratio estimated at 3.86, 95% CI 2.61-5.70.10. Blagojevic M, Jinks C, Jeffery A, Jordan KP. Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. *Osteoarthritis Cartilage*. 2010;18(1):24-33.

suggests further need for study.(223, 270) Of all risks, kneeling appears to be most consistently associated with knee OA.(170, 210, 270, 306) A registry study from Sweden has suggested increased risk among farmers, construction workers, and firefighters, while risks were not elevated among numerous other occupational groups.(309, 310) Others have suggested no increased risk of knee OA among farmers.(314)

Numerous studies of runners have been performed with a basic presumption of risk due to high force use of the knees; however, nearly all studies including long duration cohort and other studies have been negative.(315-320) There also is suggestive evidence of thicker cartilage among runners(321) and in some animal models.(322) Mixed sports and power sports have reportedly led to earlier knee OA, but not endurance sports.(318) Another study found increased risks among women with high levels of physical activity, but not among men.(323)

A few other studies may also be of interest including a lack of differences in injuries between artificial turf and natural grass in a prospective cohort study of soccer players.(324) A comparative study of cartilage from the apparently unaffected side in unicompartmental OA patients found the cartilage was inferior to the cadaveric controls,(325) suggesting the cartilage of affected patients is inherently defective.

### **Patellar Dislocation**

Patellar dislocations are, absent congenital abnormalities, consequences of significant trauma. The mechanism of the trauma determines whether the condition is work-related. In those with recurrent dislocations, there is frequently an inherited or congenital abnormality with a propensity towards recurrences. In situations where there is a congenital abnormality, dislocation may occur in the context of an “event at work” and produce a controversy regarding work-relatedness that likely will be determined largely based on the specific statutory definition of work-relatedness in the setting of pre-existing, non-occupational conditions.

### **Patellar Tendon Tendinosis and Tears**

These are believed to be degenerative tendon conditions and tears, similar to those in the rotator cuff and are considered more analogous to diseases. However, discrete accidents may contribute to these tears. It is theorized that forceful use may contribute to the condition; thus, it is possible that they may be occupational in some circumstance(s), likely involving high-force quadriceps contraction. However, there currently are no quality epidemiological studies to identify occupational risk factors. Repeated, high force stereotypical use is believed to be a risk (i.e., “jumper’s knee”).

### **Patellofemoral Joint Syndrome**

This is a disease for which there is not quality evidence of work-relatedness. There are reports that the condition is most common in those with high knee demands including military recruits(326) and among those kneeling.(327, 328) Chondromalacia patellae was previously thought to be a distinct entity,(329) although increasingly the term anterior knee pain has been used.

## **Diagnostic Criteria**

Special studies are not needed to evaluate most knee symptoms (see Table 4), unless a period of conservative care and observation has failed to lead to resolution or improvement of symptoms. The American College of Radiology (ACR), in its most recent appropriateness criteria, lists the following clinical parameters as predicting the absence of significant fracture. These parameters may be used to

support the decision *not* to obtain a radiograph following knee trauma, although the decision rests with the primary treating physician who has completed a history and physical exam:

- patient is able to walk without a limp;
- patient had a twisting injury and there is no effusion.

The clinical parameters for ordering knee radiographs following trauma, as recommended by the ACR, are:

- joint effusion within 24 hours of direct blow or fall;
- palpable tenderness over fibular head or patella;
- inability to walk (4 steps) or bear weight immediately or within a week of the trauma;
- inability to flex knee to 90°.

**Table 4. Ability of Various Techniques to Identify and Define Knee Pathology**

Technique	Meniscus Tear	Ligament Sprain	Ligament Tear	Patello-femoral Syndrome	Tendinopathy	Prepatellar Bursitis	Regional Pain
History	++	++	++	++++	+++	++	++
Physical examination	++++	++++	++++	++	++++	++++	++
Laboratory studies	0	0	0	0	0	0	0
Electromyography/nerve conduction velocity (EMG/NCV) studies	0	0	0	0	0	0	0
Imaging studies							
Radiography <sup>†</sup>	0	0	0	+	0	0	0
Bone scan <sup>†</sup>	0	0	0	+	0	0	0
Arthrography <sup>†</sup>	+++	0	+	0	0	0	0
Computed tomography (CT) <sup>†</sup>	0	0	0	0	0	0	0
Magnetic resonance imaging (MRI) <sup>†</sup>	++++	+++	++++	+++	+++	+++	0

<sup>†</sup>Risk of complications (e.g., infection, radiation) highest for arthrography, less for radiography and computer tomography (CT), and lowest for bone scan and MRI.

The criteria presented in Table 5 follow the clinical thought process, from the type of illness or injury, to symptoms and signs of a particular disorder to, finally, test results (if any tests are indicated).

**Table 5. Diagnostic Criteria for Non-red-flag Knee Disorders**

Probable Diagnosis or Injury	Symptoms	Signs	Tests and Results
Knee Osteoarthritis	Non-radiating knee pain. Morning stiffness or stiffness upon standing or after prolonged sitting. Sleep disturbance sometimes present as a result of pain, but mood disturbance usually not present. Other joints are often affected.	ROM generally reduced, especially knee flexion. May be normal when mild.	X-rays usually ordered to help secure diagnosis. Other diagnostic tests only if there is a potential for meaningful intervention

Patellofemoral Joint Syndrome (chondromalacia patella)	Anterior knee pain. Pain with stair climbing, other activities involving knee flexion, or sitting for a prolonged period of time.	Anterior knee tenderness. Crepitus on range of motion. Pain with patellofemoral compression	X-rays often ordered. Sunrise patella view particularly helpful. Other testing usually not necessary.
Patellar Dislocation and Instability	Inability to bear weight. Acute onset associated with forceful event or accident. Congenital or inherited variants tend to be recurrent. Instability if feeling of impending recurrence of subluxation with specific activities.	Unable to bear weight. Patella visibly displaced. Difficulty extending the knee.	Knee x-rays usually ordered. Other testing usually not necessary.
Patellar Tendinopathy	Focal patellar tendon pain. Pain increases with use including stair use and jumping.	Focal tenderness over patella. Resisted knee extension may reproduce pain.	X-rays may demonstrate calcification and osteophytes at inferior patellar pole (which also may be non-specific). Ultrasound may show small tears.
Fractures	Fall, motor vehicle accident, or other significant trauma. Severe pain.	Unable to bear weight. Angulation, deformity, point tenderness, and bony crepitus.	X-rays required. Other testing usually not necessary in the acute treatment setting.
Meniscal Tears	Non-radiating knee pain. Typically provoked with specific, predictable activities in specific position(s). May have symptoms of joint effusion, buckling, clicking, catching or locking. Pain may be worse with pivoting and walking or stair-climbing.	Variable findings depending on extent of tear(s). May have joint effusion and modest warmth. Knee pain often worse with ROM and extent of ROM may be restricted. Pain reproduced with knee rotation and flexion. Click and/or crepitus may be present on exam.	X-rays often ordered. MRI is sometimes ordered, and MR arthrography may be helpful.
Osteonecrosis	Non-radiating bony pain. History of systemic factors (e.g., diabetes mellitus, alcohol). Pain generally increases with weight-bearing.	Reduced ROM and pain with passive ROM usually present. May have pain with weight bearing. May be unable to bear weight if osseous collapse has occurred.	X-rays required. MRI and CT may be ordered for further evaluation of the necrotic region. Bone scans sometimes ordered.
Infrapatellar, Prepatellar, Suprapatellar, and Anserine Bursitis	Anserine bursitis may be painful, but without clear effusion or exertional component. Other types of bursitis frequently not painful, but do have effusion/swelling.	Tender over anserine bursa. Other bursitis often minimally or not tender. ROM usually normal.	X-rays usually not needed. X-rays sometimes ordered if questions of usual settings, including concerns for infection, osteomyelitis, and foreign body. Other testing usually not required.

Collateral Ligament Sprains and Tears (lateral and medial)	Focal knee joint line pain. Medial more prone to be accompanied by meniscal tear. If complete tear, will typically have instability.	May have antalgic gait, especially if moderate to severe sprain. Focal tenderness over collateral ligament. Usually no effusion.	X-rays usually ordered in acute setting to rule out fracture, particularly for moderate to severe injuries. MRI may be helpful in chronic setting to rule out associated meniscal tear. Other testing usually not required.
Iliotibial Band Syndrome	Non-radiating lateral knee pain.	Lateral knee pain with use, especially running, cycling. Tender over lateral fascia.	X-ray generally not necessary, but may be indicated if concerns of unusual diagnostic concerns, such as accompanying arthrosis.
Cruciate Ligament Sprains, Tears and Ruptures. (anterior, Posterior)	Sudden pain with accident or other traumatic event. May have giving out and immediate swelling after event. May be asymptomatic. Event usually involved exaggerated adduction and external rotation or abduction.	Effusion if acute tear. Joint laxity with complete tears, including positive posterior or anterior drawer signs.	X-ray usually ordered in acute setting to rule out fractures. MRI may be helpful.
Non-specific Knee Pain	Non-specific. No acute trauma	None	None
Non-specific Effusion	None. No acute trauma.	Effusion. No signs of infection or other abnormality.	X-ray often ordered, but by definition, normal other than effusion. Need evaluation for rheumatological disorder.

Adapted from AMA Guides to Impairment Rating – 6<sup>th</sup> edition and Sanders S, et al. Evidence-based clinical practice guidelines for interdisciplinary rehabilitation of chronic nonmalignant pain syndrome patients. *Pain Prac.* 2005;5(4):303-15.

## Follow-up Visits

Patients with knee symptoms should have follow-up approximately every three to seven days, depending on severity of the condition, limitations, and workplace accommodation of limitations. Considerations for the initial follow-up visits include: response to treatment, further education, advice to avoid static positions, medication use, activity modification, and other concerns. The practitioner can answer questions and make these sessions interactive so that the patient is fully involved in his or her recovery. If the patient has returned to work, these interactions may be done on site or by telephone to avoid interfering with modified- or full-work activities.

## Diagnostic Recommendations

### Antibodies

There are numerous antibodies that are markers for specific rheumatic diseases (e.g., rheumatoid factor, anti-nuclear antibodies, anti-Sm, anti-Ro, anti-La for rheumatoid arthritis, systemic lupus erythematosus, Sjogren's, mixed connective tissue disorder, etc.). Patients with rheumatic disorders are at increased risk for degenerative joint disease of the knee.(283, 333-339)

*Antibodies for Diagnosing Knee Pain with Suspicion of Chronic or Recurrent Rheumatological Disorder*

**Antibody levels are recommended to evaluate and diagnose patients with knee pain who have reasonable suspicion of rheumatological disorder. However, ordering of a large, diverse array of antibody levels without targeting a few specific disorders is not recommended.**

*Indications* – Knee pain with suspicion of rheumatological disorder.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Antibodies to Confirm Specific Disorders*

**Antibody levels are strongly recommended to confirm specific disorders (e.g., rheumatoid arthritis).**

*Indications* – Knee pain and presumptive diagnosis of a rheumatological disorder.

*Strength of Evidence* – **Strongly Recommended, Evidence (A)**

*Rationale for Recommendations*

Elevated antibody levels are useful for confirmation of clinical impressions of rheumatic diseases. However, routine use of these tests in knee pain patients, especially as wide-ranging, non-focused test batteries are likely to result in inaccurate diagnoses due to false positives and low pre-test probabilities. Providers should also be aware that false negative results occur. Measurement of antibody levels is recommended for focused testing of a limited number of diagnostic considerations for which there is clinical suspicion. Measuring antibody levels is minimally invasive, unlikely to have substantial adverse effects and low to moderately costly, depending on the specific test ordered.

### Arthrography

This diagnostic procedure has been replaced by MRI, which is both more sensitive and specific.

### Knee Arthroscopy

Arthroscopy of the knee has been increasingly utilized for treatment of knee disorders.(9, 137, 340-367) It has become the gold standard for measuring the utility of the clinical examination as well as the comparative standard for other treatments.(368) Disorders commonly treated arthroscopically include meniscal tears, cruciate tears, and chondral fractures.(353, 369-374) However, there are few high quality studies from which to determine indications for either diagnostic or therapeutic arthroscopic knee procedures.

*Knee Arthroscopy for Diagnosing and Treating Knee Pain with Suspicion of Meniscal Tear, Intraarticular Body, or Other Subacute or Chronic Mechanical Symptoms*

**Arthroscopy is only recommended to evaluate and diagnose patients with knee pain if there is suspicion of a clinically significant meniscal tear, intraarticular body, or other subacute or chronic mechanical symptoms and an equivocal or inconclusive MRI.**

*Indications* – Knee pain with suspicion of meniscal tear, intraarticular body, or other subacute or chronic mechanical symptoms treatable by arthroscopy.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Knee Arthroscopy for Diagnosing Acute Knee Pain*

**Arthroscopy for diagnosing acute knee pain, other than large meniscal tears, cruciate tears or intraarticular bodies, is not recommended.**

*Strength of Evidence* – **Not Recommended, Insufficient Evidence (I)**

*Knee Arthroscopy for Staging a Surgical Procedure*

**Arthroscopy is recommended for staging a surgical procedure.**

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Knee Arthroscopy for Diagnosis or Treatment in Acute, Subacute, or Chronic Osteoarthritis without Mechanical Symptoms and Other Remediable Mechanical Defect*

**Arthroscopy is not recommended for diagnosis or treatment in patients with acute, subacute, or chronic osteoarthritis in the absence of a remediable mechanical defect such as clinically significant symptomatic meniscal tear.(375)**

*Strength of Evidence* – **Not Recommended, Insufficient Evidence (I)**

*Rationale for Recommendations*

Arthroscopy of the knee is widely utilized for treatment of several knee disorders, especially meniscal tears. Complications usually occur with more serious injuries and include nerve retraction, neuropraxias, infection, and complex regional pain syndrome.(376-385) Adverse effects are minimal when small-bore arthroscopes are used. Osteoarthritis was previously thought to be treatable by arthroscopy.(369) However, arthroscopy is currently not believed to be helpful, and arthroscopy with chondroplasty has been shown not to be helpful, in the absence of remediable mechanical symptoms suggesting a clinically significant meniscal tear or intraarticular body.(375) Arthroscopy is invasive and expensive, but it is recommended for selected patients, particularly those with remediable mechanical defects such as meniscal tears.

*Evidence for the Use of Arthroscopy*

There is 1 low-quality RCT in Appendix 1.(386)

## **Bone Scans**

Bone scans involve intravenous administration of a radioactive tracer medication that is preferentially concentrated in areas of metabolic activity in bone.(387, 388) The radioactivity is then detected by a large sensor and converted into images of the skeleton. There are many causes of abnormal radioactive uptake, including metastases, infection, inflammatory arthropathies, fracture or other significant bone trauma. Thus, positive bone scans are not highly specific. Bone scans have been used for the diagnosis of early osteonecrosis, which is often not apparent on x-ray.(389-392)

*Bone Scanning for Select Use in Acute, Subacute, or Chronic Knee Pain*

**Bone scanning is recommended for select use in patients with acute, subacute, or chronic knee pain to assist in diagnosing osteonecrosis, neoplasms, or other conditions with increased polyostotic bone metabolism, particularly if more than one joint is to be evaluated.**

*Indications* – Knee pain with suspicion of osteonecrosis, Paget’s disease, neoplasm, or other increased polyostotic bone metabolism.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Routine Use of Bone Scanning for Knee Joint Evaluations*

**Bone scanning is not recommended for routine use in knee joint evaluations as it is generally thought to be inferior to MRI.**

*Strength of Evidence* – **Not Recommended, Insufficient Evidence (I)**

*Rationale for Recommendations*

Bone scanning may be a helpful diagnostic test to evaluate suspected metastases, primary bone tumors, infected bone (osteomyelitis), inflammatory arthropathies, and trauma (e.g., occult fractures). It may be helpful in those with suspected early AVN without x-ray changes. There is no indication for bone scanning in cases where the diagnosis is felt to be secure, as bone scanning does not alter management. Bone scanning is minimally invasive, has minimal potential for adverse effects (essentially equivalent to a blood test), but is costly.

*Evidence for the Use of Bone Scans*

There are no quality studies evaluating the use of bone scans for the evaluation of knee pain.

## **Computerized Tomography (CT)**

Computerized tomography is a useful imaging procedure for bony anatomy, whereas MRI is superior for soft tissue abnormalities.(393, 394) CT may be useful for certain knee joint abnormalities, including complex fractures, in which advanced imaging of the bones is required. CT may be helpful for the evaluation of AVN. CT may also be useful for evaluation of the spine in patients with contraindications for MRI, including implanted metallic-ferrous device.(394)

*Routine CT for Evaluating Acute, Subacute, or Chronic Knee Pain*

**Routine CT is not recommended for evaluating acute, subacute, or chronic knee pain.**

*Strength of Evidence* – **Not Recommended, Insufficient Evidence (I)**

*CT for Evaluating Patients with Osteonecrosis (AVN)*

**CT is recommended for evaluating patients with osteonecrosis or for those who need advanced imaging, but have contraindications for MRI.**

*Indications* – Knee pain from osteonecrosis with suspicion of subchondral fracture(s), or increased polyostotic bone metabolism.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*CT for Evaluating Patients with Periprosthetic Osteolysis after Total Knee Arthroplasty*

**CT is recommended for evaluation of total knee arthroplasty patients with potential periprosthetic osteolysis.**

*Indications* – Arthroplasty thought to have periprosthetic osteolysis.(395)

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Rationale for Recommendations*

Computerized tomography is considered superior to MRI for imaging of most knee abnormalities where advanced imaging of calcified structures is required. CT has been used to evaluate periprosthetic

osteolysis.(395) A contrast CT study is minimally invasive, has few adverse effects, but is costly. It is recommended for select use. Helical CT scan is thought to be superior to MRI for evaluating subchondral fractures; however, a large, high-quality study comparing these modalities has not yet been published.(396)

#### *Evidence for the Use of CT*

There are no quality studies evaluating the use of CT for the evaluation of knee pain.

## **C-Reactive Protein, Erythrocyte Sedimentation Rate, and Other Non-Specific Inflammatory Markers**

There are many markers of inflammation that may be measured serologically. These include C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), ferritin, and a total protein-albumin gap.(397-400)

#### *Non-specific Inflammatory Markers for Screening for Inflammatory Disorders in Subacute or Chronic Knee Pain Patients*

**Erythrocyte sedimentation rate and other inflammatory markers are recommended to evaluate for inflammatory disorders or prosthetic sepsis when there is a reasonable suspicion of an inflammatory disorder in subacute or chronic knee pain patients. However, ordering a large, diverse array of inflammatory markers without targeting specific disorders for which there is clinical suspicion is not recommended.**

*Indications* – Knee pain with suspicion of inflammatory disorder, including infection.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

#### *Rationale for Recommendation*

Erythrocyte sedimentation rate is the most commonly used systemic marker for non-specific inflammation. The ESR is elevated in numerous inflammatory conditions, including rheumatological disorders, as well as with infectious diseases. C-reactive protein is a marker of systemic inflammation that has been reported to be associated with an increased risk of coronary artery disease. However, it is also a non-specific inflammatory marker. Other non-specific markers of inflammation include an elevated ferritin and protein-albumin gap. CRP and ESR measurements are minimally invasive, have low risk of adverse effects, and are relatively inexpensive. They are recommended as a reasonable component of the evaluation when there is suspicion of a systemic inflammatory condition.

#### *Evidence for the Use of C-Reactive Protein, Erythrocyte Sedimentation Rate, and Other Non-specific Inflammatory Markers*

There are no quality studies evaluating the use of C-reactive protein, erythrocyte sedimentation rate, and other non-specific inflammatory markers for knee pain.

## **CYTOKINES**

See Chronic Pain guideline.

## **LOCAL ANESTHETIC INJECTIONS AND EPIDURALS**

Local anesthetic injections are sometimes used for diagnostic confirmation of knee conditions (see Injections). These injections are also sometimes used to differentiate pain from a distant site, such as the hip or spine. Diagnostic injections include intraarticular injections (knee, hip, or sacroiliac), ilioinguinal, genitofemoral, and saphenous nerve blocks, and lumbar epidurals.(401-404)

### *Local Anesthetic Injections to Diagnose Subacute or Chronic Knee Pain*

**Local anesthetic injections are recommended to assist in the diagnosis of subacute or chronic knee pain.**

*Indications* – Subacute or chronic knee pain from an unclear source; immediate and delayed results of injection(s) should be recorded.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

#### *Rationale for Recommendation*

Local anesthetic injections may be helpful for confirming diagnostic impressions, although there are no quality studies evaluating the use of injections for these purposes. Intraarticular knee injections are often performed with anesthetic agents and glucocorticosteroids, as this generally accomplishes both diagnostic and therapeutic purposes simultaneously. These injections are minimally invasive, have minimal potential for adverse effects, and are moderately costly.

#### *Evidence for the Use of Local Anesthetic Diagnostic Injections*

There are no quality studies evaluating the use of local anesthetic diagnostic injections for knee pain.

## **ELECTROMYOGRAPHY (including Nerve Conduction Studies)**

See the Low Back Disorders guideline for discussion regarding the use of electrodiagnostic studies for evaluation of back-related disorders that may present as knee pain. Electrodiagnostic studies have also been used to confirm diagnostic impressions of other peripheral nerve entrapments, including of the lateral cutaneous nerve of the thigh (meralgia paresthetica).(405-417)

### *Electromyography for Diagnosing Subacute or Chronic Peripheral Nerve Entrapments*

**Electrodiagnostic studies are recommended to assist in the diagnosis of subacute or chronic peripheral nerve entrapments.**

*Indications* – Subacute or chronic paresthesias with or without pain, particularly with an unclear diagnosis.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

#### *Rationale for Recommendation*

Electrodiagnostic studies may assist in confirming peripheral nerve entrapments. These studies are minimally invasive, have minimal potential for adverse effects (essentially equivalent to a blood test), and are moderately costly.

#### *Evidence for the Use of Electromyography*

There are no quality studies evaluating the use of electrodiagnostic studies for diagnosing peripheral nerve entrapments relevant to the knee.

## **FUNCTIONAL CAPACITY EVALUATIONS**

See Chronic Pain guideline.

## **MAGNETIC RESONANCE IMAGING (MRI)**

Magnetic resonance imaging (MRI) has been widely used for diagnostic purposes in patients with knee pain, particularly for evaluating the menisci and cruciate ligaments.(137, 340, 341, 343, 344, 346-352, 354-358, 360-362, 365-367, 418-420) MRI is considered the gold standard for evaluating AVN.(421-429)

*MRI for Knee Joint Pathology, Including Diagnosing Meniscal Tears, Cruciate Ligament Tears, Hamstring and other Muscular Tears, and for Select Patients with Post-arthroplasty Chronic Pain or Periarticular Masses*

**MRI is recommended for select patients with subacute or chronic knee symptoms in which mechanically disruptive internal derangement or similar soft tissue pathology is a concern. It is generally not indicated for patients with acute knee pain.**

*Indications* – Subacute or chronic knee pain in which imaging of surrounding or intraarticular soft tissues is needed (including menisci); evaluation of moderately severe and severe cruciate ligament sprains and tears to evaluate the extent of the injury and help determine whether surgery is indicated.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*MRI for Diagnosing Osteonecrosis (AVN)*

**MRI is recommended for diagnosing osteonecrosis.**

*Indications* – Subacute or chronic knee pain thought to be related to osteonecrosis (AVN), particularly if the diagnosis is unclear or if additional diagnostic evaluation and staging is needed.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*MRI for Routine Evaluation of Acute, Subacute, or Chronic Knee Joint Pathology*

**MRI is not recommended for routine evaluation of acute, subacute, or chronic knee joint pathology, including degenerative joint disease.**

*Strength of Evidence* – **Not Recommended, Insufficient Evidence (I)**

*Rationale for Recommendations*

MRI has not been evaluated in quality studies for knee joint pathology, although studies have reported accuracy estimates ranging from 82 to 96% for cruciate ligament and meniscal tears.(84, 121, 348, 356, 357, 367, 430-434) False-negative MRI interpretations are particularly likely in posterior horn meniscal tears.(368) There is concern that MRI is overutilized, particularly in cases where clinical examination is sufficient.(84, 102, 116, 435) However, most physicians believe that MRI should be performed prior to arthroscopy for meniscal or ACL tears(436) or in patients with non-specific knee pain.(437)

MRI may play a role in staging osteoarthritis,(438) although there is no quality evidence that this practice affects prognosis or treatment. MRI can detect osteophytes(439) and is better than x-ray for identifying cartilage loss and subchondral cysts, but it is relatively poor at detecting early subchondral sclerosis.(439, 440) There are no quality studies evaluating the use of MRI for osteonecrosis of the knee joint. There is low-quality evidence that MRI may be less sensitive for detection of subchondral fractures than helical CT or plain x-rays in patients with osteonecrosis.(396) MRI is not invasive, has no adverse effects, although there may be issues related to claustrophobia or complications of concomitantly administered medications, but it is costly. MRI is not recommended for routine knee imaging, but it is recommended for selected knee joint pathology, particularly suspected soft tissue pathology.

*Evidence for the Use of MRI*

There are no quality studies evaluating the use of MRI for diagnosing knee pain.

## MR Arthrogram

Magnetic resonance imaging with arthrography (MR arthrography) has been performed to evaluate meniscal and chondral lesions,(441, 442) for example following chondrocyte and meniscus implants.(442, 443)

*MR Arthrogram for Evaluation of Select Patients Needing Advanced Meniscal and Cartilage Imaging and Following Chondrocyte Implantation*

**MR arthrograms are recommended for select patients who require advanced imaging of the menisci and articular cartilage or following procedures such as chondrocyte implantation.**

*Indications* – Patients with negative or equivocal MRI imaging with ongoing suspicion of clinically significant intraarticular pathology such as meniscal tears or articular cartilage defects or following selected procedures such as chondrocyte implantation.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Rationale for Recommendation*

MR arthrograms have not been evaluated in quality studies, but appear helpful in evaluating patients with ongoing intraarticular mechanical symptoms despite negative or inconclusive MRIs. These studies are also likely to be helpful for those with certain post-operative indications, including after chondrocyte implantation. MR arthrography is minimally invasive, has no adverse effects, although there may be issues related to claustrophobia or complications of concomitantly administered medications, but it is costly. However, it is likely the best imaging procedure available for certain select patients.

*Evidence for the Use of MR Arthrogram*

There are no quality studies evaluating the use of MR arthrogram.

## ROENTGENOGRAMS (X-RAYS)

X-ray is the initial test for evaluation of most cases of knee pain.(283, 342, 438, 444-449) X-rays are considered the initial test of choice for evaluating patients with suspected knee osteoarthritis. Two or three supine views are generally performed. There are no quality studies of x-ray in the evaluation of knee pain. It should be noted that the threshold for x-ray of the lumbosacral spine and/or hip joint should be low, particularly if the findings on knee x-ray are either normal or do not readily explain the degree of clinical findings. Stress radiography (x-ray taken while a stress is applied to the joint and used to demonstrate instability) has been described for evaluation of ACL tears, but is not usually necessary to establish a diagnosis.(110) In the case of osteonecrosis, plain x-ray results differ by stage of disease. Early x-rays are usually normal or have less distinct trabecular patterns, but as the disease progresses, x-rays begin to show osteoporotic areas progressing to sclerotic areas and flattening and bony collapse.(450) X-rays are also used to evaluate post-arthroplasty knees.

*X-ray for Evaluating Acute, Subacute, or Chronic Knee Pain*

**X-ray is recommended for evaluating acute, subacute, or chronic knee pain.**

*Indications* – In the absence of red flags, knee pain of moderate to severe intensity lasting at least a few weeks, and/or limited range of motion.

*Frequency/Duration* – Obtaining x-rays once is generally sufficient. For patients with chronic or progressive knee pain, it may be reasonable to obtain a second set of x-rays, months to years after the baseline x-rays to re-evaluate the patient's condition, particularly if symptoms change.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

### *X-ray for Diagnosing Fracture*

**X-ray is recommended for diagnosing fracture.**

*Indications* – Patients thought to have fracture, particularly those with an inability to bear weight, effusion, or ecchymosis.(451)

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

### *X-ray for Diagnosing Osteonecrosis (aka Avascular Necrosis, AVN)*

**X-ray is recommended for diagnosing osteonecrosis.**

*Indications* – Patients thought to have osteonecrosis (ON).

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

### *Rationale for Recommendations*

X-ray is helpful in evaluating most knee pain, both to diagnose and to assist with narrowing the differential diagnosis. A clinical algorithm was constructed to evaluate the need for x-ray to rule out fracture, and the presence of at least one sign of fracture was deemed to be highly sensitive for fracture.(451) There are no quality studies of the use of x-ray to evaluate knee pain. There is one low-quality study suggesting x-ray has higher sensitivity than MRI for detection of subchondral fractures in patients with osteonecrosis.(396) However, x-ray has long been used to stage osteoarthritis(283, 342, 438, 452-456) and evaluate for post-arthroplasty osteolysis.(457) X-ray is non-invasive, low to moderately costly, and has little risk of adverse effects.

### *Evidence for the Use of X-rays*

There are no quality studies evaluating the use of x-rays for knee pain, including for diagnosing osteonecrosis.

## **SALINE LOAD TEST**

The saline load test has been used when there is a knee laceration to determine whether there has been penetration of the joint capsule.(458-460) The test involves injection of saline into the joint to ascertain whether the solution flows through the joint capsule and out of the trauma site.(461)

### *Saline Load Test for Select Knee Lacerations*

**A saline load test is recommended for select patients with knee lacerations that may have penetrated the joint.**

*Indications* – Lacerations in the knee region that may have penetrated the knee joint but have not clearly done so.

*Dose* – At least 150 to 200mL of saline injected with an 18-g needle. Volume required varies based on size of potential laceration (more saline required for smaller lacerations) and may differ based on location of laceration. The lateral suprapatellar instillation site has been utilized.(460) Superomedial and inferomedial locations have been compared; more volume required for the superomedial location (mean 95.2 vs. 64.0mL).(459)

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

### *Rationale for Recommendation*

There are no quality studies of the saline load test in the evaluation of joint capsule penetration. A study in 30 arthroscopy patients suggested that more than 194mL was required for the saline load test to be at least 95% sensitive.(460) Another study of knee arthroscopy patients found at least 155mL of saline must be injected to detect 95% of 1-cm inferolateral arthrotomies.(459) This procedure is minimally

invasive, has minimal potential for adverse effects, is relatively inexpensive, and is recommended for select patients.

#### *Evidence for the Use of Saline Load Test*

There are no quality studies evaluating the use of saline load test for the evaluation of knee pain.

## Ultrasound

Many of the usual causes of knee pain are better imaged with modalities other than ultrasound. Diagnostic ultrasound has been used for evaluating the patellar ligament, including for “jumper’s knee” and partial ruptures,(156, 462-468) effusions,(469) dysplasia,(470, 471) labral tears,(472) and occult fractures.(473) Ultrasound for cruciate ligament tears has been described as technically difficult.(78) Ultrasound has also been used to guide injections in deep body structures, although the knee joint is relatively accessible. The diagnostic accuracy of ultrasound for patellar partial ligament ruptures has been reported as 100% in a modest sized case series.(462)

#### *Ultrasound for Evaluating Patellar Tendinopathy, Pes Anserine Bursitis, Hamstring Strains, Quadriceps Strains or Post-arthroplasty Chronic Pain When Peri-Articular Masses Are Suspected*

**Ultrasound is recommended for evaluating patients with patellar tendinopathy, pes anserine bursitis, hamstring strains, quadriceps strains, or post-arthroplasty chronic pain, when peri-articular masses are suspected.**

*Indications* – Patients with knee pain thought to be from these disorders.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

#### *Ultrasound for Evaluating Other Knee Disorders including Osteonecrosis, Osteoarthritis, Dysplasia, or Fractures*

**There is no recommendation for or against the use of ultrasound for evaluating other knee disorders, including osteonecrosis, osteoarthritis, dysplasia, or fractures.**

*Strength of Evidence* – **No Recommendation, Insufficient Evidence (I)**

#### *Rationale for Recommendations*

Ultrasound has been found to be helpful in evaluating tendinopathy and myotendinous strains. There is no clear indication for use of ultrasound for the evaluation of osteoarthritis. Ultrasound is not invasive, has no adverse effects, is moderately costly, and is recommended for select use.

#### *Evidence for the Use of Diagnostic Ultrasound*

There are no quality studies evaluating the use of diagnostic ultrasound.

## Management Overview

Although comfort is often a patient’s first concern, the treating physician must first evaluate for remediable conditions or red flags. Nonprescription analgesics may provide sufficient pain relief for most patients with acute or subacute knee pain. If treatment response is inadequate (i.e., if symptoms and activity limitations continue) or the physician judges the condition limitations to be more significant, prescribed pharmaceuticals or physical methods can be added. Co-morbid conditions, invasiveness, adverse effects, cost, and physician and patient preferences guide the choice of recommendations. Initial care, including comfort items, may consist of non-steroidal anti-inflammatory drugs (NSAIDs),

acetaminophen, cryotherapy, heat, exercises, or education and advice on activities. Education about knee pain should begin at the first visit.

This guideline addresses the evidence for efficacy of many knee interventions. Interventions with quality evidence of proven efficacy are recommended in this guideline. Complication rates and safety profiles, if available, were considered in developing these guidelines. Interventions not supported by moderate- to high-quality studies are not recommended and are indicated as **Not Recommended, Insufficient Evidence (I)**.

# Knee Pain and Osteoarthritis

## Treatment Recommendations

Physicians should develop individualized patient treatment and follow-up plans based on the severity of the condition, co-morbidities, occupational demands, psychosocial factors, and patient motivation and need for encouragement. The ability to return to work should be considered when determining the frequency of follow-up. More frequent appointments are generally required for patients whose limitations have not been accommodated. The patient should be transitioned to work, or from modified work to full work, at the earliest date possible, and should be supported during that transition and counseled about the likelihood of increased symptoms while being reassured that pain does not equate to injury.

### Activities and Activity Modification

Activities and activity alterations are typically managed differently in patients with acute and chronic knee pain. Acute knee pain patients may benefit from activity limitations, while chronic knee pain patients almost never improve with activity limitations. Acute knee pain often improves with avoidance of occupational and non-occupational activities that result in *substantial* increases in pain. However, even in the acute pain setting, appropriate activity alterations are difficult to identify. For example, prolonged inactivity of any musculoskeletal pain usually results in increased pain upon movement. It is easy to erroneously conclude the activity aggravated the pain. Even in the acute setting, however, some activity is usually desirable. In general, activities causing a *significant* increase in knee symptoms should be reviewed with the patient and modifications advised when appropriate. These activities may include stair climbing, walking, lifting, and frequency of postural changes.

Chronic knee pain is managed differently. Almost invariably, rehabilitation of chronic knee pain involves gradually performing the occupational and non-occupational activities that result in increased pain in order to improve function. The same types of limitations may be reasonable, but progressive increases in activity frequency, intensity and/or durations is generally necessary to rehabilitate these problems.

Work limitations should take into account four main factors: 1) the job physical requirements; 2) the severity of the problem; 3) work organizational issues (e.g. ability to control job or tasks, overtime, work allocation, wage incentives); and 4) the patient's understanding of his or her condition. Sometimes it is necessary to write limitations or prescribe activity levels that are above what the patient feels he or she can do, particularly for patients who believe they should remain sedentary. Progressively increased activity is important, and restrictions that state "sedentary work" are *not* appropriate for most knee

patients. Physicians should recognize that a patient's expectations regarding return-to-work status are often set prior to the first appointment,(474) (Kapoor 06) and therefore education may be necessary to set realistic expectations and goals. It is best to communicate early in the treatment that limitations will be progressively reduced as the patient progresses. This should be reiterated at each successive visit so that the patient is well advised in advance of the treatment plan.

There are no quality studies of restrictions, so determining appropriate restrictions is often left to clinical judgment. Assessment of work activities and potential for modifications may be facilitated by a worksite visit and analysis by a healthcare provider with appropriate training (e.g., occupational therapist, physical therapist, physician, or ergonomist). Common limitations involve stair climbing and modifying the weight of objects lifted, frequency of lifts, and posture while taking into account the patient's capabilities. For severe cases of acute knee pain, initial modification of occupational and non-occupational activities often includes:

- frequent alternation of sitting and standing;
- no lifting more than 10 pounds;
- no prolonged or repeated knee bending (flexion);
- no prolonged or repeated crouching and squatting;
- avoidance of ambulation on slippery surfaces or uneven ground; and
- avoidance of frequent stairs.

These work and home activity guidelines are generally reassessed every week in the acute phase. Gradual increases in activity levels are recommended with a goal of returning to full duty in 6 to 12 weeks. The amount of weight handled can be progressively increased. Alternatively, patients can be returned to 1 to 2 hours a day of prior full duty work, with the remainder of the day spent at modified duty. The numbers of hours of full duty work can be increased every 1 to 2 weeks. Individualization of management plans is often necessary. For example, if prior job physical tasks involved frequent lifting of more than 100 pounds, then restricted work guidance may be substantially greater (e.g., 25 pounds of lifting and carrying at first). For workers who have control over their job tasks, assistance from someone else and alternating between sitting and standing as needed, may be included in the management plan.

It should be noted that some workplaces provide healthcare or rehabilitation therapy on-site, so brief periods of recumbent time during the day and on-site physical or occupational therapy may be possible. The physician should make it clear to patients and employers that:

- prolonged walking and/or stair climbing may aggravate symptoms;
- moderately heavy lifting, carrying, or working in awkward positions may aggravate symptoms; and
- any restrictions are intended to allow for recovery and time to build activity tolerance through structured exercise.

It is in the patient's best interest for the short- and long-term to maintain maximal levels of activity, including work activity. Written guidance on activity limitations, when applicable, communicates the status of the patient to the employer and gives the patient information on what he or she should or should not do both at work and at home.

## **ACTIVITY MODIFICATION**

*Activity Modification for Acute, Subacute, or Chronic Knee Pain*

**Activities that do not substantially aggravate symptoms are recommended for most patients with acute, subacute, or chronic knee pain.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

*Rationale for Recommendation*

There are no quality studies evaluating modification of activity for treatment of knee pain. Common post-arthroplasty limitations have included no lifting over a weight limit, no running, and no jumping. Lifting limits may commonly be 50 pounds, but are frequently based on prior weight-lifting capabilities and anticipated future abilities. While modification of activity is not invasive, it may result in increased disability through disuse, or increased cardiovascular morbidity through lack of exercise. It also may result in high costs through lost productivity. Thus, implementation of activity modifications should be carefully balanced against increased longer term morbidity and other costs. In cases where activity does not aggravate the symptoms or disease, activity modifications are not recommended – rather, activity is recommended.

*Evidence for the Use of Activity Modification*

There are no quality studies evaluating the use of activity modification for treatment of knee pain.

**BED REST AND NON-WEIGHT-BEARING**

*Bed Rest and Non-weight Bearing for Patients with Acute, Subacute, or Chronic Knee Pain*

**Bed rest and non-weight bearing are not recommended for patients with acute, subacute, or chronic knee pain.**

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

*Bed Rest and/or Non-weight Bearing for Unstable Fractures*

**Bed rest and/or non-weight bearing activities are recommended for patients with clear contraindications to weight-bearing, such as an unstable fracture.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

*Rationale for Recommendations*

Bed rest and/or non-weight bearing are unlikely to be beneficial and generally should be avoided for all patients other than for those with clear contraindications to weight-bearing, such as evidence of an unstable fracture.

*Evidence for the Use of Bed Rest and Non-Weight Bearing*

There are no quality studies evaluating the use of bed rest for treatment of knee pain.

**EXERCISE**

Exercises have been utilized for the prevention and treatment of osteoarthritis, including aerobic exercise, strengthening exercise, and flexibility.(475-491) Exercise is also thought to be effective for rehabilitation after knee arthroplasty.(492) Educational programs have also been used to treat knee osteoarthritis, often in combination with an exercise program.(6, 481, 493-499)

Arthritic patients tend not to engage in high levels of physical activity.(500) Some believe that exercise is an effective primary and secondary preventive intervention.(12) Opinions on the relative importance of aerobic versus strengthening versus flexibility conflict,(482, 484, 491, 501-512) and some endorse the belief that “exercise may be the most effective, malleable, and inexpensive modality available to achieve optimal outcomes for people with osteoarthritis.”(483)

Available research addressing exercise for knee OA consists of mostly low- to moderate-quality trials with few high-quality studies. In these recommendations, the entire body of exercise-related articles has been included, program.(279, 513-519) since several studies have included both inflammatory conditions,(501, 520-540) as well as osteoarthritis. Most studies have combined different exercises into programs that at least partially obscure effects of a specific exercise prescription (e.g., flexibility versus aerobic versus strengthening). However, some patterns do appear. While specific to knee or hip osteoarthritis, these recommendations also appear to apply to rheumatoid arthritis patients as well,(520, 541-543) as materially different results were not found in that population (see exercise evidence table and Hip and Groin Disorders guideline).

#### *Aerobic Exercise for Treatment of Knee Osteoarthritis*

**Aerobic exercise is strongly recommended for the treatment of knee osteoarthritis.**

*Indications* – All patients with knee osteoarthritis. However, those with significant cardiac disease or significant potential for cardiovascular disease should be evaluated prior to instituting vigorous exercises (follow *ACSM Guidelines for Exercise Testing and Prescription*, 7th ed.).(544)

*Frequency/Dose/Duration* – Dose is somewhat unclear. A self-directed program is recommended for all patients. Supervised programs may be particularly indicated for those who require supervision to initiate a program or otherwise need assistance with motivation or concomitant fear avoidant belief training. Supervision may be for a few appointments to help initiate the program. The highest quality trial prescribed walking 40 minutes per session, 3 times a week.(508, 545-547) Another common regimen is walking at least 4 times a week at 60% of predicted maximum heart rate (220 - age = maximum heart rate). Both regimens are comparable and either is recommended.(548, 549) Nearly all patients should be encouraged to continue aerobic exercises on a long-term basis for fitness purposes, including maintaining lower extremity muscle strength.

*Indications for Discontinuation* – Intolerance (rarely occurs), development of other disorders.

*Strength of Evidence* – **Strongly Recommended, Evidence (A)**

#### *Stretching Exercises for Treatment of Knee Osteoarthritis*

**Stretching exercises are recommended for select patients with knee osteoarthritis who have significant reductions in range of motion that are not thought to be fixed deficits.**

*Indications* – Patients with significant reductions in range of motion that are thought to be non-fixed deficits (e.g., limitations based on stiffness or disuse rather than osteophytes).

*Frequency/Duration* – Generally taught as home exercises over 1 to 3 appointments.

*Indications for Discontinuation* – Worsening of symptoms, identification that the deficits are fixed, or achievement of exercise program goals.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

#### *Strengthening Exercises for Treatment of Knee Osteoarthritis*

**Strengthening exercises are moderately recommended for treatment of knee osteoarthritis.**

*Indications* – Knee osteoarthritis.

*Frequency/Duration* – Home program at least 2 to 3 times a week. Supervised treatment frequency and duration is dependent on symptom severity and acuity and the presence of comorbid conditions. There is moderate-quality evidence that isometric exercises are least successful.(550) May be added with aerobic exercises to an exercise program. In limited circumstances where range-of-motion deficits are considerable, but thought to not be fixed, strengthening is sometimes added after beginning flexibility

exercises. One moderate-quality trial suggests strengthening exercises are more effective for neutrally aligned knees.(551)

*Indications for Discontinuation* – Development of a strain or failure to improve.

*Strength of Evidence* – **Moderately Recommended, Evidence (B)**

*Educational Sessions for Treatment of Knee Osteoarthritis*

**Educational sessions are recommended to help facilitate treatment of knee osteoarthritis.**

*Indications* – Knee osteoarthritis.

*Frequency/Duration* – One to 3 sessions over 6 weeks, primarily to facilitate an active exercise program and compliance. Content is suggested to be focused on active exercises rather than passive interventions or disease pathophysiology as this may be helpful, particularly in addition to an active exercise program when compliance is challenging or periodic encouragement and facilitation to overcome incapacity in patients with severe osteoarthritis.

*Indications for Discontinuation* – Noncompliance, failure to improve.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Rationale for Recommendations*

There are multiple RCTs addressing hip knee and/or hip osteoarthritis patients. Studies compare exercise to non-exercise controls,(476, 494-496, 508, 545-547, 552-566) exercise to exercise,(567-574) and exercise to other treatments(575-579) (see Exercise evidence table). As there is not a strong rationale for believing that there are major differences in efficacy for hip versus knee OA (see Hip and Groin Disorders guideline),(563) and analysis of the available evidence fails to suggest major differences, this summary assumes the outcomes are similar in both sets of patients. Most of the studies considered here combined different exercises. Some exercise programs were unstructured and some studies did not clearly describe the interventions. These limitations preclude drawing strong evidence-based conclusions regarding any single intervention. Yet, there are quality studies comparing exercise to non-exercise controls (580) that allow evidence-based conclusions to be made on the relative value of aerobic, stretching, and strengthening exercises. There also is experimental evidence that the glycosaminoglycan content in the post-meniscectomized knee is superior if exercised.

A high-quality trial of knee osteoarthritis suggests that while both aerobic and resistance training are helpful, aerobic exercises are modestly superior to resistance training and far superior to education.(508, 545-547) A moderate-quality trial using a comparable exercise regimen also suggests that walking is beneficial.(548) These studies support the idea that weight bearing is beneficial,(581) raise questions about which specific exercises are most beneficial, and suggest that aerobic exercise may be superior for knee osteoarthritis patients.

All quality studies which included a major component of documented compliance with increased aerobic exercise found benefits of aerobic exercise.(548, 560, 565) Strengthening exercise results appear similar. There is not clear superiority of aerobic or strengthening exercises or vice versa. The available quality evidence suggests aerobic and strengthening exercises are superior to flexibility or range-of-motion exercises.(476, 548) Some, but not all data, suggest increased exercise intensity results in superior outcomes. Some, but not all studies that have assessed inflammatory markers and joint scores among those with OA or RA have found reductions in erythrocyte sedimentation rates and lower joint scores among those exercising. Pool-based programs have been evaluated and evidence of superiority of water-based programs is lacking (see Aquatic Therapy). A Cochrane review of exercise for knee OA found platinum (highest) level evidence of modest beneficial effects on knee pain and disability, but

unclear evidence on the rate of disease progression.(582) A second Cochrane review found equal efficacy for both high- and low-intensity exercise.(583)

Problems with compliance and persistence with exercise programs after discharge are considerable. Evidence is mixed regarding whether supervised exercise programs are necessary or whether home-based programs are sufficient. Providers need to encourage ongoing compliance with these programs. Exercise programs are not invasive, have low adverse effects, and are low to moderate cost depending on numbers of supervised appointments. Programs emphasizing aerobic and strengthening exercises are recommended, as is stretching for those with considerable reductions in range of motion that do not appear fixed.

Educational programs are largely ineffective compared to exercise or other active treatments.(508, 545-547, 584) Trials have sometimes employed educational programs as a sham or control treatment. However, a few educational visits to emphasize need for exercise and to tailor exercise and other activities are recommended in concert with an exercise prescription, as educational interventions have low adverse effects and are not costly. There is moderate quality evidence a combination of exercise and weight loss is effective for osteoarthritis, providing additional rationale for educational interventions targeted at weight loss.(24, 585, 586)

#### *Evidence for the Use of Exercise for Knee Osteoarthritis and Rheumatoid Arthritis*

There are 5 high- and 78 moderate-quality RCTs incorporated into this analysis. There are 21 low-quality RCTs(504, 507, 511, 512, 516, 587-602) (one with two reports(603, 604)) in Appendix 1.

### **Aquatic Therapy (Hydrotherapy)**

Aquatic therapy involves the performance of aerobic and/or flexibility and/or strengthening exercises in a pool to minimize the effects of gravity, particularly where reduced weight-bearing status is believed to be desirable.(548, 605-607) However, as per the above review of exercise, there is quality evidence that weight-bearing exercise is beneficial for treatment of knee osteoarthritis.

#### *Aquatic Therapy for Knee Osteoarthritis*

**A trial of aquatic therapy is recommended for patients with knee osteoarthritis who meet the referral criteria for supervised exercise therapy, have co-morbidities (e.g., extreme obesity, significant degenerative joint disease, etc.) that preclude effective participation in a weight-bearing physical activity, and are planned to transition either to a land-based program or a self-administered water-based program.**

*Frequency/Duration* – Begin with 3 to 4 visits a week. Functional improvement should be documented within the first 2 weeks to justify additional visits. The program should include up to 4 weeks of aquatic therapy with progression towards a land-based, self-directed physical activity or self-directed aquatic therapy program by 6 weeks. For some patients with knee osteoarthritis, aquatic exercise may be the preferred method. In these cases, the program should become self managed. If any membership to a pool is covered, coverage should be continued if it can be documented that the patient is using the facility at least 3 times a week and following the prescribed exercise program.

*Indications for Discontinuation* – Non-tolerance, failure to progress, or reaching conclusion of program at 4 to 6 weeks.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Rationale for Recommendation*

Aerobic exercise is beneficial for treatment of knee osteoarthritis compared to no program(605); however, evidence of superiority to land-based programs is lacking.(548, 606-608) Instead, the quality literature appears to document comparable efficacy between land and water-based exercise programs.(548, 606, 607) These water programs are performed in lukewarm rather than higher temperature settings to allow for aerobic exercise to be performed. Spa water has been found to be no different than tap water.(609) There may be a select minority of patients in whom it is thought to be advantageous to reduce the effects of gravity. As noted previously, other forms of exercise have been shown to be effective in the treatment of knee OA, but for a few select patients who are unable to tolerate those land-based therapies, aquatic therapy is moderate costly, not invasive, and has little potential for adverse effects.

#### *Evidence for the Use of Aquatic Therapy for Knee Osteoarthritis*

There is 1 high-(605) and 7 moderate-quality(548, 557, 606-610) RCTs incorporated into this analysis.

## **Yoga**

Yoga has been used successfully for treatment of low back pain patients(611-613) (see Low Back Disorders guideline).

#### *Yoga for Chronic Knee Pain*

**There is no recommendation for or against the use of yoga for treatment of chronic knee pain.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

#### *Rationale for Recommendation*

There are no quality studies of yoga for treatment of these patients. Yoga may be appropriate for highly motivated patients; however, compliance is an issue.

## **Ergonomic Interventions**

The physician may recommend ergonomic redesign of the workplace to facilitate recovery and prevent recurrence of knee disorders.(330) Ergonomic evaluations of the workplace can be conducted on-site by a qualified professional such as an ergonomist, occupational or physical therapist, or other health safety specialist. There are no quality studies regarding ergonomic interventions to prevent knee conditions, nor are there quality studies regarding return to work and secondary prevention. Thus, suggested changes to the work environment are empiric. Knee protection for kneeling activities is recommended. Falls result in considerable knee morbidity (including fractures), and fall protection equipment has resulted in far fewer fatalities in industry over the past few decades.(331)

#### *Knee Pads for Kneeling Activities*

**Knee pads are recommended for activities which require kneeling.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

#### *Fall Protection*

**Measures to prevent falls are recommended.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

#### *Ergonomic Interventions for Knee MSDs*

**There is no recommendation for or against the use ergonomic interventions for knee MSDs.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Rationale for Recommendations*

Ergonomic interventions for spine and upper extremity disorders have been attempted in numerous occupational settings,(332) and RCTs of ergonomic interventions in these settings have been reported. However, there are no quality studies of ergonomic interventions for the lower extremity. In the upper extremity, some interventions that had been thought to be beneficial were found to be unhelpful. Thus, without quality evidence, there is no recommendation for or against ergonomic interventions for knee MSDs. Although there is no quality evidence for fall protection in preventing knee disorders, falls from heights continue to cause morbidity and deaths, and fall protection is therefore recommended.

## **Medications**

### **Non-steroidal Anti-inflammatory Drugs (NSAIDs) and Acetaminophen (Including Cytoprotection)**

NSAIDs are widely used for treatment of osteoarthritis (OA) and have been considered efficacious. However, the duration of follow-up in most studies does not exceed 6 weeks.(614-616) Most quality studies have included both knee and hip OA patients; however, outcomes in these two patient populations are similar.

Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit prostaglandin synthesis, impairing inflammation. There are several classes of NSAIDs: 1) salicylates – aspirin, diflunisal, salicyl salicylate (salsalate); 2) arylalkanoic acids – diclofenac, etodolac, ketorolac, nabumetone, sulindac, tolmetin; 3) 2-arylpropionic acids – ibuprofen, fenoprofen, ketoprofen, naproxen; 4) n-arylanthranilic acids – mefenamic acid; 5) oxicams – piroxicam, meloxicam; 6) COX-2 inhibitors – celecoxib, rofecoxib, etoricoxib; and 7) sulphonanilides – nimesulide. Acetaminophen is considered an analgesic and not an anti-inflammatory agent. Acetaminophen blocks the activation of COX by another enzyme, peroxidase. Tissues with high levels of peroxidase (i.e., platelets and immune cells) are “resistant” to acetaminophen, but tissues with low levels of peroxidase (i.e., nerve and endothelial cells that participate in pain and fever) are “sensitive” to acetaminophen.(617) There have been recent suggestions that NSAIDs may reduce cartilage synthesis.(618) However, there also are many articles documenting reductions in inflammatory mediators,(619-625) thus raising the possibility that NSAIDs delay cartilage destruction.

There are two isoenzymes of cyclooxygenase, COX-1 and Cox-2. NSAIDs are COX (non)selective to different degrees. COX-2 selective agents were designed to reduce inflammation without increasing risks for gastrointestinal (GI) bleeding. It appears that certain COX-2 selective agents may increase the risk of cardiovascular events (see Hip and Groin Disorders guideline for more information).

#### *NSAIDs for Treatment of Acute, Subacute, Chronic, or Post-operative Knee Pain*

**NSAIDs are recommended for treatment of acute, subacute, chronic, or post-operative knee pain.**

There is no consistent quality evidence that one NSAID is superior to another, thus there is **No Recommendation, Insufficient Evidence (I)**, nor is there consistent quality evidence for superiority of one dosage form(626) or enteric-coated or sustained release preparations.(627-630) Due to their inhibitory effects on platelet function, non-selective COX inhibitors should be used with caution, or avoided altogether, in the post-operative period if patients are also receiving pharmacoprophylaxis (e.g., warfarin, low molecular weight heparins) to prevent venous thromboembolic disease. Concomitant use of non-selective COX inhibitors and anti-coagulation regimens may increase the risk of hemorrhage. There is also concern that COX inhibitors, particularly COX-2 inhibitors, may inhibit bone healing. Therefore, these agents should be used with caution, or avoided altogether, in the acute post-operative

period in situations where bone healing is required, such as in fracture repair or in knee replacements where cementless components are utilized.

Acetaminophen (or the analog, paracetamol) may be a reasonable alternative for treatment of acute, subacute, chronic or post-operative knee pain,(631, 632) although quality evidence suggests that acetaminophen is less efficacious than NSAIDs.(633-639) At least two quality trials of acetaminophen compared to placebo have been negative, including one with a large sample size of 779 patients.(637, 640) Of note, a recent FDA advisory committee recommended reduction of the maximum dose of acetaminophen to 650mg, which is less than the 1gm dose used in most quality trials. Consequently, the degree of successful treatment of osteoarthritis with lower doses of acetaminophen is somewhat unclear. There is evidence that NSAIDs are as effective for pain relief as tramadol(641, 642) and dextropropoxyphene, although slightly less efficacious than codeine.(643, 644)

*Indications* – Acute, subacute, chronic, or post-operative knee pain. OTC agents may suffice and be tried first.

*Frequency/Duration* – Per manufacturer’s recommendations; essentially all NSAIDs have proven efficacious for this indication. As-needed use may be reasonable for many patients. However, nearly all trials used scheduled doses.(645) There is evidence that nocturnal dosing is superior if patient primarily has morning or nocturnal pain,(646) although this may only apply to agents with shorter half-lives, including indomethacin.(647)

*Indications for Discontinuation* – Resolution of knee pain, lack of efficacy, or development of adverse effects that necessitate discontinuation.

*Strength of Evidence* – **Strongly Recommended, Evidence (A)** – Chronic knee pain(231, 631, 637, 648-660)

**Recommended, Evidence (C)** – Acute flares(648, 661, 662)

**Recommended, Insufficient Evidence (I)** – Acute, subacute, post-operative knee pain(663)

#### *NSAIDs for Patients at Risk for GI Adverse Effects*

**Concomitant prescriptions of cytoprotective medications are recommended for patients at substantially increased risk for gastrointestinal (GI) bleeding.** There are four commonly used cytoprotective classes of drugs: misoprostol, sucralfate, histamine Type 2 receptor blockers (famotidine, ranitidine, cimetidine, etc.), and proton pump inhibitors (esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole). It is generally thought that there is no significant difference in efficacy between these classes for the prevention of GI bleeding.(664) However, evidence suggests that histamine-2 blockers are less effective for protection of the gastric mucosa and sucralfate is weaker than proton pump inhibitors. There also are combination products of NSAIDs/misoprostol that have documented reductions in the risk of endoscopic lesions.

*Indications* – Patients with high GI risk factor profiles who also have indications for NSAIDs, cytoprotective medications should be considered, particularly if longer term treatment is planned. At-risk patients include those with a history of prior GI bleeding, elderly patients, diabetics, and cigarette smokers. Providers are cautioned that H2 blockers might not protect from gastric ulcers.(665-667)

*Frequency/Dose/Duration* – Proton pump inhibitors, misoprostol, sucralfate, and H2 blockers recommended. Dose and frequency as recommended by manufacturer for duration of NSAID therapy or permanently for those with recurrent bleeds or other complications.

*Indications for Discontinuation* – Intolerance, development of adverse effects, or discontinuation of NSAID.

*Strength of Evidence – Strongly Recommended, Evidence (A)* – Proton pump inhibitors,  
misoprostol

**Moderately Recommended, Evidence (B)** – Sucralfate  
**Recommended, Evidence (C)** – H2 blockers

*NSAIDs for Patients at Risk for Cardiovascular Adverse Effects*

**Patients with known cardiovascular disease or multiple risk factors for cardiovascular disease should be counseled about the risks and benefits of NSAID therapy.**(668)

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

**Acetaminophen or aspirin should be considered as the first-line therapy for these patients with cardiovascular disease risk factors.**

*Strength of Evidence – Strongly Recommended, Evidence (A)*

If needed, NSAIDs that are non-selective are preferred over COX-2 specific drugs. In patients receiving low-dose aspirin for primary or secondary cardiovascular disease prevention, NSAID should be taken at least 30 minutes after or 8 hours before the daily aspirin to minimize the potential for the NSAID to counteract the beneficial effects of aspirin.(669)

*Acetaminophen for Treatment of Acute, Subacute, Chronic or Post-operative Knee Pain*

**Acetaminophen is recommended for treatment of acute, subacute, chronic or post-operative knee pain, particularly for those with contraindications for NSAIDs.**

*Indications* – All patients with knee pain, including acute, subacute, chronic and post-operative.

*Dose/Frequency* – Per manufacturer’s recommendations; may be utilized on an as needed basis. It has been suggested that 1gm doses are more effective than 650mg doses, particularly in post-operative patients.(670, 671) However, this dose is now above the maximum dose recommended by an FDA advisory committee of 650mg, as evidence of hepatic toxicity has been reported at 4gms per day, particularly among those consuming excessive alcohol. There is no quality evidence for superiority of 1gm dosing for treatment of osteoarthritis.

*Discontinuation* – Resolution of pain, adverse effects or intolerance.

*Strength of Evidence – Recommended, Evidence (C)*

*Rationale for Recommendations*

There is abundant quality evidence that NSAIDs improve pain and function among chronic knee pain patients, particularly those with osteoarthritis or rheumatoid arthritis. There are a few studies of NSAID use for osteoarthritis flares that consistently document benefits. There are no quality studies of NSAID use for acute, subacute or post-operative knee pain. However, by analogy to other MSDs including LBP (see Low Back Disorders guideline), successful treatment of knee pain with NSAIDs may be reasonably anticipated. Results are similar for non-selective or COX-2 (selective) NSAIDs, although the magnitude of benefit is generally not large for any given medication. There are many quality trials comparing various NSAIDs,(68, 631, 638, 639, 648, 654, 658, 659, 661, 672-722) and there is no consistent quality evidence suggesting superiority of one over another or of one class over another class. Most studies have not found cyclooxygenase-2 selective medications to be superior to other NSAIDs for pain control.(614, 615, 723) However, there is quality evidence that COX-2 selective NSAIDs reduce the risk of gastrointestinal adverse effects.(614, 615, 723) In terms of the timing of NSAID dosing, there is one quality study suggesting that evening dosing of indomethacin resulted in better pain control.(646) There is no similar result with the longer-acting agent celecoxib.(647) There is quality evidence that NSAIDs are less

impairing than opioids, yet efficacy is comparable (see Chronic Pain and Low Back Disorders guidelines). For most patients, generic ibuprofen, naproxen or other older generation NSAIDs are generally recommended as first-line medications. Second-line medications should generally include other generic medications.

There are several quality studies of acetaminophen and a few of paracetamol, a close analog.(724) All trials that compared acetaminophen with NSAIDs found either that NSAID significantly reduced pain more than acetaminophen or that differences were not statistically significant but favored NSAIDs.(633, 634, 636-639, 724-726) There is superior symptom relief at 2 hours with ibuprofen compared to paracetamol. These findings are consistent with quality evidence for the treatment of low back pain (see Low Back Disorders guideline). Subanalyses have suggested that NSAIDs are particularly more efficacious for those with more severe osteoarthritis. However, evidence also indicates higher rates of gastrointestinal adverse effects among NSAID users and lower overall adverse effects profiles for acetaminophen.

A systematic review and meta-analysis of observational studies of NSAIDs found that the risk for serious cardiovascular events was elevated in combined analyses for some NSAIDs, but not for others.(727) Many of the studies supporting these estimates were based on large pharmaceutical databases that were adequately powered to detect effects, but had limited ability to control for potential confounding. There is one reported study of NSAIDs and myocardial infarctions that controlled for two major confounders – aspirin and body mass index.(728) Summary estimates from that study for non-selective NSAIDs suggested that they are protective against cardiovascular events. Study weaknesses included a 50% participation rate and reliance on recall. However, the American Heart Association has cautioned against the use of NSAIDs, especially COX-2 inhibitors.(669) Thus, current evidence is unclear if there is increased risk, no risk, or reduced risk of cardiovascular events from the use of any NSAIDs other than rofecoxib, which appears to have a modestly elevated relative risk.(727) It is recommended that risks of NSAIDs be discussed with patients, particularly patients with cardiovascular risk factors.

Risks of gastrointestinal events should be assessed, including prior history of gastrointestinal bleeding and source, length of treatment, age, smoking, diabetes mellitus, and other medical factors. Treatment with either acetaminophen, NSAIDs plus misoprostol, proton pump inhibitors (see below) or a COX-2 selective agent should be considered in those at high risk for gastrointestinal complications.(231, 614, 615, 650, 683, 723, 729-733)

Gastrointestinal adverse events are generally considered the most significant of the risks of NSAIDs. A large volume of high and moderate quality evidence has consistently shown that proton pump inhibitors are effective for prevention and or treatment of gastric and duodenal ulcers and erosions.(734-748) Different proton pump inhibitors are probably equally effective. There is one quality head-to-head trial, and it found no difference in efficacy between pantoprazole and omeprazole.(735) Misoprostol has also been consistently shown to be effective compared with placebo.(749-759) Relatively fewer studies have shown sucralfate to be effective compared with placebo.(760) H2 blockers appear more effective for treatment of duodenal than gastric mucosa.(665-667) There are relatively few quality trials comparing efficacy of the different classes of agents. Pantoprazole but not lansoprazole has been reported to be modestly superior to misoprostol.(761, 762) No difference was found between famotidine and lansoprazole.(763) Misoprostol has been reported superior to placebo(764) and ranitidine,(765, 766) cimetidine(756) and sucralfate.(755, 767) In short, while the evidence is not definitive, available quality evidence suggests proton pump inhibitors and misoprostol appear superior to H-2 blockers and sucralfate. While COX-2 selective agents have generally been recommended as either third- or fourth-line medications for routine use in osteoarthritis patients, they are often preferred when there is a risk

of gastrointestinal complications. For patients at high risk of gastrointestinal bleeding, there is evidence that a combination of proton pump inhibitor plus COX-2 selective agent is efficacious.(768) There is consistent quality evidence that NSAIDs prevent heterotopic bone formation in post-arthroplasty patients.(769-773) but there is no quality evidence that prophylactic treatment with NSAIDs results in improved functional outcomes.(769)

NSAIDs are not invasive, have low side effect profiles in a healthy working patient population, and are low cost when generic medications are used. The potential for NSAIDs to increase the risk of cardiovascular events needs to be carefully considered

#### *Evidence for the Use of NSAIDs and Acetaminophen*

There are 26 high and 114 moderate-quality RCTs and randomized crossover trials incorporated in this analysis. *Note: Trials are aggregated within these categories to provide some structure. However, while many of these could be listed in multiple categories, they are listed only once to conserve space.*

### **OPIOIDS – Oral, Transdermal, and Parenteral (Includes Tramadol)**

Opioids are addressed in a separate guideline. The treatment recommendations are summarized below. (See Opioids guideline for all supporting evidence.)

#### **Acute Pain (Up to 4 Weeks)**

##### *Routine Use of Opioids for Treatment of Non-Severe Acute Pain*

**Routine opioid use is strongly not recommended for treatment of non-severe acute pain (e.g., low back pain [LBP], sprains, or minor injury without signs of tissue damage).**

*Harms* – May inadequately treat acute, severe pain.

*Benefits* – Faster recovery, less debility, reduced accidents risks, risks of dependency or addiction.

*Strength of Evidence* – **Strongly Not Recommended, Evidence (A)**

*Level of Confidence* – High

##### *Opioids for Treatment of Acute, Severe Pain*

**Opioids are recommended for treatment of acute, severe pain (e.g., crush injuries, large burns, severe fractures, injury with significant tissue damage) uncontrolled by other agents and/or with functional deficits caused by pain. A brief course of opioids may also be indicated at the initial visit for anticipated pain accompanying severe injuries (i.e., failure of other treatment is not mandatory). A Schedule IV<sup>iv</sup> opioid may be indicated if there is a true allergy to NSAIDs and acetaminophen, other contraindication to an alternative medication, or insufficient pain relief with an alternative. Recommend to taper off opioid use in 1 to 2 weeks.**

*Indications* – Patients should meet all of the following:

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<sup>iv</sup>USA classifies controlled substances that includes a classification system, ranging from Class 1 to Class V corresponding to lower risks of abuse and dependence. Class I includes substances with a high potential for abuse and without a recognized medical use (e.g., heroin, marijuana, LSD). Class II includes most opiates, amphetamines and cocaine. Class III includes buprenorphine, dihydrocodeine, hydrocodone/codeine when compounded with an NSAID, Marinol. Class IV includes tramadol (in some states), carisoprodol, benzodiazepines, and long-acting barbiturates. Class V includes small amounts of codeine (e.g., 30mg, 60mg).

Severe injury with a clear rationale for use (objective functional limitations due to pain resulting from the medical problem, e.g., extensive trauma such as forearm crush injury, large burns, severe radiculopathy).<sup>v</sup>

Other more efficacious treatments should have been instituted,<sup>vi</sup> and either:

- a) failed and/or
  - b) have reasonable expectations of the immediate need for an opioid to obtain sleep the evening after the injury.
- 1) Where available, prescription databases (usually referred to as a Prescription Drug Monitoring Program [PDMP]) should be checked and not show evidence for conflicting opioid prescriptions from other providers or evidence of misreporting.<sup>vii</sup>
  - 2) Non-opioid prescriptions (e.g., NSAIDs, acetaminophen) absent contraindication(s) should nearly always be the primary treatment and accompany an opioid prescription.
  - 3) Low-dose opioids may be needed in the elderly who have greater susceptibility to the adverse risks of opioids. Those of lower body weight may also require lower opioid doses.
  - 4) Dispensing quantities should be only what is needed to treat the pain. Short-acting opioids are recommended for treatment of acute pain. Long-acting opioids are not recommended.
  - 5) Due to greater than 10-fold elevated risks of adverse effects and death, considerable caution is warranted among those using other sedating medications and substances including: i) benzodiazepines; ii) anti-histamines (H<sub>1</sub>-blockers); and/or iii) illicit substances.(774-777) Patients should not receive opioids if they use illicit substances unless there is objective evidence of significant trauma or moderate to severe injuries. Considerable caution is also warranted among those who are unemployed as the reported risks of death are also greater than 10-fold.(774, 775) Due to elevated risk of death and adverse effects, caution is also warranted when considering prescribing an opioid for patients with any of the following characteristics: depression, anxiety, personality disorder, untreated sleep disorders, substance abuse history, current alcohol use or current tobacco use, attention deficit hyperactivity disorder (ADHD), post-traumatic stress disorder (PTSD), suicidal risk, impulse control problems, thought disorders, psychotropic medication use, chronic obstructive pulmonary disease (COPD), asthma, or recurrent pneumonia.(774, 778-798) Considerable caution is also warranted among those with other comorbidities such as chronic hepatitis and/or cirrhosis,(799) as well as coronary artery disease, dysrhythmias, cerebrovascular disease, orthostatic hypotension, asthma, recurrent pneumonia, thermoregulatory problems, advanced age (especially with mentation issues, fall risk, debility), osteopenia, osteoporosis, water retention, renal failure, severe obesity, testosterone deficiency, erectile dysfunction, abdominal pain, gastroparesis, constipation, prostatic hypertrophy, oligomenorrhea, pregnancy, human immunodeficiency virus (HIV), ineffective birth control, herpes, allodynia, dementia, cognitive dysfunction and impairment, gait problems, tremor, concentration problems, insomnia, coordination problems, and slow reaction time. There are considerable drug-drug interactions that have been reported (see Appendices 2-3 of Opioids guideline).

*Frequency/Duration* – Generally, opioids should be prescribed at night or while not working.(800) Lowest effective, short-acting opioid doses are preferable as they tend to have the better safety profiles, less risk of escalation,(801) less risk of lost time from work,(802) and faster return to work.(803) Short-

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<sup>v</sup>Other indications beyond the scope of this guideline include acute myocardial infarction or agitation interfering with acute trauma management.

<sup>vi</sup>Treatments to have tried generally include NSAIDs and acetaminophen. For LBP patients, additional considerations include muscle relaxants, progressive aerobic exercise, and directional exercise.

<sup>vii</sup>Exceptions such as acute, severe trauma should be documented.

acting opioids are recommended for treatment of acute pain and long-acting opioids are not recommended. Recommend opioid use as required by pain, rather than in regularly scheduled dosing.

If parenteral administration is required, ketorolac has demonstrated superior efficacy compared with opioids for acute severe pain,(804, 805) although ketorolac’s risk profile may limit use for some patients. Parenteral opioid administration outside of obvious acute trauma or surgical emergency conditions is almost never required, and requests for such treatment are clinically viewed as red flags for potential substance abuse.

*Indications for Discontinuation* – Resolution of pain, sufficient improvement in pain, intolerance or adverse effects, non-compliance, surreptitious medication use, consumption of medications or substances advised to not take concomitantly (e.g., sedating medications, alcohol, benzodiazepines), or use beyond 2 weeks.

*Harms* – Adverse effects are many (see section below on “Opioids Benefits and Harms”).

*Benefits* – Improved short-term pain control.

*Strength of Evidence* – **Recommended, Evidence (C)**

*Level of Confidence* – High

#### *Screening Patients Prior to Initiation of Opioids*

**Initial screening of patients is recommended with more detailed screening for: i) requiring continuation of opioids beyond 2 weeks for those with an acute severe injury; and ii) at consideration of initiation for severe pain but no objective evidence.** Screening should include history(ies) of depression, anxiety, personality disorder, other psychiatric disorder, substance abuse, sedating medication use (e.g., anti-histamine/anti-H<sub>1</sub> blocker(774)), benzodiazepine use, opioid dependence, alcohol abuse, current tobacco use, other substance use history, COPD, PTSD, other psychotropic medications, (severe) obesity, cognitive impairment, balance problems/fall risk, osteoporosis, and renal failure (see Appendix 1 of Opioids guideline). Those who screen positive, especially to multiple criteria, are recommended to: i) undergo greater scrutiny for appropriateness of opioids (may include psychological evaluation); ii) consideration of consultation and examination(s) for complicating conditions and/or appropriateness of opioids, and iii) if opioids are prescribed, more frequent assessments for compliance, achievement of functional gains,(775, 806, 807) adverse effects, and symptoms and signs of aberrancy.

*Harms* – Negligible. If a consultation is needed, there are additional costs that are incurred.

*Benefits* – Improved identification of more appropriate candidates for opioids. Identification of patients at increased risk of adverse effects. In cases where someone has elevated, but potentially acceptable risk, may alert the provider to improve surveillance for complications and aberrant behaviors.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Level of Confidence* – High

#### *Opioid Dose Limits in Acute Pain*

**Dispense only that which is required. The maximum daily oral dose recommended for opioid-naïve, acute pain patients based on risk of overdose/death is 50mg morphine equivalent dose (MED)<sup>viii</sup>(808).** In rare cases with documented functional improvement (see Appendix 1 of Opioids guideline), higher doses may be considered, however, risks are substantially higher and greater monitoring is also recommended (see Subacute/Chronic Opioid recommendations below). Lower doses should be used for

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<sup>viii</sup>Statistical significance present for acute and chronic pain at and above 50 mg per day of oral morphine equivalent dose.

patients at higher risk of dependency, addiction and other adverse effects. Monitoring is also recommended and consultation may be considered for those patients on higher doses.

*Harms* – Theoretical potential to undertreat pain in some patients with increased pain sensitivity.

*Benefits* – Reduced risk for adverse physical and cognitive effects, dependency, addiction and opioid-related overdoses and deaths.

*Strength of Evidence* – **Recommended, Evidence (C)**

*Level of Confidence* – Moderate

### **Post-Operative Pain Up to 4 Weeks (After 4 weeks, see Subacute Pain)**

Oral opioids are commonly prescribed after sinus surgery,(809) major noncardiac surgical procedures,(810) mastectomy and immediate breast reconstruction (IBR),(811, 812) coronary artery bypass graft surgery,(813) major abdominal surgery (abdominal laparoscopic, abdominal hysterectomy, bowel resection or radical hysterectomy),(814-817) orthopedic surgery,(818) and molar extraction.(819)

*Limited Use of Opioids for Post-operative Pain*

**Limited use of opioids is recommended for post-operative pain management as an adjunctive therapy to more effective treatments.**

*Indications* – For post-operative pain management, a brief prescription of short-acting opioids as an adjunct to more efficacious treatments (especially Cox-2 NSAIDs such as celecoxib, non-selective NSAIDs after risk of bleeding is no longer a concern).<sup>ix</sup> A brief course of opioids is often needed for minor surgical procedures. However, minor wound laceration repairs often require no opioids. Evidence suggests perioperative pregabalin for 14 days and/or continuous femoral nerve catheter analgesia instead of solely using oral opioids results in superior knee arthroplasty functional outcomes with less venous thromboses.(820) Additional considerations include:

- 1) Non-opioid prescriptions (e.g., NSAIDs, acetaminophen) should nearly always be the primary treatment and accompany an opioid prescription. Computerized programs may also assist in optimal management.(821)
- 2) The lowest effective dose of a short-acting opioid should be used,(801) as well as weaker opioids if possible.(802, 803)
- 3) Short-acting opioids are recommended for treatment of acute pain.
- 4) Dispensing should be only what is needed to treat the pain.<sup>x</sup>
- 5) Long-acting opioids are not recommended.
- 6) Low-dose opioids may be needed in the elderly who have greater susceptibility to the adverse risks of opioids. Those of lower body weight may also require lower opioid doses.
- 7) Where available, prescription databases (usually referred to as Prescription Drug Monitoring Program (PDMP)) should be checked for other opioid prescriptions. Due to greater than 10-fold elevated risks of adverse effects and death, considerable caution is warranted among those using other sedating medications and substances including: i) benzodiazepines; ii) anti-histamines (H<sub>1</sub>-blockers); and/or iii) illicit substances.(774-777) Patients should not receive opioids if they use illicit substances unless there is objective evidence of significant trauma or

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<sup>ix</sup>More efficacious treatments also include therapeutic exercises, e.g., progressive ambulation especially for moderate to extensive procedures (e.g., arthroplasty, fusion).

<sup>x</sup>Generally, this should be sufficient to cover two weeks of treatment. Prescriptions of 90-day supplies in the post-operative setting are not recommended.

moderate to severe injuries. Considerable caution is also warranted among those who are unemployed as the reported risks of death are also greater than 10-fold.(774, 775)

Due to elevated risk of death and adverse effects, caution is also warranted when considering prescribing an opioid for patients with any of the following characteristics: depression, anxiety, personality disorder, ADHD, PTSD, suicidal risk, impulse control problems, thought disorders, psychotropic medication use, substance abuse history, current alcohol use or current tobacco use, untreated sleep disorders, COPD, asthma, or recurrent pneumonia.(774, 778-798, 822) Considerable caution is also warranted among those with other comorbidities such as chronic hepatitis and/or cirrhosis,(799) as well as coronary artery disease, dysrhythmias, cerebrovascular disease, orthostatic hypotension, thermoregulatory problems, advanced age (especially with mentation issues, fall risk, debility), osteopenia, osteoporosis, water retention, renal failure, severe obesity, testosterone deficiency, erectile dysfunction, abdominal pain, gastroparesis, constipation, prostatic hypertrophy, oligomenorrhea, pregnancy, HIV, ineffective birth control, herpes, allodynia, dementia, cognitive dysfunction and impairment, gait problems, tremor, concentration problems, insomnia, coordination problems, and slow reaction time. There are considerable drug-drug interactions that have been reported (see Appendices 2-3 of Opioids guideline). Inpatient management may moderate these recommendations provided there is careful monitoring, although these same management issues then apply post-discharge.

- 8) For patients taking opioids chronically prior to surgery, consultations with anesthesiology and/or pain management are generally needed as post-operative dosing may be very high and management is often challenging.
- 9) Ongoing prescriptions of opioids after the immediate post-operative period should generally be for patients who have undergone a major surgery or have other condition(s) necessitating opioids. Most patients should be making progress towards functional restoration, pain reduction and weaning off the opioids. Patients who have not progressed should be carefully evaluated for physical complications or psychiatric comorbidity, adherence to active treatments, and pending development of addiction or dependency.

*Frequency/Duration* – For moderate and major surgeries, opioids are generally needed on a scheduled basis in the immediate post-operative period. Other post-operative situations may be sufficiently managed with an as needed opioid prescription schedule. Provision of opioids sufficient to participate in therapeutic exercise (e.g., progressive ambulation) and allow sleep may be needed. However, high dose use at night is not recommended due to respiratory depression and disruption of sleep architecture. Weaning should begin as soon as function is recovering and pain is subsiding. Subsequent weaning to as needed opioid use is recommended.

*Indications for Discontinuation* – The physician should discontinue the use of opioids based on sufficient recovery, expected resolution of pain, lack of efficacy, intolerance or adverse effects, non-compliance, surreptitious medication use, self-escalation of dose, or use beyond 3-5 days for minor procedures, and 2-3 weeks for moderate/less extensive procedures. Use for up to 3 months may occasionally be necessary during recovery from more extensive surgical procedures (e.g., spine fusion surgery). However, with rare exceptions, only nocturnal use is recommended in months 2-3 plus institution of management as discussed in the subacute/chronic guidelines below. For those requiring opioid use beyond 1 month, subacute/chronic opioid use recommendations below apply.

*Harms* – Adverse effects are many (see section on “Opioids Benefits and Harms”).

*Benefits* – Improved short-term, post-operative pain control. Some studies suggest this may modestly improve functional outcomes in the post-operative population.

*Strength of Evidence* – **Recommended, Evidence (C)**

*Level of Confidence – High*

*Screening Patients Prior to Continuation of Opioids*

**Screening of patients is recommended for those requiring continuation of opioids beyond the second post-operative week.** Screening should include history(ies) of: depression, anxiety, personality disorder, pain disorder, other psychiatric disorder, substance abuse history, sedating medication use (e.g., anti-histamine/anti-H<sub>1</sub> blocker), benzodiazepine use, opioid dependence, alcohol abuse, current tobacco use, and other substance use history, COPD, PTSD, other psychotropic medications, (severe) obesity, cognitive impairment, balance problems/fall risk, osteoporosis, and renal failure (see Appendix 1 of Opioids guideline). Those who screen positive, especially to multiple criteria, are recommended to: i) undergo greater scrutiny for appropriateness of opioids (e.g., may include psychological and/or pain evaluation); ii) compliance with active therapies (e.g., ambulation and other exercise after arthroplasty); iii) consider consultation examination(s) for complicating conditions and/or appropriateness of opioids; and iv) if ongoing opioids are prescribed, ensure more frequent assessments for treatment compliance, achievement of functional gains, (775, 806, 807) and symptoms and signs of aberrancy.

*Harms – Negligible.* If a consultation is needed, there are additional costs that are incurred.

*Benefits –* Identification of patients at increased risk of adverse effects. Improved identification of more appropriate and safe candidates for opioids compared with attempting post-operative pain control with non-opioids. This should reduce adverse effects. In cases where someone has elevated, but potentially acceptable risk, this may alert the provider to improve surveillance for complications and aberrant behaviors.

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

*Level of Confidence – High*

*Opioid Dose Limits in Post-operative Pain*

**The maximum daily oral dose recommended for opioid-naïve, acute pain patients based on risk of overdose/death is 50mg morphine equivalent dose (MED)<sup>xi</sup>(808).** Post-operative patients particularly require individualization due to factors such as the severity of the operative procedure, response to treatment(s) and variability in response. Higher doses beyond 50mg MED may be particularly needed for major surgeries in the first 2 post-operative weeks to achieve sufficient pain relief; however, greater caution and monitoring are warranted and reductions below 50mg MED at the earliest opportunity should be sought. Lower doses should be used for patients at higher risk of dependency, addiction and other adverse effects. In rare cases with documented functional improvement, ongoing use of higher doses may be considered, however, risks are substantially higher and greater monitoring is also recommended (see Subacute/Chronic Opioid recommendations below).

*Harms –* Theoretical potential to undertreat pain, which could modestly delay functional recovery.

*Benefits –* Reduced risk for adverse effects, dependency, addiction and opioid-related deaths.

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

*Level of Confidence – Low*

**Subacute (1-3 Months) and Chronic Pain (>3 Months)**

*Routine Use of Opioids for Subacute and Chronic Non-malignant Pain*

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<sup>xi</sup>Statistical significance present for acute and chronic pain at and above 50 mg per day of morphine equivalent dose.

**Opioid use is moderately not recommended for treatment of subacute and chronic non-malignant pain. Opioid prescription should be patient specific and limited to cases in which other treatments are insufficient and criteria for opioid use are met (see below).**

*Harms* – May inadequately treat severe subacute or chronic pain.

*Benefits* – Less debility, fewer adverse effects, reduced accident risks, lower risks of dependency, addiction, overdoses, and deaths.

*Strength of Evidence* – **Moderately Not Recommended, Evidence (B)**

*Level of Confidence* – High

*Opioids for Treatment of Subacute or Chronic Severe Pain*

**The use of an opioid trial is recommended if other evidence-based approaches for functional restorative pain therapy have been used with inadequate improvement in function.(823, 824) Opioids are then recommended for treatment of function impaired by subacute or chronic severe pain (e.g., inability to work due to any of the following: chronic severe radiculopathy, chronic severe peripheral neuropathies, complex regional pain syndrome (CRPS), and severe arthroses)(806) (see Appendix 1 of Opioids guideline).**

*Indications* – Patients should meet all of the following:

- 1) Reduced function is attributable to the pain. Pain or pain scales alone are insufficient reasons.(775, 806, 825-836)
- 2) A severe disorder warranting potential opioid treatment is present [e.g., CRPS, severe radiculopathy, advanced degenerative joint disease (DJD)].(827)
- 3) Other more efficacious treatments have been documented to have failed.(827) Other approaches that should have been first utilized include physical restorative approaches, behavioral interventions, self-applied modalities, non-opioid medications (including NSAIDs, acetaminophen, topical agents, norepinephrine adrenergic reuptake blocking antidepressants or dual reuptake inhibitors; also antiepileptic medications particularly for neuropathic pain) and functional restoration. For LBP patients, this also includes<sup>xii</sup> fear avoidant belief training and ongoing progressive aerobic exercise, and strengthening exercises. For CRPS patients, this includes progressive strengthening exercise. For DJD, this includes NSAIDs, weight loss, aerobic and strengthening exercises.
- 4) An ongoing active exercise program is prescribed and complied with.
- 5) Non-opioid prescriptions (e.g., NSAIDs, acetaminophen) absent a contraindication should nearly always be the primary pain medication and accompany an opioid prescription. Other medications to consider include topical agents, norepinephrine adrenergic reuptake blocking antidepressants or dual reuptake inhibitors; also antiepileptic medications particularly for neuropathic pain).
- 6) The lowest effective dose should be used.(801) Weaker opioids should be used whenever possible.(802, 803) Meperidine is not recommended for chronic pain due to bioaccumulation and adverse effects.
- 7) Low-dose opioids may be needed in the elderly who have greater susceptibility to the adverse risks of opioids. Those of lower body weight may also require lower opioid doses.
- 8) Dispensing should be only what is needed to treat the pain.<sup>xiii</sup>

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<sup>xii</sup>A previous trial of a muscle relaxant is generally recommended. However, if an opioid trial is contemplated, cessation of all depressant medications including muscle relaxants is advisable.

<sup>xiii</sup>Generally, this should be sufficient to cover one week of treatment at a time during the trial phase. If a trial is successful at improving function, prescriptions for up to 90-day supplies are recommended.

- 9) Extended-release/long-acting opioids are recommended to be used on a scheduled basis, rather than as needed.(827) As needed opioids should generally be avoided for treatment of chronic pain, although limited use for an acute painful event (e.g., fracture, sprain) is reasonable. Sublingual fentanyl is not recommended for treatment of subacute or chronic pain. Caution is warranted with fentanyl patches due to unpredictable absorption.
- 10) Where available, prescription databases (usually referred to as a Prescription Drug Monitoring Program [PDMP]) should be checked for conflicting opioid prescriptions from other providers or evidence of misreporting.
- 11) Due to greater than 10-fold elevated risks of adverse effects and death, considerable caution is warranted among those using other sedating medications and substances including: i) benzodiazepines; ii) anti-histamines (H<sub>1</sub>-blockers); and/or iii) illicit substances.(774-777) Patients should not receive opioids if they use illicit substances unless there is objective evidence of significant trauma or moderate to severe injuries. Considerable caution is also warranted among those who are unemployed as the reported risks of death are also greater than 10-fold.(774, 775)

Due to elevated risk of death and adverse effects, caution is also warranted when considering prescribing an opioid for patients with any of the following characteristics: depression, anxiety, personality disorder, untreated sleep disorders, substance abuse history, current alcohol use or current tobacco use, ADHD, PTSD, suicidal risk, impulse control problems, thought disorders, psychotropic medication use, COPD, asthma, recurrent pneumonia.(774, 778-798, 822) Considerable caution is also warranted among those with other comorbidities such as chronic hepatitis and/or cirrhosis,(799) as well as coronary artery disease, dysrhythmias, cerebrovascular disease, orthostatic hypotension, asthma, recurrent pneumonia, thermoregulatory problems, advanced age (especially with mentation issues, fall risk, debility), osteopenia, osteoporosis, water retention, renal failure, severe obesity, testosterone deficiency, erectile dysfunction, abdominal pain, gastroparesis, constipation, prostatic hypertrophy, oligomenorrhea, pregnancy, HIV, ineffective birth control, herpes, allodynia, dementia, cognitive dysfunction and impairment, gait problems, tremor, concentration problems, insomnia, coordination problems, and slow reaction time. There are considerable drug-drug interactions that have been reported (see Appendices 2-3 of Opioids guideline).

*Frequency/Duration* – Opioids use is generally initiated as a “trial” to ascertain whether the selected opioid produces functional improvement (see Appendix 1 of Opioids guideline). Opioid use is generally prescribed on a regular basis,(837) at night or when not at work.(800) Only one opioid is recommended to be prescribed in a trial. More than one opioid should rarely be used. Lower opioid doses are preferable as they tend to have the better safety profiles, less risk of dose escalation,(801) less work loss,(802) and faster return to work.(803) Patients should have ongoing visits to monitor efficacy, adverse effects, compliance and surreptitious medication use. Opioid prescriptions should be shorter rather than longer duration.(838)

*Indications for Discontinuation* – Opioids should be discontinued based on lack of functional benefit(824) (see Appendix 1), resolution of pain, improvement to the point of not requiring opioids, intolerance or adverse effects, non-compliance, surreptitious medication use, medication misuse (including self-escalation and sharing medication), aberrant drug screening results, diversion, consumption of medications or substances advised to not take concomitantly (e.g., sedating medications, alcohol, benzodiazepines).

*Harms* – Adverse effects are many (see section on “Opioids Benefits and Harms”). May initiate path to opioid dependency.

*Benefits* – Improved short-term pain ratings. Theoretical potential to improve short-term function impaired by a painful condition.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Level of Confidence* – Low

#### *Screening Patients Prior to Initiation of Opioids*

**Screening of patients is recommended prior to consideration of initiating a trial of opioids for treatment of subacute or chronic pain.** Screening should include history(ies) of depression, anxiety, personality disorder and personality profile,(803, 839, 840) other psychiatric disorder, substance abuse history, sedating medication use (e.g., anti-histamine/anti-H<sub>1</sub> blocker),(781) benzodiazepine use, opioid dependence, alcohol abuse, current tobacco use, and other substance use history, COPD, PTSD, other psychotropic medications, (severe) obesity, cognitive impairment, balance problems/fall risk, osteoporosis, and renal failure (see Appendix 1 of Opioids guideline). Those who screen positive, especially to multiple criteria, are recommended to: i) undergo greater scrutiny for appropriateness of opioids (may include psychological and/or psychiatric evaluation(s) to help assure opioids are not being used instead of appropriate mental health care); ii) consideration of consultation and examination(s) for complicating conditions and/or appropriateness of opioids; and iii) if opioids are prescribed, more frequent assessments for compliance, achievement of functional gains and symptoms and signs of aberrant use.

*Harms* – Negligible. If a consultation is needed, there are additional costs that are incurred.

*Benefits* – Identification of patients at increased risk of adverse effects. Improved identification of more appropriate and safe candidates for treatment with opioids. This should reduce adverse effects. In cases where someone has elevated, but potentially acceptable risk, this may alert the provider to improve surveillance for complications and aberrant behaviors.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Level of Confidence* – High

#### *Opioid Dose Limits in Subacute and Chronic Pain*

**The maximum daily oral dose recommended for subacute or chronic pain patients based on risk of overdose/death is 50mg Morphine Equivalent Dose (MED).**(782, 808) In rare cases with documented functional improvements occurring with use above 50mg MED, subsequent doses up to 100mg may be considered, however, risks of death are much greater and more intensive monitoring is then also recommended. Lower doses should be considered in high risk patients. Caution appears warranted in all patients as there is evidence the risk of dose escalation is present even among patients enrolled in a “hold the line (stable dose) prescribing strategy” treatment arm.(841)

For those whose daily consumption is more than 50mg MED, greater monitoring is recommended to include: i) at least monthly to not more than quarterly appointments with greater frequencies during trial, dose adjustments and with greater co-morbid risk factors and conditions; ii) at least semiannual attempts to wean below 50mg MED if not off the opioid; iii) at least semiannual documentation of persistence of functional benefit; iv) at least quarterly urine drug screening (see drug screening section); and v) at least semiannual review of medications, particularly to assure no sedating medication use (e.g., benzodiazepine, sedating anti-histamines).

*Harms* – None in a short-term trial. For chronic pain patients, theoretical potential to undertreat pain and thus impair function. However, there is no quality literature currently available to support that position.

*Benefits* – Reduced risk for adverse effects, dependency, addiction, and opioid-related deaths.

*Strength of Evidence – Recommended, Evidence (C)*

*Level of Confidence – High*

*Use of an Opioid Treatment Agreement (Opioid Contract, Doctor/Patient Agreement, Informed Consent)*

**The use of an opioid treatment agreement (opioid contract, doctor/patient agreement, or informed consent) is recommended to document patient understanding, acknowledgement of potential adverse effects, and agreement with the expectations of opioid use (see Appendix 1 of Opioids guideline). (823, 842-853) If consent is obtained, it is recommended that appropriate family members be involved in this agreement.**

*Harms – Negligible.*

*Benefits –* Educates the patient and significant others that these medications are high risk, with numerous adverse effects. It allows for a more informed choice. It provides a framework for initiation of a trial, monitoring, treatment goals, compliance requirement, treatment expectations, and conditions for opioid cessation. It should reduce risk of adverse events and opioid-related deaths, although that remains unproven to date.

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

*Level of Confidence – Moderate*

*Urine Drug Screening*

**Baseline and random urine drug screening, qualitative and quantitative, is recommended for patients prescribed opioids for the treatment of subacute or chronic pain to evaluate presence or absence of the drug, its metabolites, and other substance(s) use. In certain situations, other screenings (e.g., hair particularly for information regarding remote use(854-859) or blood (for acute toxicity) may be appropriate.**

*Indications –* All patients on opioids for subacute or chronic pain.

*Frequency –* Screening is recommended at baseline, randomly at least twice and up to 4 times a year and at termination. More intensive screening is recommended for those consuming more than 50mg MED (see above). Federal guidelines recommend at least 8 tests a year among those utilizing opioid treatment programs.(860) Screening should also be performed “for cause” (e.g., provider suspicion of substance misuse including over-sedating, drug intoxication, motor vehicle crash, other accidents and injuries, driving while intoxicated, premature prescription renewals, self-directed dose changes, lost or stolen prescriptions, using more than one provider for prescriptions, non-pain use of medication, using alcohol for pain treatment or excessive alcohol use, missed appointments, hoarding of medications, and selling medications). Standard urine drug/toxicology screening processes should be followed (consult a qualified medical review officer).(861-863) If there is an aberrant drug screen result (either positive for unexpected drugs or unexpected metabolites or unexpectedly negative results), there should be a careful evaluation of whether there is a plausible explanation (e.g., drug not tested, drug metabolite not tested, laboratory cutpoint and dosing interval would not capture the drug/metabolite, laboratory error). In the absence of a plausible explanation, those patients with aberrant test results should have the opioid discontinued or weaned.(824)

*Harms –* No adverse clinical effects if properly interpreted.

*Benefits –* Identifies aberrant medication(s) and substance(s) use. Such uses are high-risk for opioid events including fatalities (see tables below). It provides objective evidence to cease an opioid trial or ongoing treatment. Identifies patients who may be diverting medication (those screening negative for prescribed medication).

*Strength of Evidence – Recommended, Evidence (C)*  
*Level of Confidence – High*

#### *Evidence for Use of Opioids*

There are 2 high-(864, 865) and 21 moderate-quality(642, 866-885) RCTs incorporated in this analysis (see Opioids guidelines for additional evidence).

### **SKELETAL MUSCLE RELAXANTS**

Skeletal muscle relaxants comprise a diverse set of pharmaceuticals designed to produce muscle relaxation through different mechanisms of action, including central nervous system (CNS) mechanisms.(886, 887) These medications are widely used in primary care to treat painful conditions, including LBP,(888-894) muscle spasms,(895) and myalgias. They are generally not used for treatment of knee disorders.

#### *Muscle Relaxants for Acute and Subacute Knee Pain with Significant Muscle Spasm*

**There is no recommendation for or against the use of muscle relaxants for treatment of acute or subacute, moderate to severe knee pain from muscle spasm that is unrelieved by NSAIDs, avoidance of exacerbating exposures, or other conservative measures (generally not indicated for chronic knee pain).**

*Indications* – Moderate to severe chronic pain syndromes and radicular pain syndromes thought to be musculoskeletal in nature.

*Frequency/Dose* – Initial dose in evening (not during workdays or if patient operates a motor vehicle, though daytime use is acceptable if CNS-sedating effects are minimal). Duration for exacerbations of chronic pain is limited to a couple weeks. Longer term treatment is generally not indicated.

*Indications for Discontinuation* – Resolution of pain, non-tolerance, significant sedating effects that carry over into the daytime, other adverse effects.

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

#### *Rationale for Recommendation*

There are no quality studies of these agents for treatment of patients with knee pain. Skeletal muscle relaxants have been evaluated in quality studies evaluating acute LBP and also chronic back and neck pain(896-899) (see Chronic Pain and Low Back Disorders guidelines). The quality of the studies comparing these agents to placebo is limited due to probable unblinding from adverse effects. The adverse effect profile is concerning,(900) with CNS sedation rates ranging from approximately 25 to 50% and a low but definite risk of abuse.(901, 902) Thus, prescriptions for skeletal muscle relaxants for daytime use should be carefully weighed against the need to drive vehicles, operate machinery, or otherwise engage in occupations where mistakes in judgment may have serious consequences (e.g., crane operators, air traffic controllers, operators of motorized vehicles, construction workers, etc.). Skeletal muscle relaxants have beneficial uses, particularly for nocturnal administration to normalize sleep patterns disrupted by skeletal muscle pain, as well as for daytime use among the few patients who do not suffer from the CNS depressant effects. They are low cost if generic medications are prescribed. Skeletal muscle relaxants are not recommended for continuous management of subacute or chronic knee pain, although they may be reasonable options for selected patients with acute pain exacerbations or for a limited trial as a third- or fourth-line agent in more severely affected patients in whom NSAIDs and exercise have failed to control symptoms.

### *Evidence for the Use of Skeletal Muscle Relaxants*

There are no quality studies evaluating the use of skeletal muscle relaxants for treatment of patients with knee pain.

## **ANTI-DEPRESSANTS**

Antidepressants have been used for treatment of chronic pain disorders.

### *Norepinephrine Reuptake Inhibiting Anti-depressants for Knee Osteoarthritis or Subacute or Chronic Knee Pain*

**There is no recommendation for or against the use of norepinephrine reuptake inhibiting anti-depressants for treatment of knee osteoarthritis, subacute or chronic knee pain (see Chronic Pain guideline).**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Norepinephrine Reuptake Inhibiting Anti-depressants for Acute Knee Pain*

**Norepinephrine reuptake inhibiting anti-depressants are not recommended for treatment of acute knee pain.**

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

### *Selective Serotonin Reuptake Inhibitors for Acute, Subacute, or Chronic Knee Pain*

**Selective serotonin reuptake inhibitors (SSRIs) are not recommended for treatment of acute, subacute, or chronic knee pain as there is strong evidence of their lack of efficacy in treating chronic low back pain, thus they appear unlikely to be successful in treating acute, subacute, or chronic knee pain.**

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

### *Selective Serotonin Reuptake Inhibitors, SSRIs, or Tricyclic Anti-depressants for Chronic Knee Pain in Patients with Co-morbid Depression*

**Selective serotonin reuptake inhibitors (SSNRIs), SSRI, and/or tricyclic anti-depressants are recommended for patients with chronic knee pain and co-morbid depression.**

*Indications* – Patients with diagnosed depression of at least moderate severity and with chronic pain, in conjunction with a behavioral program focusing on function with chronic pain.(903)

*Duration* – Therapy for up to 12 months.(903)

*Indications for Discontinuation* – No response to medication after 3 months; adverse effects or unwillingness or incapable of participating in behavioral therapy program.

*Strength of Evidence – Recommended, Evidence (C)*

### *Rationale for Recommendations*

Norepinephrine reuptake inhibiting anti-depressants (e.g., amitriptyline, doxepin, imipramine, desipramine, nortriptyline, protriptyline, maprotiline, and clomipramine) and mixed norepinephrine and serotonin inhibitors (SNRIs) have evidence of efficacy for treatment of chronic low back pain and some other chronic pain conditions (see Low Back Disorders guideline). However, there is no quality, placebo-controlled evidence evaluating these medications for treatment of knee osteoarthritis or other knee pain. There also are no clear analogous disorders for which evidence-based guidance may be reliably derived. There is one moderate-quality study evaluating SNRI, SSRI and tricyclic antidepressants in patients with chronic low back, hip and knee pain. This study reported a significant improvement in depression severity and pain in patients taking antidepressant medications in conjunction with

education focused on how to function with chronic pain compared to usual care controls.(903) A moderate-quality study evaluated amitriptyline 50mg a day for 3 days post-operatively and reported no benefits for pain control.(904) Thus, there is not enough quality evidence of efficacy to warrant a recommendation.

#### *Evidence for the Use of Anti-depressants for Knee Pain and Osteoarthritis*

There is 1 high-quality RCT (with two reports) and 1 moderate-quality RCT incorporated into this analysis.

### **ANTI-CONVULSANT AGENTS (including Gabapentin and Pregabalin)**

Anti-convulsant agents have been utilized off-label for some chronic pain syndromes since the 1960s.(905) They have been particularly used for treating neuropathic pain.(906) Anti-convulsants are thought to have analgesic properties. Several have been used to manage chronic pain conditions include carbamazepine, valproic acid, gabapentin, phenytoin, clonazepam, lamotrigine, tiagabine, pregabalin, topiramate, levetiracetam, oxcarbazepine, and zonisamide.

#### *Topiramate for Knee Osteoarthritis or Subacute or Chronic Knee Pain*

**There is no recommendation for or against the use of topiramate for treatment of knee osteoarthritis or other subacute or chronic knee pain** (see Chronic Pain guideline).

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

#### *Topiramate for Acute Knee Pain*

**Topiramate is not recommended for treatment of acute knee pain.**

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

#### *Gabapentin for Knee Osteoarthritis or Subacute or Chronic Knee Pain*

**There is no recommendation for or against the use of gabapentin for treatment of knee osteoarthritis or subacute or chronic knee pain** (see Chronic Pain guideline).

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

#### *Gabapentin for Acute Knee Pain*

**Gabapentin is not recommended for the treatment of acute knee pain.**

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

#### *Gabapentin for Peri-Operative Pain*

**Gabapentin is recommended for the peri-operative management of pain to reduce the need for opioids, particularly in those with adverse effects from opioids.**

*Indications* – Peri-operative pain management.

*Frequency/Dose* – Limit to immediate peri-operative period, usually a few days.

*Indications for Discontinuation* – Resolution, intolerance.

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

#### *Rationale for Recommendations*

There are no quality studies involving knee pain patients, and quality evidence suggests that topiramate is weakly effective for treatment of low back pain patients and gabapentin is not helpful. However, there is quality evidence that gabapentin reduces the need for opioids when administered as part of

perioperative pain management for other patients, thus by inference, gabapentin is recommended for knee surgery patients.(907-910)

#### *Evidence for the Use of Anti-convulsant Agents*

There are no quality studies evaluating the use of topiramate or gabapentin for knee osteoarthritis or other knee pain. There are 4 high-quality RCTs incorporated in this analysis for peri-operative pain that are described in the Chronic Pain guideline. (907-910)

### **TUMOR NECROSIS FACTOR-ALPHA BLOCKERS**

A variety of tumor necrosis factor (TNF) alpha blockers, including infliximab (a chimeric monoclonal antibody directed against TNF-alpha), etanercept (a recombinant molecule comprising part of the TNF receptor plus the constant region of human immunoglobulin G1 that binds to TNF-alpha) and adalimumab (an IgG1 monoclonal antibody that binds to TNF-alpha) are in widespread use for rheumatologic and other inflammatory disorders. There may be indications for treatment of some patients with these agents in the setting of inflammatory rheumatologic disorders. However, this is beyond the scope of this guideline.

#### *Tumor Necrosis Factor-alpha Blockers for Osteoarthritis or Acute, Subacute, or Chronic Knee Pain or Other Non-inflammatory Knee Disorders*

**Tumor necrosis factor-alpha blockers are not recommended for the treatment of osteoarthritis or acute, subacute, or chronic knee pain, including other non-inflammatory knee disorders.**

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

#### *Tumor Necrosis Factor-alpha Blockers for Arthroplasty Patients with Osteolysis*

**Tumor necrosis factor-alpha blockers are not recommended for the treatment of arthroplasty patients with osteolysis.**

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

#### *Rationale for Recommendations*

One quality study has reported evaluating etanercept for attempted treatment of periacetabular osteolysis in arthroplasty patients, but found a lack of efficacy.(911)

#### *Evidence for the Use of Tumor Necrosis Factor-alpha Blockers for Knee Pain*

There is 1 moderate-quality RCT incorporated in this analysis.

### **Glucosamine, Chondroitin, and Methylsulfonylmethane (MSM)**

Glucosamine, chondroitin, and methylsulfonylmethane (MSM) are over-the-counter nutraceuticals(912) that have been advocated as safe and effective treatment alternatives to NSAIDs for the management of osteoarthritis. These supplements have also gained additional interest as agents that may potentially modify or slow the progression of osteoarthritis.

Glucosamine is an amino acid monosaccharide that occurs naturally in the human body, and is one of the principle substrates in the biosynthesis of cartilaginous glycosaminoglycans, proteoglycans, and hyaluronic acid.(913) Although the specific cause of osteoarthritis is unknown, turnover of the cartilage matrix is mediated by a multitude of complex autocrine and paracrine anabolic and catabolic factors, leading to loss of articular cartilage, subchondral bone remodeling, and low-level inflammation of the synovial membrane.(914) Glucosamine supplementation is hypothesized to beneficially affect the

imbalance between rates of synthesis and degradation of cartilage proteoglycans.(913, 915) Glucosamine reportedly has anti-inflammatory properties.(916, 917) Glucosamine preparations come in two forms, glucosamine sulfate (pill and crystalline powder) or glucosamine hydrochloride,(918, 919) and are often combined with chondroitin sulfate and sometimes combined with methylsulfonylmethane. Most studies have utilized glucosamine sulfate rather than glucosamine hydrochloride, although there are no quality comparative head-to-head trials. Glucosamine sulfate is also available in suspension for intramuscular and intra-articular injection.(920-922)

Glucosamine generally has few adverse effects with safety profiles comparable to placebo in the reviewed trials. However, there are two hypothetical risks that may suggest select patient groups to avoid these supplements. First, there is debate as to whether or not glucosamine, which is an aminoglycan, promotes insulin resistance.(923-925) However, no adverse effects have been found in patients who have well-controlled diabetes mellitus or even in persons with glucose intolerance.(926, 927) Second, glucosamine preparations are commonly produced from the shells of shrimp and crabs (chitin) – seaweed and shark cartilage has also been used,(928, 929) leading to concerns for potential allergic responses in persons with shellfish allergies. In a trial sponsored by the U.S. National Institutes of Health (NIH) of 15 patients with known systemic allergies to shrimp, administration of glucosamine sulfate was not found to result in any immediate hypersensitivity reactions.(930) Glucosamine products in the U.S. are now also commonly synthesized from grains, providing an alternate source for persons concerned with shellfish allergies. Therefore, these hypothetical risks appear to be low. The most common glucosamine dose is 1500mg per day in single or divided doses.

Chondroitin, a sulfated glycosaminoglycan matrix, provides structural elasticity. Chondroitin is thought to work via anti-inflammatory activity, stimulation of proteoglycans and hyaluronic acid synthesis, and decrease chondrocytic catabolic activity, although the exact mechanisms are unclear.(931) As with glucosamine, there are few reported adverse effects from chondroitin sulfate though some patients have GI tract effects.(932) This supplement is produced from animal cartilage such as bovine trachea, porcine and sharks. The most common dose is 1,200mg per day in single or divided dosages. Chondroitin is most commonly combined with glucosamine in commercial preparations, sometimes additionally including MSM.

#### *Glucosamine Sulfate, Chondroitin Sulfate, or Methylsulfonylmethane for Knee Osteoarthritis*

**There is no recommendation for or against the use of glucosamine sulfate 1,500mg daily (single or divided dose), chondroitin sulfate, or methylsulfonylmethane for the treatment of knee osteoarthritis.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

#### *Glucosamine Sulfate Intra-Muscular Injections for Knee Osteoarthritis*

**There is no recommendation for or against the use of glucosamine sulfate intra-muscular injections for the treatment of knee osteoarthritis.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Glucosamine Sulfate Intraarticular Injections for Knee Osteoarthritis*

**There is no recommendation for or against the use of glucosamine sulfate intraarticular injections for the treatment of knee osteoarthritis.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Glucosamine Sulfate, Chondroitin Sulfate, or Methylsulfonylmethane for Osteoarthritis Prevention*

**There is no recommendation for or against the use of glucosamine sulfate, chondroitin sulfate, or methylsulfonylmethane for prevention of osteoarthritis.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

*Level of Confidence – Low*

#### *Rationale for Recommendations*

There has been considerable debate over the efficacy of these preparations in reducing pain, improving function, and slowing the progression of the joint space narrowing in osteoarthritis. Ten quality studies have followed knee joint spaces using either MRI (2416-2418) or x-rays (933-938, 2419) to measure the joint space and one has objectively followed the hip joint (939). Six trials utilized glucosamine sulfate (936-939, 2417, 2418), four utilized chondroitin sulfate (933-935, 2416) and one used a combination (2419). One of the 3 MRI studies (33% of the studies) suggested *improvements* in the cartilage on MRI (2416), while the only sizable study of the 3 studies using MRI was negative (2417). Overall, six of the x-ray or MRI imaging studies (60% of the studies) demonstrated preservation of joint spaces compared with placebo, including multiple studies reporting either no or reduced joint space narrowing in the active treatment group over 2 years, (933, 934, 936, 937, 2419) and one reported increased cartilage volume over 2 years (2416). Thus, the studies that utilized x-rays or MRI generally suggested benefits from the treatment of knee osteoarthritis with either glucosamine sulfate or chondroitin sulfate; however, quality evidence of consistent, objective benefit utilizing x-rays of glucosamine or chondroitin for the treatment of OA is not unequivocally present. Most of the placebo-controlled studies of glucosamine and/or chondroitin report improvements in pain and/or function (506, 940-944, 933-935, 944-950). Few studies assessed MSM and some reported benefits (951, 952).

Studies compared these treatments with traditional NSAIDs (938, 945, 953-957) or acetaminophen (958, 959). Glucosamine hydrochloride, chondroitin sulfate and the combination were not superior to celecoxib 200mg per day or diclofenac 50mg TID (938, 945, 954, 2420); however, the combination was successful for treatment of moderate to severe osteoarthritis compared with placebo (945) and chondroitin sulfate had longer lasting pain relief compared to diclofenac (954). Three studies found glucosamine sulfate comparable to ibuprofen 1200mg per day (953, 955, 956). Acetaminophen was found to be inferior to glucosamine sulfate (958).

Glucosamine and chondroitin, alone or in combination, are not invasive, appear relatively safe, do not result in gastrointestinal erosions or the other common side effects of NSAIDs, are relatively inexpensive, and may provide some modest relief of knee osteoarthritis pain, particularly in patients with more advanced pain. A majority of the imaging studies suggest these medications may modify or slow the progression of knee OA as measured by slowing of cartilage destruction and joint narrowing.(938)

One major limitation of these studies is that different glucosamine formulations (hydrochloride versus sulfate), different frequencies and dosage strengths, and different durations and severities of disease of

the study populations are present in different studies.(960) The dose is not standardized and reportedly ranges widely in available preparations. There is some evidence that a single daily dose of chondroitin sulfate may be as or more effective than divided doses.(949). Thus, although there is evidence suggesting potential efficacy with 60% of the imaging-based studies reporting efficacy, and they have very low adverse effect profiles, the lack of standardized dosing prevents the formulation of an evidence-based recommendation in support of these agents. Involving the patient in a discussion for his/her personal decision-making regarding potentially self-administering these over-the-counter agents is advised.

#### *Evidence*

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: Knee Pain and Osteoarthritis controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 4 articles in PubMed, 42 in Scopus, 87 in CINAHL, 141 in Cochrane Library, 1280 in Google Scholar, and 38 from other sources. We considered for inclusion 3 from PubMed, 0 from Scopus, 9 from CINAHL, 9 from Cochrane Library, 0 from Google Scholar, and 38 from other sources. Of the 59 articles considered for inclusion, 52 randomized trials and 5 systematic reviews met the inclusion criteria.

## **COMPLEMENTARY/ALTERNATIVE TREATMENTS AND DIETARY SUPPLEMENTS**

Many treatments have been attempted to treat chronic pain conditions, including knee pain. Some of these interventions might be classified as dietary supplements or as complementary or alternative treatments.(962-965) These include homeopathic treatments, naturopathic treatments, vitamins, herbal remedies (certain exceptions discussed below), spiritual healing, touch for healing, craniosacral therapy, aromatherapy, energy healing, and neural therapy. Most of these do not have any quality evidence of efficacy. Some controversy surrounds the issue of the value of placebo effects in healing.(966) There are many interventions shown to be efficacious for the treatment of acute, subacute, and/or chronic pain and it is strongly recommended that patients be treated with therapies proven to be efficacious, whether the intervention is considered complementary.

*Complementary or Alternative Treatments, Dietary Supplements, Etc., for Acute, Subacute, or Chronic Knee Pain*

**Complementary and alternative treatments and dietary supplements, etc., are not recommended for treatment of acute, subacute, or chronic knee pain, as they have not been shown to produce meaningful benefits or improvements in functional outcomes.**

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

#### *Rationale for Recommendation*

As there is no evidence of their efficacy, complementary and alternative treatments including dietary supplements, etc., are not recommended.

*Evidence for the Use of Complementary or Alternative Treatments Dietary Supplements, Etc.*

There is 1 high-(967) and 4 moderate-quality(968-971) RCTs incorporated into this analysis. There are 2 low-quality RCTs in Appendix 1.(972, 973)

## HERBAL AND OTHER PREPARATIONS

Many complementary and alternative treatments, including herbal treatments, have been used to treat chronic knee pain, especially pain due to osteoarthritis.(974) Most of these treatments do not have any quality evidence of efficacy.(975) However, there are some remedies which may be efficacious in the management of acute LBP and osteoarthritis. White willow bark (*Salix*) extract has been studied in LBP. A principal ingredient is salicin, with salicylic acid as the principal metabolite. Daily doses of 240mg salicin, approximately equivalent to 50mg of acetylsalicylate (which was sufficiently low as to suggest that this may not be the sole reason for its analgesic effect), have been shown to be more effective than placebo in alleviating pain and improving physical impairment scores in patients with acute LBP, with gastrointestinal complaints occurring no more frequently than with placebo. Topical copper salicylates have also been used for treatment of arthrosis.(976, 977) Extract of *Harpagophytum procumbens* (devil's claw root) has been used in Europe to treat musculoskeletal symptoms, and there is some evidence that it may relieve acute LBP, acute episodes of chronic LBP, and osteoarthritis more effectively than placebo in doses that have consisted of the equivalent of 50 to 100mg of harpagoside daily. Mild gastrointestinal upset has been reported at higher doses. Other treatments include ginger extract(978-986) , rose hips,(987-996) s-adenosylmethionine,(997-1007) Camphora molmol, Maleluca alternifolia, Angelica sinensis, Aloe vera, Thymus officinalis, Menthe peperita, Arnica Montana,(1008) Curcuma longa, Tancaetum parthenium, avocado soybean unsaponifiables,(912, 1009-1019) oral enzymes,(1020-1025) and others.(1026-1029)

*Willow Bark (Salix), Ginger Extract, Rose Hips, Camphora Molmol, Maleluca Alternifolia, Angelica Sinensis, Aloe Vera, Thymus Officinalis, Menthe Peperita, Arnica Montana, Curcuma Longa, Tancaetum Parthenium, and Zingiber Officinicalis, Avocado Soybean Unsaponifiables, Oral Enzymes, Topical Copper Salicylate, S-Adenosylmethionine, and Diacerein Harpagoside for Acute, Subacute, or Chronic Knee Pain*  
**There is no recommendation for or against use of willow bark (Salix), ginger extract, rose hips, camphora molmol, maleluca alternifolia, angelica sinensis, aloe vera, thymus officinalis, menthe peperita, arnica montana, curcuma longa, tancaetum parthenium, and zingiber officinicalis, avocado soybean unsaponifiables, oral enzymes, topical copper salicylate, S-Adenosylmethionine, or diacerein harpagoside for treatment of acute, subacute, or chronic knee pain.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Rationale for Recommendation*

Most of these agents have no quality evidence available (e.g., Camphora molmol, Maleluca alternifolia, Angelica sinensis, Aloe vera, Thymus officinalis, Menthe peperita, Arnica Montana, Curcuma longa, Tancaetum parthenium, Harpagoside) for acute, subacute, or chronic knee pain. Some have conflicting results, e.g., willow bark (*Salix*),(1030, 1031) rose hips, avocado soybean unsaponifiables, and ginger extract. Still others have no quality studies comparing the active ingredient with placebo (e.g., S-Adenosylmethionine, harpagoside, oral enzymes), and one agent appears ineffective (copper salicylate).

None of these agents has had a standardized dose, resulting in a lack of clarity of patient dosing. All of the studies comparing the agent to a standard NSAID dose found the NSAID superior. Only those studies with lower doses of NSAIDs found evidence suggesting equivalency (see herbal and other preparations evidence table). These agents are not invasive, have unclear adverse effect profiles, and over time are moderate to highly costly. There is no recommendation for or against use of these agents.

### *Evidence for the Use of Herbal and Other Preparations*

There are 12 high- and 14 moderate-quality RCTs or crossover trials incorporated into this analysis. There are 4 low-quality RCTs in Appendix 1.(986, 993, 1025, 1032)

### **DIACEREIN (Diacerhein)**

Diacerein is an alternative pharmaceutical therapy developed for the treatment of osteoarthritis and purported to have inhibitory action on interleukin-1, metalloproteases and other inflammatory mediators involved in cartilage destruction in in vivo and animal models, including of inflammatory arthropathies.(1033-1041) It also stimulates prostaglandin E<sub>2</sub> synthesis without affecting phospholipase A<sub>2</sub>, cyclooxygenase (COX), or lipoxygenase, and thus does not affect the gastric mucosa.(1042) Diacerein has been used as a disease modifying agent in patients with moderately progressive joint narrowing.(1043-1046) It is available by prescription in only a few countries in Asia and Europe, and it is not currently available in the U.S. The adverse effect profile is generally significantly higher than placebo, mostly due to higher incidence of diarrhea(1034, 1047) and darkening of the urine, and the magnitude of its effects on pain are small.(1035) Diacerein is not widely available and may not be a treatment option for most patients. Optimal dose has been suggested to be 50mg twice daily.(1034) It may be an alternative to NSAIDs as a second- or third-line treatment, particularly for patients with a history of upper gastrointestinal bleeding, as it appears to be potentially associated with lower rates of gastric lesions.(1042) However, one quality study suggests NSAIDs are superior to diacerein for relief of pain.(1047) There are a few quality studies of diacerein in knee or combinations of hip and knee osteoarthritis patients in this analysis.(1034, 1048-1057)

### *Diacerein for Treatment of Osteoarthritis*

**There is no recommendation for or against the use of diacerein for the treatment of knee osteoarthritis.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Rationale for Recommendation*

Of the eight high- or moderate-quality studies evaluating diacerein, all five that compared it against placebo demonstrated modest pain relief from diacerein.(1034, 1043, 1048) A study to establish dose-response showed statistically significant improvement of symptoms with 50, 100, and 150mg daily dose, but with fewest side effects and best efficacy with the 100mg per day group.(1034) There is evidence suggesting that the effects of diacerein last weeks to months after cessation of therapy,(1047, 1048) which is not the case for NSAIDs.(1047) In addition to the symptomatic relief reported, there is one high-quality study of the hip that demonstrated a significant difference in joint space narrowing versus placebo.(1043) A 2x2 factorial study of the hip comparing diacerein, tenoxicam, diacerein with tenoxicam and placebo demonstrated early efficacy of tenoxicam. However, after 4 weeks, the diacerein plus placebo group also reached statistically significantly better symptomatic relief than placebo alone.(1047) There was no added synergistic effect; diacerein plus tenoxicam was no better or worse than each alone.

Examination of diacerein efficacy in two studies that used diacerein as one of the control arms rather than the main active research arm were not as conclusively in favor of diacerein. A comparison of diacerein to hyaluronic acid intra-articular injections over 1 year did not demonstrate diacerein to be more effective than an oral placebo, but the study had significant methodological weaknesses including a possible placebo effect of intra-articular injection masking the effect of oral diacerein treatment.(1058) Two studies comparing diacerein to Harpagophytum procumbens (Devil's Claw Root)

demonstrated both to be effective in improving pain and functional scores over baseline, but there was no placebo group for comparison.(1059, 1060)

#### *Evidence for the Use of Diacerein*

There are 6 high- and 4 moderate-quality RCTs or randomized crossover trials incorporated in this analysis.

## **Devices**

Some patients with knee pain might benefit from limited use of devices, particularly as an assistive aid while improved or full function is sought. These aids include crutches, walkers, canes, motorized scooters, heel wedges and insoles, and functional braces.(1061-1075) However, aids might also be detrimental, as they may discourage therapeutic physical activity. In general, a device is **Recommended, Insufficient Evidence (I)** when it is either part of a plan to regain better or normal function or it is essential to achieve the maximum function possible within the limits of fixed defects (see diagnostic sections for devices used for specific disorders).

## **BRACING/SLEEVES/LATERAL WEDGES**

Knee bracing has been used for some cases of knee osteoarthritis.(1076, 1077) Braces include unloader or off-loader braces designed to reduce force on one tibiofemoral compartment.(1078-1085) Most commonly, an “off-loader” brace has been utilized to attempt to reduce force on the medial compartment in cases of medial or largely medial joint OA. They also have been utilized to prevent sports injuries, especially in football athletes,(1086-1091) although there are concerns that the use of a brace leads to reduced performance.(1090) Knee sleeves and other appliances have also been utilized. Foot orthotics, most commonly lateral wedges, have been used to attempt to redirect force from the medial compartment to the lateral compartment in patients with primarily medial compartment disease.(1092-1094)

#### *Off-loader Braces for Knee Osteoarthritis*

**Off-loader braces are recommended for treatment of select patients with medial joint osteoarthritis.**

*Indications* – Patients should generally have attempted other non-operative treatments, including NSAIDs, analgesics, weight loss, exercise and glucocorticosteroid injections. Additionally, patients must be highly motivated to be compliant with the device.

*Strength of Evidence* – **Recommended, Evidence (C)**

#### *Knee Braces for Moderate to Severe Chronic Knee Osteoarthritis*

**Knee braces (e.g., unloader braces) are recommended for treatment of moderate to severe chronic knee pain due to osteoarthritis (medial or lateral joint OA) that is largely or totally unicompartmental.**

*Indications* – Moderate to severe chronic unicompartmental (e.g., medial) knee osteoarthritis, particularly if other treatments have failed and device is used in an attempt to delay surgical treatment.(1062, 1095, 1096) Patient must be motivated to comply with brace use.

*Strength of Evidence* – **Recommended, Evidence (C)**

#### *Knee Braces for All Other Osteoarthritis*

**There is no recommendation for or against the use of knee braces (e.g., unloader braces) for treatment of all other osteoarthritis including symmetrical OA.**

*Strength of Evidence* – **No Recommendation, Insufficient Evidence (I)**

*Sleeves for Knee Osteoarthritis*

**Sleeves are moderately not recommended for the treatment of knee osteoarthritis.**

*Strength of Evidence – Moderately Not Recommended, Evidence (B)*

*Neoprene Knee Sleeves for Moderate to Severe Chronic Knee Osteoarthritis*

**There is no recommendation for or against use of neoprene knee sleeves for treatment of knee osteoarthritis.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

*Lateral Wedges for Medial Compartment for Knee Osteoarthritis*

**Lateral wedges are moderately not recommended for treatment of medial compartment knee osteoarthritis.**

*Strength of Evidence – Moderately Not Recommended, Evidence (B)*

*Post-operative Braces for Knee Arthroplasty Patients*

**Post-operative knee braces are moderately not recommended for knee arthroplasty patients.**

*Strength of Evidence – Moderately Not Recommended, Evidence (B)*

*Rationale for Recommendations*

There are a few moderate-quality trials that have addressed bracing for unicompartmental osteoarthritis. Two trials comparing bracing with no bracing or usual care found bracing to be superior,(1095, 1096) while another trial comparing bracing with usual care and usual-care-only found bracing beneficial.(1062) One trial suggested bracing to be superior to neoprene sleeves.(1095) Another crossover trial suggested a valgus brace was superior to a simple hinged brace.(1097) Thus, there is moderate-quality evidence that unloader bracing is helpful in the short- to intermediate-term. There is no recommendation for or against the use of neoprene sleeves as there is moderate-quality evidence braces are superior(1095) and the evidence for neoprene sleeves compared to no treatment or another treatment is sparse. Thus, the evidence from moderate quality trials suggests these devices have modest benefits. They are not invasive and have low adverse effects, although compliance and ability to tolerate them are problematic. Thus, they are recommended for recommended for select patients with moderate to severe osteoarthritis that is either largely in the medial or lateral compartments. Patients must be willing to comply with treatment.

Knee sleeves have been evaluated in moderate quality trials and have not been found to produce clinically meaningful benefits.(1095, 1098, 1099) Thus, knee sleeves are not recommended. One trial attempted blinding of shoes with wedges and suggested no differences with lateral wedging.(1092) One trial compared lateral wedges to knee braces and found comparable results,(1094) while another trial was negative.(1093) Thus, the quality trials suggest a lack of efficacy.

Two moderate-quality trials both suggested a lack of benefit from post-arthroplasty bracing.(1100, 1101) Thus, post-operative bracing is not recommended.

*Evidence for the Use of Knee Braces, Sleeves and Lateral Wedges for Knee Osteoarthritis*

There are 12 moderate-quality RCTs or crossover trials incorporated into this analysis.

## **ORTHOSES (including wedged insoles)**

Orthoses have been used for treatment of knee osteoarthritis.(1063, 1067, 1070, 1092, 1102-1115)

*Orthoses for Moderate to Severe Chronic Knee Osteoarthritis*

**Orthoses (lateral wedges for medial joint disease) are moderately not recommended for treatment of moderate to severe chronic knee pain due to osteoarthritis.**

*Strength of Evidence – Moderately Not Recommended, Evidence (B)*

*Rationale for Recommendation*

There are eight moderate-quality trials of orthoses in osteoarthritis.(1092, 1093, 1114, 1116-1120) The highest quality trial was a randomized crossover trial that reported a lack of benefit from lateral wedging.(1116) The next highest quality studies included two reports and a 2-year follow-up report that found no meaningful benefit of orthoses.(1093, 1117) There are no trials comparing braces and orthoses. Lateral edge insoles and similar devices are not invasive, have few adverse effects, are low cost, but are not effective and thus are not recommended.

*Evidence for the Use of Orthoses for Osteoarthritis*

There are 8 moderate-quality RCTs or randomized crossover trials incorporated into this analysis. There are 6 low-quality RCTs in Appendix 1.

## **CANES AND CRUTCHES**

*Canes and Crutches for Moderate to Severe Acute, Subacute, or Chronic Knee Pain*

**Canes and crutches are recommended for treatment of moderate to severe acute knee pain or subacute and chronic knee pain when the device is used to advance the activity level.**

*Indications* – Moderate to severe acute knee pain or subacute or chronic knee pain, particularly when the device is utilized to increase activity level.

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

*Rationale for Recommendation*

Crutches and canes may be helpful for treating acute injuries during the recovery phase. They also may be helpful during the rehabilitative phase to increase functional status (e.g., from wheelchair to walker to cane). However, for chronic knee pain, crutches may paradoxically increase disability through debility. In those circumstances, institution or maintenance of advice for crutch or cane use should be carefully considered against potential risks.

*Evidence for the Use of Canes and Crutches*

There are no quality studies evaluating the use of canes and crutches for knee pain.

## **MOTORIZED SCOOTERS**

Motorized scooters have been used for treatment of severe knee arthrosis.(1121)

*Motorized Scooters for Severe Chronic Knee Osteoarthritis*

**Motorized scooters are recommended for highly select patients who have severe chronic knee pain due to osteoarthritis.**

*Indications* – Severe chronic knee osteoarthritis accompanied by major impairment in mobility that has either not responded well to arthroplasty and/or other significant impairments are present that

necessitate use of a motorized scooter. Patients should also have had inadequate response to multiple other treatments including at least 2 different NSAIDs, aerobic exercise, strengthening exercise, weight loss, and aquatic therapy program.

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

*Rationale for Recommendation*

There is one moderate-quality trial of intermittent motorized scooter use in knee osteoarthritis patients.(1121) The trial reported no meaningful increases in manual activity and long-term effects, including deconditioning, are unclear. Scooters are costly; thus, they are recommended for highly select use.

*Evidence for the Use of Motorized Scooters for Knee Osteoarthritis*

There is 1 moderate-quality RCT incorporated into this analysis.

## **MAGNETS AND MAGNETIC STIMULATION**

High intensity magnetic stimulation purportedly causes depolarization of nerves and has been found to result in an antinociceptive effect in rats.(1122) Electromagnetic fields have also been reported to increase osteoblastic activity.(1123) Therefore, proponents of magnet therapy believe that magnetic fields have value in the treatment of musculoskeletal disorders. Many studies of magnet therapy have been negative, although several studies have reported benefits.(1124, 1125) Magnets have been studied in rheumatoid arthritis,(1126) which is beyond the scope of this guideline.

*Magnets and Magnetic Stimulation for Osteoarthritis, Acute, Subacute and Chronic Knee Pain*

**There is no recommendation for or against the use of magnets and magnetic stimulation for treatment of osteoarthritis or acute, subacute and chronic knee pain.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

*Rationale for Recommendation*

There are quality sham-controlled trials that evaluate the use magnets for treatment of knee osteoarthritis. However, it cannot be assumed that subjects in these trials were successfully blinded.(1127-1131) One trial reported that most of the subjects accidentally or purposefully were unblinded to the intervention,(1127) and other trials did not report on the success of blinding. Therefore, the evidence base is limited. One trial that included a sham control (active magnets that were shielded from the skin) did not find meaningful outcomes at follow-up.(1127) While magnets are not invasive, have no adverse effects, and are relatively inexpensive, there is no quality evidence of their intermediate- or long-term efficacy and other treatments have proven efficacy; thus, there is no recommendation for or against their use.

*Evidence for the Use of Magnets and Magnetic Stimulation*

There is 1 high- and 4 moderate-quality RCTs incorporated into this analysis.

## Pulsed Electromagnetic Fields

High-intensity magnetic stimulation purportedly causes depolarization of nerves and has been found to result in an antinociceptive effect in rats.([1122](#), [1132](#)) Electromagnetic fields have been known to increase osteoblastic activity. Therefore, proponents believe that magnetic fields have therapeutic value in the treatment of musculoskeletal disorders.

*Pulsed Electromagnetic Fields for Osteoarthritis and Acute, Subacute, or Chronic Knee Pain*

**There is no recommendation regarding pulsed electromagnetic fields for the treatment of osteoarthritis or acute, subacute, or chronic knee pain.**

*Strength of Evidence- No Recommendation, Insufficient Evidence (I)*

*Level of Confidence – Low*

### *Rationale for Recommendation*

There are multiple trials of magnetic fields and the evidence substantially conflicts regarding efficacy.([1133-1139](#)) One trial for knee OA suggested benefits in VAS and WOMAC scores (2469). A moderate-quality study using PEMF after ACL reconstruction found significant recovery compared to placebo.([1140](#)) A moderate-quality study evaluated PEMF after arthroscopic surgery and reported improved recovery at 3 years and decreased NSAID use 45 days post-operatively.([1141](#)) These results require replication. Magnetic field treatments are not invasive, have no adverse effects, but as they are moderately costly and multiple studies suggest no benefit, there is no recommendation.

### *Evidence*

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: pulsed electromagnetic field; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 19 articles in PubMed, 268 in Scopus, 15 in CINAHL, 20 in Cochrane Library, 1,640 in Google Scholar, and 0 from other sources. We considered for inclusion 7 from PubMed, 2 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 9 from other sources. Of the 11 articles considered for inclusion, 16 randomized trials and 4 systematic reviews met the inclusion criteria.

## Physical Methods

### HOT AND COLD THERAPIES

It has been proposed that cold and heat have actual therapeutic benefits to modify the disease processes (e.g., cold to allegedly reduce acute inflammation and swelling and heat to speed healing through increased blood supply).(1142, 1143) However, it has been proposed that these various modalities are distractants that apparently do not materially alter the clinical course.(1144) Still, it is postulated that the distractants allow increased activity levels.(1145) Many patients with chronic pain report a temporary soothing effect from the application of heat or the use of ice packs in the home setting. Cryotherapies have also been utilized in peri- and post-operative patients to speed healing and attempt to reduce opioids requirements.(1146-1155)

## **Cryotherapies**

Cold or cryotherapies involve application of cold or cooling devices to the skin. They have been used for treatment of non-operative pain and post-operative pain.(1156)

*Home Use of Cryotherapies for Osteoarthritis or Acute, Subacute, or Chronic Knee Pain*

**Cryotherapies are recommended for home use if efficacious for the temporary relief of osteoarthritis or acute, subacute, or chronic knee pain.**

*Frequency/Duration* – Education regarding home cryotherapy application may be part of the treatment if cold is effective in reducing pain.

*Indications for Discontinuation* – Non-tolerance, including exacerbation of knee pain.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Cryotherapy for Treatment of Knee Arthroplasty and Arthroscopy and Other Surgery Patients*

**Cryotherapy is recommended for select treatment of knee arthroplasty and surgery patients.**

*Frequency/Duration* – Pain relief with cold therapy for the first several post-operative days with duration commensurate with extent of surgery. Some devices may be helpful for select patients, particularly if they are unable or unwilling to tolerate other measures to manage pain.

*Indications for Discontinuation* – Non-tolerance, adverse effects.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

### *Rationale for Recommendations*

There is one trial in non-operative patients, but it is difficult to develop evidence-based guidance as that trial is likely biased in favor of cryotherapy.(1157) While cryotherapy is generally not helpful in patients with osteoarthritis, a small minority may find benefit. Thus, cryotherapy is recommended as a potential distractant or counter-irritant and is recommended for self-application.

There are many post-operative studies, although few are moderate in quality with significant methodological limitations. The available studies confirm that there is no effect of cryotherapy on swelling. Nearly all studies also show that cryotherapy has no significant impact on blood loss. The available quality trials conflict with two suggesting no benefit (one compared cold therapy with lukewarm water(1146)) and one suggesting benefits, including opioid sparing (compared cold therapy with traditional post-operative regimens not including epidural anesthesia(1152)).

Self applications of cryotherapies using ice bags, towels or reusable devices are non-invasive, minimally costly, and without complications. Other forms of cryotherapy are moderately costly and may be reasonable for selected patients who are unwilling to undergo epidural anesthesia or have other indications for these devices.(1152)

### *Evidence for the Use of Cryotherapies*

There are 5 moderate-quality RCTs incorporated into this analysis. There are 7 low-quality RCTs in Appendix 1. requirements.(596, 1147-1149, 1151, 1154, 1158)

## Heat Therapies

Many forms of heat therapy have been used to treat musculoskeletal pain including hot packs, moist hot packs, sauna, warm baths, infrared, diathermy, and ultrasound. The depth of penetration of some heating agents is minimal since transmission is via conduction or convection, but other modalities have deeper penetration.(1159) A particular methodological problem with most studies of heat therapy is that, despite occasional attempts at, and claims of, successful blinding, it is impossible to blind the patient to these interventions, as they produce noticeable, perceptible tissue warming. Not surprisingly, some of these heat-related modalities have been shown to reduce pain ratings more than placebo for patients with low back pain. It is less clear whether there are meaningful, long-term benefits. Heat therapies are passive treatments. In chronic pain settings, use of heat should be minimized to self-treatments of flare-ups with primary emphasis on functional restoration elements (e.g., exercises).

*Self-application of Heat Therapy for Osteoarthritis or Acute, Subacute, or Chronic Knee Pain*

**Self-application of low-tech heat therapy is recommended for treatment of osteoarthritis or acute, subacute, or chronic knee pain.**

*Indications* – Applications may be periodic or continuous and should be home-based, as there is no evidence for efficacy of provider-based heat treatments. Primary emphasis should generally be on functional restoration program elements, rather than on passive treatments in patients with chronic pain.

*Frequency/Duration* – Self-applications may be periodic. Education regarding home heat application should be part of the treatment plan if heat has been effective for reducing pain.

*Indications for Discontinuation* – Intolerance, increased pain, development of a burn, other adverse event.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Rationale for Recommendation*

Self-application of heat using towels or reusable devices is non-invasive, minimally costly, and without complications. There is one trial with heat administered by a sleeve that failed to find evidence of efficacy.(1160) Another trial evaluated heat and cold as an adjunctive treatment for stretching along with a prior treatment with heat and found cold to be superior.(1157) A third trial compared ice water to lukewarm water to crushed ice, but found no benefit in the early post-operative stage due to decreased knee temperature.(1146) While they are generally not helpful in patients with osteoarthritis, heat therapy may be helpful in a small minority, and thus is recommended as self-treatment as potential distractant or counter-irritant. It may also be helpful for purposes of stretching when there is a limited range of motion. Some forms of heat can be considerably more expensive, including chemicals, and are not recommended.

*Evidence for the Use of Heat Therapy*

There are 3 moderate-quality RCTs incorporated into this analysis.

## ULTRASOUND

There are many commercial modalities that deliver heat; these generally differ on how deeply the heat is felt. None of these modalities have demonstrated major efficacy for any disorder, however there have been limited uses for treatment of specific disorders with a specific intervention (see Hand, Wrist, and Forearm Disorders, Elbow Disorders, Low Back Disorders, and Chronic Pain guidelines). There are more trials that include ultrasound to treat the knee than the hip.(1161)

### *Ultrasound for Treatment of Knee Osteoarthritis*

**There is no recommendation for or against the use of ultrasound therapy for knee osteoarthritis.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Rationale for Recommendation*

The highest quality trial comparing ultrasound with sham treatment found a lack of benefit.(1162) The moderate quality trials conflict – some suggest benefits,(577, 1163, 1164) while others suggest a lack of benefit.(575, 1165) Given that results conflict, there is no recommendation for or against ultrasound for treatment of knee OA.

### *Evidence for the Use of Ultrasound for Knee Osteoarthritis*

There is 1 high- and 5 moderate-quality RCTs incorporated into this analysis. There is 1 low-quality RCT in Appendix 1.(1166)

## PHONOPHORESIS

### *Phonophoresis for Knee Osteoarthritis*

**Phonophoresis is not recommended for knee osteoarthritis.**

*Strength of Evidence – Not Recommended, Evidence (C)*

### *Rationale for Recommendation*

There is one moderate-quality study evaluating phonophoresis with ibuprofen compared to ultrasound and found no difference between the two therapies. The authors reported that both groups were improved over the 2 weeks of therapy.(1167) Thus, as there is not evidence of efficacy, phonophoresis is not recommended.

### *Evidence for the Use of Phonophoresis for Knee Osteoarthritis*

There is 1 moderate-quality RCT incorporated into this analysis.

## MASSAGE

Massage is a commonly used treatment for chronic muscular pain and usually administered by multiple health care providers as well as family or friends. It is most typically used for treatment of spine and torso pain (see Chronic Pain and Low Back Disorders guidelines), although it has been used for the treatment of knee pain.(1168, 1169)

### *Massage for Knee Osteoarthritis or Acute, Subacute, or Chronic Knee Pain*

**There is no recommendation for or against the use of massage for knee osteoarthritis or acute, subacute, or chronic knee pain.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Rationale for Recommendation*

Massage is a commonly used treatment for musculoskeletal pain, but few studies evaluated disorders other than LBP.(1170-1172) There is one moderate-quality trial for treatment of knee OA. However, significant limitations of the study include randomization failure and use of wait-listed controls, thus biasing the study in favor of massage. While massage is not invasive and has few adverse effects, it is moderately to highly costly (when professionally administered), depending on the number of treatments. Also, other treatments with documented efficacy are available.

### *Evidence for the Use of Massage*

There are 2 moderate-quality RCTs incorporated into this analysis.

## **REFLEXOLOGY**

Reflexology is a complementary or alternative treatment. It entails the physical act of applying pressure to the feet and hands with specific thumb, finger, and hand techniques without the use of oil or lotion. Reflexology is based on a system of zones and reflex areas that reflect an image of the body on the feet and hands. Work on the feet and hands are thought to effect physical changes to the body.

### *Reflexology for Knee Osteoarthritis or Acute, Subacute, or Chronic Knee Pain*

**Reflexology is not recommended for the treatment of knee osteoarthritis or acute, subacute, or chronic knee pain.**

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

### *Rationale for Recommendation*

There are no quality studies of reflexology for knee pain. It also has not been shown to be efficacious for the treatment of chronic LBP in a moderate-quality study.(1173) Other treatments have been shown to be efficacious.

### *Evidence for the Use of Reflexology*

There are no quality studies evaluating the use of reflexology for knee osteoarthritis or acute, subacute, or chronic knee pain.

## **Acupuncture**

Acupuncture has been used to treat many musculoskeletal conditions including hip(1174) and spine pain and osteoarthritis, particularly of the knee,(486, 1175) and there is some evidence that patients seek this treatment if they have more severe pain.(1176) Multiple techniques have been used, including manual needle stimulation, electrical needle stimulation(1177-1179) (electroacupuncture), superficial dry needling, and deep dry needling.(1180, 1181) Acupuncture administration may involve moxibustion and cupping.(1182) Moxibustion is a traditional Chinese therapy involving burning of an herb (mugwort) to stimulate blood flow and balance “Qi.” Cupping is another ancient Chinese practice involving placement of a cup on the skin with negative pressure induced either through heat or suction with tension placed on the underlying tissue. Besides traditional acupuncture, there are many other types of acupuncture that have arisen, including accessing non-traditional acupuncture points.(1183) Quality evidence has documented that use of traditional acupuncture locations is not necessary to derive equivalent benefits from treatment of low back pain (see Chronic Pain and Low Back Disorders guidelines).(1184-1186)

*Acupuncture for Chronic Osteoarthritis of the Knee*

**Acupuncture is moderately recommended for select use for treatment of chronic osteoarthritis of the knee as an adjunct to more efficacious treatments.**

*Indications* – Moderate to severe chronic osteoarthritis of the knee. Prior treatments should include NSAIDs, weight loss, and exercise, including a graded walking program and strengthening exercises. Should be considered as an adjunct to a conditioning program that has resulted in insufficient clinical response.

*Frequency/Duration* – A limited course of 6 appointments(1187) with clear objective and functional goals to be achieved. Additional appointments would require documented functional benefits, lack of plateau in measures and probability of obtaining further benefits. There is quality evidence suggesting traditional acupuncture needle placement may be unnecessary(1188) and that superficial needling is as successful as deep needling.(1189, 1190) There is evidence suggesting it is not necessary to perform bilateral needling,(1191) although that result has not been replicated.

*Indications for Discontinuation* – Resolution, intolerance, and non-compliance, including non-compliance with aerobic and strengthening exercises.

*Strength of Evidence* – **Moderately Recommended, Evidence (B)**

*Acupuncture for Acute or Subacute Knee Pain*

**There is no recommendation for or against the use of acupuncture for the treatment of acute or subacute knee pain.**

*Strength of Evidence* – **No Recommendation, Insufficient Evidence (I)**

*Rationale for Recommendations*

There are several high- and moderate-quality studies that evaluated acupuncture for the treatment of knee osteoarthritis.(1190, 1192-1204) Trials of auricular acupuncture suggests efficacy in reducing analgesia requirements peri-operative,(1205) intra-operative,(1206) and post-operative.(1174) Some have concluded that the evidence suggests that there is no effect of acupuncture on pain.(1012) Some trials have combined acupuncture with electrical currents, others have applied electrical currents to acupuncture sites,(1201, 1207, 1208) and one involved periosteal stimulation.(1209) There are no quality studies to show clear benefit of electroacupuncture over needling. There continue to be some questions about efficacy of acupuncture,(1210, 1211) with concerns about biases, e.g., attention and expectation bias in these study designs as well as the adequacy of placebo acupuncture treatments.(1212, 1213) One trial demonstrated acupuncturist behaviors to set positive expectations had a significant impact on outcomes from acupuncture.(1214)

Studies reporting results after the cessation of acupuncture have nearly all found lasting benefits,(1187, 1192, 1215) although there are no long-term follow-up reports. Although not all studies have been positive,(1216) acupuncture has been found to be superior to no acupuncture ,(1192, 1217) superior to more of the same medication,(1202) superior to usual care,(1218-1221) and also an additive benefit to an NSAID.(1198) Results of three trials involving shams have indicated the sham was approximately equivalent to acupuncture,(1189, 1190, 1222) but acupuncture(1196) and electroacupuncture(1207) were superior to sham in two other trials. High-quality studies with sizable populations and long follow-up periods are needed for all of these potential indications. Acupuncture when performed by experienced professionals is minimally invasive, has minimal adverse effects, and is moderately costly. Despite significant reservations regarding its true mechanism of action, a limited course of acupuncture may be recommended for treatment of knee osteoarthritis as an adjunct to a conditioning and weight loss program. Acupuncture is recommended to assist in increasing functional activity levels more

rapidly. Primary attention should remain on the conditioning program. Acupuncture is not recommended for those not involved in a conditioning program or who are non-compliant with graded increases in activity levels.

#### *Evidence for the Use of Acupuncture*

There are 8 high- and 16 moderate-quality RCTs incorporated into this analysis. There are 4 low-quality RCTs in Appendix 1.

## **MANIPULATION AND MOBILIZATION**

Manipulation and mobilization are two types of manual therapy. Manipulation has been used to treat knee disorders.(571, 1223-1243) It has been particularly utilized for post-operative patients with inadequate range of motion that affects function that is sometimes termed arthrofibrosis.(1223, 1229, 1232, 1244, 1245) There is quality evidence of efficacy of manipulation particularly for treatment of acute low back pain and neck pain (see Low Back Disorders, and Cervical and Thoracic Spine Disorders guidelines).

#### *Manipulation or Mobilization for Acute Knee Pain, Knee Osteoarthritis, or Surgical or Knee Fracture Patients*

**There is no recommendation for or against the use of manipulation or mobilization for treatment of acute knee pain, knee osteoarthritis, or for surgical or knee fracture patients.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

#### *Manipulation or Mobilization for Subacute or Chronic Knee Pain*

**Manipulation or mobilization is recommended for patients with subacute or chronic knee pain.**

*Strength of Evidence – Recommended, Evidence (C)*

#### *Manipulation or Mobilization for Post-operative Patients with Significantly Reduced Range of Motion*

**Manipulation or mobilization is recommended for select post-operative patients with significantly reduced range of motion.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

#### *Rationale for Recommendations*

There are no quality trials of manipulation or mobilization compared with sham or incorporating a clinical prediction rule that demonstrate efficacy. There is quality evidence of efficacy for manipulation or mobilization in treating knee osteoarthritis,(571, 1226, 1246) but further quality studies are needed, as it is difficult to separate out the effect of other interventions included such as exercise. There is one high-quality study of manipulation in hospitalized knee and hip patients that found a lack of efficacy.(1247) However, this study did not include treatment to the hip or knee. Despite these study weaknesses, the orthopaedic manual physical therapy (OMPT)<sup>xiv</sup> approach(571, 1226) is believed to provide clinically important benefit for patients with knee OA. This treatment approach has been suggested to reduce the need for medication and total knee replacement. However, from the design of these pragmatic trials it cannot be determined what aspect of the OMPT approach is most responsible

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<sup>xiv</sup>OMPT is a formalized type of physical therapy based on skills developed with entry level professional programs through advanced fellowship training. OMPT generally includes: 1) a manual examination to identify impairments to movement, strength, coordination, and balance, and to identify symptom producing structures; 2) manual interventions to determine techniques and movements to reduce symptoms and improve function; 3) exercise prescription that reinforces movement from manual treatment and provides the appropriate dose of strengthening and/or balance exercises.

for the improvement. Manipulation is not invasive, has low adverse effects, but is moderately costly depending on the number of treatments. There is no recommendation for or against use in these patients, with the exception of patients with subacute or chronic knee pain or select post-operative patients.

#### *Evidence for the Use of Manipulation or Mobilization*

There are 1 high- and 8 moderate-quality RCTs incorporated in this analysis. There are 2 low-quality RCTs in Appendix 1.

### **MANIPULATION UNDER ANESTHESIA (MUA)**

#### *Manipulation under Anesthesia for Post-operative Patients with Significantly Reduced Range of Motion*

**Manipulation under anesthesia is recommended for select post-operative patients with significantly reduced range of motion.** This may be performed selectively under general or regional anesthesia typically by the operating orthopedist.(1245)

#### *Strength of Evidence – Recommended, Insufficient Evidence (I)*

#### *Rationale for Recommendation*

There is no quality evidence of efficacy of manipulation of the knee, typically performed under anesthesia but also commonly performed by physical therapists, for post-arthroplasty patients with insufficient range of motion.(1225, 1228, 1230, 1248, 1249) One low-quality trial suggested significantly improved range of motion immediately after MUA in the manipulated group compared with the group that declined manipulation with differences persisting for 2 years.(1228) For patients with insufficient range of motion, manipulation under anesthesia is modestly invasive, has adverse effects, and is moderately costly, but it appears helpful for some patients to improve range of motion. Thus, it is a viable option for selected use.

### **LOW-LEVEL LASER THERAPY**

Low-level laser treatment (LLLT) usually involves laser energy that does not induce significant heating. Low-level laser exposures are theorized to induce photoactivation of the oxidative chain.(1250-1252) LLLT is low risk and without significant reported side effects.(1253)

#### *Low-level Laser Therapy for Knee Osteoarthritis or Acute, Subacute, or Chronic Knee Pain*

**The use of low-level laser therapy is not recommended for treatment of osteoarthritis and acute, subacute, or chronic knee pain.**

#### *Strength of Evidence – Not Recommended, Evidence (C)*

#### *Rationale for Recommendation*

There are several moderate-quality trials that evaluated use of low level laser therapy for treatment of knee pain and osteoarthritis,(1252, 1254-1258) and while they conflict on efficacy to some extent,(1259) most trials with sham are negative.(1260, 1261) LLLT is not invasive, has low adverse effects, is moderately to highly costly based on the number of treatments required, has mostly negative results in quality trials for the treatment of the knee, and other effective treatment options exist. Thus, LLLT is not recommended for treatment of knee pain or osteoarthritis.

#### *Evidence for the Use of Low-Level Laser Therapy for Knee Pain or Osteoarthritis*

There is 1 high- and 7 moderate-quality RCTs incorporated into this analysis. There is 1 low-quality RCT in Appendix 1.

## Electrical Therapies

There are multiple forms of electrical therapies used to treat musculoskeletal pain. These include electrical stimulation therapies, iontophoresis, interferential therapy (IFT or IT), microcurrent therapy, percutaneous electrical nerve stimulation (PENS), and transcutaneous electrical stimulation (TENS).(1138, 1262-1268) The mechanism(s) of action, if any, are unclear.

### ELECTRICAL STIMULATION THERAPIES

Neuromuscular electrical stimulation has been used particularly to strengthen the quadriceps femoris.(1269-1272) Many studies using electrical stimulation have been reported both for treating patients with osteoarthritis,(1273) patellofemoral pain,(1274) post-surgical knee patients,(1275-1279), as well as in healthy athletes to attempt to improve performance.(1280-1289)

*Electrical Stimulation Therapies for Treatment of Knee Osteoarthritis or Acute, Subacute, or Chronic Knee Pain*

**There is no recommendation for or against the use of electrical stimulation therapies outside of research settings for the treatment of knee osteoarthritis or acute, subacute, or chronic knee pain.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

#### *Rationale for Recommendation*

There are is one moderate-quality trial of electrical stimulation in in knee osteoarthritis patients; however, the results are inconsistent.(1273) There are numerous low-quality trials attempting to address utility of electrical stimulation either alone or as an adjunct to exercise (see Appendix 1). The overall findings in those studies are exercise outperforms electrical stimulation. There are some suggestions electrical stimulation may have modest efficacy in comparison with control. Electrical stimulation is non-invasive, has low adverse effects, but is moderate to high cost with prolonged treatment. Other treatments shown to be effective are available. There is no recommendation for or against the use of these therapies.

#### *Evidence for the Use of Electrical Stimulation Therapies*

There is 1 moderate-quality study evaluating the use of electrical stimulation for knee osteoarthritis and none for acute, subacute, or chronic knee pain. There are 16 low-quality trials in Appendix 1.

### IONTOPHORESIS

*Iontophoresis for Knee Osteoarthritis*

**There is no recommendation for or against the use of iontophoresis for the treatment of knee osteoarthritis or acute, subacute or chronic knee pain.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

#### *Rationale for Recommendations*

There are no quality studies for any of these therapies in occupational populations with knee osteoarthritis. There is one quality study suggesting efficacy of iontophoresis with morphine for post-operative knee and hip patients(1265); however, applicability to outpatient knee osteoarthritis populations and others is unclear. Some of these types of electrical therapies are thought to be of greater benefit for certain types of disorders such as iontophoresis with glucocorticosteroid for rheumatoid arthritis knee patients.(1268) These therapies are mostly non-invasive with low adverse effects but are moderately to highly costly when examined in aggregate. Other treatments shown to be

effective are available. There is no recommendation for or against the use of these therapies for knee osteoarthritis.

#### *Evidence for the Use of Iontophoresis*

There are 2 moderate-quality RCTs incorporated into this analysis.

## **INTERFERENTIAL THERAPY**

### *Interferential Therapy for Post-Operative Knee Patients*

**Interferential therapy for post-operative ACL reconstruction, meniscectomy, and knee chondroplasty is recommended immediately post-operatively in an elderly population. Patients should be engaged in an appropriate post-operative rehabilitation program in combination with interferential therapy.**

*Indications* – Elderly patients, post-operative from ACL reconstruction, meniscectomy, or knee chondroplasty.(1267)

*Duration* – At home, 3 times a day for up to 9 weeks.(1267)

*Indications for Discontinuation* – Unable to participate in active rehabilitation program; no response after 1 to 3 treatments.

*Strength of Evidence* – **Recommended, Evidence (C)**

### *Rationale for Recommendation*

There is one moderate-quality placebo-controlled trial among elderly residence home patients reporting improved pain, range of motion, and post-operative edema up to 9 weeks compared to placebo therapy.(1267) (Interferential therapy is not invasive, has few adverse effects, and is moderately costly. As there is evidence of efficacy, it is recommended.

### *Evidence for the Use of Interferential Therapy*

There is 1 moderate-quality RCT incorporated into this analysis.

## **MICROCURRENT THERAPY**

### *Microcurrent Therapy for Post-Operative Total Knee Arthroplasty Patients*

**There is no recommendation for or against the use of microcurrent therapy for total knee arthroplasty post-operative pain control.**

*Strength of Evidence* – **No Recommendation, Insufficient Evidence (I)**

### *Rationale for Recommendation*

There is one moderate-quality pilot study reporting improvement in post-operative pain and pain medication use and wound healing and decreased wound drain volumes.(1266) However, that trial was not sham controlled and therefore likely biased in favor of treatment. A single pilot study with these flaws is unable to be used for development of evidence-based guidance. Therefore, there is no recommendation.

### *Evidence for the Use of Microcurrent Therapy*

There is 1 moderate-quality RCT incorporated into this analysis.

## **PERCUTANEOUS ELECTRIC THERAPY**

*Percutaneous Electric Therapy for Knee Osteoarthritis or Other Knee Pain*

**Percutaneous electric therapy is recommended for assistance with pain control for knee osteoarthritis or other knee pain.**

*Indications* – As part of an active rehabilitation and exercise program.(1138, 1263, 1264)

*Duration* – Up to 3 times a week as part of a rehabilitation program.(575, 1290, 1291)

*Indications for Discontinuation* – Patient unable to participate in active rehabilitation program. No response after first treatment.(1263)

*Strength of Evidence* – **Recommended, Evidence (C)** (Knee OA)

**Recommended, Insufficient Evidence (I)** (Other knee pain)

### *Rationale for Recommendation*

Two moderate quality sham-controlled trials evaluated patients with knee osteoarthritis reporting greater pain control compared to placebo.(1263, 1264) (A low-quality study evaluated PENS in post-operative patients and reported less muscle atrophy in the PENS group.(1292)) A moderate-quality study reported improved patient and physician rated outcomes in the active treatment group after 4 weeks of daily treatment.(1138) Percutaneous Electric Therapy is not invasive, has few adverse effects, is moderately to highly costly, depending on duration of use, and has evidence of efficacy. Thus, it is recommended.

### *Evidence for the Use of Percutaneous Electric Therapy*

There are 2 moderate-quality RCTs incorporated into this analysis. There is 1 low-quality RCT in Appendix 1.

## **TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS)**

TENS is a modality to control pain through electrical stimulation delivered by pads placed on the surface of the skin. TENS is used for the treatment of many painful conditions, including both non-inflammatory and inflammatory disorders; although it has more typically been used for spine disorders(1293-1299) (see Chronic Pain and Low Back Disorders guidelines).

*TENS for Knee Osteoarthritis or Acute, Subacute, or Chronic Knee Pain*

**There is no recommendation for or against the use of TENS for knee osteoarthritis or acute, subacute or chronic knee pain.**

*Strength of Evidence* – **No Recommendation, Insufficient Evidence (I)**

### *Rationale for Recommendation*

There are many moderate-quality trials, and one of high-quality(1300) that evaluated TENS for knee pain. Some low-quality trials have suggested modest benefits from TENS,(1301-1304) while others have suggested no benefits.(1305-1308) Seven of the moderate-quality studies did not find any significant improvement with the use of TENS,(575, 1290, 1291, 1309-1312) while nine reported some benefit compared to control.(1177, 1178, 1313-1319) TENS is not invasive, has few adverse effects, and is moderately costly. However, as there are many conflicts in the literature, there is no recommendation for or against its use to treat knee OA or pain.

### *Evidence for the Use of TENS for Knee Osteoarthritis and Knee Pain*

There is 1 high- and 16 moderate-quality RCTs incorporated into this analysis. There are 8 low-quality RCTs in Appendix 1.

## Injection Therapies

There are several types of injections that have been used for patients with knee pain using different approaches. These include intra-articular glucocorticosteroid injections,(1320-1326) viscosupplementation,(922) arthroscopic and non-arthroscopic joint lavage, and prolotherapy injections.(1320) Percutaneous needle tenotomy has been attempted for chronic tendinoses.(1327-1330) Tidal volume irrigation of the knee has been utilized for treatment of both inflammatory arthritides as well as osteoarthroses.(1331-1335) Additionally, radiation synovectomy has been utilized for treatment of patients with undifferentiated arthritis and rheumatoid arthritis.(1336, 1337)

Glucocorticosteroid injections, which have been used for the treatment of rheumatoid arthritis and juvenile idiopathic arthritits, are beyond the scope of this guideline.(1338) Intra-articular methotrexate and orgotein, which have been used for treatment of rheumatoid arthritis, psoriatic arthritis, and other arthritides(1339-1342) and oral methotrexate and leflunomide, which have been used for treatment of rheumatoid arthritis, are also beyond the scope of this guideline.(1343)

Transcranial magnetic stimulation has been used to attempt to make rehabilitation more effective. One small crossover trial with 1 hour follow-up suggested it may make rehabilitation more effective.(1344)

### **Platelet-Rich Plasma, Plasma Rich in Growth Factor, and Autologous Blood Injections**

Autologous blood injections have been used to treat osteoarthritis.(1345-1350) Autologous growth factors can be injected with autologous whole blood or platelet-rich plasma (PRP).(1351) These injections have been evaluated in studies of plantar foot pain, lateral epicondylalgia, and several other disorders.(1351, 1352)

*Intraarticular Platelet-Rich Plasma and Plasma Rich in Growth Factor, and Injections for Moderate to Severe Knee Osteoarthritis*

**Intraarticular platelet-rich plasma and plasma rich in growth factor are neither recommended nor not recommended for treatment of moderate to severe knee osteoarthritis.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

*Level of Confidence – Low*

*Autologous Blood Injections for Moderate to Severe Knee Osteoarthritis*

**There is no recommendation for or against the use of autologous blood injections for moderate to severe knee osteoarthritis.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

*Level of Confidence – Low*

*Indications* – Re. PRP injections, moderately to severe knee osteoarthritis with insufficient responses to NSAID/acetaminophen, and exercise. Generally, should also have attempted weight loss. Glucocorticosteroid should generally also be trialed first as there is moderate quality evidence suggesting comparable efficacy (2421, 2422).

*Benefits* – Improved pain and function, with somewhat conflicting evidence on duration of the benefit being 6- vs. 12+ months (2423,2424).

*Harms* – Hypertension, proteinuria, diarrhea, constipation, rare infections (2425)

*Frequency/Dose/Duration* – One injection should be evaluated to ascertain whether it is effective. Although a series of injections has been trialed, there is no clear superiority of a series of injections compared with a single injection (2423, 2424, 2426).

*Rationale* – There is one quality trial of injections of PRP vs. Hyaluronic acid vs. NSAID and used MRI imaging, and while the symptoms reportedly improved, there was not evidence of efficacy based on MRI results at one year (2427). One trial without placebo-control suggested MRI improvements in the PRP group compared with the HA group, with 48% vs. 8% improving at least one OA grade over 12 months (2418). Several moderate-quality placebo-controlled trials suggest modest benefits of PRP compared with placebo (2423-2424, 2427, 2429-2432); e.g., one trial suggested comparable benefits with either one or two injections at 6 months but superiority compared with placebo yet benefits waned after that point for either 1- or 2-injections (1349); another trial suggested durable benefits at 12 months of a series of three (3) PRP injections compared to placebo (2424); and one trial suggested PRP improved pain and disability (2433). Two moderate-quality trials suggested comparable efficacy to glucocorticoid injection (2421, 2422), with one of those trials suggesting longer duration of the PRP (2422).

There are many moderate- to high-quality trials (1346-1348, 1353, 2434), mostly comparisons against viscosupplementation. Thus, the body of evidence tends to suggest PRP injections tend to be superior to viscosupplementation injections, which appear superior to glucocorticosteroids (see below). With limited and somewhat conflicting placebo-controlled trials, the evidence was considered too limited by the panel for evidence-based recommendations.

PRP injections have also been trialed for preventing post-operative blood loss and have been suggested to improve function in knee arthroplasty patients (2435, 2436). The duration of the benefit was gone at 6 months in one trial (2435), but lasted 12 months in the other trial (2436). PRP has also been trialed with stem cells in a small-sized RCT (2437).

PRP injections are invasive and have a low risk of adverse effects but are high cost. A majority of the Evidence-based Practice Knee concluded that there should be no recommendation for platelet rich plasma injections for moderate to severe knee osteoarthritis based on the relative lack of, and conflicts among the quality placebo-controlled trials. In addition, the Evidence-base Practice Knee Panel concluded there is insufficient evidence to conclude either for or against a recommendation (57% agreed with no recommendation, 15% thought it should be not recommended and 29% felt it should be recommended) for moderate to severe knee osteoarthritis based on the lack of quality trials regarding the overall efficacy of these injections. Indications are provided above as a potential appeals process.

*Evidence* – A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: Knee Pain, Patellofemoral Pain Syndrome, Knee arthritis, Knee Osteoarthritis, Knee Arthrosis, knee degenerative joint disease, PRP, platelet rich plasma injections, autologous blood injections, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 136 articles in PubMed, 753 in Scopus, 78 in CINAHL, 51 in Cochrane Library, 1920 in Google Scholar, and 4 from other sources. We considered for inclusion 19 from PubMed, 8 from Scopus, 6 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 4 from other

sources. Of the 39 articles considered for inclusion, 35 randomized trials and 4 systematic reviews met the inclusion criteria.

## **Stem Cell Therapy**

Stem cell therapy has been used for treatment of knee osteoarthritis (2438-2441).

### *Stem Cell Therapy for Moderate to Severe Knee Osteoarthritis*

**Stem cell therapy is not recommended for the treatment of moderate to severe knee osteoarthritis.**

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

*Level of Confidence – Low*

*Rationale* – There are no sizable placebo- or sham-controlled trials of stem cells. There are only a few small trials that have been reported (2438-2441). Stem cell therapies are invasive, have some adverse effects, are costly, lack clear evidence of efficacy and thus as costs are extremely high, stem cell therapy is not recommended. Most of the panel (57%) felt the recommendation should be not recommended while 43% felt there should be no recommendation.

*Evidence* – A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2108 using the following terms: stem cells, adult stem cells, mesenchymal stem cells; knee pain, patellofemoral pain syndrome, knee arthritis, knee osteoarthritis, knee arthrosis, knee degenerative joint disease controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 22 articles in PubMed, 1949 in Scopus, 43 in CINAHL, 9 in Cochrane Library, 5530 in Google Scholar, and 5 from other sources. We considered for inclusion 8 from PubMed, 9 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 5 from other sources. Of the 24 articles considered for inclusion, 18 randomized trials and 6 systematic studies met the inclusion criteria.

## **Viscosupplementation**

Viscosupplementation has been used for knee osteoarthritis (15, 1350, 1355-1372) and to treat pain after arthroscopy and meniscectomy.(1373, 1374, 2442-2446).

### *Intraarticular Knee Viscosupplementation Injections for Moderate to Severe Knee Osteoarthritis*

**Intraarticular knee viscosupplementation injections are neither recommended nor not recommended for treatment of moderate to severe knee osteoarthritis.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

*Level of Confidence – Low*

*Indications* – Moderately to severe knee osteoarthritis with insufficient responses to NSAID/acetaminophen, and exercise. Generally, should also have attempted weight loss.

Glucocorticosteroid should generally also be trialed first as there is moderate quality evidence suggesting comparable efficacy (2421,2422).

*Benefits* – Improved pain and function, with somewhat conflicting evidence on duration of the benefit.

*Harms* – Allergic reactions, increased pain, intolerance, rare infections.

*Frequency/Dose/Duration* – One injection should be evaluated to ascertain whether it is effective. While a series of injections has been trialed, there is no clear superiority of a series of injections compared with a single injection.

*Rationale* – There are no placebo-controlled trials that used imaging as an objective outcome measure. There is one quality trial of injections of PRP vs. Hyaluronic acid vs. NSAID and used MRI imaging, and while the symptoms reportedly improved, there was not evidence of efficacy based on MRI results at one year (2427). One trial without placebo-control suggested MRI improvements in the PRP group compared with the HA group, with 48% vs. 8% improving at least one OA grade over 12 months (2428).

There are numerous moderate-quality trials comparing injections with viscosupplementation with placebo (see evidence table) (1058, 1375-1383, 2432, 2430, 2447-2449). Most trials show pain reductions from 2-weeks to 6 months and most trials suggesting superiority at approximately 3 months after injection. Yet, multiple high- and moderate-quality trials also suggest a lack of efficacy (1058, 1380, 1382, 1398, 1417, 1422, 1423, 1425, 2447, 2448).

There are many trials comparing injections with viscosupplementation with glucocorticosteroid. Most of these trials comparing viscosupplementation with glucocorticoid injection suggested glucocorticosteroid injections are inferior for the knee (1384-1390); however, for the hip the reverse may be true (1383). None of the knee trials reported superior results with glucocorticosteroid. One high-quality trial suggested comparable results until 26 weeks at which point the glucocorticoid appeared to be losing benefit while the benefits of the viscosupplementation had greater persistence.(1389) The next highest quality trial suggested comparable efficacy over 3 months.(1383, 1389)

A moderate-quality, blinded trial reported that viscosupplementation improved articular cartilage appearance significantly compared with glucocorticosteroids,(1386) but those results have not been replicated. One quality trial also documented these injections provide additive benefit over appropriate care (1391) and usual NSAID therapy.(1392)

Sparse quality placebo/sham-controlled treatment trials with follow-up beyond 1 year have been published, with one follow-up trial suggesting lack of durable efficacy (2441). There is one moderate-quality trial reporting a lack of synergism with combined glucocorticoid injection.(1393) There is no clear preponderance of evidence that high or low molecular weight preparations are superior, although one trial suggested hyaluronan tended to be superior(1394). Both resulted in approximately 40% reductions in pain ratings with benefits lasting 6 months. Various combinations of injections have not shown one regimen to be clearly superior.(1395)

Thus, the body of evidence tends to suggest PRP injections tend to be superior to viscosupplementation injections, which appear superior to glucocorticosteroids (see below).

Hyaluronic acid injections are invasive, have moderate adverse effects, are high cost, have mixed efficacy against placebo injections, have lack of durable efficacy, and have evidence suggesting PRP injections may be superior to hyaluronic acid injections. With limited and somewhat conflicting placebo-controlled trials, the evidence was considered too limited by the panel for evidence-based recommendations. The Evidence-based Practice Knee Panel has downgraded the evidence from “C” to “I” and came to a limited conclusion that these injections should be neither recommended nor not recommended for moderate to severe knee osteoarthritis based on the current understanding of the peer-reviewed literature, the adverse effects, and the overall efficacy of viscosupplementation injections. A minority of panel members (14%) felt these injections should be recommended and others (29%) felt they should be not recommended. Indications are provided for a potential appeals process.

*Evidence* – A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: viscosupplementation, hyaluronic acid, hyaluronan; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 252 articles in PubMed, 8,381 in Scopus, 162 in CINAHL, 200 in Cochrane Library, 2,370 in Google Scholar, and 87 from other sources. We considered for inclusion 46 from PubMed, 16 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 87 from other sources. Of the 149 articles considered for inclusion, 138 randomized trials and 6 systematic studies met the inclusion criteria.

### **Intraarticular Glucocorticosteroid Injections**

Intraarticular glucocorticosteroid injections are frequently performed to attempt to deliver anti-inflammatory medication to the joint with minimal systemic effects.(1336, 1337, 1383, 1390, 1436, 1476-1484) Their usual purpose is to gain sufficient relief to either resume conservative medical management or to delay operative intervention. These injections are generally performed without fluoroscopic or ultrasound guidance. Intraarticular injections have also been utilized intraoperatively at the close of procedures, including meniscectomy (1485) and arthroscopy.(1486, 1487) Periarticular injections have been used in arthroplasty patients(1488) in an attempt to facilitate recovery.

*Intraarticular Glucocorticosteroid Injections for Knee Osteoarthritis*

**Intraarticular glucocorticosteroid injections are recommended for the treatment of knee osteoarthritis, especially for short-term control of symptoms.**

*Strength of Evidence* – **Recommended, Evidence (C)**

*Level of Confidence* – **Moderate**

*Indications* – Pain from osteoarthritis sufficient that control with NSAID(s), acetaminophen, weight loss or exercise is unsatisfactory.(1320, 1321, 1332, 1333)

*Benefits* – Improved pain and function. Most evidence suggests a duration of benefit of approximately 3 months.

*Harms* – Rare infections, short-term poorer control of diabetes. One trial found steroid injections were associated with greater cartilage loss over 2-years on MRI scans compared with saline injections (2450).

*Frequency/Dose/Duration* – Only 1 injection should be scheduled to start, rather than a series of three. Medications used in RCTs include triamcinolone acetonide 40mg, 80mg, triamcinolone hexacetonide 20mg, betamethasone 6mg, hydrocortisone 25mg, and methylprednisolone 80mg and 120mg).(1320, 1321, 1333) One trial used cortivazol 3.75mg.(1332) There was no benefit of 80mg triamcinolone acetonide vs. 40mg (2472). Extended-release preparations have been suggested to produce a modestly more durable benefit (2473, 2474). Anesthetics have most often been bupivacaine or lidocaine. Whether aspiration should be performed for effusions in osteoarthritis patients is unknown; however, there is quality evidence that aspiration of effusions prior to injection results in greater effectiveness for rheumatoid arthritis patients.(1489) Many trials included aspiration prior to injection. There is moderate evidence that a superomedial or superolateral approach is superior to a lateral approach.(1434) Bed rest has been used after treatment in rheumatoid arthritis patients to theoretically reduce speed of systemic absorption; however, a moderate-quality trial demonstrated no difference and there is no reason to believe the results would be different in osteoarthritis patients.(1323, 1324) Thus, post-injection bed rest is not recommended. There is no evidence to suggest limiting the number of injections, and a high-quality trial found both evidence of efficacy of glucocorticoid injections compared to placebo and no evidence of accelerated osteoarthritis when injected 4 times a year for 2 years.(1320) Multiple doses have been utilized in trials with no head-to-head comparisons of dosing regimens. Comparative trials have suggested methylprednisolone acetate 40mg is superior to triamcinolone hexacetonide 20mg, which is superior to betamethasone 6mg.(1490, 1491) However, those results have not been replicated. Another comparative clinical trial found greater efficacy for methylprednisolone 80mg over 40mg for the hip joint.(1482)

*Indications for Discontinuation* – A 2nd glucocorticosteroid injection is not recommended if the 1st has resulted in significant reduction or resolution of symptoms. If there has been no response to a 1st injection, there is less indication for a second. If it is believed that the medication was not well placed and/or if the underlying condition is so severe that 1 steroid bolus could not be expected to adequately treat the condition, a 2nd injection may be indicated. In patients who demonstrates a pharmacologically appropriate response consisting of several weeks of temporary, partial relief of pain, but who then have worsening pain and function and who are not (yet) interested in surgical intervention, a repeat steroid injection is an option. Benefits beyond approximately 4 injections per year are not thought to exist.(1320) Patients requesting more injections should have reassessment of conservative management measures and be evaluated for irrigation/lavage and surgical intervention.

*Rationale*– There are high- and moderate-quality RCTs evaluating efficacy of glucocorticosteroid injections compared to placebo for treatment of knee OA(1341, 1492-1496). These have uniformly found efficacy (however, the magnitude and duration of benefits is modest thus the reduction in the evidence based rating to “C”).(1320, 1321, 1325, 1332) There is moderate-quality evidence that tidal irrigation appears more effective for treatment of osteoarthritis in every trial that has compared these procedures(1331-1333) and there is evidence a that combination of tidal irrigation plus glucocorticosteroid injection is superior to either alone.(1332, 1333) Moderate-quality evidence suggests intraarticular injection is more effective for treatment of rheumatoid arthritis than intramuscular injection,(1322) although there is not quality evidence for osteoarthritis patients. Thus,

there is no recommendation for intramuscular injections for osteoarthritis patients. Three moderate-quality trials have suggested viscosupplementation is superior to glucocorticoid injection (1384, 1386, 1388), although the degree of benefits do not appear large.

Intraarticular glucocorticosteroid injections are invasive, have a low risk of adverse effects, are moderately costly, have evidence of short- to intermediate-term efficacy, and are recommended for treatment of moderate-to severe osteoarthritis patients, particularly after inadequate results from NSAIDs, acetaminophen, exercise, or other non-invasive interventions. As there is quality evidence of progression of the loss of articular cartilage compared with saline injections, these should generally be reserved for advanced cases (2450).

*Evidence* – A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: intra articular glucocorticoids, intraarticular glucocorticoids, intra articular glucocorticosteroid, intraarticular glucocorticosteroid; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 59 articles in PubMed, 284 in Scopus, 22 in CINAHL, 34 in Cochrane Library, 7,080 in Google Scholar, and 0 from other sources. We considered for inclusion 16 from PubMed, 2 from Scopus, 0 from CINAHL, 2 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 20 articles considered for inclusion, 15 randomized trials and 5 systematic reviews met the inclusion criteria.

### **Tidal Knee Joint Irrigation**

Large-volume irrigation of the knee joint has been used for treatment of knee osteoarthritis.(1331-1333) Intraarticular glucocorticosteroid injections are frequently given simultaneously. This procedure may be performed in conjunction with arthroscopy, although it has also been performed without arthroscopy.

*Tidal Knee Joint Irrigation for Knee Osteoarthritis*

**Tidal knee joint irrigation is not recommended for the treatment of knee osteoarthritis.**

*Strength of Evidence* – **Not Recommended, Insufficient Evidence (I)**

*Level of Confidence* – **Low**

*Rationale* – One sham-controlled trial suggested no evidence of efficacy, although the randomization process failed and they attempted statistical adjustment (2475). There are three moderate-quality RCTs comparing the efficacy of tidal irrigation to glucocorticosteroid injection for treatment of knee OA, with all 3 trials finding evidence of superiority of irrigation to injection.(1331-1333) Two of the trials comparing the two procedures found superiority for patients undergoing irrigation followed by glucocorticoid injection(1332, 1333). One trial suggested superiority compared with conservative medical management (Ike 92). These procedures are invasive, have adverse effects, are moderate to high cost, the single sham-controlled trial suggests a lack of efficacy, and therefore, tidal irrigation is not recommended.

Adjunctive treatment with glucocorticosteroids after lavage has been assessed in many studies with mixed results. Both the highest quality study(1334) and the largest trial(1335) were largely negative.

*Evidence* – A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: Tidal Knee Joint Irrigation; Knee Pain and Osteoarthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 3 articles in PubMed, 3735 in Scopus, 10 in CINAHL, 3 in Cochrane Library, 2 in Google Scholar, and 0 from other sources. We considered for inclusion 2 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 0 from other sources. Of the 3 articles considered for inclusion, 7 randomized trials and 0 systematic reviews met the inclusion criteria.

### **Radiation Synovectomy**

Radiation synovectomy has been used for treatment of patients with knee arthritis, although mostly among those thought to have an inflammatory component or undifferentiated arthritis.(1336, 1337)

*Radiation Synovectomy for Knee Osteoarthritis*

**Radiation synovectomy is not recommended for the treatment of knee osteoarthritis.**

*Strength of Evidence* – **Not Recommended, Evidence (C)**

*Rationale for Recommendation*

There is one moderate quality trial comparing radiation synovectomy with glucocorticoid injection with a radiation sham plus glucocorticoid that suggested radiation synovectomy was ineffective for treatment of undifferentiated arthritis and rheumatoid arthritis.(1336, 1337) Radiation synovectomy is invasive, has adverse effects, is moderately costly, appears ineffective, and is not recommended.

*Evidence for the Use of Radiation Synovectomy*

There are 2 moderate-quality RCTs incorporated into this analysis.

### **Prolotherapy Injections**

Prolotherapy injections attempt to address a theoretical cause or mechanism for chronic pain. This therapy involves repeated injections of irritating, osmotic, and chemotactic agents (e.g., dextrose, glucose, glycerin, zinc sulphate, phenol, guaiacol, tannic acid, pumice flour, sodium morrhuate) combined with an injectable anesthetic agent to reduce pain, into knee structures, especially knee and other ligaments, with the theoretical construct that it will strengthen these tissues.

*Prolotherapy Injections for Acute, Subacute, or Chronic Knee Pain*

**Prolotherapy injections are not recommended for treatment of acute, subacute, or chronic knee pain.**

*Strength of Evidence* – **Not Recommended, Evidence (C)**

*Rationale for Recommendation*

There are no quality studies of prolotherapy injections compared to placebo for treatment of patients with knee OA.(1497) The data from one trial are largely negative. A second trial suggests inferiority to PRP injections (2470). Prolotherapy injections are invasive, have adverse effects, moderately to highly costly, depending on numbers of injections, lack quality evidence of efficacy, and thus they are not recommended.

#### *Evidence for the Use of Prolotherapy Injections*

There are 2 moderate-quality RCTs incorporated into this analysis.

## **Botulinum Injections**

Botulinum injections have antinociceptive properties and have been used to produce muscle paresis.(1498-1501) These injections have primarily been used for non-occupational conditions such as cervical dystonia,(1502) strabismus, blepharospasm,(1503) and severe primary axillary hyperhidrosis.(1503, 1504) In the lower extremities, there are treatments that have been used mainly for children with spasticity due to cerebral palsy.(1505-1507) These injections are thought to directly treat a taut muscle band and to have analgesic properties.(1499-1501)

#### *Botulinum Injections for Knee Osteoarthritis or Other Knee Disorders*

**There is no recommendation for or against the use of botulinum injections for knee osteoarthritis or other knee disorders.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

*Level of Confidence – Low*

*Rationale* – There are multiple randomized trials and conflicting evidence of efficacy (2450-2454). The highest quality study suggests lack of efficacy (2450). One trial was attempted in patients with refractory painful knee after arthroplasty (2455); however, baseline differences and some non-significant results make interpretation challenging. One small trial attempted to treat refractory anterior knee pain, reported significant baseline differences, and suggested some limited improvements (2456). Botulinum injections are invasive, have adverse effects including deaths (1508), are costly, lack clear evidence of efficacy and thus there is no recommendation. A minority of the panel (43%) felt these injections should be not recommended compared with 57% no recommendation.

*Evidence* – A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: Botulinum Injections, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 10 articles in PubMed, 204 in Scopus, 9 in CINAHL, 38 in Cochrane Library, 5320 in Google Scholar, and 0 from other sources. We considered for inclusion 5 from PubMed, 6 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 11 articles considered for inclusion, 7 randomized trials and 4 systematic reviews met the inclusion criteria.

## **Autologous Blood Donation and Blood Transfusion**

Autologous blood donation has been used to attempt to reduce risks of bloodborne pathogen transmission in the event a blood transfusion is required.(1509-1519)

### *Pre-operative Autologous Blood Donation*

**Selective use of pre-operative autologous blood donation is recommended.**

*Indications* – Particularly consider in those older and in more fragile health for whom the threshold for transfusion (tolerable hemoglobin loss) is lower. Also to be considered among those with procedures anticipated to be more difficult and/or resulting in greater blood loss (e.g., revisions), and difficult to transfuse patients (e.g., many prior transfusions resulting in many antibodies).

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Level of Confidence* – Low

### *Intra-operative Autologous Blood Transfusion*

**Selective use of intraoperative autologous blood transfusion is recommended.**

*Indications* – Particularly to be considered in those older and in more fragile health for whom the threshold for transfusion (tolerable hemoglobin loss) is lower. Also to be considered among those with procedures anticipated to be more difficult and/or resulting in greater blood loss (e.g., revisions), and difficult to transfuse patients (e.g., many prior transfusions resulting in many antibodies).

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Level of Confidence* – Low

### *Rationale for Recommendations*

There are two moderate-quality trials that provide different approaches to the need for post-operative transfusions. One suggests pre-operative autologous blood donation is ineffective for hip arthroplasty.(1511) The other suggests intraoperative blood salvage is effective to reduce transfusion needs for knee arthroplasty.(1520) More transfusions are required for those who have donated blood pre-operatively and the costs are higher without measurable benefits. However, there are certain clinical scenarios in which pre-operative autologous blood donation may be beneficial, and the patient's age and health status needs to be considered. Therefore, pre-operative autologous blood donation is recommended for selective use.

There is one moderate-quality trial indicating that intra-operative autologous blood transfusion is associated with less need for blood transfusion,(1520) and thus is recommended.

### *Evidence for Autologous Blood Donation and Blood Transfusion*

There are 2 moderate-quality RCTs incorporated in this analysis. There is 1 low-quality RCT in Appendix 1.(1521)

## Interleukin-1 Receptor Antagonists

Interleukin-1 receptor antagonists have been used to treat rheumatoid arthritis. They have been investigated for treatment of osteoarthritis.(1522, 1523)

*Interleukin-1 Receptor Antagonists for Knee Osteoarthritis*

**Interleukin-1 receptor antagonists are not recommended for treatment of osteoarthritis.**

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

*Level of Confidence – LowLow*

*Rationale* – There are two high-quality RCTs that somewhat conflict. One suggests slight benefits in some secondary outcome measures(1522) while the other suggests no benefits.(1523) Taken together, these results suggest additional studies are warranted. Meanwhile, the treatment is associated with significant adverse effects and there are other treatments with documented efficacy, thus interleukin-1 receptor antagonists are not recommended without consistent evidence of efficacy and clear indications.

*Evidence* – A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: Interleukin-1 Receptor Antagonists, IL-1RA; Knee Pain, Patellofemoral Pain Syndrome, Knee Arthritis, Knee Osteoarthritis, Knee Arthrosis controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 12 articles in PubMed, 403 in Scopus, 7 in CINAHL, 18 in Cochrane Library, 1,100 in Google Scholar, and 0 from other sources. We considered for inclusion 2 from PubMed, 1 from Scopus, 1 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 5 articles considered for inclusion, 4 randomized trials and 0 systematic reviews met the inclusion criteria.

## Surgical Considerations

### Chondroplasty and Debridement

Chondroplasty and debridement have been used to treat knee osteoarthritis.(1441, 1524, 1525)

**Chondroplasty and debridement are moderately not recommended for treatment of knee osteoarthritis.**

*Strength of Evidence – Moderately Not Recommended, Evidence (B)*

*Level of Confidence – Moderate*

*Rationale* – A high-quality, sham-controlled trial suggested there is no benefit of chondroplasty and debridement for treatment of knee osteoarthritis.(375) A second trial suggested debridement was not helpful in comparison with joint lavage.(1526) One substantially lower quality trial provided conflicting evidence regarding how debridement compared with lavage.(1527) Other trials evaluating

electrocautery and radiofrequency treatments suggest no benefits.(1528, 1529) Thus, the higher quality trials and balance of evidence indicate that chondroplasty and debridement are ineffective and are not recommended for treatment of knee osteoarthritis. However, there are lesions that are thought to be mechanical in nature and require debridement, typically in the context of arthroscopic evaluation of meniscal tears with mechanical symptoms.

*Evidence* – A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: Chondroplasty, Debridement; Knee Pain, Patellofemoral Pain Syndrome, Knee arthritis, Knee Osteoarthritis, Knee Arthritis controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 27 articles in PubMed, 93 in Scopus, 11 in CINAHL, 33 in Cochrane Library, 207 in Google Scholar, and 8 from other sources. We considered for inclusion 5 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 7 from other sources. Of the 14 articles considered for inclusion, 8 randomized trials and 6 systematic reviews met the inclusion criteria.

## **CARTILAGE GRAFTS, OSTEOCHONDRAL AUTOGRAFTS, AND/OR TRANSPLANTATION**

Cartilage grafts and/or transplantations for osteochondral defects are used for treatment of articular cartilaginous defects.(349, 581, 1530-1564) These procedures are technically difficult and require specific physician expertise. They are thought to be effective in select patients generally less than 40 years old with active lifestyles having a traumatically induced, modest sized cartilage defect. These procedures are believed to delay or possibly prevent the development of osteoarthritis. However, a Cochrane review concluded there was insufficient evidence, opining that long-term studies are needed.(1530, 1565)

*Cartilage Grafts, Osteochondral Autografts, and/or Transplantation*

**Cartilage grafting, osteochondral autografts, and/or transplantation is moderately recommended for select patients.**

*Indications* – Select patients less than 40 years old with active lifestyles with a single, traumatically caused Grade III or IV femoral condyle deficit. Deficit diameter recommended not to exceed 20mm for osteochondral autograft transplants, although criteria up to 4cm<sup>2</sup> has been used. Grafts and transplants not recommended for those with obesity, inflammatory conditions or osteoarthritis, other chondral defects, associated ligamentous or meniscus pathology, or who are older than 55 years of age.

*Strength of Evidence* – **Moderately Recommended, Evidence (B)**

*Rationale for Recommendation*

There are no sham-controlled trials. However, there are quality trials that have compared different management approaches for these cartilaginous defects.(1566-1570) One trial with multiple reports suggests that at up to 10 years, autologous osteochondral transplantation is superior to microfracture in competitive athletes(349, 1540, 1571) and another trial by the same author also found superiority when performed in conjunction with ACL reconstruction.(1572)

Trials have included rigorous enrollment criteria that have on at least one occasion only included conditioned athletes.(349) As most trials have excluded obesity, it appears likely that at least 50% of the potential population would be excluded solely by that criterion. Thus, it is unclear how few patients would actually be eligible for these procedures. There are increasing numbers of longer term studies that have followed treated patients from 3-10 years(349, 1531, 1540, 1546, 1571, 1572) that have reported persistent benefits.Although, further studies with long follow-ups and larger sample sizes are needed. Cartilage grafts and/or transplants are invasive, have potential for adverse effects, and are high cost. These procedures have evidence of efficacy and are recommended for select patients.

#### *Evidence for the Use of Cartilage Grafts and/or Transplantation*

There is 1 high-(1571) and 4 moderate-quality(349, 1540, 1572, 1573) RCTs incorporated into this analysis.

*A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: autografts, osteochondral autograft transplant system, OATS, mosaicplasty, knee pain , patellar tendonitis, patellar tendinitis, patellar tendinopathy, knee arthritis, knee osteoarthritis, degenerative joint disease, meniscal tears, meniscus tear controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed we found and reviewed 12 articles, and considered 2 for inclusion. In Scopus, we found and reviewed 155 articles, and considered zero for inclusion. In CINAHL, we found and reviewed 13 articles, and considered zero for inclusion. In Cochrane Library, we found and reviewed 4 articles, and considered zero for inclusion. We also considered for inclusion one article from other sources. Of the 6 articles considered for inclusion, 2 randomized trials and 4 systematic studies met the inclusion criteria.*

## **Knee Arthroplasty**

Knee arthroplasty has been long used for treatment of end-stage knee degenerative joint disease. Outcomes have generally been excellent with 5 to 10 year survival rates of 95 to 99%.(1574-1585) A modestly worse prognosis including higher infection rates has been reported in rheumatoid arthritis patients.(1585, 1586) Unicompartmental arthroplasty has been used for medial joint arthrosis. However, patellar resurfacing is controversial.(1587)

Pain and functional loss have been shown to be predictors of arthroplasties(1588, 1589) ( $p < 0.0001$ ), as have visual analog scale ratings. Primary reasons for surgical failure are loosening, as well as infected, prostheses. Other predictors of suboptimal results include presence of effusion,(1590) older age(1591) more pre-operative debility,(1591, 1592) longer duration of disease,(1590) depressive symptoms,(1593) helplessness(1594) and catastrophizing.(1593, 1595, 1596) Similar to all arthroplasties, the literature has advanced more slowly than the technology resulting in challenges in analyzing the literature for purposes of evidence-based guidance.

#### *Knee Arthroplasty for Moderate to Severe Arthritides*

### **Knee arthroplasty is strongly recommended for severe arthritides.**

*Indications* – All of the following present: 1) severe knee degenerative joint disease that is unresponsive to non-operative treatment (rare cases may include osteonecrosis of the distal femur or tibial plateau with collapse or lack of response to non-operative treatment); 2) sufficient symptoms and functional

limitations, such as impairments of activities of daily living or occupational tasks, and 3) failure to successfully manage symptoms after a prolonged period of a conservative management plan that included NSAIDs, exercise, physical or occupational therapy, and where appropriate, weight reduction, intraarticular viscosupplementation, and corticosteroids. Carefully selected patients may be candidates for bilateral arthroplastic procedures. However, particular attention should be paid to pre-operative medical fitness and psychological fortitude.

*Strength of Evidence – Strongly Recommended, Evidence (A)*

*Unicompartmental Knee Arthroplasty for Largely Unicompartmental Disease*

**Unicompartmental arthroplasty is recommended for largely unicompartmental disease.**(1597, 1598)

*Strength of Evidence – Recommended, Evidence (C)*

*Knee Arthroplasty for Bilateral Disease*

**For bilateral disease, carefully selected patients may safely undergo simultaneous bilateral knee replacement.**

*Strength of Evidence – Recommended, Evidence (C)*

*Autologous Blood Re-infusion Systems*

**Autologous blood re-infusion systems are moderately recommended for arthroplasty patients.**

*Strength of Evidence – Moderately Recommended, Evidence (B)*

*Rationale for Recommendations*

There are numerous trials that have been performed of arthroplasty.(1599-1682) There are no trials that have compared arthroplasty or other surgical procedures with non-operative management. However, all quality trials have reported marked improvements in all surgical arms of the trials, thus arthroplasty is strongly recommended for select patients who fail non-operative management.

For largely unicompartmental disease, one moderate-quality trial has reported 5 and 15 year follow-ups and found better range of motion and “excellent” results with unicompartmental arthroplasty compared with total joint arthroplasty.(1597, 1598) Thus, unicompartmental arthroplasty is recommended for that select group of patients. One trial has compared high tibial osteotomy with unicompartmental arthroplasty and found that arthroplasty resulted in a longer time to failure, as defined as total joint arthroplasty, but most results were reasonably comparable.(1683)

There are several trials of surgical approaches, but data somewhat conflict. A quadriceps sparing or subvastus approach has been found to result in superior short-term results or trends towards superiority in most(1684-1687) but not all trials.(1688) Two older trials were negative.(1689, 1690) A mini-incision medial parapatellar approach has also been found to be associated with a shorter hospital stay in one trial,(1691) but was not found to be superior to a quadriceps sparing approach in another trial.(1692) As there are minimal differences in outcomes, there is no recommendation, although the subvastus approach has some evidence of very short-term superiority.

Computer navigation systems have been reported in many studies and quality trials.(1672, 1693-1705) Short-term results include better function,(1699) worse function,(1706) and no differences in fat emboli.(1705) All trials that have reported on alignment found superior anatomic alignment with those systems. Superior alignment is presumed to result in superior outcomes long-term; however, to date only one trial has reported some results suggesting better outcomes at 1 year.(1693) While the reduction in malposition is hopeful, the increased cost and the lack of data to support a change in failure rate result in no formal recommendation for or against those systems.

Different prosthetic designs have been reported in quality trials.(1707-1715) (1716) Components have also been coated, uncoated, cemented and uncemented.(1717-1737) Quality trials demonstrating clear superiority of one design over another are not reported. Cemented prostheses tend to migrate less in the short term, but over the intermediate term, cemented prostheses migrate equivalent amounts, and longer term results are unclear comparing the two options.

Patellar resurfacing has been used in conjunction with arthroplasty. There are numerous trials that have been performed with durations of follow-up exceeding 10 years in two studies. A high-quality study found comparable results regardless of whether the patella was resurfaced or not.(1738) Moderate-quality trials also found no differences in outcomes for patellar resurfacing compared with patellar retention/non-resurfacing.(1739-1751) Four of the trials suggested modestly better results with patellar resurfacing that included less anterior knee pain and less need for reoperation.(1752-1755) Available studies have also suggested appearance of the patella does not predict need for resurfacing. Thus, there is no recommendation for or against patellar resurfacing; however, some caution appears warranted in the surgical performance of patellar resurfacing, particularly as complications that are difficult to treat may occur though infrequently.

Autologous blood reinfusion systems have been shown to reduce transfusion needs of patients in all studies.(1756-1762) Two low-quality trials also suggest efficacy,(1763, 1764) and thus autologous blood re-infusion systems are moderately recommended.

Drains have been used indwelling, as well as intraarticular.(1765-1772) One moderate-quality trial of hip and knee arthroplasty patients reported not using drains and found no advantage to drains.(1766) Comparative data suggest no differences in outcomes. Drains that have used higher suction pressures have resulted in greater fluid removal,(1767) but no documented improvements in outcomes. Thus, there is no recommendation for or against drains. There is evidence that drains become colonized within 48 hours and thus provide a theoretical conduit for infection, and prompt removal is generally indicated.

Tourniquets have been used to keep the operative field free of blood, but concerns about failure to identify bleeders after tourniquet release and subsequent impairments of lower extremity function have been addressed in research studies.(1773-1781) Two trials have compared tourniquet use with no tourniquet use.(1776, 1782) One high-quality trial suggested comparable results although there was earlier straight-leg raising capacity in the non-tourniquet group.(1782) The second study reported moderate to heavy bleeding issues in 15% without use of a tourniquet, but otherwise good outcomes.(1776) Other trials evaluated early tourniquet release vs. late release and have variously reported early release resulted in superior function,(1773) trends towards more complications in the late release group,(1773, 1775) and modestly higher blood loss with early release.(1777) Another trial found no differences between tourniquet at 350mm Hg vs. systolic blood pressure plus 100mm Hg,(1781) suggesting lower pressures may be preferable.

Infected prostheses are catastrophic events and infectious disease precautions including at least some barrier methods (e.g., surgical 'moon suits,' surgical masks, ventilation) combined with antibiotics are universally utilized. Antibiotic impregnated cement combined with intravenous antibiotics is used. There is increasing use of air flow controls(1783) and supplied air in operating suites to attempt to reduce these infections.

#### *Evidence for the Use of Knee Arthroplasty*

There are 10 high- and 144 moderate-quality RCTs or crossover trials incorporated into this analysis. There are 30 low-quality RCTs in Appendix 1.

## **Bisphosphonates and Calcitonin**

Bisphosphonates have been used to attempt to reduce periprosthetic bone resorption in the immediate peri-operative period.(1730, 1784, 1785) Calcitonin has been used to attempt to develop better healing after hip fracture fixation.(1786)

### *Routine Peri-operative Use of Bisphosphonates*

**There is no recommendation for or against the routine peri-operative use of bisphosphonates.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Routine Post-operative Use of Calcitonin*

**There is no recommendation for or against the routine post-operative use of calcitonin.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Rationale for Recommendations*

Multiple studies have shown less bone loss with cemented prostheses.(1787-1790) A high-quality trial of intranasal calcitonin also found better healing after internal fixation of hip fractures compared to placebo.(1786) However, these studies are of short-term duration and there is no long-term follow-up. Thus, the utility of these medications for this purpose is unclear. Among those patients with osteoporosis however, these medications may be indicated.

### *Evidence for the Use of Bisphosphonates and Calcitonin*

There are 1 high- and 4 moderate-quality RCTs incorporated in this analysis.

## **Antibiotics**

Antibiotics have been utilized systemically and added to cement for many years.(1791-1814)

### *One-day Use of Systemic Antibiotics for Knee Surgery*

**One-day use of systemic antibiotics is moderately recommended for patients undergoing surgical knee procedures.** Antibiotic-impregnated cement also appears effective compared with cement without antibiotics with evidence particularly in the hip and by inference assumed likely to be true of the knee as well.

*Strength of Evidence – Moderately Recommended, Evidence (B)*

### *Rationale for Recommendation*

There are trials comparing multiple doses with a single day of antibiotics, (1815) finding no differences in outcomes. This is a similar finding to the hip as there is evidence from a non-randomized registry data of 10,905 hip prostheses that the risk of revision due to infection was reduced 75 to 78% with a systemic antibiotic combined with antibiotic-impregnated cement compared with either systemic antibiotic administration or antibiotic-impregnated cement alone.(1816) The risk, if there was only antibiotic in the cement, was 6.3-fold higher, and, if the antibiotic was only systemic risk, was 4.3-fold greater. There is a belief that some cases of aseptic loosening are undiagnosed infections(1796) as there were lower rates of aseptic loosening among those with both routes of antibiotic administration compared with either alone(1816) and those with gentamicin cement appear to have lower rates of aseptic loosening compare with systemic antibiotics.(1817, 1818) Thus, there is quality evidence that a combination of systemic and antibiotic-impregnated cement is important to prevent infections.

### *Evidence for the Use of Antibiotics*

There are 2 high-quality and 10 moderate-quality RCTs incorporated into this analysis. There are 4 low-quality RCTs in Appendix 1(1778, 1819-1821) (see Hip and Groin Disorders guideline for additional studies).

### **Glucocorticosteroid Injections after Arthroscopy and Meniscectomy**

Intra-articular glucocorticosteroid injections are frequently performed after arthroscopy and meniscectomy.(1485)

#### *Glucocorticosteroid Injections after Arthroscopy*

**Intraarticular glucocorticosteroid injections are recommended for select patients after arthroscopy and meniscectomy.**

*Indications* – Patients undergoing arthroscopy, particularly if osteoarthritis is identified and patient is believed to potentially benefit from glucocorticoid injection, although there may be no long-term benefit.(1485)

*Frequency/Dose/Duration* – Injection performed at end of procedure.

*Strength of Evidence* – **Recommended, Evidence (C)**

#### *Rationale for Recommendation*

Two moderate-quality trials suggest superior short-term results from injection with glucocorticosteroid if chondromalacia is identified,(1485) or compared with placebo among patients with osteoarthritis.(1486) There is generally no additional invasiveness of this adjunctive procedure and the complication rate (primarily due to infection) is believed to be quite low. As there is evidence of efficacy,(1325) these injections are recommended.

#### *Evidence for the Use of Glucocorticosteroid Injections after Arthroscopy and Meniscectomy*

There are 3 moderate-quality RCTs incorporated into this analysis.

### **Periarticular Glucocorticosteroid Injections for Arthroplasty Patients**

Periarticular glucocorticoid injections have been used for arthroplasty patients.(1488)

#### *Periarticular Glucocorticosteroid Injections for Arthroplasty Patients*

**There is no recommendation for or against the use of periarticular glucocorticosteroid injections for arthroplasty patients.**

*Strength of Evidence* – **No Recommendation, Insufficient Evidence (I)**

#### *Rationale for Recommendation*

There is one moderate-quality trial comparing a mixture of pharmaceuticals with and without a glucocorticosteroid.(1488) While most outcomes including pain scores and narcotics consumed were negative, the length of hospital stay was inexplicably shorter in the steroid group and produced a mixed picture regarding efficacy of this intervention. Thus, there is no recommendation for or against these injections.

#### *Evidence for the Use of Periarticular Glucocorticosteroid Injections for Arthroplasty Patients*

There is 1 moderate-quality RCT incorporated into this analysis.

## PRE- AND POST-OPERATIVE REHABILITATION PROGRAMS FOR KNEE ARTHROPLASTY

Numerous studies have evaluated post-operative rehabilitation and activity levels that appear important for recovery from knee procedures, especially for arthroplasty.(1839, 1840) Considerations have included pre-operative exercise programs, post-operative activity limitations, post-operative rehabilitation programs and late rehabilitation programs several months after surgery.(1841, 1842) Compliance is noted to be problematic.

### Preoperative Education

Educational interventions have been utilized for rehabilitation of arthroplasty patients, particularly for pre-operative preparation.(1822-1824) These interventions may include various combinations of procedural, sensory information, cognitive coping strategies, reassurance, and relaxation and hypnosis training.(1825, 1826) Multiple modes of instruction are frequently incorporated, including oral, written, and video.

#### *Pre-operative Educational Program Prior to Arthroplasty*

**A pre-operative educational program is moderately recommended prior to arthroplasty.** Components should include procedural and recovery information and use at least two modes of teaching (e.g., oral and written).

*Strength of Evidence – Moderately Recommended, Evidence (B)*

#### *Rationale for Recommendation*

Most studies of educational interventions involved hip and not knee patients and have demonstrated benefits.(565, 1827-1829) Lengths of contact have ranged widely, although most studies do not report educational contact time. Some programs encourage involvement of family members and other care givers. Better post-operative compliance with rehabilitation has been shown in patients who have participated in educational interventions.(1830) Numerous studies have combined exercises and other interventions with educational interventions. However, nearly all studies reporting length of hospital stay have shown earlier hospital discharge after hip arthroplasty with educational interventions.(1822-1824, 1831, 1832) Other studies have shown earlier performance of activities such as stair climbing(1833) and reductions in pain and anxiety.(1834)

#### *Evidence for the Use of Pre-operative Education Prior to Arthroplasty*

There are 12 moderate-quality RCTs incorporated in this analysis. There are 5 low-quality RCTs in Appendix 1.(1822, 1835-1838)

## PRE-OPERATIVE EXERCISE

Pre-operative exercise programs have been prescribed to attempt to improve arthroplasty results and reduce complications.(1828, 1833, 1843-1849)

#### *Pre-operative Exercise Program*

**A pre-operative exercise program particularly emphasizing cardiovascular fitness and strengthening prior to knee arthroplasty is recommended for a select, fairly small minority of patients who exhibit evidence of considerable weakness, debility or unsteady gait. Flexibility components may be reasonable in those without fixed deficits.**(1833, 1846, 1848)

*Indications* – Highly select pre-operative arthroplasty patients who have considerable muscle weakness and/or debility, particularly sufficient weakness to have impairments such as unsteady gait or difficulty with ADLs.

*Frequency/Duration* – Most program elements require an initial appointment to teach exercises followed by a home exercise program prescription. Two or 3 follow-up appointments for adherence and additional exercise instruction may be needed. Patients with severe deficits may require 2 to 3 appointments a week for 4 to 6 weeks in advance of arthroplasty.(1848) Patients with minimal deficits may benefit from a single appointment to teach programmatic elements for a self-directed program.

*Indications for Discontinuation* – Achievement of program goals, resolution of strength or gait deficits, intolerance or other adverse effects.

***Strength of Evidence – Recommended, Insufficient Evidence (I)***

***Rationale for Recommendation***

There are few quality trials that evaluate pre-operative exercise programs for the treatment of knee arthroplasty, and there is no consistent evidence of benefits in either knee or hip arthroplasty patients.(1850, 1851) One trial has suggested benefits, but most have not.(588, 1852) One moderate-quality study demonstrated there were benefits from a 6-week pre-operative exercise program that consisted of several elements broadly including cardiovascular, strengthening and flexibility exercises with 30 to 60-minute sessions 3 times a week.(1848) The benefits included reduced post-operative complications, earlier discharge and higher probability to be discharged directly to the patient's home. A second moderate-quality study demonstrated benefits of a peri-operative exercise program and also demonstrated benefits lasting 6 months after surgery.(1846) Another moderate-quality study was reported as negative using the author's main outcome of changes in Harris Hip Scores. However, all 5 post-operative milestones (e.g., walking, chair transfer, stair climbing) statistically favored the exercise group.(1833) Pre-operative rehabilitation may be useful as a component of pre-operative education and exercise programs for selected high risk, deconditioned patients. However, most typical patients do not require preoperative programs.

***Evidence for the Use of a Pre-operative Exercise Program***

There are 4 moderate-quality RCT incorporated in this analysis. There is 1 low-quality RCT in Appendix 1.

## **POST-OPERATIVE REHABILITATION**

Exercise, physical therapy and rehabilitation have been used pre-operatively as well as post-operatively for rehabilitation of arthroplasty patients.(580, 1850, 1851, 1853-1858) Continuous passive-motion machines have also been used in rehabilitation of arthroplasty patients.(1859, 1860)

***Post-Operative Rehabilitation of Knee Arthroplasty Patients***

**Post-operative rehabilitation is recommended for knee arthroplasty patients.**

***Strength of Evidence – Recommended, Insufficient Evidence (I)***

*Indications* – Patients having undergone knee arthroplasty.

*Duration* – Treatment may need individualization based on factors including pre-operative conditioning and immediate post-operative results. Treatment is often daily while hospitalized, then 2 to 3 sessions a week. One trial suggested an educational kneeling intervention had demonstrable long-term benefits.(1854) Three trials have suggested benefits of accelerated and/or early rehabilitation.(1839, 1855, 1861)

*Indications for Discontinuation* – Achievement of goals, non-compliance with clinic or home-based exercises or intolerance.

*Continuous Passive Motion for Knee Arthroplasty Patients*

**Continuous passive motion is not recommended for routine use for arthroplasty patients. It may be useful for select, substantially physically inactive patients post-operatively.**

*Strength of Evidence* – **Not Recommended, Evidence (C)**

*Rationale for Recommendations*

Most of the available quality trials concern continuous passive-motion (CPM) devices in the immediate post-operative period.(1862-1867) This literature base has many older, lower quality trials(1307, 1860, 1868-1878) (see Appendix 1). Trials comparing CPM with splinting have suggested efficacy.(1879) However, over the past 25 years, patients have gradually been ambulated earlier and are now generally placed on immediate weight bearing status, which appears a likely reason that both of the more recent and higher quality studies have failed to show benefits from use of CPM.(1862, 1863) This device is likely preferable to no activity; however, for most patients, active exercise appears superior. Thus, CPM is not recommended for most patients, but it may retain some utility for selected, relatively inactive patients in the immediate postoperative period.

Accelerated rehabilitation programs have been assessed and appear to be superior to usual care(1839, 1855, 1861) or CPM.(1880) There is no demonstrable difference between clinic- and home-based rehabilitation programs or between home and hospital-based care after arthroplasty.(1881, 1882) One trial has suggested neuromuscular electrical stimulation was not of significant additive benefits.(1883) Exercise and rehabilitation are not invasive, have low adverse effects, and are moderately costly, depending on numbers of appointments required; thus, they are recommended for select patients who have functional deficits.

*Evidence for the Use of Post-operative Rehabilitation*

There is 1 high- and 12 moderate-quality RCTs incorporated into this analysis. There are 13 low-quality RCTs in Appendix 1.

## **Post-Operative Activities and Sports**

There is a greater volume and quality of literature on post-operative hip arthroplasty patients than knee arthroplasty patients(1797) (see Hip and Groin Disorders guideline). Researchers summarizing this literature have concluded there is somewhat less return to sports in knee than hip arthroplasty patients.(1884, 1885) There are three primary methods to assess appropriate sports or activities for knee arthroplasty patients: epidemiological studies, biomechanical models, and experimental studies. While there are more hip data, the available studies for the knee also produce conflicts that are not readily resolved. Since the evidence conflicts and the epidemiological studies are the gold standard for the development of quality guidance,(1886-1888) this review emphasizes epidemiological studies.

There are many studies suggesting sizable proportions of individuals successfully returning to sports and manual labor, including high impact sports that have not been generally recommended for these patients. One study has suggested 91% of knee arthroplasty patients return to low impact sports compared with 20% to high impact activities.(1889) A small case series reported no apparent complications with high impact sports, including jogging, downhill skiing, tennis, racquetball, squash and basketball, although it may be underpowered for adverse effects.(1890) One study found 16% of

arthroplasty patients were involved in heavy manual labor or sports that were “not recommended” by the Knee Society.(1891, 1892) Yet, there are neither randomized controlled trials of returning to sports,<sup>xv</sup> nor are there large prospective cohort studies that have used return to sports as a primary indicator, thus the overall quality of this literature from which to draw conclusions is quite limited. Data for hip arthroplasty patients is similarly conflicted (see Hip and Groin Disorders guideline).

One concern has been increased wear rates for prosthetic joints subjected to sports or manual labor. While joint use has been thought to be an important factor, the evidence is primarily derived from biomechanical studies and not quality epidemiological studies with large sample sizes. Wear rates for knee arthroplasties are reportedly worse with activity reported in a small necropsy study.(1893) However, that study which also evaluated multiple factors found body mass index as the most important factor, which creates a conflict between physical activity and body mass index. Another large case series reported worse outcomes with increased body mass index, higher Deyo-Charlson index, female gender, age over 80 years and comorbidities.(1894) Younger patients are presumed to be more active on average than older patients, yet such a cohort of younger active patients reported a 94% 18-year arthroplasty survival rate.(1895) Thus, the importance of activity for joint survival is somewhat unclear.

Among unicondylar knee arthroplasty patients, one report noted 93 to 95% of patients returned to sports.(1896, 1897) Others have similarly found more patients with unicondylar arthroplasties return to sports compared with total knee arthroplasty patients,(1898) although these studies could be confounded by other factors.

A related issue is lack of use after arthroplasty from fear of use or fear of excessive wear, which could worsen outcomes and incur worse health outcomes associated with inactivity. For example, one descriptive study found few golfers walked the course after arthroplasty and suggested education to increase exercise is needed.(1899) Among the determinants of post-operative activity levels, pre-operative condition is thought to be an important, if not the most important factor.

Operative approaches in relation to return to sports have not been well studied, although evidence suggests minimal differences in return to usual functions (see Arthroplasty above). Minimally invasive approaches have been hypothesized to potentially be better for return to sports activity, particularly in the early phases. No differences by type of operation have been found.

The Knee Society survey of opinions on returning to sports(1900) included the following sports recommendations by category: recommended allowed sports were low impact aerobics, stationary bicycling, bowling, golfing, dancing, horseback riding, croquet, walking, swimming, shooting, shuffleboard, and horseshoes. Sports allowed with experience were road bicycling, canoeing, hiking, rowing, cross country skiing, speed walking, tennis, weight machines and ice skating. Sports not recommended were racquetball, squash, rock climbing, soccer, singles tennis, volleyball, football, gymnastics, lacrosse, hockey, basketball, jogging, and handball. Sports with no conclusion were fencing, roller blading/in-line skating, downhill skiing, and weight lifting. However, these recommendations do not necessarily conform with epidemiological evidence (see above).

Studies on prosthetic wear rates have been used to imply appropriate work limitations for the post-arthroplasty patient. However, no quality studies have been reported that address the appropriateness of work limitations. Additionally, the avocational studies reviewed above do not provide quality

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<sup>xv</sup>Almost no RCTs have addressed return to activity other than a number of post-operative rehabilitation studies such as a study of ergometer cycling that found it ineffective in contrast with hip rehabilitation (see Hip and Groin Disorders guideline).

evidence in support of activity limitations. Thus, although reduced return-to-work status has been reported among patients with more physically demanding work, there is not a strong rationale for work restrictions in the post-surgical knee population.

#### *Post-Operative Vocational or Avocational Activities*

**There is no recommendation for or against specific vocational or avocational pursuits post-operatively.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

#### *Rationale for Recommendation*

Quality evidence does not sufficiently support evidence-based guidance and therefore there is no recommendation for or against specific vocational or avocational activities.

#### *Evidence for the Use of Vocational or Avocational Activities*

There are no quality studies evaluating the use of vocational or avocational activities.

## **Psychological Services**

Psychological issues appear to be substantially less prevalent among patients with osteoarthritis compared with spine disorders for unclear reasons. Thus, psychological services are rarely needed for knee pain patients (see Chronic Pain guideline for further discussion of psychological evaluation).

## **Psychological Evaluation**

#### *Psychological Evaluation for Chronic Knee Pain*

**A psychological evaluation is recommended as part of the evaluation and management of patients with chronic knee pain with any of the below indications in order to assess whether psychological factors will need to be considered and treated as part of the overall treatment plan.**

*Indications* – 1) Knee pain or dysfunction that persists longer than typical for the condition; 2) disability or impairments thought to be disproportionate to usual or expected findings; 3) demonstration or suspicion of significant psychosocial dysfunction; 4) medication issues and/or drug problems(1901-1904); 5) current or premorbid major psychiatric symptoms or disorder thought to be impacting disorder; 6) non-compliance with the prescribed treatment regimen; or 7) experiencing delayed functional recovery.

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## **Cognitive Behavioral Therapy**

#### *Cognitive Behavioral Therapy (CBT) for Patients with Subacute or Chronic Knee Pain*

**Cognitive-behavioral therapy is recommended as an adjunct to an interdisciplinary program for treatment of subacute or chronic knee pain.**

*Indications* – Specific indications for CBT in chronic pain conditions are:

1. Management of clinically significant behavioral aberrations and/or anxiety during opiate weaning or detoxification;
2. A component therapy integrated into an interdisciplinary or other functional restoration program;
3. Clinically significant problems of noncompliance or non-adherence to prescribed medical or physical regimens;

4. Vocational counseling for resolution of psychosocial barriers in return to work (requires a current or imminent medical release to return to work);
5. Resolution of interpersonal, behavioral, or occupational self-management problems in the workplace, during/after return to work, where such problems are risk factors for loss of work or are impeding resumption of full duty or work consistent with permanent restrictions.

*Frequency/Duration* – Therapy provided for the above indications should be limited to 6 sessions or less. When therapy is provided as a component of an interdisciplinary or functional restoration program, the number of sessions is based on the needs of the program to provide relevant treatment objectives.

*Indications for Discontinuation* – Noncompliance, failure to obtain functional or behavioral improvement, or resolution of problems.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

#### *Rationale for Recommendations*

There are no quality studies specifically addressing knee pain as nearly all studies evaluated low back pain patients (see Chronic Pain and Low Back Disorders guidelines). Psychological assessments are routinely accomplished for the purposes given above, including treatments for which various levels of evidence are provided herein, e.g., functional rehabilitation or interdisciplinary pain programs, candidacy for certain procedures, or chronic use of opioid medications. Evaluations are moderate cost and, when done appropriately, present little risk of harm.

#### *Evidence for the Use of Psychological Evaluations/Cognitive-Behavioral Therapy*

There are no quality studies evaluating the use of psychological evaluations for patients with chronic knee pain. However, there are quality studies evaluating spine patients (see Low Back Disorders and Chronic Pain guidelines).

## **REHABILITATION FOR DELAYED RECOVERY**

### **Biofeedback**

Biofeedback is a behavioral medicine method providing automated information and training to improve control of certain physiologic processes which are normally inaccessible to a subject's perception. Biofeedback most commonly involves surface EMG input to a monitor with audible or visual feedback of the degree to which there is muscle activity.(1905) Through this feedback, the patient may learn to control the degree of muscle contraction.

#### *Biofeedback for Chronic Knee Pain*

**There is no recommendation for or against the use of biofeedback for chronic knee pain.**

*Strength of Evidence* – **No Recommendation, Insufficient Evidence (I)**

#### *Rationale for Recommendation*

Biofeedback is not invasive, has no complications, and is moderately costly. However, there are other efficacious treatment strategies.

#### *Evidence for the Use of Biofeedback*

There are no quality studies for use of biofeedback for treatment of knee pain patients.

## **Functional Restoration**

Functional restoration is both a type of interdisciplinary pain management and rehabilitation program and a general approach to medical care. Fundamental elements of a functional restoration approach include assessment of the patient's dynamic physical and functional status including traditional tests for strength, sensation, and range of motion. Psychosocial strengths and stressors must also be assessed including the patient's support system, evidence of mood disorders, medication use, presence of litigation, work capacity, and assessment of education and skills. Following this evaluation, the emphasis is on expectation management, directed conditioning and exercise, cognitive behavioral therapy, setting functional goals and decreased medication use. An ongoing assessment of patient participation and compliance (with documentation of complicating problems and progress toward specific goals, including reduction in disability and medical utilization) is needed.

In functional restoration, the treatment team members are educators. Passive therapies and invasive interventions are de-emphasized while home exercise/self-management efforts are stressed. There should be a shift of health, function, and well-being responsibility (locus of control) from physicians and therapists to the patient. A functional restoration approach may include the limited/adjunctive use of medications and interventional measures (where specifically indicated) however, these should not be viewed as ongoing solutions. It may also involve institution of preventive measures, education for relapse prevention, proper activity and work pacing, ergonomic accommodation, and when appropriate, transitional return to employment.

Functional restoration's goals are returning to a productive life despite having a chronic pain problem and mitigation of a patient's suffering. If an individual fails to recover within the appropriate biological healing time frame, the acute care paradigms of specific diagnosis and treatment change to biopsychosocial approaches that address pain, function, work, and psychological factors impeding progress. Treatment programs focus on restoration of work-related function. These programs include work conditioning and work hardening, interdisciplinary pain rehabilitation programs and functional rehabilitation. Because functional restoration is an approach, not just a specific program, the approaches taken both overlap on a continuum.

## **Work Conditioning, Work Hardening, AND Early Intervention Programs**

Work conditioning and work hardening programs are often recommended for patients who are not able to return to work because of persistent symptoms and functional limitations following acute care and rehabilitation. Early intervention functional restoration programs are sometimes recommended during the first 3 to 6 months if the injured worker is noted to have increased risk factors and evidence of delayed recovery. These risks and delays suggest that a more coordinated functional restoration approach with a psychosocial emphasis is needed beyond conditioning or hardening alone.

### **Work Conditioning and Work Hardening Programs**

Differentiating work conditioning from work hardening is problematic as the terms are sometimes used interchangeably. The American Physical Therapy Association (APTA) defines work conditioning as "an intensive, work-related, goal-oriented conditioning program designed specifically to restore systemic neuromusculoskeletal functions (e.g., joint integrity and mobility, muscle performance (including strength, power, and endurance), motor function (motor control and motor learning), range of motion (including muscle length), and cardiovascular/ pulmonary functions (e.g., aerobic capacity/endurance, circulation, and ventilation and respiration/gas exchange)." (1906) APTA classifies work conditioning as a single-discipline program and work hardening program as interdisciplinary. The Commission on

Accreditation of Rehabilitation Facilities (CARF) defines occupational rehabilitation as work conditioning, and comprehensive occupational rehabilitation as work hardening. Although not universally accepted, some physicians consider work conditioning as a generalized endurance and strengthening program that includes work simulation activities, whereas work hardening is a program where a specific job has been identified and stresses involvement in sets of occupationally-related tasks and functional activities that are directly related to a patient's work. Work conditioning and work hardening programs in the U.S. are heterogeneous and are often provided by a single-therapy discipline, either physical or occupational therapy.(1907-1909)

Work conditioning and work hardening programs generally involve structured programs of gradually increased levels of exertion to bridge a significant gap between the patient's current physical or perceived capabilities and the requirements needed to return to everyday activities and work. Regardless of the terminology used, the most successful programs involve a detailed appreciation of the worker's capabilities, a detailed knowledge of the job physical requirements (if possible, obtained from on-site analysis or familiarity), and individualization of the program to address specific deficits that are barriers to return to work. These programs can be somewhat heterogeneous with varying components and there is some overlap with multidisciplinary programs.

Work conditioning and work hardening programs focus on increasing physical efforts, using fear avoidance belief training if necessary. These programs may also use a cognitive-behavioral model and overlap with early intervention programs. In the majority of return-to-work situations, work conditioning or work hardening programs are not required as the gap between worker abilities and capabilities are not sufficiently large to justify either the time or expense. These programs are generally utilized for workers involved in significant demanding jobs for the knees that may include materials handling tasks that commonly involve high-force expenditures or highly repetitious activities. Not infrequently, work conditioning or work hardening programs are the next step after conventional physical or occupational therapy is exhausted and a gap remains to return the patient back to work, particularly in the subacute pain setting. These programs are also utilized for patients who have tried to return to work but failed due to either the gap between abilities and capacities or the lack of modified duty in physically demanding occupations. These programs are not invasive and have low adverse effects, but are moderate to high cost depending on program length.

Patients who may benefit from work conditioning or hardening include those who: 1) remain completely off work or are on modified duty for 6 to 12 weeks; 2) have not responded to less costly interventions including a 4 to 6 week physical or occupational therapy program or a graded therapy program of at least 6 to 8 weeks that includes aerobic and knee strengthening exercise components; 3) have a stated strong interest and expectation to return to work; 4) involve cooperation of the employer; 5) are supervised by a qualified physical or occupational therapist; 6) have had a careful assessment of their occupational demands; 7) have a FCE that indicated appropriate performance effort and consistency at a level of work lower than that to which they need or wish to return; and 8) are in a program that includes a cognitive-behavioral approach with a focus on function rather than pain, a conditioning or aerobic exercise component and simulated graded work tasks, and is tailored to their needs and identifies gaps between current capabilities and job demands.

### **Early Intervention (Functional Restoration) Programs**

Early identification and appropriate management of patients exhibiting signs of delayed recovery is believed to decrease the likelihood that they will go on to develop chronic pain.(1910) These patients may benefit from a limited but intense program of physical restoration with a strong emphasis on education that identifies barriers to recovery and return to work. They may require an abbreviated early

intervention interdisciplinary rehabilitation program (IPRP), preferably using functional restoration principles, rather than a longer program utilized for more complex cases. Early intervention programs are an alternative to work conditioning and work hardening programs for subacute or patients with early chronic pain who have evidence for delayed recovery with an increased need for education and psychological assessment and intervention. These programs are usually appropriate in cases of work incapacity lasting 3 to 6 months. The interdisciplinary functional restoration program used for early intervention contains the features of a functional restoration IPRP, but involves lower intensity and duration of services than a program for patients with greater chronicity of disability. The type, intensity, and duration of services is dictated by the patient's unique rehabilitation needs and may be used for those who fail work conditioning and work hardening programs, usually within 6 months of onset of disability post-injury. The time frame of 3 to 6 months post-injury is vital for intervening with the most effective treatment possible in order to avoid the negative sequelae that come with increasing duration of disability. During this time, normal musculoskeletal healing generally occurs, eliminating any remaining physical barriers to intensive rehabilitation. Such programs are appropriate for prevention, before the patient is entrenched in a chronic pain syndrome or before severe pain and illness behavior evolves.

*Work Conditioning, Work Hardening, or Early Intervention Programs for Chronic Knee Pain Syndromes*  
**Work conditioning, work hardening, and early intervention programs are recommended for treatment of chronic knee pain syndromes.**

*Frequency/Duration* – Three (3) to 5 times a week for work conditioning and early intervention programs; daily for work hardening. Weekly evaluations demonstrating sufficient levels of physical effort and consistency, compliance with the plan of care, and functionally significant progress toward the return-to-work goal must be documented to justify continuation. Program length and intensity is dictated by each patient's unique rehabilitation needs.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

#### *Rationale for Recommendation*

There are no quality studies of knee pain patients and limited evidence that work conditioning, work hardening, or early intervention programs are effective for chronic spinal pain, nevertheless there is a longstanding belief and experience that they are highly effective. While there is potential for overlap, work conditioning, work hardening, and early intervention are distinct programs and are not intended for sequential use, although this might be appropriate in certain situations depending on program components. In acute cases, where delayed recovery is not an issue, these programs are inappropriate. In more chronic cases, particularly with pain and illness behavior and a high level of reported dysfunction, a more intense IPRP should be considered. Although less costly, work conditioning, work-hardening, and early intervention programs do not need to be attempted before moving to an IPRP as long as a quality interdisciplinary program with proven outcomes is accessible to the patient. Program choice depends on availability and matching patient needs to the services offered to provide the most cost-effective and beneficial outcome. Hence, these programs might provide the greatest potential impact when used to manage patients during the subacute phases of injury, although they might also be appropriate for use in those with chronic pain who do not, after evaluation, have significant psychosocial factors contributing to their clinical presentation.

#### *Evidence for the Use of Work Conditioning, Work Hardening, and Early Intervention Programs*

There are no quality studies evaluating the use of work conditioning, work hardening, and early intervention programs for chronic knee pain.

## INTERDISCIPLINARY PAIN REHABILITATION PROGRAMS

An interdisciplinary pain rehabilitation program (IPRP) is a type of chronic pain management program that uses a biopsychosocial paradigm (preferably employing a functional restoration approach), that can enhance function, reduce pain and illness behavior, and mitigate chronic pain associated disability. These programs are intended to manage psychological, social, physical and occupational factors and are discussed in detail in the Chronic Pain guideline. All IPRP programs involve an integrated team of professionals who provide intensive, coordinated care. This team may include physical and occupational therapists, psychologists, vocational counselors, nurses, and case managers. Quality programs emphasize functional recovery and active, progressive physical activity and generally involve intensive 5-days-a-week treatment regimens that should be individualized. **All medical and therapy services must be supervised by a physician who is directly involved with the program and regularly interviews and examines the patient for relevant parameters.** For reasons that are unclear, there appear to be few lower extremity pain patients, including knee pain patients who require these programs. Nevertheless, a minority of patients may derive benefits (see Chronic Pain guideline).

### *IPRPs for Chronic Knee Pain*

**A multidisciplinary or interdisciplinary program (IPRP) with a focus on behavioral or cognitive-behavioral approaches combined with conditioning exercise is recommended for patients who due to chronic knee pain demonstrate partial/total work incapacity.**

*Indications* – Chronic knee pain in patients who are not working, or unable to return to full duty, and have significant, pain-related limitations in activities of daily living. Patients should have failed other standard approaches (e.g., physical therapy, occupational therapy, interventions, medication) and have reasonable probability of recovery.

*Frequency/Duration* – Median 20 days, with trial of the first 10 days to assess patient compliance, attendance, and progress. Program duration is variable due to the patient's needs, the rehabilitation strategies used, and the demonstrated program outcomes. IPRP treatment is generally provided 5 full days per week, though slightly fewer hours and longer calendar durations are utilized in some programs. Complicating problems involving activities of daily living (such as coordinating part-time employment, transportation, or child care needs) or limitations imposed by co-morbid medical conditions which preclude the patient from participating in the program full-time (thus preventing them an assessment at 10 days) are considerations that might necessitate program modification.

*Indications for Discontinuation* – Failure to improve, noncompliance, resolution of symptoms and disability, exhaustion of reasonable program duration for a specific condition.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

### *Rationale for Recommendation*

Participation in an IPRP to treat chronic knee pain patients has not been evaluated in quality studies. These programs may be helpful if there is medical need to wean the patient from opioids or other medications and/or if the patient has shown demonstrable clinical progress with less intense rehabilitation but “pain limitation” has impeded adequate recovery. Development of entrenched psychosocial barriers to recovery and a chronic pain syndrome as sequelae of the original physical components of the injury may be associated with this group of patients. Functional restoration might be appropriate, as well as vocational re-entry in positions not requiring the same job physical characteristics when all previous treatments have failed. With the possible exception of workplace-based interventions, most successful multidisciplinary programs appear to utilize either a cognitive-behavioral approach or involve psychologists.(1911-1914) While exercise is a major focus in many of these successful programs that primarily treat spine pain,(1911-1915) the one trial that compared a

graded exercise approach with a participatory ergonomics approach found exercise inferior.(1916) This suggests that of the options available, the participatory ergonomics approach may be superior to other approaches.(1917) These heterogeneous studies also suggest that multidisciplinary programs that focus on functional improvements are superior.

IPRPs of the types described in the literature are not invasive, have few adverse effects, but are high cost. Some U.S.-based programs involve significant interventions, but there is no documentation of superior outcomes from such programs which can cost \$20,000 to \$50,000. IPRPs are indicated for select, more severely affected patients, including those who have failed appropriate conservative management (e.g., appropriate medications, specific exercises, etc.). Generally, these referrals are most indicated in the early chronic pain management timeframe (3 to 6 months). However, there are times when earlier referral in the mid- to late-subacute interval is indicated. (Physicians should be aware that there is a belief that earlier referral results in higher probability of successful treatment, but that supposition has not been rigorously tested and is prone to a strong spectrum bias whereby all patients tend to do worse the longer they have a acute, subacute, or chronic pain condition.) Referrals beyond 6 months might also be indicated if there has been failure to progress with numerous interventions and there is reasonable expectation for potential benefits. Referrals during the subacute phase best occur when there is a quality program with proven outcome efficacy is available, the patient has documented delayed recovery, yet there is interdisciplinary assessment that the patient is likely to benefit from the program.

## PREVENTION OF VENOUS THROMBOEMBOLIC DISEASE

Venous thromboembolic disease (VTED) is a high-risk complication among post-operative knee and hip arthroplasty patients resulting in morbidity and mortality. This topic is extensively reviewed in the Hip and Groin Disorders guideline. Only the recommendations are reviewed here, and the reader is referred to the Hip and Groin Disorders guideline for further details.

Reported risk factors in these post-operative patients include age, general anesthesia, and obesity. There has been some review of risk of VTED from cement; however, the evidence conflicts.(1735, 1918) Treatments have included early ambulation (discussed elsewhere), compression boots or stockings(1919) and other methods,(1920) and medications.(1921-1929) There are currently four classes of medications used to prevent VTED: warfarin/ coumadin,(1930, 1931) low molecular weight heparin,(1932-1942) Factor Xa inhibitors,(1943) and direct thrombin inhibitors. (670) Of these options, all are currently available in the U.S. with the exception of oral direct thrombin inhibitors. While initially believed to be a complication of hospitalization, post-hospital discharge surveillance data suggest high risks of thromboembolism continue well after discharge,(1944) with many studies treating patients for 30 days for longer.

### *Prevention of Venous Thromboembolic Disease*

**Prevention of venous thromboembolic disease is strongly recommended for post-operative knee patients, particularly arthroplasty patients or other post-operative patients with prolonged reductions in activity. Early ambulation is recommended.**

*Strength of Evidence – Strongly Recommended, Evidence (A)*

### *Compressions Stockings for Prevention of Venous Thromboembolic Disease*

**The use of post-operative graded compression stockings is moderately recommended for the prevention of venous thromboembolic disease.(1945, 1946)**

*Indications* – All post-operative major knee surgical patients (e.g., knee fractures, knee arthroplasties, or any other patients thought at increased risk of VTED in the post-operative period).

*Duration* – Duration unclear and longer use does not add expense. As risk of VTED is high, particularly for these major procedures, threshold for use of 2 weeks or longer should be generally low.

*Strength of Evidence* – **Moderately Recommended, Evidence (B)**

*Lower Extremity Pumps for Prevention of Venous Thromboembolic Disease*

**The use of lower extremity pump devices is moderately recommended for the prevention of venous thromboembolic disease.**(1947-1950)

*Indications* – All post-operative major knee surgical patients (e.g., knee fractures, knee arthroplasties, or any other patients thought at increased risk of VTED in the post-operative period).

*Devices* – Devices include foot pumps, foot plus calf pumps, entire lower extremity intermittent compression devices and various other combinations. As there are no quality comparative trials, there is no recommendation for a particular device.

*Duration* – Duration unclear. Most have utilized devices for the duration of hospitalization. As risk of VTED is high, particularly for these major procedures, threshold for use of 2 weeks or longer should be generally low, including while at home.

*Indications for Discontinuation* – Discontinuation is generally recommended by 14 days unless there are continuing ongoing issues, such as delayed rehabilitation and ambulation that result in a judgment of increased risk. Some patients are also unable to tolerate devices.(1951)

*Strength of Evidence* – **Moderately Recommended, Evidence (B)**

*Low-molecular Weight Heparin for Prevention of Venous Thromboembolic Disease*

**Low-molecular weight heparin is strongly recommended for prevention of venous thromboembolic disease.**

*Indications* – Post-operative arthroplasty, knee fracture, and other major knee surgery patients, particularly those with either prolonged inactivity or prolonged reduced or sedentary activity levels.(1941, 1945, 1952-1962) There is some evidence LMWH is generally preferable to warfarin for VTED prophylaxis. Patients with prior reactions to LMWH should generally receive other treatments first.

*Dose/Frequency* – Subcutaneous injections of enoxaparin (Lovenox) 4,000 IU or 40mg SC QD(1945, 1952-1954, 1956, 1963-1968) for variable durations ranging from 5 to 9 post-operative days(1965-1967) to 8 to 14 days(1964) to 10 to 14 days,(1963) 21 days,(1952, 1953) 30 days,(1956) to 12 weeks.(1954) There is no consensus on duration of treatment, and individualization based on activity level appears indicated.

*Duration* – Duration unclear. Available quality studies utilized treatment courses ranging from 4 days(1960) to 12 weeks.(1954) A plurality of studies utilized a course of 30 to 35 days.(1955-1957, 1961) There is quality evidence that treatment is generally required beyond hospitalization; there is evidence of deep venous thromboses many months later (reviewed above). One quality trial suggested no benefits from extending 4 to 10 days treatment out to 12 weeks.(1958) In the absence of substantive quality data comparing various durations of treatment, it is suggested that approximately 30 days of treatment after surgery may be required for average patients (a single trial suggested 30 to 42 days after arthroplasty).(1944) Patients with prior histories of venous thrombi, prolonged inactivity, delayed recovery or recurrences of thromboses, or family histories of venous thrombi likely require longer

courses. Those with major risk of bleeding may warrant individualized shorter courses. Patients who regain activity rapidly may be appropriate candidates for shorter courses of treatment.

*Indications for Discontinuation* – Completion of course of treatment, development of major complication (e.g., major bleeding) or other adverse effect.

*Strength of Evidence* – **Strongly Recommended, Evidence (A)**

*Factor Xa Inhibitors for Prevention of Venous Thromboembolic Disease*

**Factor Xa inhibitors are strongly recommended for the prevention of venous thromboembolic disease.**

*Indications* – Post-operative arthroplasty, knee fracture, or other major knee surgery patients, particularly those with prolonged inactivity or prolonged reduced or sedentary activity levels.(1918, 1969-1972) Patients with prior reactions should generally receive other treatments first. Patients with renal failure or renal insufficiency should generally receive a different medication due to renal excretion of this compound.

*Dose/Frequency* – Subcutaneous injections of Fondaparinux (Arixtra) 2.5mg SC QD. Currently Rivaroxaban (Xarelto) is investigational in the U.S.

*Duration* – Duration unclear. Literature suggests duration be individualized based on factors such as prolonged inactivity, delayed recovery or thrombotic recurrences, prior history, and risks of bleeding.

*Indications for Discontinuation* – Completion of course of treatment, development of major complication (e.g., major bleeding) or other adverse effect.

*Strength of Evidence* – **Strongly Recommended, Evidence (A)**

*Warfarin and Heparin for Prevention of Venous Thromboembolic Disease*

**Warfarin and heparin are moderately recommended for prevention of venous thromboembolic disease.**

*Indications* – Post-operative arthroplasty, knee fracture, other major knee surgery.(1973, 1974) Patients with adverse reactions to warfarin may be maintained on heparin throughout the treatment course. Patients with reactions to heparin, but at increased risk of thrombosis may be started on the other agents and switched to warfarin.

*Dose/Frequency* – Subcutaneous injections of Heparin, which can be titrated to the activated partial thromboplastin time (aPTT). Warfarin dose titrated to International Normalized Ratio (INR). Magnitude of anticoagulation is recommended to be individualized, and include risks of thrombi versus risks of bleeding and it is notable that the quality studies utilized a range of INRs.

*Duration* – Duration unclear. Literature suggests duration be individualized based on factors such as prolonged inactivity, delayed recovery or thrombotic recurrences, prior history, and risks of bleeding.

*Indications for Discontinuation* – Completion of course of treatment, development of major complication (e.g., major bleeding) or other adverse effect.

*Strength of Evidence* – **Moderately Recommended, Evidence (B)**

*Prevention of Venous Thromboembolic Disease*

**Aspirin is moderately recommended for the prevention of deep venous thrombosis.**

*Indications* – Post-operative arthroplasty, knee fracture, and other major knee surgery patients, particularly after cessation of other treatments such as LMWH, heparin, or other anticoagulants.(1975)

*Dose/Frequency* – Aspirin 160mg per day was used in PEP trial. Other studies have found 85mg/day sufficient for heart attack prevention.

*Duration* – Duration unclear; 1 month is suggested, however due to other risk factors, prolonged or indefinite treatment may be recommended.

*Indications for Discontinuation* – Completion of course of treatment, development of major complication (e.g., major bleeding) or other adverse effect.

*Strength of Evidence* – **Moderately Recommended, Evidence (B)**

*Evidence for the Prevention of Venous Thromboembolic Disease*

There are 9 high- and 23 moderate-quality RCTs incorporated into this analysis. There are 3 low-quality RCTs in Appendix 1.(1976-1978)

## Hamstring and Hip Flexor Strains

See Hip and Groin Disorders guideline.

## Iliotibial Band Syndrome

### Introduction

Iliotibial band syndrome is believed to occur in susceptible individuals with exposure to forceful, repeated movement of the iliotibial band over the lateral femoral condyle with resultant friction.(129, 141, 177, 183, 187, 189, 190) This disorder has been reported mostly in discrete, physically active populations, including runners, military recruits, weight lifters, bicyclers, and downhill skiers.(127, 175, 176, 178-184, 189, 191-196, 1979, 1980) Quality epidemiological studies are absent, but purported risk factors include increased activity, genu varus, leg length discrepancies, running surface and shoe wear.(141, 1981, 1982) The results are thought to include tendinopathy-like changes involving the iliotibial tract with accompanying inflammation of the lateral synovial recess.(131, 132, 141, 183, 189, 1983-1987)

The diagnosis is mostly clinical, although MRI has been used for evaluation of IT band syndrome.(131, 132, 1988) Treatment has largely been empiric, as quality evidence has been notably sparse.(130) Conservative treatment has been thought to be successful.(1984, 1985, 1989) Treatments have predominantly included: reducing the exposure factor(s) and rest,(177, 185, 191, 192, 1984, 1989-1991) NSAIDs, gradual return to activity, ice,(141, 192, 196, 1980, 1992) massage,(1980, 1992, 1993) physical therapy, stretching of the IT band,(192, 194, 1994) and local injections.

### Treatment Recommendations

#### NSAIDs

Anti-inflammatory medications have been used for treatment of IT band syndrome.(141, 177, 189, 191-193, 1980, 1984, 1989, 1990, 1995, 1996)

*NSAIDs for Iliotibial Band Syndrome*

**NSAIDs are recommended for the treatment of iliotibial band syndrome.**

*Indications* – Iliotibial band syndrome patients with sufficient symptoms to require treatment.

*Frequency/Dose/Duration* – Per manufacturers' recommendations.

*Indications for Discontinuation* – Sufficient clinical results (NSAIDs no longer required), resolution of symptoms, intolerance, adverse effects. A trial with a different class of NSAID is reasonable for treatment failures.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

#### *Rationale for Recommendation*

There is one moderate-quality placebo-controlled trial; however, it did not document improvements compared to placebo.(1980) That trial included patients with acute symptoms and baseline differences that may have impacted the results. It also involved very short follow-up of 1 week with continued treadmill exercise in athletes resulting in difficulty extrapolating to working populations. The use of acute patients may have resulted in underpowering due to favorable prognoses in all treatment groups. NSAIDs are thought to be helpful, are not invasive, have few adverse, effects especially in young patients, are of low cost, and are thus recommended.

#### *Evidence for the Use of NSAIDs*

There is 1 moderate-quality RCT incorporated into this analysis.

## **Knee Immobilization**

Knee immobilization has been used for treatment of IT band syndrome.(1997)

#### *Knee Immobilization for Iliotibial Band Syndrome*

**Knee immobilization is not recommended for treatment of Iliotibial band syndrome.**

*Strength of Evidence* – **Not Recommended, Evidence (C)**

#### *Rationale for Recommendation*

There are no placebo-controlled trials that evaluate knee immobilization for treatment of IT band syndrome. There are also no quality trials comparing knee immobilization with an intervention with known efficacy. There is one moderate-quality trial comparing knee immobilization with phonophoresis that found the phonophoresis superior.(1997) While that study is likely biased in favor of phonophoresis, it does suggest that knee immobilization is not effective, and knee immobilization is thus not recommended.

#### *Evidence for Knee Immobilization*

There is 1 moderate-quality RCT incorporated into this analysis.

## **Transverse Friction Massage**

Transverse friction massage has been used for treatment of IT band syndrome.(1980, 1992, 1993)

#### *Transverse Friction Massage for Iliotibial Band Syndrome*

**There is no recommendation for or against the use of transverse friction massage for the treatment of iliotibial band syndrome.**

*Strength of Evidence* – **No Recommendation, Insufficient Evidence (I)**

#### *Rationale for Recommendation*

There is one moderate-quality trial assessing additive benefit in addition to stretching, ice and ultrasound.(197) It failed to show improvement, although it may have been underpowered. Thus, there

is no recommendation for or against the use of transverse friction massage for treatment of iliotibial band syndrome.

#### *Evidence for the Use of Transverse Friction Massage*

There is 1 moderate-quality RCT incorporated into this analysis.

## **PHONOPHORESIS**

Phonophoresis has been used for treatment of IT band syndrome.(1997)

#### *Phonophoresis for Iliotibial Band Syndrome*

**There is no recommendation for or against the use of phonophoresis for the treatment of iliotibial band syndrome.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

#### *Rationale for Recommendation*

There are no placebo-controlled trials that evaluate phonophoresis for treatment of IT band syndrome. There are also no quality trials comparing phonophoresis with an intervention with known efficacy. There is one moderate-quality trial comparing phonophoresis with knee immobilization that found phonophoresis superior.(1997) However, the study was likely biased in favor of phonophoresis. Therefore, there is no recommendation for or against the use of phonophoresis.

#### *Evidence for the Use of Phonophoresis*

There is 1 moderate-quality RCT incorporated into this analysis.

## **Glucocorticosteroid Injections**

Glucocorticoid injections have been used for treatment of IT band syndrome.(1998)

#### *Glucocorticosteroid Injections for Iliotibial Band Syndrome*

**Glucocorticosteroid injections are recommended for the treatment of iliotibial band syndrome in a subset of patients with insufficient results from other treatments.**

*Indications* – Iliotibial band syndrome patients with insufficient results from activity modification, relative rest, NSAIDs, and local applications of ice or heat.

*Frequency/Dose/Duration* – One quality trial used methylprednisolone acetate 40mg mixed with 1% lidocaine, injected between the IT band and lateral femoral condyle.(1998) If there is insufficient response, consideration may be given to a second injection, often with a modestly higher dose.

*Indications for Discontinuation* – A second glucocorticosteroid injection is not recommended if the first has resulted in significant reduction or resolution of symptoms. If there has not been any response to a first injection, there is also less indication for a second. If the interventionalist believes the medication was not well placed and/or if the underlying condition is so severe that one steroid bolus could not be expected to adequately treat the condition, a second injection may be indicated. In patients who respond with several weeks of pharmacologically appropriate, temporary, partial relief of pain, but then have worsening pain and function and are not (yet) interested in surgical intervention, a repeat steroid injection is an option. There is unlikely to be benefit with greater than about 3 injections per year.

*Strength of Evidence – Recommended, Evidence (C)*

#### *Rationale for Recommendation*

There is one moderate-quality placebo-controlled trial that suggested benefits of injection with glucocorticoid compared with placebo anesthetic for treatment of iliotibial band syndrome.(1998)

Although the trial was small, the results were statistically significant, thus meeting minimum criteria for an evidence-based recommendation. These injections are mildly invasive, have adverse effects, are moderately costly, and appear effective and are therefore recommended.

#### *Evidence for the Use of Glucocorticosteroid Injections*

There is 1 moderate-quality RCT incorporated into this analysis.

## **Surgery**

Surgical procedures have been used for treatment of iliotibial band syndrome, which have included x-lengthening.(192, 1990)

#### *Surgery for Iliotibial Band Syndrome*

**There is no recommendation for or against surgery for treatment of iliotibial band syndrome.**

*Indications* – Iliotibial band syndrome patients with insufficient results from activity modification, relative rest, NSAIDs, local applications of ice or heat, and 2 glucocorticoid injections.

*Strength of Evidence* – **No Recommendation, Insufficient Evidence (I)**

#### *Rationale for Recommendation*

There are no quality trials comparing surgery with sham surgery for treatment of iliotibial band syndrome. There are also no quality trials comparing surgery with a non-interventional control group. There also are no quality comparative trials for different operative approaches. Therefore, surgery would be a last resort for the small minority of patients with unsatisfactory results from other treatments that generally include at least 2 glucocorticoid injections. Surgery is invasive, has adverse effects, and is highly costly. Therefore, there is no recommendation for or against its use in this small group of patients as data are insufficient and inconclusive.

# **QUADRICEPS, GASTROCNEMIUS, AND SOLEUS STRAINS**

## **Introduction**

Quadriceps, gastrocnemius and soleus strains are thought to be true muscular strains (i.e., disrupted myotendinous junctions). These problems are usually precipitated by a high-force maneuver, including sports injuries in sprinting, football or soccer,(1999-2001) with near maximum voluntary contraction capabilities. Prior injury is likely the greatest predictor of future risk. Patients have pain exacerbated by use, stiffness and weakness.

## **Diagnostic Recommendations**

### **X-RAYS and MRI**

*X-ray and/or MRI for Severe Quadriceps, Gastrocnemius, or Soleus Strains*

In the more severe cases of quadriceps, gastrocnemius, and soleus strains, evaluation with x-ray and/or MRI are recommended for evaluation of the underlying bony structure as well as the degree of muscle tear.

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

#### *Rationale for Recommendation*

The examination findings for these types of strains are tenderness, usually at either the muscle origin or insertion (e.g., high vs. low hamstring strains), with swelling or large ecchymoses in more severe cases. Some cases involve complete ruptures and require surgical repair. Clinical tests are generally not necessary, although in the more severe cases, evaluation with x-ray and/or MRI are recommended for evaluation of the underlying bony structure as well as the degree of muscle tear, as severe cases may require surgery.

## Treatment Recommendations

### WORK LIMITATIONS

#### *Work Limitations for Select Cases of Quadriceps, Gastrocnemius, or Soleus Strains*

**Work limitations are recommended for those with quadriceps, gastrocnemius, or soleus strains performing high physical demand tasks or those who have no ability to avoid repeating physically demanding job tasks thought to have resulted in the condition.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

#### *Work Limitations for Other Cases of Quadriceps, Gastrocnemius, or Soleus Strains*

**There is no recommendation for or against work limitations for other cases of quadriceps, gastrocnemius, or soleus strains.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

#### *Rationale for Recommendations*

Work limitations may be necessary depending on the severity of the condition and the required job demands.

### BED REST

#### *Bed Rest for Quadriceps, Gastrocnemius, or Soleus Strains*

**Bed rest is not recommended for treatment quadriceps, gastrocnemius, or soleus strains, although relative rest may be required for many patients.**

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

### NSAIDs

#### *NSAIDs for Quadriceps, Gastrocnemius, and Soleus Strains*

**Nonsteroidal anti-inflammatory medications are recommended for quadriceps, gastrocnemius, and soleus strains.**

*Dose/Duration* – See NSAID section for dose, frequency, discontinuation information.

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## ICE/HEAT

*Ice/Heat for Quadriceps, Gastrocnemius, or Soleus Strains*

**Ice and/or heat are recommended for treatment of quadriceps, gastrocnemius, or soleus strains.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## WRAPS

*Ace Wraps for Quadriceps, Gastrocnemius, or Soleus Strains*

**Ace wraps are recommended for treatment of quadriceps, gastrocnemius, or soleus strains.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## REHABILITATION THERAPY

*Rehabilitation Therapy for Quadriceps, Gastrocnemius, or Soleus Strains*

**A course of rehabilitation therapy is recommended for patients with persisting pain from quadriceps, gastrocnemius, or soleus strains.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## Progressive Agility, Trunk Stabilization, and Icing (PATS)

*PATS for Quadriceps, Gastrocnemius, or Soleus Strains*

**PATS is recommended for quadriceps, gastrocnemius, or soleus strains.**

*Dose/Duration – See Exercise section for exercise dose, frequency, discontinuation information.*

*Strength of Evidence – Recommended, Evidence (C)*

### *Rationale for Recommendations*

There is one quality study of treatment options, however, it only addressed exercise(2002); thus nearly all treatment recommendations are empiric.(2003-2005) Bed rest is not recommended due to concern regarding deep venous thrombosis and other adverse effects of bed rest. A course of rehabilitation therapy is recommended for those with persisting pain, although long term compliance is a noted problem.(2003) Quality evidence suggests stretching and isolated progressive resistance training are not successful compared with progressive agility, trunk stabilization and icing (PATS)(2002); thus PATS is recommended.

### *Evidence for the Use of PATS for Hamstring Strains*

There is 1 moderate-quality RCT incorporated in this analysis. There are 2 low-quality RCTs in Appendix 1.

# KNEE SPRAINS (including Medial and Lateral Collateral Ligaments; Anterior and Posterior Cruciate Ligaments)

## Introduction

Knee sprains are partial or complete disruptions of ligaments.(104, 2006, 2007) Thus, these injuries are usually a result of high force events, particularly including sporting injuries, slips, trips, falls, motor vehicle accidents and work injuries.(104, 2006, 2008, 2009) The 4 major ligaments of the knee are all susceptible to knee sprains.(104, 2006) These are the medial and lateral collateral ligaments, along with the anterior and posterior cruciate ligaments. Sprains are typically graded from I to III ranging from an intact ligament without laxity but with fiber disruption (I) to complete disruption (III).(104, 2006, 2007) Low grade sprains are considered to have excellent prognoses.(2006, 2010-2012) Grade III sprains are more susceptible to concomitant injuries such as the ACL and menisci.(2006) A careful history will usually result in a presumptive diagnosis that is confirmed on physical examination (see History and Physical Examination sections). Patients have pain exacerbated by use and ligament stretching. The examination findings are focal tenderness over the collateral ligament and pain augmentation with ligamentous stressing for collateral ligament sprains. Examination findings may be normal for Grade I cruciate ligament sprains or include laxity with complete disruptions. Some cases involve complete ruptures and may require surgical repair (see ACL section). Combined ruptures (e.g., MCL plus ACL) are beyond the scope of this guideline as there are few quality studies to define treatment options and both operative and non-operative care has been attempted with successes.

## Diagnostic Recommendations

### X-RAY AND MRI

*X-rays and MRI for Evaluation of Knee Sprains*

**X-ray and/or MRI are recommended for the evaluation of knee sprains, particularly to rule out fracture.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

### ULTRASOUND

*Ultrasound for Evaluation of Knee Sprains*

**There is no recommendation for or against the use of diagnostic ultrasound for the evaluation of knee sprains.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Rationale for Recommendations*

Clinical tests are generally not necessary for mild sprains, although in more severe cases, evaluation with x-ray and/or MRI are recommended, particularly to rule out fracture, and MRI is helpful for defining

cruciate ligament tears. There is no recommendation for or against the use of diagnostic ultrasound to evaluate knee sprains.

## Treatment Recommendations

### WORK LIMITATIONS

*Work Limitations for Select Knee Sprains*

**Work limitations are recommended for those with knee sprains performing high physical demand tasks or those who have no ability to avoid repeating physically demanding job tasks thought to have resulted in the condition.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

*Work Limitations for Other Cases of Knee Sprains*

**There is no recommendation for or against the use of work limitations for other cases of knee sprains.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### BED REST AND KNEE IMMOBILIZATION

*Bed Rest and Knee Immobilization for Knee Sprains*

**Bed rest and knee immobilization are not recommended for treatment of knee sprains, although relative rest may be required for many patients.**

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

### NSAIDs

*NSAIDs for Knee Sprains*

**Nonsteroidal anti-inflammatory medications are recommended for treatment of knee sprains.**

*Dose/Duration – See NSAID section for dose, frequency, discontinuation information.*

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

### ICE/HEAT

*Ice/Heat for Knee Sprains*

**Ice and/or heat are recommended for treatment of knee sprains.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

### WRAPS AND KNEE BRACES

*Ace Wraps and Knee Braces for Knee Sprains*

**Ace wraps and knee braces are recommended for treatment of knee sprains.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

### REHABILITATION THERAPY

*Rehabilitation Therapy for Knee Sprains*

**A course of rehabilitation therapy is recommended for those with persisting pain from a knee sprain.**

*Dose/Duration* – See exercise section for dose, frequency and discontinuation.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

## **OTHER PHYSICAL MODALITIES/INJECTIONS**

*Other Modalities/Injections for Knee Sprains*

**There is no recommendation for or against the use of therapeutic ultrasound, diathermy, electrical stimulation, iontophoresis, low-level laser therapy, phonophoresis, acupuncture, manipulation, mobilization or manual therapy, autologous blood injections, plasma rich platelet injections, glucocorticosteroid injections, and hyaluronic acid injections for knee sprains.**

*Strength of Evidence* – **No Recommendation, Insufficient Evidence (I)**

## **SURGERY**

*Surgery for Grade III LCL Tears*

**Surgery is recommended in isolated Grade III LCL tears, recognizing that they are rare.**

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Surgery for Select Cases of Grade III MCL Tears*

**Surgery in isolated Grade III MCL tears is usually not necessary because of the documented excellent healing potential of this ligament with closed (i.e., non-operative) treatment. Surgery is only recommended in those rare select cases of failure of non-operative management.**

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Rationale for Recommendations*

There are no quality studies of treatment options aside from surgery and rehabilitation for complete ACL tears (see next section) and one trial comparing NSAIDs(719) and one with DHEP gel.(2013) Of necessity, guidance for treatment relies upon ankle sprains for analogy as there are considerable quality trials for ankle sprains (2014, 2015) (evidence ratings are all “Insufficient Evidence” due to the analogy with the ankle). Work limitations may be necessary depending on the severity of the condition and the required job demands.(2016) Those performing high physical demand tasks or those who have no ability to avoid repeating physically demanding job tasks thought to have resulted in the condition are recommended to have work limitations.

Bed rest and knee immobilization are not recommended due to risks of venous thromboembolisms and other adverse effects of bed rest, although relative rest may be required for many patients. NSAIDs, ice and/or heat, Ace wraps, and knee braces are recommended. A low-quality trial suggested a less bulky elastic support bandage was superior to a Robert Jones bandage.(2017) Those with persisting pain are recommended to have a course of rehabilitation therapy. There is no recommendation for or against autologous blood injections, plasma rich platelet injections, glucocorticosteroid injections, hyaluronic acid injections, therapeutic ultrasound, diathermy, electrical stimulation, iontophoresis, low level laser therapy, phonophoresis, acupuncture, manipulation, and mobilization or manual therapy. RCTs and a systematic review suggested neuromuscular training for sports injury prevention was effective.(2018-2021) However, this topic is beyond the scope of these *Guidelines* but may be of interest to some readers. Warm-up stretching has been shown to increase flexibility(2022); however, its relationship to preventing injury is unclear. Surgery is recommended in isolated Grade III LCL tears, recognizing that they are rare. Surgery in isolated Grade III MCL tears is usually not necessary because of the documented excellent healing potential of this ligament with closed (i.e., non-operative) treatment. Surgery is only recommended in those rare select cases of failure of non-operative management.

### *Evidence for Knee Sprains*

There are 5 moderate-quality RCTs incorporated into this analysis. There are 3 low-quality RCTs in Appendix 1.

# Anterior and Posterior Cruciate Ligament Tears

## Introduction

This section addresses complete disruptions of the cruciate ligaments. These injuries are most commonly experienced in athletics, as well as acute discrete, forceful traumatic events.(2, 4, 1061, 1064-1066, 1068, 1069, 1072-1075, 2023-2031) The history and physical examination findings have been previously discussed (see History and Physical Examination and Knee Sprain sections). There are concerns regarding subsequent development of osteoarthritis, and a positive pivot shift after surgical repair has been reported to predict osteoarthritis.(2032)

The anterior cruciate ligament (ACL) is considered the most important stabilizing knee ligament. Thus, this section will primarily address ACL tears. Posterior cruciate ligament tears are uncommon, and rarely require surgery in non-professional athletes. PCL ligament tears are thought to be best rehabilitated with progressive exercises which are **Recommended, Insufficient Evidence (I)** (see ACL exercise section above).

Whereas ACL tears were once universally thought to require surgical repair, there is now quality evidence of successful non-operative rehabilitation in well selected patients (see below). This has somewhat increased the complexity of patient management. For many interventions, there is not quality evidence, and either inference from treatment of other body parts, consensus, and/or expert opinion guide treatments.

## Diagnostic Recommendations

### X-RAYS

*X-ray for Evaluation of ACL Tears*

**X-ray is recommended for many cases of ACL tears, particularly accompanying trauma, to rule out fractures.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

### MRI

*MRI for the Evaluation of ACL Tears*

**MRI is recommended for ACL tears, particularly if there are concerns for other soft tissue damage including meniscal tears and other sprains. However, some cases also may be managed clinically without MRI.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## ULTRASOUND

*Ultrasound for the Evaluation of ACL Tears*

**There is no recommendation for or against the use of diagnostic ultrasound for evaluation of ACL tears.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

*Rationale for Recommendations*

Clinical tests may or may not be necessary depending on the mechanism of severity, physical examination findings and potential for complicating injuries. X-ray is recommended particularly in cases with accompanying trauma to rule out fractures. MRI is helpful, particularly if there are concerns for other soft tissue damage including meniscal tears and other sprains. However, some cases also may be managed clinically without MRI. There is no recommendation for or against the use of diagnostic ultrasound to evaluate ACL tears.

## Treatment Recommendations

Rest, splints, ice and heat have been utilized for treatment of ACL injuries.(1066, 1068, 1072, 1074, 2023, 2033, 2034) Functional bracing has been used to prevent and treat ACL injuries; they have also been used post-operatively as part of the rehabilitation program.(1064, 1065, 1069) There are no quality studies of treatment options aside from exercise, rehabilitation, braces and surgical treatment.

## BRACING

Knee bracing is commonly performed for ACL tears.(1061, 1064-1066, 1068, 1069, 1072-1077, 2023-2031, 2033, 2035, 2036) Most often, hinged braces are used, although there are different models in use.

*Functional Bracing for Treatment of Non-Operative Anterior Cruciate Ligament Injuries*

**There is no recommendation for or against the use of functional bracing for treatment of non-operative ACL injuries.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

*Functional Bracing for Anterior Cruciate Ligament Injuries Post-operatively*

**Functional bracing is not recommended for ACL injuries post-operatively.**

*Strength of Evidence – Not Recommended, Evidence (C)*

*Rationale for Recommendations*

There are many RCTs that evaluate the use of braces to treat and rehabilitate post-operative and non-operative patients with ACL tears. However, nearly all of the trials for non-operative treatment are of low quality. Thus, there is no recommendation for or against the use of braces for non-operative treatment of ACL tears. Use of braces in these patients must balance theoretical stabilization against disuse and delayed progression. If braces are prescribed it is suggested patients be monitored for progress and generally be engaged in an active exercise program.

There are four moderate-quality trials that evaluated post-operative patients. Three of these studies suggested no differences in outcome,(1076, 2035, 2036) and the other suggested modestly less reduction in range of motion in a post-operative group.(1077) Bracing is not invasive, has low adverse effects, and is low to moderately costly. However, available evidence does not suggest significant

benefits; therefore bracing is generally not recommended. Exceptions may include suboptimal surgical repairs and other extenuating factors.

*Evidence for the Use of Bracing for ACL Tears*

There are 5 moderate-quality RCTs incorporated into this analysis. There are 8 low-quality RCTs in Appendix 1.(2037-2044)

**Rehabilitation after ACL Injury With or Without Reconstruction**

Exercise, physical therapy, and rehabilitation have been used for treatment of ACL tears either instead of surgery or post-operatively.(224, 2008, 2009, 2045-2054) The early objectives of rehabilitation include restoration of knee range of motion, pain management, reduction of swelling, early ambulation and increasing muscle strength.(2047, 2051)

*Post ACL Injury Rehabilitation with or without Surgical Repair*

**Rehabilitation is recommended after ACL injury with or without surgical reconstruction.**

*Indications* – ACL injury with or without surgery.

*Duration* – One to 6 weeks, 2 to 3 sessions a week, decreasing over time with active treatment up to 12 weeks.(2009, 2055) There is quality evidence that a home-based program is as effective as a therapy based program for motivated post-operative patients(2047, 2056) (see Table 6).

*Indications for Discontinuation* – Achievement of goals, non-compliance with clinic or home-based exercises or intolerance.

*Strength of Evidence* – **Recommended, Evidence (C)**

**Table 6. Post-operative Rehabilitation after ACL Injury**

		<b>0-4 weeks</b>	<b>5-8 weeks</b>	<b>9-12 weeks</b>	<b>13-16 weeks</b>	<b>17-24 weeks</b>
<b>Unloaded ROM</b>		As tolerated	As tolerated	Normal	Normal	Normal
<b>Muscle Function</b>	<i>Quadriceps</i>	Unloaded, full control	Loaded, non-weight bearing in 40-120°; weight-bearing exercises in 0-80°	Closed chain exercises without limitations		
	<i>Hamstrings</i>	Loaded exercises	No limitations	No limitations	No limitations	No limitations
	<i>All other lower limb muscles</i>	Initiated	No limitations	No limitations	No limitations	No limitations
<b>Symptoms</b>	<i>Pain</i>	As tolerated; treat if necessary	As tolerated; treat if necessary	No pain	No pain	No pain
	<i>Swelling</i>	As tolerated; treat if necessary	As tolerated; treat if necessary	Occasional activity-related swelling, no treatment	Occasional activity-related swelling, no treatment	Occasional activity-related swelling, no treatment

<b>Walking</b>		As tolerated; may use crutches until walk backwards without limping	Full weight bearing. Daily walking without restriction	Slow and fast walking on treadmill	Running on treadmill/even surface. Non-surgical: unrestricted running	Surgical: unrestricted running
<b>Balance/Coordination</b>	<i>One-leg standing</i>	Stand in functional positions	Stand in functional positions on soft ground and Babs-board	More demanding surfaces	Two legged bounces, easy sport-specific movements. Easy agility exercises	One-legged bounces. Provoked sport-specific movement. Provoked agility exercises.
<b>Activities</b>		Unloaded and loaded biking on stationary bike backwards and forwards	Stationary biking without restrictions. Water based running. Non-surgical: outdoor biking with restrictions.	Slide-board training	Non-surgical: introduction of sport-specific exercises. Surgical: Outdoor biking without restrictions	Surgical: introduction of sport-specific exercises.

Adapted from Frobell, et al. 2007.

### *Home-Based Physical Therapy for Post-ACL Operative Repair Patients*

**Home-based physical therapy is recommended for post-ACL operative repair patients.**

*Indications* – ACL post-operative patients.(2047, 2056, 2057)

*Duration* – From 3 to 5 supervised physical therapy visits focusing on a home-based exercise program that lasts up to a total of 3 months post-operatively.(2047, 2056, 2057) The idea is to develop a continual exercise program indefinitely.

*Indications for Discontinuation:* Discontinuation of intermittent supervision based on achievement of goals, non-compliance or intolerance.

*Strength of Evidence* – **Recommended, Evidence (C)**

#### *Rationale for Recommendations*

A moderate-quality trial has shown equivalent results whether treatment is surgical or non-surgical (see Surgical section below).(2009) There are no quality studies comparing post ACL-injury with rehabilitation compared with no rehabilitation. Two moderate-quality studies evaluated home exercises after 0 to 4 supervised physical therapy sessions compared with a total of 17 or more sessions and reported no differences in several objective and subjective outcomes.(2047, 2056) A low-quality study evaluated home therapy after supervised physical therapy to supervised physical therapy and reported no significant differences in favor of a fully-supervised physical therapy program.(2057) A second low-quality study evaluated a home exercise program versus clinic-based exercises and found no significant differences.(2058) Another low-quality study evaluated a supervised home exercise program versus a knee exercise class for a minimum of 6 months after ACL reconstruction and concluded there was no difference between groups.(2059) Physical therapy appears beneficial in ACL-injured patients with no reported significant adverse events. One trial suggested supervised training to be superior to self-monitoring; however, the trial appears to have instructed the self-monitored group to avoid use, thus biasing against that treatment.(2060) Home based exercises programs appear as efficient as supervised

programs, cost less, and are recommended for most motivated post-operative patients.(2058) It is recommended that several types of exercises be included in the post injury rehabilitation program (see above).(1275, 1292, 2009, 2049, 2061-2065) Rehabilitation is not invasive, has few adverse effects and is moderately costly using the regimen noted above. Given the evidence of efficacy, rehabilitation is recommended.

#### *Perturbation Training As Part of a Rehabilitation Program for ACL Injured Patients*

**Perturbation training is recommended as part of a comprehensive exercise program in patients with injured ACL with or without surgery.**

*Indications* – ACL injured patients who choose to undergo ACL reconstruction surgery, or patients who opt for nonsurgical management. To be done as part of a comprehensive exercise therapy program that includes strength training exercises.(2066, 2067)

*Duration* – As part of a therapy program, both supervised and unsupervised. Available studies have examined up to 10 sessions of therapy with perturbation as a part of the therapy program.(2066, 2067)

*Indications for Discontinuation* – Achievement of goals, non-compliance, or lack of benefits.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

#### *Rationale for Recommendation*

A low-quality study evaluated ACL-injured patients who opted to be treated non-operatively. The study compared physical therapy with or without perturbation training and reported slightly better improvements in the perturbation group.(2066) Perturbation training can be included in a therapy program. A low-quality study evaluated perturbation and strength training versus strength training alone prior to ACL surgery. Both groups increased strength post-operatively, but the group that included perturbation training had better gait mechanics results 6 months after surgery.(2067) It appears to have low adverse events and encourages physical activity. One trial has suggested that patients, classified as non-copers performed better with perturbation training and quadriceps strength training than quadriceps strength training.(2068)

#### *Early Post-operative Rehabilitation After ACL Reconstruction Surgery*

**Early post-operative rehabilitation after ACL reconstruction surgery is recommended.**

*Indications* – ACL reconstruction patients starting as early as the first post-operative day.(2051, 2061, 2069)

*Duration* – Two to 3 times a week for up to 6 weeks for guided therapy.(2062, 2070)

*Indications for Discontinuation* – Complications causing a need for further intervention and/or surgery.

*Strength of Evidence* – **Recommended, Evidence (C)**

#### *Rationale for Recommendation*

A moderate-quality study evaluated isokinetic hamstring exercises as part of a post-operative rehabilitation program. One group started the exercises 3 weeks post-operatively, the other 9 weeks post-operatively. They reported benefits of starting exercises earlier in an athletic cohort.(2071) A moderate-quality study compared patients who started quadriceps exercises on post-operative day 2 with patients who started therapy 1 to 2 weeks following surgery. They reported no increase in adverse events and faster recovery of knee range of motion and stability in the group that started therapy earlier.(2051) Earlier rehabilitation has not been reported to increase adverse events, and it has been reported to increase benefits.(2061) A low-quality study evaluated knee continuous passive range of motion starting post-operative day two to range of motion on post-operative day seven. They reported

no increase in adverse events with starting therapy earlier.(2069) Early rehabilitation is not invasive, has low adverse effects, is low cost, has documented efficacy, and is therefore recommended.

#### *Evidence for Post ACL Injury Rehabilitation*

There are 9 moderate-quality RCTs incorporated into this analysis. There are 5 low-quality RCTs in Appendix 1.

## **Work Limitations**

#### *Work Limitations for Select Cases of ACL Tears*

**Work limitations for ACL tears are usually necessary, especially in the acute phase, although required job demands must be incorporated. Severe cases may be unable to perform any work for a few days. Those performing high physical demand tasks or those who cannot avoid repeating physically demanding job tasks similar to those that resulted in the condition are especially recommended to have work limitations.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

#### *Work Limitations for Other Cases of ACL Tears*

**There is no recommendation for or against work limitations in other cases of ACL tears, particularly where the worker has the ability to modulate work tasks.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

## **BED REST AND KNEE IMMOBILIZATION**

#### *Bed Rest and Knee Immobilization for ACL Tears*

**Bed rest and knee immobilization are not recommended for ACL tears, although relative rest may be required for most patients.**

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

## **NSAIDs**

#### *NSAIDs for ACL Tears*

**Nonsteroidal anti-inflammatory medications are recommended for ACL tears. (See NSAID section for dose, frequency, discontinuation information.)**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## **ICE/HEAT**

#### *Ice/Heat for ACL Tears*

**Ice and/or heat are recommended for ACL tears.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## **OTHER MODALITIES/INJECTIONS**

#### *Other Modalities/Injections for ACL Tears*

**There is no recommendation for or against therapeutic ultrasound, diathermy, electrical stimulation, iontophoresis, low-level laser therapy, phonophoresis, acupuncture, manipulation and mobilization or manual therapy, autologous blood injections, plasma rich platelet injections, glucocorticosteroid injections, and hyaluronic acid injections.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Rationale for Recommendations*

There are no quality trials specifically addressing patients with ACL and PCL tears. Work limitations are usually necessary, especially in the acute phase, although required job demands must be incorporated. Those performing high physical demand tasks or those who cannot avoid repeating physically demanding job tasks similar to those that resulted in the condition are especially recommended to have work limitations. In other cases, particularly where the worker has the ability to modulate work tasks, there is no recommendation for or against work limitations. Bed rest and knee immobilization are not recommended due to risks of venous thromboembolisms and other adverse effects of bed rest, although relative rest may be required for most patients. Nonsteroidal anti-inflammatory medications and ice/heat are recommended. There is no recommendation for or against the use of therapeutic ultrasound, diathermy, electrical stimulation, iontophoresis, low-level laser therapy, phonophoresis, acupuncture, manipulation and mobilization or manual therapy, autologous blood injections, plasma-rich platelet injections, glucocorticosteroid injections, or hyaluronic acid injections for treatment of ACL tears.

### **Surgery**

Surgery has been utilized for reconstruction of torn ACLs.(1, 581, 1538, 1555, 1557, 1559, 1560, 1562, 1566-1570, 2008, 2009, 2045, 2048, 2072-2107) Recently, studies have documented equivalent success with non-operative management of ACL tears.(2009) The crossover rate to surgery from the non-operative arm was 37% (23 of 59), potentially signaling that significant numbers of patients may still require surgery for successful outcomes from ACL tears. There also are some concerns that meniscal injuries may occur more readily in cruciate deficient knees, and subsequent surgical repairs may be less successful.(2108-2112)

#### *Surgery for ACL Tears*

**Surgical reconstruction of ACL tears is sometimes recommended for treatment of select patients with ACL tears.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

*Level of Confidence – Low*

*Indications* – Patients should generally have attempted non-operative treatment that included progressive exercise implemented after the acute phase of swelling, if any, has subsided. Duration of a non-operative treatment plan to determine success or failure is unclear and likely requires individualization. A study evaluated grafting at 2 weeks versus 8 to 12 weeks and reported no significant differences after 52 weeks of follow up.(2113) Most patients who fail non-operative treatment appear to require surgery within 3 months of the ACL tear.(2009) There is no quality evidence surgery outperforms primary rehabilitation at 5 years of follow-up (2471). Some patients, particularly those with high demand jobs or high performance athletes, may be candidates for early surgical reconstruction, as they are believed to more frequently fail non-operative rehabilitation.(1, 2113) There is moderate-quality evidence that delay in surgical reconstruction does not impair outcomes,(2009, 2113) thus there is no rush to operate that has been shown in quality studies.

*Benefits* – Theoretically better ability to suddenly pivot on the knee and less instability.

*Harms* – Increased risk of osteoarthritis in the operated knee, risk of infection, longer period of debility than with a primary rehabilitation approach.

*Rationale* – There is one moderate-quality trial comparing rehabilitation with surgical reconstruction of ACLs and which found no differences over time intervals up to 2 years.(2009) Four low-quality trials comparing surgical ACL reconstruction with non-operative care have also been published, with one trial suggesting mostly comparable results but more instability in the non-surgical group,(2045) one suggesting fewer subsequent meniscal tears after surgical ACL reconstruction,(2048) one suggesting comparable functional outcomes,(2008) and one suggesting superior stability with surgery.(2109)

There are numerous quality trials comparing different surgical approaches, most commonly a patellar tendon autograft or hamstring tendon autograft (see evidence table). Most RCTs have participants that are actively participating in various levels of sports, which may somewhat limit generalizability, although presumably less active patients may derive comparable benefits.

Patellar tendon autografts have been associated with fewer graft failures and less knee laxity. Hamstring tendon autografts have been associated with less anterior knee pain and less extension deficit.(2114-2116) Use of hamstring autograft compared to patellar reportedly results in less anterior knee pain up to 3 years post-operatively,(2117-2122) and other studies reported no differences up to 7 years post-operatively.(2114, 2123-2126)

Different hamstring autograft techniques have been used. There are studies evaluating the double-bundle technique versus the single-bundle technique.(378, 2127-2132) The argument for the more technically demanding anatomic double-bundle technique is that the results are more anatomical compared to the single-bundle technique.(2115, 2133, 2134) Two moderate-quality studies comparing hamstring autograft double-bundle to single-bundle techniques reported superior anterior and rotational stability, but no subjective difference.(2115, 2133) One study evaluated the double bundle hamstring autograft done with 4 strands versus 8, and reported superior outcomes in terms of laxity and subjective results in the 8-strand double-bundle group.(2134) There is no clear evidence supporting one surgical treatment over another; thus there is no recommendation regarding specific autologous tendon harvest sites or surgical techniques.

Thus, currently available quality evidence suggests autologous grafting may be superior to prosthetics or allografts,(2135-2138) although individual patient factors should be considered. This precludes a formal recommendation for or against prosthetics and allografts. Surgical reconstruction is invasive, has adverse effects, and is highly costly, but may be necessary for selected patients and is thus selectively recommended.

*Evidence* – A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: Ipsilateral Hamstring Autografts; Anterior cruciate ligament, posterior cruciate ligament, ACL, PCL, repair, injury; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 17 articles in PubMed, 56 in Scopus, 1 in CINAHL, 6 in Cochrane Library, 1330 in Google Scholar, and 4 from other sources. We considered for inclusion 2 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 2 from Google Scholar, and 4 from other sources. Of the 9 articles considered for inclusion, 8 randomized trials and 1 systematic review met the inclusion criteria.

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: LAD technique, ligament augmentation device, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 32 articles in PubMed, 57 in Scopus, 26 in CINAHL, 10 in Cochrane Library, 5340 in Google Scholar, and 0 from other sources. We considered for inclusion 8 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 8 articles considered for inclusion, 7 randomized trials and 1 systematic review met the inclusion criteria

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: Anterior cruciate ligament, Posterior cruciate ligament, ACL, injuries, sprain, tear, Leeds-Keio graft, artificial ligament, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 3 articles in PubMed, 101 in Scopus, 7 in CINAHL, 1 in Cochrane Library, 198 in Google Scholar, and 1 from other sources. We considered for inclusion 1 from PubMed, 6 from Scopus, 2 from CINAHL, 0 from Cochrane Library, 3 from Google Scholar, and 1 from other sources. Of the 13 articles considered for inclusion, 3 randomized trials and 3 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: Patellar Tendon Graft, Bone-patellar tendon-bone grafting, Anterior Cruciate Ligament Tears and Posterior Ligament Tears, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 106 articles in PubMed, 2513 in Scopus, 16 in CINAHL, 33 in Cochrane Library, 2180 in Google Scholar, and 7 from other sources. We considered for inclusion 15 from PubMed, 0 from Scopus, 0 from CINAHL, 7 from Cochrane Library, 2 from Google Scholar, and 7 from other sources. Of the 31 articles considered for inclusion, 25 randomized trials and 6 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: quadriceps tendon graft;

Anterior Cruciate Ligament Tears, Posterior Ligament Tears, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 18 articles in PubMed, 1 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 0 in Google Scholar, and 2 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 3 articles considered for inclusion, 3 randomized trial and 0 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: Semitendinosus Graft, Anterior cruciate ligament, Posterior cruiate ligament, ACL, injuries, sprain, tear controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 69 articles in PubMed, 29 in Scopus, 0 in CINAHL, 1 in Cochrane Library, 1460 in Google Scholar, and 19 from other sources. We considered for inclusion 8 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 7 from Google Scholar, and 0 from other sources. Of the 17 articles considered for inclusion, 7 randomized trials and 2 systematic reviews met the inclusion criteria.

### **Post-operative Rehabilitation for ACL Tears**

See above.

## **Meniscal Tears**

### **Diagnostic Recommendations**

Magnetic resonance imaging of asymptomatic individuals has shown that among those 60 to 69 years of age, the anterior horns were normal in only 20% of the lateral menisci, and all medial menisci were abnormal.(2139) Similarly, all of the posterior horns were also showing some degenerative changes among the elderly with strong trends towards increased degeneration with age.(2139) Another study reported severity of changes and also found a strong correlation between increased degenerative changes and age.(2140) Thus, tears of the medial or lateral knee menisci are quite common. They have often been classified as trauma-related or degenerative.(2139-2141) However, due to the high prevalence of tears on MRI, designations of trauma-related tears may be a somewhat arbitrary distinction in many cases, particularly when the inciting event involves normal use or minimal exertion, rather than sporting events.

A careful history will usually result in a presumptive diagnosis that may be confirmed with physical examination (see History and Physical Examination sections above). Patients tend to have pain that lateralizes to the affected compartment and tends to not radiate and may or may not have swelling, presumably depending on factors such as the acuity and magnitude of the tear. Quality of physical examination tests has been called “poor to fair,”(138, 2142) and many examination maneuvers have relatively poor operant characteristics.(74, 75, 80, 83, 137, 2143-2146) A composite of physical

examination maneuvers has been thought to be more helpful.(108) As there is a high prevalence rate of asymptomatic tears, the examination also may be normal, but an MRI may be abnormal.(2139, 2140) Clinical tests are generally not necessary for initial presentation and evaluation of mild meniscal tears as they do not tend to affect management.

## X-RAY AND MRI

*X-ray and MRI for Evaluation of Meniscal Tears*

**X-ray and MRI are recommended in more severe cases of meniscal tears, including cases involving significant trauma, particularly to rule out fracture. MRI is also helpful for defining other injuries that may accompany tears such as cruciate and other ligament tears.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## ULTRASOUND

*Ultrasound for Evaluation of Meniscal Tears*

**There is no recommendation for or against the use of diagnostic ultrasound for the evaluation of meniscal tears.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

*Rationale for Recommendations*

MRI has been commonly performed to evaluate meniscal tears.(430, 433, 2147-2177) However, MRIs have been thought to be able to be reserved for complicated and confusing cases,(2178) as they do not usually contribute to management.(2179, 2180) There also are concerns that have been raised regarding increasing unnecessary surgery by over-reliance on MRI findings(2181); although a clinical trial suggested this may not be the case.(2180) Ultrasound,(2182-2186) CT, CT arthrography, spiral CT,(2187-2190) SPECT,(2191-2193) and SPET(2194) have all been used for diagnostic purposes. There are no quality studies of treatment options aside from surgery and rehabilitation for meniscal tears (see next section). Out of necessity, guidance for treatment relies by analogy upon ankle sprains, as there are considerable quality trials for ankle sprains.

*Evidence for the Use of MRI for Meniscal Tears*

There are 1 moderate-quality RCT incorporated into this analysis.

## Treatment Recommendations

Rest, splints, ice and heat have been utilized for treatment of meniscal tears.

### Work Limitations

*Work Limitations for Select Cases of Meniscal Tears*

**Work limitations are recommended for those with meniscal tears performing high physical demand tasks or those who have no ability to avoid repeating physically demanding job tasks that may have resulted in the condition.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

*Work Limitations for Other Cases of Meniscal Tears*

**There is no recommendation for or against work limitations in other cases of meniscal tears.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

## **BED REST AND KNEE IMMOBILIZATION**

*Bed Rest and Knee Immobilization for Meniscal Tears*

**Bed rest and knee immobilization are not recommended for meniscal tears, although relative rest may be required for some patients, particularly those more severely affected.**

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

## **NSAIDs**

*NSAIDs for Meniscal Tears*

**Nonsteroidal anti-inflammatory medications are recommended for meniscal tears. (See NSAIDs section for dose, frequency, discontinuation information).**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## **ICE/HEAT**

*Ice/Heat for Meniscal Tears*

**Ice and/or heat are recommended for meniscal tears.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## **WRAPS/SUPPORTS/SLEEVES**

*Ace Wraps, Supports or Sleeves for Meniscal Tears*

**Ace wraps, supports, or sleeves are recommended for meniscal tears.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## **REHABILITATION THERAPY**

*Rehabilitation Therapy for Meniscal Tears*

**A course of rehabilitation therapy is recommended for those with meniscal tears with persisting pain thought to not be clearly surgical.**

*Dose – See exercise section for dose, frequency and discontinuation.*

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## **Glucocorticosteroid Injections**

Glucocorticosteroid injections have been used to treat meniscal tears (2457).

*Glucocorticosteroid Injections for Meniscal Tears*

**Glucocorticosteroid injections are not recommended for the treatment of meniscal tears.**

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

*Level of Confidence – Low*

*Rationale* – There is no quality evidence of efficacy of these injections for meniscal tears and thus they are not recommended. There are other indications for steroid injections. The medical expert panel differed on this recommendation with 43% supporting not recommended, 29% no recommendation and 29% recommended.

*Evidence* – A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: Glucocorticoids, glucocorticosteroids, steroid injections, glucocorticosteroid injections, Meniscus Injuries, Lateral Meniscus injury, Tibial Meniscus Injuries, Meniscal tears, Meniscus tears controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 5 articles in PubMed, 19 in Scopus, 0 in CINAHL, 0 in Cochrane Library, 175 in Google Scholar, and 2 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 3 articles considered for inclusion, 3 randomized trials and 0 systematic reviews met the inclusion criteria.

## **Low-Level Laser Therapy**

Low-level laser therapy has been trialed for treatment of meniscal tears (2458).

### *Low-Level Laser Therapy for Meniscal Tears*

Low-level laser therapy is not recommended for the treatment of meniscal tears.

*Strength of Evidence* – **Not Recommended, Insufficient Evidence (I)**

*Level of Confidence* – **Low**

*Rationale:* There are sparse trials of LLLT for treatment of meniscal tears (2458). There is no quality evidence of efficacy in large, sham-controlled trials, thus the panel (57%) felt this should be no recommended and 43% felt it should have no recommendation.

*Evidence:* A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: Low-level laser therapy, Meniscus Injuries, Tibial Meniscus Injuries, Lateral Meniscus injury, Meniscal tears, Meniscus tears controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 1 article in PubMed, 168 in Scopus, 0 in CINAHL, 1 in Cochrane Library, 149 in Google Scholar, and 0 from other sources. We considered for inclusion 1 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 1 article considered for inclusion, 1 randomized trial and 0 systematic reviews met the inclusion criteria.

## Manipulation and Mobilization

Manual therapy and manipulation have been used to treat meniscal tears (2459).

### *Manual Therapy and Manipulation for Meniscal Tears*

Manual therapy and manipulation are not recommended for the treatment of meniscal tears.

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

*Level of Confidence – Low*

*Rationale* – One small, 2-week trial attempted a sham and suggested modest benefits of a manual technique for meniscal tear (2459). Manual therapy has low adverse effects, but in the absence of durable effects, the panel recommendation is not recommended (57%), while a minority felt this should have no recommendation.

*Evidence* – A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: Manipulation, mobilization, Meniscus Injuries, Lateral Meniscus injury, Tibial Meniscus Injuries, Meniscal tears, Meniscus tears controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 106 articles in PubMed, 489 in Scopus, 2 in CINAHL, 11 in Cochrane Library, 1110 in Google Scholar, and 1 from other sources. We considered for inclusion 0 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 1 from other sources. Of the 1 article considered for inclusion, 1 randomized controlled trial and 0 systematic reviews met the inclusion criteria.

## OTHER MODALITIES/INJECTIONS

### *Other Modalities and Injections for Meniscal Tears*

**There is no recommendation for or against therapeutic ultrasound, diathermy, electrical stimulation, iontophoresis, phonophoresis, acupuncture, autologous blood injections, plasma rich platelet injections, and hyaluronic acid injections for meniscal tears.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Rationale for Recommendations*

Work limitations may be necessary depending on the severity of the condition and the required job demands. Those performing high physical demand tasks or those who have no ability to avoid repeating physically demanding job tasks that may have resulted in the condition are recommended to have work limitations. In other cases, there is no recommendation for or against work limitations. Bed rest and knee immobilization are not recommended due to risks of venous thromboembolisms and other adverse effects of bed rest, although relative rest may be required for some patients, particularly those more severely affected. Nonsteroidal anti-inflammatory medications, ice, heat, Ace wraps, supports or sleeves are recommended. Those with persisting pain thought to not be clearly surgical are recommended to have a course of rehabilitation therapy. There is no recommendation for or against therapeutic ultrasound, diathermy, electrical stimulation, iontophoresis, phonophoresis, acupuncture,

manual therapy, autologous blood injections, plasma rich platelet injections, and hyaluronic acid injections. Hyaluronic acid injections have been used to treat knee osteoarthritis,(1424) and have been reported to have additive benefit for arthroscopy patients found to have arthrosis at the time of meniscal surgery.(2195)

*Evidence for the Use of Hyaluronate Injections for Meniscal Tears*

There are 2 moderate-quality RCTs incorporated into this analysis.

## **Rehabilitation of Meniscal Tears with or without Surgical Repair**

Exercise, physical therapy, and rehabilitation have been used for treatment of meniscal tears.(2196-2198) Inferential current therapy has also been used.(1267)

*Meniscal Tear Rehabilitation without Surgical Repair*

**Rehabilitation for select patients after meniscal tears without surgical repair is recommended.**

*Indications* – Select patients with meniscal tears resolving without surgery, but particularly those with functional deficits, such as residual muscle weakness.

*Duration* – One to 4 weeks, 2 to 3 sessions a week.

*Indications for Discontinuation* – Achievement of goals, non-compliance with clinic or home based exercises or intolerance.

*Strength of Evidence* – **Recommended, Evidence (C)**

*Meniscal Tear Rehabilitation after Surgical Repair*

**Meniscal tear rehabilitation for select patients after surgical repair is recommended.**

*Indications* – Patients with meniscal tears having undergone surgical repair, particularly with functional deficits such as residual muscle weakness.

*Duration* – One to 6 weeks, 2 to 3 sessions a week.

*Indications for Discontinuation* – Achievement of goals, non-compliance with clinic or home-based exercises or intolerance.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

*Rationale for Recommendations*

There is one moderate-quality trial comparing surgery plus exercise with exercise alone suggesting equivalency.(2199) This provides some evidence for successful non-operative rehabilitation. Most trials of exercise and rehabilitation enrolled post-meniscectomy patients.(2200) Most of these trials compared supervised therapy with either a home exercise program or advice compared to a home program,(2201) physiotherapy with oral and written advice,(2202) and stationary bicycling with no treatment.(2203) One trial found functional strengthening exercises superior to a control for post-operative rehabilitation.(2204) Thus, the balance of studies implies the post-operative results are good and many patients do not appear to require formal post-operative therapy aside from advice and education. Nevertheless, exercise is thought to be helpful for select patients with weakness or other functional limitations who were not the main enrollment criteria for the available evidence-base. Some may require few appointments for teaching while others require more supervision and assistance with advancement of the program towards independence in the presence of significant deficits. One trial evaluated early rehabilitation and its suggested superiority; however, baseline differences negate the ability to utilize the trial for the development of evidence-based guidance.(1861) Exercise is not invasive,

has low adverse effects and is moderately costly, depending on numbers of appointments required, and is recommended for select patients with functional deficits.

#### *Evidence for the Use of Rehabilitation for Meniscal Tears*

There are 7 moderate-quality RCTs incorporated into this analysis. There is 1 low-quality RCT in Appendix 1.

## **Platelet-Rich Plasma and Autologous Blood Injections**

Platelet rich plasma, as well as autologous blood injections, have been used to treat several tendinopathies including lateral epicondylalgia,(2363, 2364) Achilles' tendinopathies,(2365, 2366) and patellar tendinopathy. (2367, 2368) These injections have also been used for treatment of osteoarthritis.(1346-1349, 2369-2371)

#### *Platelet-Rich Plasma and Autologous Blood Injections for Meniscal Tears*

**There is no recommendation for or against the use of platelet-rich plasma or autologous blood injections.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

*Level of Confidence – Low*

*Rationale* – There is only one research group has reported a placebo-controlled trial suggested PRP was associated with improved healing of chronic meniscal tears and limited the need for future surgical repairs significantly (8% vs 28%), while the failure rate (non-union of the meniscal tear) was 48% in PRP group vs 70% in controls (2460). As there is only one research group reporting favorable results, there is no recommendation until reproducible and durable efficacy has been demonstrated.

*Evidence* – A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2108 using the following terms: Plasma rich platelet injection, platelet rich plasma; Meniscus Injuries, Tibial Meniscus Injuries, Meniscal tears, Meniscus tears controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 9 articles in PubMed, 126 in Scopus, 2 in CINAHL, 1 in Cochrane Library, 435 in Google Scholar, and 2 from other sources. We considered for inclusion 0 from PubMed, 1 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 2 articles considered for inclusion, 2 were randomized controlled trials and 0 were systematic reviews.

## **Surgery for Meniscal Tears**

Surgical partial meniscectomy has been used for treatment of meniscal tears,(2205-2213) particularly by arthroscopic means.(2214-2236) The short-term prognosis (2237, 2238) as well as the degree of subsequent arthrosis has been correlated with the amount of meniscus removed.(207, 2214, 2239-2241) Meniscal repairs have a higher operation rate than partial meniscectomies; however, reportedly more likely result in better long-term outcomes.(2242) All-inside repair has been utilized as a surgical technique.(2243-2245) There also are concerns that a lateral meniscus tear may have a worse prognosis.(2217) However, a Cochrane review concluded the lack of RCTs impaired the ability to draw conclusions regarding surgical versus non-surgical management as well as repair versus excision of torn

menisci. There also are investigational techniques, including use of stem cells to attempt to regenerate menisci.(2246-2248) Allograft transplantation,(2249-2274) collagen implants(1678, 2275) , and synthetic materials (2276) have also been utilized.

### *Surgery for Meniscal Tears*

**Arthroscopic partial meniscectomy and/or meniscal repairs for symptomatic, torn menisci is recommended for highly select patients.**

*Strength of Evidence* – Recommended, Insufficient Evidence (I)

*Level of Confidence* – **Low**

*Indications* – Relatively few patients with meniscal tears appear to be candidates for this surgery. Possible expectations include those with locking symptoms, severe tears, and/or frank traumatic onset that does not generally include onset after “exercise,” “hard work,” or “twisting” events.(2277) Thus, patients should be highly selected and have attempted non-operative treatment that generally included passage of at least a few weeks, NSAIDs, and activity modulation, and also may have included formal therapy.(2199) Patients with marked mechanical symptoms (e.g., mechanical locking with effusions) are candidates for early operative intervention. Patients trending towards improvement generally warrant longer periods of non-operative management, while patients failing to trend towards improvement over at least 3 to 4 weeks are candidates for earlier surgical treatment.

*Benefits* – Theoretical potential for faster healing, but limited to those who would not have healed or recovered without surgery.

*Harms* – Inherent risks of surgery, including infection and post-operative debility.

*Rationale* – There is one high-quality trial comparing partial meniscectomy with sham in knees without osteoarthritis and found a lack of efficacy including at 2-year follow-up.(2277, 2461) There is one moderate-quality trial comparing meniscectomy with versus without exercise that suggested no differences in outcomes.(2199) Another trial found a lack of benefit of medial meniscectomy for horizontal tears at 2 years (2462). As noted above, meniscal degenerative tears become universal with age. These data suggest that there are many cases of meniscal tears that do not require meniscectomy. Additionally, surgical indications have not been clearly defined. Those with marked mechanical symptoms have not been evaluated in randomized, quality trials and are believed to require operative treatment. Meniscal repairs have a higher re-operation rate than partial meniscectomies; however, reportedly more likely result in better long-term outcomes.(2242) One moderate-quality trial suggested a radiofrequency device was superior to a mechanical shaver to accomplish the meniscectomy.(2278) Surgery is invasive, has adverse effects, is costly, and the highest quality evidence does not support efficacy; but surgery is thought to be required for treatment of selected meniscal tears, particularly those including significant mechanical symptoms. Surgery is thus highly selectively recommended.

Available evidence suggests that preservation of more meniscal tissue is superior to removal of greater quantities of the menisci for both short- to intermediate-term function,(2205, 2206, 2275, 2279-2281) as well as for reduction in subsequent risk of osteoarthritis.(207, 2214, 2239-2241) There is no quality evidence to address utility of meniscectomy by peripheral/vascular vs. avascular zone involvement, although there are opinions about these tears.(2282-2285)

*Evidence* – A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: Partial Meniscectomy, Meniscus Injuries, Meniscal tears, Meniscus tears, Lateral Meniscus injury, Medial Meniscus injury controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 305 articles in PubMed, 1698 in Scopus, 7 in CINAHL, 81 in Cochrane Library, 1560 in Google Scholar, and 15 from other sources. We considered for inclusion 15 from PubMed, 2 from Scopus, 1 from CINAHL, 1 from Cochrane Library, 0 from Google Scholar, and 0 from other sources. Of the 19 articles considered for inclusion, 8 randomized trials and 11 systematic reviews met the inclusion criteria.

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without publication dates limits and then an updated search was conducted using multiple search engines including: PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2018 using the following terms: Total Meniscectomy, Meniscus Injuries, Tibial Meniscus Injuries, Meniscal tears, Meniscus tears, Meniscal tears, Total meniscal tear, Lateral meniscus Injury, Medial Mesicuas Injury controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 123 articles in PubMed, 1144 in Scopus, 1 in CINAHL, 30 in Cochrane Library, 2940 in Google Scholar, and 6 from other sources. We considered for inclusion 2 from PubMed, 2 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 1 from Google Scholar, and 6 from other sources. Of the 11 articles considered for inclusion, 7 randomized trials and 2 systematic reviews met the inclusion criteria.

## **Post-operative Rehabilitation for Meniscal Tears**

See above.

# **Knee Bursitis**

## **Introduction**

Knee bursitis is usually associated with a painless effusion of one or more of the knee bursae. (2291-2294) Acute knee bursitis may be slightly warm, but is generally non-tender or minimally tender. Septic (infected) bursitis is either a complication of aseptic knee bursitis or a direct consequence of trauma. (96, 2291, 2295, 2296) Generally, to be a complication of aseptic knee, bursitis also requires introduction of organisms through the skin, such as via abraded skin or an injection, although systemic seeding may also occur. Signs include swelling, pain, tenderness, and pain on range of motion. (2291, 2292, 2294, 2297) Bursitis due to crystal arthropathies also tends to present with findings similar to those of septic bursitis. (2292, 2298)

## Diagnostic Recommendations

There are no recommended special studies for most cases of knee bursitis. If the bursa is thought to be infected, aspiration of the fluid and analyses including Gram stain and culture and sensitivity are recommended.

### *Fluid Aspiration and Analyses for Knee Bursitis*

**Aspiration of the fluid and analyses including Gram stain and culture and sensitivity are recommended to evaluate for septic bursitis in patients with suspected infection.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

### *X-ray for Bursitis*

**X-ray is recommended to rule out osteomyelitis or joint effusion in cases of significant septic knee bursitis.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## Treatment Recommendations

Most patients with knee bursitis are treated with soft knee padding or an ace wrap, are instructed to avoid kneeling, and require no further care other than monitoring to assure resolution.

### **Initial Care**

#### *Soft Knee Padding and Ace Wraps for Knee Bursitis*

**Soft padding of the knee and ace wraps are recommended for treatment of knee bursitis.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

#### *Rationale for Recommendation*

There are no quality trials evaluating these modifications for treatment of knee bursitis. Most cases of bursitis appear to resolve with non-invasive options. Soft padding and ace wraps are not invasive, have few adverse effects, are low cost, thus they are recommended.

#### *Evidence for the Use of Soft Padding and Ace Wraps for Knee Bursitis*

There are no quality studies evaluating the use of soft padding or ace wraps for knee bursitis.

#### *Modifying Activities to Avoid Kneeling or other Pressure Over the Knee*

**Modifying activities to avoid kneeling or pressure over the knee and allowing time to reabsorb the fluid are recommended for treatment of knee bursitis.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

#### *Rationale for Recommendation*

There are no quality trials evaluating modification of activities for treatment of knee bursitis. Most cases appear to resolve with non-invasive options including avoiding kneeling and pressure on the knee. Activity modification is not invasive, has low or no adverse effects, is low cost and is recommended.

#### *Evidence for the Use of Modifying Activities*

There are no quality studies evaluating the use of modifying activities for knee bursitis.

## Non-steroidal Antiinflammatory Drugs (NSAIDs)

Some patients with knee bursitis have been treated with NSAIDs, particularly if there is some accompanying discomfort.

### *NSAIDs for Knee Bursitis*

**There is no recommendation for or against the use of NSAIDs for the treatment of knee bursitis.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Rationale for Recommendation*

There is no quality evidence that NSAIDs alter the clinical course, thus there is no recommendation for or against their use for knee bursitis. The threshold for a trial of these medications should generally be low.

### *Evidence for the Use of NSAIDs for Knee Bursitis*

There are no quality studies evaluating the use of NSAIDs for knee bursitis.

## ASPIRATION

Aspiration of the swollen bursa has been used for diagnosing septic knee bursitis, or if it is thought to be potentially infected. (2292, 2294, 2299)

### *Aspiration for Infected Bursa*

**Aspiration of a clinically infected or questionably infected bursa is recommended.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

### *Rationale for Recommendation*

Aspiration has been used for diagnosis, particularly when combined with Gram stain, culture and sensitivity, and complete cell count of the aspirated fluid are performed. Crystal examination (light polarizing microscopy) should also be performed at least once on the aspirated fluid. Aspiration of a bursa is invasive, has relatively low adverse effects, although it can introduce an infection, and is low to moderately costly, but is recommended for diagnosis and planning of treatment.

## GLUCOCORTICOSTEROID INJECTIONS

Injection with a glucocorticosteroid (typically doses of methylprednisolone approximately 20 to 40mg or equivalent), often accompanied by aspiration, is widely used for aseptic knee bursitis.(2299)

### *Glucocorticosteroid Injections for Knee Bursitis*

**There is no recommendation for or against the use of glucocorticosteroid injections for the treatment of knee bursitis.** This may be a reasonable option for patients who are failing to resolve prior to consideration of surgery.

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Rationale for Recommendation*

There are no quality studies evaluating the use of glucocorticosteroid injections to treat knee bursitis. These injections sometimes appear to help speed resolution in cases not trending towards resorption. However, these injections potentially introduce bacteria, thus the one drawback is the potential to create a septic bursitis, which then often requires surgical drainage. If attempted, these injections appear to be reserved for patients thought to not be infected and/or who are not resolving with activity modifications and observation. If attempted, generally only 1 aspiration/injection is performed followed by careful observation. Some physicians aspirate and then inject, while others only inject the steroid. If

the bursitis is not satisfactorily resolved, a second aspiration/injection is often attempted, although usually not sooner than 3 to 4 weeks later. Doses of steroid are approximately, e.g., methylprednisolone 20 to 40mg or equivalent. Aspirated fluid should be sent at least once for studies including crystals (light polarizing microscopy), Gram stain, culture, and sensitivity and complete cell count. Glucocorticosteroid injection is invasive, has relatively low adverse effects, although it can introduce an infection, and is moderately costly; thus, it is recommended in those cases not trending towards resolution.

## **Surgical Considerations**

Surgery has been used to treat knee bursitis that has not responded to activity modifications and injections or if infection is believed to be present.(2300-2304)

### *Surgical Drainage for Knee Bursitis*

**Surgical drainage is recommended for treatment of knee bursitis.**

*Indications* – Knee bursitis that is either infected, clinically thought to be infected, or not infected but present for at least approximately 6 to 8 weeks without trending towards resolution despite being treated with soft padding and activity modifications.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

### *Surgical Resection for Chronic Knee Bursitis*

**Surgical resection of the bursa is recommended for chronic knee bursitis with recurrent drainage.**

*Indications* – Knee bursitis with recurrent drainage.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

### *Rationale for Recommendations*

There are no quality trials addressing surgery for the treatment of knee bursitis. Surgical drainage of a swollen knee bursa has been successfully used for treatment. As it is not without potential complications, it is recommended to be reserved for selected cases either involving infection or failure to respond to an adequate trial of non-operative measures. Surgical drainage is invasive, has modest adverse effects, and is moderately to highly cost, but is recommended in those cases not trending towards resolution or which are thought to be infected.

# Patellar Tendinosis, Patellar Tendinopathy (“Jumper’s Knee”), and Anterior Knee Pain

## Introduction

Anterior knee pain is caused by several different entities that include patellar tendinosis as well as patellofemoral joint-related pain.(101, 159, 2305, 2306) The diagnosis is primarily clinical (see History and Physical Examination), and a careful history will usually result in a presumptive diagnosis that may be confirmed with physical examination. Patients have anterior knee pain, and those with patellar tendinosis have pain localized to the affected area of the patellar tendon. Those with patellofemoral joint disorders tend to have peripatellar knee pain that often is worse with use of stairs.(2305, 2307)

## Diagnostic Recommendations

### X-RAY

X-ray is commonly utilized, especially for evaluation of pain felt to be attributable to the patellofemoral joint.

*X-ray for Evaluation of Patellofemoral Joint Pain*

**X-ray is recommended to evaluate patellofemoral joint pain.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

### ULTRASOUND AND MRI

*Ultrasound or MRI for the Evaluation of Patellofemoral Joint Pain*

**There is no recommendation for or against the use of diagnostic ultrasound or MRI to evaluate patellofemoral joint pain.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

Rest, splints, ice, and heat have been utilized for treatment of tendinoses, as well as for patellofemoral joint disorders. There are no quality studies of treatment options, aside from surgery and rehabilitation for patellofemoral pain or tendinosis (see next section). Out of necessity, guidance for treatment relies upon other musculoskeletal disorders for inferences on projected treatment efficacy.

## Treatment Recommendations

### Work Limitations

*Work Limitations for Select Cases of Patellofemoral Joint Pain*

**Work limitations are recommended for patients with patellofemoral joint pain who perform physically demanding tasks or who have no ability to avoid repeating physically demanding job**

tasks that have resulted in the condition, especially jumping for patellar tendinosis and stair use for patellofemoral joint pain.

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

*Work Limitations for Other Cases of Patellofemoral Joint Pain*

**There is no recommendation for or against the use of work limitations for treatment of other cases of patellofemoral joint pain.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

## **BED REST AND KNEE IMMOBILIZATION**

*Bed Rest and Knee Immobilization for Patellofemoral Joint Pain*

**Bed rest and knee immobilization are not recommended for treatment of patellofemoral joint pain, although relative rest may be required for some patients, particularly those more severely affected.**

*Strength of Evidence – Not Recommended, Insufficient Evidence (I)*

## **NSAIDs**

*NSAIDs for Patellofemoral Joint Pain*

**Nonsteroidal anti-inflammatory medications are recommended for treatment of patellofemoral joint pain.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## **ICE/HEAT**

*Ice/Heat for Patellofemoral Joint Pain*

**Ice and/or heat are recommended for treatment of patellofemoral joint pain.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## **WRAPS, SUPPORTS, AND SLEEVES**

*Wraps, Supports, or Sleeves for Patellofemoral Joint Pain*

**Ace wraps, supports, or sleeves are recommended for treatment patellofemoral joint pain.**

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## **REHABILITATION THERAPY**

*Rehabilitation Therapy for Patellofemoral Joint Pain*

**A course of rehabilitation therapy is recommended for treatment of patellofemoral joint pain in patients with persisting pain thought to not be clearly surgical.**

*Dose/Duration – See exercise section for dose, frequency, and discontinuation.*

*Strength of Evidence – Recommended, Insufficient Evidence (I)*

## **OTHER MODALITIES/INJECTIONS**

*Other Modalities/Injections for Patellofemoral Joint Pain*

**There is no recommendation for or against the use of therapeutic ultrasound, diathermy, iontophoresis, low-level laser therapy, phonophoresis, autologous blood injections, or hyaluronic acid injections for treatment of patellofemoral joint pain.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

#### *Rationale for Recommendations*

Work limitations may be necessary depending on the severity of the condition and the required job demands. Those performing physically demanding tasks or those who have no ability to avoid repeating physically demanding job tasks that have resulted in the condition are recommended to have work limitations. In other cases, there is no recommendation for or against work limitations. Bed rest and knee immobilization are not recommended due to risks of venous thromboembolisms and other adverse effects of bed rest, although relative rest may be required for some patients, particularly those more severely affected. NSAIDs, ice, heat, Ace wraps, supports, and sleeves are recommended. Those with persisting pain thought to not be clearly surgical are recommended to have a course of rehabilitation therapy. There is no recommendation for or against therapeutic ultrasound, diathermy, iontophoresis, low-level laser therapy, phonophoresis, autologous blood injections, or hyaluronic acid injections for treatment of patellofemoral joint pain.

## **Exercise**

Exercise, physical therapy, and rehabilitation have been used for treatment of anterior knee pain.(2308-2331) However, evidence to support physical interventions has been labeled “limited.”(2332)

#### *Exercise for Patellofemoral Joint Pain*

**Exercise is moderately recommended for patellofemoral joint pain.**

*Indications* – Patients with patellofemoral joint pain, especially if insufficiently responsive to treatment with NSAIDs and activity modification.

*Duration* – One to 4 weeks, 2 to 3 sessions a week; additional appointments based on continuing objective improvements.

*Indications for Discontinuation* – Achievement of goals, non-compliance with clinic or home-based exercises, intolerance.

*Strength of Evidence – Moderately Recommended, Evidence (B)*

#### *Rationale for Recommendation*

Two moderate-quality trials compared exercise therapy with no treatment and found exercise of modest efficacy.(2333-2335) Results from another trial of specific exercise approaches, including static, dynamic, vastus medialis obliquus selective activation (VMO), is unclear,(2335) and there is no recommendation for a specific exercise approach. There also is one trial suggesting a patellar brace is of equal efficacy.(2336) One high-quality trial with two reports included multiple co-interventions and suggested benefit, but an assessment of which intervention was effective is not possible.(2310, 2337) Exercises are not invasive, have low adverse effects, are low to moderately costly depending on numbers of appointments, and thus are recommended.

#### *Evidence for the Use of Exercise for Anterior Knee Pain*

There are 2 high- and 20 moderate-quality (one with two reports) RCTs incorporated into this analysis. There are 3 low-quality RCTs in Appendix 1.(594, 2338, 2339)

## TAPING

Patellar taping has been used to treat anterior knee pain.(2340-2342) There is experimental evidence supporting the idea that taping and bracing provide coronal plane and torsional control of the knee in eccentric stair step descent.(1071)

### *Taping for Anterior Knee Pain*

**Taping is not recommended for anterior knee pain.**

*Strength of Evidence- Not Recommended, Evidence (C)*

### *Rationale for Recommendation*

One moderate-quality trial attempted sham taping and found no efficacy of taping(2343); two other trials also suggested that taping is ineffective.(2344, 2345) While one trial suggested taping may be superior,(2346) the balance of studies suggest that it is not effective. There were two crossover trials, but both were of very short duration, precluding their use in guidance.(2347, 2348) Taping is not invasive, but is not tolerated by some patients and compliance is reportedly problematic. Taping is low cost for one application, but rapidly becomes costly over time. As most quality evidence suggests a lack of efficacy, taping is not recommended for treating anterior knee pain.

### *Evidence for the Use of Taping for Anterior Knee Pain*

There are 6 moderate-quality RCTs or crossover trials incorporated into this analysis. There are 1 low-quality RCTs or crossover trials in Appendix 1.(2349)

## ORTHOTICS AND KNEE SPLINTS

Orthotics has been used for treatment of patellofemoral joint pain.(594, 1118, 2336, 2350, 2351)

### *Orthotics or Knee Splints for Patellofemoral Knee Pain*

**There is no recommendation for or against the use of orthotics or knee splints for patellofemoral joint pain.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Functional Bracing for Prevention of Anterior Knee Pain*

**There is no recommendation for or against the use of functional bracing for prevention of anterior knee pain.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Rationale for Recommendations*

There are no quality studies addressing the use of knee splints, orthotics, or bracing for treatment of patellofemoral knee pain. There is one moderate-quality study comparing bracing with no bracing in prevention of anterior knee pain in military recruits and that study reported a significant decrease in the development of anterior knee pain after 6 weeks.(2352) There is one high-quality trial comparing foot orthoses, flat inserts, physiotherapy and a combination of foot orthoses plus physiotherapy and found minimal differences(2308);. Braces may be helpful for those with high-demand positions, particularly if they are not acclimated to the demands of the position. These devices are not invasive, have few adverse effects, are low cost, but absent evidence of efficacy, there is no recommendation regarding their use.

### *Evidence for the Use of Orthotics and Knee Splints*

There are 1 high- and 3 moderate-quality RCTs or crossover trials incorporated into this analysis. There are 4 low-quality RCTs in Appendix 1.(594, 2353-2355)

## Electrical Stimulation

Electrical stimulation has been used for treatment of anterior knee pain.(1269)

*Electrical Stimulation for Anterior Knee Pain*

**Electrical stimulation is not recommended for treatment of anterior knee pain.**

*Strength of Evidence – Not Recommended, Evidence (C)*

*Rationale for Recommendation*

There are no quality placebo- or sham-controlled clinical trials evaluating electrical stimulation for anterior knee pain. One trial found electrical stimulation to be of no added benefit in addition to exercises.(2356) Another moderate-quality trial that used two different active treatments failed to find differences.(1269) Electrical stimulation is not invasive, has low adverse effects, and is moderately costly. It appears ineffective in treating anterior knee pain and thus, is not recommended.

*Evidence for the Use of Electrical Stimulation for Anterior Knee Pain*

There are 2 moderate-quality RCTs incorporated into this analysis.

## Manipulation and Mobilization

Manipulation and mobilization and have been used to treat anterior knee pain, often in conjunction with axial joints.(1223, 1235, 1240, 1242, 2357)

*Mobilization and Manipulation for Anterior Knee Pain*

**There is no recommendation for or against the use of manipulation and mobilization for treatment of anterior knee pain.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

*Rationale for Recommendation*

There are no quality trials comparing manipulation or mobilization with sham or no treatment controls to treat anterior knee pain. The few, small available studies comparing active treatments have methodological flaws. Thus, there is no recommendation for or against the use of mobilization or manipulation to treat anterior knee pain.

*Evidence for the Use of Manipulation and Mobilization for Anterior Knee Pain*

There are 2 moderate-quality RCTs incorporated into this analysis. There are 2 low-quality RCTs in Appendix 1.

## Acupuncture

Acupuncture has been used for treatment of anterior knee and patellofemoral pain.(1208, 2358)

*Acupuncture for Anterior Knee Pain*

**There is no recommendation for or against the use of acupuncture for anterior knee pain.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Rationale for Recommendation*

There are two moderate-quality trials with somewhat conflicting results. One trial compared electroacupuncture with minimal superficial acupuncture and failed to find evidence of efficacy,(1208) while the other suggested slight benefits compared with no treatment controls.(2358) Thus, there is no recommendation for or against the use of acupuncture to treat anterior knee pain.

### *Evidence for the Use of Acupuncture for Anterior Knee Pain*

There are 2 moderate-quality RCTs incorporated into this analysis.

## **Biofeedback**

Biofeedback has been used for treatment of patellofemoral pain.(2359, 2360)

### *Biofeedback for Patellofemoral Pain*

**Biofeedback is not recommended for the treatment of patellofemoral pain.**

*Strength of Evidence – Not Recommended, Evidence (C)*

### *Rationale for Recommendation*

Biofeedback has been evaluated in two moderate-quality trials for treatment of patellofemoral pain syndrome.(2359, 2360) In both trials, there was no additive benefit for biofeedback in addition to exercise. Biofeedback is not invasive, has few adverse effects, and is low cost, but it is ineffective and thus is not recommended.

### *Evidence for the Use of Biofeedback*

There are 2 moderate-quality RCTs incorporated into this analysis. There is 1 low-quality RCT in Appendix 1.(2361)

## **GLUCOCORTICOSTEROID INJECTIONS**

Glucocorticosteroid injections have been utilized for treatment of patellar tendinopathy.

### *Glucocorticosteroid Injections for Select Patients with Patellar Tendinopathy*

**Glucocorticosteroid injections are recommended for select patents to treat patellar tendinopathy.**

*Indications* – Chronic patellar tendinopathy that is unresponsive to other treatments including NSAID(s), activity modification and exercises.(1326, 2362)

*Strength of Evidence – Recommended, Insufficient Evidence (C)*

### *Rationale for Recommendation*

There is one moderate-quality placebo-controlled trial that evaluated the use of glucocorticosteroid injections for the treatment of patellar tendinopathy and found some evidence of efficacy, although somewhat less than with aprotinin.(2362) There is also one moderate-quality trial comparing glucocorticosteroid injections with two different exercise regimens that suggested that the steroid injections are inferior to heavy slow-resistance training exercises.(1326) These injections are mildly invasive, have adverse effects, are moderately costly, and have some evidence of efficacy, thus they are recommended for those select patients who fail a quality exercise program.

### *Evidence for the Use of Glucocorticosteroid Injections for Patellar Tendinopathy*

There are 2 moderate-quality RCTs incorporated into this analysis.

## PLATELET-RICH PLASMA AND AUTOLOGOUS BLOOD INJECTIONS

Platelet-rich plasma, as well as autologous blood injections, have been used to treat several tendinopathies including patellar tendinopathy. (2367, 2368) These injections have also been used for treatment of osteoarthritis.(1346-1349, 2369-2371)

*Platelet-Rich Plasma and Autologous Blood Injections for Patellar Tendinopathy*

**Platelet-rich plasma and autologous blood injections are not recommended for the treatment of patellar tendinopathy.**

*Strength of Evidence – Not Recommended, Evidence (C)*

*Level of Confidence – Low*

*Rationale* – One small, placebo-controlled trial for patellar tendinopathy suggested a lack of efficacy (2463). Another trial found no differences between 1 and 2 injections (2464) while another found 2 injections better than one (2465). There is one moderate-quality study suggesting efficacy of PRP over dry-needling.(2372) There are two moderate-quality trials suggesting PRP is superior to extracorporeal shockwave therapy, but ESWT appears ineffective (see ESWT).(2373, 2374) PRP injections are invasive, have adverse effects, are costly, and the sole placebo-controlled trial suggests lack of efficacy; thus, they are not recommended.

*Evidence*– A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2108 using the following terms: Patellar tendinopathy, Patellar tendinosis, Patellar tendinitis, Jumpers knee, Anterior knee pain, PRP, platelet rich plasma injections, autologous blood injections, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 50 articles in PubMed, 286 in Scopus, 26 in CINAHL, 10 in Cochrane Library, 120 in Google Scholar, and 2 from other sources. We considered for inclusion 9 from PubMed, 4 from Scopus, 3 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 2 from other sources. Of the 19 articles considered for inclusion, 7 randomized trials and 12 systematic studies met the inclusion criteria.

## APROTININ INJECTIONS

Aprotinin injections have been utilized for treatment of patellar tendinopathy as an anti-inflammatory treatment.(2362)

*Aprotinin Injections for Patellar Tendinopathy*

**Aprotinin injections are recommended for select patients to treat patellar tendinopathy.**

*Indications* – Chronic patellar tendinopathy that is unresponsive to other treatments including NSAID(s), exercise, and activity modification.

*Strength of Evidence – Recommended, Evidence (C)*

*Rationale for Recommendation*

There is one moderate-quality placebo-controlled trial that evaluated the use of paratendon, bursal, and tendinous insertion area aprotinin injections for the treatment of patellar tendinopathy and found suggested some efficacy.(2362) This trial did not utilize ultrasound, thus there is no recommendation for or against imaging to accomplish the injections. These injections are invasive, have adverse effects, and are moderately costly. They are recommended for use in highly select cases.

### *Evidence for the Use of Aprotinin Injections for Patellar Tendinopathy*

There is 1 moderate-quality RCT incorporated into this analysis.

## **PROLOTHERAPY, INCLUDING POLIDOCANOL AND HYPERTONIC GLUCOSE INJECTIONS**

Prolotherapy is performed with various sclerosing agents, including polidocanol and hypertonic saline. These have been used to treat chronic patellar tendinopathy.

### *Prolotherapy Injections for Chronic Patellar Tendinopathy*

**Prolotherapy injections are recommended for select patients to treat chronic patellar tendinopathy.**

*Indications* – Athletes with chronic patellar tendinopathy with neovascularization corresponding to the painful area that is unresponsive to other treatments including NSAID(s) and activity modification. Whether these injections are appropriate for others, including workers, is unclear. Ultrasound guidance is recommended for accomplishing the injections.

*Strength of Evidence – Recommended, Evidence (I)*

### *Polidocanol Injection for Acute, Subacute, or Post-operative Patellar Tendinopathy*

**There is no recommendation for or against the use of polidocanol injection for acute, subacute, or post-operative patellar tendinopathy.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

### *Rationale for Recommendations*

There is one high-quality trial among athletes suggesting efficacy of a sclerosing agent (polidocanol) for chronic patellar tendinopathy although there are some weaknesses in the trial.(2377) These injections are invasive, have adverse effects, and are moderately costly. They are recommended for use in highly select cases.

### *Evidence for the Use of Polidocanol Injections*

There is 1 high-quality RCT incorporated into this analysis.

## **GLYCOSAMINOGLYCAN INJECTIONS**

Glycosaminoglycan injections have been used for treatment of patellar tendinosis.

### *Glycosaminoglycan Injections for Patellar Tendinosis*

**Glycosaminoglycan injections are not recommended for treatment of patellar tendinosis.**

*Strength of Evidence – Not Recommended, Evidence (C)*

### *Rationale for Recommendation*

One moderate-quality trial has suggested a lack of efficacy.(2378) Thus, these injections are not recommended.

### *Evidence for the Use of Glycosaminoglycan Injections for Patellar Tendinopathy*

There is 1 moderate-quality RCTs incorporated into this analysis.

## **PERCUTANEOUS NEEDLE TENOTOMY**

Percutaneous needle tenotomy has been attempted to treat chronic tendinosis.(1327-1330, 2379)

### *Percutaneous Needle Tenotomy for Chronic Tendinosis*

**There is no recommendation for or against the use of percutaneous needle tenotomy for treatment of chronic tendinosis.**

*Strength of Evidence – No Recommendation, Insufficient Evidence (I)*

#### *Rationale for Recommendation*

There are no quality studies of percutaneous needle tenotomy as a treatment for chronic tendinosis. This procedure is invasive, has adverse effects, and is moderate to highly costly; thus, there is no recommendation.

#### *Evidence for Percutaneous Needle Tenotomy*

There are no quality studies evaluating the use of percutaneous needle tenotomy.

## **EXTRACORPOREAL SHOCKWAVE THERAPY (“Shockwave”)**

Extracorporeal shockwave therapy (ESWT) has been utilized for treatment of tendinoses, especially in the shoulder and ankle. It has been documented to have efficacy for treatment of calcific tendinitis in the shoulder (see Shoulder Disorders guideline).(2380-2385)

### *Extracorporeal Shockwave Therapy for Patellar Tendinosis*

**Extracorporeal shockwave therapy is not recommended for treatment of patellar tendinosis.**

*Strength of Evidence – Moderately Not Recommended, Evidence (B)*

*Level of Confidence – Moderate*

*Rationale* – One sham-controlled trial found a lack of efficacy of ESWT for treatment of patellar tendinopathy in active athletes (2466) and another trial found a lack of effectiveness for adding ESWT to eccentric exercises (2467). One trial found no difference between focused ESWT and radial shockwave therapy (2468). There is one low-quality trial comparing extracorporeal shockwave therapy with either sham or low-energy treatment for patellar tendinosis.(2386) There are two trials suggesting ESWT is inferior to platelet-rich plasma injections (see above). For most body parts, there is evidence that ESWT is ineffective (see Elbow Disorders, Shoulder Disorders, and Ankle and Foot Disorders guidelines), with the primary exception being efficacy for the treatment of rotator cuff calcific tendinosis. ESWT is minimally invasive, is often performed with an injected anesthetic, has some adverse effects, is moderate to highly costly depending on numbers of treatments, and has two placebo-controlled trials showing lack of efficacy and thus it is not recommended.

*Evidence* – A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar between 1/1/2013 and 11/15/2108 using the following terms Extracorporeal Shockwave Therapy, Patellar tendinopathy, Patellar tendinosis, Patellar tendinitis, Jumpers knee, Anterior knee pain, Extracorporeal Shockwave Therapy, Shock Wave Therapy, Extracorporeal High Intensity Focused Ultrasound Therapy, High-Intensity Focused Ultrasound Therapy, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random\*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 116 articles in PubMed, 225 in Scopus, 7 in CINAHL, 0 in Cochrane Library, 1650 in Google Scholar, and 2 from other sources. We considered for inclusion 4 from PubMed, 3 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 2 from Google

Scholar, and 2 from other sources. Of the 11 articles considered for inclusion, 7 randomized trials and 4 systematic studies met the inclusion criteria.

## **Surgery for Anterior Knee Pain and Patellofemoral Syndrome**

Several surgical procedures have been performed for anterior knee pain and patellofemoral pain syndrome. These have included chondroplasty and patellar shaving and resurfacing. Lateral retinacular release or lengthening and arthroscopic lateral retinacular release has been performed for recurrent subluxation, and surgical realignment of the extensor mechanism has been used for some patients.(2387-2398) Lateral release has been performed without,(1245, 2399-2404) as well as in conjunction with, medial soft-tissue realignment for recurrent patellar instability.(2405-2411) Although, there are no RCTs, a comparison of these procedures concluded that medial soft-tissue realignment is superior.(2408)

### *Surgery for Anterior Knee Pain*

**Surgery is recommended in patients with anterior knee pain after a 6-month period of failed non-operative treatment provided the patient also has one or more of the below indications.**

*Indications* – Moderate to severe anterior knee pain of at least 6 months duration with failed non-operative treatment (including 2 to 3 months of supervised exercises and home-exercise program components with which the patient has been compliant) and one or more of the following: 1) clinical and radiographical evidence of patellar malalignment; 2) clinically and/or radiographically proven subluxation; and/or 3) repeated episodes of patellar dislocation.

*Strength of Evidence* – **Recommended, Insufficient Evidence (I)**

### *Rationale for Recommendation*

One trial has suggested arthroscopic surgery for patellofemoral syndrome was of no additive benefit to a home exercise program, although it included techniques that are no longer recommended such as chondroplasty.(2315) Other trials have compared operative techniques,(2412) including one suggesting no differences between open and arthroscopic lateral release.(2413) Thus, there is one trial comparing operative with non-operative management,(2414) but no trials available that include optimal techniques. Patients who have failed non-operative management are very difficult to treat, and surgery should be carefully weighed against potential failure to improve. For select patients who have significant functional impairment due to patellar malalignment, subluxation, or recurrent dislocation and have failed exercises and non-operative management with which they have been compliant, an attempt at surgical intervention is recommended.

### *Evidence for the Use of Surgery for Anterior Knee Pain*

There are 4 moderate-quality RCTs incorporated into this analysis.

# Appendix 1

## **Low-quality Randomized Controlled Trials and Non-randomized Studies**

The following low-quality randomized controlled studies (RCTs) and other non-randomized studies were reviewed by the Evidence-based Practice Knee Panel to be all inclusive, but were not relied upon for purpose of developing this document's guidance on treatments because they were not of high quality due to one or more errors (e.g., lack of defined methodology, incomplete database searches, selective use of the studies and inadequate or incorrect interpretation of the studies' results, etc.), which may render the conclusions invalid. ACOEM's Methodology requires that only moderate- to high-quality literature be used in making recommendations.(2415)

# References

1. Frank CB, Jackson DW. The science of reconstruction of the anterior cruciate ligament. *J Bone Joint Surg Am.* 1997;79(10):1556-76.
2. Griffin LY, Agel J, Albohm MJ, et al. Noncontact anterior cruciate ligament injuries: risk factors and prevention strategies. *J Am Acad Orthop Surg.* 2000;8(3):141-50.
3. Boden BP, Dean GS, Feagin JA, Jr., Garrett WE, Jr. Mechanisms of anterior cruciate ligament injury. *Orthopedics.* 2000;23(6):573-8.
4. Hughes G, Watkins J. A risk-factor model for anterior cruciate ligament injury. *Sports Med.* 2006;36(5):411-28.
5. Gottlob CA, Baker CL, Jr., Pellissier JM, Colvin L. Cost effectiveness of anterior cruciate ligament reconstruction in young adults. *Clin Orthop Relat Res.* 1999(367):272-82.
6. Murphy SL, Strasburg DM, Lyden AK, et al. Effects of activity strategy training on pain and physical activity in older adults with knee or hip osteoarthritis: a pilot study. *Arthritis Rheum.* 2008;59(10):1480-7.
7. Centers for Disease Control and Prevention. "Arthritis." Arthritis types - overview. 2008. <https://www.cdc.gov/arthritis/basics/osteoarthritis.htm>.
8. Reason for Visits to Emergency Room – National Hospital Ambulatory Medical Care Survey 1998-2006. U.S. Department of Health and Human Services; Centers for Disease Control and Prevention; National Center for Health Statistics.
9. Selesnick FH, Noble HB, Bachman DC, Steinberg FL. Internal derangement of the knee: diagnosis by arthrography, arthroscopy, and arthrotomy. *Clin Orthop Relat Res.* 1985(198):26-30.
10. Blagojevic M, Jinks C, Jeffery A, Jordan KP. Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. *Osteoarthritis Cartilage.* 2010;18(1):24-33.
11. Valdes AM, Loughlin J, Oene MV, et al. Sex and ethnic differences in the association of ASPN, CALM1, COL2A1, COMP, and FRZB with genetic susceptibility to osteoarthritis of the knee. *Arthritis Rheum.* 2007;56(1):137-46.
12. Bliddal H, Christensen R. The treatment and prevention of knee osteoarthritis: a tool for clinical decision-making. *Expert Opin Pharmacother.* 2009;10(11):1793-804.
13. Christiansen T, Bruun JM, Madsen EL, Richelsen B. Weight loss maintenance in severely obese adults after an intensive lifestyle intervention: 2- to 4-year follow-up. *Obesity (Silver Spring).* 2007;15(2):413-20.
14. Chua SD, Jr., Messier SP, Legault C, Lenz ME, Thonar EJ, Loeser RF. Effect of an exercise and dietary intervention on serum biomarkers in overweight and obese adults with osteoarthritis of the knee. *Osteoarthritis Cartilage.* 2008;16(9):1047-53.
15. Conrozier T, Chevalier X. Long-term experience with hylan GF-20 in the treatment of knee osteoarthritis. *Expert Opin Pharmacother.* 2008;9(10):1797-804.
16. Felson DT. Weight and osteoarthritis. *Am J Clin Nutr.* 1996;63(3 Suppl):430S-2S.
17. Felson DT, Chaisson CE. Understanding the relationship between body weight and osteoarthritis. *Baillieres Clin Rheumatol.* 1997;11(4):671-81.
18. Flugsrud GB, Nordsletten L, Espehaug B, Havelin LI, Meyer HE. Weight change and the risk of total hip replacement. *Epidemiology.* 2003;14(5):578-84.
19. Glazier RH, Badley EM, Wright JG, et al. Patient and provider factors related to comprehensive arthritis care in a community setting in Ontario, Canada. *J Rheumatol.* 2003;30(8):1846-50.
20. Lee MS, Pittler MH, Ernst E. Tai chi for osteoarthritis: a systematic review. *Clin Rheumatol.* 2008;27(2):211-8.
21. Manek NJ, Lane NE. Osteoarthritis: current concepts in diagnosis and management. *Am Fam Physician.* 2000;61(6):1795-804.
22. Messier SP. Obesity and osteoarthritis: disease genesis and nonpharmacologic weight management. *Rheum Dis Clin North Am.* 2008;34(3):713-29.
23. Messier SP. Obesity and osteoarthritis: disease genesis and nonpharmacologic weight management. *Med Clin North Am.* 2009;93(1):145-59, xi-xii.

24. Messier SP, Loeser RF, Miller GD, et al. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. *Arthritis Rheum.* 2004;50(5):1501-10.
25. Miller GD, Nicklas BJ, Loeser RF. Inflammatory biomarkers and physical function in older, obese adults with knee pain and self-reported osteoarthritis after intensive weight-loss therapy. *J Am Geriatr Soc.* 2008;56(4):644-51.
26. Misso ML, Pitt VJ, Jones KM, Barnes HN, Piterman L, Green SE. Quality and consistency of clinical practice guidelines for diagnosis and management of osteoarthritis of the hip and knee: a descriptive overview of published guidelines. *Med J Aust.* 2008;189(7):394-9.
27. O'Reilly S, Doherty M. Lifestyle changes in the management of osteoarthritis. *Best Pract Res Clin Rheumatol.* 2001;15(4):559-68.
28. Paans N, van den Akker-Scheek I, van der Meer K, Bulstra SK, Stevens M. The effects of exercise and weight loss in overweight patients with hip osteoarthritis: design of a prospective cohort study. *BMC Musculoskelet Disord.* 2009;1024.
29. Pelletier JP, Raynauld JP, Berthiaume MJ, et al. Risk factors associated with the loss of cartilage volume on weight-bearing areas in knee osteoarthritis patients assessed by quantitative magnetic resonance imaging: a longitudinal study. *Arthritis Res Ther.* 2007;9(4):R74.
30. Vingard E, Alfredsson L, Malchau H. Lifestyle factors and hip arthrosis. A case referent study of body mass index, smoking and hormone therapy in 503 Swedish women. *Acta Orthop Scand.* 1997;68(3):216-20.
31. Wendelboe AM, Hegmann KT, Biggs JJ, et al. Relationships between body mass indices and surgical replacements of knee and hip joints. *Am J Prev Med.* 2003;25(4):290-5.
32. Altman RD, Lozada CJ. Practice guidelines in the management of osteoarthritis. *Osteoarthritis Cartilage.* 1998;6 Suppl A22-4.
33. Arokoski JP. Physical therapy and rehabilitation programs in the management of hip osteoarthritis. *Eura Medicophys.* 2005;41(2):155-61.
34. Christiansen T, Richelsen B, Bruun JM. Monocyte chemoattractant protein-1 is produced in isolated adipocytes, associated with adiposity and reduced after weight loss in morbid obese subjects. *Int J Obes (Lond).* 2005;29(1):146-50.
35. Messier SP, Gutekunst DJ, Davis C, DeVita P. Weight loss reduces knee-joint loads in overweight and obese older adults with knee osteoarthritis. *Arthritis Rheum.* 2005;52(7):2026-32.
36. Toda Y, Toda T, Takemura S, Wada T, Morimoto T, Ogawa R. Change in body fat, but not body weight or metabolic correlates of obesity, is related to symptomatic relief of obese patients with knee osteoarthritis after a weight control program. *J Rheumatol.* 1998;25(11):2181-6.
37. Kocher MS, Tucker R, Ganley TJ, Flynn JM. Management of osteochondritis dissecans of the knee: current concepts review. *Am J Sports Med.* 2006;34(7):1181-91.
38. Stattin EL, Wiklund F, Lindblom K, et al. A missense mutation in the aggrecan C-type lectin domain disrupts extracellular matrix interactions and causes dominant familial osteochondritis dissecans. *Am J Hum Genet.* 2010;86(2):126-37.
39. Aglietti P, Ciardullo A, Giron F, Ponteggia F. Results of arthroscopic excision of the fragment in the treatment of osteochondritis dissecans of the knee. *Arthroscopy.* 2001;17(7):741-6.
40. Aichroth P. Osteochondral fractures and their relationship to osteochondritis dissecans of the knee. An experimental study in animals. *J Bone Joint Surg Br.* 1971;53(3):448-54.
41. Aichroth P. Osteochondritis dissecans of the knee. A clinical survey. *J Bone Joint Surg Br.* 1971;53(3):440-7.
42. Bramer JA, Maas M, Dallinga RJ, te Slaa RL, Vergroesen DA. Increased external tibial torsion and osteochondritis dissecans of the knee. *Clin Orthop Relat Res.* 2004(422):175-9.
43. Cahill BR. Osteochondritis Dissecans of the Knee: Treatment of Juvenile and Adult Forms. *J Am Acad Orthop Surg.* 1995;3(4):237-47.
44. Glancy GL. Juvenile osteochondritis dissecans. *Am J Knee Surg.* 1999;12(2):120-4.
45. Green WT, Banks HH. Osteochondritis dissecans in children. *J Bone Joint Surg Am.* 1953;35-A(1):26-47; passim.
46. Langer F, Percy EC. Osteochondritis dissecans and anomalous centres of ossification: a review of 80 lesions in 61 patients. *Can J Surg.* 1971;14(3):208-15.

47. Linden B. The incidence of osteochondritis dissecans in the condyles of the femur. *Acta Orthop Scand*. 1976;47(6):664-7.
48. Mubarak SJ, Carroll NC. Juvenile osteochondritis dissecans of the knee: etiology. *Clin Orthop Relat Res*. 1981(157):200-11.
49. Rowe SM, Moon ES, Yoon TR, Jung ST, Lee KB, Lee JJ. Fate of the osteochondral fragments in osteochondritis dissecans after Legg-Calve-Perthes' disease. *J Bone Joint Surg Br*. 2002;84(7):1025-9.
50. Schindler OS, Cannon SR, Briggs TW, Blunn GW. Use of a novel bone graft substitute in peri-articular bone tumours of the knee. *Knee*. 2007;14(6):458-64.
51. Wall E, Von Stein D. Juvenile osteochondritis dissecans. *Orthop Clin North Am*. 2003;34(3):341-53.
52. Ahmad CS, McCarthy M, Gomez JA, Shubin Stein BE. The moving patellar apprehension test for lateral patellar instability. *Am J Sports Med*. 2009;37(4):791-6.
53. Dejour D, Le Coultre B. Osteotomies in patello-femoral instabilities. *Sports Med Arthrosc*. 2007;15(1):39-46.
54. Mizuno Y, Kumagai M, Mattessich SM, et al. Q-angle influences tibiofemoral and patellofemoral kinematics. *J Orthop Res*. 2001;19(5):834-40.
55. Senavongse W, Amis AA. The effects of articular, retinacular, or muscular deficiencies on patellofemoral joint stability. *J Bone Joint Surg Br*. 2005;87(4):577-82.
56. Mannion AF, Muntener M, Taimela S, Dvorak J. Comparison of three active therapies for chronic low back pain: results of a randomized clinical trial with one-year follow-up. *Rheumatology*. 2001;40(7):772-8.
57. Kankaanpaa M, Taimela S, Airaksinen O, Hanninen O. The efficacy of active rehabilitation in chronic low back pain. Effect on pain intensity, self-experienced disability, and lumbar fatigability. *Spine (Phila Pa 1976)*. 1999;24(10):1034-42.
58. Cohen I, Rainville J. Aggressive exercise as treatment for chronic low back pain. *Sports Med*. 2002;32(1):75-82.
59. Danielsen JM, Johnsen R, Kibsgaard SK, Hellevik E. Early aggressive exercise for postoperative rehabilitation after discectomy. *Spine*. 2000;25(8):1015-20.
60. Gross DP, Battie MC, Asante A. Development and validation of a short-form functional capacity evaluation for use in claimants with low back disorders. *J Occup Rehabil*. 2006;16(1):53-62.
61. Mayer T, Gatchel R. *Functional Restoration for Spinal Disorders: The Sports Medicine Approach*. Philadelphia: Lea & Febiger; 1988.
62. Mayer T, Gatchel R, Kishino N, et al. Objective assessment of spine function following industrial accident. A prospective study with comparison group and one-year follow-up. *Spine*. 1985;10(6):482-93.
63. Mayer TG, Gatchel RJ, Kishino N, et al. A prospective short-term study of chronic low back pain patients utilizing novel objective functional measurement. *Pain*. 1986;25(1):53-68.
64. Mayer TG, Gatchel RJ, Mayer H, Kishino ND, Keeley J, Mooney V. A prospective two-year study of functional restoration in industrial low back injury. An objective assessment procedure. *JAMA*. 1987;258(13):1763-7.
65. Rainville J, Kim RS, Katz JN. A review of 1985 Volvo Award winner in clinical science: objective assessment of spine function following industrial injury: a prospective study with comparison group and 1-year follow-up. *Spine (Phila Pa 1976)*. 2007;32(18):2031-4.
66. Jousset N, Fanello S, Bontoux L, et al. Effects of functional restoration versus 3 hours per week physical therapy: a randomized controlled study. *Spine (Phila Pa 1976)*. 2004;29(5):487-93; discussion 94.
67. Hildebrandt J, Pflingsten M, Saur P, Jansen J. Prediction of success from a multidisciplinary treatment program for chronic low back pain. *Spine*. 1997;22(9):990-1001.
68. Bellamy N, Buchanan W, Goldsmith C, Campbell J, Stitt L. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol*. 1988;15(12):1833-40.
69. Leshner JM, Dreyfuss P, Hager N, Kaplan M, Furman M. Hip joint pain referral patterns: a descriptive study. *Pain Med*. 2008;9(1):22-5.
70. Rahme D, Comley A, Foster B, Cundy P. Consequences of diagnostic delays in slipped capital femoral epiphysis. *J Pediatr Orthop B*. 2006;15(2):93-7.
71. Flatman JG. Hip diseases with referred pain to the knee. *JAMA*. 1975;234(9):967-8.

72. Henningsen P, Zipfel S, Herzog W. Management of functional somatic syndromes. *Lancet*. 2007;369(9565):946-55.
73. Diermann N, Schumacher T, Schanz S, Raschke MJ, Petersen W, Zantop T. Rotational instability of the knee: internal tibial rotation under a simulated pivot shift test. *Arch Orthop Trauma Surg*. 2009;129(3):353-8.
74. Akseki D, Ozcan O, Boya H, Pinar H. A new weight-bearing meniscal test and a comparison with McMurray's test and joint line tenderness. *Arthroscopy*. 2004;20(9):951-8.
75. Anderson AF, Lipscomb AB. Clinical diagnosis of meniscal tears. Description of a new manipulative test. *Am J Sports Med*. 1986;14(4):291-3.
76. Bae JH, Choi IC, Suh SW, et al. Evaluation of the reliability of the dial test for posterolateral rotatory instability: a cadaveric study using an isotonic rotation machine. *Arthroscopy*. 2008;24(5):593-8.
77. Garavaglia G, Lubbeke A, Dubois-Ferriere V, Suva D, Fritschy D, Menetrey J. Accuracy of stress radiography techniques in grading isolated and combined posterior knee injuries: a cadaveric study. *Am J Sports Med*. 2007;35(12):2051-6.
78. Gebhard F, Authenrieth M, Strecker W, Kinzl L, Hehl G. Ultrasound evaluation of gravity induced anterior drawer following anterior cruciate ligament lesion. *Knee Surg Sports Traumatol Arthrosc*. 1999;7(3):166-72.
79. Hoshino Y, Kuroda R, Nagamune K, et al. In vivo measurement of the pivot-shift test in the anterior cruciate ligament-deficient knee using an electromagnetic device. *Am J Sports Med*. 2007;35(7):1098-104.
80. Karachalios T, Hantes M, Zibis AH, Zachos V, Karantanias AH, Malizos KN. Diagnostic accuracy of a new clinical test (the Thessaly test) for early detection of meniscal tears. *J Bone Joint Surg Am*. 2005;87(5):955-62.
81. Kostogiannis I, Ageberg E, Neuman P, Dahlberg LE, Friden T, Roos H. Clinically assessed knee joint laxity as a predictor for reconstruction after an anterior cruciate ligament injury: a prospective study of 100 patients treated with activity modification and rehabilitation. *Am J Sports Med*. 2008;36(8):1528-33.
82. Kundra RK, Moorehead JD, Barton-Hanson N, Montgomery SC. Magnetic tracking: a novel method of assessing anterior cruciate ligament deficiency. *Ann R Coll Surg Engl*. 2006;88(1):16-7.
83. Kurosaka M, Yagi M, Yoshiya S, Muratsu H, Mizuno K. Efficacy of the axially loaded pivot shift test for the diagnosis of a meniscal tear. *Int Orthop*. 1999;23(5):271-4.
84. Liu SH, Osti L, Henry M, Bocchi L. The diagnosis of acute complete tears of the anterior cruciate ligament. Comparison of MRI, arthrometry and clinical examination. *J Bone Joint Surg Br*. 1995;77(4):586-8.
85. Logan MC, Williams A, Lavelle J, Gedroyc W, Freeman M. What really happens during the Lachman test? A dynamic MRI analysis of tibiofemoral motion. *Am J Sports Med*. 2004;32(2):369-75.
86. Lopomo N, Zaffagnini S, Bignozzi S, Visani A, Marcacci M. Pivot-shift test: analysis and quantification of knee laxity parameters using a navigation system. *J Orthop Res*. 2010;28(2):164-9.
87. Lucie RS, Wiedel JD, Messner DG. The acute pivot shift: clinical correlation. *Am J Sports Med*. 1984;12(3):189-91.
88. Oliver JH, Coughlin LP. Objective knee evaluation using the Genucom Knee Analysis System. Clinical implications. *Am J Sports Med*. 1987;15(6):571-8.
89. Pookarnjanamorakot C, Korsantirat T, Woratanarat P. Meniscal lesions in the anterior cruciate insufficient knee: the accuracy of clinical evaluation. *J Med Assoc Thai*. 2004;87(6):618-23.
90. Sakai H, Yajima H, Kobayashi N, et al. Gravity-assisted pivot-shift test for anterior cruciate ligament injury: a new procedure to detect anterolateral rotatory instability of the knee joint. *Knee Surg Sports Traumatol Arthrosc*. 2006;14(1):2-6.
91. Wiertsema SH, van Hooff HJ, Migchelsen LA, Steultjens MP. Reliability of the KT1000 arthrometer and the Lachman test in patients with an ACL rupture. *Knee*. 2008;15(2):107-10.
92. Reveille JD. Soft-tissue rheumatism: diagnosis and treatment. *Am J Med*. 1997;102(1A):23S-9S.
93. Handy JR. Anserine bursitis: a brief review. *South Med J*. 1997;90(4):376-7.
94. Wood LR, Peat G, Thomas E, Duncan R. The contribution of selected non-articular conditions to knee pain severity and associated disability in older adults. *Osteoarthritis Cartilage*. 2008;16(6):647-53.
95. Alvarez-Nemegyei J. Risk factors for pes anserinus tendinitis/bursitis syndrome: a case control study. *J Clin Rheumatol*. 2007;13(2):63-5.
96. Price N. Prepatellar bursitis. *Emerg Nurse*. 2008;16(3):20-4.

97. Aydingoz U, Oguz B, Aydingoz O, Comert RB, Akgun I. The deep infrapatellar bursa: prevalence and morphology on routine magnetic resonance imaging of the knee. *J Comput Assist Tomogr.* 2004;28(4):557-61.
98. Ho G, Jr., Tice AD, Kaplan SR. Septic bursitis in the prepatellar and olecranon bursae: an analysis of 25 cases. *Ann Intern Med.* 1978;89(1):21-7.
99. Smith DL, McAfee JH, Lucas LM, Kumar KL, Romney DM. Septic and nonseptic olecranon bursitis. Utility of the surface temperature probe in the early differentiation of septic and nonseptic cases. *Arch Intern Med.* 1989;149(7):1581-5.
100. Wijdicks CA, Ewart DT, Nuckley DJ, Johansen S, Engebretsen L, Laprade RF. Structural properties of the primary medial knee ligaments. *Am J Sports Med.* 2010;38(8):1638-46.
101. Scotney B. Sports knee injuries - assessment and management. *Aust Fam Physician.* 2010;39(1-2):30-4.
102. O'Shea KJ, Murphy KP, Heekin RD, Herzwurm PJ. The diagnostic accuracy of history, physical examination, and radiographs in the evaluation of traumatic knee disorders. *Am J Sports Med.* 1996;24(2):164-7.
103. Kastelein M, Wagemakers HP, Luijsterburg PA, Verhaar JA, Koes BW, Bierma-Zeinstra SM. Assessing medial collateral ligament knee lesions in general practice. *Am J Med.* 2008;121(11):982-8 e2.
104. Miyamoto RG, Bosco JA, Sherman OH. Treatment of medial collateral ligament injuries. *J Am Acad Orthop Surg.* 2009;17(3):152-61.
105. Noyes FR, Grood ES, Butler DL, Raterman L. Knee ligament tests: what do they really mean? *Phys Ther.* 1980;60(12):1578-81.
106. Yoon KH, Bae DK, Song SJ, Cho HJ, Lee JH. A Prospective Randomized Study Comparing Arthroscopic Single-Bundle and Double-Bundle Posterior Cruciate Ligament Reconstructions Preserving Remnant Fibers. *Am J Sports Med.* 2010;XX(X, XXXX).
107. Guillodo Y, Rannou N, Dubrana F, Lefevre C, Saraux A. Diagnosis of anterior cruciate ligament rupture in an emergency department. *J Trauma.* 2008;65(5):1078-82.
108. Solomon DH, Simel DL, Bates DW, Katz JN, Schaffer JL. The rational clinical examination. Does this patient have a torn meniscus or ligament of the knee? Value of the physical examination. *JAMA.* 2001;286(13):1610-20.
109. Hurley WL, Boros RL, Challis JH. Influences of variation in force application on tibial displacement and strain in the anterior cruciate ligament during the Lachman test. *Clin Biomech (Bristol, Avon).* 2004;19(1):95-8.
110. Lerat JL, Moyen BL, Cladiere F, Besse JL, Abidi H. Knee instability after injury to the anterior cruciate ligament. Quantification of the Lachman test. *J Bone Joint Surg Br.* 2000;82(1):42-7.
111. Kim SJ, Kim HK. Reliability of the anterior drawer test, the pivot shift test, and the Lachman test. *Clin Orthop Relat Res.* 1995(317):237-42.
112. Gurtler RA, Stine R, Torg JS. Lachman test evaluated. Quantification of a clinical observation. *Clin Orthop Relat Res.* 1987(216):141-50.
113. Schraeder TL, Terek RM, Smith CC. Clinical evaluation of the knee. *N Engl J Med.* 2010;363(4):e5.
114. Logerstedt DS, Snyder-Mackler L, Ritter RC, Axe MJ. Knee pain and mobility impairments: meniscal and articular cartilage lesions. *J Orthop Sports Phys Ther.* 2010;40(6):A1-A35.
115. Sandberg R, Balkfors B, Henricson A, Westlin N. Stability tests in knee ligament injuries. *Arch Orthop Trauma Surg.* 1986;106(1):5-7.
116. Gelb HJ, Glasgow SG, Sapega AA, Torg JS. Magnetic resonance imaging of knee disorders. Clinical value and cost-effectiveness in a sports medicine practice. *Am J Sports Med.* 1996;24(1):99-103.
117. Torg JS, Conrad W, Kalen V. Clinical diagnosis of anterior cruciate ligament instability in the athlete. *Am J Sports Med.* 1976;4(2):84-93.
118. Jonsson T, Althoff B, Peterson L, Renstrom P. Clinical diagnosis of ruptures of the anterior cruciate ligament: a comparative study of the Lachman test and the anterior drawer sign. *Am J Sports Med.* 1982;10(2):100-2.
119. Donaldson WF, 3rd, Warren RF, Wickiewicz T. A comparison of acute anterior cruciate ligament examinations. Initial versus examination under anesthesia. *Am J Sports Med.* 1985;13(1):5-10.
120. Zarins B, Rowe CR. Combined anterior cruciate-ligament reconstruction using semitendinosus tendon and iliotibial tract. *J Bone Joint Surg Am.* 1986;68(2):160-77.

121. Lee JK, Yao L, Phelps CT, Wirth CR, Czajka J, Lozman J. Anterior cruciate ligament tears: MR imaging compared with arthroscopy and clinical tests. *Radiology*. 1988;166(3):861-4.
122. Katz JW, Fingerth RJ. The diagnostic accuracy of ruptures of the anterior cruciate ligament comparing the Lachman test, the anterior drawer sign, and the pivot shift test in acute and chronic knee injuries. *Am J Sports Med*. 1986;14(1):88-91.
123. Heiderscheid BC. Lower extremity injuries: is it just about hip strength? *J Orthop Sports Phys Ther*. 2010;40(2):39-41.
124. Mason JB, Fehring TK, Estok R, Banel D, Fahrbach K. Meta-analysis of alignment outcomes in computer-assisted total knee arthroplasty surgery. *J Arthroplasty*. 2007;22(8):1097-106.
125. Warren P GB, Schneider-Kolsky M. Clinical predictors of time to return to competition and of recurrence following hamstring strain in elite Australian footballers. *Br J Sports Med*. 2008(Aug).
126. Falvey EC, Clark RA, Franklyn-Miller A, Bryant AL, Briggs C, McCrory PR. Iliotibial band syndrome: an examination of the evidence behind a number of treatment options. *Scand J Med Sci Sports*. 2010;20(4):580-7.
127. Jordaan G, Schweltnus MP. The incidence of overuse injuries in military recruits during basic military training. *Mil Med*. 1994;159(6):421-6.
128. Fairclough J, Hayashi K, Toumi H, et al. The functional anatomy of the iliotibial band during flexion and extension of the knee: implications for understanding iliotibial band syndrome. *J Anat*. 2006;208(3):309-16.
129. Orchard JW, Fricker PA, Abud AT, Mason BR. Biomechanics of iliotibial band friction syndrome in runners. *Am J Sports Med*. 1996;24(3):375-9.
130. Ellis R, Hing W, Reid D. Iliotibial band friction syndrome--a systematic review. *Man Ther*. 2007;12(3):200-8.
131. Ekman EF, Pope T, Martin DF, Curl WW. Magnetic resonance imaging of iliotibial band syndrome. *Am J Sports Med*. 1994;22(6):851-4.
132. Nishimura G, Yamato M, Tamai K, Takahashi J, Uetani M. MR findings in iliotibial band syndrome. *Skeletal Radiol*. 1997;26(9):533-7.
133. Stiell IG, Wells GA, McDowell I, et al. Use of radiography in acute knee injuries: need for clinical decision rules. *Acad Emerg Med*. 1995;2(11):966-73.
134. Jackson JL, O'Malley PG, Kroenke K. Evaluation of acute knee pain in primary care. *Ann Intern Med*. 2003;139(7):575-88.
135. Kapur S, Wissman RD, Robertson M, Verma S, Kreeger MC, Oostveen RJ. Acute knee dislocation: review of an elusive entity. *Curr Probl Diagn Radiol*. 2009;38(6):237-50.
136. Apley AG. The diagnosis of meniscus injuries; some new clinical methods. *J Bone Joint Surg Am*. 1947;29(1):78-84.
137. Oberlander MA, Shalvoy RM, Hughston JC. The accuracy of the clinical knee examination documented by arthroscopy. A prospective study. *Am J Sports Med*. 1993;21(6):773-8.
138. Meserve BB, Cleland JA, Boucher TR. A meta-analysis examining clinical test utilities for assessing meniscal injury. *Clin Rehabil*. 2008;22(2):143-61.
139. Fowler PJ, Lubliner JA. The predictive value of five clinical signs in the evaluation of meniscal pathology. *Arthroscopy*. 1989;5(3):184-6.
140. Evans PJ, Bell GD, Frank C. Prospective evaluation of the McMurray test. *Am J Sports Med*. 1993;21(4):604-8.
141. Noble CA. Iliotibial band friction syndrome in runners. *Am J Sports Med*. 1980;8(4):232-4.
142. Konan S, Rayan F, Haddad FS. Do physical diagnostic tests accurately detect meniscal tears? *Knee Surg Sports Traumatol Arthrosc*. 2009;17(7):806-11.
143. Corea JR, Moussa M, al Othman A. McMurray's test tested. *Knee Surg Sports Traumatol Arthrosc*. 1994;2(2):70-2.
144. Lowery DJ, Farley TD, Wing DW, Sterett WI, Steadman JR. A clinical composite score accurately detects meniscal pathology. *Arthroscopy*. 2006;22(11):1174-9.
145. Bansal P, Deehan DJ, Gregory RJ. Diagnosing the acutely locked knee. *Injury*. 2002;33(6):495-8.
146. Benjaminse A, Gokeler A, van der Schans CP. Clinical diagnosis of an anterior cruciate ligament rupture: a meta-analysis. *J Orthop Sports Phys Ther*. 2006;36(5):267-88.

147. Wadey VM, Mohtadi NG, Bray RC, Frank CB. Positive predictive value of maximal posterior joint-line tenderness in diagnosing meniscal pathology: a pilot study. *Can J Surg*. 2007;50(2):96-100.
148. Felson DT. Glucosamine and chondroitin sulfate in knee osteoarthritis: where now? *Nat Clin Pract Rheumatol*. 2006;2(7):356-7.
149. Felson DT. Clinical practice. Osteoarthritis of the knee. *N Engl J Med*. 2006;354(8):841-8.
150. Faucher M, Poiraudau S, Lefevre-Colau MM, Rannou F, Fermanian J, Revel M. Assessment of the test-retest reliability and construct validity of a modified WOMAC index in knee osteoarthritis. *Joint Bone Spine*. 2004;71(2):121-7.
151. Tanner SM, Garth WP, Jr., Soileau R, Lemons JE. A modified test for patellar instability: the biomechanical basis. *Clin J Sport Med*. 2003;13(6):327-38.
152. Sallay PI, Poggi J, Speer KP, Garrett WE. Acute dislocation of the patella. A correlative pathoanatomic study. *Am J Sports Med*. 1996;24(1):52-60.
153. Blazina ME, Kerlan RK, Jobe FW, Carter VS, Carlson GJ. Jumper's knee. *Orthop Clin North Am*. 1973;4(3):665-78.
154. King JB, Perry DJ, Mourad K, Kumar SJ. Lesions of the patellar ligament. *J Bone Joint Surg Br*. 1990;72(1):46-8.
155. Martens M, Wouters P, Burssens A, Mulier JC. Patellar tendinitis: pathology and results of treatment. *Acta Orthop Scand*. 1982;53(3):445-50.
156. Myllymaki T, Bondestam S, Suramo I, Cederberg A, Peltokallio P. Ultrasonography of jumper's knee. *Acta Radiol*. 1990;31(2):147-9.
157. Clayton RA, Court-Brown CM. The epidemiology of musculoskeletal tendinous and ligamentous injuries. *Injury*. 2008;39(12):1338-44.
158. White DW, Wenke JC, Mosely DS, Mountcastle SB, Basamania CJ. Incidence of major tendon ruptures and anterior cruciate ligament tears in US Army soldiers. *Am J Sports Med*. 2007;35(8):1308-14.
159. Pihlajamaki HK, Kuikka PI, Leppanen VV, Kiuru MJ, Mattila VM. Reliability of clinical findings and magnetic resonance imaging for the diagnosis of chondromalacia patellae. *J Bone Joint Surg Am*. 2010;92(4):927-34.
160. Thomee R, Augustsson J, Karlsson J. Patellofemoral pain syndrome: a review of current issues. *Sports Med*. 1999;28(4):245-62.
161. Brattstroem H. Shape of the Intercondylar Groove Normally and in Recurrent Dislocation of Patella. a Clinical and X-Ray-Anatomical Investigation. *Acta Orthop Scand Suppl*. 1964;68SUPPL 68:1-148.
162. Schulthies SS, Francis RS, Fisher AG, Van de Graaff KM. Does the Q angle reflect the force on the patella in the frontal plane? *Phys Ther*. 1995;75(1):24-30.
163. Aglietti P, Insall JN, Cerulli G. Patellar pain and incongruence. I: Measurements of incongruence. *Clin Orthop Relat Res*. 1983(176):217-24.
164. Niskanen RO, Paavilainen PJ, Jaakkola M, Korkala OL. Poor correlation of clinical signs with patellar cartilaginous changes. *Arthroscopy*. 2001;17(3):307-10.
165. Nijs J, Van Geel C, Van der auwera C, Van de Velde B. Diagnostic value of five clinical tests in patellofemoral pain syndrome. *Man Ther*. 2006;11(1):69-77.
166. Jensen LK, Eenberg W. Occupation as a risk factor for knee disorders. *Scand J Work Environ Health*. 1996;22(3):165-75.
167. Sharrard WJ. Pressure Effects on the Knee in Kneeling Miners. *Ann R Coll Surg Engl*. 1965;36309-24.
168. Thun M, Tanaka S, Smith AB, et al. Morbidity from repetitive knee trauma in carpet and floor layers. *Br J Ind Med*. 1987;44(9):611-20.
169. Myllymaki T, Tikkakoski T, Typpo T, Kivimaki J, Suramo I. Carpet-layer's knee. An ultrasonographic study. *Acta Radiol*. 1993;34(5):496-9.
170. Kivimaki J. Occupationally related ultrasonic findings in carpet and floor layers' knees. *Scand J Work Environ Health*. 1992;18(6):400-2.
171. Hawkins RD, Fuller CW. A prospective epidemiological study of injuries in four English professional football clubs. *Br J Sports Med*. 1999;33(3):196-203.
172. Beynon BD, Uh BS, Johnson RJ, et al. Rehabilitation after anterior cruciate ligament reconstruction: a prospective, randomized, double-blind comparison of programs administered over 2 different time intervals. *Am J Sports Med*. 2005;33(3):347-59.

173. Drawer S, Fuller CW. Perceptions of retired professional soccer players about the provision of support services before and after retirement. *Br J Sports Med.* 2002;36(1):33-8.
174. Drawer S, Fuller CW. Evaluating the level of injury in English professional football using a risk based assessment process. *Br J Sports Med.* 2002;36(6):446-51.
175. Almeida SA, Trone DW, Leone DM, Shaffer RA, Patheal SL, Long K. Gender differences in musculoskeletal injury rates: a function of symptom reporting? *Med Sci Sports Exerc.* 1999;31(12):1807-12.
176. Almeida SA, Williams KM, Shaffer RA, Brodine SK. Epidemiological patterns of musculoskeletal injuries and physical training. *Med Sci Sports Exerc.* 1999;31(8):1176-82.
177. Barber FA, Sutker AN. Iliotibial band syndrome. *Sports Med.* 1992;14(2):144-8.
178. Fredericson M, Cookingham CL, Chaudhari AM, Dowdell BC, Oestreicher N, Sahrmann SA. Hip abductor weakness in distance runners with iliotibial band syndrome. *Clin J Sport Med.* 2000;10(3):169-75.
179. Hodge JC. Clinics in diagnostic imaging (40). Iliotibial band syndrome. *Singapore Med J.* 1999;40(8):547-9.
180. Holmes JC, Pruitt AL, Whalen NJ. Iliotibial band syndrome in cyclists. *Am J Sports Med.* 1993;21(3):419-24.
181. Kelly A, Winston I. Iliotibial band syndrome in cyclists. *Am J Sports Med.* 1994;22(1):150.
182. Linenger JM, West LA. Epidemiology of soft-tissue/musculoskeletal injury among U.S. Marine recruits undergoing basic training. *Mil Med.* 1992;157(9):491-3.
183. McNicol K, Taunton JE, Clement DB. Iliotibial tract friction syndrome in athletes. *Can J Appl Sport Sci.* 1981;6(2):76-80.
184. Messier SP, Edwards DG, Martin DF, et al. Etiology of iliotibial band friction syndrome in distance runners. *Med Sci Sports Exerc.* 1995;27(7):951-60.
185. Newell SG BS. Overuse injuries to the knee in runners. *Phys Sportsmed.* 1984;1281-92.
186. Noble J, Erat K. In defence of the meniscus. A prospective study of 200 meniscectomy patients. *J Bone Joint Surg Br.* 1980;62-B(1):7-11.
187. Novacheck TF. Running injuries: a biomechanical approach. *Instr Course Lect.* 1998;47397-406.
188. Novacheck TF. The biomechanics of running. *Gait Posture.* 1998;7(1):77-95.
189. Orava S. Iliotibial tract friction syndrome in athletes--an uncommon exertion syndrome on the lateral side of the knee. *Br J Sports Med.* 1978;12(2):69-73.
190. Puniello MS. Iliotibial band tightness and medial patellar glide in patients with patellofemoral dysfunction. *J Orthop Sports Phys Ther.* 1993;17(3):144-8.
191. Renne JW. The iliotibial band friction syndrome. *J Bone Joint Surg Am.* 1975;57(8):1110-1.
192. Richards DP, Alan Barber F, Troop RL. Iliotibial band Z-lengthening. *Arthroscopy.* 2003;19(3):326-9.
193. Sutker AN, Barber FA, Jackson DW, Pagliano JW. Iliotibial band syndrome in distance runners. *Sports Med.* 1985;2(6):447-51.
194. Sutker AN, Jackson DW, Pagliano JW. Iliotibial band syndrome in distance runners. *Phys Sportmed.* 1981;9(10):69-73.
195. Taunton JE, Ryan MB, Clement DB, McKenzie DC, Lloyd-Smith DR, Zumbo BD. A retrospective case-control analysis of 2002 running injuries. *Br J Sports Med.* 2002;36(2):95-101.
196. Pinshaw R, Atlas V, Noakes TD. The nature and response to therapy of 196 consecutive injuries seen at a runners' clinic. *S Afr Med J.* 1984;65(8):291-8.
197. Schweltnus MP, Machintosh L, Mee J. Deep transverse friction in the treatment of Iliotibial Band Friction syndrome in athletes: a clinical trial. *Physiotherapy.* 1992;78(8):564-8.
198. Lange AK, Fiatarone Singh MA, Smith RM, et al. Degenerative meniscus tears and mobility impairment in women with knee osteoarthritis. *Osteoarthritis Cartilage.* 2007;15(6):701-8.
199. Lohmander LS, Roos H. Knee ligament injury, surgery and osteoarthritis. Truth or consequences? *Acta Orthop Scand.* 1994;65(6):605-9.
200. Englund M. The role of the meniscus in osteoarthritis genesis. *Rheum Dis Clin North Am.* 2008;34(3):573-9.
201. Englund M. Meniscal tear--a feature of osteoarthritis. *Acta Orthop Scand Suppl.* 2004;75(312):1-45, backcover.
202. Englund M, Guermazi A, Lohmander SL. The role of the meniscus in knee osteoarthritis: a cause or consequence? *Radiol Clin North Am.* 2009;47(4):703-12.
203. Englund M, Lohmander LS. Risk factors for symptomatic knee osteoarthritis fifteen to twenty-two years after meniscectomy. *Arthritis Rheum.* 2004;50(9):2811-9.

204. Englund M, Niu J, Guermazi A, et al. Effect of meniscal damage on the development of frequent knee pain, aching, or stiffness. *Arthritis Rheum.* 2007;56(12):4048-54.
205. Englund M, Paradowski PT, Lohmander LS. Association of radiographic hand osteoarthritis with radiographic knee osteoarthritis after meniscectomy. *Arthritis Rheum.* 2004;50(2):469-75.
206. Englund M, Roos EM, Lohmander LS. Impact of type of meniscal tear on radiographic and symptomatic knee osteoarthritis: a sixteen-year followup of meniscectomy with matched controls. *Arthritis Rheum.* 2003;48(8):2178-87.
207. Englund M, Roos EM, Roos HP, Lohmander LS. Patient-relevant outcomes fourteen years after meniscectomy: influence of type of meniscal tear and size of resection. *Rheumatology (Oxford).* 2001;40(6):631-9.
208. Baker P, Coggon D, Reading I, Barrett D, McLaren M, Cooper C. Sports injury, occupational physical activity, joint laxity, and meniscal damage. *J Rheumatol.* 2002;29(3):557-63.
209. Rytter S, Jensen LK, Bonde JP. Clinical knee findings in floor layers with focus on meniscal status. *BMC Musculoskelet Disord.* 2008;9:144.
210. Rytter S, Jensen LK, Bonde JP, Jurik AG, Egund N. Occupational kneeling and meniscal tears: a magnetic resonance imaging study in floor layers. *J Rheumatol.* 2009;36(7):1512-9.
211. Atkins JB. Internal derangement of the knee joint in miners. *Br J Ind Med.* 1957;14(2):121-6.
212. Sharrard WJ, Liddell FD. Injuries to the semilunar cartilages of the knee in miners. *Br J Ind Med.* 1962;19:195-202.
213. Allen PM, White RD, McFarland PH. A diagnostic dilemma: osteoclasia with tissue necrosis. *Oral Surg Oral Med Oral Pathol.* 1974;38(5):698-702.
214. Wickstrom G, Hanninen K, Mattsson T, et al. Knee degeneration in concrete reinforcement workers. *Br J Ind Med.* 1983;40(2):216-9.
215. Johnson RJ, Kettelkamp DB, Clark W, Leaverton P. Factors effecting late results after meniscectomy. *J Bone Joint Surg Am.* 1974;56(4):719-29.
216. Fairbank TJ. Knee joint changes after meniscectomy. *J Bone Joint Surg Br.* 1948;30B(4):664-70.
217. Appel H. Late results after meniscectomy in the knee joint. A clinical and roentgenologic follow-up investigation. *Acta Orthop Scand Suppl.* 1970;1331-111.
218. Jackson JP. Degenerative changes in the knee after meniscectomy. *Br Med J.* 1968;2(5604):525-7.
219. Jorgensen U, Sonne-Holm S, Lauridsen F, Rosenklint A. Long-term follow-up of meniscectomy in athletes. A prospective longitudinal study. *J Bone Joint Surg Br.* 1987;69(1):80-3.
220. Cooper C, McAlindon T, Snow S, et al. Mechanical and constitutional risk factors for symptomatic knee osteoarthritis: differences between medial tibiofemoral and patellofemoral disease. *J Rheumatol.* 1994;21(2):307-13.
221. Ding C, Martel-Pelletier J, Pelletier JP, et al. Knee meniscal extrusion in a largely non-osteoarthritic cohort: association with greater loss of cartilage volume. *Arthritis Res Ther.* 2007;9(2):R21.
222. Louboutin H, Debarge R, Richou J, et al. Osteoarthritis in patients with anterior cruciate ligament rupture: a review of risk factors. *Knee.* 2009;16(4):239-44.
223. Lohmander LS, Englund PM, Dahl LL, Roos EM. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. *Am J Sports Med.* 2007;35(10):1756-69.
224. Roos H, Ornell M, Gardsell P, Lohmander LS, Lindstrand A. Soccer after anterior cruciate ligament injury--an incompatible combination? A national survey of incidence and risk factors and a 7-year follow-up of 310 players. *Acta Orthop Scand.* 1995;66(2):107-12.
225. Kohatsu ND, Schurman DJ. Risk factors for the development of osteoarthrosis of the knee. *Clin Orthop Relat Res.* 1990(261):242-6.
226. Davis MA. Epidemiology of osteoarthritis. *Clin Geriatr Med.* 1988;4(2):241-55.
227. Gelber AC, Hochberg MC, Mead LA, Wang NY, Wigley FM, Klag MJ. Joint injury in young adults and risk for subsequent knee and hip osteoarthritis. *Ann Intern Med.* 2000;133(5):321-8.
228. Moretz JA, 3rd, Harlan SD, Goodrich J, Walters R. Long-term followup of knee injuries in high school football players. *Am J Sports Med.* 1984;12(4):298-300.
229. Bauer DC, Hunter DJ, Abramson SB, et al. Classification of osteoarthritis biomarkers: a proposed approach. *Osteoarthritis Cartilage.* 2006;14(8):723-7.

230. Lohmander LS, Atley LM, Pietka TA, Eyre DR. The release of crosslinked peptides from type II collagen into human synovial fluid is increased soon after joint injury and in osteoarthritis. *Arthritis Rheum.* 2003;48(11):3130-9.
231. Lohmander LS, McKeith D, Svensson O, et al. A randomised, placebo controlled, comparative trial of the gastrointestinal safety and efficacy of AZD3582 versus naproxen in osteoarthritis. *Ann Rheum Dis.* 2005;64(3):449-56.
232. Dean DD. Proteinase-mediated cartilage degradation in osteoarthritis. *Semin Arthritis Rheum.* 1991;20(6 Suppl 2):2-11.
233. Lohmander LS, Hoerrner LA, Dahlberg L, Roos H, Bjornsson S, Lark MW. Stromelysin, tissue inhibitor of metalloproteinases and proteoglycan fragments in human knee joint fluid after injury. *J Rheumatol.* 1993;20(8):1362-8.
234. Lohmander LS, Hoerrner LA, Lark MW. Metalloproteinases, tissue inhibitor, and proteoglycan fragments in knee synovial fluid in human osteoarthritis. *Arthritis Rheum.* 1993;36(2):181-9.
235. Pelletier JP, Martel-Pelletier J. In vivo protective effects of prophylactic treatment with tiaprofenic acid or intraarticular corticosteroids on osteoarthritic lesions in the experimental dog model. *J Rheumatol Suppl.* 1991;27:127-30.
236. Agramson SB. Inflammation in osteoarthritis. *J Rheumatol Suppl.* 2004;70:70-6.
237. Sharif M, Saxne T, Shepstone L, et al. Relationship between serum cartilage oligomeric matrix protein levels and disease progression in osteoarthritis of the knee joint. *Br J Rheumatol.* 1995;34(4):306-10.
238. Melrose J, Fuller ES, Roughley PJ, et al. Fragmentation of decorin, biglycan, lumican and keratocan is elevated in degenerate human meniscus, knee and hip articular cartilages compared with age-matched macroscopically normal and control tissues. *Arthritis Res Ther.* 2008;10(4):R79.
239. Neidhart M, Hauser N, Paulsson M, DiCesare PE, Michel BA, Hauselmann HJ. Small fragments of cartilage oligomeric matrix protein in synovial fluid and serum as markers for cartilage degradation. *Br J Rheumatol.* 1997;36(11):1151-60.
240. Sharif M, George E, Shepstone L, et al. Serum hyaluronic acid level as a predictor of disease progression in osteoarthritis of the knee. *Arthritis Rheum.* 1995;38(6):760-7.
241. Wilson MG, Michet CJ, Jr., Ilstrup DM, Melton LJ, 3rd. Idiopathic symptomatic osteoarthritis of the hip and knee: a population-based incidence study. *Mayo Clin Proc.* 1990;65(9):1214-21.
242. Kellgren JH. Osteoarthrosis in patients and populations. *Br Med J.* 1961;2(5243):1-6.
243. Kellgren JH, Lawrence JS. Osteoarthrosis and disk degeneration in an urban population. *Ann Rheum Dis.* 1958;17(4):388-97.
244. Bagge E, Bjelle A, Eden S, Svanborg A. Factors associated with radiographic osteoarthritis: results from the population study 70-year-old people in Goteborg. *J Rheumatol.* 1991;18(8):1218-22.
245. Bagge E, Bjelle A, Svanborg A. Radiographic osteoarthritis in the elderly. A cohort comparison and a longitudinal study of the "70-year old people in Goteborg". *Clin Rheumatol.* 1992;11(4):486-91.
246. Felson DT. The epidemiology of knee osteoarthritis: results from the Framingham Osteoarthritis Study. *Semin Arthritis Rheum.* 1990;20(3 Suppl 1):42-50.
247. Acheson RM, Collart AB. New Haven survey of joint diseases. XVII. Relationship between some systemic characteristics and osteoarthrosis in a general population. *Ann Rheum Dis.* 1975;34(5):379-87.
248. Davis MA, Ettinger WH, Neuhaus JM, Mallon KP. Knee osteoarthritis and physical functioning: evidence from the NHANES I Epidemiologic Followup Study. *J Rheumatol.* 1991;18(4):591-8.
249. Hernborg J, Nilsson BE. The relationship between osteophytes in the knee joint, osteoarthritis and aging. *Acta Orthop Scand.* 1973;44(1):69-74.
250. Hart DJ, Doyle DV, Spector TD. Incidence and risk factors for radiographic knee osteoarthritis in middle-aged women: the Chingford Study. *Arthritis Rheum.* 1999;42(1):17-24.
251. Peyron JG. Epidemiologic and etiologic approach of osteoarthritis. *Semin Arthritis Rheum.* 1979;8(4):288-306.
252. Allander E. Prevalence, incidence, and remission rates of some common rheumatic diseases or syndromes. *Scand J Rheumatol.* 1974;3(3):145-53.
253. Lawrence JS, Bremner JM, Bier F. Osteoarthrosis. Prevalence in the population and relationship between symptoms and x-ray changes. *Ann Rheum Dis.* 1966;25(1):1-24.

254. Lethbridge-Cejku M, Tobin JD, Scott WW, Jr., Reichle R, Plato CC, Hochberg MC. The relationship of age and gender to prevalence and pattern of radiographic changes of osteoarthritis of the knee: data from Caucasian participants in the Baltimore Longitudinal Study of Aging. *Aging (Milano)*. 1994;6(5):353-7.
255. Cheung PP, Gossec L, Dougados M. What are the best markers for disease progression in osteoarthritis (OA)? *Best Pract Res Clin Rheumatol*. 24(1):81-92.
256. Anderson JJ, Felson DT. Factors associated with osteoarthritis of the knee in the first national Health and Nutrition Examination Survey (HANES I). Evidence for an association with overweight, race, and physical demands of work. *Am J Epidemiol*. 1988;128(1):179-89.
257. Felson DT. Epidemiology of hip and knee osteoarthritis. *Epidemiol Rev*. 1988;101-28.
258. Felson DT. Obesity and osteoarthritis of the knee. *Bull Rheum Dis*. 1992;41(2):6-7.
259. Felson DT, Anderson JJ, Naimark A, Walker AM, Meenan RF. Obesity and knee osteoarthritis. The Framingham Study. *Ann Intern Med*. 1988;109(1):18-24.
260. Felson DT, Lawrence RC, Dieppe PA, et al. Osteoarthritis: new insights. Part 1: the disease and its risk factors. *Ann Intern Med*. 2000;133(8):635-46.
261. Spector TD, Hart DJ, Doyle DV. Incidence and progression of osteoarthritis in women with unilateral knee disease in the general population: the effect of obesity. *Ann Rheum Dis*. 1994;53(9):565-8.
262. Sturmer T, Gunther KP, Brenner H. Obesity, overweight and patterns of osteoarthritis: the Ulm Osteoarthritis Study. *J Clin Epidemiol*. 2000;53(3):307-13.
263. Coggon D, Reading I, Croft P, McLaren M, Barrett D, Cooper C. Knee osteoarthritis and obesity. *Int J Obes Relat Metab Disord*. 2001;25(5):622-7.
264. Davis MA, Ettinger WH, Neuhaus JM, Cho SA, Hauck WW. The association of knee injury and obesity with unilateral and bilateral osteoarthritis of the knee. *Am J Epidemiol*. 1989;130(2):278-88.
265. Lau EC, Cooper C, Lam D, Chan VN, Tsang KK, Sham A. Factors associated with osteoarthritis of the hip and knee in Hong Kong Chinese: obesity, joint injury, and occupational activities. *Am J Epidemiol*. 2000;152(9):855-62.
266. Hartz AJ, Fischer ME, Bril G, et al. The association of obesity with joint pain and osteoarthritis in the HANES data. *J Chronic Dis*. 1986;39(4):311-9.
267. Gelber AC, Hochberg MC, Mead LA, Wang NY, Wigley FM, Klag MJ. Body mass index in young men and the risk of subsequent knee and hip osteoarthritis. *Am J Med*. 1999;107(6):542-8.
268. Bergstrom G, Bjelle A, Sorensen LB, Sundh V, Svanborg A. Prevalence of rheumatoid arthritis, osteoarthritis, chondrocalcinosis and gouty arthritis at age 79. *J Rheumatol*. 1986;13(3):527-34.
269. Manninen P, Riihimaki H, Heliovaara M, Makela P. Overweight, gender and knee osteoarthritis. *Int J Obes Relat Metab Disord*. 1996;20(6):595-7.
270. Coggon D, Croft P, Kellingray S, Barrett D, McLaren M, Cooper C. Occupational physical activities and osteoarthritis of the knee. *Arthritis Rheum*. 2000;43(7):1443-9.
271. Silberberg M, Silberberg R. Age factor and high-fat diets in the evolution of osteoarthritis in mice. *J Gerontol*. 1957;12(1):9-13.
272. Leach RE, Baumgard S, Broom J. Obesity: its relationship to osteoarthritis of the knee. *Clin Orthop Relat Res*. 1973(93):271-3.
273. Hochberg MC, Lethbridge-Cejku M, Scott WW, Jr., Reichle R, Plato CC, Tobin JD. The association of body weight, body fatness and body fat distribution with osteoarthritis of the knee: data from the Baltimore Longitudinal Study of Aging. *J Rheumatol*. 1995;22(3):488-93.
274. Schouten JS, van den Ouweland FA, Valkenburg HA. A 12 year follow up study in the general population on prognostic factors of cartilage loss in osteoarthritis of the knee. *Ann Rheum Dis*. 1992;51(8):932-7.
275. Oliveria SA, Felson DT, Cirillo PA, Reed JI, Walker AM. Body weight, body mass index, and incident symptomatic osteoarthritis of the hand, hip, and knee. *Epidemiology*. 1999;10(2):161-6.
276. Hart DJ, Spector TD. The relationship of obesity, fat distribution and osteoarthritis in women in the general population: the Chingford Study. *J Rheumatol*. 1993;20(2):331-5.
277. van Saase JL, Vandenbroucke JP, van Romunde LK, Valkenburg HA. Osteoarthritis and obesity in the general population. A relationship calling for an explanation. *J Rheumatol*. 1988;15(7):1152-8.
278. Huang J, Ushiyama T, Inoue K, Kawasaki T, Hukuda S. Vitamin D receptor gene polymorphisms and osteoarthritis of the hand, hip, and knee: a case-control study in Japan. *Rheumatology (Oxford)*. 2000;39(1):79-84.

279. Messier SP, Loeser RF, Mitchell MN, et al. Exercise and weight loss in obese older adults with knee osteoarthritis: a preliminary study. *J Am Geriatr Soc*. 2000;48(9):1062-72.
280. Loughlin J. Polymorphism in signal transduction is a major route through which osteoarthritis susceptibility is acting. *Curr Opin Rheumatol*. 2005;17(5):629-33.
281. Loughlin J. The genetic epidemiology of human primary osteoarthritis: current status. *Expert Rev Mol Med*. 2005;7(9):1-12.
282. Valdes AM, Van Oene M, Hart DJ, et al. Reproducible genetic associations between candidate genes and clinical knee osteoarthritis in men and women. *Arthritis Rheum*. 2006;54(2):533-9.
283. Altman RD. Criteria for the Classification of Osteoarthritis of the Knee and Hip. *Scand J Rheumatol*. 1987;16(s65):31-9.
284. Bunim JJ. Research activities in rheumatic diseases. *Public Health Rep*. 1954;69(5):437-40.
285. Lawrence JS. Generalized osteoarthrosis in a population sample. *Am J Epidemiol*. 1969;90(5):381-9.
286. Doherty M, Watt I, Dieppe P. Influence of primary generalised osteoarthritis on development of secondary osteoarthritis. *Lancet*. 1983;2(8340):8-11.
287. Kellgren JH, Lawrence JS, Bier F. Genetic Factors in Generalized Osteo-Arthrosis. *Ann Rheum Dis*. 1963;22:237-55.
288. Kellgren JH, Moore R. Generalized osteoarthritis and Heberden's nodes. *Br Med J*. 1952;1(4751):181-7.
289. Ledingham J, Regan M, Jones A, Doherty M. Factors affecting radiographic progression of knee osteoarthritis. *Ann Rheum Dis*. 1995;54(1):53-8.
290. Hirsch R, Lethbridge-Cejku M, Scott WW, Jr., et al. Association of hand and knee osteoarthritis: evidence for a polyarticular disease subset. *Ann Rheum Dis*. 1996;55(1):25-9.
291. Waldron HA. Association between osteoarthritis of the hand and hip in a skeletal population from London, UK. *J Rheumatol*. 1997;24(7):1452-3.
292. Hall KD, Hayes KW, Falconer J. Differential strength decline in patients with osteoarthritis of the knee: revision of a hypothesis. *Arthritis Care Res*. 1993;6(2):89-96.
293. Hootman JM. Editorial: New Section in JAT: Evidence-Based Practice. *J Athl Train*. 2004;39(1):9.
294. Hurley MV. The role of muscle weakness in the pathogenesis of osteoarthritis. *Rheum Dis Clin North Am*. 1999;25(2):283-98, vi.
295. Sharma H. Osteoarthritis: a review. *J Indian Med Assoc*. 2001;99(6):322-4.
296. Sharma L, Dunlop DD, Cahue S, Song J, Hayes KW. Quadriceps strength and osteoarthritis progression in malaligned and lax knees. *Ann Intern Med*. 2003;138(8):613-9.
297. Siemenda CW LC, Zhou L, Hui SL, Peacock M, Johnston CC. Sex steroids and bone mass in older men. *J Clin Invest*. 1997(100):1755-9.
298. Tan J, Balci N, Sepici V, Gener FA. Isokinetic and isometric strength in osteoarthrosis of the knee. A comparative study with healthy women. *Am J Phys Med Rehabil*. 1995;74(5):364-9.
299. Thorstensson CA, Petersson IF, Jacobsson LT, Boegard TL, Roos EM. Reduced functional performance in the lower extremity predicted radiographic knee osteoarthritis five years later. *Ann Rheum Dis*. 2004;63(4):402-7.
300. Harvey WF YM, Cooke, T, et al. Association of leg-length inequality with knee osteoarthritis: a cohort study. *Ann Internal Med*. 2010;152(5):287-95.
301. Felson DT MS, Gogins J, et al. Bone marrow edema and its relation to progression of knee osteoarthritis. *Ann Internal Med*. 2003;139(5):330-6.
302. McAlindon TE, Wilson PW, Aliabadi P, Weissman B, Felson DT. Level of physical activity and the risk of radiographic and symptomatic knee osteoarthritis in the elderly: the Framingham study. *Am J Med*. 1999;106(2):151-7.
303. Maetzel A, Makela M, Hawker G, Bombardier C. Osteoarthritis of the hip and knee and mechanical occupational exposure--a systematic overview of the evidence. *J Rheumatol*. 1997;24(8):1599-607.
304. Lawrence JS. Rheumatism in coal miners. III. Occupational factors. *Br J Ind Med*. 1955;12(3):249-61.
305. Lawrence JS, Aitken-Swan J. Rheumatism in miners. Part I: Rheumatic complaints. *Br J Ind Med*. 1952;9(1):1-18.
306. Felson DT, Hannan MT, Naimark A, et al. Occupational physical demands, knee bending, and knee osteoarthritis: results from the Framingham Study. *J Rheumatol*. 1991;18(10):1587-92.

307. Manninen P, Heliövaara M, Riihimäki H, Suoma-lainen O. Physical workload and the risk of severe knee osteoarthritis. *Scand J Work Environ Health*. 2002;28(1):25-32.
308. Sahlström A, Montgomery F. Risk analysis of occupational factors influencing the development of arthrosis of the knee. *Eur J Epidemiol*. 1997;13(6):675-9.
309. Sandmark H, Hogstedt C, Vingard E. Primary osteoarthritis of the knee in men and women as a result of lifelong physical load from work. *Scand J Work Environ Health*. 2000;26(1):20-5.
310. Vingard E, Alfredsson L, Goldie I, Hogstedt C. Occupation and osteoarthritis of the hip and knee: a register-based cohort study. *Int J Epidemiol*. 1991;20(4):1025-31.
311. Lindberg H, Montgomery F. Heavy labor and the occurrence of gonarthrosis. *Clin Orthop Relat Res*. 1987(214):235-6.
312. O'Reilly SC, Muir KR, Doherty M. Occupation and knee pain: a community study. *Osteoarthritis Cartilage*. 2000;8(2):78-81.
313. Jensen LK, Mikkelsen S, Loft IP, Eenberg W, Bergmann I, Logager V. Radiographic knee osteoarthritis in floorlayers and carpenters. *Scand J Work Environ Health*. 2000;26(3):257-62.
314. Holmberg S, Thelin A, Thelin N. Is there an increased risk of knee osteoarthritis among farmers? A population-based case-control study. *Int Arch Occup Environ Health*. 2004;77(5):345-50.
315. Lane NE, Bloch DA, Hubert HB, Jones H, Simpson U, Fries JF. Running, osteoarthritis, and bone density: initial 2-year longitudinal study. *Am J Med*. 1990;88(5):452-9.
316. Lane NE, Michel B, Björkengren A, et al. The risk of osteoarthritis with running and aging: a 5-year longitudinal study. *J Rheumatol*. 1993;20(3):461-8.
317. Sohn RS, Micheli LJ. The effect of running on the pathogenesis of osteoarthritis of the hips and knees. *Clin Orthop Relat Res*. 1985(198):106-9.
318. Kujala UM, Kaprio J, Sarna S. Osteoarthritis of weight bearing joints of lower limbs in former elite male athletes. *Bmj*. 1994;308(6923):231-4.
319. Spector TD, Harris PA, Hart DJ, et al. Risk of osteoarthritis associated with long-term weight-bearing sports: a radiologic survey of the hips and knees in female ex-athletes and population controls. *Arthritis Rheum*. 1996;39(6):988-95.
320. Konradsen L, Hansen EM, Sondergaard L. Long distance running and osteoarthritis. *Am J Sports Med*. 1990;18(4):379-81.
321. Lane NE, Bloch DA, Jones HH, Marshall WH, Jr., Wood PD, Fries JF. Long-distance running, bone density, and osteoarthritis. *JAMA*. 1986;255(9):1147-51.
322. Kiviranta I, Tammi M, Jurvelin J, Saamanen AM, Helminen HJ. Moderate running exercise augments glycosaminoglycans and thickness of articular cartilage in the knee joint of young beagle dogs. *J Orthop Res*. 1988;6(2):188-95.
323. Imeokparia RL, Barrett JP, Arrieta MI, et al. Physical activity as a risk factor for osteoarthritis of the knee. *Ann Epidemiol*. 1994;4(3):221-30.
324. Steffen R, O'Rourke K, Gill HS, Murray DW. The anterolateral approach leads to less disruption of the femoral head-neck blood supply than the posterior approach during hip resurfacing. *J Bone Joint Surg Br*. 2007;89(10):1293-8.
325. Obeid EM, Adams MA, Newman JH. Mechanical properties of articular cartilage in knees with unicompartmental osteoarthritis. *J Bone Joint Surg Br*. 1994;76(2):315-9.
326. Milgrom C, Finestone A, Eldad A, Shlamkovitch N. Patellofemoral pain caused by overactivity. A prospective study of risk factors in infantry recruits. *J Bone Joint Surg Am*. 1991;73(7):1041-3.
327. Kivimäki J, Hanninen K, Kujala UM, Osterman K, Riihimäki H. Knee laxity in carpet and floor layers and painters. *Ann Chir Gynaecol*. 1994;83(3):229-33.
328. Kivimäki J, Riihimäki H, Alaranta H. Knee disorders in carpet and floor layers and painters. Part I. Isometric knee extension and flexion torques. *Scand J Rehabil Med*. 1994;26(2):91-5.
329. Bentley G, Dowd G. Current concepts of etiology and treatment of chondromalacia patellae. *Clin Orthop Relat Res*. 1984(189):209-28.
330. Keogh JP, Nuwayhid I, Gordon JL, Gucer PW. The impact of occupational injury on injured worker and family: outcomes of upper extremity cumulative trauma disorders in Maryland workers. *Am J Ind Med*. 2000;38(5):498-506.

331. Derr J, Forst L, Chen HY, Conroy L. Fatal falls in the US construction industry, 1990 to 1999. *J Occup Environ Med.* 2001;43(10):853-60.
332. Verhagen AP, Karels C, Bierma-Zeinstra SM, et al. Ergonomic and physiotherapeutic interventions for treating work-related complaints of the arm, neck or shoulder in adults. *Cochrane Database Syst Rev.* 2006;3CD003471.
333. Witherington R, Branan WJ, Jr., Wray BB, Best GK. Malacoplakia associated with vesicoureteral reflux and selective immunoglobulin A deficiency. *J Urol.* 1984;132(5):975-7.
334. Zendman AJ, van Venrooij WJ, Pruijn GJ. Use and significance of anti-CCP autoantibodies in rheumatoid arthritis. *Rheumatology (Oxford).* 2006;45(1):20-5.
335. Tan EM, Feltkamp TE, Smolen JS, et al. Range of antinuclear antibodies in "healthy" individuals. *Arthritis Rheum.* 1997;40(9):1601-11.
336. Lyons R, Narain S, Nichols C, Satoh M, Reeves WH. Effective use of autoantibody tests in the diagnosis of systemic autoimmune disease. *Ann N Y Acad Sci.* 2005;1050217-28.
337. Ratnoff WD. Inherited deficiencies of complement in rheumatic diseases. *Rheum Dis Clin North Am.* 1996;22(1):75-94.
338. Walport MJ. Complement. First of two parts. *N Engl J Med.* 2001;344(14):1058-66.
339. Walport MJ. Complement. Second of two parts. *N Engl J Med.* 2001;344(15):1140-4.
340. Blackburn WD, Jr., Bernreuter WK, Rominger M, Loose LL. Arthroscopic evaluation of knee articular cartilage: a comparison with plain radiographs and magnetic resonance imaging. *J Rheumatol.* 1994;21(4):675-9.
341. Bryan S, Bungay HP, Weatherburn G, Field S. Magnetic resonance imaging for investigation of the knee joint: a clinical and economic evaluation. *Int J Technol Assess Health Care.* 2004;20(2):222-9.
342. Buckland-Wright C. Current status of imaging procedures in the diagnosis, prognosis and monitoring of osteoarthritis. *Baillieres Clin Rheumatol.* 1997;11(4):727-48.
343. Bui-Mansfield LT, Youngberg RA, Warme W, Pitcher JD, Nguyen PL. Potential cost savings of MR imaging obtained before arthroscopy of the knee: evaluation of 50 consecutive patients. *AJR Am J Roentgenol.* 1997;168(4):913-8.
344. Chissell HR, Allum RL, Keightley A. MRI of the knee: its cost-effective use in a district general hospital. *Ann R Coll Surg Engl.* 1994;76(1):26-9.
345. Denti M, Arosio A, Trevisan C. Comparison of "catheter" and conventional arthroscopy in the diagnosis of knee derangements. *Arthroscopy.* 1994;10(6):614-7.
346. Duncan JB, Hunter R, Purnell M, Freeman J. Injured stable knee with acute effusion: MRI evaluation. *J South Orthop Assoc.* 1996;5(1):13-9.
347. Friemert B, Oberlander Y, Schwarz W, et al. Diagnosis of chondral lesions of the knee joint: can MRI replace arthroscopy? A prospective study. *Knee Surg Sports Traumatol Arthrosc.* 2004;12(1):58-64.
348. Glashow JL, Katz R, Schneider M, Scott WN. Double-blind assessment of the value of magnetic resonance imaging in the diagnosis of anterior cruciate and meniscal lesions. *J Bone Joint Surg Am.* 1989;71(1):113-9.
349. Gudas R, Kalesinskas RJ, Kimtys V, et al. A prospective randomized clinical study of mosaic osteochondral autologous transplantation versus microfracture for the treatment of osteochondral defects in the knee joint in young athletes. *Arthroscopy.* 2005;21(9):1066-75.
350. Henderson I, Francisco R, Oakes B, Cameron J. Autologous chondrocyte implantation for treatment of focal chondral defects of the knee--a clinical, arthroscopic, MRI and histologic evaluation at 2 years. *Knee.* 2005;12(3):209-16.
351. Heron CW, Calvert PT. Three-dimensional gradient-echo MR imaging of the knee: comparison with arthroscopy in 100 patients. *Radiology.* 1992;183(3):839-44.
352. Irie K, Yamada T, Inoue K. A comparison of magnetic resonance imaging and arthroscopic evaluation of chondral lesions of the knee. *Orthopedics.* 2000;23(6):561-4.
353. Johannsen HV, Fruensgaard S. Arthroscopy in the diagnosis of acute injuries to the knee joint. *Int Orthop.* 1988;12(4):283-6.
354. Kolman BH, Daffner RH, Sciulli RL, Soehnen MW. Correlation of joint fluid and internal derangement on knee MRI. *Skeletal Radiol.* 2004;33(2):91-5.

355. Lundberg M, Odensten M, Thuomas KA, Messner K. The diagnostic validity of magnetic resonance imaging in acute knee injuries with hemarthrosis. A single-blinded evaluation in 69 patients using high-field MRI before arthroscopy. *Int J Sports Med.* 1996;17(3):218-22.
356. Mink JH, Levy T, Crues JV, 3rd. Tears of the anterior cruciate ligament and menisci of the knee: MR imaging evaluation. *Radiology.* 1988;167(3):769-74.
357. Munk B, Madsen F, Lundorf E, et al. Clinical magnetic resonance imaging and arthroscopic findings in knees: a comparative prospective study of meniscus anterior cruciate ligament and cartilage lesions. *Arthroscopy.* 1998;14(2):171-5.
358. Nho SJ, Freedman KB, Bansal SL, et al. The effect of radiofrequency energy on nonweight-bearing areas of bone following shoulder and knee arthroscopy. *Orthopedics.* 2005;28(4):392-9.
359. Nickinson R, Darrah C, Donell S. Accuracy of clinical diagnosis in patients undergoing knee arthroscopy. *Int Orthop.* 2010;34(1):39-44.
360. Ruwe PA, Wright J, Randall RL, Lynch JK, Jokl P, McCarthy S. Can MR imaging effectively replace diagnostic arthroscopy? *Radiology.* 1992;183(2):335-9.
361. Schneider F, Schroeder JH, Labs K. Failed meniscus repair. *Arthroscopy.* 2003;19(8):E93-6.
362. Servant CT, Ramos JP, Thomas NP. The accuracy of magnetic resonance imaging in diagnosing chronic posterior cruciate ligament injury. *Knee.* 2004;11(4):265-70.
363. Sumen Y, Ochi M, Adachi N, Urabe Y, Ikuta Y. Anterior laxity and MR signals of the knee after exercise. A comparison of 9 normal knees and 6 anterior cruciate ligament reconstructed knees. *Acta Orthop Scand.* 1999;70(3):256-60.
364. Trieshmann HW, Jr. Knee arthroscopy: a cost analysis of general and local anesthesia. *Arthroscopy.* 1996;12(1):60-3.
365. Uppal A, Disler DG, Short WB, McCauley TR, Cooper JA. Internal derangements of the knee: rates of occurrence at MR imaging in patients referred by orthopedic surgeons compared with rates in patients referred by physicians who are not orthopedic surgeons. *Radiology.* 1998;207(3):633-6.
366. Vallotton JA, Meuli RA, Leyvraz PF, Landry M. Comparison between magnetic resonance imaging and arthroscopy in the diagnosis of patellar cartilage lesions: a prospective study. *Knee Surg Sports Traumatol Arthrosc.* 1995;3(3):157-62.
367. Weinstabl R, Muellner T, Vecsei V, Kainberger F, Kramer M. Economic considerations for the diagnosis and therapy of meniscal lesions: can magnetic resonance imaging help reduce the expense? *World J Surg.* 1997;21(4):363-8.
368. Quinn SF, Brown TF. Meniscal tears diagnosed with MR imaging versus arthroscopy: how reliable a standard is arthroscopy? *Radiology.* 1991;181(3):843-7.
369. Ike RW. The role of arthroscopy in the differential diagnosis of osteoarthritis of the knee. *Rheum Dis Clin North Am.* 1993;19(3):673-96.
370. Bert JM. Role of abrasion arthroplasty and debridement in the management of osteoarthritis of the knee. *Rheum Dis Clin North Am.* 1993;19(3):725-39.
371. Gillquist J, Hagberg G, Oretorp N. Arthroscopic examination of the posteromedial compartment of the knee joint. *Int Orthop.* 1979;3(1):13-8.
372. Lysholm J, Gillquist J, Liljedahl SO. Arthroscopy in the early diagnosis of injuries to the knee joint. *Acta Orthop Scand.* 1981;52(1):111-8.
373. Lysholm J, Gillquist J, Liljedahl SO. Long-term results after early treatment of knee injuries. *Acta Orthop Scand.* 1982;53(1):109-18.
374. Simonsen O, Jensen J, Lauritzen J. Arthroscopy in acute knee injuries. *Acta Orthop Scand.* 1986;57(2):126-9.
375. Moseley JB, O'Malley K, Petersen NJ, et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med.* 2002;347(2):81-8.
376. Sampson TG. Complications of hip arthroscopy. *Clin Sports Med.* 2001;20(4):831-5.
377. Yacub JN, Rice JB, Dillingham TR. Nerve injury in patients after hip and knee arthroplasties and knee arthroscopy. *Am J Phys Med Rehabil.* 2009;88(8):635-41; quiz 42-4, 91.
378. Wang JQ, Ao YF, Yu CL, Liu P, Xu Y, Chen LX. Clinical evaluation of double-bundle anterior cruciate ligament reconstruction procedure using hamstring tendon grafts: a prospective, randomized and controlled study. *Chin Med J (Engl).* 2009;122(6):706-11.

379. Judd D, Bottoni C, Kim D, Burke M, Hooker S. Infections following arthroscopic anterior cruciate ligament reconstruction. *Arthroscopy*. 2006;22(4):375-84.
380. Clarke HD, Scott WN. The role of debridement: through small portals. *J Arthroplasty*. 2003;18(3 Suppl 1):10-3.
381. Griffin DR, Villar RN. Complications of arthroscopy of the hip. *J Bone Joint Surg Br*. 1999;81(4):604-6.
382. Narvani AA, Tsiroidis E, Tai CC, Thomas P. Acetabular labrum and its tears. *Br J Sports Med*. 2003;37(3):207-11.
383. Byrd RG, Byrd RP, Jr., Roy TM. Axillary artery injuries after proximal fracture of the humerus. *Am J Emerg Med*. 1998;16(2):154-6.
384. Kim YH, Cho SH, Kim RS. Drainage versus nondrainage in simultaneous bilateral total knee arthroplasties. *Clin Orthop Relat Res*. 1998(347):188-93.
385. Funke EL, Munzinger U. Complications in hip arthroscopy. *Arthroscopy*. 1996;12(2):156-9.
386. Ingram C, Stoker DJ. Contrast media in double-contrast arthrography of the knee: a comparison of ioxaglate and iothalamate preparations. *Br J Radiol*. 1986;59(698):143-6.
387. McKillop JH, Maharaj D, Boyce BF, Fogelman I. Bone scan appearances following biopsy of bone and bone marrow. *Radiology*. 1984;153(1):241-2.
388. Van der Wall H, Fogelman I. Scintigraphy of benign bone disease. *Semin Musculoskelet Radiol*. 2007;11(4):281-300.
389. Arce K, Assael LA, Weissman JL, Markiewicz MR. Imaging findings in bisphosphonate-related osteonecrosis of jaws. *J Oral Maxillofac Surg*. 2009;67(5 Suppl):75-84.
390. Slade JF, 3rd, Gillon T. Retrospective review of 234 scaphoid fractures and nonunions treated with arthroscopy for union and complications. *Scand J Surg*. 2008;97(4):280-9.
391. Malizos KN, Karantanas AH, Varitimidis SE, Dailiana ZH, Bargiotas K, Maris T. Osteonecrosis of the femoral head: etiology, imaging and treatment. *Eur J Radiol*. 2007;63(1):16-28.
392. Murakami H, Kawahara N, Gabata T, Nambu K, Tomita K. Vertebral body osteonecrosis without vertebral collapse. *Spine (Phila Pa 1976)*. 2003;28(16):E323-8.
393. Bahrs C, Rolaufts B, Sudkamp NP, et al. Indications for computed tomography (CT-) diagnostics in proximal humeral fractures: a comparative study of plain radiography and computed tomography. *BMC Musculoskelet Disord*. 2009;1033.
394. Ohashi K, El-Khoury GY. Musculoskeletal CT: recent advances and current clinical applications. *Radiol Clin North Am*. 2009;47(3):387-409.
395. Reish TG, Clarke HD, Scuderi GR, Math KR, Scott WN. Use of multi-detector computed tomography for the detection of periprosthetic osteolysis in total knee arthroplasty. *J Knee Surg*. 2006;19(4):259-64.
396. Stevens K, Tao C, Lee SU, et al. Subchondral fractures in osteonecrosis of the femoral head: comparison of radiography, CT, and MR imaging. *AJR Am J Roentgenol*. 2003;180(2):363-8.
397. Miller JW, Castor CW. Connective tissue activation XXVI: IgG stimulation of glycosaminoglycan synthesis in human synovial cultures. *J Rheumatol*. 1983;10(2):190-6.
398. Bridgen A, Kocherhans R, Tobler K, Carvajal A, Ackermann M. Further analysis of the genome of porcine epidemic diarrhoea virus. *Adv Exp Med Biol*. 1998;440781-6.
399. Morley KD, Hughes GR. Systemic lupus erythematosus: causative factors and treatment. *Drugs*. 1982;23(6):481-8.
400. Wener MH, Daum PR, McQuillan GM. The influence of age, sex, and race on the upper reference limit of serum C-reactive protein concentration. *J Rheumatol*. 2000;27(10):2351-9.
401. Redborg KE, Sites BD, Chinn CD, et al. Ultrasound improves the success rate of a sural nerve block at the ankle. *Reg Anesth Pain Med*. 2009;34(1):24-8.
402. Akkaya T, Ersan O, Ozkan D, et al. Saphenous nerve block is an effective regional technique for post-meniscectomy pain. *Knee Surg Sports Traumatol Arthrosc*. 2008;16(9):855-8.
403. Tran de QH, Clemente A, Tran DQ, Finlayson RJ. A comparison between ultrasound-guided infraclavicular block using the "double bubble" sign and neurostimulation-guided axillary block. *Anesth Analg*. 2008;107(3):1075-8.
404. Benzon HT. The neuropathic pain scales. *Reg Anesth Pain Med*. 2005;30(5):417-21.
405. Shapiro BE, Preston DC. Repetitive nerve stimulation and exercise testing. *Phys Med Rehabil Clin N Am*. 2003;14(2):185-206.

406. Shapiro BE, Preston DC. Entrapment and compressive neuropathies. *Med Clin North Am.* 2009;93(2):285-315, vii.
407. Masakado Y, Ushiba J, Tsutsumi N, et al. EEG-EMG coherence changes in postural tasks. *Electromyogr Clin Neurophysiol.* 2008;48(1):27-33.
408. Chiodo A, Spiegelberg T, Tong HC. Comparing saphenous nerve conduction study techniques at the knee and at the ankle and their relationship to body mass index. *Arch Phys Med Rehabil.* 2007;88(4):477-80.
409. Buxton WG, Dominick JE. Electromyography and nerve conduction studies of the lower extremity: uses and limitations. *Clin Podiatr Med Surg.* 2006;23(3):531-43.
410. Tankisi H, Pugdahl K, Fuglsang-Frederiksen A, et al. Pathophysiology inferred from electrodiagnostic nerve tests and classification of polyneuropathies. Suggested guidelines. *Clin Neurophysiol.* 2005;116(7):1571-80.
411. Thomas SA. Spinal stenosis: history and physical examination. *Phys Med Rehabil Clin N Am.* 2003;14(1):29-39.
412. Yee T. Recurrent idiopathic lumbosacral plexopathy. *Muscle Nerve.* 2000;23(9):1439-42.
413. Robinson LR. Role of neurophysiologic evaluation in diagnosis. *J Am Acad Orthop Surg.* 2000;8(3):190-9.
414. Blando AV. Lower extremity sensory nerve conduction studies. *Phys Med Rehabil Clin N Am.* 1998;9(4):853-70, vii.
415. Fisher MA. AAEM Minimonograph #13: H reflexes and F waves: physiology and clinical indications. *Muscle Nerve.* 1992;15(11):1223-33.
416. Sonck WA, Francx MM, Engels HL. Innervation anomalies in upper and lower extremities: potential clinical implications. How to identify with electrophysiologic techniques. *Electromyogr Clin Neurophysiol.* 1991;31(2):67-80.
417. Weber GA. Nerve conduction studies and their clinical applications. *Clin Podiatr Med Surg.* 1990;7(1):151-78.
418. Gardner MJ, Demetrakopoulos D, Briggs SM, Helfet DL, Lorich DG. The ability of the Lauge-Hansen classification to predict ligament injury and mechanism in ankle fractures: an MRI study. *J Orthop Trauma.* 2006;20(4):267-72.
419. Sumen Y, Ochi M, Deie M, Adachi N, Ikuta Y. Ganglion cysts of the cruciate ligaments detected by MRI. *Int Orthop.* 1999;23(1):58-60.
420. Triesmann HW, Jr., Mosure JC. The impact of magnetic resonance imaging of the knee on surgical decision making. *Arthroscopy.* 1996;12(5):550-5.
421. Theodorou DJ, Theodorou SJ, Fithian DC, Paxton L, Garelick DH, Resnick D. Posterolateral complex knee injuries: magnetic resonance imaging with surgical correlation. *Acta Radiol.* 2005;46(3):297-305.
422. Scheiber C, Meyer ME, Dumitresco B, et al. The pitfalls of planar three-phase bone scintigraphy in nontraumatic hip avascular osteonecrosis. *Clin Nucl Med.* 1999;24(7):488-94.
423. Helenius I, Jalanko H, Remes V, et al. Avascular bone necrosis of the hip joint after solid organ transplantation in childhood: a clinical and MRI analysis. *Transplantation.* 2006;81(12):1621-7.
424. Sakai T, Sugano N, Nishii T, Hananouchi T, Yoshikawa H. Extent of osteonecrosis on MRI predicts humeral head collapse. *Clin Orthop Relat Res.* 2008;466(5):1074-80.
425. Jones LC, Hungerford DS. Osteonecrosis: etiology, diagnosis, and treatment. *Curr Opin Rheumatol.* 2004;16(4):443-9.
426. Koo KH, Kim R. Quantifying the extent of osteonecrosis of the femoral head. A new method using MRI. *J Bone Joint Surg Br.* 1995;77(6):875-80.
427. Coombs RR, Thomas RW. Avascular necrosis of the hip. *Br J Hosp Med.* 1994;51(6):275-80.
428. Cherian SF, Laorr A, Saleh KJ, Kuskowski MA, Bailey RF, Cheng EY. Quantifying the extent of femoral head involvement in osteonecrosis. *J Bone Joint Surg Am.* 2003;85-A(2):309-15.
429. Radke S, Rader C, Kenn W, Kirschner S, Walther M, Eulert J. Transient marrow edema syndrome of the hip: results after core decompression. A prospective MRI-controlled study in 22 patients. *Arch Orthop Trauma Surg.* 2003;123(5):223-7.
430. Boeree NR, Watkinson AF, Ackroyd CE, Johnson C. Magnetic resonance imaging of meniscal and cruciate injuries of the knee. *J Bone Joint Surg Br.* 1991;73(3):452-7.
431. Falconiero RP, DiStefano VJ. Comparison of revascularization and ligamentization of autograft and allograft tissue for anterior cruciate ligament reconstruction in humans. *Orthop Trans.* 1994;18:1096.

432. Fischer SP, Fox JM, Del Pizzo W, Friedman MJ, Snyder SJ, Ferkel RD. Accuracy of diagnoses from magnetic resonance imaging of the knee. A multi-center analysis of one thousand and fourteen patients. *J Bone Joint Surg Am.* 1991;73(1):2-10.
433. Jackson DW, Jennings LD, Maywood RM, Berger PE. Magnetic resonance imaging of the knee. *Am J Sports Med.* 1988;16(1):29-38.
434. Spiers AS, Meagher T, Ostlere SJ, Wilson DJ, Dodd CA. Can MRI of the knee affect arthroscopic practice? A prospective study of 58 patients. *J Bone Joint Surg Br.* 1993;75(1):49-52.
435. Brooks S, Morgan M. Accuracy of clinical diagnosis in knee arthroscopy. *Ann R Coll Surg Engl.* 2002;84(4):265-8.
436. Crawford R, Walley G, Bridgman S, Maffulli N. Magnetic resonance imaging versus arthroscopy in the diagnosis of knee pathology, concentrating on meniscal lesions and ACL tears: a systematic review. *Br Med Bull.* 2007;845-23.
437. Chapman-Jones D, Paterson A, Johnston S. Plain radiography of the knee: a useful diagnostic modality for patients with non-specific knee pain? A retrospective study of plain radiography of the knee in comparison with MRI in patients with non-specific knee pain. *Radiography.* 1998;4:183-7.
438. Guermazi A, Hunter DJ, Roemer FW. Plain radiography and magnetic resonance imaging diagnostics in osteoarthritis: validated staging and scoring. *J Bone Joint Surg Am.* 2009;91 Suppl 154-62.
439. Chan WP, Lang P, Stevens MP, et al. Osteoarthritis of the knee: comparison of radiography, CT, and MR imaging to assess extent and severity. *AJR Am J Roentgenol.* 1991;157(4):799-806.
440. McAlindon TE, Watt I, McCrae F, Goddard P, Dieppe PA. Magnetic resonance imaging in osteoarthritis of the knee: correlation with radiographic and scintigraphic findings. *Ann Rheum Dis.* 1991;50(1):14-9.
441. Mathieu L, Bouchard A, Marchaland JP, et al. Knee MR-arthrography in assessment of meniscal and chondral lesions. *Orthop Traumatol Surg Res.* 2009;95(1):40-7.
442. Ciliz D, Ciliz A, Elverici E, Sakman B, Yuksel E, Akbulut O. Evaluation of postoperative menisci with MR arthrography and routine conventional MRI. *Clin Imaging.* 2008;32(3):212-9.
443. Streitparth F, Schottle P, Schell H, et al. Indirect MR-arthrography in osteochondral autograft and crushed bone graft with a collagen membrane--correlation with histology. *Eur J Radiol.* 2009;70(1):155-64.
444. Ornetti P, Brandt K, Hellio-Le Graverand MP, et al. OARSI-OMERACT definition of relevant radiological progression in hip/knee osteoarthritis. *Osteoarthritis Cartilage.* 2009;17(7):856-63.
445. Bedson J, Croft PR. The discordance between clinical and radiographic knee osteoarthritis: a systematic search and summary of the literature. *BMC Musculoskelet Disord.* 2008;9:116.
446. Peat G, Thomas E, Handy J, et al. The Knee Clinical Assessment Study--CAS(K). A prospective study of knee pain and knee osteoarthritis in the general population. *BMC Musculoskelet Disord.* 2004;54.
447. Salaffi F, Piva S, Barreca C, et al. Validation of an Italian version of the arthritis impact measurement scales 2 (ITALIAN-AIMS2) for patients with osteoarthritis of the knee. Gonarthrosis and Quality of Life Assessment (GOQOLA) Study Group. *Rheumatology (Oxford).* 2000;39(7):720-7.
448. Seaberg DC, Jackson R. Clinical decision rule for knee radiographs. *Am J Emerg Med.* 1994;12(5):541-3.
449. Hamerman D. Osteoarthritis. *Orthop Rev.* 1988;17(4):353-60.
450. Ficat RP. Idiopathic bone necrosis of the femoral head. Early diagnosis and treatment. *J Bone Joint Surg Br.* 1985;67(1):3-9.
451. Bauer SJ, Hollander JE, Fuchs SH, Thode HC, Jr. A clinical decision rule in the evaluation of acute knee injuries. *J Emerg Med.* 1995;13(5):611-5.
452. Ahlback S. Osteoarthrosis of the knee. A radiographic investigation. *Acta Radiol Diagn (Stockh).* 1968Suppl 277:7-72.
453. Buckland-Wright JC, Macfarlane DG, Lynch JA, Jasani MK, Bradshaw CR. Joint space width measures cartilage thickness in osteoarthritis of the knee: high resolution plain film and double contrast macroradiographic investigation. *Ann Rheum Dis.* 1995;54(4):263-8.
454. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Ann Rheum Dis.* 1957;16(4):494-502.
455. Bellamy N, Tesar P, Walker D, et al. Perceptual variation in grading hand, hip and knee radiographs: observations based on an Australian twin registry study of osteoarthritis. *Ann Rheum Dis.* 1999;58(12):766-9.
456. Thomas RH, Resnick D, Alazraki NP, Daniel D, Greenfield R. Compartmental evaluation of osteoarthritis of the knee. A comparative study of available diagnostic modalities. *Radiology.* 1975;116(3):585-94.

457. Marx A, Saxler G, Landgraeber S, Loer F, Holland-Letz T, von Knoch M. Comparison of subtraction arthrography, radionuclide arthrography and conventional plain radiography to assess loosening of total knee arthroplasty. *Biomed Tech (Berl)*. 2005;50(5):143-7.
458. Marvel JE, Marsh HO. Management of penetrating injuries of the knee. *Clin Orthop Relat Res*. 1977(122):268-72.
459. Nord RM, Quach T, Walsh M, Pereira D, Tejwani NC. Detection of traumatic arthrotomy of the knee using the saline solution load test. *J Bone Joint Surg Am*. 2009;91(1):66-70.
460. Keese GR, Boody AR, Wongworawat MD, Jobe CM. The accuracy of the saline load test in the diagnosis of traumatic knee arthrotomies. *J Orthop Trauma*. 2007;21(7):442-3.
461. Voit GA, Irvine G, Beals RK. Saline load test for penetration of periarticular lacerations. *J Bone Joint Surg Br*. 1996;78(5):732-3.
462. Kalebo P, Sward L, Karlsson J, Peterson L. Ultrasonography in the detection of partial patellar ligament ruptures (jumper's knee). *Skeletal Radiol*. 1991;20(4):285-9.
463. Mourad K, King J, Guggiana P. Computed tomography and ultrasound imaging of jumper's knee-patellar tendinitis. *Clin Radiol*. 1988;39(2):162-5.
464. Laine HR, Harjula A, Peltokallio P. Ultrasound in the evaluation of the knee and patellar regions. *J Ultrasound Med*. 1987;6(1):33-6.
465. Fornage BD, Rifkin MD. Ultrasound examination of tendons. *Radiol Clin North Am*. 1988;26(1):87-107.
466. Fornage BD, Rifkin MD, Touche DH, Segal PM. Sonography of the patellar tendon: preliminary observations. *AJR Am J Roentgenol*. 1984;143(1):179-82.
467. De Flaviis L, Nessi R, Scaglione P, Balconi G, Albisetti W, Derchi LE. Ultrasonic diagnosis of Osgood-Schlatter and Sinding-Larsen-Johansson diseases of the knee. *Skeletal Radiol*. 1989;18(3):193-7.
468. Fritschy D, de Gautard R. Jumper's knee and ultrasonography. *Am J Sports Med*. 1988;16(6):637-40.
469. Vieira RL, Levy JA. Bedside ultrasonography to identify hip effusions in pediatric patients. *Ann Emerg Med*. 2010;55(3):284-9.
470. Mahan ST, Katz JN, Kim YJ. To screen or not to screen? A decision analysis of the utility of screening for developmental dysplasia of the hip. *J Bone Joint Surg Am*. 2009;91(7):1705-19.
471. Visser F, Sprij AJ, Bos CF. Comment on: Clinical examination versus ultrasonography in detecting developmental dysplasia of the hip. *Int Orthop*. 2009;33(3):883-4; author reply 5-6.
472. Troelsen A, Jacobsen S, Bolvig L, Gelineck J, Romer L, Soballe K. Ultrasound versus magnetic resonance arthrography in acetabular labral tear diagnostics: a prospective comparison in 20 dysplastic hips. *Acta Radiol*. 2007;48(9):1004-10.
473. Safran O, Goldman V, Applbaum Y, et al. Posttraumatic painful hip: sonography as a screening test for occult hip fractures. *J Ultrasound Med*. 2009;28(11):1447-52.
474. Kapoor S, Shaw WS, Pransky G, Patterson W. Initial patient and clinician expectations of return to work after acute onset of work-related low back pain. *J Occup Environ Med*. 2006;48(11):1173-80.
475. Cibulka MT, White DM, Woehrle J, et al. Hip pain and mobility deficits--hip osteoarthritis: clinical practice guidelines linked to the international classification of functioning, disability, and health from the orthopaedic section of the American Physical Therapy Association. *J Orthop Sports Phys Ther*. 2009;39(4):A1-25.
476. Petrella RJ. Is exercise effective treatment for osteoarthritis of the knee? *Br J Sports Med*. 2000;34(5):326-31.
477. Smidt N, de Vet HC, Bouter LM, et al. Effectiveness of exercise therapy: a best-evidence summary of systematic reviews. *Aust J Physiother*. 2005;51(2):71-85.
478. Kettunen JA, Kujala UM. Exercise therapy for people with rheumatoid arthritis and osteoarthritis. *Scand J Med Sci Sports*. 2004;14(3):138-42.
479. Bischoff HA, Roos EM. Effectiveness and safety of strengthening, aerobic, and coordination exercises for patients with osteoarthritis. *Curr Opin Rheumatol*. 2003;15(2):141-4.
480. Bennell K, Hinman R. Exercise as a treatment for osteoarthritis. *Curr Opin Rheumatol*. 2005;17(5):634-40.
481. Devos-Comby L, Cronan T, Roesch SC. Do exercise and self-management interventions benefit patients with osteoarthritis of the knee? A meta-analytic review. *J Rheumatol*. 2006;33(4):744-56.
482. Roddy E, Zhang W, Doherty M. Aerobic walking or strengthening exercise for osteoarthritis of the knee? A systematic review. *Ann Rheum Dis*. 2005;64(4):544-8.

483. Minor MA. Exercise in the treatment of osteoarthritis. *Rheum Dis Clin North Am*. 1999;25(2):397-415, viii.
484. van Baar ME, Assendelft WJ, Dekker J, Oostendorp RA, Bijlsma JW. Effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee: a systematic review of randomized clinical trials. *Arthritis Rheum*. 1999;42(7):1361-9.
485. Ytterberg SR, Mahowald ML, Krug HE. Exercise for arthritis. *Baillieres Clin Rheumatol*. 1994;8(1):161-89.
486. Balint G, Szebenyi B. Non-pharmacological therapies in osteoarthritis. *Baillieres Clin Rheumatol*. 1997;11(4):795-815.
487. Leivseth G, Torstensson J, Reikeras O. Effect of passive muscle stretching in osteoarthritis of the hip. *Clin Sci (Lond)*. 1989;76(1):113-7.
488. Sisto SA, Malanga G. Osteoarthritis and therapeutic exercise. *Am J Phys Med Rehabil*. 2006;85(11 Suppl):S69-78; quiz S9-81.
489. Westby MD, Wade JP, Rangno KK, Berkowitz J. A randomized controlled trial to evaluate the effectiveness of an exercise program in women with rheumatoid arthritis taking low dose prednisone. *J Rheumatol*. 2000;27(7):1674-80.
490. O'Grady M, Fletcher J, Ortiz S. Therapeutic and physical fitness exercise prescription for older adults with joint disease: an evidence-based approach. *Rheum Dis Clin North Am*. 2000;26(3):617-46.
491. Hernandez-Molina G, Reichenbach S, Zhang B, Lavalley M, Felson DT. Effect of therapeutic exercise for hip osteoarthritis pain: results of a meta-analysis. *Arthritis Rheum*. 2008;59(9):1221-8.
492. Brander V, Stulberg SD. Rehabilitation after hip- and knee-joint replacement. An experience- and evidence-based approach to care. *Am J Phys Med Rehabil*. 2006;85(11 Suppl):S98-118; quiz S9-23.
493. Maurer BT, Stern AG, Kinossian B, Cook KD, Schumacher HR, Jr. Osteoarthritis of the knee: isokinetic quadriceps exercise versus an educational intervention. *Arch Phys Med Rehabil*. 1999;80(10):1293-9.
494. van Baar ME, Dekker J, Oostendorp RA, et al. The effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee: a randomized clinical trial. *J Rheumatol*. 1998;25(12):2432-9.
495. Baker KR, Nelson ME, Felson DT, Layne JE, Sarno R, Roubenoff R. The efficacy of home based progressive strength training in older adults with knee osteoarthritis: a randomized controlled trial. *J Rheumatol*. 2001;28(7):1655-65.
496. Halbert J, Crotty M, Weller D, Ahern M, Silagy C. Primary care-based physical activity programs: effectiveness in sedentary older patients with osteoarthritis symptoms. *Arthritis Rheum*. 2001;45(3):228-34.
497. O'Reilly SC, Muir KR, Doherty M. Effectiveness of home exercise on pain and disability from osteoarthritis of the knee: a randomised controlled trial. *Ann Rheum Dis*. 1999;58(1):15-9.
498. Ravaud P, Flipo RM, Boutron I, et al. ARTIST (osteoarthritis intervention standardized) study of standardised consultation versus usual care for patients with osteoarthritis of the knee in primary care in France: pragmatic randomised controlled trial. *Bmj*. 2009;338b421.
499. Dias RC, Dias JM, Ramos LR. Impact of an exercise and walking protocol on quality of life for elderly people with OA of the knee. *Physiother Res Int*. 2003;8(3):121-30.
500. Hootman JM, Macera CA, Ham SA, Helmick CG, Sniezek JE. Physical activity levels among the general US adult population and in adults with and without arthritis. *Arthritis Rheum*. 2003;49(1):129-35.
501. Ekdahl C, Andersson SI, Moritz U, Svensson B. Dynamic versus static training in patients with rheumatoid arthritis. *Scand J Rheumatol*. 1990;19(1):17-26.
502. Stenstrom CH, Lindell B, Swanberg E, Swanberg P, Harms-Ringdahl K, Nordemar R. Intensive dynamic training in water for rheumatoid arthritis functional class II--a long-term study of effects. *Scand J Rheumatol*. 1991;20(5):358-65.
503. Jan MH, Lai JS. The effects of physiotherapy on osteoarthritic knees of females. *J Formos Med Assoc*. 1991;90(10):1008-13.
504. Peterson MG, Kovar-Toledano PA, Otis JC, et al. Effect of a walking program on gait characteristics in patients with osteoarthritis. *Arthritis Care Res*. 1993;6(1):11-6.
505. Chamberlain MA, Care G, Harfield B. Physiotherapy in osteoarthrosis of the knees. A controlled trial of hospital versus home exercises. *Int Rehabil Med*. 1982;4(2):101-6.
506. Messier SP, Mihalko S, Loeser RF, et al. Glucosamine/chondroitin combined with exercise for the treatment of knee osteoarthritis: a preliminary study. *Osteoarthritis Cartilage*. 2007;15(11):1256-66.

507. Schilke JM, Johnson GO, Housh TJ, O'Dell JR. Effects of muscle-strength training on the functional status of patients with osteoarthritis of the knee joint. *Nurs Res*. 1996;45(2):68-72.
508. Ettinger WH, Jr., Burns R, Messier SP, et al. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. The Fitness Arthritis and Seniors Trial (FAST). *JAMA*. 1997;277(1):25-31.
509. Borjesson M, Robertson E, Weidenhielm L, Mattsson E, Olsson E. Physiotherapy in knee osteoarthritis: effect on pain and walking. *Physiother Res Int*. 1996;1(2):89-97.
510. Bautch JC, Malone DG, Vailas AC. Effects of exercise on knee joints with osteoarthritis: a pilot study of biologic markers. *Arthritis Care Res*. 1997;10(1):48-55.
511. Callaghan MJ, Oldham JA. An evaluation of exercise regimes for patients with osteoarthritis of the knee: a single-blind randomized controlled trial. *Clin Rehabil*. 1995;9:213-8.
512. Kovar PA, Allegrante JP, MacKenzie CR, Peterson MG, Gutin B, Charlson ME. Supervised fitness walking in patients with osteoarthritis of the knee. A randomized, controlled trial. *Ann Intern Med*. 1992;116(7):529-34.
513. Barton GR, Sach TH, Jenkinson C, Doherty M, Avery AJ, Muir KR. Lifestyle interventions for knee pain in overweight and obese adults aged > or = 45: economic evaluation of randomised controlled trial. *Bmj*. 2009;339b2273.
514. Brinkworth GD, Noakes M, Clifton PM, Buckley JD. Effects of a Low Carbohydrate Weight Loss Diet on Exercise Capacity and Tolerance in Obese Subjects. *Obesity (Silver Spring)*. 2009.
515. Focht BC, Rejeski WJ, Ambrosius WT, Katula JA, Messier SP. Exercise, self-efficacy, and mobility performance in overweight and obese older adults with knee osteoarthritis. *Arthritis Rheum*. 2005;53(5):659-65.
516. Jenkinson CM, Doherty M, Avery AJ, et al. Effects of dietary intervention and quadriceps strengthening exercises on pain and function in overweight people with knee pain: randomised controlled trial. *Bmj*. 2009;339b3170.
517. Sevick MA, Bradham DD, Muender M, et al. Cost-effectiveness of aerobic and resistance exercise in seniors with knee osteoarthritis. *Med Sci Sports Exerc*. 2000;32(9):1534-40.
518. Sevick MA, Miller GD, Loeser RF, Williamson JD, Messier SP. Cost-effectiveness of exercise and diet in overweight and obese adults with knee osteoarthritis. *Med Sci Sports Exerc*. 2009;41(6):1167-74.
519. van Gool CH, Penninx BW, Kempen GI, et al. Effects of exercise adherence on physical function among overweight older adults with knee osteoarthritis. *Arthritis Rheum*. 2005;53(1):24-32.
520. Baillet A, Zeboulon N, Gossec L, et al. Efficacy of cardiorespiratory aerobic exercise in rheumatoid arthritis: meta-analysis of randomized controlled trials. *Arthritis Care Res (Hoboken)*. 62(7):984-92.
521. van den Ende CH, Breedveld FC, le Cessie S, Dijkmans BA, de Mug AW, Hazes JM. Effect of intensive exercise on patients with active rheumatoid arthritis: a randomised clinical trial. *Ann Rheum Dis*. 2000;59(8):615-21.
522. Hall J, Skevington SM, Maddison PJ, Chapman K. A randomized and controlled trial of hydrotherapy in rheumatoid arthritis. *Arthritis Care Res*. 1996;9(3):206-15.
523. Lyngberg KK, Harreby M, Bentzen H, Frost B, Danneskiold-Samsøe B. Elderly rheumatoid arthritis patients on steroid treatment tolerate physical training without an increase in disease activity. *Arch Phys Med Rehabil*. 1994;75(11):1189-95.
524. Lyngberg K, Danneskiold-Samsøe B, Halskov O. The effect of physical training on patients with rheumatoid arthritis: changes in disease activity, muscle strength and aerobic capacity. A clinically controlled minimized cross-over study. *Clin Exp Rheumatol*. 1988;6(3):253-60.
525. Baslund B, Lyngberg K, Andersen V, et al. Effect of 8 wk of bicycle training on the immune system of patients with rheumatoid arthritis. *J Appl Physiol*. 1993;75(4):1691-5.
526. van den Ende CH, Hazes JM, le Cessie S, et al. Comparison of high and low intensity training in well controlled rheumatoid arthritis. Results of a randomised clinical trial. *Ann Rheum Dis*. 1996;55(11):798-805.
527. Daltroy LH, Robb-Nicholson C, Iversen MD, Wright EA, Liang MH. Effectiveness of minimally supervised home aerobic training in patients with systemic rheumatic disease. *Br J Rheumatol*. 1995;34(11):1064-9.

528. Hansen TM, Hansen G, Langgaard AM, Rasmussen JO. Longterm physical training in rheumatoid arthritis. A randomized trial with different training programs and blinded observers. *Scand J Rheumatol*. 1993;22(3):107-12.
529. Smith SS, MacKay-Lyons M. Therapeutisch nut van aquaerobics voor patiënten met reumatoïde artritis. *Stimulus*. 1998;18(2):79-81.
530. McMeeken J, Stillman B, Story I, Kent P, Smith J. The effects of knee extensor and flexor muscle training on the timed-up-and-go test in individuals with rheumatoid arthritis. *Physiother Res Int*. 1999;4(1):55-67.
531. Harkcom TM, Lampman RM, Banwell BF, Castor CW. Therapeutic value of graded aerobic exercise training in rheumatoid arthritis. *Arthritis Rheum*. 1985;28(1):32-9.
532. Hakkinen A, Sokka T, Kotaniemi A, Hannonen P. A randomized two-year study of the effects of dynamic strength training on muscle strength, disease activity, functional capacity, and bone mineral density in early rheumatoid arthritis. *Arthritis Rheum*. 2001;44(3):515-22.
533. de Jong Z, Munneke M, Zwinderman AH, et al. Is a long-term high-intensity exercise program effective and safe in patients with rheumatoid arthritis? Results of a randomized controlled trial. *Arthritis Rheum*. 2003;48(9):2415-24.
534. de Jong Z, Munneke M, Zwinderman AH, et al. Slowing of bone loss in patients with rheumatoid arthritis by long-term high-intensity exercise: results of a randomized, controlled trial. *Arthritis Rheum*. 2004;50(4):1066-76.
535. Stenstrom C. Home exercise in rheumatoid arthritis functional class II: goal setting versus pain attention. *J Rheumatol*. 1994;21(4):627-34.
536. Melikoglu M, Karatay S, Senel K, Akcay F. Association between dynamic exercise therapy and IGF-1 and IGFBP-3 concentrations in the patients with rheumatoid arthritis. *Rheumatol Int*. 2006;26(4):309-13.
537. Bilberg A, Ahlmen M, Mannerkorpi K. Moderately intensive exercise in a temperate pool for patients with rheumatoid arthritis: a randomized controlled study. *Rheumatology (Oxford)*. 2005;44(4):502-8.
538. Neuberger G, Aaronson LS, Gajewski B, et al. Predictors of exercise and effects of exercise on symptoms, function, aerobic fitness, and disease outcomes of rheumatoid arthritis. *Arthritis Rheum*. 2007;57(6):943-52.
539. Komatireddy GLR, Cella K, Browning G, Minor M. Efficacy of low load resistive muscle training in patients with rheumatoid arthritis functional class II and III. *J Rheumatol*. 1997;24(8):1531-9.
540. van den Berg M, Runday HK, Peeters AJ, et al. Using internet technology to deliver a home-based physical activity intervention for patients with rheumatoid arthritis: a randomized controlled trial. *Arthritis Rheum*. 2006;55(6):935-45.
541. Metsios GS, Stavropoulos-Kalinoglou A, Veldhuijzen van Zanten JJ, et al. Rheumatoid arthritis, cardiovascular disease and physical exercise: a systematic review. *Rheumatology (Oxford)*. 2008;47(3):239-48.
542. Ekblom B, Lovgren O, Alderin M, Fridstrom M, Satterstrom G. Effect of short-term physical training on patients with rheumatoid arthritis. a six-month follow-up study. *Scand J Rheumatol*. 1975;4(2):87-91.
543. Ekblom B, Lovgren O, Alderin M, Fridstrom M, Satterstrom G. Effect of short-term physical training on patients with rheumatoid arthritis I. *Scand J Rheumatol*. 1975;4(2):80-6.
544. Armstrong L. *ACSM's Guidelines for Exercise Testing and Prescription*. 7th ed. Baltimore, Md: Lippincott Williams & Wilkins; 2005.
545. Rejeski WJ, Brawley LR, Ettinger W, Morgan T, Thompson C. Compliance to exercise therapy in older participants with knee osteoarthritis: implications for treating disability. *Med Sci Sports Exerc*. 1997;29(8):977-85.
546. Mangani I, Cesari M, Kritchevsky SB, et al. Physical exercise and comorbidity. Results from the Fitness and Arthritis in Seniors Trial (FAST). *Aging Clin Exp Res*. 2006;18(5):374-80.
547. Rejeski WJ, Ettinger WH, Jr., Martin K, Morgan T. Treating disability in knee osteoarthritis with exercise therapy: a central role for self-efficacy and pain. *Arthritis Care Res*. 1998;11(2):94-101.
548. Minor MA, Hewett JE, Webel RR, Anderson SK, Kay DR. Efficacy of physical conditioning exercise in patients with rheumatoid arthritis and osteoarthritis. *Arthritis Rheum*. 1989;32(11):1396-405.
549. Mangione KK, McCully K, Gloviak A, Lefebvre I, Hofmann M, Craik R. The effects of high-intensity and low-intensity cycle ergometry in older adults with knee osteoarthritis. *J Gerontol A Biol Sci Med Sci*. 1999;54(4):M184-90.

550. Huang MH, Lin YS, Yang RC, Lee CL. A comparison of various therapeutic exercises on the functional status of patients with knee osteoarthritis. *Semin Arthritis Rheum*. 2003;32(6):398-406.
551. Lim BW, Hinman RS, Wrigley TV, Sharma L, Bennell KL. Does knee malalignment mediate the effects of quadriceps strengthening on knee adduction moment, pain, and function in medial knee osteoarthritis? A randomized controlled trial. *Arthritis Rheum*. 2008;59(7):943-51.
552. Lin DH, Lin CH, Lin YF, Jan MH. Efficacy of 2 non-weight-bearing interventions, proprioception training versus strength training, for patients with knee osteoarthritis: a randomized clinical trial. *J Orthop Sports Phys Ther*. 2009;39(6):450-7.
553. Fransen M, Crosbie J, Edmonds J. Physical therapy is effective for patients with osteoarthritis of the knee: a randomized controlled clinical trial. *J Rheumatol*. 2001;28(1):156-64.
554. Thomas KS, Miller P, Doherty M, Muir KR, Jones AC, O'Reilly SC. Cost effectiveness of a two-year home exercise program for the treatment of knee pain. *Arthritis Rheum*. 2005;53(3):388-94.
555. Thomas KS, Muir KR, Doherty M, Jones AC, O'Reilly SC, Bassej EJ. Home based exercise programme for knee pain and knee osteoarthritis: randomised controlled trial. *Bmj*. 2002;325(7367):752.
556. Hay EM, Foster NE, Thomas E, et al. Effectiveness of community physiotherapy and enhanced pharmacy review for knee pain in people aged over 55 presenting to primary care: pragmatic randomised trial. *Bmj*. 2006;333(7576):995.
557. Nguyen M, Revel M, Dougados M. Prolonged effects of 3 week therapy in a spa resort on lumbar spine, knee and hip osteoarthritis: follow-up after 6 months. A randomized controlled trial. *Br J Rheumatol*. 1997;36(1):77-81.
558. Ravaud P, Giraudeau B, Logeart I, et al. Management of osteoarthritis (OA) with an unsupervised home based exercise programme and/or patient administered assessment tools. A cluster randomised controlled trial with a 2x2 factorial design. *Ann Rheum Dis*. 2004;63(6):703-8.
559. Thorstensson CA, Roos EM, Petersson IF, Ekdahl C. Six-week high-intensity exercise program for middle-aged patients with knee osteoarthritis: a randomized controlled trial [ISRCTN20244858]. *BMC Musculoskelet Disord*. 2005;627.
560. Tak E, Staats P, Van Hespden A, Hopman-Rock M. The effects of an exercise program for older adults with osteoarthritis of the hip. *J Rheumatol*. 2005;32(6):1106-13.
561. Rogind H, Bibow-Nielsen B, Jensen B, Moller HC, Frimodt-Moller H, Bliddal H. The effects of a physical training program on patients with osteoarthritis of the knees. *Arch Phys Med Rehabil*. 1998;79(11):1421-7.
562. Peloquin L, Bravo G, Gauthier P, Lacombe G, Billiard JS. Effects of a Cross-Training Exercise Program in Persons with Osteoarthritis of the Knee A Randomized Controlled Trial. *J Clin Rheumatol*. 1999;5(3):126-36.
563. Roos EM, Dahlberg L. Positive effects of moderate exercise on glycosaminoglycan content in knee cartilage: a four-month, randomized, controlled trial in patients at risk of osteoarthritis. *Arthritis Rheum*. 2005;52(11):3507-14.
564. Topp R, Woolley S, Hornyak J, 3rd, Khuder S, Kahaleh B. The effect of dynamic versus isometric resistance training on pain and functioning among adults with osteoarthritis of the knee. *Arch Phys Med Rehabil*. 2002;83(9):1187-95.
565. Hopman-Rock M, Westhoff MH. The effects of a health educational and exercise program for older adults with osteoarthritis for the hip or knee. *J Rheumatol*. 2000;27(8):1947-54.
566. Jan MH, Lin JJ, Liao JJ, Lin YF, Lin DH. Investigation of clinical effects of high- and low-resistance training for patients with knee osteoarthritis: a randomized controlled trial. *Phys Ther*. 2008;88(4):427-36.
567. Hoeksma HL, Dekker J, Runday HK, et al. Comparison of manual therapy and exercise therapy in osteoarthritis of the hip: a randomized clinical trial. *Arthritis Rheum*. 2004;51(5):722-9.
568. McCarthy CJ, Mills PM, Pullen R, Roberts C, Silman A, Oldham JA. Supplementing a home exercise programme with a class-based exercise programme is more effective than home exercise alone in the treatment of knee osteoarthritis. *Rheumatology (Oxford)*. 2004;43(7):880-6.
569. Jan MH, Lin CH, Lin YF, Lin JJ, Lin DH. Effects of weight-bearing versus nonweight-bearing exercise on function, walking speed, and position sense in participants with knee osteoarthritis: a randomized controlled trial. *Arch Phys Med Rehabil*. 2009;90(6):897-904.
570. Weng MC, Lee CL, Chen CH, et al. Effects of different stretching techniques on the outcomes of isokinetic exercise in patients with knee osteoarthritis. *Kaohsiung J Med Sci*. 2009;25(6):306-15.

571. Deyle GD, Allison SC, Matekel RL, et al. Physical therapy treatment effectiveness for osteoarthritis of the knee: a randomized comparison of supervised clinical exercise and manual therapy procedures versus a home exercise program. *Phys Ther*. 2005;85(12):1301-17.
572. Jessep SA, Walsh NE, Ratcliffe J, Hurley MV. Long-term clinical benefits and costs of an integrated rehabilitation programme compared with outpatient physiotherapy for chronic knee pain. *Physiotherapy*. 2009;95(2):94-102.
573. Chaipinyo K, Karoonsupcharoen O. No difference between home-based strength training and home-based balance training on pain in patients with knee osteoarthritis: a randomised trial. *Aust J Physiother*. 2009;55(1):25-30.
574. McKnight PE, Kasle S, Going S, et al. A comparison of strength training, self-management, and the combination for early osteoarthritis of the knee. *Arthritis Care Res (Hoboken)*. 2010;62(1):45-53.
575. Cetin N, Aytar A, Atalay A, Akman MN. Comparing hot pack, short-wave diathermy, ultrasound, and TENS on isokinetic strength, pain, and functional status of women with osteoarthritic knees: a single-blind, randomized, controlled trial. *Am J Phys Med Rehabil*. 2008;87(6):443-51.
576. Kawasaki T, Kurosawa H, Ikeda H, et al. Therapeutic home exercise versus intraarticular hyaluronate injection for osteoarthritis of the knee: 6-month prospective randomized open-labeled trial. *J Orthop Sci*. 2009;14(2):182-91.
577. Huang MH, Yang RC, Lee CL, Chen TW, Wang MC. Preliminary results of integrated therapy for patients with knee osteoarthritis. *Arthritis Rheum*. 2005;53(6):812-20.
578. Doi T, Akai M, Fujino K, et al. Effect of home exercise of quadriceps on knee osteoarthritis compared with nonsteroidal antiinflammatory drugs: a randomized controlled trial. *Am J Phys Med Rehabil*. 2008;87(4):258-69.
579. Karatosun V, Unver B, Gocen Z, Sen A, Gunal I. Intra-articular hyaluranic acid compared with progressive knee exercises in osteoarthritis of the knee: a prospective randomized trial with long-term follow-up. *Rheumatol Int*. 2006;26(4):277-84.
580. Liebs TR, Herzberg W, Ruther W, Haasters J, Russlies M, Hassenpflug J. Ergometer cycling after hip or knee replacement surgery: a randomized controlled trial. *J Bone Joint Surg Am*. 2010;92(4):814-22.
581. Ebert JR, Robertson WB, Lloyd DG, Zheng MH, Wood DJ, Ackland T. Traditional vs accelerated approaches to post-operative rehabilitation following matrix-induced autologous chondrocyte implantation (MACI): comparison of clinical, biomechanical and radiographic outcomes. *Osteoarthritis Cartilage*. 2008;16(10):1131-40.
582. Fransen M, McConnell S, Hernandez-Molina G, Reichenbach S. Exercise for osteoarthritis of the hip. *Cochrane Database Syst Rev*. 2009(3):CD007912.
583. Brosseau L, MacLeay L, Robinson V, Wells G, Tugwell P. Intensity of exercise for the treatment of osteoarthritis. *Cochrane Database Syst Rev*. 2003(2):CD004259.
584. Veenhof C, Koke AJ, Dekker J, et al. Effectiveness of behavioral graded activity in patients with osteoarthritis of the hip and/or knee: A randomized clinical trial. *Arthritis Rheum*. 2006;55(6):925-34.
585. Miller GD, Rejeski WJ, Williamson JD, et al. The Arthritis, Diet and Activity Promotion Trial (ADAPT): design, rationale, and baseline results. *Control Clin Trials*. 2003;24(4):462-80.
586. Rejeski WJ, Focht BC, Messier SP, Morgan T, Pahor M, Penninx B. Obese, older adults with knee osteoarthritis: weight loss, exercise, and quality of life. *Health Psychol*. 2002;21(5):419-26.
587. Keefe FJ, Blumenthal J, Baucom D, et al. Effects of spouse-assisted coping skills training and exercise training in patients with osteoarthritic knee pain: a randomized controlled study. *Pain*. 2004;110(3):539-49.
588. Topp R, Swank AM, Quesada PM, Nyland J, Malkani A. The effect of prehabilitation exercise on strength and functioning after total knee arthroplasty. *Pm R*. 2009;1(8):729-35.
589. Gur H, Cakin N, Akova B, Okay E, Kucukoglu S. Concentric versus combined concentric-eccentric isokinetic training: effects on functional capacity and symptoms in patients with osteoarthrosis of the knee. *Arch Phys Med Rehabil*. 2002;83(3):308-16.
590. Yip YB, Sit JW, Wong DY, Chong SY, Chung LH. A 1-year follow-up of an experimental study of a self-management arthritis programme with an added exercise component of clients with osteoarthritis of the knee. *Psychol Health Med*. 2008;13(4):402-14.

591. Sullivan T, Allegrante JP, Peterson MG, Kovar PA, MacKenzie CR. One-year followup of patients with osteoarthritis of the knee who participated in a program of supervised fitness walking and supportive patient education. *Arthritis Care Res.* 1998;11(4):228-33.
592. Talbot LA, Gaines JM, Huynh TN, Metter EJ. A home-based pedometer-driven walking program to increase physical activity in older adults with osteoarthritis of the knee: a preliminary study. *J Am Geriatr Soc.* 2003;51(3):387-92.
593. Mikesky AE, Mazzuca SA, Brandt KD, Perkins SM, Damush T, Lane KA. Effects of strength training on the incidence and progression of knee osteoarthritis. *Arthritis Rheum.* 2006;55(5):690-9.
594. Schneider F, Labs K, Wagner S. Chronic patellofemoral pain syndrome: alternatives for cases of therapy resistance. *Knee Surg Sports Traumatol Arthrosc.* 2001;9(5):290-5.
595. Cochrane T, Davey RC, Matthes Edwards SM. Randomised controlled trial of the cost-effectiveness of water-based therapy for lower limb osteoarthritis. *Health Technol Assess.* 2005;9(31):iii-iv, ix-xi, 1-114.
596. Hecht PJ, Bachmann S, Booth RE, Jr., Rothman RH. Effects of thermal therapy on rehabilitation after total knee arthroplasty. A prospective randomized study. *Clin Orthop Relat Res.* 1983(178):198-201.
597. Jan MH, Tang PF, Lin JJ, Tseng SC, Lin YF, Lin DH. Efficacy of a target-matching foot-stepping exercise on proprioception and function in patients with knee osteoarthritis. *J Orthop Sports Phys Ther.* 2008;38(1):19-25.
598. Hurley MV, Walsh NE, Mitchell HL, et al. Clinical effectiveness of a rehabilitation program integrating exercise, self-management, and active coping strategies for chronic knee pain: a cluster randomized trial. *Arthritis Rheum.* 2007;57(7):1211-9.
599. Hurley MV, Walsh NE, Mitchell HL, et al. Economic evaluation of a rehabilitation program integrating exercise, self-management, and active coping strategies for chronic knee pain. *Arthritis Rheum.* 2007;57(7):1220-9.
600. Hakkinen A, Sokka T, Lietsalmi AM, Kautiainen H, Hannonen P. Effects of dynamic strength training on physical function, Valpar 9 work sample test, and working capacity in patients with recent-onset rheumatoid arthritis. *Arthritis Rheum.* 2003;49(1):71-7.
601. Hakkinen A, Sokka T, Hannonen P. A home-based two-year strength training period in early rheumatoid arthritis led to good long-term compliance: a five-year followup. *Arthritis Rheum.* 2004;51(1):56-62.
602. Hakkinen A, Sokka T, Kotaniemi A, et al. Dynamic strength training in patients with early rheumatoid arthritis increases muscle strength but not bone mineral density. *J Rheumatol.* 1999;26(6):1257-63.
603. Yip YB, Sit JW, Fung KK, et al. Effects of a self-management arthritis programme with an added exercise component for osteoarthritic knee: randomized controlled trial. *J Adv Nurs.* 2007;59(1):20-8.
604. Yip YB, Sit JW, Fung KK, et al. Impact of an Arthritis Self-Management Programme with an added exercise component for osteoarthritic knee sufferers on improving pain, functional outcomes, and use of health care services: An experimental study. *Patient Educ Couns.* 2007;65(1):113-21.
605. Hinman RS, Heywood SE, Day AR. Aquatic physical therapy for hip and knee osteoarthritis: results of a single-blind randomized controlled trial. *Phys Ther.* 2007;87(1):32-43.
606. Foley A, Halbert J, Hewitt T, Crotty M. Does hydrotherapy improve strength and physical function in patients with osteoarthritis--a randomised controlled trial comparing a gym based and a hydrotherapy based strengthening programme. *Ann Rheum Dis.* 2003;62(12):1162-7.
607. Sylvester K. Investigation of the effect of hydrotherapy in the treatment of osteoarthritic hips. *Clin Rehabil.* 1990;4(3):223-8.
608. Silva LE, Valim V, Pessanha AP, et al. Hydrotherapy versus conventional land-based exercise for the management of patients with osteoarthritis of the knee: a randomized clinical trial. *Phys Ther.* 2008;88(1):12-21.
609. Yurtkuran M, Yurtkuran M, Alp A, et al. Balneotherapy and tap water therapy in the treatment of knee osteoarthritis. *Rheumatol Int.* 2006;27(1):19-27.
610. Fioravanti A, Iacoponi F, Bellisai B, Cantarini L, Galeazzi M. Short- and long-term effects of spa therapy in knee osteoarthritis. *Am J Phys Med Rehabil.* 2010;89(2):125-32.
611. Williams KA, Petronis J, Smith D, et al. Effect of Iyengar yoga therapy for chronic low back pain. *Pain.* 2005;115(1-2):107-17.
612. Sherman KJ, Cherkin DC, Erro J, Miglioretti DL, Deyo RA. Comparing yoga, exercise, and a self-care book for chronic low back pain: a randomized, controlled trial. *Ann Intern Med.* 2005;143(12):849-56.

613. Galantino ML, Bzdewka TM, Eissler-Russo JL, et al. The impact of modified Hatha yoga on chronic low back pain: a pilot study. *Altern Ther Health Med*. 2004;10(2):56-9.
614. Garner SE, Fidan DD, Frankish R, Maxwell L. Rofecoxib for osteoarthritis. *Cochrane Database Syst Rev*. 2005(1):CD005115.
615. Berenbaum F, Grifka J, Brown JP, et al. Efficacy of lumiracoxib in osteoarthritis: a review of nine studies. *J Int Med Res*. 2005;33(1):21-41.
616. Jagtap SA, Lahoti S, Anwaruddin K, Ram S, Ballary C, Desai A. Evaluation of efficacy, safety and tolerability of valdecoxib in osteo-arthritis patients--an Indian study. *J Indian Med Assoc*. 2002;100(11):673-4.
617. Boutaud O, Aronoff DM, Richardson JH, Marnett LJ, Oates JA. Determinants of the cellular specificity of acetaminophen as an inhibitor of prostaglandin H(2) synthases. *Proc Natl Acad Sci U S A*. 2002;99(10):7130-5.
618. Dingle JT. The effect of nonsteroidal antiinflammatory drugs on human articular cartilage glycosaminoglycan synthesis. *Osteoarthritis Cartilage*. 1999;7(3):313-4.
619. Chu SC, Yang SF, Lue KH, Hsieh YS, Li TJ, Lu KH. Naproxen, meloxicam and methylprednisolone inhibit urokinase plasminogen activator and inhibitor and gelatinases expression during the early stage of osteoarthritis. *Clin Chim Acta*. 2008;387(1-2):90-6.
620. Clutterbuck AL, Mobasheri A, Shakibaei M, Allaway D, Harris P. Interleukin-1beta-induced extracellular matrix degradation and glycosaminoglycan release is inhibited by curcumin in an explant model of cartilage inflammation. *Ann N Y Acad Sci*. 2009;1171:428-35.
621. de Boer TN, Huisman AM, Polak AA, et al. The chondroprotective effect of selective COX-2 inhibition in osteoarthritis: ex vivo evaluation of human cartilage tissue after in vivo treatment. *Osteoarthritis Cartilage*. 2009;17(4):482-8.
622. de Grauw JC, van de Lest CH, van Weeren PR. Inflammatory mediators and cartilage biomarkers in synovial fluid after a single inflammatory insult: a longitudinal experimental study. *Arthritis Res Ther*. 2009;11(2):R35.
623. Kullich W, Fagerer N, Schwann H. Effect of the NSAID nimesulide on the radical scavenger glutathione S-transferase in patients with osteoarthritis of the knee. *Curr Med Res Opin*. 2007;23(8):1981-6.
624. Lakey RL, Cawston TE. Sulfasalazine blocks the release of proteoglycan and collagen from cytokine stimulated cartilage and down-regulates metalloproteinases. *Rheumatology (Oxford)*. 2009;48(10):1208-12.
625. Yang SF, Hsieh YS, Lue KH, Chu SC, Chang IC, Lu KH. Effects of nonsteroidal anti-inflammatory drugs on the expression of urokinase plasminogen activator and inhibitor and gelatinases in the early osteoarthritic knee of humans. *Clin Biochem*. 2008;41(1-2):109-16.
626. Wagenitz A, Mueller EA, Frentzel A, Cambon N. Comparative efficacy and tolerability of two sustained-release formulations of diclofenac: results of a double-blind, randomised study in patients with osteoarthritis and a reappraisal of diclofenac's use in this patient population. *Curr Med Res Opin*. 2007;23(8):1957-66.
627. Bakshi R. Comparative efficacy and tolerability of two diclofenac formulations in the treatment of painful osteoarthritis. *Br J Clin Pract*. 1996;50(6):294-7.
628. Bakshi R, Ezzet N, Frey L, Lasry D, Salliere D. Efficacy and tolerability of diclofenac dispersible in painful osteoarthrosis. *Clin Rheumatol*. 1993;12(1):57-61.
629. Toft B, Christophersen J, Christensen N, et al. A double-blind, crossover study of a sustained-release tablet of ketoprofen and normal ketoprofen capsules in the treatment of patients with osteoarthritis. *Curr Med Res Opin*. 1985;9(10):708-12.
630. Bacon P, Luqmani RA, Bossingham DH, et al. A comparison of two formulations of indomethacin ('Flexin Continus' tablets and 'Indocid' capsules) in the treatment of osteoarthritis. *Curr Med Res Opin*. 1990;12(2):128-34.
631. Pincus T, Koch G, Lei H, et al. Patient Preference for Placebo, Acetaminophen (paracetamol) or Celecoxib Efficacy Studies (PACES): two randomised, double blind, placebo controlled, crossover clinical trials in patients with knee or hip osteoarthritis. *Ann Rheum Dis*. 2004;63(8):931-9.
632. Amadio P, Cummings D. Evaluation of acetaminophen in the management of osteoarthritis of the knee. *Curr Ther Res*. 1983;34(1):59-66.

633. Golden HE, Moskowitz RW, Minic M. Analgesic efficacy and safety of nonprescription doses of naproxen sodium compared with acetaminophen in the treatment of osteoarthritis of the knee. *Am J Ther.* 2004;11(2):85-94.
634. Temple AR, Benson GD, Zinsenheim JR, Schweinle JE. Multicenter, randomized, double-blind, active-controlled, parallel-group trial of the long-term (6-12 months) safety of acetaminophen in adult patients with osteoarthritis. *Clin Ther.* 2006;28(2):222-35.
635. Pincus T, Koch GG, Sokka T, et al. A randomized, double-blind, crossover clinical trial of diclofenac plus misoprostol versus acetaminophen in patients with osteoarthritis of the hip or knee. *Arthritis Rheum.* 2001;44(7):1587-98.
636. Boureau F, Schneid H, Zeghari N, Wall R, Bourgeois P. The IPSO study: ibuprofen, paracetamol study in osteoarthritis. A randomised comparative clinical study comparing the efficacy and safety of ibuprofen and paracetamol analgesic treatment of osteoarthritis of the knee or hip. *Ann Rheum Dis.* 2004;63(9):1028-34.
637. Case JP, Baliunas AJ, Block JA. Lack of efficacy of acetaminophen in treating symptomatic knee osteoarthritis: a randomized, double-blind, placebo-controlled comparison trial with diclofenac sodium. *Arch Intern Med.* 2003;163(2):169-78.
638. Geba GP, Weaver AL, Polis AB, Dixon ME, Schnitzer TJ. Efficacy of rofecoxib, celecoxib, and acetaminophen in osteoarthritis of the knee: a randomized trial. *JAMA.* 2002;287(1):64-71.
639. Bradley JD, Brandt KD, Katz BP, Kalasinski LA, Ryan SI. Comparison of an antiinflammatory dose of ibuprofen, an analgesic dose of ibuprofen, and acetaminophen in the treatment of patients with osteoarthritis of the knee. *N Engl J Med.* 1991;325(2):87-91.
640. Miceli-Richard C, Le Bars M, Schmidely N, Dougados M. Paracetamol in osteoarthritis of the knee. *Ann Rheum Dis.* 2004;63(8):923-30.
641. Beaulieu AD, Peloso PM, Haraoui B, et al. Once-daily, controlled-release tramadol and sustained-release diclofenac relieve chronic pain due to osteoarthritis: a randomized controlled trial. *Pain Res Manag.* 2008;13(2):103-10.
642. Pavelka K, Peliskova Z, Stehlikova H, Ratcliffe S, Repas C. Intraindividual differences in pain relief and functional improvement in osteoarthritis with diclofenac or tramadol. *Clin Drug Investig.* 1998;16(6):421-9.
643. Quiding H, Grimstad J, Rusten K, Stubhaug A, Bremnes J, Breivik H. Ibuprofen plus codeine, ibuprofen, and placebo in a single- and multidose cross-over comparison for coxarthrosis pain. *Pain.* 1992;50(3):303-7.
644. Kjaersgaard-Andersen P, Nafei A, Skov O, et al. Codeine plus paracetamol versus paracetamol in longer-term treatment of chronic pain due to osteoarthritis of the hip. A randomised, double-blind, multi-centre study. *Pain.* 1990;43(3):309-18.
645. Vinje O, Fagertun HE, Laerum E, Lund H, Larsen S. Ketoprofen controlled release (CR) in the treatment of osteoarthritis; a double blind, randomized multicentre study of single morning versus evening dose. Norwegian Study Group of General Practitioners. *Scand J Prim Health Care.* 1993;11(2):91-7.
646. Levi F, Le Louarn C, Reinberg A. Timing optimizes sustained-release indomethacin treatment of osteoarthritis. *Clin Pharmacol Ther.* 1985;37(1):77-84.
647. Stengaard-Pedersen K, Ekesbo R, Karvonen AL, Lyster M. Celecoxib 200 mg q.d. is efficacious in the management of osteoarthritis of the knee or hip regardless of the time of dosing. *Rheumatology (Oxford).* 2004;43(5):592-5.
648. Yocum D, Fleischmann R, Dalgin P, Caldwell J, Hall D, Roszko P. Safety and efficacy of meloxicam in the treatment of osteoarthritis: a 12-week, double-blind, multiple-dose, placebo-controlled trial. The Meloxicam Osteoarthritis Investigators. *Arch Intern Med.* 2000;160(19):2947-54.
649. Berry H, Bird HA, Black C, et al. A double blind, multicentre, placebo controlled trial of lornoxicam in patients with osteoarthritis of the hip and knee. *Ann Rheum Dis.* 1992;51(2):238-42.
650. Bocanegra TS, Weaver AL, Tindall EA, et al. Diclofenac/misoprostol compared with diclofenac in the treatment of osteoarthritis of the knee or hip: a randomized, placebo controlled trial. Arthrotec Osteoarthritis Study Group. *J Rheumatol.* 1998;25(8):1602-11.
651. Caroit M, Forette B, Hubault A, Pasquier P. Double-blind study of ketoprofen against a placebo in osteoarthritis of the hip. *Scand J Rheumatol Suppl.* 1976;1976(0):123-7.

652. Famaey JP, Colinet E. A double-blind trial of ketoprofen in the treatment of osteoarthritis of the hip. *Rheumatol Rehabil*. 1976;Suppl45-9.
653. Kivitz AJ, Moskowitz RW, Woods E, et al. Comparative efficacy and safety of celecoxib and naproxen in the treatment of osteoarthritis of the hip. *J Int Med Res*. 2001;29(6):467-79.
654. Kogstad O. Double blind crossover trial of piroxicam and naproxen in the treatment of osteoarthritis of hip and knee. *Br J Clin Pract*. 1981;35(1):45-50.
655. Kruger K, Klasser M, Mossinger J, Becker U. Oxaceprol--a randomised, placebo-controlled clinical study in osteoarthritis with a non-conventional non-steroidal anti-inflammatory drug. *Clin Exp Rheumatol*. 2007;25(1):29-34.
656. Petrick TJ, Black ME. Double-blind multicenter studies with meclofenamate sodium in the treatment of rheumatoid arthritis in the United States and Canada. *Arzneimittelforschung*. 1983;33(4A):631-5.
657. Pope JE, McCrear K, Stevens A, Ouimet JM. Treatment of osteoarthritis of the hip and knee: a comparison of NSAID use in patients for whom surgery was and was not recommended. *Clin Exp Rheumatol*. 2004;22(2):171-6.
658. Puopolo A, Boice JA, Fidelholtz JL, et al. A randomized placebo-controlled trial comparing the efficacy of etoricoxib 30 mg and ibuprofen 2400 mg for the treatment of patients with osteoarthritis. *Osteoarthritis Cartilage*. 2007;15(12):1348-56.
659. Saag K, van der Heijde D, Fisher C, et al. Rofecoxib, a new cyclooxygenase 2 inhibitor, shows sustained efficacy, comparable with other nonsteroidal anti-inflammatory drugs: a 6-week and a 1-year trial in patients with osteoarthritis. Osteoarthritis Studies Group. *Arch Fam Med*. 2000;9(10):1124-34.
660. Gillgrass J, Grahame R. Nabumetone: a double-blind study in osteoarthritis. *Pharmatherapeutica*. 1984;3(9):592-4.
661. Levenstein JH. Isoxicam and indomethacin in acute osteo-arthritis. A GP multicentre double-blind comparison. *S Afr Med J*. 1985;67(17):676-9.
662. Averbuch M, Katzper M. Assessment of visual analog versus categorical scale for measurement of osteoarthritis pain. *J Clin Pharmacol*. 2004;44(4):368-72.
663. Ogilvie-Harris DJ, Bauer M, Corey P. Prostaglandin inhibition and the rate of recovery after arthroscopic meniscectomy. A randomised double-blind prospective study. *J Bone Joint Surg Br*. 1985;67(4):567-71.
664. Graham DY, Opekun AR, Willingham FF, Qureshi WA. Visible small-intestinal mucosal injury in chronic NSAID users. *Clin Gastroenterol Hepatol*. 2005;3(1):55-9.
665. Robinson M, Mills RJ, Euler AR. Ranitidine prevents duodenal ulcers associated with non-steroidal anti-inflammatory drug therapy. *Aliment Pharmacol Ther*. 1991;5(2):143-50.
666. Robinson MG, Griffin JW, Jr., Bowers J, et al. Effect of ranitidine on gastroduodenal mucosal damage induced by nonsteroidal antiinflammatory drugs. *Dig Dis Sci*. 1989;34(3):424-8.
667. Ehsanullah RS, Page MC, Tildesley G, Wood JR. Prevention of gastroduodenal damage induced by non-steroidal anti-inflammatory drugs: controlled trial of ranitidine. *Bmj*. 1988;297(6655):1017-21.
668. Edworthy SM, Devins GM. Improving medication adherence through patient education distinguishing between appropriate and inappropriate utilization. Patient Education Study Group. *J Rheumatol*. 1999;26(8):1793-801.
669. Antman EM, Bennett JS, Daugherty A, Furberg C, Roberts H, Taubert KA. Use of nonsteroidal antiinflammatory drugs: an update for clinicians: a scientific statement from the American Heart Association. *Circulation*. 2007;115(12):1634-42.
670. Prevention of venous thromboembolism in orthopedic surgery. *The Medical Letter*; 2008:86.
671. McQuay HJ, Edwards JE, Moore RA. Evaluating analgesia: the challenges. *Am J Ther*. 2002;9(3):179-87.
672. Zacher J, Feldman D, Gerli R, et al. A comparison of the therapeutic efficacy and tolerability of etoricoxib and diclofenac in patients with osteoarthritis. *Curr Med Res Opin*. 2003;19(8):725-36.
673. Bellamy N, Bensen WG, Ford PM, Huang SH, Lang JY. Double-blind randomized controlled trial of flurbiprofen-SR (ANSAID-SR) and diclofenac sodium-SR (Voltaren-SR) in the treatment of osteoarthritis. *Clin Invest Med*. 1992;15(5):427-33.
674. Bellamy N, Buchanan WW, Grace E. Double-blind randomized controlled trial of isoxicam vs piroxicam in elderly patients with osteoarthritis of the hip and knee. *Br J Clin Pharmacol*. 1986;22 Suppl 2149S-55S.

675. Hawel R, Klein G, Singer F, Mayrhofer F, Kahler ST. Comparison of the efficacy and tolerability of dexibuprofen and celecoxib in the treatment of osteoarthritis of the hip. *Int J Clin Pharmacol Ther*. 2003;41(4):153-64.
676. Fleischmann R, Tannenbaum H, Patel NP, Nottter M, Sallstig P, Reginster JY. Long-term retention on treatment with lumiracoxib 100 mg once or twice daily compared with celecoxib 200 mg once daily: a randomised controlled trial in patients with osteoarthritis. *BMC Musculoskelet Disord*. 2008;932.
677. Day R, Morrison B, Luza A, et al. A randomized trial of the efficacy and tolerability of the COX-2 inhibitor rofecoxib vs ibuprofen in patients with osteoarthritis. Rofecoxib/Ibuprofen Comparator Study Group. *Arch Intern Med*. 2000;160(12):1781-7.
678. Fioravanti A, Storri L, Di Martino S, et al. A randomized, double-blind, multicenter trial of nimesulide-beta-cyclodextrin versus naproxen in patients with osteoarthritis. *Clin Ther*. 2002;24(4):504-19.
679. Le Loet X, Dreiser RL, Le Gros V, Febvre N. Therapeutic equivalence of diclofenac sustained-released 75 mg tablets and diclofenac enteric-coated 50 mg tablets in the treatment of painful osteoarthritis. *Int J Clin Pract*. 1997;51(6):389-93.
680. Leung AT, Malmstrom K, Gallacher AE, et al. Efficacy and tolerability profile of etoricoxib in patients with osteoarthritis: A randomized, double-blind, placebo and active-comparator controlled 12-week efficacy trial. *Curr Med Res Opin*. 2002;18(2):49-58.
681. Reginster JY, Malmstrom K, Mehta A, et al. Evaluation of the efficacy and safety of etoricoxib compared with naproxen in two, 138-week randomised studies of patients with osteoarthritis. *Ann Rheum Dis*. 2007;66(7):945-51.
682. Kidd B, Frenzel W. A multicenter, randomized, double blind study comparing lornoxicam with diclofenac in osteoarthritis. *J Rheumatol*. 1996;23(9):1605-11.
683. Lisse JR, Perlman M, Johansson G, et al. Gastrointestinal tolerability and effectiveness of rofecoxib versus naproxen in the treatment of osteoarthritis: a randomized, controlled trial. *Ann Intern Med*. 2003;139(7):539-46.
684. Wegman AC, van der Windt DA, de Haan M, Deville WL, Fo CT, de Vries TP. Switching from NSAIDs to paracetamol: a series of n of 1 trials for individual patients with osteoarthritis. *Ann Rheum Dis*. 2003;62(12):1156-61.
685. Smugar SS, Schnitzer TJ, Weaver AL, Rubin BR, Polis AB, Tershakovec AM. Rofecoxib 12.5 mg, rofecoxib 25 mg, and celecoxib 200 mg in the treatment of symptomatic osteoarthritis: results of two similarly designed studies. *Curr Med Res Opin*. 2006;22(7):1353-67.
686. Perpignano G, Bogliolo A, Puccetti L. Double-blind comparison of the efficacy and safety of etodolac SR 600 mg u.i.d. and of tenoxicam 20 mg u.i.d. in elderly patients with osteoarthritis of the hip and of the knee. *Int J Clin Pharmacol Res*. 1994;14(5-6):203-16.
687. Bellamy N, Bensen WG, Beaulieu A, et al. A multicenter study of nabumetone and diclofenac SR in patients with osteoarthritis. *J Rheumatol*. 1995;22(5):915-20.
688. Lussier A, Elie R, Gareau J. A placebo-controlled trial of floctafenine (idarac) against enteric-coated acetylsalicylic acid in osteoarthritic patients. *Rheumatol Rehabil*. 1980;19(1):52-9.
689. Myllykangas-Luosujarvi R, Lu HS, Chen SL, et al. Comparison of low-dose rofecoxib versus 1000 mg naproxen in patients with osteoarthritis. Results of two randomized treatment trials of six weeks duration. *Scand J Rheumatol*. 2002;31(6):337-44.
690. Hosie J, Distel M, Bluhmki E. Meloxicam in osteoarthritis: a 6-month, double-blind comparison with diclofenac sodium. *Br J Rheumatol*. 1996;35 Suppl 139-43.
691. Herrmann G, Steeger D, Klasser M, et al. Oxaceprol is a well-tolerated therapy for osteoarthritis with efficacy equivalent to diclofenac. *Clin Rheumatol*. 2000;19(2):99-104.
692. Ginsberg F, Famaey JP. A double-blind, parallel trial of oxaprozin versus naproxen in the treatment of osteoarthritis. *Curr Med Res Opin*. 1984;8(10):689-95.
693. Schnitzer TJ, Beier J, Geusens P, et al. Efficacy and safety of four doses of lumiracoxib versus diclofenac in patients with knee or hip primary osteoarthritis: a phase II, four-week, multicenter, randomized, double-blind, placebo-controlled trial. *Arthritis Rheum*. 2004;51(4):549-57.
694. Morgan GJ, Jr., Kaine J, DeLapp R, Palmer R. Treatment of elderly patients with nabumetone or diclofenac: gastrointestinal safety profile. *J Clin Gastroenterol*. 2001;32(4):310-4.

695. Cannon GW, Caldwell JR, Holt P, et al. Rofecoxib, a specific inhibitor of cyclooxygenase 2, with clinical efficacy comparable with that of diclofenac sodium: results of a one-year, randomized, clinical trial in patients with osteoarthritis of the knee and hip. Rofecoxib Phase III Protocol 035 Study Group. *Arthritis Rheum.* 2000;43(5):978-87.
696. Alho A, Jaer O, Slungaard U, Holme I. Piroxicam and naproxen in patients with osteoarthritis of the hip waiting for total hip replacement. *Clin Rheumatol.* 1988;7(2):208-13.
697. Baumgartner H, Schwarz HA, Blum W, et al. Ibuprofen and diclofenac sodium in the treatment of osteoarthritis: a comparative trial of two once-daily sustained-release NSAID formulations. *Curr Med Res Opin.* 1996;13(8):435-44.
698. Shipley M, Berry H, Broster G, Jenkins M, Clover A, Williams I. Controlled trial of homoeopathic treatment of osteoarthritis. *Lancet.* 1983;1(8316):97-8.
699. Brown BL, Johnson JH, Hearron MS. Double-blind comparison of flurbiprofen and sulindac for the treatment of osteoarthritis. *Am J Med.* 1986;80(3A):112-7.
700. Cardoe N, Hart FD. Double-blind multicentre UK hospital studies of isoxicam vs naproxen. *Br J Clin Pharmacol.* 1986;22 Suppl 2167S-72S.
701. Gordin A, Karppinen I, Holttinen K. Comparison of slow-release indomethacin and diflunisal in patients with arthrosis. *Curr Med Res Opin.* 1984;9(4):275-9.
702. Bauer HW, Klasser M, von Hanstein KL, et al. Oxaceprol is as effective as diclofenac in the therapy of osteoarthritis of the knee and hip. *Clin Rheumatol.* 1999;18(1):4-9.
703. Adelowo OO, Chukwuani CM, Grange JJ, Ojeasebhulo EE, Onabowale BO. Comparative double blind study of the efficacy and safety of tenoxicam vs. piroxicam in osteoarthritis of knee and hip joints. *West Afr J Med.* 1998;17(3):194-8.
704. Ginsberg F, Famaey JP. Double-blind crossover study of nabumetone versus naproxen in the treatment of osteoarthritis of the knee and hip. *J Int Med Res.* 1982;10(4):209-13.
705. Telhag H, Bach-Andersen R, Persson B. A double-blind comparative evaluation of tolmetin versus naproxen in osteoarthritis. *Curr Med Res Opin.* 1981;7(6):392-400.
706. Cortes Giner JR, Garcia Borrás JJ. Double-blind, randomized and parallel comparison between droxicam and diclofenac sodium in patients with coxarthrosis and gonarthrosis. *Eur J Rheumatol Inflamm.* 1991;11(4):29-34.
707. Bingham CO, 3rd, Sebba AI, Rubin BR, et al. Efficacy and safety of etoricoxib 30 mg and celecoxib 200 mg in the treatment of osteoarthritis in two identically designed, randomized, placebo-controlled, non-inferiority studies. *Rheumatology (Oxford).* 2007;46(3):496-507.
708. Kiff PS, Stead H, Morant SV, Shield MJ. Arthrotec, diclofenac and ibuprofen in general practice. *Eur J Rheumatol Inflamm.* 1994;14(3 Suppl):31-8.
709. Clarke AK. A Double-blind comparison of naproxen against indometacin in osteoarthritis. *Arzneimittelforschung.* 1975;25(2A):302-4.
710. Singer F, Mayrhofer F, Klein G, Hawel R, Kollenz CJ. Evaluation of the efficacy and dose-response relationship of dexibuprofen (S(+)-ibuprofen) in patients with osteoarthritis of the hip and comparison with racemic ibuprofen using the WOMAC osteoarthritis index. *Int J Clin Pharmacol Ther.* 2000;38(1):15-24.
711. Meurice J. Treatment of osteoarthritis: a 3-month comparison between tiaprofenic acid and indomethacin. *Curr Med Res Opin.* 1983;8(5):295-301.
712. Kriegel W, Korff KJ, Ehrlich JC, et al. Double-blind study comparing the long-term efficacy of the COX-2 inhibitor nimesulide and naproxen in patients with osteoarthritis. *Int J Clin Pract.* 2001;55(8):510-4.
713. Keet JG. A comparative clinical trial of diflunisal and ibuprofen in the control of pain in osteoarthritis. *J Int Med Res.* 1979;7(4):272-6.
714. Bjorkenheim JM, Helland J, Peltonen J. A double-blind crossover evaluation of naproxen and piroxicam in osteoarthritis of hip or knee. *J Int Med Res.* 1985;13(5):263-9.
715. Valtonen EJ. Clinical comparison of fenbufen and aspirin in osteoarthritis. *Scand J Rheumatol Suppl.* 1979(27):1-7.
716. Liyanage S, Steele C. Tolmetin in osteoarthritis of the hip and knee: double-blind crossover trials. *Curr Med Res Opin.* 1977-1978;5(4):299-305.

717. Lund B, Andersen RB, Fossgreen J, et al. A long-term randomised trial on tenoxicam and piroxicam in osteoarthritis of the hip or knee: a 24-month interim report focusing on the 12-24 month interval. *Eur J Rheumatol Inflamm*. 1987;9(2):58-67.
718. Chikanza IC, Clarke B, Hopkins R, MacFarlane DG, Bird H, Grahame R. A comparative study of the efficacy and toxicity of etodolac and naproxen in the treatment of osteoarthritis. *Br J Clin Pract*. 1994;48(2):67-9.
719. McIlwain HH, Platt RD. Piroxicam versus naproxen in the treatment of acute musculoskeletal disorders in athletes. *Am J Med*. 1988;84(5A):56-60.
720. The Manchester General Practitioner Group. A study of naproxen and ibuprofen in patients with osteoarthritis seen in general practice. The Manchester General Practitioner Group. *Curr Med Res Opin*. 1984;9(1):41-6.
721. Gordin A, Sotka S, Nuutila J. Comparison of a slow-release indomethacin tablet and naproxen in osteoarthrosis. *Curr Med Res Opin*. 1985;9(7):500-4.
722. Verbruggen LA, Cytryn E, Pintens H. Double-blind crossover study of nabumetone versus naproxen in the treatment of osteoarthritis. *J Int Med Res*. 1982;10(4):214-8.
723. Fenton C, Keating GM, Wagstaff AJ. Valdecoxib: a review of its use in the management of osteoarthritis, rheumatoid arthritis, dysmenorrhoea and acute pain. *Drugs*. 2004;64(11):1231-61.
724. Towheed TE, Maxwell L, Judd MG, Catton M, Hochberg MC, Wells G. Acetaminophen for osteoarthritis. *Cochrane Database Syst Rev*. 2006(1):CD004257.
725. Pincus T, Koch G, Sokka T. Are NSAIDs more effective than acetaminophen in patients with osteoarthritis? *J Fam Pract*. 2001;50(10):894-5.
726. Blandino D. Are NSAIDs more effective than acetaminophen in patients with osteoarthritis? *J Fam Pract*. 2001;50(10):894.
727. McGettigan P, Han P, Henry D. Cyclooxygenase-2 inhibitors and coronary occlusion--exploring dose-response relationships. *Br J Clin Pharmacol*. 2006;62(3):358-65.
728. Kimmel SE, Berlin JA, Reilly M, et al. Patients exposed to rofecoxib and celecoxib have different odds of nonfatal myocardial infarction. *Ann Intern Med*. 2005;142(3):157-64.
729. Agrawal NM, Caldwell J, Kivitz AJ, et al. Comparison of the upper gastrointestinal safety of Arthrotec 75 and nabumetone in osteoarthritis patients at high risk for developing nonsteroidal anti-inflammatory drug-induced gastrointestinal ulcers. *Clin Ther*. 1999;21(4):659-74.
730. Gomes J, Roth SH, Zeeh J, Bruyn GAW, Woods EM, Geis GS. Double-blind comparison of efficacy and gastroduodenal safety of diclofenac/misoprostol, piroxicam, and naproxen in the treatment of osteoarthritis. *Annals of the Rheumatic Diseases*. 1993;52:881-5.
731. Hayllar J, Bjarnason I. Gastroduodenal tolerability of highly specific cyclo-oxygenase-2 inhibitor. *Ital J Gastroenterol*. 1996;28 Suppl 430-2.
732. Becvar R, Urbanova Z, Vlasakova V, et al. Nabumetone induces less gastrointestinal mucosal changes than diclofenac retard. *Clin Rheumatol*. 1999;18(4):273-8.
733. Hoyeraal HM, Fagertun H, Ingemann-Hansen T, Ersmark H, Ronn O. Characterization of responders and nonresponders to tiaprofenic acid and naproxen in the treatment of patients with osteoarthritis. *J Rheumatol*. 1993;20(10):1747-52.
734. Scheiman JM, Behler EM, Loeffler KM, Elta GH. Omeprazole ameliorates aspirin-induced gastroduodenal injury. *Dig Dis Sci*. 1994;39(1):97-103.
735. Scheiman JM, Yeomans ND, Talley NJ, et al. Prevention of ulcers by esomeprazole in at-risk patients using non-selective NSAIDs and COX-2 inhibitors. *Am J Gastroenterol*. 2006;101(4):701-10.
736. Yeomans N, Lanos A, Labenz J, et al. Efficacy of esomeprazole (20 mg once daily) for reducing the risk of gastroduodenal ulcers associated with continuous use of low-dose aspirin. *Am J Gastroenterol*. 2008;103(10):2465-73.
737. Bergmann JF, Chassany O, Simoneau G, Lemaire M, Segrestaa JM, Caulin C. Protection against aspirin-induced gastric lesions by lansoprazole: simultaneous evaluation of functional and morphologic responses. *Clin Pharmacol Ther*. 1992;52(4):413-6.
738. Chan FK, Hung LC, Suen BY, et al. Celecoxib versus diclofenac and omeprazole in reducing the risk of recurrent ulcer bleeding in patients with arthritis. *N Engl J Med*. 2002;347(26):2104-10.

739. Desai JC, Sanyal SM, Goo T, et al. Primary prevention of adverse gastroduodenal effects from short-term use of non-steroidal anti-inflammatory drugs by omeprazole 20 mg in healthy subjects: a randomized, double-blind, placebo-controlled study. *Dig Dis Sci*. 2008;53(8):2059-65.
740. Hawkey C, Talley NJ, Yeomans ND, et al. Improvements with esomeprazole in patients with upper gastrointestinal symptoms taking non-steroidal anti-inflammatory drugs, including selective COX-2 inhibitors. *Am J Gastroenterol*. 2005;100(5):1028-36.
741. Regula J, Butruk E, Dekkers CP, et al. Prevention of NSAID-associated gastrointestinal lesions: a comparison study pantoprazole versus omeprazole. *Am J Gastroenterol*. 2006;101(8):1747-55.
742. Bianchi Porro G, Lazzaroni M, Imbesi V, Montrone F, Santagada T. Efficacy of pantoprazole in the prevention of peptic ulcers, induced by non-steroidal anti-inflammatory drugs: a prospective, placebo-controlled, double-blind, parallel-group study. *Dig Liver Dis*. 2000;32(3):201-8.
743. Bianchi Porro G, Lazzaroni M, Petrillo M, Manzionna G, Montrone F, Caruso I. Prevention of gastroduodenal damage with omeprazole in patients receiving continuous NSAIDs treatment. A double blind placebo controlled study. *Ital J Gastroenterol Hepatol*. 1998;3043-7.
744. Cullen D, Bardhan KD, Eisner M, et al. Primary gastroduodenal prophylaxis with omeprazole for non-steroidal anti-inflammatory drug users. *Aliment Pharmacol Ther*. 1998;12(2):135-40.
745. Labenz J, Blum AL, Bolten WW, et al. Primary prevention of diclofenac associated ulcers and dyspepsia by omeprazole or triple therapy in Helicobacter pylori positive patients: a randomised, double blind, placebo controlled, clinical trial. *Gut*. 2002;51(3):329-35.
746. Dorta G, Nicolet M, Vouillamoz D, et al. The effects of omeprazole on healing and appearance of small gastric and duodenal lesions during dosing with diclofenac in healthy subjects. *Aliment Pharmacol Ther*. 2000;14(5):535-41.
747. Niwa Y, Nakamura M, Ohmiya N, et al. Efficacy of rebamipide for diclofenac-induced small-intestinal mucosal injuries in healthy subjects: a prospective, randomized, double-blinded, placebo-controlled, cross-over study. *J Gastroenterol*. 2008;43(4):270-6.
748. Pilotto A, Di Mario F, Franceschi M, et al. Pantoprazole versus one-week Helicobacter pylori eradication therapy for the prevention of acute NSAID-related gastroduodenal damage in elderly subjects. *Aliment Pharmacol Ther*. 2000;14(8):1077-82.
749. Graham DY, White RH, Moreland LW, et al. Duodenal and gastric ulcer prevention with misoprostol in arthritis patients taking NSAIDs. Misoprostol Study Group. *Ann Intern Med*. 1993;119(4):257-62.
750. Chandrasekaran AN, Sambandam PR, Lal HM, et al. Double blind, placebo controlled trial on the cytoprotective effect of misoprostol in subjects with rheumatoid arthritis, osteoarthritis and seronegative spondyloarthritis on NSAIDs. *J Assoc Physicians India*. 1991;39(12):919-21.
751. Donnelly MT, Goddard AF, Filipowicz B, Morant SV, Shield MJ, Hawkey CJ. Low-dose misoprostol for the prevention of low-dose aspirin-induced gastroduodenal injury. *Aliment Pharmacol Ther*. 2000;14(5):529-34.
752. Elliott SL, Yeomans ND, Buchanan RR, Smallwood RA. Efficacy of 12 months' misoprostol as prophylaxis against NSAID-induced gastric ulcers. A placebo-controlled trial. *Scand J Rheumatol*. 1994;23(4):171-6.
753. Jiranek GC, Kimmey MB, Saunders DR, Willson RA, Shanahan W, Silverstein FE. Misoprostol reduces gastroduodenal injury from one week of aspirin: an endoscopic study. *Gastroenterology*. 1989;96(2 Pt 2 Suppl):656-61.
754. Koch M, Dezi A, Tarquini M, Capurso L. Prevention of non-steroidal anti-inflammatory drug-induced gastrointestinal mucosal injury: risk factors for serious complications. *Dig Liver Dis*. 2000;32(2):138-51.
755. Lanza F, Peace K, Gustitus L, Rack MF, Dickson B. A blinded endoscopic comparative study of misoprostol versus sucralfate and placebo in the prevention of aspirin-induced gastric and duodenal ulceration. *Am J Gastroenterol*. 1988;83(2):143-6.
756. Lanza FL, Aspinall RL, Swabb EA, Davis RE, Rack MF, Rubin A. Double-blind, placebo-controlled endoscopic comparison of the mucosal protective effects of misoprostol versus cimetidine on tolmetin-induced mucosal injury to the stomach and duodenum. *Gastroenterology*. 1988;95(2):289-94.
757. Raskin JB, White RH, Jackson JE, et al. Misoprostol dosage in the prevention of nonsteroidal anti-inflammatory drug-induced gastric and duodenal ulcers: a comparison of three regimens. *Ann Intern Med*. 1995;123(5):344-50.

758. Bardhan KD, Bjarnason I, Scott DL, et al. The prevention and healing of acute non-steroidal anti-inflammatory drug-associated gastroduodenal mucosal damage by misoprostol. *Br J Rheumatol*. 1993;32(11):990-5.
759. Medina Santillan R, Reyes Garcia G, Mateos Garcia E. Prevention of gastroduodenal injury induced by NSAIDs with low-dose misoprostol. *Proc West Pharmacol Soc*. 1999;4233-4.
760. Miglioli M, Bianchi Porro G, Vaira D, et al. Prevention with sucralfate gel of NSAID-induced gastroduodenal damage in arthritic patients. *Am J Gastroenterol*. 1996;91(11):2367-71.
761. Stupnicki T, Dietrich K, Gonzalez-Carro P, et al. Efficacy and tolerability of pantoprazole compared with misoprostol for the prevention of NSAID-related gastrointestinal lesions and symptoms in rheumatic patients. *Digestion*. 2003;68(4):198-208.
762. Graham DY, Agrawal NM, Campbell DR, et al. Ulcer prevention in long-term users of nonsteroidal anti-inflammatory drugs: results of a double-blind, randomized, multicenter, active- and placebo-controlled study of misoprostol vs lansoprazole. *Arch Intern Med*. 2002;162(2):169-75.
763. Miyake K, Ueki N, Suzuki K, et al. Preventive therapy for non-steroidal anti-inflammatory drug-induced ulcers in Japanese patients with rheumatoid arthritis: the current situation and a prospective controlled-study of the preventive effects of lansoprazole or famotidine. *Aliment Pharmacol Ther*. 2005;21 Suppl 267-72.
764. Silverstein FE, Kimmey MB, Saunders DR, Levine DS. Gastric protection by misoprostol against 1300 mg of aspirin. An endoscopic study. *Dig Dis Sci*. 1986;31(2 Suppl):137S-41S.
765. Bianchi Porro G, Lazzaroni M, Petrillo M. Double-blind, double-dummy endoscopic comparison of the mucosal protective effects of misoprostol versus ranitidine on naproxen-induced mucosal injury to the stomach and duodenum in rheumatic patients. *Am J Gastroenterol*. 1997;92(4):663-7.
766. Raskin JB, White RH, Jaszewski R, Korsten MA, Schubert TT, Fort JG. Misoprostol and ranitidine in the prevention of NSAID-induced ulcers: a prospective, double-blind, multicenter study. *Am J Gastroenterol*. 1996;91(2):223-7.
767. Agrawal NM, Roth S, Graham DY, et al. Misoprostol compared with sucralfate in the prevention of nonsteroidal anti-inflammatory drug-induced gastric ulcer. A randomized, controlled trial. *Ann Intern Med*. 1991;115(3):195-200.
768. Goldstein JL, Cryer B, Amer F, Hunt B. Celecoxib plus aspirin versus naproxen and lansoprazole plus aspirin: a randomized, double-blind, endoscopic trial. *Clin Gastroenterol Hepatol*. 2007;5(10):1167-74.
769. Franssen M, Anderson C, Douglas J, et al. Safety and efficacy of routine postoperative ibuprofen for pain and disability related to ectopic bone formation after hip replacement surgery (HIPAID): randomised controlled trial. *Br Med J*. 2006;333(7567):519.
770. Sell S, Phillips O, Handel M. No difference between two doses of diclofenac in prophylaxis of heterotopic ossifications after total hip arthroplasty. *Acta Orthop Scand*. 2004;75(1):45-9.
771. Kjaersgaard-Andersen P, Schmidt SA, Pedersen NW, Kristensen SS, Pedersen P. Erythrocyte sedimentation rate and heterotopic bone formation after cemented total hip arthroplasty. *Clin Orthop Relat Res*. 1989(248):189-94.
772. Persson PE, Sodemann B, Nilsson OS. Preventive effects of ibuprofen on periarticular heterotopic ossification after total hip arthroplasty. A randomized double-blind prospective study of treatment time. *Acta Orthop Scand*. 1998;69(2):111-5.
773. Dorn U, Grethen C, Effenberger H, Berka H, Ramsauer T, Drekonja T. Indomethacin for prevention of heterotopic ossification after hip arthroplasty. A randomized comparison between 4 and 8 days of treatment. *Acta Orthop Scand*. 1998;69(2):107-10.
774. Cheng M, Sauer B, Johnson E, Porucznik C, Hegmann K. Comparison of opioid-related deaths by work-related injury. *Am J Industrial Med*. 2013;56308-16.
775. Eriksen J, Sjogren P, Bruera E, Ekholm O, Rasmussen NK. Critical issues on opioids in chronic non-cancer pain: an epidemiological study. *Pain*. 2006;125(1-2):172-9.
776. Atluri S, Sudarshan G. Development of a screening tool to detect the risk of inappropriate prescription opioid use in patients with chronic pain. *Pain Physician*. 2004;7(3):333-8.
777. Green TC, Grau LE, Carver HW, Kinzly M, Heimer R. Epidemiologic trends and geographic patterns of fatal opioid intoxications in Connecticut, USA: 1997-2007. *Drug Alcohol Depend*. 2011;115(3):221-8.

778. Shah NG, Lathrop SL, Reichard RR, Landen MG. Unintentional drug overdose death trends in New Mexico, USA, 1990-2005: combinations of heroin, cocaine, prescription opioids and alcohol. *Addiction*. 2008;103(1):126-36.
779. Hall A, Logan J, Toblin R, et al. Patterns of abuse among unintentional pharmaceutical overdose fatalities. *JAMA*. 2008;300(22):2613-20.
780. Wunsch M, Nakamoto K, Behonick G, Massello W. Opioid deaths in rural Virginia: a description of the high prevalence of accidental fatalities involving prescribed medications. *Am J Addict*. 2009;18(1).
781. Webster L, Cochella S, Dasgupta N, et al. An analysis of the root causes for opioid-related overdose deaths in the United States. *Pain Med*. 2011;12(Suppl 2):S26-35.
782. Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a cohort study. *Ann Intern Med*. 2010;152(2):85-92.
783. Paulozzi L, Baldwin G, Franklin G, et al. CDC Grand Rounds: Prescription Drug Overdoses-a U.S. Epidemic. *MMWR*. 2012;61(1):10-3.
784. Paulozzi LJ, Logan JE, Hall AJ, McKinstry E, Kaplan JA, Crosby AE. A comparison of drug overdose deaths involving methadone and other opioid analgesics in West Virginia. *Addiction*. 2009;104(9):1541-8.
785. Toblin RL, Paulozzi LJ, Logan JE, Hall AJ, Kaplan JA. Mental illness and psychotropic drug use among prescription drug overdose deaths: a medical examiner chart review. *J Clin Psychiatry*. 2010;71(4):491-6.
786. Grattan A, Sullivan M, Saunders K, Campbell C, Von Korff M. Depression and prescription opioid misuse among chronic opioid therapy recipients with no history of substance abuse. *Annals Fam Med*. 2012;10(4):304-11.
787. Centers for Disease Control and Prevention. Unintentional deaths from drug poisoning by urbanization of area — New Mexico, 1994–2003. *MMWR*. 2005;54(35):870-3.
788. Centers for Disease Control and Prevention. Adult Use of Prescription Opioid Pain Medications --- Utah, 2008. *MMWR*. 2010;59(6):153-7.
789. Dean M. Opioids in renal failure and dialysis patients. *J Pain Symptom Manage*. 2004;28(5):497-504.
790. Deyo RA, Smith DH, Johnson ES, et al. Opioids for back pain patients: primary care prescribing patterns and use of services. *J Am Board Fam Med*. 2011;24(6):717-27.
791. Fareed A, Casarella J, Roberts M, et al. High dose versus moderate dose methadone maintenance: is there a better outcome? *J Addict Dis*. 2009;28(4):399-405.
792. Goodridge D, Lawson J, Rocker G, Marciniuk D, Rennie D. Factors associated with opioid dispensation for patients with COPD and lung cancer in the last year of life: A retrospective analysis. *Int J Chron Obstruct Pulmon Dis*. 2010;599-105.
793. Hadidi MS, Ibrahim MI, Abdallat IM, Hadidi KA. Current trends in drug abuse associated fatalities - Jordan, 2000-2004. *Forensic Sci Int*. 2009;186(1-3):44-7.
794. Mills K, Teesson M, Ross J, Darke S, Shanahan M. The costs and outcomes of treatment for opioid dependence associated with posttraumatic stress disorder. *Psychiatr Serv*. 2005;56(8):940-5.
795. Nyhlen A, Fridell M, Backstrom M, Hesse M, Krantz P. Substance abuse and psychiatric co-morbidity as predictors of premature mortality in Swedish drug abusers: a prospective longitudinal study 1970-2006. *BMC Psychiatry*. 2011;11122.
796. Seal KH, Shi Y, Cohen G, et al. Association of mental health disorders with prescription opioids and high-risk opioid use in US veterans of Iraq and Afghanistan. *JAMA*. 2012;307(9):940-7.
797. Wysowski DK. Surveillance of prescription drug-related mortality using death certificate data. *Drug Saf*. 2007;30(6):533-40.
798. Wysowski DK, Governale LA, Swann J. Trends in outpatient prescription drug use and related costs in the US: 1998-2003. *Pharmacoeconomics*. 2006;24(3):233-6.
799. Walter SR, Thein HH, Amin J, et al. Trends in mortality after diagnosis of hepatitis B or C infection: 1992-2006. *J Hepatol*. 2011;54(5):879-86.
800. Gomes T, Redelmeier DA, Juurlink DN, Dhalla IA, Camacho X, Mamdani MM. Opioid dose and risk of road trauma in Canada: a population-based study. *JAMA Intern Med*. 2013;173(3):196-201.
801. Cifuentes M, Webster B, Genevay S, Pransky G. The course of opioid prescribing for a new episode of disabling low back pain: opioid features and dose escalation. *Pain*. 2010;151(1):22-9.
802. Volinn E, Fargo JD, Fine PG. Opioid therapy for nonspecific low back pain and the outcome of chronic work loss. *Pain*. 2009;142(3):194-201.

803. Dersh J, Mayer T, Gatchel R, Polatin P, Theodore B, Mayer E. Prescription opioid dependence is associated with poorer outcomes in disabling spinal disorders. *Spine*. 2008;33(20):2219-27.
804. Innes GD, Croskerry P, Worthington J, Beveridge R, Jones D. Ketorolac versus acetaminophen-codeine in the emergency department treatment of acute low back pain. *J Emerg Med*. 1998;16(4):549-56.
805. Veenema K, Leahey N, S. S. Ketorolac versus meperidine: ED treatment of severe musculoskeletal low back pain. *Am J Emerg Med*. 2000;18(4):404-7.
806. Reneman MF, Jorritsma W, Schellekens JM, Goeken LN. Concurrent validity of questionnaire and performance-based disability measurements in patients with chronic nonspecific low back pain. *J Occup Rehabil*. 2002;12(3):119-29.
807. Swinkels-Meewisse IE, Roelofs J, Oostendorp RA, Verbeek AL, Vlaeyen JW. Acute low back pain: pain-related fear and pain catastrophizing influence physical performance and perceived disability. *Pain*. 2006;120(1-2):36-43.
808. Bohnert AS, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA*. 2011;305(13):1315-21.
809. Church CA, Stewart Ct, TJ OL, Wallace D. Rofecoxib versus hydrocodone/acetaminophen for postoperative analgesia in functional endoscopic sinus surgery. *Laryngoscope*. 2006;116(4):602-6.
810. Nussmeier NA, Whelton AA, Brown MT, et al. Safety and efficacy of the cyclooxygenase-2 inhibitors parecoxib and valdecoxib after noncardiac surgery. *Anesthesiology*. 2006;104(3):518-26.
811. Dirks J, Fredensborg BB, Christensen D, Fomsgaard JS, Flyger H, Dahl JB. A randomized study of the effects of single-dose gabapentin versus placebo on postoperative pain and morphine consumption after mastectomy. *Anesthesiology*. 2002;97(3):560-4.
812. Legeby M, Sandelin K, Wickman M, Olofsson C. Analgesic efficacy of diclofenac in combination with morphine and paracetamol after mastectomy and immediate breast reconstruction. *Acta Anaesthesiol Scand*. 2005;49(9):1360-6.
813. Pettersson PH, Jakobsson J, Owall A. Intravenous acetaminophen reduced the use of opioids compared with oral administration after coronary artery bypass grafting. *J Cardiothorac Vasc Anesth*. 2005;19(3):306-9.
814. Buchler MW, Seiler CM, Monson JR, et al. Clinical trial: alvimopan for the management of post-operative ileus after abdominal surgery: results of an international randomized, double-blind, multicentre, placebo-controlled clinical study. *Aliment Pharmacol Ther*. 2008;28(3):312-25.
815. Dierking G, Duedahl TH, Rasmussen ML, et al. Effects of gabapentin on postoperative morphine consumption and pain after abdominal hysterectomy: a randomized, double-blind trial. *Acta Anaesthesiol Scand*. 2004;48(3):322-7.
816. Wininger SJ, Miller H, Minkowitz HS, et al. A randomized, double-blind, placebo-controlled, multicenter, repeat-dose study of two intravenous acetaminophen dosing regimens for the treatment of pain after abdominal laparoscopic surgery. *Clin Ther*. 2010;32(14):2348-69.
817. Wolff BG, Michelassi F, Gerkin TM, et al. Alvimopan, a novel, peripherally acting mu opioid antagonist: results of a multicenter, randomized, double-blind, placebo-controlled, phase III trial of major abdominal surgery and postoperative ileus. *Ann Surg*. 2004;240(4):728-34; discussion 34-5.
818. Pizzi LT, Toner R, Foley K, et al. Relationship between potential opioid-related adverse effects and hospital length of stay in patients receiving opioids after orthopedic surgery. *Pharmacotherapy*. 2012;32(6):502-14.
819. Christensen KS, Cohen AE, Mermelstein FH, et al. The analgesic efficacy and safety of a novel intranasal morphine formulation (morphine plus chitosan), immediate release oral morphine, intravenous morphine, and placebo in a postsurgical dental pain model. *Anesth Analg*. 2008;107(6):2018-24.
820. Nader A, Kendall MC, Wixson RL, Chung B, Polakow LM, McCarthy RJ. A randomized trial of epidural analgesia followed by continuous femoral analgesia compared with oral opioid analgesia on short- and long-term functional recovery after total knee replacement. *Pain Med*. 2012;13(7):937-47.
821. Belknap SM, Moore H, Lanzotti SA, et al. Application of software design principles and debugging methods to an analgesia prescription reduces risk of severe injury from medical use of opioids. *Clin Pharmacol Ther*. 2008;84(3):385-92.

822. Manchikanti L, Damron KS, McManus CD, Barnhill RC. Patterns of illicit drug use and opioid abuse in patients with chronic pain at initial evaluation: a prospective, observational study. *Pain Physician*. 2004;7(4):431-7.
823. Federation of State Medical Boards. Model Policy on the Use of Opioid Analgesics in the Treatment of Chronic Pain. 2013.
824. International Association of Industrial Accident Boards and Commissions. Reducing Inappropriate Opioid Use in Treatment of Injured Workers. A Policy Guide. 2013.
825. Brouwer S, Dijkstra PU, Stewart RE, Goeken LN, Groothoff JW, Geertzen JH. Comparing self-report, clinical examination and functional testing in the assessment of work-related limitations in patients with chronic low back pain. *Disabil Rehabil*. 2005;27(17):999-1005.
826. Buelow AK, Haggard R, Gatchel RJ. Additional validation of the pain medication questionnaire in a heterogeneous sample of chronic pain patients. *Pain Pract*. 2009;9(6):428-34.
827. Food and Drug Administration. Letter to Dr. Andrew Kolodny in Response to the Citizen Petition Submitted by Physicians for Responsible Opioid Prescribing. 2013.
828. Fox CD, Steger HG, Jennison JH. Ratio scaling of pain perception with the submaximum effort tourniquet technique. *Pain*. 1979;7(1):21-9.
829. Gross DP, Battie MC. Construct validity of a kinesiophysical functional capacity evaluation administered within a worker's compensation environment. *J Occup Rehabil*. 2003;13(4):287-95.
830. Hartrick CT, Kovan JP, Shapiro S. The numeric rating scale for clinical pain measurement: a ratio measure? *Pain Pract*. 2003;3(4):310-6.
831. Lund I, Lundeberg T, Sandberg L, Budh CN, Kowalski J, Svensson E. Lack of interchangeability between visual analogue and verbal rating pain scales: a cross sectional description of pain etiology groups. *BMC Med Res Methodol*. 2005;5:31.
832. Mahowald ML, Singh JA, Majeski P. Opioid use by patients in an orthopedics spine clinic. *Arthritis Rheum*. 2005;52(1):312-21.
833. Morasco BJ, Cavanagh R, Gritzner S, Dobscha SK. Care management practices for chronic pain in veterans prescribed high doses of opioid medications. *Fam Pract*. 2013.
834. Reneman MF, Schiphorts Preuper HR, Kleen M, Geertzen JH, Dijkstra PU. Are pain intensity and pain related fear related to functional capacity evaluation performances of patients with chronic low back pain? *J Occup Rehabil*. 2007;17(2):247-58.
835. Schiphorst Preuper H, Reneman M, Boonstra A, et al. Relationship between psychological factors and performance-based and self-reported disability in chronic low back pain. *Eur Spine J*. 2008;17(11):1448-56.
836. Smeets RJ, van Geel AC, Kester AD, Knottnerus JA. Physical capacity tasks in chronic low back pain: what is the contributing role of cardiovascular capacity, pain and psychological factors? *Disabil Rehabil*. 2007;29(7):577-86.
837. Von Korff M, Merrill JO, Rutter CM, Sullivan M, Campbell CI, Weisner C. Time-scheduled vs. pain-contingent opioid dosing in chronic opioid therapy. *Pain*. 2011;152(6):1256-62.
838. Cifuentes M, Powell R, Webster B. Shorter time between opioid prescriptions associated with reduced work disability among acute low back pain opioid users. *J Occup Environ Med*. 2012;54(4):491-6.
839. Hartrick C, Gatchel R, Conroy S. Identification and management of pain medication abuse and misuse: current state and future directions. *Expert Rev Neurother*. 2012;12(5).
840. Kidner CL, Gatchel RJ, Mayer TG. MMPI disability profile is associated with degree of opioid use in chronic work-related musculoskeletal disorders. *Clin J Pain*. 2010;26(1):9-15.
841. Naliboff BD, Wu SM, Schieffer B, et al. A randomized trial of 2 prescription strategies for opioid treatment of chronic nonmalignant pain. *J Pain*. 2011;12(2):288-96.
842. Burchman S, Pagel P. Implementation of a formal treatment agreement for outpatient management of chronic nonmalignant pain with opioid analgesics. *J Pain Symptom Manage*. 1995;10(7):556-63.
843. Chelminski PR, Ives TJ, Felix KM, et al. A primary care, multi-disciplinary disease management program for opioid-treated patients with chronic non-cancer pain and a high burden of psychiatric comorbidity. *BMC Health Serv Res*. 2005;5(1):3.
844. Chou R, Fanciullo GJ, Fine PG, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain*. 2009;10(2):113-30.

845. Compton PA, Wu SM, Schieffer B, Pham Q, Naliboff BD. Introduction of a self-report version of the Prescription Drug Use Questionnaire and relationship to medication agreement noncompliance. *J Pain Symptom Manage*. 2008;36(4):383-95.
846. Goldberg K, Simel D, Oddone E. Effect of an opioid management system on opioid prescribing and unscheduled visits in a large primary care clinic. *JCOM*. 2005;12(12):621-8.
847. Hariharan J, Lamb GC, Neuner JM. Long-term opioid contract use for chronic pain management in primary care practice. A five year experience. *J Gen Intern Med*. 2007;22(4):485-90.
848. Ives TJ, Chelminski PR, Hammett-Stabler CA, et al. Predictors of opioid misuse in patients with chronic pain: a prospective cohort study. *BMC Health Serv Res*. 2006;6:46.
849. Manchikanti L, Manchukonda R, Damron KS, Brandon D, McManus CD, Cash K. Does adherence monitoring reduce controlled substance abuse in chronic pain patients? *Pain Physician*. 2006;9(1):57-60.
850. Manchikanti L, Manchukonda R, Pampati V, et al. Does random urine drug testing reduce illicit drug use in chronic pain patients receiving opioids? *Pain Physician*. 2006;9(2):123-9.
851. Starrels JL, Becker WC, Alford DP, Kapoor A, Williams AR, Turner BJ. Systematic review: treatment agreements and urine drug testing to reduce opioid misuse in patients with chronic pain. *Ann Intern Med*. 2010;152(11):712-20.
852. Vaglianti RM, Huber SJ, Noel KR, Johnstone RE. Misuse of prescribed controlled substances defined by urinalysis. *W V Med J*. 2003;99(2):67-70.
853. Wiedemer N, Harden P, Arndt I, Gallagher R. The opioid renewal clinic: a primary care, managed approach to opioid therapy in chronic pain patients at risk for substance abuse. *Pain Med*. 2007;8(7):573-84.
854. Appenzeller BM, Agirman R, Neuberg P, Yegles M, Wennig R. Segmental determination of ethyl glucuronide in hair: a pilot study. *Forensic Sci Int*. 2007;173(2-3):87-92.
855. Cooper GA, Kronstrand R, Kintz P. Society of Hair Testing guidelines for drug testing in hair. *Forensic Sci Int*. 2012;218(1-3):20-4.
856. Kulaga V, Velazquez-Armenta Y, Aleksa K, Vergee Z, Koren G. The effect of hair pigment on the incorporation of fatty acid ethyl esters (FAEE). *Alcohol Alcohol*. 2009;44(3):287-92.
857. Lamoureux F, Gaulier JM, Sauvage FL, Mercerolle M, Vallejo C, Lachatre G. Determination of ethyl-glucuronide in hair for heavy drinking detection using liquid chromatography-tandem mass spectrometry following solid-phase extraction. *Anal Bioanal Chem*. 2009;394(7):1895-901.
858. Lees R, Kingston R, Williams TM, Henderson G, Lingford-Hughes A, Hickman M. Comparison of ethyl glucuronide in hair with self-reported alcohol consumption. *Alcohol Alcohol*. 2012;47(3):267-72.
859. Politi L, Zucchella A, Morini L, Stramesi C, Poletini A. Markers of chronic alcohol use in hair: comparison of ethyl glucuronide and cocaethylene in cocaine users. *Forensic Sci Int*. 2007;172(1):23-7.
860. Substance Abuse and Mental Health Services Administration. Federal Guidelines for Opioid Treatment. 2013.
861. Auerbach K. Drug testing methods. In: Lessenger J, Roper G, eds. *Drug Courts: A New Approach to Treatment and Rehabilitation*. New York, NY: Springer Science+Business Media; 2007:215-33.
862. Heit H, Gourlay D. Urine drug testing in pain medicine. *J Pain Symptom Manage*. 2004;27(3):260-7.
863. Jortani S, Stauble E, Wong S. Chapter 1. Pharmacogenetics in clinical and forensic toxicology: opioid overdoses and deaths. In: Mozayani A, Raymon L, eds. *Handbook of Drug Interactions A Clinical and Forensic Guide*. New York, NY: Humana Press; 2012:3-22.
864. Caldwell JR, Hale ME, Boyd RE, et al. Treatment of osteoarthritis pain with controlled release oxycodone or fixed combination oxycodone plus acetaminophen added to nonsteroidal antiinflammatory drugs: a double blind, randomized, multicenter, placebo controlled trial. *J Rheumatol*. 1999;26(4):862-9.
865. Silverfield JC, Kamin M, Wu SC, Rosenthal N. Tramadol/acetaminophen combination tablets for the treatment of osteoarthritis flare pain: a multicenter, outpatient, randomized, double-blind, placebo-controlled, parallel-group, add-on study. *Clin Ther*. 2002;24(2):282-97.
866. Babul N, Noveck R, Chipman H, Roth SH, Gana T, Albert K. Efficacy and safety of extended-release, once-daily tramadol in chronic pain: a randomized 12-week clinical trial in osteoarthritis of the knee. *J Pain Symptom Manage*. 2004;28(1):59-71.
867. Burch F, Fishman R, Messina N, et al. A comparison of the analgesic efficacy of Tramadol Contramid OAD versus placebo in patients with pain due to osteoarthritis. *J Pain Symptom Manage*. 2007;34(3):328-38.

868. Caldwell JR, Rapoport RJ, Davis JC, et al. Efficacy and safety of a once-daily morphine formulation in chronic, moderate-to-severe osteoarthritis pain: results from a randomized, placebo-controlled, double-blind trial and an open-label extension trial. *J Pain Symptom Manage*. 2002;23(4):278-91.
869. Emkey R, Rosenthal N, Wu SC, Jordan D, Kamin M. Efficacy and safety of tramadol/acetaminophen tablets (Ultracet) as add-on therapy for osteoarthritis pain in subjects receiving a COX-2 nonsteroidal antiinflammatory drug: a multicenter, randomized, double-blind, placebo-controlled trial. *J Rheumatol*. 2004;31(1):150-6.
870. Fishman RL, Kistler CJ, Ellerbusch MT, et al. Efficacy and safety of 12 weeks of osteoarthritic pain therapy with once-daily tramadol (Tramadol Contramid OAD). *J Opioid Manag*. 2007;3(5):273-80.
871. Fleischmann R, Caldwell J, Roth S, Tesser J, Olson W, Kamin M. Tramadol for the treatment of joint pain associated with osteoarthritis: a randomized, double-blind, placebo-controlled trial. *Curr Ther Res*. 2001;62(2):113-28.
872. Florete OG, Xiang J, Vorsanger GJ. Effects of extended-release tramadol on pain-related sleep parameters in patients with osteoarthritis. *Expert Opin Pharmacother*. 2008;9(11):1817-27.
873. Gana TJ, Pascual ML, Fleming RR, et al. Extended-release tramadol in the treatment of osteoarthritis: a multicenter, randomized, double-blind, placebo-controlled clinical trial. *Curr Med Res Opin*. 2006;22(7):1391-401.
874. Kean WF, Bouchard S, Roderich Gossen E. Women with pain due to osteoarthritis: the efficacy and safety of a once-daily formulation of tramadol. *Pain Med*. 2009;10(6):1001-11.
875. Langford R, McKenna F, Ratcliffe S, Vojtassak J, Richarz U. Transdermal fentanyl for improvement of pain and functioning in osteoarthritis: a randomized, placebo-controlled trial. *Arthritis Rheum*. 2006;54(6):1829-37.
876. Lloyd RS, Costello F, Eves MJ, James IG, Miller AJ. The efficacy and tolerability of controlled-release dihydrocodeine tablets and combination dextropropoxyphene/paracetamol tablets in patients with severe osteoarthritis of the hips. *Curr Med Res Opin*. 1992;13(1):37-48.
877. Malonne H, Coffiner M, Sonet B, Sereno A, Vanderbist F. Efficacy and tolerability of sustained-release tramadol in the treatment of symptomatic osteoarthritis of the hip or knee: a multicenter, randomized, double-blind, placebo-controlled study. *Clin Ther*. 2004;26(11):1774-82.
878. Markenson JA, Croft J, Zhang PG, Richards P. Treatment of persistent pain associated with osteoarthritis with controlled-release oxycodone tablets in a randomized controlled clinical trial. *Clin J Pain*. 2005;21(6):524-35.
879. Matsumoto AK, Babul N, Ahdieh H. Oxymorphone extended-release tablets relieve moderate to severe pain and improve physical function in osteoarthritis: results of a randomized, double-blind, placebo- and active-controlled phase III trial. *Pain Med*. 2005;6(5):357-66.
880. Parr G, Darekar B, Fletcher A, Bulpitt CJ. Joint pain and quality of life; results of a randomised trial. *Br J Clin Pharmacol*. 1989;27(2):235-42.
881. Peloso PM, Bellamy N, Bensen W, et al. Double blind randomized placebo control trial of controlled release codeine in the treatment of osteoarthritis of the hip or knee. *J Rheumatol*. 2000;27(3):764-71.
882. Roth SH. Efficacy and safety of tramadol HCl in breakthrough musculoskeletal pain attributed to osteoarthritis. *The Journal Of Rheumatology*. 1998;25(7):1358-63.
883. Roth SH, Fleischmann RM, Burch FX, et al. Around-the-clock, controlled-release oxycodone therapy for osteoarthritis-related pain: placebo-controlled trial and long-term evaluation. *Arch Intern Med*. 2000;160(6):853-60.
884. Schnitzer TJ, Kamin M, Olson WH. Tramadol allows reduction of naproxen dose among patients with naproxen-responsive osteoarthritis pain: a randomized, double-blind, placebo-controlled study. *Arthritis Rheum*. 1999;42(7):1370-7.
885. Zautra AJ, Smith BW. Impact of controlled-release oxycodone on efficacy beliefs and coping efforts among osteoarthritis patients with moderate to severe pain. *Clin J Pain*. 2005;21(6):471-7.
886. Abbruzzese G. The medical management of spasticity. *Eur J Neurol*. 2002;9 Suppl 130-4; discussion 53-61.
887. Elenbaas JK. Centrally acting oral skeletal muscle relaxants. *Am J Hosp Pharm*. 1980;37(10):1313-23.
888. Cherkin DC, Wheeler KJ, Barlow W, Deyo RA. Medication use for low back pain in primary care. *Spine (Phila Pa 1976)*. 1998;23(5):607-14.

889. Di Iorio D, Henley E, Doughty A. A survey of primary care physician practice patterns and adherence to acute low back problem guidelines. *Arch Fam Med*. 2000;9(10):1015-21.
890. van Tulder M, Koes B, Bouter L. Conservative treatment of acute and chronic nonspecific low back pain: A systematic review of randomized controlled trials of the most common interventions. *Spine*. 1997;22:128-56.
891. Schnitzer TJ, Ferraro A, Hunsche E, Kong SX. A comprehensive review of clinical trials on the efficacy and safety of drugs for the treatment of low back pain. *J Pain Symptom Manage*. 2004;28(1):72-95.
892. Deyo RA, Loeser JD, Bigos SJ. Herniated lumbar intervertebral disk. *Ann Intern Med*. 1990;112(8):598-603.
893. Baratta RR. A double-blind comparative study of carisoprodol, propoxyphene, and placebo in the management of low back syndrome. *Curr Ther Res Clin Exp*. 1976;20(3):233-40.
894. Arbus L, Fajadet B, Aubert D, et al. Activity of tetrazepam (myolastan) in low back pain: a double-blind trial v. placebo. *Clin Trials J*. 1990;27(4):258-67.
895. Preston E, Miller C, Herbertson R. A double-blind, multicenter trial of methocarbamol (Robaxin (R)) and cyclobenzaprine (Flexeril (R)) in acute musculoskeletal conditions. *Today's Therapeutic Trends*. 1984;11-11.
896. Brown BR, Jr., Womble J. Cyclobenzaprine in intractable pain syndromes with muscle spasm. *JAMA*. 1978;240(11):1151-2.
897. Hingorani K. Orphenadrin-paracetamol in backache—a double-blind controlled trial. *Br J Clin Pract*. 1971;25(5):227-31.
898. Bercel N. Cyclobenzaprine in the treatment of skeletal muscle spasm in osteoarthritis of the cervical and lumbar spine. *Curr Ther Res*. 1977;22(4):462-8.
899. Salzmann E, Pforringer W, Paal G, Gierend M. Treatment of chronic low-back syndrome with tetrazepam in a placebo controlled double-blind trial. *J Drug Dev*. 1992;4(4):219-28.
900. Lofland JH, Szarlej D, Buttaro T, Shermock S, Jalali S. Cyclobenzaprine hydrochloride is a commonly prescribed centrally acting muscle relaxant, which is structurally similar to tricyclic antidepressants (TCAs) and differs from amitriptyline by only one double bond. *Clin J Pain*. 2001;17(1):103-4.
901. Littrell RA, Hayes LR, Stillner V. Carisoprodol (Soma): a new and cautious perspective on an old agent. *South Med J*. 1993;86(7):753-6.
902. Toth PP, Urtis J. Commonly used muscle relaxant therapies for acute low back pain: a review of carisoprodol, cyclobenzaprine hydrochloride, and metaxalone. *Clin Ther*. 2004;26(9):1355-67.
903. Kroenke K, Bair MJ, Damush TM, et al. Optimized antidepressant therapy and pain self-management in primary care patients with depression and musculoskeletal pain: a randomized controlled trial. *JAMA*. 2009;301(20):2099-110.
904. Kerrick JM, Fine PG, Lipman AG, Love G. Low-dose amitriptyline as an adjunct to opioids for postoperative orthopedic pain: a placebo-controlled trial. *Pain*. 1993;52(3):325-30.
905. Wiffen P, Collins S, McQuay H, Carroll D, Jadad A, Moore A. Anticonvulsant drugs for acute and chronic pain. *Cochrane Database Syst Rev*. 2005(3):CD001133.
906. Challapalli V, Tremont-Lukats IW, McNicol ED, Lau J, Carr DB. Systemic administration of local anesthetic agents to relieve neuropathic pain. *Cochrane Database Syst Rev*. 2005(4):CD003345.
907. Pandey CK, Navkar DV, Giri PJ, et al. Evaluation of the optimal preemptive dose of gabapentin for postoperative pain relief after lumbar discectomy: a randomized, double-blind, placebo-controlled study. *J Neurosurg Anesthesiol*. 2005;17(2):65-8.
908. Pandey CK, Priye S, Singh S, Singh U, Singh RB, Singh PK. Preemptive use of gabapentin significantly decreases postoperative pain and rescue analgesic requirements in laparoscopic cholecystectomy. *Can J Anaesth*. 2004;51(4):358-63.
909. Turan A, Karamanlioglu B, Memis D, et al. Analgesic effects of gabapentin after spinal surgery. *Anesthesiology*. 2004;100(4):935-8.
910. Radhakrishnan M, Bithal PK, Chaturvedi A. Effect of preemptive gabapentin on postoperative pain relief and morphine consumption following lumbar laminectomy and discectomy: a randomized, double-blinded, placebo-controlled study. *J Neurosurg Anesthesiol*. 2005;17(3):125-8.
911. Schwarz EM, Campbell D, Totterman S, Boyd A, O'Keefe RJ, Looney RJ. Use of volumetric computerized tomography as a primary outcome measure to evaluate drug efficacy in the prevention of peri-prosthetic osteolysis: a 1-year clinical pilot of etanercept vs. placebo. *J Orthop Res*. 2003;21(6):1049-55.

912. Gregory PJ, Sperry M, Wilson AF. Dietary supplements for osteoarthritis. *Am Fam Physician*. 2008;77(2):177-84.
913. Houpt JB, McMillan R, Wein C, Paget-Dellio SD. Effect of glucosamine hydrochloride in the treatment of pain of osteoarthritis of the knee. *J Rheumatol*. 1999;26(11):2423-30.
914. Martel-Pelletier J, Boileau C, Pelletier JP, Roughley PJ. Cartilage in normal and osteoarthritis conditions. *Best Pract Res Clin Rheumatol*. 2008;22(2):351-84.
915. Bassleer C, Rovati L, Franchimont P. Stimulation of proteoglycan production by glucosamine sulfate in chondrocytes isolated from human osteoarthritic articular cartilage in vitro. *Osteoarthritis Cartilage*. 1998;6(6):427-34.
916. Largo R, Alvarez-Soria MA, Diez-Ortego I, et al. Glucosamine inhibits IL-1beta-induced NFkappaB activation in human osteoarthritic chondrocytes. *Osteoarthritis Cartilage*. 2003;11(4):290-8.
917. Jomphe C, Gabriac M, Hale TM, et al. Chondroitin sulfate inhibits the nuclear translocation of nuclear factor-kappaB in interleukin-1beta-stimulated chondrocytes. *Basic Clin Pharmacol Toxicol*. 2008;102(1):59-65.
918. Das A, Jr., Hammad TA. Efficacy of a combination of FCHG49 glucosamine hydrochloride, TRH122 low molecular weight sodium chondroitin sulfate and manganese ascorbate in the management of knee osteoarthritis. *Osteoarthritis Cartilage*. 2000;8(5):343-50.
919. Braham R, Dawson B, Goodman C. The effect of glucosamine supplementation on people experiencing regular knee pain. *Br J Sports Med*. 2003;37(1):45-9; discussion 9.
920. Reichelt A, Forster KK, Fischer M, Rovati LC, Setnikar I. Efficacy and safety of intramuscular glucosamine sulfate in osteoarthritis of the knee. A randomised, placebo-controlled, double-blind study. *Arzneimittelforschung*. 1994;44(1):75-80.
921. Vajjaradul Y. Double-blind clinical evaluation of intra-articular glucosamine in outpatients with gonarthrosis. *Clin Ther*. 1981;3(5):336-43.
922. Gramajo RJ, Cutroneo EJ, Fernandez DE, et al. A single-blind, placebo-controlled study of glycosaminoglycan-peptide complex ('Rumalon') in patients with osteoarthritis of the hip or knee. *Curr Med Res Opin*. 1989;11(6):366-73.
923. Muniyappa R, Karne RJ, Hall G, et al. Oral glucosamine for 6 weeks at standard doses does not cause or worsen insulin resistance or endothelial dysfunction in lean or obese subjects. *Diabetes*. 2006;55(11):3142-50.
924. Biggee BA, Blinn CM, Nuite M, Silbert JE, McAlindon TE. Effects of oral glucosamine sulphate on serum glucose and insulin during an oral glucose tolerance test of subjects with osteoarthritis. *Ann Rheum Dis*. 2007;66(2):260-2.
925. Pham T, Cornea A, Blick KE, Jenkins A, Scofield RH. Oral glucosamine in doses used to treat osteoarthritis worsens insulin resistance. *Am J Med Sci*. 2007;333(6):333-9.
926. Marshall PD, Poddar S, Tweed EM, Brandes L. Clinical inquiries: Do glucosamine and chondroitin worsen blood sugar control in diabetes? *J Fam Pract*. 2006;55(12):1091-3.
927. Scroggie DA, Albright A, Harris MD. The effect of glucosamine-chondroitin supplementation on glycosylated hemoglobin levels in patients with type 2 diabetes mellitus: a placebo-controlled, double-blinded, randomized clinical trial. *Arch Intern Med*. 2003;163(13):1587-90.
928. Frestedt JL, Walsh M, Kuskowski MA, Zenk JL. A natural mineral supplement provides relief from knee osteoarthritis symptoms: a randomized controlled pilot trial. *Nutr J*. 2008;79.
929. Cohen M, Wolfe R, Mai T, Lewis D. A randomized, double blind, placebo controlled trial of a topical cream containing glucosamine sulfate, chondroitin sulfate, and camphor for osteoarthritis of the knee. *J Rheumatol*. 2003;30(3):523-8.
930. Villacis J, Rice TR, Bucci LR, et al. Do shrimp-allergic individuals tolerate shrimp-derived glucosamine? *Clin Exp Allergy*. 2006;36(11):1457-61.
931. Monfort J, Pelletier JP, Garcia-Giralt N, Martel-Pelletier J. Biochemical basis of the effect of chondroitin sulphate on osteoarthritis articular tissues. *Ann Rheum Dis*. 2008;67(6):735-40.
932. Felson D, Lawrence R, Dieppe P. NIH Conferences - Osteoarthritis: New Insights. Part 1: The disease and its risk factors. *Ann Intern Med*. 2000;133(8):635-46.

933. Kahan A, Uebelhart D, De Vathaire F, Delmas PD, Reginster JY. Long-term effects of chondroitins 4 and 6 sulfate on knee osteoarthritis: the study on osteoarthritis progression prevention, a two-year, randomized, double-blind, placebo-controlled trial. *Arthritis Rheum.* 2009;60(2):524-33.
934. Michel BA, Stucki G, Frey D, et al. Chondroitins 4 and 6 sulfate in osteoarthritis of the knee: a randomized, controlled trial. *Arthritis Rheum.* 2005;52(3):779-86.
935. Uebelhart D, Malaise M, Marcolongo R, et al. Intermittent treatment of knee osteoarthritis with oral chondroitin sulfate: a one-year, randomized, double-blind, multicenter study versus placebo. *Osteoarthritis Cartilage.* 2004;12(4):269-76.
936. Pavelka K, Gatterova J, Olejarova M, Machacek S, Giacomelli G, Rovati LC. Glucosamine sulfate use and delay of progression of knee osteoarthritis: a 3-year, randomized, placebo-controlled, double-blind study. *Arch Intern Med.* 2002;162(18):2113-23.
937. Reginster JY, Deroisy R, Rovati LC, et al. Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial. *Lancet.* 2001;357(9252):251-6.
938. Sawitzke AD, Shi H, Finco MF, et al. The effect of glucosamine and/or chondroitin sulfate on the progression of knee osteoarthritis: a report from the glucosamine/chondroitin arthritis intervention trial. *Arthritis Rheum.* 2008;58(10):3183-91.
939. Rozendaal RM, Koes BW, van Osch GJ, et al. Effect of glucosamine sulfate on hip osteoarthritis: a randomized trial. *Ann Intern Med.* 2008;148(4):268-77.
940. Hughes R, Carr A. A randomized, double-blind, placebo-controlled trial of glucosamine sulphate as an analgesic in osteoarthritis of the knee. *Rheumatology (Oxford).* 2002;41(3):279-84.
941. McAlindon T, Formica M, LaValley M, Lehmer M, Kabbara K. Effectiveness of glucosamine for symptoms of knee osteoarthritis: results from an internet-based randomized double-blind controlled trial. *Am J Med.* 2004;117(9):643-9.
942. Mehta K, Gala J, Bhasale S, et al. Comparison of glucosamine sulfate and a polyherbal supplement for the relief of osteoarthritis of the knee: a randomized controlled trial [ISRCTN25438351]. *BMC Complement Altern Med.* 2007;734.
943. Noack W, Fischer M, Forster KK, Rovati LC, Setnikar I. Glucosamine sulfate in osteoarthritis of the knee. *Osteoarthritis Cartilage.* 1994;2(1):51-9.
944. Mazieres B, Hucher M, Zaim M, Garnero P. Effect of chondroitin sulphate in symptomatic knee osteoarthritis: a multicentre, randomised, double-blind, placebo-controlled study. *Ann Rheum Dis.* 2007;66(5):639-45.
945. Clegg DO, Reda DJ, Harris CL, et al. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. *N Engl J Med.* 2006;354(8):795-808.
946. Mazieres B, Combe B, Phan Van A, Tondut J, Grynfeldt M. Chondroitin sulfate in osteoarthritis of the knee: a prospective, double blind, placebo controlled multicenter clinical study. *J Rheumatol.* 2001;28(1):173-81.
947. Bucsi L, Poor G. Efficacy and tolerability of oral chondroitin sulfate as a symptomatic slow-acting drug for osteoarthritis (SYSADOA) in the treatment of knee osteoarthritis. *Osteoarthritis Cartilage.* 1998;6 Suppl A31-6.
948. Kerzberg EM, Roldan EJ, Castelli G, Huberman ED. Combination of glycosaminoglycans and acetylsalicylic acid in knee osteoarthrosis. *Scand J Rheumatol.* 1987;16(5):377-80.
949. Bourgeois P, Chales G, Dehais J, Delcambre B, Kuntz JL, Rozenberg S. Efficacy and tolerability of chondroitin sulfate 1200 mg/day vs chondroitin sulfate 3 x 400 mg/day vs placebo. *Osteoarthritis Cartilage.* 1998;6 Suppl A25-30.
950. Uebelhart D, Thonar EJ, Delmas PD, Chantraine A, Vignon E. Effects of oral chondroitin sulfate on the progression of knee osteoarthritis: a pilot study. *Osteoarthritis Cartilage.* 1998;6 Suppl A39-46.
951. Usha PR, Naidu MU. Randomised, Double-Blind, Parallel, Placebo-Controlled Study of Oral Glucosamine, Methylsulfonylmethane and their Combination in Osteoarthritis. *Clin Drug Investig.* 2004;24(6):353-63.
952. Kim LS, Axelrod LJ, Howard P, Buratovich N, Waters RF. Efficacy of methylsulfonylmethane (MSM) in osteoarthritis pain of the knee: a pilot clinical trial. *Osteoarthritis Cartilage.* 2006;14(3):286-94.
953. Muller-Fassbender H, Bach GL, Haase W, Rovati LC, Setnikar I. Glucosamine sulfate compared to ibuprofen in osteoarthritis of the knee. *Osteoarthritis Cartilage.* 1994;2(1):61-9.

954. Morreale P, Manopulo R, Galati M, Boccanera L, Saponati G, Bocchi L. Comparison of the antiinflammatory efficacy of chondroitin sulfate and diclofenac sodium in patients with knee osteoarthritis. *J Rheumatol*. 1996;23(8):1385-91.
955. Lopes Vaz A. Double-blind clinical evaluation of the relative efficacy of ibuprofen and glucosamine sulphate in the management of osteoarthrosis of the knee in out-patients. *Curr Med Res Opin*. 1982;8(3):145-9.
956. Qiu GX, Gao SN, Giacobelli G, Rovati L, Setnikar I. Efficacy and safety of glucosamine sulfate versus ibuprofen in patients with knee osteoarthritis. *Arzneimittelforschung*. 1998;48(5):469-74.
957. Cibere J, Kopec JA, Thorne A, et al. Randomized, double-blind, placebo-controlled glucosamine discontinuation trial in knee osteoarthritis. *Arthritis Rheum*. 2004;51(5):738-45.
958. Herrero-Beaumont G, Ivorra JA, Del Carmen Trabado M, et al. Glucosamine sulfate in the treatment of knee osteoarthritis symptoms: a randomized, double-blind, placebo-controlled study using acetaminophen as a side comparator. *Arthritis Rheum*. 2007;56(2):555-67.
959. Marti-Bonmati L, Sanz-Requena R, Rodrigo JL, Alberich-Bayarri A, Carot JM. Glucosamine sulfate effect on the degenerated patellar cartilage: preliminary findings by pharmacokinetic magnetic resonance modeling. *Eur Radiol*. 2009;19(6):1512-8.
960. Vlad SC, LaValley MP, McAlindon TE, Felson DT. Glucosamine for pain in osteoarthritis: why do trial results differ? *Arthritis Rheum*. 2007;56(7):2267-77.
961. Kawasaki T, Kurosawa H, Ikeda H, et al. Additive effects of glucosamine or risedronate for the treatment of osteoarthritis of the knee combined with home exercise: a prospective randomized 18-month trial. *J Bone Miner Metab*. 2008;26(3):279-87.
962. Wolsko PM, Eisenberg DM, Davis RB, Kessler R, Phillips RS. Patterns and perceptions of care for treatment of back and neck pain: results of a national survey. *Spine (Phila Pa 1976)*. 2003;28(3):292-7; discussion 8.
963. Sherman KJ, Cherkin DC, Kahn J, et al. A survey of training and practice patterns of massage therapists in two US states. *BMC Complement Altern Med*. 2005;513.
964. Abbot NC, Harkness EF, Stevinson C, Marshall FP, Conn DA, Ernst E. Spiritual healing as a therapy for chronic pain: a randomized, clinical trial. *Pain*. 2001;91(1-2):79-89.
965. Zaproudina N, Hanninen OO, Airaksinen O. Effectiveness of traditional bone setting in chronic neck pain: randomized clinical trial. *J Manipulative Physiol Ther*. 2007;30(6):432-7.
966. Kaptchuk TJ. The placebo effect in alternative medicine: can the performance of a healing ritual have clinical significance? *Ann Intern Med*. 2002;136(11):817-25.
967. Jacquet A, Girodet PO, Pariente A, Forest K, Mallet L, Moore N. Phytalgic, a food supplement, vs placebo in patients with osteoarthritis of the knee or hip: a randomised double-blind placebo-controlled clinical trial. *Arthritis Res Ther*. 2009;11(6):R192.
968. Frestedt JL, Kuskowski MA, Zenk JL. A natural seaweed derived mineral supplement (Aquamin F) for knee osteoarthritis: a randomised, placebo controlled pilot study. *Nutr J*. 2009;87.
969. Ruff KJ, Winkler A, Jackson RW, DeVore DP, Ritz BW. Eggshell membrane in the treatment of pain and stiffness from osteoarthritis of the knee: a randomized, multicenter, double-blind, placebo-controlled clinical study. *Clin Rheumatol*. 2009;28(8):907-14.
970. Wluka A, Stuckey S, Brand C, Cicuttini FM. Supplementary vitamin E does not affect the loss of cartilage volume in knee osteoarthritis: a 2 year double blind randomized placebo controlled study. *J Rheumatol*. 2002;29(12):2585-91.
971. Tao Q, Xu Y, Jin DE, Yan XP. Clinical efficacy and safety of Gubitong Recipe in treating osteoarthritis of knee joint. *Chin J Integr Med*. 2009;15(6):458-61.
972. Colker CM, Swain M, Lynch L, Gingerich DA. Effects of a milk-based bioactive micronutrient beverage on pain symptoms and activity of adults with osteoarthritis: a double-blind, placebo-controlled clinical evaluation. *Nutrition*. 2002;18(5):388-92.
973. Oben J, Enonchong E, Kothari S, Chambliss W, Garrison R, Dolnick D. Phellodendron and Citrus extracts benefit joint health in osteoarthritis patients: a pilot, double-blind, placebo-controlled study. *Nutr J*. 2009;838.
974. Chrubasik JE, Roufogalis BD, Chrubasik S. Evidence of effectiveness of herbal antiinflammatory drugs in the treatment of painful osteoarthritis and chronic low back pain. *Phytother Res*. 2007;21(7):675-83.

975. Gagnier JJ, van Tulder MW, Berman B, Bombardier C. Herbal medicine for low back pain: a Cochrane review. *Spine*. 2007;32(1):82-92.
976. Shackel NA, Day RO, Kellett B, Brooks PM. Copper-salicylate gel for pain relief in osteoarthritis: a randomised controlled trial. *Med J Aust*. 1997;167(3):134-6.
977. Boettcher B. Copper-salicylate gel for pain relief in osteoarthritis. *Med J Aust*. 1998;168(6):312.
978. Leach MJ, Saravana Kumar. The clinical effectiveness of Ginger (*Zingiber officinale*) in adults with osteoarthritis. *Intl J Evidence-Based Healthcare*. 2008;6(3):311 - 20.
979. Altman RD, Marcussen KC. Effects of a ginger extract on knee pain in patients with osteoarthritis. *Arthritis Rheum*. 2001;44(11):2531-8.
980. Bliddal H, Rosetzky A, Schlichting P, et al. A randomized, placebo-controlled, cross-over study of ginger extracts and ibuprofen in osteoarthritis. *Osteoarthritis Cartilage*. 2000;8(1):9-12.
981. Marcus DM, Suarez-Almazor ME. Is there a role for ginger in the treatment of osteoarthritis? *Arthritis Rheum*. 2001;44(11):2461-2.
982. Shen CL, Hong KJ, Kim SW. Comparative effects of ginger root (*Zingiber officinale* Rosc.) on the production of inflammatory mediators in normal and osteoarthrotic sow chondrocytes. *J Med Food*. 2005;8(2):149-53.
983. Westermarck TS, Guntars; Sauka, Melita; Aboltina, Laima; Davidova, Alla; Pilmane, Mara;. Effects Of Dietary Supplemetation With Ginger Extract In Osteoarthritis. A Double-blind Controlled Study: 190. *Therapeutic Drug Monitoring*. 2005;27(2):259.
984. Wigler I, Grotto I, Caspi D, Yaron M. The effects of Zintona EC (a ginger extract) on symptomatic gonarthritis. *Osteoarthritis Cartilage*. 2003;11(11):783-9.
985. Haghighi M, Khalvat A, Toliat T, Jallaei S. Comparing the effects of ginger (*Zingiber officinale*) extract and ibuprofen on patients with osteoarthritis. *Arch Iranian Med*. 2005;8:267-71.
986. Kuptniratsaikul V, Thanakhumtorn S, Chinswangwatanakul P, Wattanamongkonsil L, Thamlikitkul V. Efficacy and safety of Curcuma domestica extracts in patients with knee osteoarthritis. *J Altern Complement Med*. 2009;15(8):891-7.
987. Christensen R, Bartels EM, Altman RD, Astrup A, Bliddal H. Does the hip powder of *Rosa canina* (rosehip) reduce pain in osteoarthritis patients?--a meta-analysis of randomized controlled trials. *Osteoarthritis Cartilage*. 2008;16(9):965-72.
988. Chrubasik C, Duke RK, Chrubasik S. The evidence for clinical efficacy of rose hip and seed: a systematic review. *Phytother Res*. 2006;20(1):1-3.
989. Kharazmi A, Winther K. Rose hip inhibits chemotaxis and chemiluminescence of human peripheral blood neutrophils in vitro and reduces certain inflammatory parameters in vivo. *Inflammopharmacology*. 1999;7(4):377-86.
990. Rein E, Kharazmi A, Winther K. A herbal remedy, Hyben Vital (stand. powder of a subspecies of *Rosa canina* fruits), reduces pain and improves general wellbeing in patients with osteoarthritis--a double-blind, placebo-controlled, randomised trial. *Phytomedicine*. 2004;11(5):383-91.
991. Rossnagel K, Roll S, Willich SN. The clinical effectiveness of rosehip powder in patients with osteoarthritis. A systematic review. *MMW Fortschr Med*. 2007;149(11):51-6.
992. Rossnagel K, Willich SN. Value of complementary medicine exemplified by rose-hips. *Gesundheitswesen*. 2001;63(6):412-6.
993. Warholm O, Skaar S, Hedman E, Molmen H, Eik L. The effects of a standardized herbal remedy made from a subtype of *rosa canina* in patients wit osteoarthritis: A double-blind, randomized, placebo-controlled clinical trial. *Current Therapeutic Research*. 2003;61(1):21-31.
994. Warholm O, Skaar S, Hedman E, Molmer H, Elk L. Hyben vital, a herbal remedy, reduces pain and stiffness of the hip, in a group of patietns suffering from severe osteoarthrosis. *The 9th APLAR Congress of Rheumatology*. Beijing, China; 2000.
995. Winther K, Apel K, Thamsborg G. A powder made from seeds and shells of a rose-hip subspecies (*Rosa canina*) reduces symptoms of knee and hip osteoarthritis: a randomized, double-blind, placebo-controlled clinical trial. *Scand J Rheumatol*. 2005;34(4):302-8.
996. Winther K, Rein E, Kharazmi A. The anti-inflammatory properties of rose-hip. *Inflammopharmacology*. 1999;7(1):63-8.

997. Fetrow CW, Avila JR. Efficacy of the dietary supplement S-adenosyl-L-methionine. *Ann Pharmacother*. 2001;35(11):1414-25.
998. Glorioso S, Todesco S, Mazzi A, et al. Double-blind multicentre study of the activity of S-adenosylmethionine in hip and knee osteoarthritis. *Int J Clin Pharmacol Res*. 1985;5(1):39-49.
999. Gualano M, Stramentinoli G, Berti F. Anti-inflammatory activity of S-adenosyl-L-methionine: interference with the eicosanoid system. *Pharmacol Res Commun*. 1983;15(7):683-96.
1000. Harmand MF, Vilamitjana J, Maloche E, Duphil R, Ducassou D. Effects of S-adenosylmethionine on human articular chondrocyte differentiation. An in vitro study. *Am J Med*. 1987;83(5A):48-54.
1001. Konig B. A long-term (two years) clinical trial with S-adenosylmethionine for the treatment of osteoarthritis. *Am J Med*. 1987;83(5A):89-94.
1002. Rutjes AW, Nuesch E, Reichenbach S, Juni P. S-Adenosylmethionine for osteoarthritis of the knee or hip. *Cochrane Database Syst Rev*. 2009(4):CD007321.
1003. Schreiber A, Warren G, Sutherland E, Simon F. Enhancement of taurocholate secretory maximum: S-Adenosyl Methionine (SAME)-induced cytoprotection. *Clin Res*. 1983;31(1):86A.
1004. Vetter G. Double-blind comparative clinical trial with S-adenosylmethionine and indomethacin in the treatment of osteoarthritis. *Am J Med*. 1987;83(5A):78-80.
1005. Najm WI, Reinsch S, Hoehler F, Tobis JS, Harvey PW. S-adenosyl methionine (SAME) versus celecoxib for the treatment of osteoarthritis symptoms: a double-blind cross-over trial. [ISRCTN36233495]. *BMC Musculoskelet Disord*. 2004;56.
1006. Maccagno A, Di Giorgio EE, Caston OL, Sagasta CL. Double-blind controlled clinical trial of oral S-adenosylmethionine versus piroxicam in knee osteoarthritis. *Am J Med*. 1987;83(5A):72-7.
1007. Muller-Fassbender H. Double-blind clinical trial of S-adenosylmethionine versus ibuprofen in the treatment of osteoarthritis. *Am J Med*. 1987;83(5A):81-3.
1008. Brinkhaus B, Wilkens JM, Ludtke R, Hunger J, Witt CM, Willich SN. Homeopathic arnica therapy in patients receiving knee surgery: results of three randomised double-blind trials. *Complement Ther Med*. 2006;14(4):237-46.
1009. Knuesel O, Weber M, Suter A. Arnica montana gel in osteoarthritis of the knee: an open, multicenter clinical trial. *Adv Ther*. 2002;19(5):209-18.
1010. Kraemer WJ, Ratamess NA, Maresch CM, et al. A cetylated fatty acid topical cream with menthol reduces pain and improves functional performance in individuals with arthritis. *J Strength Cond Res*. 2005;19(2):475-80.
1011. Maheu E, Mazieres B, Valat JP, et al. Symptomatic efficacy of avocado/soybean unsaponifiables in the treatment of osteoarthritis of the knee and hip: a prospective, randomized, double-blind, placebo-controlled, multicenter clinical trial with a six-month treatment period and a two-month followup demonstrating a persistent effect. *Arthritis Rheum*. 1998;41(1):81-91.
1012. Moe RH, Haavardsholm EA, Christie A, Jamtvedt G, Dahm KT, Hagen KB. Effectiveness of nonpharmacological and nonsurgical interventions for hip osteoarthritis: an umbrella review of high-quality systematic reviews. *Phys Ther*. 2007;87(12):1716-27.
1013. Blotman F, Maheu E, Wulwik A, Caspard H, Lopez A. Efficacy and safety of avocado/soybean unsaponifiables in the treatment of symptomatic osteoarthritis of the knee and hip. A prospective, multicenter, three-month, randomized, double-blind, placebo-controlled trial. *Rev Rhum Engl Ed*. 1997;64(12):825-34.
1014. Christensen R, Bartels EM, Astrup A, Bliddal H. Symptomatic efficacy of avocado-soybean unsaponifiables (ASU) in osteoarthritis (OA) patients: a meta-analysis of randomized controlled trials. *Osteoarthritis Cartilage*. 2008;16(4):399-408.
1015. Ernst E. Avocado-soybean unsaponifiables (ASU) for osteoarthritis - a systematic review. *Clin Rheumatol*. 2003;22(4-5):285-8.
1016. Lequesne M, Maheu E, Cadet C, Dreiser RL. Structural effect of avocado/soybean unsaponifiables on joint space loss in osteoarthritis of the hip. *Arthritis Rheum*. 2002;47(1):50-8.
1017. Little CV, Parsons T. Herbal therapy for treating osteoarthritis. *Cochrane Database Syst Rev*. 2001(1):CD002947.
1018. Wegener T, Lupke NP. Treatment of patients with arthrosis of hip or knee with an aqueous extract of devil's claw (*Harpagophytum procumbens* DC.). *Phytother Res*. 2003;17(10):1165-72.

1019. Appelboom T, Schuermans J, Verbruggen G, Henrotin Y, Reginster JY. Symptoms modifying effect of avocado/soybean unsaponifiables (ASU) in knee osteoarthritis. A double blind, prospective, placebo-controlled study. *Scand J Rheumatol*. 2001;30(4):242-7.
1020. Akhtar NM, Naseer R, Farooqi AZ, Aziz W, Nazir M. Oral enzyme combination versus diclofenac in the treatment of osteoarthritis of the knee--a double-blind prospective randomized study. *Clin Rheumatol*. 2004;23(5):410-5.
1021. Klein G, Kullich W, Schnitker J, Schwann H. Efficacy and tolerance of an oral enzyme combination in painful osteoarthritis of the hip. A double-blind, randomised study comparing oral enzymes with non-steroidal anti-inflammatory drugs. *Clin Exp Rheumatol*. 2006;24(1):25-30.
1022. Wittenborg A, Bock PR, Hanisch J, Saller R, Schneider B. Comparative epidemiological study in patients with rheumatic diseases illustrated in a example of a treatment with non-steroidal anti-inflammatory drugs versus an oral enzyme combination preparation. *Arzneimittelforschung*. 2000;50(8):728-38.
1023. Singer F, Singer C, Oberleitner H. Phlogenzym versus diclofenac in the treatment of activated osteoarthritis of the knee. *Int J Immunotherapy*. 2001;XVII(2/3/4):135-4.
1024. van Tulder MW, Furlan AD, Gagnier JJ. Complementary and alternative therapies for low back pain. *Best Pract Res Clin Rheumatol*. 2005;19(4):639-54.
1025. Tilwe GH, Beria S, Turakhia NH, Daftary GV, Schiess W. Efficacy and tolerability of oral enzyme therapy as compared to diclofenac in active osteoarthrosis of knee joint: an open randomized controlled clinical trial. *J Assoc Physicians India*. 2001;49:617-21.
1026. Paris A, Gonnet N, Chaussard C, et al. Effect of homeopathy on analgesic intake following knee ligament reconstruction: a phase III monocentre randomized placebo controlled study. *Br J Clin Pharmacol*. 2008;65(2):180-7.
1027. Teekachunhatean S, Kunanusorn P, Rojanasthien N, et al. Chinese herbal recipe versus diclofenac in symptomatic treatment of osteoarthritis of the knee: a randomized controlled trial [ISRCTN70292892]. *BMC Complement Altern Med*. 2004;4:19.
1028. Manicourt DH, Azria M, Mindeholm L, Thonar EJ, Devogelaer JP. Oral salmon calcitonin reduces Lequesne's algofunctional index scores and decreases urinary and serum levels of biomarkers of joint metabolism in knee osteoarthritis. *Arthritis Rheum*. 2006;54(10):3205-11.
1029. Lung YB, Seong SC, Lee MC, et al. A four-week, randomized, double-blind trial of the efficacy and safety of SKI306X: a herbal anti-arthritis agent versus diclofenac in osteoarthritis of the knee. *Am J Chin Med*. 2004;32(2):291-301.
1030. Biegert C, Wagner I, Ludtke R, et al. Efficacy and safety of willow bark extract in the treatment of osteoarthritis and rheumatoid arthritis: results of 2 randomized double-blind controlled trials. *J Rheumatol*. 2004;31(11):2121-30.
1031. Schmid B, Ludtke R, Selbmann HK, et al. Efficacy and tolerability of a standardized willow bark extract in patients with osteoarthritis: randomized placebo-controlled, double blind clinical trial. *Phytother Res*. 2001;15(4):344-50.
1032. Grube B, Grunwald J, Krug L, Staiger C. Efficacy of a comfrey root (*Symphyti offic. radix*) extract ointment in the treatment of patients with painful osteoarthritis of the knee: results of a double-blind, randomised, bicenter, placebo-controlled trial. *Phytomedicine*. 2007;14(1):2-10.
1033. Pelletier JP, Mineau F, Fernandes JC, Duval N, Martel-Pelletier J. Diacerhein and rhein reduce the interleukin 1beta stimulated inducible nitric oxide synthesis level and activity while stimulating cyclooxygenase-2 synthesis in human osteoarthritic chondrocytes. *J Rheumatol*. 1998;25(12):2417-24.
1034. Pelletier JP, Yaron M, Haraoui B, et al. Efficacy and safety of diacerein in osteoarthritis of the knee: a double-blind, placebo-controlled trial. The Diacerein Study Group. *Arthritis Rheum*. 2000;43(10):2339-48.
1035. Fidelix TS, Soares BG, Trevisani VF. Diacerein for osteoarthritis. *Cochrane Database Syst Rev*. 2006(1):CD005117.
1036. Moore AR, Greenslade KJ, Alam CA, Willoughby DA. Effects of diacerhein on granuloma induced cartilage breakdown in the mouse. *Osteoarthritis Cartilage*. 1998;6(1):19-23.
1037. Del Rosso M, Fibbi G, Magnelli L, et al. Modulation of urokinase receptors on human synovial cells and osteoarthritis condrocytes by diacetylrhein. *Internal Journal of Tissue Reactions*. 1990;12(2):91-100.

1038. Douni E, Sfrikakis PP, Haralambous S, Fernandes P, Kollias G. Attenuation of inflammatory polyarthritis in TNF transgenic mice by diacerein: comparative analysis with dexamethasone, methotrexate and anti-TNF protocols. *Arthritis Res Ther*. 2004;6(1):R65-R72.
1039. Bendele A, Bendele R, Hulman J, Swann B. A chronic study of the efficacy and toxicity of diacerhein treatment of guinea pigs with osteoarthritis. *The 2nd OARS International Congress Symposium: Research and Therapeutics in Osteoarthritis*. Nice, France; 1995.
1040. Smith GN, Jr., Myers SL, Brandt KD, Mickler EA, Albrecht ME. Diacerhein treatment reduces the severity of osteoarthritis in the canine cruciate-deficiency model of osteoarthritis. *Arthritis Rheum*. 1999;42(3):545-54.
1041. Brandt KD, Smith G, Kang SY, Myers S, O'Connor B, Albrecht M. Effects of diacerhein in an accelerated canine model of osteoarthritis. *Osteoarthritis Cartilage*. 1997;5(6):438-49.
1042. Petrillo M, Montrone F, Ardizzone S ea. Endoscopic evaluation of diacetylrhein-induced gastric mucosal lesions. *Curr Ther Res*. 1991;49(1):10-5.
1043. Dougados M, Nguyen M, Berdah L, Mazieres B, Vignon E, Lequesne M. Evaluation of the structure-modifying effects of diacerein in hip osteoarthritis: ECHODIAH, a three-year, placebo-controlled trial. Evaluation of the Chondromodulating Effect of Diacerein in OA of the Hip. *Arthritis Rheum*. 2001;44(11):2539-47.
1044. Mattara L. DAR "controlled" studies in treatment of osteoarthritis. *The LXXXVI Congress of the Italian National Society of Internal Medicine*. Sorrento, Italy; 1985.
1045. Mordini M, Nencioni C, Lavagni A, Camarri E. Diacerhein vs naproxen in coxogonarthrosis: double-blind randomized study. *The 27th Congress of the Italian Society of Rheumatology*. Montecatini, Italy; 1986.
1046. Rintelen B, Neumann K, Leeb BF. A meta-analysis of controlled clinical studies with diacerein in the treatment of osteoarthritis. *Arch Intern Med*. 2006;166(17):1899-906.
1047. Nguyen M, Dougados M, Berdah L, Amor B. Diacerhein in the treatment of osteoarthritis of the hip. *Arthritis Rheum*. 1994;37(4):529-36.
1048. Pavelka K, Trc T, Karpas K, et al. The efficacy and safety of diacerein in the treatment of painful osteoarthritis of the knee: a randomized, multicenter, double-blind, placebo-controlled study with primary end points at two months after the end of a three-month treatment period. *Arthritis Rheum*. 2007;56(12):4055-64.
1049. Mathieu P. Interleukin 1: Its role, its dosage, the difficulties in advances in arthritis. Results of a "pilot" study with diacerheine (ART 50) in gonarthrosis. *Rev Prat*. 1999;Suppl 13S15-8.
1050. Ascherl R. Double-blind, placebo-controlled multicentre, phase iii study of the efficacy and tolerability of diacerein (DA39) in patients with osteoarthritis of the knee. Koln, Germany: University of Lubeck; 1994.
1051. Tang F, Wu D, Lu Z, Huang F, Zhou Y. The efficacy and safety of diacerein in the treatment of painful osteoarthritis of the knee. *The 11th Asia Pacific League of Associations for Rheumatology (APLAR) congress, International Convention Center (ICC)*. Jeju, Korea; 2004.
1052. Schulz K. Clinical investigation of the efficacy and tolerance of idacetylrhein (DAR) in the treatment of osteoarthritis of the knee. Koln, Germany: Madaus AG; 1994.
1053. Louthrenoo W, Nilganuwong S, Aksaranugraha S. The efficacy and safety of diacerin in the treatment of painful osteoarthritis of the knee: a randomised, multicentre, double-blind, piroxicam-controlled, parallel-group, phase III study *The 11th Asia Pacific League of Associations for Rheumatology (APLAR) Congress, International Convention Center (ICC)*. Jeju, Korea; 2004.
1054. Fioravanti A, Marcolongo R. Therapeutic effectiveness of diacerhein (DAR) in arthrosis of knee and hip. *The Toscana Medicina Symposium on Diacereina*. Pisa, Italy; 1985.
1055. Portioli I. Naproxen-controlled study on the efficacy and tolerability of diacetylrhein in the functional manifestations of osteoarthritis of the knee and hip: a double-blind study versus naproxen. Reggio Emilia, Italy: Santa Maria Nuova Hospital; 1987.
1056. Mantia C. A controlled study of the efficacy and tolerability of diacetylrhein in the functional manifestations of osteoarthritis of the hip and the knee: a doubleblind study versus diclofenac. Palermo, Italy: Palermo Hospital; 1987.
1057. Pietrogrande V, Leonardi M, Pacchioni C. Results of a clinical trial with a new drug, diacerhein in arthrosic patients. *The LXXXVI Congress of the Italian national Society of Internal Medicine*. Sorrento, Italy; 1985.

1058. Pham T, Le Henanff A, Ravaud P, Dieppe P, Paolozzi L, Dougados M. Evaluation of the symptomatic and structural efficacy of a new hyaluronic acid compound, NRD101, in comparison with diacerein and placebo in a 1 year randomised controlled study in symptomatic knee osteoarthritis. *Ann Rheum Dis*. 2004;63(12):1611-7.
1059. Chantre P, Cappelaere A, Leblan D, Guedon D, Vandermander J, Fournie B. Efficacy and tolerance of Harpagophytum procumbens versus diacerhein in treatment of osteoarthritis. *Phytomedicine*. 2000;7(3):177-83.
1060. Leblan D, Chantre P, Fournie B. Harpagophytum procumbens in the treatment of knee and hip osteoarthritis. Four-month results of a prospective, multicenter, double-blind trial versus diacerhein. *Joint Bone Spine*. 2000;67(5):462-7.
1061. Acierno SP, D'Ambrosia C, Solomonow M, Baratta RV, D'Ambrosia RD. Electromyography and biomechanics of a dynamic knee brace for anterior cruciate ligament deficiency. *Orthopedics*. 1995;18(11):1101-7.
1062. Brouwer RW, van Raaij TM, Verhaar JA, Coene LN, Bierma-Zeinstra SM. Brace treatment for osteoarthritis of the knee: a prospective randomized multi-centre trial. *Osteoarthritis Cartilage*. 2006;14(8):777-83.
1063. Crenshaw SJ, Pollo FE, Calton EF. Effects of lateral-wedged insoles on kinetics at the knee. *Clin Orthop Relat Res*. 2000(375):185-92.
1064. Kartus J, Stener S, Kohler K, Sernert N, Eriksson BI, Karlsson J. Is bracing after anterior cruciate ligament reconstruction necessary? A 2-year follow-up of 78 consecutive patients rehabilitated with or without a brace. *Knee Surg Sports Traumatol Arthrosc*. 1997;5(3):157-61.
1065. Marans HJ, Jackson RW, Piccinin J, Silver RL, Kennedy DK. Functional testing of braces for anterior cruciate ligament-deficient knees. *Can J Surg*. 1991;34(2):167-72.
1066. Mishra DK, Daniel DM, Stone ML. The use of functional knee braces in the control of pathologic anterior knee laxity. *Clin Orthop Relat Res*. 1989(241):213-20.
1067. Nakajima K, Kakihana W, Nakagawa T, et al. Addition of an arch support improves the biomechanical effect of a laterally wedged insole. *Gait Posture*. 2009;29(2):208-13.
1068. Ramsey DK, Wretenberg PF, Lamontagne M, Nemeth G. Electromyographic and biomechanical analysis of anterior cruciate ligament deficiency and functional knee bracing. *Clin Biomech (Bristol, Avon)*. 2003;18(1):28-34.
1069. Rink PC, Scott RA, Lupo RL, Guest SJ. Team physician #7. A comparative study of functional bracing in the anterior cruciate deficient knee. *Orthop Rev*. 1989;18(6):719-27.
1070. Sasaki T, Yasuda K. Clinical evaluation of the treatment of osteoarthritic knees using a newly designed wedged insole. *Clin Orthop Relat Res*. 1987(221):181-7.
1071. Selfe J, Richards J, Thewlis D, Kilmurray S. The biomechanics of step descent under different treatment modalities used in patellofemoral pain. *Gait Posture*. 2008;27(2):258-63.
1072. Singer JC, Lamontagne M. The effect of functional knee brace design and hinge misalignment on lower limb joint mechanics. *Clin Biomech (Bristol, Avon)*. 2008;23(1):52-9.
1073. Tegner Y, Pettersson G, Lysholm J, Gillquist J. The effect of derotation braces on knee motion. *Acta Orthop Scand*. 1988;59(3):284-7.
1074. Wojtys EM, Huston LJ. "Custom-fit" versus "off-the-shelf" ACL functional braces. *Am J Knee Surg*. 2001;14(3):157-62.
1075. Wojtys EM, Kothari SU, Huston LJ. Anterior cruciate ligament functional brace use in sports. *Am J Sports Med*. 1996;24(4):539-46.
1076. Moller E, Forssblad M, Hansson L, Wange P, Weidenhielm L. Bracing versus nonbracing in rehabilitation after anterior cruciate ligament reconstruction: a randomized prospective study with 2-year follow-up. *Knee Surg Sports Traumatol Arthrosc*. 2001;9(2):102-8.
1077. Mikkelsen C, Cerulli G, Lorenzini M, Bergstrand G, Werner S. Can a post-operative brace in slight hyperextension prevent extension deficit after anterior cruciate ligament reconstruction? A prospective randomised study. *Knee Surg Sports Traumatol Arthrosc*. 2003;11(5):318-21.
1078. Gross KD, Hillstrom HJ. Noninvasive devices targeting the mechanics of osteoarthritis. *Rheum Dis Clin North Am*. 2008;34(3):755-76.
1079. Beaudreuil J, Bendaya S, Faucher M, et al. Clinical practice guidelines for rest orthosis, knee sleeves, and unloading knee braces in knee osteoarthritis. *Joint Bone Spine*. 2009;76(6):629-36.

1080. Pollo FE, Jackson RW. Knee bracing for unicompartmental osteoarthritis. *J Am Acad Orthop Surg*. 2006;14(1):5-11.
1081. Richmond J, Hunter D, Irrgang J, et al. Treatment of osteoarthritis of the knee (nonarthroplasty). *J Am Acad Orthop Surg*. 2009;17(9):591-600.
1082. Lunsford T, Lunsford B, Greenfield J, Ross S. Response of eight knee orthoses to valgus, varus and axial rotation loads. *Journal of prosthetics and orthotics*. 1990;2(4):274-88
1083. Butler PB, Evans GA, Rose GK, Patrick JH. A review of selected knee orthoses. *Br J Rheumatol*. 1983;22(2):109-20.
1084. Vertullo C. Management of the osteoarthritic knee. New advances in nonoperative therapy. *Aust Fam Physician*. 2001;30(9):853-7.
1085. Chew KT, Lew HL, Date E, Fredericson M. Current evidence and clinical applications of therapeutic knee braces. *Am J Phys Med Rehabil*. 2007;86(8):678-86.
1086. Sitler M, Ryan J, Hopkinson W, et al. The efficacy of a prophylactic knee brace to reduce knee injuries in football. A prospective, randomized study at West Point. *Am J Sports Med*. 1990;18(3):310-5.
1087. Requa RK, Garrick JG. Clinical significance and evaluation of prophylactic knee brace studies in football. *Clin Sports Med*. 1990;9(4):853-69.
1088. Pietrosimone BG, Grindstaff TL, Linens SW, Uczekaj E, Hertel J. A systematic review of prophylactic braces in the prevention of knee ligament injuries in collegiate football players. *J Athl Train*. 2008;43(4):409-15.
1089. Rishiraj N, Taunton JE, Lloyd-Smith R, Woollard R, Regan W, Clement DB. The potential role of prophylactic/functional knee bracing in preventing knee ligament injury. *Sports Med*. 2009;39(11):937-60.
1090. Najibi S, Albright JP. The use of knee braces, part 1: Prophylactic knee braces in contact sports. *Am J Sports Med*. 2005;33(4):602-11.
1091. Baker BE. The effect of bracing on the collateral ligaments of the knee. *Clin Sports Med*. 1990;9(4):843-51.
1092. Barrios JA, Crenshaw JR, Royer TD, Davis IS. Walking shoes and laterally wedged orthoses in the clinical management of medial tibiofemoral osteoarthritis: a one-year prospective controlled trial. *Knee*. 2009;16(2):136-42.
1093. Maillefert JF, Hudry C, Baron G, et al. Laterally elevated wedged insoles in the treatment of medial knee osteoarthritis: a prospective randomized controlled study. *Osteoarthritis Cartilage*. 2001;9(8):738-45.
1094. van Raaij T, Reijman M, Brouwer RW, Bierma-Zeinstra SM, Verhaar JA. Medial knee osteoarthritis treated by insoles or braces: a randomized trial. *Clin Orthop Relat Res*. 2010;468(7):1926-32.
1095. Kirkley A, Webster-Bogaert S, Litchfield R, et al. The effect of bracing on varus gonarthrosis. *J Bone Joint Surg Am*. 1999;81(4):539-48.
1096. Draganich L, Reider B, Rimington T, Piotrowski G, Mallik K, Nasson S. The effectiveness of self-adjustable custom and off-the-shelf bracing in the treatment of varus gonarthrosis. *J Bone Joint Surg Am*. 2006;88(12):2645-52.
1097. Richards JD, Sanchez-Ballester J, Jones RK, Darke N, Livingstone BN. A comparison of knee braces during walking for the treatment of osteoarthritis of the medial compartment of the knee. *J Bone Joint Surg Br*. 2005;87(7):937-9.
1098. Pajareya K, Chadchavalpanichaya N, Timdang S. Effectiveness of an elastic knee sleeve for patients with knee osteoarthritis: a randomized single-blinded controlled trial. *J Med Assoc Thai*. 2003;86(6):535-42.
1099. Chuang SH, Huang MH, Chen TW, Weng MC, Liu CW, Chen CH. Effect of knee sleeve on static and dynamic balance in patients with knee osteoarthritis. *Kaohsiung J Med Sci*. 2007;23(8):405-11.
1100. Zenios M, Wykes P, Johnson DS, Clayson AD, Kay P. The use of knee splints after total knee replacements. *Knee*. 2002;9(3):225-8.
1101. Horton TC, Jackson R, Mohan N, Hambidge JE. Is routine splintage following primary total knee replacement necessary? A prospective randomised trial. *Knee*. 2002;9(3):229-31.
1102. Brouwer RW, Jakma TS, Verhagen AP, Verhaar JA, Bierma-Zeinstra SM. Braces and orthoses for treating osteoarthritis of the knee. *Cochrane Database Syst Rev*. 2005(1):CD004020.
1103. Toda Y, Segal N. Usefulness of an insole with subtalar strapping for analgesia in patients with medial compartment osteoarthritis of the knee. *Arthritis Rheum*. 2002;47(5):468-73.
1104. Toda Y, Segal N, Kato A, Yamamoto S, Irie M. Effect of a novel insole on the subtalar joint of patients with medial compartment osteoarthritis of the knee. *J Rheumatol*. 2001;28(12):2705-10.

1105. Toda Y, Tsukimura N. A 2-year follow-up of a study to compare the efficacy of lateral wedged insoles with subtalar strapping and in-shoe lateral wedged insoles in patients with varus deformity osteoarthritis of the knee. *Osteoarthritis Cartilage*. 2006;14(3):231-7.
1106. Toda Y, Tsukimura N, Segal N. An optimal duration of daily wear for an insole with subtalar strapping in patients with varus deformity osteoarthritis of the knee. *Osteoarthritis Cartilage*. 2005;13(4):353-60.
1107. Rodrigues PT, Ferreira AF, Pereira RM, Bonfa E, Borba EF, Fuller R. Effectiveness of medial-wedge insole treatment for valgus knee osteoarthritis. *Arthritis Rheum*. 2008;59(5):603-8.
1108. Tohyama H, Yasuda K, Kaneda K. Treatment of osteoarthritis of the knee with heel wedges. *Int Orthop*. 1991;15(1):31-3.
1109. Reilly KA, Barker KL, Shamley D. A systematic review of lateral wedge orthotics--how useful are they in the management of medial compartment osteoarthritis? *Knee*. 2006;13(3):177-83.
1110. Gelis A, Coudeyre E, Hudry C, Pelissier J, Revel M, Rannou F. Is there an evidence-based efficacy for the use of foot orthotics in knee and hip osteoarthritis? Elaboration of French clinical practice guidelines. *Joint Bone Spine*. 2008;75(6):714-20.
1111. Krohn K. Footwear alterations and bracing as treatments for knee osteoarthritis. *Curr Opin Rheumatol*. 2005;17(5):653-6.
1112. Marks R, Penton L. Are foot orthotics efficacious for treating painful medial compartment knee osteoarthritis? A review of the literature. *Int J Clin Pract*. 2004;58(1):49-57.
1113. Hinman RS, Bennell KL. Advances in insoles and shoes for knee osteoarthritis. *Curr Opin Rheumatol*. 2009;21(2):164-70.
1114. Hinman RS, Bowles KA, Bennell KL. Laterally wedged insoles in knee osteoarthritis: do biomechanical effects decline after one month of wear? *BMC Musculoskelet Disord*. 2009;10:146.
1115. Toda Y, Tsukimura N, Kato A. The effects of different elevations of laterally wedged insoles with subtalar strapping on medial compartment osteoarthritis of the knee. *Arch Phys Med Rehabil*. 2004;85(4):673-7.
1116. Baker K, Goggins J, Xie H, et al. A randomized crossover trial of a wedged insole for treatment of knee osteoarthritis. *Arthritis Rheum*. 2007;56(4):1198-203.
1117. Pham T, Maillfert JF, Hudry C, et al. Laterally elevated wedged insoles in the treatment of medial knee osteoarthritis. A two-year prospective randomized controlled study. *Osteoarthritis Cartilage*. 2004;12(1):46-55.
1118. Trotter LC, Pierrynowski MR. Changes in gait economy between full-contact custom-made foot orthoses and prefabricated inserts in patients with musculoskeletal pain: a randomized clinical trial. *J Am Podiatr Med Assoc*. 2008;98(6):429-35.
1119. Berry H. Controlled trial of a knee support ("Genustrain") in patients with osteoarthritis of the knee. *Eur J Rheumatol Inflamm*. 1992;12(3):30-4.
1120. Horlick S, Loomer RL. Valgus Knee Bracing for medical gonarthrosis. *Clin J Sport Med*. 1993;3(4):251-5.
1121. Hoenig H, Pieper C, Branch LG, Cohen HJ. Effect of motorized scooters on physical performance and mobility: a randomized clinical trial. *Arch Phys Med Rehabil*. 2007;88(3):279-86.
1122. Lin VW, Hsiao I, Kingery WS. High intensity magnetic stimulation over the lumbosacral spine evokes antinociception in rats. *Clin Neurophysiol*. 2002;113(7):1006-12.
1123. Bassett C. Beneficial effects of electromagnetic fields. *J Cell Biochem*. 1993;51:387-93.
1124. Pittler MH, Brown EM, Ernst E. Static magnets for reducing pain: systematic review and meta-analysis of randomized trials. *CMAJ*. 2007;177(7):736-42.
1125. Eccles NK. A critical review of randomized controlled trials of static magnets for pain relief. *J Altern Complement Med*. 2005;11(3):495-509.
1126. Segal NA, Toda Y, Huston J, et al. Two configurations of static magnetic fields for treating rheumatoid arthritis of the knee: a double-blind clinical trial. *Arch Phys Med Rehabil*. 2001;82(10):1453-60.
1127. Wolsko PM, Eisenberg DM, Simon LS, et al. Double-blind placebo-controlled trial of static magnets for the treatment of osteoarthritis of the knee: results of a pilot study. *Altern Ther Health Med*. 2004;10(2):36-43.
1128. Harlow T, Greaves C, White A, Brown L, Hart A, Ernst E. Randomised controlled trial of magnetic bracelets for relieving pain in osteoarthritis of the hip and knee. *Bmj*. 2004;329(7480):1450-4.
1129. Chen CY, Chen CL, Hsu SC, Chou SW, Wang KC. Effect of magnetic knee wrap on quadriceps strength in patients with symptomatic knee osteoarthritis. *Arch Phys Med Rehabil*. 2008;89(12):2258-64.

1130. Jacobson JI, Gorman R, Yamanashi WS, Saxena BB, Clayton L. Low-amplitude, extremely low frequency magnetic fields for the treatment of osteoarthritic knees: a double-blind clinical study. *Altern Ther Health Med*. 2001;7(5):54-64, 6-9.
1131. Hinman MR, Ford J, Heyl H. Effects of static magnets on chronic knee pain and physical function: a double-blind study. *Altern Ther Health Med*. 2002;8(4):50-5.
1132. McCarthy CJ, Callaghan MJ, Oldham JA. Pulsed electromagnetic energy treatment offers no clinical benefit in reducing the pain of knee osteoarthritis: a systematic review. *BMC Musculoskelet Disord*. 2006;751.
1133. Trock DH, Bollet AJ, Dyer RH, Jr., Fielding LP, Miner WK, Markoll R. A double-blind trial of the clinical effects of pulsed electromagnetic fields in osteoarthritis. *J Rheumatol*. 1993;20(3):456-60.
1134. Trock DH, Bollet AJ, Markoll R. The effect of pulsed electromagnetic fields in the treatment of osteoarthritis of the knee and cervical spine. Report of randomized, double blind, placebo controlled trials. *J Rheumatol*. 1994;21(10):1903-11.
1135. Thamsborg G, Florescu A, Oturai P, Fallentin E, Tritsarlis K, Dissing S. Treatment of knee osteoarthritis with pulsed electromagnetic fields: a randomized, double-blind, placebo-controlled study. *Osteoarthritis Cartilage*. 2005;13(7):575-81.
1136. Gremion G, Gaillard D, Leyvraz PF, Jolles BM. Effect of biomagnetic therapy versus physiotherapy for treatment of knee osteoarthritis: a randomized controlled trial. *J Rehabil Med*. 2009;41(13):1090-5.
1137. Ay S, Evcik D. The effects of pulsed electromagnetic fields in the treatment of knee osteoarthritis: a randomized, placebo-controlled trial. *Rheumatol Int*. 2009;29(6):663-6.
1138. Zizic TM, Hoffman KC, Holt PA, et al. The treatment of osteoarthritis of the knee with pulsed electrical stimulation. *J Rheumatol*. 1995;22(9):1757-61.
1139. Pipitone N, Scott DL. Magnetic pulse treatment for knee osteoarthritis: a randomised, double-blind, placebo-controlled study. *Curr Med Res Opin*. 2001;17(3):190-6.
1140. Benazzo F, Zanon G, Pederzini L, et al. Effects of biophysical stimulation in patients undergoing arthroscopic reconstruction of anterior cruciate ligament: prospective, randomized and double blind study. *Knee Surg Sports Traumatol Arthrosc*. 2008;16(6):595-601.
1141. Zorzi C, Dall'Oca C, Cadossi R, Setti S. Effects of pulsed electromagnetic fields on patients' recovery after arthroscopic surgery: prospective, randomized and double-blind study. *Knee Surg Sports Traumatol Arthrosc*. 2007;15(7):830-4.
1142. Grana WA. Physical agents in musculoskeletal problems: heat and cold therapy modalities. *Instr Course Lect*. 1993;42439-42.
1143. Michlovitz S. *Thermal Agents in Rehabilitation*. Philadelphia: FA Davis; 1996.
1144. Melzack R, Jeans ME, Stratford JG, Monks RC. Ice massage and transcutaneous electrical stimulation: comparison of treatment for low-back pain. *Pain*. 1980;9(2):209-17.
1145. Nadler SF. Nonpharmacologic management of pain. *J Am Osteopath Assoc*. 2004;104(11 Suppl 8):S6-12.
1146. Konrath GA, Lock T, Goitz HT, Scheidler J. The use of cold therapy after anterior cruciate ligament reconstruction. A prospective, randomized study and literature review. *Am J Sports Med*. 1996;24(5):629-33.
1147. Dervin GF, Taylor DE, Keene GC. Effects of cold and compression dressings on early postoperative outcomes for the arthroscopic anterior cruciate ligament reconstruction patient. *J Orthop Sports Phys Ther*. 1998;27(6):403-6.
1148. Barber FA, McGuire DA, Click S. Continuous-flow cold therapy for outpatient anterior cruciate ligament reconstruction. *Arthroscopy*. 1998;14(2):130-5.
1149. Schroder D, Passler HH. Combination of cold and compression after knee surgery. A prospective randomized study. *Knee Surg Sports Traumatol Arthrosc*. 1994;2(3):158-65.
1150. Smith J, Stevens J, Taylor M, Tibbey J. A randomized, controlled trial comparing compression bandaging and cold therapy in postoperative total knee replacement surgery. *Orthop Nurs*. 2002;21(2):61-6.
1151. Woolf SK, Barfield WR, Merrill KD, McBryde AM, Jr. Comparison of a continuous temperature-controlled cryotherapy device to a simple icing regimen following outpatient knee arthroscopy. *J Knee Surg*. 2008;21(1):15-9.
1152. Holmstrom A, Hardin BC. Cryo/Cuff compared to epidural anesthesia after knee unicompartmental arthroplasty: a prospective, randomized and controlled study of 60 patients with a 6-week follow-up. *J Arthroplasty*. 2005;20(3):316-21.

1153. Raynor MC, Pietrobon R, Guller U, Higgins LD. Cryotherapy after ACL reconstruction: a meta-analysis. *J Knee Surg*. 2005;18(2):123-9.
1154. Gibbons CE, Solan MC, Ricketts DM, Patterson M. Cryotherapy compared with Robert Jones bandage after total knee replacement: a prospective randomized trial. *Int Orthop*. 2001;25(4):250-2.
1155. Ivey M, Johnston RV, Uchida T. Cryotherapy for postoperative pain relief following knee arthroplasty. *J Arthroplasty*. 1994;9(3):285-90.
1156. Saito N, Horiuchi H, Kobayashi S, Nawata M, Takaoka K. Continuous local cooling for pain relief following total hip arthroplasty. *J Arthroplasty*. 2004;19(3):334-7.
1157. Lin YH. Effects of thermal therapy in improving the passive range of knee motion: comparison of cold and superficial heat applications. *Clin Rehabil*. 2003;17(6):618-23.
1158. Scarcella JB, Cohn BT. The effect of cold therapy on the postoperative course of total hip and knee arthroplasty patients. *Am J Orthop (Belle Mead NJ)*. 1995;24(11):847-52.
1159. Vasudevan SV. Physical rehabilitation in managing pain. *Pain: Clinical Updates*. 1997;V.
1160. Mazzuca S, Page, MC, Meldrum RD, Brandt KD, Petty-Saphon S. Pilot study of the effects of a heat-retaining knee sleeve on joint pain, stiffness, and function in patients with knee osteoarthritis. *Arthritis Care Res*. 2004;51(5):716-21.
1161. Rutjes AW, Nuesch E, Sterchi R, Juni P. Therapeutic ultrasound for osteoarthritis of the knee or hip. *Cochrane Database Syst Rev*. 2010(1):CD003132.
1162. Reed BV, Ashikaga T, Fleming BC, Zimny NJ. Effects of ultrasound and stretch on knee ligament extensibility. *J Orthop Sports Phys Ther*. 2000;30(6):341-7.
1163. Huang MH, Lin YS, Lee CL, Yang RC. Use of ultrasound to increase effectiveness of isokinetic exercise for knee osteoarthritis. *Arch Phys Med Rehabil*. 2005;86(8):1545-51.
1164. Ozgonenel L, Aytekin E, Durmusoglu G. A double-blind trial of clinical effects of therapeutic ultrasound in knee osteoarthritis. *Ultrasound Med Biol*. 2009;35(1):44-9.
1165. Falconer J, Hayes KW, Chang RW. Effect of ultrasound on mobility in osteoarthritis of the knee. A randomized clinical trial. *Arthritis Care Res*. 1992;5(1):29-35.
1166. Tsumaki N, Kakiuchi M, Sasaki J, Ochi T, Yoshikawa H. Low-intensity pulsed ultrasound accelerates maturation of callus in patients treated with opening-wedge high tibial osteotomy by hemicallotaxis. *J Bone Joint Surg Am*. 2004;86-A(11):2399-405.
1167. Kozanoglu E, Basaran S, Guzel R, Guler-Uysal F. Short term efficacy of ibuprofen phonophoresis versus continuous ultrasound therapy in knee osteoarthritis. *Swiss Med Wkly*. 2003;133(23-24):333-8.
1168. Perlman AI, Sabina A, Williams AL, Njike VY, Katz DL. Massage therapy for osteoarthritis of the knee: a randomized controlled trial. *Arch Intern Med*. 2006;166(22):2533-8.
1169. Yip YB, Tam AC. An experimental study on the effectiveness of massage with aromatic ginger and orange essential oil for moderate-to-severe knee pain among the elderly in Hong Kong. *Complement Ther Med*. 2008;16(3):131-8.
1170. Melzack R, Vetere P, Finch L. Transcutaneous electrical nerve stimulation for low back pain. A comparison of TENS and massage for pain and range of motion. *Phys Ther*. 1983;63(4):489-93.
1171. Preyde M. Effectiveness of massage therapy for subacute low-back pain: a randomized controlled trial. *CMAJ*. 2000;162(13):1815-20.
1172. Kalauokalani D, Cherkin DC, Sherman KJ, Koepsell TD, Deyo RA. Lessons from a trial of acupuncture and massage for low back pain: patient expectations and treatment effects. *Spine (Phila Pa 1976)*. 2001;26(13):1418-24.
1173. Poole H, Glenn S, Murphy P. A randomised controlled study of reflexology for the management of chronic low back pain. *Eur J Pain*. 2007;11(8):878-87.
1174. Usichenko TI, Dinse M, Hermsen M, Witstruck T, Pavlovic D, Lehmann C. Auricular acupuncture for pain relief after total hip arthroplasty - a randomized controlled study. *Pain*. 2005;114(3):320-7.
1175. Ezzo J, Hadhazy V, Birch S, et al. Acupuncture for osteoarthritis of the knee: a systematic review. *Arthritis Rheum*. 2001;44(4):819-25.
1176. Andersson HI, Ejlertsson G, Leden I, Schersten B. Impact of chronic pain on health care seeking, self care, and medication. Results from a population-based Swedish study. *J Epidemiol Community Health*. 1999;53(8):503-9.

1177. Yurtkuran M, Kocagil T. TENS, electroacupuncture and ice massage: comparison of treatment for osteoarthritis of the knee. *Am J Acupunct*. 1999;27(3-4):133-40.
1178. Ng MM, Leung MC, Poon DM. The effects of electro-acupuncture and transcutaneous electrical nerve stimulation on patients with painful osteoarthritic knees: a randomized controlled trial with follow-up evaluation. *J Altern Complement Med*. 2003;9(5):641-9.
1179. Ahsin S, Saleem S, Bhatti AM, Iles RK, Aslam M. Clinical and endocrinological changes after electro-acupuncture treatment in patients with osteoarthritis of the knee. *Pain*. 2009;147(1-3):60-6.
1180. Baldry P. Superficial versus deep dry needling. *Acupunct Med*. 2002;20(2-3):78-81.
1181. Huguenin L, Brukner PD, McCrory P, Smith P, Wajswelner H, Bennell K. Effect of dry needling of gluteal muscles on straight leg raise: a randomised, placebo controlled, double blind trial. *Br J Sports Med*. 2005;39(2):84-90.
1182. Erqing D, Haiying L. One hundred and eighty-nine cases of acute articular soft tissue injury treated by blood-letting puncture with plum-blossom needle and cupping. 2005;25(2):104-5.
1183. MacPherson H, Mercer SW, Scullion T, Thomas KJ. Empathy, enablement, and outcome: an exploratory study on acupuncture patients' perceptions. *J Altern Complement Med*. 2003;9(6):869-76.
1184. Brinkhaus B, Witt CM, Jena S, et al. Interventions and physician characteristics in a randomized multicenter trial of acupuncture in patients with low-back pain. *J Altern Complement Med*. 2006;12(7):649-57.
1185. Haake M, Muller HH, Schade-Brittinger C, et al. German Acupuncture Trials (GERAC) for chronic low back pain: randomized, multicenter, blinded, parallel-group trial with 3 groups. *Arch Intern Med*. 2007;167(17):1892-8.
1186. Leibing E, Leonhardt U, Koster G, et al. Acupuncture treatment of chronic low-back pain -- a randomized, blinded, placebo-controlled trial with 9-month follow-up. *Pain*. 2002;96(1-2):189-96.
1187. Haslam R. A comparison of acupuncture with advice and exercises on the symptomatic treatment of osteoarthritis of the hip--a randomised controlled trial. *Acupunct Med*. 2001;19(1):19-26.
1188. Fink MG, Kunsebeck H, Wipperman B, Gehrke A. Non-specific effects of traditional Chinese acupuncture in osteoarthritis of the hip. *Complement Ther Med*. 2001;9(2):82-9.
1189. Scharf HP, Mansmann U, Streitberger K, et al. Acupuncture and knee osteoarthritis: a three-armed randomized trial. *Ann Intern Med*. 2006;145(1):12-20.
1190. Takeda W, Wessel J. Acupuncture for the treatment of pain of osteoarthritic knees. *Arthritis Care Res*. 1994;7(3):118-22.
1191. Tillu A, Roberts C, Tillu S. Unilateral versus bilateral acupuncture on knee function in advanced osteoarthritis of the knee--a prospective randomised trial. *Acupunct Med*. 2001;19(1):15-8.
1192. Witt CM, Jena S, Brinkhaus B, Liecker B, Wegscheider K, Willich SN. Acupuncture in patients with osteoarthritis of the knee or hip: a randomized, controlled trial with an additional nonrandomized arm. *Arthritis Rheum*. 2006;54(11):3485-93.
1193. Christensen BV, Iuhl IU, Vilbek H, Bulow HH, Dreijer NC, Rasmussen HF. Acupuncture treatment of severe knee osteoarthrosis. A long-term study. *Acta Anaesthesiol Scand*. 1992;36(6):519-25.
1194. Petrou P, Winkler V, Genti G, Balint G. Double-blind trial to evaluate the effect of acupuncture treatment on knee osteoarthrosis. *Scand J Acupunct*. 1988;3112-5.
1195. Molsberger A, Bowing G, Jensen KU, Lorek M. [Acupuncture treatment for the relief of gonarthrosis pain-a controlled clinical trial.]. *Schmerz*. 1994;8(1):37-42.
1196. Berman BM, Lao L, Langenberg P, Lee WL, Gilpin AM, Hochberg MC. Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. *Ann Intern Med*. 2004;141(12):901-10.
1197. Berman BM, Singh BB, Lao L, et al. A randomized trial of acupuncture as an adjunctive therapy in osteoarthritis of the knee. *Rheumatology (Oxford)*. 1999;38(4):346-54.
1198. Vas J, Mendez C, Perea-Milla E, et al. Acupuncture as a complementary therapy to the pharmacological treatment of osteoarthritis of the knee: randomised controlled trial. *Bmj*. 2004;329(7476):1216.
1199. Ammer K, Petschnig R. [Comparison of the effectiveness of acupuncture and physical therapy in ambulatory patients with gonarthrosis]. *Wien Med Wochenschr*. 1988;138(22):566-9.
1200. Jia J, al. e. Acupuncture combined with function exercise for the elder patients with knee osteoarthritis. *Chin J Clin Rehab*. 2005;918-9.

1201. Sangdee C, Teekachunhatean S, Sananpanich K, et al. Electroacupuncture versus diclofenac in symptomatic treatment of osteoarthritis of the knee: a randomized controlled trial. *BMC Complement Altern Med*. 2002;23.
1202. Tukmachi E, Jubb R, Dempsey E, Jones P. The effect of acupuncture on the symptoms of knee osteoarthritis--an open randomised controlled study. *Acupunct Med*. 2004;22(1):14-22.
1203. Kim EJ, Jang MK, Yoon EH, et al. Efficacy of pharmacopuncture using root bark of *Ulmus davidiana* Planch in patients with knee osteoarthritis: a double-blind randomized controlled trial. *J Acupunct Meridian Stud*. 2010;3(1):16-23.
1204. Nejrup K, Olivarius Nde F, Jacobsen JL, Siersma V. Randomised controlled trial of extraarticular gold bead implantation for treatment of knee osteoarthritis: a pilot study. *Clin Rheumatol*. 2008;27(11):1363-9.
1205. Usichenko TI, Kuchling S, Witstruck T, et al. Auricular acupuncture for pain relief after ambulatory knee surgery: a randomized trial. *CMAJ*. 2007;176(2):179-83.
1206. Usichenko TI, Dinse M, Lysenyuk VP, Wendt M, Pavlovic D, Lehmann C. Auricular acupuncture reduces intraoperative fentanyl requirement during hip arthroplasty--a randomized double-blinded study. *Acupunct Electrother Res*. 2006;31(3-4):213-21.
1207. Jubb RW, Tukmachi ES, Jones PW, Dempsey E, Waterhouse L, Brailsford S. A blinded randomised trial of acupuncture (manual and electroacupuncture) compared with a non-penetrating sham for the symptoms of osteoarthritis of the knee. *Acupunct Med*. 2008;26(2):69-78.
1208. Naslund J, Naslund UB, Odenbring S, Lundeberg T. Sensory stimulation (acupuncture) for the treatment of idiopathic anterior knee pain. *J Rehabil Med*. 2002;34(5):231-8.
1209. Weiner DK, Rudy TE, Morone N, Glick R, Kwok CK. Efficacy of periosteal stimulation therapy for the treatment of osteoarthritis-associated chronic knee pain: an initial controlled clinical trial. *J Am Geriatr Soc*. 2007;55(10):1541-7.
1210. Manheimer E, Ezzo J, Hadhazy V, Berman B. Published reports of acupuncture trials showed important limitations. *J Clin Epidemiol*. 2006;59(2):107-13.
1211. Manheimer E, White A, Berman B, Forsy K, Ernst E. Meta-analysis: acupuncture for low back pain. *Ann Intern Med*. 2005;142(8):651-63.
1212. White P, Lewith G, Hopwood V, Prescott P. The placebo needle, is it a valid and convincing placebo for use in acupuncture trials? A randomised, single-blind, cross-over pilot trial. *Pain*. 2003;106(3):401-9.
1213. Boutron I, Tubach F, Giraudeau B, Ravaud P. Methodological differences in clinical trials evaluating nonpharmacological and pharmacological treatments of hip and knee osteoarthritis. *JAMA*. 2003;290(8):1062-70.
1214. Suarez-Almazor ME, Looney C, Liu Y, et al. A randomized controlled trial of acupuncture for osteoarthritis of the knee: effects of patient-provider communication. *Arthritis Care Res (Hoboken)*. 2010;62(9):1229-36.
1215. Stener-Victorin E, Kruse-Smidje C, Jung K. Comparison between electro-acupuncture and hydrotherapy, both in combination with patient education and patient education alone, on the symptomatic treatment of osteoarthritis of the hip. *Clin J Pain*. 2004;20(3):179-85.
1216. Foster NE, Thomas E, Barlas P, et al. Acupuncture as an adjunct to exercise based physiotherapy for osteoarthritis of the knee: randomised controlled trial. *Bmj*. 2007;335(7617):436.
1217. Witt C, Brinkhaus B, Jena S, et al. Acupuncture in patients with osteoarthritis of the knee: a randomised trial. *Lancet*. 2005;366(9480):136-43.
1218. Berman BM, Singh BB, Lao L, et al. A randomized trial of acupuncture as an adjunctive therapy in osteoarthritis of the knee. *Rheumatology*. 1999;38(4):346-54.
1219. Williamson L, Wyatt MR, Yein K, Melton JT. Severe knee osteoarthritis: a randomized controlled trial of acupuncture, physiotherapy (supervised exercise) and standard management for patients awaiting knee replacement. *Rheumatology (Oxford)*. 2007;46(9):1445-9.
1220. Lansdown H, Howard K, Brealey S, MacPherson H. Acupuncture for pain and osteoarthritis of the knee: a pilot study for an open parallel-arm randomised controlled trial. *BMC Musculoskelet Disord*. 2009;10:130.
1221. Reinhold T, Witt CM, Jena S, Brinkhaus B, Willich SN. Quality of life and cost-effectiveness of acupuncture treatment in patients with osteoarthritis pain. *Eur J Health Econ*. 2008;9(3):209-19.
1222. Tsang RC, Tsang PL, Ko CY, Kong BC, Lee WY, Yip HT. Effects of acupuncture and sham acupuncture in addition to physiotherapy in patients undergoing bilateral total knee arthroplasty--a randomized controlled trial. *Clin Rehabil*. 2007;21(8):719-28.

1223. Brantingham JW, Globe GA, Jensen ML, et al. A feasibility study comparing two chiropractic protocols in the treatment of patellofemoral pain syndrome. *J Manipulative Physiol Ther.* 2009;32(7):536-48.
1224. Cibulka MT, Delitto A. A comparison of two different methods to treat hip pain in runners. *J Orthop Sports Phys Ther.* 1993;17(4):172-6.
1225. Daluga D, Lombardi AV, Jr., Mallory TH, Vaughn BK. Knee manipulation following total knee arthroplasty. Analysis of prognostic variables. *J Arthroplasty.* 1991;6(2):119-28.
1226. Deyle GD, Henderson NE, Matekel RL, Ryder MG, Garber MB, Allison SC. Effectiveness of manual physical therapy and exercise in osteoarthritis of the knee. A randomized, controlled trial. *Ann Intern Med.* 2000;132(3):173-81.
1227. Eastwood NB. Manipulation for locked knee. *J R Coll Gen Pract.* 1978;28(189):219-20.
1228. Esler CN, Lock K, Harper WM, Gregg PJ. Manipulation of total knee replacements. Is the flexion gained retained? *J Bone Joint Surg Br.* 1999;81(1):27-9.
1229. Fitzsimmons SE, Vazquez EA, Bronson MJ. How to treat the stiff total knee arthroplasty?: a systematic review. *Clin Orthop Relat Res.* 2010;468(4):1096-106.
1230. Fox JL, Poss R. The role of manipulation following total knee replacement. *J Bone Joint Surg Am.* 1981;63(3):357-62.
1231. Hoskins W, McHardy A, Pollard H, Windsham R, Onley R. Chiropractic treatment of lower extremity conditions: a literature review. *J Manipulative Physiol Ther.* 2006;29(8):658-71.
1232. Magit D, Wolff A, Sutton K, Medvecky MJ. Arthrofibrosis of the knee. *J Am Acad Orthop Surg.* 2007;15(11):682-94.
1233. Maloney WJ. The stiff total knee arthroplasty: evaluation and management. *J Arthroplasty.* 2002;17(4 Suppl 1):71-3.
1234. Mook WR, Miller MD, Diduch DR, Hertel J, Boachie-Adjei Y, Hart JM. Multiple-ligament knee injuries: a systematic review of the timing of operative intervention and postoperative rehabilitation. *J Bone Joint Surg Am.* 2009;91(12):2946-57.
1235. Rowlands BW, Brantingham JW. The efficacy of patella mobilization in patients suffering from patellofemoral pain syndrome. *Journal of the Neuromusculoskeletal system.* 1999;7(4):142-9.
1236. Suter E, McMorland G, Herzog W, Bray R. Conservative lower back treatment reduces inhibition in knee-extensor muscles: a randomized controlled trial. *J Manipulative Physiol Ther.* 2000;23(2):76-80.
1237. Tucker M, Brantingham JW, Myburgh C. Relative effectiveness of a non-steroidal anti-inflammatory medication (Meloxicam) versus manipulation in the treatment of osteo-arthritis of the knee. *European Journal of Chiropractic.* 2003;50:163-83.
1238. Van Herck P, Vanhaecht K, Deneckere S, et al. Key interventions and outcomes in joint arthroplasty clinical pathways: a systematic review. *J Eval Clin Pract.* 2010;16(1):39-49.
1239. Pollard H, Ward G, Hoskins W, Hardy K. The effect of a manual therapy knee protocol on osteoarthritic knee pain: a randomised controlled trial. *J Can Chiropr Assoc.* 2008;52(4):229-42.
1240. Stakes NO, Myburgh C, Brantingham JW, Moyer RJ, Jensen M, Globe G. A prospective randomized clinical trial to determine efficacy of combined spinal manipulation and patella mobilization compared to patella mobilization alone in the conservative management of patellofemoral pain syndrome. *Journal of the American Chiropractic Association online.* 2006;43(7).
1241. Bennell KL, Hinman RS, Metcalf BR, et al. Efficacy of physiotherapy management of knee joint osteoarthritis: a randomised, double blind, placebo controlled trial. *Ann Rheum Dis.* 2005;64(6):906-12.
1242. Taylor K, Brantingham J. N INVESTIGATION INTO THE EFFECT OF EXERCISE COMBINED WITH PATELLA MOBILIZATION/MANIPULATION IN THE TREATMENT OF PATELLOFEMORAL PAIN SYNDROME: A RANDOMIZED, ASSESSOR-BLINDED, CONTROLLED CLINICAL PILOT TRIAL  
URL *Eur J Chiropr.* 2003;51(1):5-17.
1243. Hoskins W, Pollard H. The effect of a sports chiropractic manual therapy intervention on the prevention of back pain, hamstring and lower limb injuries in semi-elite Australian Rules footballers: a randomized controlled trial. *BMC Musculoskelet Disord.* 2010;1164.
1244. Keating EM, Ritter MA, Harty LD, et al. Manipulation after total knee arthroplasty. *J Bone Joint Surg Am.* 2007;89(2):282-6.
1245. Panni AS, Tartarone M, Patricola A, Paxton EW, Fithian DC. Long-term results of lateral retinacular release. *Arthroscopy.* 2005;21(5):526-31.

1246. Hart LE. Combination of manual physical therapy and exercises for osteoarthritis of the knee. *Clin J Sport Med*. 2000;10(4):305.
1247. Licciardone JC, Stoll ST, Cardarelli KM, Gamber RG, Swift JN, Jr., Winn WB. A randomized controlled trial of osteopathic manipulative treatment following knee or hip arthroplasty. *J Am Osteopath Assoc*. 2004;104(5):193-202.
1248. Namba RS, Inacio M. Early and late manipulation improve flexion after total knee arthroplasty. *J Arthroplasty*. 2007;22(6 Suppl 2):58-61.
1249. Pariente GM, Lombardi AV, Jr., Berend KR, Mallory TH, Adams JB. Manipulation with prolonged epidural analgesia for treatment of TKA complicated by arthrofibrosis. *Surg Technol Int*. 2006;15221-4.
1250. Fitz-Ritson D. Lasers and their therapeutic applications in chiropractic. *J Can Chiropr Assoc*. 2001;45(1):26-34.
1251. Simunovic Z, Ivankovich AD, Depolo A. Wound healing of animal and human body sport and traffic accident injuries using low-level laser therapy treatment: a randomized clinical study of seventy-four patients with control group. *J Clin Laser Med Surg*. 2000;18(2):67-73.
1252. Gur A, Cosut A, Sarac AJ, Cevik R, Nas K, Uyar A. Efficacy of different therapy regimes of low-power laser in painful osteoarthritis of the knee: a double-blind and randomized-controlled trial. *Lasers Surg Med*. 2003;33(5):330-8.
1253. Bjordal JM, Johnson MI, Lopes-Martins RA, Bogen B, Chow R, Ljunggren AE. Short-term efficacy of physical interventions in osteoarthritic knee pain. A systematic review and meta-analysis of randomised placebo-controlled trials. *BMC Musculoskelet Disord*. 2007;851.
1254. Bulow PM, Jensen H, Danneskiold-Samsøe B. Low power Ga-Al-As laser treatment of painful osteoarthritis of the knee. A double-blind placebo-controlled study. *Scand J Rehabil Med*. 1994;26(3):155-9.
1255. Hegedus B, Viharos L, Gervain M, Galfi M. The effect of low-level laser in knee osteoarthritis: a double-blind, randomized, placebo-controlled trial. *Photomed Laser Surg*. 2009;27(4):577-84.
1256. Tascioglu F, Armagan O, Tabak Y, Corapci I, Oner C. Low power laser treatment in patients with knee osteoarthritis. *Swiss Med Wkly*. 2004;134(17-18):254-8.
1257. Shen X, Zhao L, Ding G, et al. Effect of combined laser acupuncture on knee osteoarthritis: a pilot study. *Lasers Med Sci*. 2009;24(2):129-36.
1258. Montes-Molina R, Madronero-Agreda MA, Romojaro-Rodriguez AB, et al. Efficacy of interferential low-level laser therapy using two independent sources in the treatment of knee pain. *Photomed Laser Surg*. 2009;27(3):467-71.
1259. Brosseau L, Welch V, Wells G, et al. Low level laser therapy (Classes I, II and III) for treating osteoarthritis. *Cochrane Database Syst Rev*. 2004(3):CD002046.
1260. Rogvi-Hansen B, Ellitsgaard N, Funch M, Dall-Jensen M, Prieske J. Low level laser treatment of chondromalacia patellae. *Int Orthop*. 1991;15(4):359-61.
1261. Yurtkuran M, Alp A, Konur S, Ozcakir S, Bingol U. Laser acupuncture in knee osteoarthritis: a double-blind, randomized controlled study. *Photomed Laser Surg*. 2007;25(1):14-20.
1262. Rutjes AW, Nuesch E, Sterchi R, et al. Transcutaneous electrostimulation for osteoarthritis of the knee. *Cochrane Database Syst Rev*. 2009(4):CD002823.
1263. Kang RW, Lewis PB, Kramer A, Hayden JK, Cole BJ. Prospective randomized single-blinded controlled clinical trial of percutaneous neuromodulation pain therapy device versus sham for the osteoarthritic knee: a pilot study. *Orthopedics*. 2007;30(6):439-45.
1264. Garland D, Holt P, Harrington JT, Caldwell J, Zizic T, Cholewczynski J. A 3-month, randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of a highly optimized, capacitively coupled, pulsed electrical stimulator in patients with osteoarthritis of the knee. *Osteoarthritis Cartilage*. 2007;15(6):630-7.
1265. Ashburn MA, Stephen RL, Ackerman E, et al. Iontophoretic delivery of morphine for postoperative analgesia. *J Pain Symptom Manage*. 1992;7(1):27-33.
1266. El-Husseini T, El-Kawy S, Shalaby H, El-Sebai M. Microcurrent skin patches for postoperative pain control in total knee arthroplasty: a pilot study. *Int Orthop*. 2007;31(2):229-33.
1267. Jarit GJ, Mohr KJ, Waller R, Glousman RE. The effects of home interferential therapy on post-operative pain, edema, and range of motion of the knee. *Clin J Sport Med*. 2003;13(1):16-20.

1268. Li LC, Scudds RA. Iontophoresis: an overview of the mechanisms and clinical application. *Arthritis Care Res.* 1995;8(1):51-61.
1269. Callaghan MJ, Oldham JA. Electric muscle stimulation of the quadriceps in the treatment of patellofemoral pain. *Arch Phys Med Rehabil.* 2004;85(6):956-62.
1270. Bax L, Staes F, Verhagen A. Does neuromuscular electrical stimulation strengthen the quadriceps femoris? A systematic review of randomised controlled trials. *Sports Med.* 2005;35(3):191-212.
1271. Selkowitz D. Improvement in isometric strength of the quadriceps femoris muscle after training with electrical stimulation. *Phys Ther.* 1985;65:186-96.
1272. Hainaut K, Duchateau J. Neuromuscular electrical stimulation and voluntary exercise. *Sports Med.* 1992;14:100-13.
1273. Oldham JA HT, Petterson T, Smith GP, Rallis RC. Electrotherapeutic rehabilitation of the quadriceps in elderly osteoarthritic patients: a double blind assessment of patterned neuromuscular stimulation. *Clin Rehabil.* 1995;9(1):10-20.
1274. Callaghan M, Oldham JA, Winstanley J. A comparison of two types of electrical stimulation of the quadriceps in the treatment of patellofemoral pain syndrome. A pilot study. *Clin Rehabil.* 2001;15(6):637-46.
1275. Delitto A, Rose SJ, McKowen JM, Lehman RC, Thomas JA, Shively RA. Electrical stimulation versus voluntary exercise in strengthening thigh musculature after anterior cruciate ligament surgery. *Phys Ther.* 1988;68(5):660-3.
1276. Snyder-Mackler L, Delitto A, Bailey SL, Stralka SW. Strength of the quadriceps femoris muscle and functional recovery after reconstruction of the anterior cruciate ligament. A prospective, randomized clinical trial of electrical stimulation. *J Bone Joint Surg Am.* 1995;77(8):1166-73.
1277. Wigerstad-Lossing I, Grimby G, Jonsson T, Morelli B, Peterson L, Renstrom P. Effects of electrical muscle stimulation combined with voluntary contractions after knee ligament surgery. *Med Sci Sports Exerc.* 1988;20(1):93-8.
1278. Draper V, Ballard L. Electrical stimulation versus electromyographic biofeedback in the recovery of quadriceps femoris muscle function following anterior cruciate ligament surgery. *Phys Ther.* 1991;71(6):455-61; discussion 61-4.
1279. Snyder-Mackler L, Ladin Z, Schepsis AA, Young JC. Electrical stimulation of the thigh muscles after reconstruction of the anterior cruciate ligament. Effects of electrically elicited contraction of the quadriceps femoris and hamstring muscles on gait and on strength of the thigh muscles. *J Bone Joint Surg Am.* 1991;73(7):1025-36.
1280. Hortobagyi T, Lambert J, Scott K. Incomplete muscle activation after training with electromyostimulation. *Can J Appl Physiol.* 1998;23(3):261-70.
1281. Kubiak R, Whitman KM, Johnston RM. Changes in quadriceps femoris muscle strength using isometric exercise versus electrical stimulation. *J Orthop Sports Phys Ther.* 1987;8(11):537-41.
1282. Balogun J, Onilari OO, Akeju OA, Marzouk DK. High voltage electrical stimulation in the augmentation of muscle strength: effects of pulse frequency. *Arch Phys Med Rehabil.* 1993;74(9):910-6.
1283. Caggiano E, Emrey T, Shirley S, Craik RL. Effects of electrical stimulation or voluntary contraction for strengthening the quadriceps femoris muscles in an aged male population. *J Orthop Sports Phys Ther.* 1994;20(1):22-8.
1284. Laughman K, Youdas JW, Garrett TR, Chao EY. Strength changes in the normal quadriceps femoris muscle as a result of electrical stimulation. *Phys Ther.* 1983;63:494-9.
1285. Mohr T, Carlson B, Sulentic C, Landry R. Comparison of isometric exercise and high volt galvanic stimulation on quadriceps femoris muscle strength. *Phys Ther.* 1985;65(5):606-9.
1286. Maffiuletti N, Cometti G, Amiridis IG, Martin A, Pousson M, Chartard J-C. The effects of electromyostimulation training and basketball practice on muscle strength and jumping ability. *Int J Sports Med.* 2000;21:437-43.
1287. Currier D, Mann R. Muscular strength development by electrical stimulation in healthy individuals. *Phys Ther.* 1983;63:915-21.
1288. Fahey T, Harvey M, Schroeder RV, Ferguson F. Influence of sex differences and knee joint position on electrical stimulation-modulated strength increases. *Med Sci Sports Exerc.* 1985;17(1):144-7.

1289. Romero J, Sanford TL, Schroeder RV, Fahey TD. The effects of electrical stimulation of normal quadriceps on strength and girth. *Med Sci Sports Exerc.* 1982;14(3):194-7.
1290. Cheing GL, Hui-Chan CW. Would the addition of TENS to exercise training produce better physical performance outcomes in people with knee osteoarthritis than either intervention alone? *Clin Rehabil.* 2004;18(5):487-97.
1291. Adedoyin R, Olaogun M, Oyeyemi A. Transcutaneous electrical nerve stimulation and interferential current combined with exercise for the treatment of knee osteoarthritis: a randomised controlled trial. *Hong Kong Physiotherapy Journal.* 2005;2313-9
1292. Eriksson E, Haggmark T. Comparison of isometric muscle training and electrical stimulation supplementing isometric muscle training in the recovery after major knee ligament surgery. A preliminary report. *Am J Sports Med.* 1979;7(3):169-71.
1293. Gemignani G, Olivieri I, Ruju G, Pasero G. Transcutaneous electrical nerve stimulation in ankylosing spondylitis: a double-blind study. *Arthritis Rheum.* 1991;34(6):788-9.
1294. van Tulder MW, Koes B, Malmivaara A. Outcome of non-invasive treatment modalities on back pain: an evidence-based review. *Eur Spine J.* 2006;15 Suppl 1S64-81.
1295. Long DM. Fifteen years of transcutaneous electrical stimulation for pain control. *Stereotact Funct Neurosurg.* 1991;56(1):2-19.
1296. Khadilkar A, Milne S, Brosseau L, et al. Transcutaneous electrical nerve stimulation (TENS) for chronic low-back pain. *Cochrane Database Syst Rev.* 2005(3):CD003008.
1297. Shealy CN. Transcutaneous electrical nerve stimulation: the treatment of choice for pain and depression. *J Altern Complement Med.* 2003;9(5):619-23.
1298. Richardson RR, Arbit J, Siqueira EB, Zagar R. Transcutaneous electrical neurostimulation in functional pain. *Spine (Phila Pa 1976).* 1981;6(2):185-8.
1299. Rushton DN. Electrical stimulation in the treatment of pain. *Disabil Rehabil.* 2002;24(8):407-15.
1300. Burch FX, Tarro JN, Greenberg JJ, Carroll WJ. Evaluating the benefits of patterned stimulation in the treatment of osteoarthritis of the knee: a multi-center, randomized, single-blind, controlled study with an independent masked evaluator. *Osteoarthritis Cartilage.* 2008;16(8):865-72.
1301. Fargas-Babjak A, Rooney P, Gerecz E. Randomized trial of Codetron for pain control in osteoarthritis of the hip/knee. *Clin J Pain.* 1989;5(2):137-41.
1302. Smith MJ, Hutchins RC, Hehenberger D. Transcutaneous neural stimulation use in postoperative knee rehabilitation. *Am J Sports Med.* 1983;11(2):75-82.
1303. Cheing GL, Hui-Chan CW, Chan KM. Does four weeks of TENS and/or isometric exercise produce cumulative reduction of osteoarthritic knee pain? *Clin Rehabil.* 2002;16(7):749-60.
1304. Cheing GL, Tsui AY, Lo SK, Hui-Chan CW. Optimal stimulation duration of tens in the management of osteoarthritic knee pain. *J Rehabil Med.* 2003;35(2):62-8.
1305. Jensen H, Zesler R, Christensen T. Transcutaneous electrical nerve stimulation (TNS) for painful osteoarthrosis of the knee. *Int J Rehabil Res.* 1991;14(4):356-8.
1306. Anderson AF, Lipscomb AB. Analysis of rehabilitation techniques after anterior cruciate reconstruction. *Am J Sports Med.* 1989;17(2):154-60.
1307. Walker RH, Morris BA, Angulo DL, Schneider J, Colwell CW, Jr. Postoperative use of continuous passive motion, transcutaneous electrical nerve stimulation, and continuous cooling pad following total knee arthroplasty. *J Arthroplasty.* 1991;6(2):151-6.
1308. Alcidì L, Beneforti E, Maresca M, Santosuosso U, Zoppi M. Low power radiofrequency electromagnetic radiation for the treatment of pain due to osteoarthritis of the knee. *Reumatismo.* 2007;59(2):140-5.
1309. Breit R, Van der Wall H. Transcutaneous electrical nerve stimulation for postoperative pain relief after total knee arthroplasty. *J Arthroplasty.* 2004;19(1):45-8.
1310. Grimmer K. A controlled double blind study comparing the effects of strong Burst Mode TENS and High Rate TENS on painful osteoarthritic knees. *Australian Journal of Physiotherapy.* 1992;38(1):49-56.
1311. Paternostro-Sluga T, Fialka C, Alacamlioglu Y, Saradeth T, Fialka-Moser V. Neuromuscular electrical stimulation after anterior cruciate ligament surgery. *Clin Orthop Relat Res.* 1999(368):166-75.
1312. Lewis B, Lewis D, Cumming G. The comparative analgesic efficacy of transcutaneous electrical nerve stimulation and a non-steroidal anti-inflammatory drug for painful osteoarthritis. *Br J Rheumatol.* 1994;33(5):455-60.

1313. Lewis D, Lewis B, Sturrock RD. Transcutaneous electrical nerve stimulation in osteoarthritis: a therapeutic alternative? *Ann Rheum Dis*. 1984;43(1):47-9.
1314. Law PP, Cheing GL. Optimal stimulation frequency of transcutaneous electrical nerve stimulation on people with knee osteoarthritis. *J Rehabil Med*. 2004;36(5):220-5.
1315. Law PP, Cheing GL, Tsui AY. Does Transcutaneous Electrical Nerve Stimulation Improve the Physical Performance of People With Knee Osteoarthritis? *J Clin Rheumatol*. 2004;10(6):295-9.
1316. Itoh K, Hirota S, Katsumi Y, Ochi H, Kitakoji H. A pilot study on using acupuncture and transcutaneous electrical nerve stimulation (TENS) to treat knee osteoarthritis (OA). *Chin Med*. 2008;32.
1317. Taylor P, Hallett M, Flaherty L. Treatment of osteoarthritis of the knee with transcutaneous electrical nerve stimulation. *Pain*. 1981;11(2):233-40.
1318. Lone A, Wafai Z, Buth B, Wani T, Koul P, SH K. Analgesic efficacy of transcutaneous electrical nerve stimulation compared with diclofenac sodium in osteo-arthritis of the knee. *Physiotherapy*. 2003;89(8):478-85.
1319. Parker N, Tekdos D, Kesiktas N, Soy D. Comparison of the therapeutic efficacy of TENS versus intra-articular hyaluronic acid injection in patients with knee osteoarthritis: a prospective randomized study. *Adv Ther*. 2006;23(2):342-53.
1320. Raynauld JP, Buckland-Wright C, Ward R, et al. Safety and efficacy of long-term intraarticular steroid injections in osteoarthritis of the knee: a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum*. 2003;48(2):370-7.
1321. Gaffney K, Ledingham J, Perry JD. Intra-articular triamcinolone hexacetonide in knee osteoarthritis: factors influencing the clinical response. *Annals Of The Rheumatic Diseases*. 1995;54(5):379-81.
1322. Konai MS, Vilar Furtado RN, Dos Santos MF, Natour J. Monoarticular corticosteroid injection versus systemic administration in the treatment of rheumatoid arthritis patients: a randomized double-blind controlled study. *Clin Exp Rheumatol*. 2009;27(2):214-21.
1323. Weitoft T, Larsson A, Saxne T, Ronnblom L. Changes of cartilage and bone markers after intra-articular glucocorticoid treatment with and without postinjection rest in patients with rheumatoid arthritis. *Annals Of The Rheumatic Diseases*. 2005;64(12):1750-3.
1324. Weitoft T, Ronnblom L. Glucocorticoid resorption and influence on the hypothalamic-pituitary-adrenal axis after intra-articular treatment of the knee in resting and mobile patients. *Annals Of The Rheumatic Diseases*. 2006;65(7):955-7.
1325. Young L, Katrib A, Cuello C, et al. Effects of intraarticular glucocorticoids on macrophage infiltration and mediators of joint damage in osteoarthritis synovial membranes: findings in a double-blind, placebo-controlled study. *Arthritis Rheum*. 2001;44(2):343-50.
1326. Kongsgaard M, Kovanen V, Aagaard P, et al. Corticosteroid injections, eccentric decline squat training and heavy slow resistance training in patellar tendinopathy. *Scand J Med Sci Sports*. 2009;19(6):13p.
1327. Housner JA, Jacobson JA, Misko R. Sonographically guided percutaneous needle tenotomy for the treatment of chronic tendinosis. *J Ultrasound Med*. 2009;28(9):1187-92.
1328. McShane JM, Nazarian LN, Harwood MI. Sonographically guided percutaneous needle tenotomy for treatment of common extensor tendinosis in the elbow. *J Ultrasound Med*. 2006;25(10):1281-9.
1329. Testa V, Capasso G, Benazzo F, Maffulli N. Management of Achilles tendinopathy by ultrasound-guided percutaneous tenotomy. *Med Sci Sports Exerc*. 2002;34(4):573-80.
1330. Testa V, Capasso G, Maffulli N, Bifulco G. Ultrasound-guided percutaneous longitudinal tenotomy for the management of patellar tendinopathy. *Med Sci Sports Exerc*. 1999;31(11):1509-15.
1331. Arden NK, Reading IC, Jordan KM, et al. A randomised controlled trial of tidal irrigation vs corticosteroid injection in knee osteoarthritis: the KIVIS Study. *Osteoarthritis Cartilage*. 2008;16(6):733-9.
1332. Ravaud P, Moulinier L, Giraudeau B, et al. Effects of joint lavage and steroid injection in patients with osteoarthritis of the knee: results of a multicenter, randomized, controlled trial. *Arthritis Rheum*. 1999;42(3):475-82.
1333. van Oosterhout M, Sont JK, Bajema IM, Breedveld FC, van Laar JM. Comparison of efficacy of arthroscopic lavage plus administration of corticosteroids, arthroscopic lavage plus administration of placebo, and joint aspiration plus administration of corticosteroids in arthritis of the knee: A randomized controlled trial. *Arthritis Rheum*. 2006;55(6):964-70.

1334. Smith MD, Wetherall M, Darby T, et al. A randomized placebo-controlled trial of arthroscopic lavage versus lavage plus intra-articular corticosteroids in the management of symptomatic osteoarthritis of the knee. *Rheumatology (Oxford)*. 2003;42(12):1477-85.
1335. Frias G, Caracuel MA, Escudero A, et al. Assessment of the efficacy of joint lavage versus joint lavage plus corticoids in patients with osteoarthritis of the knee. *Curr Med Res Opin*. 2004;20(6):861-7.
1336. Jahangier ZN, Jacobs JW, Kraan MC, et al. Pretreatment macrophage infiltration of the synovium predicts the clinical effect of both radiation synovectomy and intra-articular glucocorticoids. *Annals Of The Rheumatic Diseases*. 2006;65(10):1286-92.
1337. Jahangier ZN, Jacobs JW, Lafeber FP, et al. Is radiation synovectomy for arthritis of the knee more effective than intraarticular treatment with glucocorticoids? Results of an eighteen-month, randomized, double-blind, placebo-controlled, crossover trial. *Arthritis Rheum*. 2005;52(11):3391-402.
1338. Wallen M, Gillies D. Intra-articular steroids and splints/rest for children with juvenile idiopathic arthritis and adults with rheumatoid arthritis. *Cochrane Database Syst Rev*. 2006(1):CD002824.
1339. Blyth T, Stirling A, Coote J, Land D, Hunter JA. Injection of the rheumatoid knee: does intra-articular methotrexate or rifampicin add to the benefits of triamcinolone hexacetonide? *Br J Rheumatol*. 1998;37(7):770-2.
1340. Goebel KM, Storck U. Effect of intra-articular orgotein versus a corticosteroid on rheumatoid arthritis of the knees. *Am J Med*. 1983;74(1):124-8.
1341. Hasso N, Maddison PJ, Breslin A. Intra-articular methotrexate in knee synovitis. *Rheumatology (Oxford)*. 2004;43(6):779-82.
1342. Bird HA, Ring EF, Daniel R, Bacon PA. Comparison of intra-articular methotrexate with intra-articular triamcinolone hexacetonide by thermography. *Curr Med Res Opin*. 1977;5(2):141-6.
1343. Kraan MC, Reece RJ, Barg EC, et al. Modulation of inflammation and metalloproteinase expression in synovial tissue by leflunomide and methotrexate in patients with active rheumatoid arthritis. Findings in a prospective, randomized, double-blind, parallel-design clinical trial in thirty-nine patients at two centers. *Arthritis Rheum*. 2000;43(8):1820-30.
1344. Urbach D, Berth A, Awiszus F. Effect of transcranial magnetic stimulation on voluntary activation in patients with quadriceps weakness. *Muscle Nerve*. 2005;32(2):164-9.
1345. Frizziero A, Giannotti E, Oliva F, Masiero S, Maffulli N. Autologous conditioned serum for the treatment of osteoarthritis and other possible applications in musculoskeletal disorders. *Br Med Bull*. 2013;105:169-84.
1346. Sanchez M, Fiz N, Azofra J, et al. A randomized clinical trial evaluating plasma rich in growth factors (PRGF-Endoret) versus hyaluronic acid in the short-term treatment of symptomatic knee osteoarthritis. *Arthroscopy*. 2012;28(8):1070-8.
1347. Filardo G, Kon E, Di Martino A, et al. Platelet-rich plasma vs hyaluronic acid to treat knee degenerative pathology: study design and preliminary results of a randomized controlled trial. *BMC Musculoskelet Disord*. 2012;13:229.
1348. Cerza F, Carni S, Carcangiu A, et al. Comparison between hyaluronic acid and platelet-rich plasma, intra-articular infiltration in the treatment of gonarthrosis. *Am J Sports Med*. 2012;40(12):2822-7.
1349. Patel S, Dhillon MS, Aggarwal S, Marwaha N, Jain A. Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial. *Am J Sports Med*. 2013;41(2):356-64.
1350. Miltner O, Schneider U, Siebert CH, Niedhart C, Niethard FU. Efficacy of intraarticular hyaluronic acid in patients with osteoarthritis—a prospective clinical trial. *Osteoarthritis Cartilage*. 2002;10(9):680-6.
1351. de Vos R, Weir A, van Schie H, et al. Platelet-rich plasma injection for chronic Achilles tendinopathy: a randomized controlled trial. *JAMA*. 2010;303(2):144-9.
1352. Sandrey MA. Autologous growth factor injections in chronic tendinopathy. *J Athl Train*. 2014;49(3):428-30.
1353. Vaquerizo V, Plasencia MA, Arribas I, et al. Comparison of intra-articular injections of plasma rich in growth factors (PRGF-Endoret) versus Durolane hyaluronic acid in the treatment of patients with symptomatic osteoarthritis: a randomized controlled trial. *Arthroscopy*. 2013;29(10):1635-43.
1354. Baltzer AW, Moser C, Jansen SA, Krauspe R. Autologous conditioned serum (Orthokine) is an effective treatment for knee osteoarthritis. *Osteoarthritis Cartilage*. 2009;17(2):152-60.
1355. Evanich JD, Evanich CJ, Wright MB, Rydlewicz JA. Efficacy of intraarticular hyaluronic acid injections in knee osteoarthritis. *Clin Orthop Relat Res*. 2001(390):173-81.

1356. Frizziero L, Govoni E, Bacchini P. Intra-articular hyaluronic acid in the treatment of osteoarthritis of the knee: clinical and morphological study. *Clin Exp Rheumatol*. 1998;16(4):441-9.
1357. Goorman SD, Watanabe TK, Miller EH, Perry C. Functional outcome in knee osteoarthritis after treatment with hylan G-F 20: a prospective study. *Arch Phys Med Rehabil*. 2000;81(4):479-83.
1358. Grecomoro G, Piccione F, Letizia G. Therapeutic synergism between hyaluronic acid and dexamethasone in the intra-articular treatment of osteoarthritis of the knee: a preliminary open study. *Curr Med Res Opin*. 1992;13(1):49-55.
1359. Lussier A, Cividino AA, McFarlane CA, Olszynski WP, Potashner WJ, De Medicis R. Viscosupplementation with hylan for the treatment of osteoarthritis: findings from clinical practice in Canada. *J Rheumatol*. 1996;23(9):1579-85.
1360. Wen DY. Intra-articular hyaluronic acid injections for knee osteoarthritis. *Am Fam Physician*. 2000;62(3):565-70, 72.
1361. Caglar-Yagci H, Unsal S, Yagci I, Dulgeroglu D, Ozel S. Safety and efficacy of ultrasound-guided intra-articular hylan G-F 20 injection in osteoarthritis of the hip: a pilot study. *Rheumatol Int*. 2005;25(5):341-4.
1362. Cefalu CA, Waddell DS. Viscosupplementation: treatment alternative for osteoarthritis of the knee. *Geriatrics*. 1999;54(10):51-4, 7.
1363. Petrella RJ. Hyaluronic acid for the treatment of knee osteoarthritis: long-term outcomes from a naturalistic primary care experience. *Am J Phys Med Rehabil*. 2005;84(4):278-83; quiz 84, 93.
1364. Tikiz C, Unlu Z, Sener A, Efe M, Tuzun C. Comparison of the efficacy of lower and higher molecular weight viscosupplementation in the treatment of hip osteoarthritis. *Clin Rheumatol*. 2005;24(3):244-50.
1365. Abate M, Pelotti P, De Amicis D, Di Iorio A, Galletti S, Salini V. Viscosupplementation with hyaluronic acid in hip osteoarthritis (a review). *Ups J Med Sci*. 2008;113(3):261-77.
1366. Aggarwal A, Sempowski IP. Hyaluronic acid injections for knee osteoarthritis. Systematic review of the literature. *Can Fam Physician*. 2004;50:249-56.
1367. Arrich J, Piribauer F, Mad P, Schmid D, Klaushofer K, Mullner M. Intra-articular hyaluronic acid for the treatment of osteoarthritis of the knee: systematic review and meta-analysis. *CMAJ*. 2005;172(8):1039-43.
1368. Kotz R, Kolarz G. Intra-articular hyaluronic acid: duration of effect and results of repeated treatment cycles. *Am J Orthop (Belle Mead NJ)*. 1999;28(11 Suppl):5-7.
1369. Modawal A, Ferrer M, Choi HK, Castle JA. Hyaluronic acid injections relieve knee pain. *J Fam Pract*. 2005;54(9):758-67.
1370. Reichenbach S, Blank S, Rutjes AW, et al. Hylan versus hyaluronic acid for osteoarthritis of the knee: a systematic review and meta-analysis. *Arthritis Rheum*. 2007;57(8):1410-8.
1371. Stitik TP, Blacksins MF, Stiskal DM, et al. Efficacy and safety of hyaluronan treatment in combination therapy with home exercise for knee osteoarthritis pain. *Arch Phys Med Rehabil*. 2007;88(2):135-41.
1372. Wang CT, Lin J, Chang CJ, Lin YT, Hou SM. Therapeutic effects of hyaluronic acid on osteoarthritis of the knee. A meta-analysis of randomized controlled trials. *J Bone Joint Surg Am*. 2004;86-A(3):538-45.
1373. Huskin JP, Vandekerckhove B, Delince P, et al. Multicentre, prospective, open study to evaluate the safety and efficacy of hylan G-F 20 in knee osteoarthritis subjects presenting with pain following arthroscopic meniscectomy. *Knee Surg Sports Traumatol Arthrosc*. 2008;16(8):747-52.
1374. Zietz PM, Selesnick H. The use of hylan G-F 20 after knee arthroscopy in an active patient population with knee osteoarthritis. *Arthroscopy*. 2008;24(4):416-22.
1375. Altman RD, Akermark C, Beaulieu AD, Schnitzer T. Efficacy and safety of a single intra-articular injection of non-animal stabilized hyaluronic acid (NASHA) in patients with osteoarthritis of the knee. *Osteoarthritis Cartilage*. 2004;12(8):642-9.
1376. Altman RD, Rosen JE, Bloch DA, Hatoum HT, Korner P. A double-blind, randomized, saline-controlled study of the efficacy and safety of EUFLEXXA for treatment of painful osteoarthritis of the knee, with an open-label safety extension (the FLEXX trial). *Semin Arthritis Rheum*. 2009;39(1):1-9.
1377. Brandt KD, Block JA, Michalski JP, Moreland LW, Caldwell JR, Lavin PT. Efficacy and safety of intraarticular sodium hyaluronate in knee osteoarthritis. ORTHOVISC Study Group. *Clin Orthop Relat Res*. 2001(385):130-43.
1378. DeCaria JE, Montero-Odasso M, Wolfe D, Chesworth BM, Petrella RJ. The effect of intra-articular hyaluronic acid treatment on gait velocity in older knee osteoarthritis patients: a randomized, controlled study. *Arch Gerontol Geriatr*. 2012;55(2):310-5.

1379. Huang TL, Chang CC, Lee CH, Chen SC, Lai CH, Tsai CL. Intra-articular injections of sodium hyaluronate (Hyalgan(R)) in osteoarthritis of the knee. a randomized, controlled, double-blind, multicenter trial in the Asian population. *BMC Musculoskelet Disord*. 2011;12221.
1380. Jorgensen A, Stengaard-Pedersen K, Simonsen O, et al. Intra-articular hyaluronan is without clinical effect in knee osteoarthritis: a multicentre, randomised, placebo-controlled, double-blind study of 337 patients followed for 1 year. *Ann Rheum Dis*. 2010;69(6):1097-102.
1381. Kul-Panza E, Berker N. Is hyaluronate sodium effective in the management of knee osteoarthritis? A placebo-controlled double-blind study. *Minerva Med*. 2010;101(2):63-72.
1382. Neustadt D, Caldwell J, Bell M, Wade J, Gimbel J. Clinical effects of intraarticular injection of high molecular weight hyaluronan (Orthovisc) in osteoarthritis of the knee: a randomized, controlled, multicenter trial. *J Rheumatol*. 2005;32(10):1928-36.
1383. Qvistgaard E, Christensen R, Torp-Pedersen S, Bliddal H. Intra-articular treatment of hip osteoarthritis: a randomized trial of hyaluronic acid, corticosteroid, and isotonic saline. *Osteoarthritis Cartilage*. 2006;14(2):163-70.
1384. Caborn D, Rush J, Lanzer W, Parenti D, Murray C. A randomized, single-blind comparison of the efficacy and tolerability of hylan G-F 20 and triamcinolone hexacetonide in patients with osteoarthritis of the knee. *J Rheumatol*. 2004;31(2):333-43.
1385. Frederico T, Carlson BV, Mastroleo RC, Tomio L, Hussein MS. Inclusive annihilation of antiprotons on deuterium. *Phys Rev C Nucl Phys*. 1990;42(1):138-41.
1386. Frizziero L, Ronchetti IP. Intra-articular treatment of osteoarthritis of the knee: an arthroscopic and clinical comparison between sodium hyaluronate (500–730 kDa) and methylprednisolone acetate *Journal of Orthopaedics and Traumatology*. 2002;3(2):89-96.
1387. Guidolin DD, Ronchetti IP, Lini E, Guerra D, Frizziero L. Morphological analysis of articular cartilage biopsies from a randomized, clinical study comparing the effects of 500-730 kDa sodium hyaluronate (Hyalgan) and methylprednisolone acetate on primary osteoarthritis of the knee. *Osteoarthritis Cartilage*. 2001;9(4):371-81.
1388. Leardini G, Mattara L, Franceschini M, Perbellini A. Intra-articular treatment of knee osteoarthritis. A comparative study between hyaluronic acid and 6-methyl prednisolone acetate. *Clin Exp Rheumatol*. 1991;9(4):375-81.
1389. Leighton R, Akermark C, Therrien R, et al. NASHA hyaluronic acid vs. methylprednisolone for knee osteoarthritis: a prospective, multi-centre, randomized, non-inferiority trial. *Osteoarthritis Cartilage*. 2014;22(1):17-25.
1390. Pietrogrande V, Melanotte P, D'Agnolo B, et al. Hyaluronic acid versus methylprednisolone intra-articular injected for treatment of osteoarthritis of the knee. *Curr Ther Res*. 1991;50(5):691-701.
1391. Raynauld JP, Torrance GW, Band PA, et al. A prospective, randomized, pragmatic, health outcomes trial evaluating the incorporation of hylan G-F 20 into the treatment paradigm for patients with knee osteoarthritis (Part 1 of 2): clinical results. *Osteoarthritis Cartilage*. 2002;10(7):506-17.
1392. Adams ME, Atkinson MH, Lussier AJ, et al. The role of viscosupplementation with hylan G-F 20 (Synvisc) in the treatment of osteoarthritis of the knee: a Canadian multicenter trial comparing hylan G-F 20 alone, hylan G-F 20 with non-steroidal anti-inflammatory drugs (NSAIDs) and NSAIDs alone. *Osteoarthritis Cartilage*. 1995;3(4):213-25.
1393. Ozturk C, Atamaz F, Hepguler S, Argin M, Arkun R. The safety and efficacy of intraarticular hyaluronan with/without corticosteroid in knee osteoarthritis: 1-year, single-blind, randomized study. *Rheumatol Int*. 2006;26(4):314-9.
1394. Raman R, Dutta A, Day N, Sharma HK, Shaw CJ, Johnson GV. Efficacy of Hylan G-F 20 and Sodium Hyaluronate in the treatment of osteoarthritis of the knee -- a prospective randomized clinical trial. *Knee*. 2008;15(4):318-24.
1395. Conrozier T, Jerosch J, Beks P, et al. Prospective, multi-centre, randomised evaluation of the safety and efficacy of five dosing regimens of viscosupplementation with hylan G-F 20 in patients with symptomatic tibio-femoral osteoarthritis: a pilot study. *Arch Orthop Trauma Surg*. 2009;129(3):417-23.
1396. Chevalier X, Jerosch J, Goupille P, et al. Single, intra-articular treatment with 6 ml hylan G-F 20 in patients with symptomatic primary osteoarthritis of the knee: a randomised, multicentre, double-blind, placebo controlled trial. *Ann Rheum Dis*. 2010;69(1):113-9.

1397. Day R, Brooks P, Conaghan PG, Petersen M. A double blind, randomized, multicenter, parallel group study of the effectiveness and tolerance of intraarticular hyaluronan in osteoarthritis of the knee. *J Rheumatol*. 2004;31(4):775-82.
1398. Lundsgaard C, Dufour N, Fallentin E, Winkel P, Gluud C. Intra-articular sodium hyaluronate 2 mL versus physiological saline 20 mL versus physiological saline 2 mL for painful knee osteoarthritis: a randomized clinical trial. *Scand J Rheumatol*. 2008;37(2):142-50.
1399. Puhl W, Bernau A, Greiling H, et al. Intra-articular sodium hyaluronate in osteoarthritis of the knee: a multicenter, double-blind study. *Osteoarthritis Cartilage*. 1993;1(4):233-41.
1400. Wobig M, Dickhut A, Maier R, Vetter G. Viscosupplementation with hylan G-F 20: a 26-week controlled trial of efficacy and safety in the osteoarthritic knee. *Clin Ther*. 1998;20(3):410-23.
1401. Berenbaum F, Grifka J, Cazzaniga S, et al. A randomised, double-blind, controlled trial comparing two intra-articular hyaluronic acid preparations differing by their molecular weight in symptomatic knee osteoarthritis. *Ann Rheum Dis*. 2012;71(9):1454-60.
1402. Jüni P, Reichenbach S, Trelle S, et al. Efficacy and safety of intraarticular hylan or hyaluronic acids for osteoarthritis of the knee: a randomized controlled trial. *Arthritis Rheum*. 2007;56(11):3610-9.
1403. Kirchner M, Marshall D. A double-blind randomized controlled trial comparing alternate forms of high molecular weight hyaluronan for the treatment of osteoarthritis of the knee. *Osteoarthritis Cartilage*. 2006;14(2):154-62.
1404. Petrella RJ, Petrella M. A prospective, randomized, double-blind, placebo controlled study to evaluate the efficacy of intraarticular hyaluronic acid for osteoarthritis of the knee. *J Rheumatol*. 2006;33(5):951-6.
1405. Wobig M, Bach G, Beks P, et al. The role of elastoviscosity in the efficacy of viscosupplementation for osteoarthritis of the knee: a comparison of hylan G-F 20 and a lower-molecular-weight hyaluronan. *Clin Ther*. 1999;21(9):1549-62.
1406. Baker JF, Solayar GN, Byrne DP, Moran R, Mulhall KJ. Analgesic control and functional outcome after knee arthroscopy: results of a randomized double-blinded trial comparing a hyaluronic acid supplement with bupivacaine. *Clin J Sport Med*. 2012;22(2):109-15.
1407. Housman L, Arden N, Schnitzer TJ, et al. Intra-articular hylastan versus steroid for knee osteoarthritis. *Knee Surg Sports Traumatol Arthrosc*. 2014;22(7):1684-92.
1408. Nahler G, Metelmann H, Sperber H. Treating osteoarthritis of the knee with a homeopathic preparation. Results of a randomized, controlled clinical trial in comparison to hyaluronic acid. *Biomedical Ther*. 1998;XVI(2):186-91.
1409. Giarratana LS, Marelli BM, Crapanzano C, et al. A randomized double-blind clinical trial on the treatment of knee osteoarthritis: the efficacy of polynucleotides compared to standard hyaluronian viscosupplementation. *Knee*. 2014;21(3):661-8.
1410. Khanasuk Y, Dechmaneein T, Tanavalee A. Prospective randomized trial comparing the efficacy of single 6-ml injection of hylan G-F 20 and hyaluronic acid for primary knee arthritis: a preliminary study. *J Med Assoc Thai*. 2012;95 Suppl 10S92-7.
1411. Maheu E, Zaim M, Appelboom T, et al. Comparative efficacy and safety of two different molecular weight (MW) hyaluronans F60027 and Hylan G-F20 in symptomatic osteoarthritis of the knee (KOA). Results of a non inferiority, prospective, randomized, controlled trial. *Clin Exp Rheumatol*. 2011;29(3):527-35.
1412. Pavelka K, Uebelhart D. Efficacy evaluation of highly purified intra-articular hyaluronic acid (Sinovial((R))) vs hylan G-F20 (Synvisc((R))) in the treatment of symptomatic knee osteoarthritis. A double-blind, controlled, randomized, parallel-group non-inferiority study. *Osteoarthritis Cartilage*. 2011;19(11):1294-300.
1413. Strand V, Baraf HS, Lavin PT, Lim S, Hosokawa H. A multicenter, randomized controlled trial comparing a single intra-articular injection of Gel-200, a new cross-linked formulation of hyaluronic acid, to phosphate buffered saline for treatment of osteoarthritis of the knee. *Osteoarthritis Cartilage*. 2012;20(5):350-6.
1414. Altman RD, Moskowitz R. Intraarticular sodium hyaluronate (Hyalgan) in the treatment of patients with osteoarthritis of the knee: a randomized clinical trial. Hyalgan Study Group. *J Rheumatol*. 1998;25(11):2203-12.
1415. Chareancholvanich K, Pornrattanamaneewong C, Narkbunnam R. Increased cartilage volume after injection of hyaluronic acid in osteoarthritis knee patients who underwent high tibial osteotomy. *Knee Surg Sports Traumatol Arthrosc*. 2014;22(6):1415-23.

1416. Diracoglu D, Vural M, Baskent A, Dikici F, Aksoy C. The effect of viscosupplementation on neuromuscular control of the knee in patients with osteoarthritis. *J Back Musculoskelet Rehabil.* 2009;22(1):1-9.
1417. Karlsson J, Sjogren LS, Lohmander LS. Comparison of two hyaluronan drugs and placebo in patients with knee osteoarthritis. A controlled, randomized, double-blind, parallel-design multicentre study. *Rheumatology (Oxford).* 2002;41(11):1240-8.
1418. Lohmander LS, Dalen N, Englund G, et al. Intra-articular hyaluronan injections in the treatment of osteoarthritis of the knee: a randomised, double blind, placebo controlled multicentre trial. Hyaluronan Multicentre Trial Group. *Ann Rheum Dis.* 1996;55(7):424-31.
1419. Vangsness CT, Jr., Farr J, 2nd, Boyd J, Dellaero DT, Mills CR, LeRoux-Williams M. Adult human mesenchymal stem cells delivered via intra-articular injection to the knee following partial medial meniscectomy: a randomized, double-blind, controlled study. *J Bone Joint Surg Am.* 2014;96(2):90-8.
1420. Bunyaratavej N, Chan KM, Subramanian N. Treatment of painful osteoarthritis of the knee with hyaluronic acid. Results of a multicenter Asian study. *J Med Assoc Thai.* 2001;84 Suppl 2S576-81.
1421. Carrabba M, Paresce E, Angelini M, Re K, Torchiana E, Perbellini A. The safety and efficacy of different dose schedules of hyaluronic acid in the treatment of painful osteoarthritis of the knee with joint effusion. *Eur J Rhem Inflammation.* 1995;15(1):25-31.
1422. Dahlberg L, Lohmander LS, Ryd L. Intraarticular injections of hyaluronan in patients with cartilage abnormalities and knee pain. A one-year double-blind, placebo-controlled study. *Arthritis Rheum.* 1994;37(4):521-8.
1423. Dixon AS, Jacoby RK, Berry H, Hamilton EB. Clinical trial of intra-articular injection of sodium hyaluronate in patients with osteoarthritis of the knee. *Curr Med Res Opin.* 1988;11(4):205-13.
1424. Dougados M, Nguyen M, Listrat V, Amor B. High molecular weight sodium hyaluronate (hyalectin) in osteoarthritis of the knee: a 1 year placebo-controlled trial. *Osteoarthritis Cartilage.* 1993;1(2):97-103.
1425. Henderson EB, Smith EC, Pegley F, Blake DR. Intra-articular injections of 750 kD hyaluronan in the treatment of osteoarthritis: a randomised single centre double-blind placebo-controlled trial of 91 patients demonstrating lack of efficacy. *Ann Rheum Dis.* 1994;53(8):529-34.
1426. Huskisson EC, Donnelly S. Hyaluronic acid in the treatment of osteoarthritis of the knee. *Rheumatology (Oxford).* 1999;38(7):602-7.
1427. Kotevoglou N, Iyibozkurt PC, Hiz O, Toktas H, Kuran B. A prospective randomised controlled clinical trial comparing the efficacy of different molecular weight hyaluronan solutions in the treatment of knee osteoarthritis. *Rheumatol Int.* 2006;26(4):325-30.
1428. Navarro-Sarabia F, Coronel P, Collantes E, et al. A 40-month multicentre, randomised placebo-controlled study to assess the efficacy and carry-over effect of repeated intra-articular injections of hyaluronic acid in knee osteoarthritis: the AMELIA project. *Ann Rheum Dis.* 2011;70(11):1957-62.
1429. Payne MW, Petrella RJ. Viscosupplementation effect on proprioception in the osteoarthritic knee. *Arch Phys Med Rehabil.* 2000;81(5):598-603.
1430. Scale D, Wobig M, Wolpert W. Viscosupplementation of osteoarthritic knees with hylan: a treatment schedule study. *Current Therapeutic Research.* 1994;55(3):220-32.
1431. de Campos G, Rezende M, Pailo A, Frucchi R, Camargo O. Adding triamcinolone improves viscosupplementation: a randomized clinical trial. *Clin Orthop Relat Res.* 2013;471(2):613-20.
1432. Lee P, Kim Y, Lee C, et al. Comparison between high and low molecular weight hyaluronates in knee osteoarthritis patients: open-label, randomized, multicentre clinical trial. *J Intl Med Res.* 2006;3477-87.
1433. Palmieri B, Rottigni V, Iannitti T. Preliminary study of highly cross-linked hyaluronic acid-based combination therapy for management of knee osteoarthritis-related pain. *Drug Des Devel Ther.* 2013;77-12.
1434. Wind WM, Jr., Smolinski RJ. Reliability of common knee injection sites with low-volume injections. *J Arthroplasty.* 2004;19(7):858-61.
1435. Jones AC, Patrick M, Doherty S, Doherty M. Intra-articular hyaluronic acid compared to intra-articular triamcinolone hexacetonide in inflammatory knee osteoarthritis. *Osteoarthritis Cartilage.* 1995;3(4):269-73.
1436. Shimizu M, Higuchi H, Takagishi K, Shinozaki T, Kobayashi T. Clinical and biochemical characteristics after intra-articular injection for the treatment of osteoarthritis of the knee: prospective randomized study of sodium hyaluronate and corticosteroid. *J Orthop Sci.* 2010;15(1):51-6.

1437. Torrance GW, Raynauld JP, Walker V, et al. A prospective, randomized, pragmatic, health outcomes trial evaluating the incorporation of hylan G-F 20 into the treatment paradigm for patients with knee osteoarthritis (Part 2 of 2): economic results. *Osteoarthritis Cartilage*. 2002;10(7):518-27.
1438. Vanelli R, Costa P, Rossi SM, Benazzo F. Efficacy of intra-articular polynucleotides in the treatment of knee osteoarthritis: a randomized, double-blind clinical trial. *Knee Surg Sports Traumatol Arthrosc*. 2010;18(7):901-7.
1439. Chen WL, Hsu WC, Lin YJ, Hsieh LF. Comparison of intra-articular hyaluronic acid injections with transcutaneous electric nerve stimulation for the management of knee osteoarthritis: a randomized controlled trial. *Arch Phys Med Rehabil*. 2013;94(8):1482-9.
1440. Chevillard M, Galanti A, Paresce E, Wolf A, Carrabba M. Efficacy and tolerability of galactosaminoglycuronoglycan-sulfate in osteoarthritis of the knee: an 11-month experience. *Int J Clin Pharmacol Res*. 1993;13 Suppl49-53.
1441. Forster MC, Straw R. A prospective randomised trial comparing intra-articular Hyalgan injection and arthroscopic washout for knee osteoarthritis. *Knee*. 2003;10(3):291-3.
1442. Graf J, Neusel E, Schneider E, Niethard FU. Intra-articular treatment with hyaluronic acid in osteoarthritis of the knee joint: a controlled clinical trial versus mucopolysaccharide polysulfuric acid ester. *Clin Exp Rheumatol*. 1993;11(4):367-72.
1443. Kahan A, Lleu PL, Salin L. Prospective randomized study comparing the medicoeconomic benefits of Hylan GF-20 vs. conventional treatment in knee osteoarthritis. *Joint Bone Spine*. 2003;70(4):276-81.
1444. Katona G. A clinical trial of glycosaminoglycan-peptide complex ('Rumalon') in patients with osteoarthritis of the knee. *Curr Med Res Opin*. 1987;10(9):625-33.
1445. Lee SC, Rha DW, Chang WH. Rapid analgesic onset of intra-articular hyaluronic acid with ketorolac in osteoarthritis of the knee. *J Back Musculoskelet Rehabil*. 2011;24(1):31-8.
1446. Leopold SS, Redd BB, Warme WJ, Wehrle PA, Pettis PD, Shott S. Corticosteroid compared with hyaluronic acid injections for the treatment of osteoarthritis of the knee. A prospective, randomized trial. *J Bone Joint Surg Am*. 2003;85-A(7):1197-203.
1447. Listrat V, Ayral X, Patarnello F, et al. Arthroscopic evaluation of potential structure modifying activity of hyaluronan (Hyalgan) in osteoarthritis of the knee. *Osteoarthritis Cartilage*. 1997;5(3):153-60.
1448. Mathies B. Effects of Viscosel, a synovial fluid substitute, on recovery after arthroscopic partial meniscectomy and joint lavage. *Knee Surg Sports Traumatol Arthrosc*. 2006;14(1):32-9.
1449. McDonald C, Hantel S, Strohmeier M. A randomised controlled study to compare the performance and safety of two sources of sodium hyaluronate given as a viscosupplement by intra-articular injection to patients with osteoarthritis of the knee. *J Clin Res*. 2000;341-50.
1450. Paker N, Tekdos D, Kesiktas N, Soy D. Comparison of the therapeutic efficacy of TENS versus intra-articular hyaluronic acid injection in patients with knee osteoarthritis: a prospective randomized study. *Adv Ther*. 2006;23(2):342-53.
1451. Petrella RJ, DiSilvestro MD, Hildebrand C. Effects of hyaluronate sodium on pain and physical functioning in osteoarthritis of the knee: a randomized, double-blind, placebo-controlled clinical trial. *Arch Intern Med*. 2002;162(3):292-8.
1452. Rossini M, Viapiana O, Ramonda R, et al. Intra-articular clodronate for the treatment of knee osteoarthritis: dose ranging study vs hyaluronic acid. *Rheumatology (Oxford)*. 2009;48(7):773-8.
1453. Atamaz F, Kirazli Y, Akkoc Y. A comparison of two different intra-articular hyaluronan drugs and physical therapy in the management of knee osteoarthritis. *Rheumatol Int*. 2006;26(10):873-8.
1454. Bayramoglu M, Karatas M, Cetin N, Akman N, Sozay S, Dilek A. Comparison of two different viscosupplements in knee osteoarthritis -- a pilot study. *Clin Rheumatol*. 2003;22(2):118-22.
1455. Bragantini A, Cassini M, De B, Perbellini A. Controlled single-blind trial of intra-articularly injected hyaluronic acid (Hyalgan®) in osteoarthritis of the knee. *Clin Trials J*. 1987;24333-40.
1456. Corrado EM, Peluso GF, Gigliotti S, de Durante C, Palmieri D, Savoia Mea. The effects of intra-articular administration of hyaluronic acid on osteoarthritis of the knee: a clinical study with immunological and biochemical evaluations. *Eur J Rheumatol Inflamm*. 1995;1547-56.
1457. Creamer P, Sharif M, George E, et al. Intra-articular hyaluronic acid in osteoarthritis of the knee: an investigation into mechanisms of action. *Osteoarthritis Cartilage*. 1994;2(2):133-40.

1458. Cubukcu D, Ardic F, Karabulut N, Topuz O. Hylan G-F 20 efficacy on articular cartilage quality in patients with knee osteoarthritis: clinical and MRI assessment. *Clin Rheumatol*. 2005;24(4):336-41.
1459. Grecomoro G, Martorana U, Di Marco C. Intra-articular treatment with sodium hyaluronate in gonarthrosis: a controlled clinical trial versus placebo. *Pharmatherapeutica*. 1987;5(2):137-41.
1460. Jubb RW, Piva S, Beinat L, Dacre J, Gishen P. A one-year, randomised, placebo (saline) controlled clinical trial of 500-730 kDa sodium hyaluronate (Hyalgan) on the radiological change in osteoarthritis of the knee. *Int J Clin Pract*. 2003;57(6):467-74.
1461. Spakova T, Rosocha J, Lacko M, Harvanova D, Gharaibeh A. Treatment of knee joint osteoarthritis with autologous platelet-rich plasma in comparison with hyaluronic acid. *Am J Phys Med Rehabil*. 2012;91(5):411-7.
1462. Tamir E, Robinson D, Koren R, Agar G, Halperin N. Intra-articular hyaluronan injections for the treatment of osteoarthritis of the knee: a randomized, double blind, placebo controlled study. *Clin Exp Rheumatol*. 2001;19(3):265-70.
1463. Tashiro T, Seino S, Sato T, Matsuoka R, Masuda Y, Fukui N. Oral administration of polymer hyaluronic acid alleviates symptoms of knee osteoarthritis: a double-blind, placebo-controlled study over a 12-month period. *ScientificWorldJournal*. 2012;2012167928.
1464. Wu J, Shih L, Hsu H, Chen T. The double-blind test of sodium hyaluronate (ARTZ) on osteoarthritis knee. *Zhonghua Yi Xue Za Zhi (Taipei)*. 1997;59(2):99-106.
1465. Onel E, Kolsun K, Kauffman JI. Post-Hoc analysis of a head-to-head hyaluronic acid comparison in knee osteoarthritis using the 2004 OMERACT-OARSI responder criteria. *Clin Drug Investig*. 2008;28(1):37-45.
1466. Pasquali Ronchetti I, Guerra D, Taparelli F, et al. Morphological analysis of knee synovial membrane biopsies from a randomized controlled clinical study comparing the effects of sodium hyaluronate (Hyalgan) and methylprednisolone acetate (Depomedrol) in osteoarthritis. *Rheumatol*. 2001;40(2):158-69.
1467. Roman JA, Chismol J, Morales M, Donderis JL. Intra-articular treatment with hyaluronic acid. Comparative study of Hyalgan and Adant. *Clin Rheumatol*. 2000;19(3):204-6.
1468. Sezgin M, Demirel AC, Karaca C, et al. Does hyaluronan affect inflammatory cytokines in knee osteoarthritis? *Rheumatol Int*. 2005;25(4):264-9.
1469. Tasciotoaglu F, Oner C. Efficacy of intra-articular sodium hyaluronate in the treatment of knee osteoarthritis. *Clin Rheumatol*. 2003;22(2):112-7.
1470. Formiguera Sala S, Esteve de Miguel R. Intra-articular hyaluronic acid in the treatment osteoarthritis of the knee: A short term study. *Eur J Rhem Inflammation*. 1995;15(1):33-8.
1471. Frampton JE. Hylan G-F 20 single-injection formulation. *Drugs Aging*. 2010;27(1):77-85.
1472. Iannitti T, Rottigni V, Palmieri B. A pilot study to compare two different hyaluronic acid compounds for treatment of knee osteoarthritis. *Int J Immunopathol Pharmacol*. 2012;25(4):1093-8.
1473. Karatay S, Kiziltunc A, Yildirim K, Karanfil RC, Senel K. Effects of different hyaluronic acid products on synovial fluid levels of intercellular adhesion molecule-1 and vascular cell adhesion molecule-1 in knee osteoarthritis. *Ann Clin Lab Sci*. 2004;34(3):330-5.
1474. Karatay S, Kiziltunc A, Yildirim K, Karanfil RC, Senel K. Effects of different hyaluronic acid products on synovial fluid NO levels in knee osteoarthritis. *Clin Rheumatol*. 2005;24(5):497-501.
1475. Zoboli AA, de Rezende MU, de Campos GC, Pasqualin T, Frucchi R, de Camargo OP. Prospective randomized clinical trial: single and weekly viscosupplementation. *Acta Ortop Bras*. 2013;21(5):271-5.
1476. Kullenberg B, Runesson R, Tuvhag R, Olsson C, Resch S. Intraarticular corticosteroid injection: pain relief in osteoarthritis of the hip? *J Rheumatol*. 2004;31(11):2265-8.
1477. Hollander J, Brown E, Jessar R, Brown C. Hydrocortisone and cortisone injected into arthritic joints; comparative effects of and use of hydrocortisone as a local antiarthritic agent. *J Am Med Assoc* 1951;147(17):1629-35.
1478. Lambert RG, Hutchings EJ, Grace MG, Jhangri GS, Conner-Spady B, Maksymowych WP. Steroid injection for osteoarthritis of the hip: a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum*. 2007;56(7):2278-87.
1479. van den Bekerom MP, Lamme B, Sermon A, Mulier M. What is the evidence for viscosupplementation in the treatment of patients with hip osteoarthritis? Systematic review of the literature. *Arch Orthop Trauma Surg*. 2008;128(8):815-23.

1480. Zhang W, Moskowitz RW, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage*. 2008;16(2):137-62.
1481. Flanagan J, Casale FF, Thomas TL, Desai KB. Intra-articular injection for pain relief in patients awaiting hip replacement. *Ann R Coll Surg Engl*. 1988;70(3):156-7.
1482. Robinson P, Keenan AM, Conaghan PG. Clinical effectiveness and dose response of image-guided intra-articular corticosteroid injection for hip osteoarthritis. *Rheumatology (Oxford)*. 2007;46(2):285-91.
1483. Leopold S, Redd B, Warme W, Wehrle P, Pettis P, Shott S. Corticosteroid compared with hyaluronic acid injections for the treatment of osteoarthritis of the knee: a prospective, randomized trial. *Journal of Bone & Joint Surgery, American Volume*. 2003;85A(7):1197-203.
1484. Sambrook PN, Champion GD, Browne CD, et al. Corticosteroid injection for osteoarthritis of the knee: peripatellar compared to intra-articular route. *Clin Exp Rheumatol*. 1989;7(6):609-13.
1485. Koyonos L, Yanke AB, McNickle AG, et al. A randomized, prospective, double-blind study to investigate the effectiveness of adding DepoMedrol to a local anesthetic injection in postmeniscectomy patients with osteoarthritis of the knee. *Am J Sports Med*. 2009;37(6):1077-82.
1486. Wang JJ, Ho ST, Lee SC, Tang JJ, Liaw WJ. Intraarticular triamcinolone acetonide for pain control after arthroscopic knee surgery. *Anesth Analg*. 1998;87(5):1113-6.
1487. Kirkley A, Birmingham TB, Litchfield RB, et al. A randomized trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med*. 2008;359(11):1097-107.
1488. Christensen CP, Jacobs CA, Jennings HR. Effect of periarticular corticosteroid injections during total knee arthroplasty. A double-blind randomized trial. *J Bone Joint Surg Am*. 2009;91(11):2550-5.
1489. Weitoft T, Uddenfeldt P. Importance of synovial fluid aspiration when injecting intra-articular corticosteroids. *Annals Of The Rheumatic Diseases*. 2000;59(3):233-5.
1490. Valtonen EJ. Clinical comparison of triamcinolonehexacetonide and betamethasone in the treatment of osteoarthrosis of the knee-joint. *Scand J Rheumatol Suppl*. 1981;411-7.
1491. Pyne D, Ioannou Y, Mootoo R, Bhanji A. Intra-articular steroids in knee osteoarthritis: a comparative study of triamcinolone hexacetonide and methylprednisolone acetate. *Clin Rheumatol*. 2004;23(2):116-20.
1492. Dieppe PA, Sathapatayavongs B, Jones HE, Bacon PA, Ring EF. Intra-articular steroids in osteoarthritis. *Rheumatol Rehabil*. 1980;19(4):212-7.
1493. Jones A, Doherty M. Intra-articular corticosteroids are effective in osteoarthritis but there are no clinical predictors of response. *Annals Of The Rheumatic Diseases*. 1996;55(11):829-32.
1494. Miller JH, White J, Norton TH. The value of intra-articular injections in osteoarthritis of the knee. *J Bone Joint Surg Br*. 1958;40-B(4):636-43.
1495. Friedman DM, Moore ME. The efficacy of intraarticular steroids in osteoarthritis: a double-blind study. *J Rheumatol*. 1980;7(6):850-6.
1496. Cederlof S, Jonson G. Intraarticular prednisolone injection for osteoarthritis of the knee. A double blind test with placebo. *Acta Chir Scand*. 1966;132(5):532-7.
1497. Reeves KD, Hassanein K. Randomized prospective double-blind placebo-controlled study of dextrose prolotherapy for knee osteoarthritis with or without ACL laxity. *Altern Ther Health Med*. 2000;6(2):68-74, 7-80.
1498. Gobel H, Heinze A, Reichel G, Hefter H, Benecke R. Efficacy and safety of a single botulinum type A toxin complex treatment (Dysport) for the relief of upper back myofascial pain syndrome: results from a randomized double-blind placebo-controlled multicentre study. *Pain*. 2006;125(1-2):82-8.
1499. Qerama E, Fuglsang-Frederiksen A, Kasch H, Bach FW, Jensen TS. A double-blind, controlled study of botulinum toxin A in chronic myofascial pain. *Neurology*. 2006;67(2):241-5.
1500. Richards BA, Jensen. A double-blind, controlled study of botulinum toxin A in chronic myofascial pain. *Neurology*. 2007;68(12):963; author reply -4.
1501. Ferrante FM, Bearn L, Rothrock R, King L. Evidence against trigger point injection technique for the treatment of cervicothoracic myofascial pain with botulinum toxin type A. *Anesthesiology*. 2005;103(2):377-83.
1502. Lew MF, Adornato BT, Duane DD, et al. Botulinum toxin type B: a double-blind, placebo-controlled, safety and efficacy study in cervical dystonia. *Neurology*. 1997;49(3):701-7.

1503. Charles PD. Botulinum neurotoxin serotype A: a clinical update on non-cosmetic uses. *Am J Health Syst Pharm.* 2004;61(22 Suppl 6):S11-23.
1504. Naumann M, Lowe NJ. Botulinum toxin type A in treatment of bilateral primary axillary hyperhidrosis: randomised, parallel group, double blind, placebo controlled trial. *Bmj.* 2001;323(7313):596-9.
1505. Graham HK, Boyd R, Carlin JB, et al. Does botulinum toxin a combined with bracing prevent hip displacement in children with cerebral palsy and "hips at risk"? A randomized, controlled trial. *J Bone Joint Surg Am.* 2008;90(1):23-33.
1506. Galli M, Cimolin V, Valente EM, Crivellini M, Ialongo T, Albertini G. Computerized gait analysis of botulinum toxin treatment in children with cerebral palsy. *Disabil Rehabil.* 2007;29(8):659-64.
1507. Rousseaux M, Launay MJ, Kozlowski O, Daveluy W. Botulinum toxin injection in patients with hereditary spastic paraparesis. *Eur J Neurol.* 2007;14(2):206-12.
1508. Li M, Goldberger BA, Hopkins C. Fatal case of BOTOX-related anaphylaxis? *J Forensic Sci.* 2005;50(1):169-72.
1509. Billote DB, Abdoue AG, Wixson RL. Comparison of acute normovolemic hemodilution and preoperative autologous blood donation in clinical practice. *J Clin Anesth.* 2000;12(1):31-5.
1510. Billote DB, Glisson SN, Green D, Wixson RL. Efficacy of preoperative autologous blood donation: analysis of blood loss and transfusion practice in total hip replacement. *J Clin Anesth.* 2000;12(7):537-42.
1511. Billote DB, Glisson SN, Green D, Wixson RL. A prospective, randomized study of preoperative autologous donation for hip replacement surgery. *J Bone Joint Surg Am.* 2002;84-A(8):1299-304.
1512. Bierbaum BE, Callaghan JJ, Galante JO, Rubash HE, Tooms RE, Welch RB. An analysis of blood management in patients having a total hip or knee arthroplasty. *J Bone Joint Surg Am.* 1999;81(1):2-10.
1513. Biesma DH, Marx JJ, Kraaijenhagen RJ, Franke W, Messinger D, van de Wiel A. Lower homologous blood requirement in autologous blood donors after treatment with recombinant human erythropoietin. *Lancet.* 1994;344(8919):367-70.
1514. Birkmeyer JD, Goodnough LT, AuBuchon JP, Noordsij PG, Littenberg B. The cost-effectiveness of preoperative autologous blood donation for total hip and knee replacement. *Transfusion.* 1993;33(7):544-51.
1515. Woolson ST, Marsh JS, Tanner JB. Transfusion of previously deposited autologous blood for patients undergoing hip-replacement surgery. *J Bone Joint Surg Am.* 1987;69(3):325-8.
1516. Woolson ST, Watt JM. Use of autologous blood in total hip replacement. A comprehensive program. *J Bone Joint Surg Am.* 1991;73(1):76-80.
1517. Etchason J, Petz L, Keeler E, et al. The cost effectiveness of preoperative autologous blood donations. *N Engl J Med.* 1995;332(11):719-24.
1518. Grosvenor D, Goyal V, Goodman S. Efficacy of postoperative blood salvage following total hip arthroplasty in patients with and without deposited autologous units. *J Bone Joint Surg Am.* 2000;82-A(7):951-4.
1519. NHLBI. Transfusion alert: use of autologous blood. National Heart, Lung, and Blood Institute Expert Panel on the use of Autologous Blood. *Transfusion.* 1995;35(8):703-11.
1520. Thomas D, Wareham K, Cohen D, Hutchings H. Autologous blood transfusion in total knee replacement surgery. *Br J Anaesth.* 2001;86(5):669-73.
1521. Tsumara N, Yoshiya S, Chin T, Shiba R, Kohso K, Doita M. A prospective comparison of clamping the drain or post-operative salvage of blood in reducing blood loss after total knee arthroplasty. *J Bone Joint Surg Br.* 2006;88(1):49-53.
1522. Auw Yang K, Raijmakers N, van Arkel E, et al. Autologous interleukin-1 receptor antagonist improves function and symptoms in osteoarthritis when compared to placebo in a prospective randomized controlled trial. *Osteoarthritis Cartilage.* 2008;16(4):498-505.
1523. Chevalier X, Goupille P, Beaulieu AD, et al. Intraarticular injection of anakinra in osteoarthritis of the knee: a multicenter, randomized, double-blind, placebo-controlled study. *Arthritis Rheum.* 2009;61(3):344-52.
1524. Gibson JN, White MD, Chapman VM, Strachan RK. Arthroscopic lavage and debridement for osteoarthritis of the knee. *J Bone Joint Surg Br.* 1992;74(4):534-7.
1525. Kalunian KC, Moreland LW, Klashman DJ, et al. Visually-guided irrigation in patients with early knee osteoarthritis: a multicenter randomized, controlled trial. *Osteoarthritis Cartilage.* 2000;8(6):412-8.

1526. Chang RW, Falconer J, Stulberg SD, Arnold WJ, Manheim LM, Dyer AR. A randomized, controlled trial of arthroscopic surgery versus closed-needle joint lavage for patients with osteoarthritis of the knee. *Arthritis Rheum.* 1993;36(3):289-96.
1527. Hubbard MJ. Articular debridement versus washout for degeneration of the medial femoral condyle. A five-year study. *J Bone Joint Surg Br.* 1996;78(2):217-9.
1528. Kang RW, Gomoll AH, Nho SJ, Pylawka TK, Cole BJ. Outcomes of mechanical debridement and radiofrequency ablation in the treatment of chondral defects: a prospective randomized study. *J Knee Surg.* 2008;21(2):116-21.
1529. Stein DT, Ricciardi CA, Viehe T. The effectiveness of the use of electrocautery with chondroplasty in treating chondromalacic lesions: A randomized prospective study. *Arthroscopy.* 2002;18(2):190-3.
1530. Vasiliadis H. Autologous chondrocyte implantation for full thickness articular cartilage defects of the knee (knee). *The Cochrane Collaboration.* 2010.
1531. Behrens P, Bitter T, Kurz B, Russlies M. Matrix-associated autologous chondrocyte transplantation/implantation (MACT/MACI)--5-year follow-up. *Knee.* 2006;13(3):194-202.
1532. Bekkers JE, Inklaar M, Saris DB. Treatment selection in articular cartilage lesions of the knee: a systematic review. *Am J Sports Med.* 2009;37 Suppl 1148S-55S.
1533. Bentley G. A prospective, randomised comparison of autologous chondrocyte implantation versus mosaicplasty for osetochondral defects in the knee. *The Journal of Bone and Joint Surgery.* 2003;85(2):223-30.
1534. Blevins FT, Steadman JR, Rodrigo JJ, Silliman J. Treatment of articular cartilage defects in athletes: an analysis of functional outcome and lesion appearance. *Orthopedics.* 1998;21(7):761-7; discussion 7-8.
1535. Cerynik DL, Lewullis GE, Joves BC, Palmer MP, Tom JA. Outcomes of microfracture in professional basketball players. *Knee Surg Sports Traumatol Arthrosc.* 2009;17(9):1135-9.
1536. Crawford DC, Heveran CM, Cannon WD, Jr., Foo LF, Potter HG. An autologous cartilage tissue implant NeoCart for treatment of grade III chondral injury to the distal femur: prospective clinical safety trial at 2 years. *Am J Sports Med.* 2009;37(7):1334-43.
1537. Dozin B, Malpeli M, Cancedda R, et al. Comparative evaluation of autologous chondrocyte implantation and mosaicplasty: a multicentered randomized clinical trial. *Clin J Sport Med.* 2005;15(4):220-6.
1538. Gobbi A, Domzalski M, Pascual J, Zanazzo M. Hamstring anterior cruciate ligament reconstruction: Is it necessary to sacrifice the gracilis? *Arthroscopy: The Journal of Arthroscopic & Related Surgery.* 2005;21(3):275-80.
1539. Gobbi A, Francisco RA, Lubowitz JH, Allegra F, Canata G. Osteochondral lesions of the talus: randomized controlled trial comparing chondroplasty, microfracture, and osteochondral autograft transplantation. *Arthroscopy.* 2006;22(10):1085-92.
1540. Gudas R, Stankevicius E, Monastyreckiene E, Pranys D, Kalesinskas RJ. Osteochondral autologous transplantation versus microfracture for the treatment of articular cartilage defects in the knee joint in athletes. *Knee Surg Sports Traumatol Arthrosc.* 2006;14(9):834-42.
1541. Harris JD, Brophy RH, Siston RA, Flanigan DC. Treatment of chondral defects in the athlete's knee. *Arthroscopy.* 2010;26(6):841-52.
1542. Horas U, Pelinkovic D, Herr G, Aigner T, Schnettler R. Autologous chondrocyte implantation and osteochondral cylinder transplantation in cartilage repair of the knee joint. A prospective, comparative trial. *J Bone Joint Surg Am.* 2003;85-A(2):185-92.
1543. Kon E, Gobbi A, Filardo G, Delcogliano M, Zaffagnini S, Marcacci M. Arthroscopic second-generation autologous chondrocyte implantation compared with microfracture for chondral lesions of the knee: prospective nonrandomized study at 5 years. *Am J Sports Med.* 2009;37(1):33-41.
1544. Kreuz PC, Muller S, Ossendorf C, Kaps C, Erggelet C. Treatment of focal degenerative cartilage defects with polymer-based autologous chondrocyte grafts: four-year clinical results. *Arthritis Res Ther.* 2009;11(2):R33.
1545. Magnussen RA, Dunn WR, Carey JL, Spindler KP. Treatment of focal articular cartilage defects in the knee: a systematic review. *Clin Orthop Relat Res.* 2008;466(4):952-62.
1546. Micheli LJ, Browne JE, Erggelet C, et al. Autologous chondrocyte implantation of the knee: multicenter experience and minimum 3-year follow-up. *Clin J Sport Med.* 2001;11(4):223-8.

1547. Mithoefer K, Williams RJ, 3rd, Warren RF, et al. Chondral resurfacing of articular cartilage defects in the knee with the microfracture technique. Surgical technique. *J Bone Joint Surg Am*. 2006;88 Suppl 1 Pt 2294-304.
1548. Mithoefer K, Williams RJ, 3rd, Warren RF, et al. The microfracture technique for the treatment of articular cartilage lesions in the knee. A prospective cohort study. *J Bone Joint Surg Am*. 2005;87(9):1911-20.
1549. Mithofer K, Peterson L, Mandelbaum BR, Minas T. Articular cartilage repair in soccer players with autologous chondrocyte transplantation: functional outcome and return to competition. *Am J Sports Med*. 2005;33(11):1639-46.
1550. Namdari S, Baldwin K, Anakwenze O, Park MJ, Huffman GR, Sennett BJ. Results and performance after microfracture in National Basketball Association athletes. *Am J Sports Med*. 2009;37(5):943-8.
1551. Pinker K, Szomolanyi P, Welsch GC, et al. Longitudinal evaluation of cartilage composition of matrix-associated autologous chondrocyte transplants with 3-T delayed gadolinium-enhanced MRI of cartilage. *AJR Am J Roentgenol*. 2008;191(5):1391-6.
1552. Riyami M, Rolf C. Evaluation of microfracture of traumatic chondral injuries to the knee in professional football and rugby players. *J Orthop Surg Res*. 2009;413.
1553. Steadman JR, Briggs KK, Rodrigo JJ, Kocher MS, Gill TJ, Rodkey WG. Outcomes of microfracture for traumatic chondral defects of the knee: average 11-year follow-up. *Arthroscopy*. 2003;19(5):477-84.
1554. Steadman JR, Miller BS, Karas SG, Schlegel TF, Briggs KK, Hawkins RJ. The microfracture technique in the treatment of full-thickness chondral lesions of the knee in National Football League players. *J Knee Surg*. 2003;16(2):83-6.
1555. Visna P. Treatment of deep cartilage defects of the knee us. *Acta chirurgica Belgica*. 2004;104(6):709-14.
1556. Zengerink M. Treatment of osteochondral lesions of the talus: a systemic review. *Knee Surg Sports Traumatol Arthrosc*. 2010;18:238-46.
1557. Bartlett W, Skinner JA, Gooding CR, et al. Autologous chondrocyte implantation versus matrix-induced autologous chondrocyte implantation for osteochondral defects of the knee: a prospective, randomised study. *J Bone Joint Surg Br*. 2005;87(5):640-5.
1558. Bentley G, Biant LC, Carrington RW, et al. A prospective, randomised comparison of autologous chondrocyte implantation versus mosaicplasty for osteochondral defects in the knee. *J Bone Joint Surg Br*. 2003;85(2):223-30.
1559. Wondrasch B, Zak L, Welsch GH, Marlovits S. Effect of accelerated weightbearing after matrix-associated autologous chondrocyte implantation on the femoral condyle on radiographic and clinical outcome after 2 years: a prospective, randomized controlled pilot study. *Am J Sports Med*. 2009;37 Suppl 188S-96S.
1560. Bartlett W. Collagen-Covered versus matrix-induced autologous chondrocyte implantation for osteochondral defects of the knee: a comparison of tourniquet times. *Eur J Orthop Surgery Traumatol*. 2006;16:315-3317.
1561. Benthien JP, Schwaninger M, Behrens P. We do not have evidence based methods for the treatment of cartilage defects in the knee. *Knee Surg Sports Traumatol Arthrosc*. 2011;19(4):543-52.
1562. Gooding CR, Bartlett W, Bentley G, Skinner JA, Carrington R, Flanagan A. A prospective, randomised study comparing two techniques of autologous chondrocyte implantation for osteochondral defects in the knee: Periosteum covered versus type I/III collagen covered. *Knee*. 2006;13(3):203-10.
1563. Mithoefer K, McAdams T, Williams RJ, Kreuz PC, Mandelbaum BR. Clinical efficacy of the microfracture technique for articular cartilage repair in the knee: an evidence-based systematic analysis. *Am J Sports Med*. 2009;37(10):2053-63.
1564. Vavken P, Samartzis D. Effectiveness of autologous chondrocyte implantation in cartilage repair of the knee: a systematic review of controlled trials. *Osteoarthritis Cartilage*. 2010;18(6):857-63.
1565. Vasiliadis HS, Lindahl A, Georgoulis AD, Peterson L. Malalignment and cartilage lesions in the patellofemoral joint treated with autologous chondrocyte implantation. *Knee Surg Sports Traumatol Arthrosc*. 2011;19(3):452-7.
1566. Knutsen G, Engebretsen L, Ludvigsen TC, et al. Autologous chondrocyte implantation compared with microfracture in the knee. A randomized trial. *J Bone Joint Surg Am*. 2004;86-A(3):455-64.
1567. Knutsen G, Drogset JO, Engebretsen L, et al. A randomized trial comparing autologous chondrocyte implantation with microfracture. Findings at five years. *J Bone Joint Surg Am*. 2007;89(10):2105-12.

1568. Van Assche D, Staes F, Van Caspel D, et al. Autologous chondrocyte implantation versus microfracture for knee cartilage injury: a prospective randomized trial, with 2-year follow-up. *Knee Surg Sports Traumatol Arthrosc.* 2010;18(4):486-95.
1569. Saris DB, Vanlauwe J, Victor J, et al. Characterized chondrocyte implantation results in better structural repair when treating symptomatic cartilage defects of the knee in a randomized controlled trial versus microfracture. *Am J Sports Med.* 2008;36(2):235-46.
1570. Saris DB, Vanlauwe J, Victor J, et al. Treatment of symptomatic cartilage defects of the knee: characterized chondrocyte implantation results in better clinical outcome at 36 months in a randomized trial compared to microfracture. *Am J Sports Med.* 2009;37 Suppl 110S-9S.
1571. Gudas R, Gudaite A, Pocius A, et al. Ten-year follow-up of a prospective, randomized clinical study of mosaic osteochondral autologous transplantation versus microfracture for the treatment of osteochondral defects in the knee joint of athletes. *Am J Sports Med.* 2012;40(11):2499-508.
1572. Gudas R, Gudaite A, Mickevicius T, et al. Comparison of osteochondral autologous transplantation, microfracture, or debridement techniques in articular cartilage lesions associated with anterior cruciate ligament injury: a prospective study with a 3-year follow-up. *Arthroscopy.* 2013;29(1):89-97.
1573. Ulstein S, Aroen A, Rotterud JH, Loken S, Engebretsen L, Heir S. Microfracture technique versus osteochondral autologous transplantation mosaicplasty in patients with articular chondral lesions of the knee: a prospective randomized trial with long-term follow-up. *Knee Surg Sports Traumatol Arthrosc.* 2014;22(6):1207-15.
1574. Knutson K, Robertsson O. The Swedish Knee Arthroplasty Register ([www.knee.se](http://www.knee.se)). *Acta Orthop.* 2010;81(1):5-7.
1575. Kolettis GT, Wixson RL, Peruzzi WT, Blake MJ, Wardell S, Stulberg SD. Safety of 1-stage bilateral total knee arthroplasty. *Clin Orthop Relat Res.* 1994(309):102-9.
1576. Paxton EW, Inacio MC, Khatod M, Yue EJ, Namba RS. Kaiser Permanente National Total Joint Replacement Registry: aligning operations with information technology. *Clin Orthop Relat Res.* 2010;468(10):2646-63.
1577. Pearse AJ, Hooper GJ, Rothwell A, Frampton C. Survival and functional outcome after revision of a unicompartmental to a total knee replacement: the New Zealand National Joint Registry. *J Bone Joint Surg Br.* 2010;92(4):508-12.
1578. Ranstam J, Robertsson O. Statistical analysis of arthroplasty register data. *Acta Orthop.* 2010;81(1):10-4.
1579. Robertsson O, Bizjajeva S, Fenstad AM, et al. Knee arthroplasty in Denmark, Norway and Sweden. *Acta Orthop.* 2010;81(1):82-9.
1580. Robertsson O, Dunbar MJ. Patient satisfaction compared with general health and disease-specific questionnaires in knee arthroplasty patients. *J Arthroplasty.* 2001;16(4):476-82.
1581. Robertsson O, Knutson K, Lewold S, Lidgren L. The routine of surgical management reduces failure after unicompartmental knee arthroplasty. *J Bone Joint Surg Br.* 2001;83(1):45-9.
1582. Robertsson O, Knutson K, Lewold S, Lidgren L. The Swedish Knee Arthroplasty Register 1975-1997: an update with special emphasis on 41,223 knees operated on in 1988-1997. *Acta Orthop Scand.* 2001;72(5):503-13.
1583. Schwartz AJ, Della Valle CJ, Rosenberg AG, Jacobs JJ, Berger RA, Galante JO. Cruciate-retaining TKA using a third-generation system with a four-pegged tibial component: a minimum 10-year followup note. *Clin Orthop Relat Res.* 2010;468(8):2160-7.
1584. Tagil M, Hansson U, Sigfusson R, et al. Bone morphology in relation to the migration of porous-coated anatomic knee arthroplasties : a roentgen stereophotogrammetric and histomorphometric study in 23 knees. *J Arthroplasty.* 2003;18(5):649-53.
1585. Schrama JC, Espehaug B, Hallan G, et al. Risk of revision for infection in primary total hip and knee arthroplasty in patients with rheumatoid arthritis compared with osteoarthritis: a prospective, population-based study on 108,786 hip and knee joint arthroplasties from the Norwegian Arthroplasty Register. *Arthritis Care Res (Hoboken).* 2010;62(4):473-9.
1586. Bongartz T, Halligan CS, Osmon DR, et al. Incidence and risk factors of prosthetic joint infection after total hip or knee replacement in patients with rheumatoid arthritis. *Arthritis Rheum.* 2008;59(12):1713-20.
1587. Pakos EE, Ntzani EE, Trikalinos TA. Patellar resurfacing in total knee arthroplasty. A meta-analysis. *J Bone Joint Surg Am.* 2005;87(7):1438-45.

1588. Baumann C, Rat AC, Osnowycz G, Mainard D, Cuny C, Guillemin F. Satisfaction with care after total hip or knee replacement predicts self-perceived health status after surgery. *BMC Musculoskelet Disord*. 2009;10:150.
1589. Riddle DL, Kong X, Jiranek WA. Two-year incidence and predictors of future knee arthroplasty in persons with symptomatic knee osteoarthritis: preliminary analysis of longitudinal data from the osteoarthritis initiative. *Knee*. 2009;16(6):494-500.
1590. Conaghan PG, D'Agostino MA, Le Bars M, et al. Clinical and ultrasonographic predictors of joint replacement for knee osteoarthritis: results from a large, 3-year, prospective EULAR study. *Ann Rheum Dis*. 2010;69(4):644-7.
1591. Zeni JA, Jr., Axe MJ, Snyder-Mackler L. Clinical predictors of elective total joint replacement in persons with end-stage knee osteoarthritis. *BMC Musculoskelet Disord*. 2010;11:86.
1592. Meier WA, Marcus RL, Dibble LE, et al. The long-term contribution of muscle activation and muscle size to quadriceps weakness following total knee arthroplasty. *J Geriatr Phys Ther*. 2009;32(2):35-8.
1593. Edwards RR, Haythornthwaite JA, Smith MT, Klick B, Katz JN. Catastrophizing and depressive symptoms as prospective predictors of outcomes following total knee replacement. *Pain Res Manag*. 2009;14(4):307-11.
1594. Gandhi R, Razak F, Tso P, Davey JR, Mahomed NN. Greater perceived helplessness in osteoarthritis predicts outcome of joint replacement surgery. *J Rheumatol*. 2009;36(7):1507-11.
1595. Riddle DL, Wade JB, Jiranek WA, Kong X. Preoperative pain catastrophizing predicts pain outcome after knee arthroplasty. *Clin Orthop Relat Res*. 2010;468(3):798-806.
1596. Witvrouw E, Pattyn E, Almqvist KF, et al. Catastrophic thinking about pain as a predictor of length of hospital stay after total knee arthroplasty: a prospective study. *Knee Surg Sports Traumatol Arthrosc*. 2009;17(10):1189-94.
1597. Newman JH, Ackroyd CE, Shah NA. Unicompartmental or total knee replacement? Five-year results of a prospective, randomised trial of 102 osteoarthritic knees with unicompartmental arthritis. *J Bone Joint Surg Br*. 1998;80(5):862-5.
1598. Newman J, Pydisetty RV, Ackroyd C. Unicompartmental or total knee replacement: the 15-year results of a prospective randomised controlled trial. *J Bone Joint Surg Br*. 2009;91(1):52-7.
1599. Hilding MB, Backbro B, Ryd L. Quality of life after knee arthroplasty. A randomized study of 3 designs in 42 patients, compared after 4 years. *Acta Orthop Scand*. 1997;68(2):156-60.
1600. Hilding MB, Yuan X, Ryd L. The stability of three different cementless tibial components. A randomized radiostereometric study in 45 knee arthroplasty patients. *Acta Orthop Scand*. 1995;66(1):21-7.
1601. Masri BA, Laskin RS, Windsor RE, Haas SB. Knee closure in total knee replacement: a randomized prospective trial. *Clin Orthop Relat Res*. 1996(331):81-6.
1602. Kim YH, Choi Y, Kim JS. Range of motion of standard and high-flexion posterior cruciate-retaining total knee prostheses a prospective randomized study. *J Bone Joint Surg Am*. 2009;91(8):1874-81.
1603. Kim YH, Choi Y, Kwon OR, Kim JS. Functional outcome and range of motion of high-flexion posterior cruciate-retaining and high-flexion posterior cruciate-substituting total knee prostheses. A prospective, randomized study. *J Bone Joint Surg Am*. 2009;91(4):753-60.
1604. Nutton RW, van der Linden ML, Rowe PJ, Gaston P, Wade FA. A prospective randomised double-blind study of functional outcome and range of flexion following total knee replacement with the NexGen standard and high flexion components. *J Bone Joint Surg Br*. 2008;90(1):37-42.
1605. Harato K, Bourne RB, Victor J, Snyder M, Hart J, Ries MD. Midterm comparison of posterior cruciate-retaining versus -substituting total knee arthroplasty using the Genesis II prosthesis. A multicenter prospective randomized clinical trial. *Knee*. 2008;15(3):217-21.
1606. Chaudhary R, Beaupre LA, Johnston DW. Knee range of motion during the first two years after use of posterior cruciate-stabilizing or posterior cruciate-retaining total knee prostheses. A randomized clinical trial. *J Bone Joint Surg Am*. 2008;90(12):2579-86.
1607. Tanzer M, Smith K, Burnett S. Posterior-stabilized versus cruciate-retaining total knee arthroplasty: balancing the gap. *J Arthroplasty*. 2002;17(7):813-9.
1608. McCalden RW, MacDonald SJ, Bourne RB, Marr JT. A randomized controlled trial comparing "high-flex" vs "standard" posterior cruciate substituting polyethylene tibial inserts in total knee arthroplasty. *J Arthroplasty*. 2009;24(6 Suppl):33-8.

1609. Uvehammer J, Karrholm J, Regner L, Carlsson L, Herberts P. Concave versus posterior-stabilized tibial joint surface in total knee arthroplasty: randomized evaluation of 47 knees. *J Arthroplasty*. 2001;16(1):25-32.
1610. Weeden SH, Schmidt R. A randomized, prospective study of primary total knee components designed for increased flexion. *J Arthroplasty*. 2007;22(3):349-52.
1611. Matsuda Y, Ishii Y, Noguchi H, Ishii R. Varus-valgus balance and range of movement after total knee arthroplasty. *J Bone Joint Surg Br*. 2005;87(6):804-8.
1612. Matsumoto T, Kuroda R, Kubo S, Muratsu H, Mizuno K, Kurosaka M. The intra-operative joint gap in cruciate-retaining compared with posterior-stabilised total knee replacement. *J Bone Joint Surg Br*. 2009;91(4):475-80.
1613. Saari T, Uvehammer J, Carlsson LV, Regner L, Karrholm J. Posterior stabilized component increased femoral bone loss after total knee replacement. 5-year follow-up of 47 knees using dual energy X-ray absorptiometry. *Knee*. 2006;13(6):435-9.
1614. Shoji H, Wolf A, Packard S, Yoshino S. Cruciate retained and excised total knee arthroplasty. A comparative study in patients with bilateral total knee arthroplasty. *Clin Orthop Relat Res*. 1994(305):218-22.
1615. Snider MG, Macdonald SJ. The influence of the posterior cruciate ligament and component design on joint line position after primary total knee arthroplasty. *J Arthroplasty*. 2009;24(7):1093-8.
1616. Lee SY, Matsui N, Kurosaka M, et al. A posterior-stabilized total knee arthroplasty shows condylar lift-off during deep knee bends. *Clin Orthop Relat Res*. 2005(435):181-4.
1617. Swanik CB, Lephart SM, Rubash HE. Proprioception, kinesthesia, and balance after total knee arthroplasty with cruciate-retaining and posterior stabilized prostheses. *J Bone Joint Surg Am*. 2004;86-A(2):328-34.
1618. Ishii Y, Noguchi H, Matsuda Y, Takeda M, Kiga H, Toyabe S. Range of motion during the perioperative period in total knee arthroplasty. *Arch Orthop Trauma Surg*. 2008;128(8):795-9.
1619. Aigner C, Windhager R, Pechmann M, Rehak P, Engeleke K. The influence of an anterior-posterior gliding mobile bearing on range of motion after total knee arthroplasty. A prospective, randomized, double-blinded study. *J Bone Joint Surg Am*. 2004;86-A(10):2257-62.
1620. Beard DJ, Pandit H, Price AJ, et al. Introduction of a new mobile-bearing total knee prosthesis: minimum three year follow-up of an RCT comparing it with a fixed-bearing device. *Knee*. 2007;14(6):448-51.
1621. Price AJ, Rees JL, Beard D, et al. A mobile-bearing total knee prosthesis compared with a fixed-bearing prosthesis. A multicentre single-blind randomised controlled trial. *J Bone Joint Surg Br*. 2003;85(1):62-7.
1622. Hasegawa M, Sudo A, Uchida A. Staged bilateral mobile-bearing and fixed-bearing total knee arthroplasty in the same patients: a prospective comparison of a posterior-stabilized prosthesis. *Knee Surg Sports Traumatol Arthrosc*. 2009;17(3):237-43.
1623. Munro JT, Pandit S, Walker CG, Clatworthy M, Pitto RP. Loss of tibial bone density in patients with rotating- or fixed-platform TKA. *Clin Orthop Relat Res*. 2010;468(3):775-81.
1624. Kim YH, Kim JS. Comparison of anterior-posterior-glide and rotating-platform low contact stress mobile-bearing total knee arthroplasties. *J Bone Joint Surg Am*. 2004;86-A(6):1239-47.
1625. Kim YH, Sohn KS, Kim JS. Range of motion of standard and high-flexion posterior stabilized total knee prostheses. A prospective, randomized study. *J Bone Joint Surg Am*. 2005;87(7):1470-5.
1626. Kim YH, Kim DY, Kim JS. Simultaneous mobile- and fixed-bearing total knee replacement in the same patients. A prospective comparison of mid-term outcomes using a similar design of prosthesis. *J Bone Joint Surg Br*. 2007;89(7):904-10.
1627. Kim YH, Kook HK, Kim JS. Comparison of fixed-bearing and mobile-bearing total knee arthroplasties. *Clin Orthop Relat Res*. 2001(392):101-15.
1628. Breugem SJ, Sierveelt IN, Schafroth MU, Blankevoort L, Schaap GR, van Dijk CN. Less anterior knee pain with a mobile-bearing prosthesis compared with a fixed-bearing prosthesis. *Clin Orthop Relat Res*. 2008;466(8):1959-65.
1629. Gioe TJ, Glynn J, Sembrano J, Suthers K, Santos ER, Singh J. Mobile and fixed-bearing (all-polyethylene tibial component) total knee arthroplasty designs. A prospective randomized trial. *J Bone Joint Surg Am*. 2009;91(9):2104-12.
1630. Gleeson RE, Evans R, Ackroyd CE, Webb J, Newman JH. Fixed or mobile bearing unicompartmental knee replacement? A comparative cohort study. *Knee*. 2004;11(5):379-84.

1631. Hansson U, Toksvig-Larsen S, Jorn LP, Ryd L. Mobile vs. fixed meniscal bearing in total knee replacement: a randomised radiostereometric study. *Knee*. 2005;12(6):414-8.
1632. Harrington MA, Hopkinson WJ, Hsu P, Manion L. Fixed- vs mobile-bearing total knee arthroplasty: does it make a difference?--a prospective randomized study. *J Arthroplasty*. 2009;24(6 Suppl):24-7.
1633. Henricson A, Dalen T, Nilsson KG. Mobile bearings do not improve fixation in cemented total knee arthroplasty. *Clin Orthop Relat Res*. 2006;448:114-21.
1634. Ladermann A, Lubbeke A, Stern R, Riand N, Fritschy D. Fixed-bearing versus mobile-bearing total knee arthroplasty: a prospective randomised, clinical and radiological study with mid-term results at 7 years. *Knee*. 2008;15(3):206-10.
1635. Li MG, Yao F, Joss B, Ioppolo J, Nivbrant B, Wood D. Mobile vs. fixed bearing unicondylar knee arthroplasty: A randomized study on short term clinical outcomes and knee kinematics. *Knee*. 2006;13(5):365-70.
1636. Seon JK, Park SJ, Lee KB, Yoon TR, Kozanek M, Song EK. Range of motion in total knee arthroplasty: a prospective comparison of high-flexion and standard cruciate-retaining designs. *J Bone Joint Surg Am*. 2009;91(3):672-9.
1637. Wylde V, Learmonth I, Potter A, Bettinson K, Lingard E. Patient-reported outcomes after fixed- versus mobile-bearing total knee replacement: a multi-centre randomised controlled trial using the Kinemax total knee replacement. *J Bone Joint Surg Br*. 2008;90(9):1172-9.
1638. Confalonieri N, Manzotti A, Pullen C. Comparison of a mobile with a fixed tibial bearing unicompartmental knee prosthesis: a prospective randomized trial using a dedicated outcome score. *Knee*. 2004;11(5):357-62.
1639. Pagnano MW, Trousdale RT, Stuart MJ, Hanssen AD, Jacofsky DJ. Rotating platform knees did not improve patellar tracking: a prospective, randomized study of 240 primary total knee arthroplasties. *Clin Orthop Relat Res*. 2004(428):221-7.
1640. Aglietti P, Baldini A, Buzzi R, Lup D, De Luca L. Comparison of mobile-bearing and fixed-bearing total knee arthroplasty: a prospective randomized study. *J Arthroplasty*. 2005;20(2):145-53.
1641. Garling EH, Valstar ER, Nelissen RG. Comparison of micromotion in mobile bearing and posterior stabilized total knee prostheses: a randomized RSA study of 40 knees followed for 2 years. *Acta Orthop*. 2005;76(3):353-61.
1642. Wohlrab D, Hube R, Zeh A, Hein W. Clinical and radiological results of high flex total knee arthroplasty: a 5 year follow-up. *Arch Orthop Trauma Surg*. 2009;129(1):21-4.
1643. Saari T, Uvehammer J, Carlsson LV, Herberts P, Regner L, Karrholm J. Kinematics of three variations of the Freeman-Samuelson total knee prosthesis. *Clin Orthop Relat Res*. 2003(410):235-47.
1644. Gao F, Waters B, Seager J, Dowling C, Vickers MD. Comparison of bupivacaine plus buprenorphine with bupivacaine alone by caudal blockade for post-operative pain relief after hip and knee arthroplasty. *Eur J Anaesthesiol*. 1995;12(5):471-6.
1645. Reiter A, Zulus E, Hartmann T, Hoerauf K. Preoperative oral administration of fast-release morphine sulfate reduces postoperative piritramide consumption. *Wien Klin Wochenschr*. 2003;115(12):417-20.
1646. Tarradell R, Pol O, Farre M, Barrera E, Puig MM. Respiratory and analgesic effects of meperidine and tramadol in patients undergoing orthopedic surgery. *Methods Find Exp Clin Pharmacol*. 1996;18(3):211-8.
1647. Grattidge P. Nausea and vomiting after major arthroplasty with spinal anaesthesia including morphine: a randomised trial of subhypnotic propofol infusion as prophylaxis. *Acta Anaesthesiol Scand*. 1998;42(1):124-7.
1648. Toksvig-Larsen S, Ryd L, Lindstrand A. Effect of a cooled saw blade on prosthesis fixation. Randomized radiostereometry of 33 knee cases. *Acta Orthop Scand*. 1994;65(5):533-7.
1649. Pandit H, Jenkins C, Beard DJ, et al. Cementless Oxford unicompartmental knee replacement shows reduced radiolucency at one year. *J Bone Joint Surg Br*. 2009;91(2):185-9.
1650. Reed MR, Bliss W, Sher JL, Emmerson KP, Jones SM, Partington PF. Extramedullary or intramedullary tibial alignment guides: a randomised, prospective trial of radiological alignment. *J Bone Joint Surg Br*. 2002;84(6):858-60.
1651. Carpiniello VL, Cendron M, Altman HG, Malloy TR, Booth R. Treatment of urinary complications after total joint replacement in elderly females. *Urology*. 1988;32(3):186-8.

1652. Hansson U, Toksvig-Larsen S, Ryd L, Aspenberg P. Once-weekly oral medication with alendronate does not prevent migration of knee prostheses: A double-blind randomized RSA study. *Acta Orthop*. 2009;80(1):41-5.
1653. Usichenko TI, Edinger H, Witstruck T, et al. Millimetre wave therapy for pain relief after total knee arthroplasty: a randomised controlled trial. *Eur J Pain*. 2008;12(5):617-23.
1654. Levy AS, Marmar E. The role of cold compression dressings in the postoperative treatment of total knee arthroplasty. *Clin Orthop Relat Res*. 1993(297):174-8.
1655. Andersen LO, Husted H, Otte KS, Kristensen BB, Kehlet H. A compression bandage improves local infiltration analgesia in total knee arthroplasty. *Acta Orthop*. 2008;79(6):806-11.
1656. Webb JM, Williams D, Ivory JP, Day S, Williamson DM. The use of cold compression dressings after total knee replacement: a randomized controlled trial. *Orthopedics*. 1998;21(1):59-61.
1657. Berti M, Casati A, Torri G, Aldegheri G, Lugani D, Fanelli G. Active warming, not passive heat retention, maintains normothermia during combined epidural-general anesthesia for hip and knee arthroplasty. *J Clin Anesth*. 1997;9(6):482-6.
1658. Hester RA, Nelson CL, Harrison S. Control of contamination of the operative team in total joint arthroplasty. *J Arthroplasty*. 1992;7(3):267-9.
1659. Maruyama S, Yoshiya S, Matsui N, Kuroda R, Kurosaka M. Functional comparison of posterior cruciate-retaining versus posterior stabilized total knee arthroplasty. *J Arthroplasty*. 2004;19(3):349-53.
1660. Gioe TJ, Bowman KR. A randomized comparison of all-polyethylene and metal-backed tibial components. *Clin Orthop Relat Res*. 2000(380):108-15.
1661. Gioe TJ, Killeen KK, Mehle S, Grimm K. Implementation and application of a community total joint registry: a twelve-year history. *J Bone Joint Surg Am*. 2006;88(6):1399-404.
1662. Higuchi H, Hatayama K, Shimizu M, Kobayashi A, Kobayashi T, Takagishi K. Relationship between joint gap difference and range of motion in total knee arthroplasty: a prospective randomised study between different platforms. *Int Orthop*. 2009;33(4):997-1000.
1663. Ishii Y, Matsuda Y, Sakata S, Onda N, Omori G. Primary total knee arthroplasty using the Genesis I total knee prosthesis: a 5- to 10-year follow-up study. *Knee*. 2005;12(5):341-5.
1664. Toksvig-Larsen S, Jorn LP, Ryd L, Lindstrand A. Hydroxyapatite-enhanced tibial prosthetic fixation. *Clin Orthop Relat Res*. 2000(370):192-200.
1665. Baker PN, Khaw FM, Kirk LM, Esler CN, Gregg PJ. A randomised controlled trial of cemented versus cementless press-fit condylar total knee replacement: 15-year survival analysis. *J Bone Joint Surg Br*. 2007;89(12):1608-14.
1666. Khaw FM, Kirk LM, Morris RW, Gregg PJ. A randomised, controlled trial of cemented versus cementless press-fit condylar total knee replacement. Ten-year survival analysis. *J Bone Joint Surg Br*. 2002;84(5):658-66.
1667. Nilsson KG, Karrholm J. Increased varus-valgus tilting of screw-fixed knee prostheses. Stereoradiographic study of uncemented versus cemented tibial components. *J Arthroplasty*. 1993;8(5):529-40.
1668. Nilsson KG, Karrholm J, Ekelund L, Magnusson P. Evaluation of micromotion in cemented vs uncemented knee arthroplasty in osteoarthritis and rheumatoid arthritis. Randomized study using roentgen stereophotogrammetric analysis. *J Arthroplasty*. 1991;6(3):265-78.
1669. Nilsson KG, Karrholm J, Linder L. Femoral component migration in total knee arthroplasty: randomized study comparing cemented and uncemented fixation of the Miller-Galante I design. *J Orthop Res*. 1995;13(3):347-56.
1670. Regner L, Carlsson L, Karrholm J. Bone mineral and migratory patterns in uncemented total knee arthroplasties: A randomized 5-year follow-up study of 38 knees. *Acta Orthop Scand*. 1999;70(6):603-8.
1671. Ensini A, Catani F, Leardini A, Romagnoli M, Giannini S. Alignments and clinical results in conventional and navigated total knee arthroplasty. *Clin Orthop Relat Res*. 2007;457:156-62.
1672. Park SE, Lee CT. Comparison of robotic-assisted and conventional manual implantation of a primary total knee arthroplasty. *J Arthroplasty*. 2007;22(7):1054-9.
1673. Brown AR, Taylor GJ, Gregg PJ. Air contamination during skin preparation and draping in joint replacement surgery. *J Bone Joint Surg Br*. 1996;78(1):92-4.

1674. Healy WL, Seidman J, Pfeifer BA, Brown DG. Cold compressive dressing after total knee arthroplasty. *Clin Orthop Relat Res.* 1994(299):143-6.
1675. Kirk PG, Rorabeck CH, Bourne RB. Clinical comparison of the Miller Galante I and AMK total knee systems. *J Arthroplasty.* 1994;9(2):131-6.
1676. Laskin RS. An oxidized Zr ceramic surfaced femoral component for total knee arthroplasty. *Clin Orthop Relat Res.* 2003(416):191-6.
1677. Laskin RS, Maruyama Y, Villaneuva M, Bourne R. Deep-dish congruent tibial component use in total knee arthroplasty: a randomized prospective study. *Clin Orthop Relat Res.* 2000(380):36-44.
1678. Linke RD, Ulmer M, Imhoff AB. [Replacement of the meniscus with a collagen implant (CMI)]. *Oper Orthop Traumatol.* 2006;18(5-6):453-62.
1679. Michelson JD, Lotke PA, Steinberg ME. Urinary-bladder management after total joint-replacement surgery. *N Engl J Med.* 1988;319(6):321-6.
1680. Parker DA, Rorabeck CH, Bourne RB. Long-term followup of cementless versus hybrid fixation for total knee arthroplasty. *Clin Orthop Relat Res.* 2001(388):68-76.
1681. Stern SH, Sharrock N, Kahn R, Insall JN. Hematologic and circulatory changes associated with total knee arthroplasty surgical instrumentation. *Clin Orthop Relat Res.* 1994(299):179-89.
1682. Wallace DF, Emmett SR, Kang KK, et al. The safety of peri-articular local anaesthetic injection for patients undergoing total knee replacement with autologous blood transfusion: a randomised trial. *J Bone Joint Surg Br.* 2012;94(12):1632-6.
1683. Stukenborg-Colsman C, Wirth CJ, Lazovic D, Wefer A. High tibial osteotomy versus unicompartmental joint replacement in unicompartmental knee joint osteoarthritis: 7-10-year follow-up prospective randomised study. *Knee.* 2001;8(3):187-94.
1684. Roysam GS, Oakley MJ. Subvastus approach for total knee arthroplasty: a prospective, randomized, and observer-blinded trial. *J Arthroplasty.* 2001;16(4):454-7.
1685. Karachalios T, Giotikas D, Roidis N, Poultides L, Bargiotas K, Malizos KN. Total knee replacement performed with either a mini-midvastus or a standard approach: a prospective randomised clinical and radiological trial. *J Bone Joint Surg Br.* 2008;90(5):584-91.
1686. Juosponis R, Tarasevicius S, Smailys A, Kalesinskas RJ. Functional and radiological outcome after total knee replacement performed with mini-midvastus or conventional arthrotomy: controlled randomised trial. *Int Orthop.* 2009;33(5):1233-7.
1687. B athis H, Perlick L, Blum C, L uring C, Perlick C, Grifka J. Midvastus approach in total knee arthroplasty: a randomized, double-blinded study on early rehabilitation. *Knee Surgery, Sports Traumatology, Arthroscopy.* 2005;13(7):545-50.
1688. Aglietti P, Baldini A, Sensi L. Quadriceps-sparing versus mini-subvastus approach in total knee arthroplasty. *Clin Orthop Relat Res.* 2006;452:106-11.
1689. Faure BT, Benjamin JB, Lindsey B, Volz RG, Schutte D. Comparison of the subvastus and paramedian surgical approaches in bilateral knee arthroplasty. *J Arthroplasty.* 1993;8(5):511-6.
1690. Engh GA, Holt BT, Parks NL. A midvastus muscle-splitting approach for total knee arthroplasty. *J Arthroplasty.* 1997;12(3):322-31.
1691. Carlsson LV, Albrektsson BE, Regner LR. Minimally invasive surgery vs conventional exposure using the Miller-Galante unicompartmental knee arthroplasty: a randomized radiostereometric study. *J Arthroplasty.* 2006;21(2):151-6.
1692. Lin W, Lin J, Horng LC, Chang SM, Jiang CC. Quadriceps-sparing, minimal-incision total knee arthroplasty: a comparative study. *J Arthroplasty.* 2009;24(7):1024-32.
1693. Choong PF, Dowsey MM, Stoney JD. Does accurate anatomical alignment result in better function and quality of life? Comparing conventional and computer-assisted total knee arthroplasty. *J Arthroplasty.* 2009;24(4):560-9.
1694. Confalonieri N, Manzotti A, Pullen C, Ragone V. Mini-incision versus mini-incision and computer-assisted surgery in total knee replacement: a radiological prospective randomised study. *Knee.* 2007;14(6):443-7.
1695. Cobb J, Henckel J, Gomes P, et al. Hands-on robotic unicompartmental knee replacement: a prospective, randomised controlled study of the acrobot system. *J Bone Joint Surg Br.* 2006;88(2):188-97.
1696. Stockl B, Nogler M, Rosiek R, Fischer M, Krismer M, Kessler O. Navigation improves accuracy of rotational alignment in total knee arthroplasty. *Clin Orthop Relat Res.* 2004(426):180-6.

1697. Oberst M, Bertsch C, Konrad G, Lahm A, Holz U. CT analysis after navigated versus conventional implantation of TKA. *Arch Orthop Trauma Surg.* 2008;128(6):561-6.
1698. Kalairajah Y, Cossey AJ, Verrall GM, Ludbrook G, Spriggins AJ. Are systemic emboli reduced in computer-assisted knee surgery?: A prospective, randomised, clinical trial. *J Bone Joint Surg Br.* 2006;88(2):198-202.
1699. Dutton AQ, Yeo SJ, Yang KY, Lo NN, Chia KU, Chong HC. Computer-assisted minimally invasive total knee arthroplasty compared with standard total knee arthroplasty. A prospective, randomized study. *J Bone Joint Surg Am.* 2008;90(1):2-9.
1700. van Strien T, van der Linden-van der Zwaag E, Kaptein B, van Erkel A, Valstar E, Nelissen R. Computer assisted versus conventional cemented total knee prostheses alignment accuracy and micromotion of the tibial component. *Int Orthop.* 2009;33(5):1255-61.
1701. Chin PL, Yang KY, Yeo SJ, Lo NN. Randomized control trial comparing radiographic total knee arthroplasty implant placement using computer navigation versus conventional technique. *J Arthroplasty.* 2005;20(5):618-26.
1702. Sparmann M, Wolke B, Czupalla H, Banzer D, Zink A. Positioning of total knee arthroplasty with and without navigation support. A prospective, randomised study. *J Bone Joint Surg Br.* 2003;85(6):830-5.
1703. Hall J, Copp SN, Adelson WS, D'Lima DD, Colwell CW, Jr. Extensor mechanism function in single-radius vs multiradius femoral components for total knee arthroplasty. *J Arthroplasty.* 2008;23(2):216-9.
1704. Hurschler C, Seehaus F, Emmerich J, Kaptein BL, Windhagen H. Accuracy of model-based RSA contour reduction in a typical clinical application. *Clin Orthop Relat Res.* 2008;466(8):1978-86.
1705. Kim YH, Kim JS, Hong KS, Kim YJ, Kim JH. Prevalence of fat embolism after total knee arthroplasty performed with or without computer navigation. *J Bone Joint Surg Am.* 2008;90(1):123-8.
1706. Weinrauch P, Myers N, Wilkinson M, Dodsworth J, Fitzpatrick P, Whitehouse S. Comparison of early postoperative rehabilitation outcome following total knee arthroplasty using different surgical approaches and instrumentation. *J Orthop Surg (Hong Kong).* 2006;14(1):47-52.
1707. Hyldahl H, Regner L, Carlsson L, Karrholm J, Weidenhielm L. All-polyethylene vs. metal-backed tibial component in total knee arthroplasty-a randomized RSA study comparing early fixation of horizontally and completely cemented tibial components: part 2. Completely cemented components: MB not superior to AP components. *Acta Orthop.* 2005;76(6):778-84.
1708. Hyldahl H, Regner L, Carlsson L, Karrholm J, Weidenhielm L. All-polyethylene vs. metal-backed tibial component in total knee arthroplasty-a randomized RSA study comparing early fixation of horizontally and completely cemented tibial components: part 1. Horizontally cemented components: AP better fixated than MB. *Acta Orthop.* 2005;76(6):769-77.
1709. Mattsson P, Alberts A, Dahlberg G, Sohlman M, Hyldahl HC, Larsson S. Resorbable cement for the augmentation of internally-fixed unstable trochanteric fractures. A prospective, randomised multicentre study. *J Bone Joint Surg Br.* 2005;87(9):1203-9.
1710. Norgren B, Dalen T, Nilsson KG. All-poly tibial component better than metal-backed: a randomized RSA study. *Knee.* 2004;11(3):189-96.
1711. Muller SD, Deehan DJ, Holland JP, et al. Should we reconsider all-polyethylene tibial implants in total knee replacement? *J Bone Joint Surg Br.* 2006;88(12):1596-602.
1712. Adalberth G, Nilsson KG, Bystrom S, Kolstad K, Milbrink J. All-polyethylene versus metal-backed and stemmed tibial components in cemented total knee arthroplasty. A prospective, randomised RSA study. *J Bone Joint Surg Br.* 2001;83(6):825-31.
1713. Adalberth G, Nilsson KG, Bystrom S, Kolstad K, Milbrink J. Low-conforming all-polyethylene tibial component not inferior to metal-backed component in cemented total knee arthroplasty: prospective, randomized radiostereometric analysis study of the AGC total knee prosthesis. *J Arthroplasty.* 2000;15(6):783-92.
1714. Hyldahl HC, Regner L, Carlsson L, Karrholm J, Weidenhielm L. Does metal backing improve fixation of tibial component in unicondylar knee arthroplasty? A randomized radiostereometric analysis. *J Arthroplasty.* 2001;16(2):174-9.
1715. Bettinson KA, Pinder IM, Moran CG, Weir DJ, Lingard EA. All-polyethylene compared with metal-backed tibial components in total knee arthroplasty at ten years. A prospective, randomized controlled trial. *J Bone Joint Surg Am.* 2009;91(7):1587-94.

1716. Nilsson KG, Dalen T. Inferior performance of Boneloc bone cement in total knee arthroplasty: a prospective randomized study comparing Boneloc with Palacos using radiostereometry (RSA) in 19 patients. *Acta Orthop Scand*. 1998;69(5):479-83.
1717. Onsten I, Nordqvist A, Carlsson AS, Besjakov J, Shott S. Hydroxyapatite augmentation of the porous coating improves fixation of tibial components. A randomised RSA study in 116 patients. *J Bone Joint Surg Br*. 1998;80(3):417-25.
1718. Carlsson A, Bjorkman A, Besjakov J, Onsten I. Cemented tibial component fixation performs better than cementless fixation: a randomized radiostereometric study comparing porous-coated, hydroxyapatite-coated and cemented tibial components over 5 years. *Acta Orthop*. 2005;76(3):362-9.
1719. Nilsson KG, Henricson A, Norgren B, Dalen T. Uncemented HA-coated implant is the optimum fixation for TKA in the young patient. *Clin Orthop Relat Res*. 2006;448:129-39.
1720. Nilsson KG, Karrholm J, Carlsson L, Dalen T. Hydroxyapatite coating versus cemented fixation of the tibial component in total knee arthroplasty: prospective randomized comparison of hydroxyapatite-coated and cemented tibial components with 5-year follow-up using radiostereometry. *J Arthroplasty*. 1999;14(1):9-20.
1721. Nelissen RG, Valstar ER, Rozing PM. The effect of hydroxyapatite on the micromotion of total knee prostheses. A prospective, randomized, double-blind study. *J Bone Joint Surg Am*. 1998;80(11):1665-72.
1722. Beaupre LA, al-Yamani M, Huckell JR, Johnston DW. Hydroxyapatite-coated tibial implants compared with cemented tibial fixation in primary total knee arthroplasty. A randomized trial of outcomes at five years. *J Bone Joint Surg Am*. 2007;89(10):2204-11.
1723. Uvehammer J, Karrholm J, Carlsson L. Cemented versus hydroxyapatite fixation of the femoral component of the Freeman-Samuels total knee replacement: a radiostereometric analysis. *J Bone Joint Surg Br*. 2007;89(1):39-44.
1724. Regner L, Carlsson L, Karrholm J, Herberts P. Tibial component fixation in porous- and hydroxyapatite-coated total knee arthroplasty: a radiostereometric evaluation of migration and inducible displacement after 5 years. *J Arthroplasty*. 2000;15(6):681-9.
1725. Regner L, Carlsson L, Karrholm J, Herberts P. Ceramic coating improves tibial component fixation in total knee arthroplasty. *J Arthroplasty*. 1998;13(8):882-9.
1726. Hansson U, Ryd L, Toksvig-Larsen S. A randomised RSA study of Peri-Apatite HA coating of a total knee prosthesis. *Knee*. 2008;15(3):211-6.
1727. Petersen MM, Gehrchen PM, Ostgaard SE, Nielsen PK, Lund B. Effect of hydroxyapatite-coated tibial components on changes in bone mineral density of the proximal tibia after uncemented total knee arthroplasty: a prospective randomized study using dual-energy x-ray absorptiometry. *J Arthroplasty*. 2005;20(4):516-20.
1728. Gao F, Henricson A, Nilsson KG. Cemented versus uncemented fixation of the femoral component of the NexGen CR total knee replacement in patients younger than 60 years: a prospective randomised controlled RSA study. *Knee*. 2009;16(3):200-6.
1729. Dalen T, Nilsson KG. VersaBond bone cement prospective randomized study of the clinical properties of a new bone cement in total knee replacement. *Knee*. 2005;12(4):311-7.
1730. Hilding M, Ryd L, Toksvig-Larsen S, Aspenberg P. Clodronate prevents prosthetic migration: a randomized radiostereometric study of 50 total knee patients. *Acta Orthop Scand*. 2000;71(6):553-7.
1731. Dunbar MJ, Wilson DA, Hennigar AW, Amirault JD, Gross M, Reardon GP. Fixation of a trabecular metal knee arthroplasty component. A prospective randomized study. *J Bone Joint Surg Am*. 2009;91(7):1578-86.
1732. Toksvig-Larsen S, Ryd L, Lindstrand A. Early inducible displacement of tibial components in total knee prostheses inserted with and without cement: a randomized study with roentgen stereophotogrammetric analysis. *J Bone Joint Surg Am*. 1998;80(1):83-9.
1733. van der Linde MJ, Garling EH, Valstar ER, Tonino AJ, Nelissen RG. Periapatite may not improve micromotion of knee prostheses in rheumatoid arthritis. *Clin Orthop Relat Res*. 2006;448:122-8.
1734. Albrektsson BE, Carlsson LV, Freeman MA, Herberts P, Ryd L. Proximally cemented versus uncemented Freeman-Samuels knee arthroplasty. A prospective randomised study. *J Bone Joint Surg Br*. 1992;74(2):233-8.

1735. Clarke MT, Green JS, Harper WM, Gregg PJ. Cement as a risk factor for deep-vein thrombosis. Comparison of cemented TKR, uncemented TKR and cemented THR. *J Bone Joint Surg Br.* 1998;80(4):611-3.
1736. McCaskie AW, Deehan DJ, Green TP, et al. Randomised, prospective study comparing cemented and cementless total knee replacement: results of press-fit condylar total knee replacement at five years. *J Bone Joint Surg Br.* 1998;80(6):971-5.
1737. Saari T, Li MG, Wood D, Nivbrant B. Comparison of cementing techniques of the tibial component in total knee replacement. *Int Orthop.* 2009;33(5):1239-42.
1738. Myles CM, Rowe PJ, Nutton RW, Burnett R. The effect of patella resurfacing in total knee arthroplasty on functional range of movement measured by flexible electrogoniometry. *Clin Biomech (Bristol, Avon).* 2006;21(7):733-9.
1739. Smith AJ, Wood DJ, Li MG. Total knee replacement with and without patellar resurfacing: a prospective, randomised trial using the profix total knee system. *J Bone Joint Surg Br.* 2008;90(1):43-9.
1740. Barrack RL, Bertot AJ, Wolfe MW, Waldman DA, Milicic M, Myers L. Patellar resurfacing in total knee arthroplasty. A prospective, randomized, double-blind study with five to seven years of follow-up. *J Bone Joint Surg Am.* 2001;83-A(9):1376-81.
1741. Barrack RL, Wolfe MW, Waldman DA, Milicic M, Bertot AJ, Myers L. Resurfacing of the patella in total knee arthroplasty. A prospective, randomized, double-blind study. *J Bone Joint Surg Am.* 1997;79(8):1121-31.
1742. Burnett RS, Boone JL, McCarthy KP, Rosenzweig S, Barrack RL. A prospective randomized clinical trial of patellar resurfacing and nonresurfacing in bilateral TKA. *Clin Orthop Relat Res.* 2007;464:65-72.
1743. Burnett RS, Boone JL, Rosenzweig SD, Steger-May K, Barrack RL. Patellar resurfacing compared with nonresurfacing in total knee arthroplasty. A concise follow-up of a randomized trial. *J Bone Joint Surg Am.* 2009;91(11):2562-7.
1744. Burnett RS, Bourne RB. Indications for patellar resurfacing in total knee arthroplasty. *Instr Course Lect.* 2004;53:167-86.
1745. Campbell DG, Duncan WW, Ashworth M, et al. Patellar resurfacing in total knee replacement: a ten-year randomised prospective trial. *J Bone Joint Surg Br.* 2006;88(6):734-9.
1746. Bourne RB, Rorabeck CH, Vaz M, Kramer J, Hardie R, Robertson D. Resurfacing versus not resurfacing the patella during total knee replacement. *Clin Orthop Relat Res.* 1995(321):156-61.
1747. Partio E WJ. Comparison of patellar resurfacing and nonresurfacing in total knee arthroplasty: A prospective randomized study. *J Orthop Rheum.* 1995;8:69-74.
1748. Feller JA, Bartlett RJ, Lang DM. Patellar resurfacing versus retention in total knee arthroplasty. *J Bone Joint Surg Br.* 1996;78(2):226-8.
1749. Kajino A, Yoshino S, Kameyama S, Kohda M, Nagashima S. Comparison of the results of bilateral total knee arthroplasty with and without patellar replacement for rheumatoid arthritis. A follow-up note. *J Bone Joint Surg Am.* 1997;79(4):570-4.
1750. Keblish PA, Varma AK, Greenwald AS. Patellar resurfacing or retention in total knee arthroplasty. A prospective study of patients with bilateral replacements. *J Bone Joint Surg Br.* 1994;76(6):930-7.
1751. Mayman D, Bourne RB, Rorabeck CH, Vaz M, Kramer J. Resurfacing versus not resurfacing the patella in total knee arthroplasty: 8- to 10-year results. *J Arthroplasty.* 2003;18(5):541-5.
1752. Waters TS, Bentley G. Patellar resurfacing in total knee arthroplasty. A prospective, randomized study. *J Bone Joint Surg Am.* 2003;85-A(2):212-7.
1753. Wood DJ, Smith AJ, Collopy D, White B, Brankov B, Bulsara MK. Patellar resurfacing in total knee arthroplasty: a prospective, randomized trial. *J Bone Joint Surg Am.* 2002;84-A(2):187-93.
1754. Newman JH, Ackroyd CE, Shah NA, Karachalios T. Should the patella be resurfaced during total knee replacement? *Knee.* 2000;7(1):17-23.
1755. Schroeder-Boersch H, Scheller G, Synnatschke M, Arnold P, Jani L. [Patellar resurfacing. Results of a prospective randomized study]. *Orthopade.* 1998;27(9):642-50.
1756. Healy WL, Pfeifer BA, Kurtz SR, et al. Evaluation of autologous shed blood for autotransfusion after orthopaedic surgery. *Clin Orthop Relat Res.* 1994(299):53-9.
1757. Simpson MB, Murphy KP, Chambers HG, Bucknell AL. The effect of postoperative wound drainage reinfusion in reducing the need for blood transfusions in elective total joint arthroplasty: a prospective, randomized study. *Orthopedics.* 1994;17(2):133-7.

1758. Majkowski RS, Currie IC, Newman JH. Postoperative collection and reinfusion of autologous blood in total knee arthroplasty. *Ann R Coll Surg Engl*. 1991;73(6):381-4.
1759. Newman JH, Bowers M, Murphy J. The clinical advantages of autologous transfusion. A randomized, controlled study after knee replacement. *J Bone Joint Surg Br*. 1997;79(4):630-2.
1760. Faris P. Use of recombinant human erythropoietin in the perioperative period of orthopedic surgery. *Am J Med*. 1996;101(2A):285-325.
1761. Gannon DM, Lombardi AV, Jr., Mallory TH, Vaughn BK, Finney CR, Niemcryk S. An evaluation of the efficacy of postoperative blood salvage after total joint arthroplasty. A prospective randomized trial. *J Arthroplasty*. 1991;6(2):109-14.
1762. Kristensen PW, Sorensen LS, Thyregod HC. Autotransfusion of drainage blood in arthroplasty. A prospective, controlled study of 31 operations. *Acta Orthop Scand*. 1992;63(4):377-80.
1763. Mah ET, Davis R, Seshadri P, Nyman TL, Seshadri R. The role of autologous blood transfusion in joint replacement surgery. *Anaesth Intensive Care*. 1995;23(4):472-7.
1764. Slagis SV, Benjamin JB, Volz RG, Giordano GF. Postoperative blood salvage in total hip and knee arthroplasty. A randomised controlled trial. *J Bone Joint Surg Br*. 1991;73(4):591-4.
1765. Seo ES, Yoon SW, Koh IJ, Chang CB, Kim TK. Subcutaneous versus intraarticular indwelling closed suction drainage after TKA: a randomized controlled trial. *Clin Orthop Relat Res*. 2010;468(8):2168-76.
1766. Ovardia D, Luger E, Bickels J, Menachem A, Dekel S. Efficacy of closed wound drainage after total joint arthroplasty. A prospective randomized study. *J Arthroplasty*. 1997;12(3):317-21.
1767. Berman AT, Fabiano D, Bosacco SJ, Weiss AA. Comparison between intermittent (spring-loaded) and continuous closed suction drainage of orthopedic wounds: a controlled clinical trial. *Orthopedics*. 1990;13(3):309-14.
1768. Ritter MA, Fechtman RW. Closed wound drainage systems: the Stryker Constavac versus the Snyder Hemovac. *Orthop Rev*. 1988;17(5):496-8.
1769. Ritter MA, Herbst SA, Keating EM, Faris PM, Meding JB. Long-term survival analysis of a posterior cruciate-retaining total condylar total knee arthroplasty. *Clin Orthop Relat Res*. 1994(309):136-45.
1770. Willemens D, Paul J, White SH, Crook DW. Closed suction drainage following knee arthroplasty. Effectiveness and risks. *Clin Orthop Relat Res*. 1991(264):232-4.
1771. Confalonieri N, Manzotti A, Pullen C. Is closed-suction drain necessary in unicompartmental knee replacement? A prospective randomised study. *Knee*. 2004;11(5):399-402.
1772. Amin A, Watson A, Mangwani J, Nawabi DH, Ahluwalia R, Loeffler M. A prospective randomised controlled trial of autologous retransfusion in total knee replacement. *J Bone Joint Surg Br*. 2008;90(4):451-4.
1773. Barwell J, Anderson G, Hassan A, Rawlings I. The effects of early tourniquet release during total knee arthroplasty: a prospective randomized double-blind study. *J Bone Joint Surg Br*. 1997;79(2):265-8.
1774. Burkart BC, Bourne RB, Rorabeck CH, Kirk PG, Nott L. The efficacy of tourniquet release in blood conservation after total knee arthroplasty. *Clin Orthop Relat Res*. 1994(299):147-52.
1775. Christodoulou AG, Ploumis AL, Terzidis IP, Chantzidis P, Metsovitis SR, Nikiforos DG. The role of timing of tourniquet release and cementing on perioperative blood loss in total knee replacement. *Knee*. 2004;11(4):313-7.
1776. Wakankar HM, Nicholl JE, Koka R, D'Arcy JC. The tourniquet in total knee arthroplasty. A prospective, randomised study. *J Bone Joint Surg Br*. 1999;81(1):30-3.
1777. Jorn LP, Lindstrand A, Toksvig-Larsen S. Tourniquet release for hemostasis increases bleeding. A randomized study of 77 knee replacements. *Acta Orthop Scand*. 1999;70(3):265-7.
1778. Friedman RJ, Friedrich LV, White RL, Kays MB, Brundage DM, Graham J. Antibiotic prophylaxis and tourniquet inflation in total knee arthroplasty. *Clin Orthop Relat Res*. 1990(260):17-23.
1779. Friedrich LV, White RL, Brundage DM, Kays MB, Friedman RJ. The effect of tourniquet inflation on cefazolin tissue penetration during total knee arthroplasty. *Pharmacotherapy*. 1990;10(6):373-7.
1780. Steffin B, Green-Riviere E, Giori NJ. Timing of tourniquet release in total knee arthroplasty when using a postoperative blood salvage drain. *J Arthroplasty*. 2009;24(4):539-42.
1781. Ishii Y, Matsuda Y. Effect of tourniquet pressure on perioperative blood loss associated with cementless total knee arthroplasty: a prospective, randomized study. *J Arthroplasty*. 2005;20(3):325-30.
1782. Abdel-Salam A, Eyres KS. Effects of tourniquet during total knee arthroplasty. A prospective randomised study. *J Bone Joint Surg Br*. 1995;77(2):250-3.

1783. Ahl T, Dalen N, Jorbeck H, Hoborn J. Air contamination during hip and knee arthroplasties. Horizontal laminar flow randomized vs. conventional ventilation. *Acta Orthop Scand*. 1995;66(1):17-20.
1784. Bhandari M, Bajammal S, Guyatt GH, et al. Effect of bisphosphonates on periprosthetic bone mineral density after total joint arthroplasty. A meta-analysis. *J Bone Joint Surg Am*. 2005;87(2):293-301.
1785. Hilding M, Aspenberg P. Local peroperative treatment with a bisphosphonate improves the fixation of total knee prostheses: a randomized, double-blind radiostereometric study of 50 patients. *Acta Orthop*. 2007;78(6):795-9.
1786. Huusko TM, Karppi P, Kautiainen H, Suominen H, Avikainen V, Sulkava R. Randomized, double-blind, clinically controlled trial of intranasal calcitonin treatment in patients with hip fracture. *Calcif Tissue Int*. 2002;71(6):478-84.
1787. Wilkinson JM, Stockley I, Peel NF, et al. Effect of pamidronate in preventing local bone loss after total hip arthroplasty: a randomized, double-blind, controlled trial. *J Bone Miner Res*. 2001;16(3):556-64.
1788. Venesmaa PK, Kroger HP, Miettinen HJ, Jurvelin JS, Suomalainen OT, Alhav EM. Alendronate reduces periprosthetic bone loss after uncemented primary total hip arthroplasty: a prospective randomized study. *J Bone Miner Res*. 2001;16(11):2126-31.
1789. Soininvaara TA, Jurvelin JS, Miettinen HJ, Suomalainen OT, Alhava EM, Kroger PJ. Effect of alendronate on periprosthetic bone loss after total knee arthroplasty: a one-year, randomized, controlled trial of 19 patients. *Calcif Tissue Int*. 2002;71(6):472-7.
1790. Hennigs T, Arabmotlagh M, Schwarz A, Zichner L. Dose-dependent prevention of early periprosthetic bone loss by alendronate. *Z Orthop Ihre Grenzgeb*. 2002;140(1):42-7.
1791. Amstutz HC, Le Duff MJ, Harvey N, Hoberg M. Improved survivorship of hybrid metal-on-metal hip resurfacing with second-generation techniques for Crowe-I and II developmental dysplasia of the hip. *J Bone Joint Surg Am*. 2008;90 Suppl 312-20.
1792. Buergi ML, Walter WL. Hip resurfacing arthroplasty: the Australian experience. *J Arthroplasty*. 2007;22(7 Suppl 3):61-5.
1793. Grecula MJ. Resurfacing arthroplasty in osteonecrosis of the hip. *Orthop Clin North Am*. 2005;36(2):231-42, x.
1794. Greenfield S, Apolone G, McNeil BJ, Cleary PD. The importance of co-existent disease in the occurrence of postoperative complications and one-year recovery in patients undergoing total hip replacement. Comorbidity and outcomes after hip replacement. *Med Care*. 1993;31(2):141-54.
1795. Hartl A, Schillinger M, Wanivenhaus A. Cemented versus cementless total hip arthroplasty for osteoarthritis and other non-traumatic diseases (Protocol). *Cochrane Database Syst Rev*. 2004;Art. No.: CD004850. DOI: 10.1002/14651858.CD004850.(3).
1796. Havelin LI, Engesaeter LB, Espehaug B, Furnes O, Lie SA, Vollset SE. The Norwegian Arthroplasty Register: 11 years and 73,000 arthroplasties. *Acta Orthop Scand*. 2000;71(4):337-53.
1797. Healy WL, Sharma S, Schwartz B, Iorio R. Athletic activity after total joint arthroplasty. *J Bone Joint Surg Am*. 2008;90(10):2245-52.
1798. Howie DW, McGee MA, Costi K, Graves SE. Metal-on-metal resurfacing versus total hip replacement-the value of a randomized clinical trial. *Orthop Clin North Am*. 2005;36(2):195-201, ix.
1799. Jager M, Begg M, Krauspe R. Partial hemi-resurfacing of the hip joint--a new approach to treat local osteochondral defects? *Biomed Tech*. 2006;51(5-6):371-6.
1800. McQueen M, Littlejohn A, Hughes SP. A comparison of systemic cefuroxime and cefuroxime loaded bone cement in the prevention of early infection after total joint replacement. *Int Orthop*. 1987;11(3):241-3.
1801. Ong KL, Manley MT, Kurtz SM. Have contemporary hip resurfacing designs reached maturity? A review. *J Bone Joint Surg Am*. 2008;90 Suppl 381-8.
1802. Onsten I, Carlsson AS, Ohlin A, Nilsson JA. Migration of acetabular components, inserted with and without cement, in one-stage bilateral hip arthroplasty. A controlled, randomized study using roentgenstereophotogrammetric analysis. *J Bone Joint Surg Am*. 1994;76(2):185-94.
1803. Rodway NV, Rodway GW. Return to mountain sports after minimally invasive two-incision hip arthroplasty. *Wilderness Environ Med*. 2008;19(4):316-7.
1804. Schmalzried TP. Total resurfacing for osteonecrosis of the hip. *Clin Orthop Relat Res*. 2004(429):151-6.
1805. Wymenga AB, Hekster YA, Theeuwes A, Muyltjens HL, van Horn JR, Slooff TJ. Antibiotic use after cefuroxime prophylaxis in hip and knee joint replacement. *Clin Pharmacol Ther*. 1991;50(2):215-20.

1806. Gatell JM, Riba J, Lozano ML, Mana J, Ramon R, Garcia SanMiguel J. Prophylactic cefamandole in orthopaedic surgery. *J Bone Joint Surg Am*. 1984;66(8):1219-22.
1807. Bryan CS, Morgan SL, Caton RJ, Lunceford EM, Jr. Cefazolin versus cefamandole for prophylaxis during total joint arthroplasty. *Clin Orthop Relat Res*. 1988(228):117-22.
1808. Periti P, Stringa G, Mini E. Comparative multicenter trial of teicoplanin versus cefazolin for antimicrobial prophylaxis in prosthetic joint implant surgery. Italian Study Group for Antimicrobial Prophylaxis in Orthopedic Surgery. *Eur J Clin Microbiol Infect Dis*. 1999;18(2):113-9.
1809. DeBenedictis KJ, Rowan NM, Boyer BL. A double-blind study comparing cefonicid with cefazolin as prophylaxis in patients undergoing total hip or knee replacement. *Rev Infect Dis*. 1984;6 Suppl 4S901-4.
1810. Vainionpaa S, Wilppula E, Lalla M, Renkonen OV, Rokkanen P. Cefamandole and isoxazolyl penicillins in antibiotic prophylaxis of patients undergoing total hip or knee-joint arthroplasty. *Arch Orthop Trauma Surg*. 1988;107(4):228-30.
1811. Soave R, Hirsch JC, Salvati EA, Brause BD, Roberts RB. Comparison of ceforanide and cephalothin prophylaxis in patients undergoing total joint arthroplasty. *Orthopedics*. 1986;9(12):1657-60.
1812. Chiu FY, Chen CM, Lin CF, Lo WH. Cefuroxime-impregnated cement in primary total knee arthroplasty: a prospective, randomized study of three hundred and forty knees. *J Bone Joint Surg Am*. 2002;84-A(5):759-62.
1813. Chiu FY, Lin CF, Chen CM, Lo WH, Chaung TY. Cefuroxime-impregnated cement at primary total knee arthroplasty in diabetes mellitus. A prospective, randomised study. *J Bone Joint Surg Br*. 2001;83(5):691-5.
1814. Josefsson G, Lindberg L, Wiklander B. Systemic antibiotics and gentamicin-containing bone cement in the prophylaxis of postoperative infections in total hip arthroplasty. *Clin Orthop Relat Res*. 1981(159):194-200.
1815. Mauerhan DR, Nelson CL, Smith DL, et al. Prophylaxis against infection in total joint arthroplasty. One day of cefuroxime compared with three days of cefazolin. *J Bone Joint Surg Am*. 1994;76(1):39-45.
1816. Espehaug B, Engesaeter LB, Vollset SE, Havelin LI, Langeland N. Antibiotic prophylaxis in total hip arthroplasty. Review of 10,905 primary cemented total hip replacements reported to the Norwegian arthroplasty register, 1987 to 1995. *J Bone Joint Surg Br*. 1997;79(4):590-5.
1817. Josefsson G, Gudmundsson G, Kolmert L, Wijkstrom S. Prophylaxis with systemic antibiotics versus gentamicin bone cement in total hip arthroplasty. A five-year survey of 1688 hips. *Clin Orthop Relat Res*. 1990(253):173-8.
1818. Josefsson G, Kolmert L. Prophylaxis with systematic antibiotics versus gentamicin bone cement in total hip arthroplasty. A ten-year survey of 1,688 hips. *Clin Orthop Relat Res*. 1993(292):210-4.
1819. Nelson CL, Evans RP, Blaha JD, Calhoun J, Henry SL, Patzakis MJ. A comparison of gentamicin-impregnated polymethylmethacrylate bead implantation to conventional parenteral antibiotic therapy in infected total hip and knee arthroplasty. *Clin Orthop Relat Res*. 1993(295):96-101.
1820. Richardson JB, Roberts A, Robertson JF, John PJ, Sweeney G. Timing of antibiotic administration in knee replacement under tourniquet. *J Bone Joint Surg Br*. 1993;75(1):32-5.
1821. Mollan RA, Haddock M, Webb CH. Teicoplanin vs cephamandole for antimicrobial prophylaxis in prosthetic joint implant surgery: (preliminary results). *Eur J Surg Suppl*. 1992(567):19-21.
1822. Wong J, Wong S, Nolde T, Yabsley RH. Effects of an experimental program on post-hospital adjustment of early discharged patients. *Int J Nurs Stud*. 1990;27(1):7-20.
1823. Gammon J, Mulholland CW. Effect of preparatory information prior to elective total hip replacement on post-operative physical coping outcomes. *Int J Nurs Stud*. 1996;33(6):589-604.
1824. Gammon J, Mulholland CW. Effect of preparatory information prior to elective total hip replacement on psychological coping outcomes. *J Adv Nurs*. 1996;24(2):303-8.
1825. Johnston M, Vogeles C. Benefits of psychological preparation for surgery: a meta-analysis. *Ann Behav Med*. 1993;15(4):245-56.
1826. Daltroy LH, Morlino CI, Eaton HM, Poss R, Liang MH. Preoperative education for total hip and knee replacement patients. *Arthritis Care Res*. 1998;11(6):469-78.
1827. Mancuso CA, Graziano S, Briskie LM, et al. Randomized trials to modify patients' preoperative expectations of hip and knee arthroplasties. *Clin Orthop Relat Res*. 2008;466(2):424-31.
1828. Vukomanovic A, Popovic Z, Durovic A, Krstic L. The effects of short-term preoperative physical therapy and education on early functional recovery of patients younger than 70 undergoing total hip arthroplasty. *Vojnosanit Pregl*. 2008;65(4):291-7.

1829. Butler GS, Hurley CA, Buchanan KL, Smith-VanHorne J. Prehospital education: effectiveness with total hip replacement surgery patients. *Patient Educ Couns*. 1996;29(2):189-97.
1830. Wong J, Wong S. A randomized controlled trial of a new approach to preoperative teaching and patient compliance. *Int J Nurs Stud*. 1985;22(2):105-15.
1831. Siggeirsdottir K, Olafsson O, Jonsson H, Iwarsson S, Gudnason V, Jonsson BY. Short hospital stay augmented with education and home-based rehabilitation improves function and quality of life after hip replacement: randomized study of 50 patients with 6 months of follow-up. *Acta Orthop*. 2005;76(4):555-62.
1832. Pour AE, Parvizi J, Sharkey PF, Hozack WJ, Rothman RH. Minimally invasive hip arthroplasty: what role does patient preconditioning play? *J Bone Joint Surg Am*. 2007;89(9):1920-7.
1833. Gocen Z, Sen A, Unver B, Karatosun V, Gunal I. The effect of preoperative physiotherapy and education on the outcome of total hip replacement: a prospective randomized controlled trial. *Clin Rehabil*. 2004;18(4):353-8.
1834. Giraudet-Le Quintrec J, Coste J, Vastel L, Pacault V, Jeanne L, Lamas JP, Kerboull L, Fougeray M, Conseiller C, Kahan A, Courpied JP. Positive effect of patient education for hip surgery: a randomized trial. *Clin Orthop Relat Res*. 2003(414):112-20.
1835. McGregor AH, Rylands H, Owen A, Dore CJ, Hughes SP. Does preoperative hip rehabilitation advice improve recovery and patient satisfaction? *J Arthroplasty*. 2004;19(4):464-8.
1836. Burns DD, Nolen-Hoeksema S. Therapeutic empathy and recovery from depression in cognitive-behavioral therapy: a structural equation model. *J Consult Clin Psychol*. 1992;60(3):441-9.
1837. Santavirta N, Lillqvist G, Sarvimaki A, Honkanen V, Konttinen YT, Santavirta S. Teaching of patients undergoing total hip replacement surgery. *Int J Nurs Stud*. 1994;31(2):135-42.
1838. Lilja Y, Ryden S, Fridlund B. Effects of extended preoperative information on perioperative stress: an anaesthetic nurse intervention for patients with breast cancer and total hip replacement. *Intensive Crit Care Nurs*. 1998;14(6):276-82.
1839. Munin MC, Rudy TE, Glynn NW, Crossett LS, Rubash HE. Early inpatient rehabilitation after elective hip and knee arthroplasty. *JAMA*. 1998;279(11):847-52.
1840. Brander V, Stulberg S, Chang R. Rehabilitation Following Hip and Knee Arthroplasty. *Physical medicine and rehabilitation clinics of north america*. 1994;5(4):815.
1841. Munin M, Hockenberry P, Flynn P, Toplak W. Chapter 7: Rehabilitation after total joint arthroplasty. In: Callaghan J, Rosenberg A, Rubash H, eds. *The Adult Hip*. Philadelphia: Lippencott Raven Publishers; 1998:1571-79.
1842. Naylor J, Harmer A, Fransen M, Crosbie J, Innes L. Status of physiotherapy rehabilitation after total knee replacement in Australia. *Physiother Res Int*. 2006;11(1):35-47.
1843. Flanagan SR, Ragnarsson KT, Ross MK, Wong DK. Rehabilitation of the geriatric orthopaedic patient. *Clin Orthop Relat Res*. 1995(316):80-92.
1844. Hicks JE, Gerber LH. Rehabilitation of the patient with arthritis and connective tissue disease. In: Delisa JA, Gans BM, eds. *Rehabilitation medicine principles and practice*. Philadelphia Lippincott Raven Publishers; 1998:1478-97.
1845. Gilbey HJ, Ackland TR, Wang AW, Morton AR, Trouchet T, Tapper J. Exercise improves early functional recovery after total hip arthroplasty. *Clin Orthop Relat Res*. 2003(408):193-200.
1846. Wang AW, Gilbey HJ, Ackland TR. Perioperative exercise programs improve early return of ambulatory function after total hip arthroplasty: a randomized, controlled trial. *Am J Phys Med Rehabil*. 2002;81(11):801-6.
1847. Wijgman AJ, Dekkers GH, Waltje E, Krekels T, Arens HJ. No positive effect of preoperative exercise therapy and teaching in patients to be subjected to hip arthroplasty. *Ned Tijdschr Geneesk*. 1994;138(19):949-52.
1848. Rooks DS, Huang J, Bierbaum BE, et al. Effect of preoperative exercise on measures of functional status in men and women undergoing total hip and knee arthroplasty. *Arthritis Rheum*. 2006;55(5):700-8.
1849. Rodgers JA, Garvin KL, Walker CW, Morford D, Urban J, Bedard J. Preoperative physical therapy in primary total knee arthroplasty. *J Arthroplasty*. 1998;13(4):414-21.
1850. D'Lima DD, Colwell CW, Jr., Morris BA, Hardwick ME, Kozin F. The effect of preoperative exercise on total knee replacement outcomes. *Clin Orthop Relat Res*. 1996(326):174-82.

1851. Weidenhielm L, Mattsson E, Brostrom LA, Wersall-Robertsson E. Effect of preoperative physiotherapy in unicompartmental prosthetic knee replacement. *Scand J Rehabil Med*. 1993;25(1):33-9.
1852. Beaupre LA, Lier D, Davies DM, Johnston DB. The effect of a preoperative exercise and education program on functional recovery, health related quality of life, and health service utilization following primary total knee arthroplasty. *J Rheumatol*. 2004;31(6):1166-73.
1853. Roos EM. Effectiveness and practice variation of rehabilitation after joint replacement. *Curr Opin Rheumatol*. 2003;15(2):160-2.
1854. Jenkins C, Barker KL, Pandit H, Dodd CA, Murray DW. After partial knee replacement, patients can kneel, but they need to be taught to do so: a single-blind randomized controlled trial. *Phys Ther*. 2008;88(9):1012-21.
1855. Reilly KA, Beard DJ, Barker KL, Dodd CA, Price AJ, Murray DW. Efficacy of an accelerated recovery protocol for Oxford unicompartmental knee arthroplasty--a randomised controlled trial. *Knee*. 2005;12(5):351-7.
1856. Lenssen AF, Crijns YH, Waltje EM, et al. Efficiency of immediate postoperative inpatient physical therapy following total knee arthroplasty: an RCT. *BMC Musculoskelet Disord*. 2006;771.
1857. Frost H, Lamb SE, Robertson S. A randomized controlled trial of exercise to improve mobility and function after elective knee arthroplasty. Feasibility, results and methodological difficulties. *Clin Rehabil*. 2002;16(2):200-9.
1858. Davies DM, Johnston DW, Beaupre LA, Lier DA. Effect of adjunctive range-of-motion therapy after primary total knee arthroplasty on the use of health services after hospital discharge. *Can J Surg*. 2003;46(1):30-6.
1859. Lenssen AF, Koke AJ, De Bie RA, Gennsink RGT. Continuous passive motion following primary total knee arthroplasty: short- and long- term effects on range of motion. *Physical Therapy Reviews*. 2003;8:113-21.
1860. Ververeli PA, Sutton DC, Hearn SL, Booth RE, Jr., Hozack WJ, Rothman RR. Continuous passive motion after total knee arthroplasty. Analysis of cost and benefits. *Clin Orthop Relat Res*. 1995(321):208-15.
1861. Moffet H, Collet JP, Shapiro SH, Paradis G, Marquis F, Roy L. Effectiveness of intensive rehabilitation on functional ability and quality of life after first total knee arthroplasty: A single-blind randomized controlled trial. *Arch Phys Med Rehabil*. 2004;85(4):546-56.
1862. Beaupre LA, Davies DM, Jones CA, Cinats JG. Exercise combined with continuous passive motion or slider board therapy compared with exercise only: a randomized controlled trial of patients following total knee arthroplasty. *Phys Ther*. 2001;81(4):1029-37.
1863. Denis M, Moffet H, Caron F, Ouellet D, Paquet J, Nolet L. Effectiveness of continuous passive motion and conventional physical therapy after total knee arthroplasty: a randomized clinical trial. *Phys Ther*. 2006;86(2):174-85.
1864. McInnes J, Larson MG, Daltroy LH, et al. A controlled evaluation of continuous passive motion in patients undergoing total knee arthroplasty. *JAMA*. 1992;268(11):1423-8.
1865. Montgomery F, Eliasson M. Continuous passive motion compared to active physical therapy after knee arthroplasty: similar hospitalization times in a randomized study of 68 patients. *Acta Orthop Scand*. 1996;67(1):7-9.
1866. Ritter MA, Gandolf VS, Holston KS. Continuous passive motion versus physical therapy in total knee arthroplasty. *Clin Orthop Relat Res*. 1989(244):239-43.
1867. Chen B, Zimmerman JR, Soulen L, DeLisa JA. Continuous passive motion after total knee arthroplasty: a prospective study. *Am J Phys Med Rehabil*. 2000;79(5):421-6.
1868. Chiarello CM, Gundersen L, O'Halloran T. The effect of continuous passive motion duration and increment on range of motion in total knee arthroplasty patients. *J Orthop Sports Phys Ther*. 1997;25(2):119-27.
1869. Gotlin RS, Hershkowitz S, Juris PM, Gonzalez EG, Scott WN, Insall JN. Electrical stimulation effect on extensor lag and length of hospital stay after total knee arthroplasty. *Arch Phys Med Rehabil*. 1994;75(9):957-9.
1870. Harms M, Engstrom B. Continuous passive motion as an adjunct to treatment in the physiotherapy management of the total knee arthroplasty patient. *Physiotherapy*. 1991;77(4):301-7.
1871. Johnson DP, Eastwood DM. Beneficial effects of continuous passive motion after total condylar knee arthroplasty. *Ann R Coll Surg Engl*. 1992;74(6):412-6.
1872. Kumar PJ, McPherson EJ, Dorr LD, Wan Z, Baldwin K. Rehabilitation after total knee arthroplasty: a comparison of 2 rehabilitation techniques. *Clin Orthop Relat Res*. 1996(331):93-101.

1873. Lau SK, Chiu KY. Use of continuous passive motion after total knee arthroplasty. *J Arthroplasty*. 2001;16(3):336-9.
1874. Lotke PA, Faralli VJ, Orenstein EM, Ecker ML. Blood loss after total knee replacement. Effects of tourniquet release and continuous passive motion. *J Bone Joint Surg Am*. 1991;73(7):1037-40.
1875. May LM, Busse W, Zayac D, Whitridge MR. Comparison of continuous passive motion (CPM) machines and lower limb mobility boards (LLiMB) in the rehabilitation of patients with total knee arthroplasty. *Canadian Journal of Rehabilitation*. 1999;12(4):257-63.
1876. Pope RO, Corcoran S, McCaul K, Howie DW. Continuous passive motion after primary total knee arthroplasty. Does it offer any benefits? *J Bone Joint Surg Br*. 1997;79(6):914-7.
1877. Vince KG, Kelly MA, Beck J, Insall JN. Continuous passive motion after total knee arthroplasty. *J Arthroplasty*. 1987;2(4):281-4.
1878. Worland RL, Arredondo J, Angles F, Lopez-Jimenez F, Jessup DE. Home continuous passive motion machine versus professional physical therapy following total knee replacement. *J Arthroplasty*. 1998;13(7):784-7.
1879. Johnson DP. The effect of continuous passive motion on wound-healing and joint mobility after knee arthroplasty. *J Bone Joint Surg Am*. 1990;72(3):421-6.
1880. Nielsen PT, Rechnagel K, Nielsen SE. No effect of continuous passive motion after arthroplasty of the knee. *Acta Orthop Scand*. 1988;59(5):580-1.
1881. Kramer JF, Speechley M, Bourne R, Rorabeck C, Vaz M. Comparison of clinic- and home-based rehabilitation programs after total knee arthroplasty. *Clin Orthop Relat Res*. 2003(410):225-34.
1882. Shepperd S, Harwood D, Jenkinson C, Gray A, Vessey M, Morgan P. Randomised controlled trial comparing hospital at home care with inpatient hospital care. I: three month follow up of health outcomes. *Bmj*. 1998;316(7147):1786-91.
1883. Petterson SC, Mizner RL, Stevens JE, et al. Improved function from progressive strengthening interventions after total knee arthroplasty: a randomized clinical trial with an imbedded prospective cohort. *Arthritis Rheum*. 2009;61(2):174-83.
1884. Mallon WJ, Callaghan JJ. Total knee arthroplasty in active golfers. *J Arthroplasty*. 1993;8(3):299-306.
1885. Mallon WJ, Callaghan JJ. Total hip arthroplasty in active golfers. *J Arthroplasty*. 1992;7 Suppl339-46.
1886. Melhorn J, Ackerman W. *Guides to the Evaluation of Disease and Injury Causation*. Chicago: AMA Press; 2008.
1887. Glass L. *Occupational Medicine Practice Guidelines: Evaluation and Mangement of Common Health Problems and Functional Recovery in Workers, Second Edition*. Elk Grove Village: American College of Occupational and Environmental Medicine; 2004.
1888. Hegmann K. *Occupational Medicine Practice Guidelines: Evaluation and Mangement of Common Health Problems and Functional Recovery in Workers, Second Edition, 2008 Revision*. Elk Grove Village: American College of Occupational and Environmental Medicine; 2008.
1889. Bradbury N BD, Spoo G, et al. Participation in sports after total knee replacement. *Am J Sports Med*. 1998;26;530-5.
1890. Mont M, Marker DR, Seyler TM, Jones LC, Kolisek FR, Hungerford DS. High-impact sports after total knee arthroplasty. *J Arthroplasty*. 2008;23(6):80-4.
1891. Dahm D, Barnes SA, Harrington JR, Berry DJ. Patient reported activity after revision total knee arthroplasty. *J Arthroplasty*. 2007;22(6 Suppl 2):106-10.
1892. Dahm D, Barnes SA, Harrington JR, Sayeed SA, Berry DJ. Patient-reported activity level after total knee arthroplasty. *J Arthroplasty*. 2008;23(3):401-7.
1893. Lavernia C, Sierra RJ, Hungerford DS, Krackow K. Activity level and wear in total knee arthroplasty: a study of autopsy retrieved specimens. *J Arthroplasty*. 2001;16(4):446-53.
1894. Singh J, O'Byrne M, Harmsen S, Lewallen D. Predictors of moderate-severe functional limitation after primary Total Knee Arthroplasty (TKA): 4701 TKAs at 2-years and 2935 TKAs at 5-years. *Osteoarthr Cartil*. 2010;18(4):515-21.
1895. Diduch DR, Insall JN, Scott WN, Scuderi GR, Font-Rodriguez D. Total knee replacement in young, active patients. Long-term follow-up and functional outcome. *J Bone Joint Surg Am*. 1997;79(4):575-82.
1896. Naal FD FM, Preuss A, et al. Return to sports and recreational activity after unicompartmental knee arthroplasty. *Am J Sports Med*. 2007;35(10):1688-95.

1897. Fisher N, Agarwal M, Reuben SF, Johnson DS, Turner PG. Sporting and physical activity following Oxford medial unicompartmental knee arthroplasty. *Knee*. 2006;13(4):296-300.
1898. Walton N, Jahromi I, Lewis PL, Dobson PJ, Angel KR, Campbell DG. Patient-perceived outcomes and return to sport and work: TKA versus mini-incision unicompartmental knee arthroplasty. *J Knee Surg*. 2006;19(2):112-6.
1899. Jackson J, Smith J, Shah JP, Wisniewski SJ, Dahm D. Golf after total knee arthroplasty: do patients return to walking the course? *Am J Sports Med*. 2009;37(11):2201-4.
1900. Healy W, Iorio R, Lemos MJ. Athletic activity after joint replacement. *Am J Sports Med*. 2001;29(3):377-88.
1901. Fishbain DA, Cutler RB, Rosomoff HL, Rosomoff RS. Are opioid-dependent/tolerant patients impaired in driving-related skills? A structured evidence-based review. *J Pain Symptom Manage*. 2003;25(6):559-77.
1902. Ballantyne JC. Opioid analgesia: perspectives on right use and utility. *Pain Physician*. 2007;10(3):479-91.
1903. Manchikanti L, Giordano J, Boswell MV, Fellows B, Manchukonda R, Pampati V. Psychological factors as predictors of opioid abuse and illicit drug use in chronic pain patients. *J Opioid Manag*. 2007;3(2):89-100.
1904. Savage S, Covington E, Heit H, et al. *Definitions Related to the Use of Opioids for the Treatment of Pain: A Consensus Statement from the American Academy of Pain Medicine, American Pain Society, and the American Society of Addiction Medicine*. Glenview; 2001.
1905. Flor H, Birbaumer N. Comparison of the efficacy of electromyographic biofeedback, cognitive-behavioral therapy, and conservative medical interventions in the treatment of chronic musculoskeletal pain. *J Consult Clin Psychol*. 1993;61(4):653-8.
1906. American Physical Therapy Association. Guidelines: Occupational Health Physical Therapy: Work Conditioning and Work Hardening Programs.
1907. Niemeyer LO, Jacobs K, Reynolds-Lynch K, Bettencourt C, Lang S. Work hardening: past, present, and future--the work programs special interest section national work-hardening outcome study. *Am J Occup Ther*. 1994;48(4):327-39.
1908. Lechner DE. Work hardening and work conditioning interventions: do they affect disability? *Phys Ther*. 1994;74(5):471-93.
1909. Haig AJ, Linton P, McIntosh M, Moneta L, Mead PB. Aggressive early medical management by a specialist in physical medicine and rehabilitation: effect on lost time due to injuries in hospital employees. *J Occup Med*. 1990;32(3):241-4.
1910. Jordan A, Bendix T, Nielsen H, Hansen FR, Host D, Winkel A. Intensive training, physiotherapy, or manipulation for patients with chronic neck pain. A prospective, single-blinded, randomized clinical trial. *Spine*. 1998;23(3):311-8; discussion 9.
1911. Staal JB, Hlobil H, Twisk JW, Smid T, Koke AJ, van Mechelen W. Graded activity for low back pain in occupational health care: a randomized, controlled trial. *Ann Intern Med*. 2004;140(2):77-84.
1912. Fairbank J, Frost H, Wilson-MacDonald J, Yu LM, Barker K, Collins R. Randomised controlled trial to compare surgical stabilisation of the lumbar spine with an intensive rehabilitation programme for patients with chronic low back pain: the MRC spine stabilisation trial. *Br Med J*. 2005;330(7502):1233.
1913. Haldorsen EM, Grasdahl AL, Skouen JS, Risa AE, Kronholm K, Ursin H. Is there a right treatment for a particular patient group? Comparison of ordinary treatment, light multidisciplinary treatment, and extensive multidisciplinary treatment for long-term sick-listed employees with musculoskeletal pain. *Pain*. 2002;95(1-2):49-63.
1914. Jensen IB, Bergstrom G, Ljungquist T, Bodin L. A 3-year follow-up of a multidisciplinary rehabilitation programme for back and neck pain. *Pain*. 2005;115(3):273-83.
1915. Lindstrom I, Ohlund C, Eek C, Wallin L, Peterson LE, Nachemson A. Mobility, strength, and fitness after a graded activity program for patients with subacute low back pain. A randomized prospective clinical study with a behavioral therapy approach. *Spine (Phila Pa 1976)*. 1992;17(6):641-52.
1916. Anema JR, Steenstra IA, Bongers PM, et al. Multidisciplinary rehabilitation for subacute low back pain: graded activity or workplace intervention or both? A randomized controlled trial. *Spine*. 2007;32(3):291-8; discussion 9-300.
1917. Loisel P, Abenhaim L, Durand P, et al. A population-based, randomized clinical trial on back pain management. *Spine (Phila Pa 1976)*. 1997;22(24):2911-8.

1918. Eriksson BI, Wille-Jorgensen P, Kalebo P, et al. A comparison of recombinant hirudin with a low-molecular-weight heparin to prevent thromboembolic complications after total hip replacement. *N Engl J Med*. 1997;337(19):1329-35.
1919. Robinson KS, Anderson DR, Gross M, et al. Ultrasonographic screening before hospital discharge for deep venous thrombosis after arthroplasty: the post-arthroplasty screening study. A randomized, controlled trial. *Ann Intern Med*. 1997;127(6):439-45.
1920. Wilson NV, Das SK, Kakkar VV, et al. Thrombo-embolic prophylaxis in total knee replacement. Evaluation of the A-V Impulse System. *J Bone Joint Surg Br*. 1992;74(1):50-2.
1921. McKenna R, Galante J, Bachmann F, Wallace DL, Kaushal PS, Meredith P. Prevention of venous thromboembolism after total knee replacement by high-dose aspirin or intermittent calf and thigh compression. *Br Med J*. 1980;280(6213):514-7.
1922. Karnezis TA, Stulberg SD, Wixson RL, Reilly P. The hemostatic effects of desmopressin on patients who had total joint arthroplasty. A double-blind randomized trial. *J Bone Joint Surg Am*. 1994;76(10):1545-50.
1923. Hiippala S, Strid L, Wennerstrand M, et al. Tranexamic acid (Cyklokapron) reduces perioperative blood loss associated with total knee arthroplasty. *Br J Anaesth*. 1995;74(5):534-7.
1924. Hiippala ST, Strid LJ, Wennerstrand MI, et al. Tranexamic acid radically decreases blood loss and transfusions associated with total knee arthroplasty. *Anesth Analg*. 1997;84(4):839-44.
1925. Benoni G, Fredin H. Fibrinolytic inhibition with tranexamic acid reduces blood loss and blood transfusion after knee arthroplasty: a prospective, randomised, double-blind study of 86 patients. *J Bone Joint Surg Br*. 1996;78(3):434-40.
1926. Orpen NM, Little C, Walker G, Crawford EJ. Tranexamic acid reduces early post-operative blood loss after total knee arthroplasty: a prospective randomised controlled trial of 29 patients. *Knee*. 2006;13(2):106-10.
1927. Garneti N, Field J. Bone bleeding during total hip arthroplasty after administration of tranexamic acid. *J Arthroplasty*. 2004;19(4):488-92.
1928. Engel JM, Hohaus T, Ruwoldt R, Menges T, Jurgensen I, Hempelmann G. Regional hemostatic status and blood requirements after total knee arthroplasty with and without tranexamic acid or aprotinin. *Anesth Analg*. 2001;92(3):775-80.
1929. Francis CW, Pellegrini VD, Jr., Stulberg BN, Miller ML, Totterman S, Marder VJ. Prevention of venous thrombosis after total knee arthroplasty. Comparison of antithrombin III and low-dose heparin with dextran. *J Bone Joint Surg Am*. 1990;72(7):976-82.
1930. Wilson MG, Pei LF, Malone KM, Polak JF, Creager MA, Goldhaber SZ. Fixed low-dose versus adjusted higher-dose warfarin following orthopedic surgery. A randomized prospective trial. *J Arthroplasty*. 1994;9(2):127-30.
1931. Vives MJ, Hozack WJ, Sharkey PF, Moriarty L, Sokoloff B, Rothman RH. Fixed minidose versus-adjusted low-dose warfarin after total joint arthroplasty: a randomized prospective study. *J Arthroplasty*. 2001;16(8):1030-7.
1932. Heit JA, Berkowitz SD, Bona R, et al. Efficacy and safety of low molecular weight heparin (ardeparin sodium) compared to warfarin for the prevention of venous thromboembolism after total knee replacement surgery: a double-blind, dose-ranging study. Ardeparin Arthroplasty Study Group. *Thromb Haemost*. 1997;77(1):32-8.
1933. Hull R, Raskob G, Pineo G, et al. A comparison of subcutaneous low-molecular-weight heparin with warfarin sodium for prophylaxis against deep-vein thrombosis after hip or knee implantation. *N Engl J Med*. 1993;329(19):1370-6.
1934. Marlovits S, Striessnig G, Schuster R, et al. Extended-duration thromboprophylaxis with enoxaparin after arthroscopic surgery of the anterior cruciate ligament: a prospective, randomized, placebo-controlled study. *Arthroscopy*. 2007;23(7):696-702.
1935. Ofosu FA, Leclerc J, Delorme F, et al. The low molecular weight heparin Enoxaparin inhibits the consumption of factor VII and prothrombin activation in vivo associated with elective knee replacement surgery. *Br J Haematol*. 1992;82(2):391-9.
1936. Lassen MR, Ageno W, Borris LC, et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty. *N Engl J Med*. 2008;358(26):2776-86.

1937. Fauno P, Suomalainen O, Rehnberg V, et al. Prophylaxis for the prevention of venous thromboembolism after total knee arthroplasty. A comparison between unfractionated and low-molecular-weight heparin. *J Bone Joint Surg Am*. 1994;76(12):1814-8.
1938. Colwell CW, Jr., Spiro TE, Trowbridge AA, Stephens JW, Gardiner GA, Jr., Ritter MA. Efficacy and safety of enoxaparin versus unfractionated heparin for prevention of deep venous thrombosis after elective knee arthroplasty. Enoxaparin Clinical Trial Group. *Clin Orthop Relat Res*. 1995(321):19-27.
1939. Perhoniemi V, Vuorinen J, Myllynen P, Kivioja A, Lindevall K. The effect of enoxaparin in prevention of deep venous thrombosis in hip and knee surgery--a comparison with the dihydroergotamine-heparin combination. *Ann Chir Gynaecol*. 1996;85(4):359-63.
1940. Hamulyak K, Lensing AW, van der Meer J, Smid WM, van Ooy A, Hoek JA. Subcutaneous low-molecular weight heparin or oral anticoagulants for the prevention of deep-vein thrombosis in elective hip and knee replacement? Fraxiparine Oral Anticoagulant Study Group. *Thromb Haemost*. 1995;74(6):1428-31.
1941. RD heparin compared with warfarin for prevention of venous thromboembolic disease following total hip or knee arthroplasty. RD Heparin Arthroplasty Group. *J Bone Joint Surg Am*. 1994;76(8):1174-85.
1942. Schmidt B, Michler R, Klein M, Faulmann G, Weber C, Schellong S. Ultrasound screening for distal vein thrombosis is not beneficial after major orthopedic surgery. A randomized controlled trial. *Thromb Haemost*. 2003;90(5):949-54.
1943. Turpie AG, Bauer KA, Davidson BL, et al. A randomized evaluation of betrixaban, an oral factor Xa inhibitor, for prevention of thromboembolic events after total knee replacement (EXPERT). *Thromb Haemost*. 2009;101(1):68-76.
1944. Eikelboom JW, Quinlan DJ, Douketis JD. Extended-duration prophylaxis against venous thromboembolism after total hip or knee replacement: a meta-analysis of the randomised trials. *Lancet*. 2001;358(9275):9-15.
1945. Kalodiki EP, Hoppensteadt DA, Nicolaides AN, et al. Deep venous thrombosis prophylaxis with low molecular weight heparin and elastic compression in patients having total hip replacement. A randomised controlled trial. *Int Angiol*. 1996;15(2):162-8.
1946. Hui AC, Heras-Palou C, Dunn I, et al. Graded compression stockings for prevention of deep-vein thrombosis after hip and knee replacement. *J Bone Joint Surg Br*. 1996;78(4):550-4.
1947. Hull RD, Raskob GE, Gent M, et al. Effectiveness of intermittent pneumatic leg compression for preventing deep vein thrombosis after total hip replacement. *JAMA*. 1990;263(17):2313-7.
1948. Bradley JG, Krugener GH, Jager HJ. The effectiveness of intermittent plantar venous compression in prevention of deep venous thrombosis after total hip arthroplasty. *J Arthroplasty*. 1993;8(1):57-61.
1949. Gallus A, Raman K, Darby T. Venous thrombosis after elective hip replacement--the influence of preventive intermittent calf compression and of surgical technique. *Br J Surg*. 1983;70(1):17-9.
1950. Kaempffe FA, Lifeso RM, Meinking C. Intermittent pneumatic compression versus coumadin. Prevention of deep vein thrombosis in lower-extremity total joint arthroplasty. *Clin Orthop Relat Res*. 1991(269):89-97.
1951. Pitto RP, Hamer H, Heiss-Dunlop W, Kuehle J. Mechanical prophylaxis of deep-vein thrombosis after total hip replacement a randomised clinical trial. *J Bone Joint Surg Br*. 2004;86(5):639-42.
1952. Planes A, Vochelle N, Darmon JY, et al. Efficacy and safety of postdischarge administration of enoxaparin in the prevention of deep venous thrombosis after total hip replacement. A prospective randomised double-blind placebo-controlled trial. *Drugs*. 1996;52 Suppl 747-54.
1953. Planes A, Vochelle N, Darmon JY, Fagola M, Bellaud M, Huet Y. Risk of deep-venous thrombosis after hospital discharge in patients having undergone total hip replacement: double-blind randomised comparison of enoxaparin versus placebo. *Lancet*. 1996;348(9022):224-8.
1954. Comp PC, Spiro TE, Friedman RJ, et al. Prolonged enoxaparin therapy to prevent venous thromboembolism after primary hip or knee replacement. Enoxaparin Clinical Trial Group. *J Bone Joint Surg Am*. 2001;83-A(3):336-45.
1955. Arnesen H, Dahl OE, Aspelin T, Seljeflot I, Kierulf P, Lyberg T. Sustained prothrombotic profile after hip replacement surgery: the influence of prolonged prophylaxis with dalteparin. *J Thromb Haemost*. 2003;1(5):971-5.
1956. Bergqvist D, Benoni G, Bjorgell O, et al. Low-molecular-weight heparin (enoxaparin) as prophylaxis against venous thromboembolism after total hip replacement. *N Engl J Med*. 1996;335(10):696-700.

1957. Dahl OE, Andreassen G, Aspelin T, et al. Prolonged thromboprophylaxis following hip replacement surgery--results of a double-blind, prospective, randomised, placebo-controlled study with dalteparin (Fragmin). *Thromb Haemost.* 1997;77(1):26-31.
1958. Heit JA, Elliott CG, Trowbridge AA, Morrey BF, Gent M, Hirsh J. Ardeparin sodium for extended out-of-hospital prophylaxis against venous thromboembolism after total hip or knee replacement. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med.* 2000;132(11):853-61.
1959. Hoek JA, Nurmohamed MT, Hamelynck KJ, et al. Prevention of deep vein thrombosis following total hip replacement by low molecular weight heparinoid. *Thromb Haemost.* 1992;67(1):28-32.
1960. Jorgensen PS, Knudsen JB, Broeng L, et al. The thromboprophylactic effect of a low-molecular-weight heparin (Fragmin) in hip fracture surgery. A placebo-controlled study. *Clin Orthop Relat Res.* 1992(278):95-100.
1961. Lassen MR, Borris LC, Anderson BS, et al. Efficacy and safety of prolonged thromboprophylaxis with a low molecular weight heparin (dalteparin) after total hip arthroplasty--the Danish Prolonged Prophylaxis (DaPP) Study. *Thromb Res.* 1998;89(6):281-7.
1962. Turpie AG, Levine MN, Hirsh J, et al. A randomized controlled trial of a low-molecular-weight heparin (enoxaparin) to prevent deep-vein thrombosis in patients undergoing elective hip surgery. *N Engl J Med.* 1986;315(15):925-9.
1963. Planes A, Vochelle N, Fagola M, Bellaud M. Comparison of two low-molecular-weight heparins for the prevention of postoperative venous thromboembolism after elective hip surgery. Reviparin Study Group. *Blood Coagul Fibrinolysis.* 1998;9(6):499-505.
1964. Bara L, Planes A, Samama MM. Occurrence of thrombosis and haemorrhage, relationship with anti-Xa, anti-IIa activities, and D-dimer plasma levels in patients receiving a low molecular weight heparin, enoxaparin or tinzaparin, to prevent deep vein thrombosis after hip surgery. *Br J Haematol.* 1999;104(2):230-40.
1965. Eriksson BI, Borris L, Dahl OE, et al. Oral, direct Factor Xa inhibition with BAY 59-7939 for the prevention of venous thromboembolism after total hip replacement. *J Thromb Haemost.* 2006;4(1):121-8.
1966. Eriksson BI, Borris LC, Dahl OE, et al. A once-daily, oral, direct Factor Xa inhibitor, rivaroxaban (BAY 59-7939), for thromboprophylaxis after total hip replacement. *Circulation.* 2006;114(22):2374-81.
1967. Eriksson BI, Dahl OE, Rosencher N, et al. Oral dabigatran etexilate vs. subcutaneous enoxaparin for the prevention of venous thromboembolism after total knee replacement: the RE-MODEL randomized trial. *J Thromb Haemost.* 2007;5(11):2178-85.
1968. Spiro TE, Johnson GJ, Christie MJ, et al. Efficacy and safety of enoxaparin to prevent deep venous thrombosis after hip replacement surgery. Enoxaparin Clinical Trial Group. *Ann Intern Med.* 1994;121(2):81-9.
1969. Agnelli G, Haas S, Ginsberg JS, Krueger KA, Dmitrienko A, Brandt JT. A phase II study of the oral factor Xa inhibitor LY517717 for the prevention of venous thromboembolism after hip or knee replacement. *J Thromb Haemost.* 2007;5(4):746-53.
1970. Eriksson BI, Agnelli G, Cohen AT, et al. The direct thrombin inhibitor melagatran followed by oral ximelagatran compared with enoxaparin for the prevention of venous thromboembolism after total hip or knee replacement: the EXPRESS study. *J Thromb Haemost.* 2003;1(12):2490-6.
1971. Eriksson BI, Bauer KA, Lassen MR, Turpie AG. Fondaparinux compared with enoxaparin for the prevention of venous thromboembolism after hip-fracture surgery. *N Engl J Med.* 2001;345(18):1298-304.
1972. Thorpe CM, Murphy WG, Logan M. Use of aprotinin in knee replacement surgery. *Br J Anaesth.* 1994;73(3):408-10.
1973. Beisaw NE, Comerota AJ, Groth HE, et al. Dihydroergotamine/heparin in the prevention of deep-vein thrombosis after total hip replacement. A controlled, prospective, randomized multicenter trial. *J Bone Joint Surg Am.* 1988;70(1):2-10.
1974. Powers PJ, Gent M, Jay RM, et al. A randomized trial of less intense postoperative warfarin or aspirin therapy in the prevention of venous thromboembolism after surgery for fractured hip. *Arch Intern Med.* 1989;149(4):771-4.
1975. Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention (PEP) trial. *Lancet.* 2000;355:1295-302.

1976. Stulberg BN, Francis CW, Pellegrini VD, et al. Antithrombin III/low-dose heparin in the prevention of deep-vein thrombosis after total knee arthroplasty. A preliminary report. *Clin Orthop Relat Res.* 1989(248):152-7.
1977. Francis CW, Pellegrini VD, Jr., Marder VJ, et al. Prevention of venous thrombosis after total hip arthroplasty. Antithrombin III and low-dose heparin compared with dextran 40. *J Bone Joint Surg Am.* 1989;71(3):327-35.
1978. Westrich GH, Sculco TP. Prophylaxis against deep venous thrombosis after total knee arthroplasty. Pneumatic plantar compression and aspirin compared with aspirin alone. *J Bone Joint Surg Am.* 1996;78(6):826-34.
1979. Nilsson S SP. Tendoperiostitis in the lateral femoral condyle in long distance runners. *Br J Sports Med.* 1973(7):87-9.
1980. Schwellnus MP, Theunissen L, Noakes TD, Reinach SG. Anti-inflammatory and combined anti-inflammatory/analgesic medication in the early management of iliotibial band friction syndrome. A clinical trial. *S Afr Med J.* 1991;79(10):602-6.
1981. Krissoff W, Ferris W. Runner's injuries. *Physician Sportsmed.* 1979;7(12):55-64.
1982. Lindenberg G, Pinshaw R. Iliotibial band friction syndrome in runners. *Physician Sportsmed.* 1984.
1983. Austermuehle PD. Common knee injuries in primary care. *Nurse Pract.* 2001;26(10):26, 32-45; quiz 6-7.
1984. Kirk KL, Kuklo T, Klemme W. Iliotibial band friction syndrome. *Orthopedics.* 2000;23(11):1209-14; discussion 14-5; quiz 16-7.
1985. Levin J. Run down: battling IT band syndrome in runners. *Biomechanics.* 2003;122-5.
1986. Nemeth WC, Sanders BL. The lateral synovial recess of the knee: anatomy and role in chronic Iliotibial band friction syndrome. *Arthroscopy.* 1996;12(5):574-80.
1987. Noble CA. The treatment of iliotibial band friction syndrome. *Br J Sports Med.* 1979;13(2):51-4.
1988. Murphy BJ, Hechtman KS, Uribe JW, Selesnick H, Smith RL, Zlatkin MB. Iliotibial band friction syndrome: MR imaging findings. *Radiology.* 1992;185(2):569-71.
1989. Anderson GS. Iliotibial band friction syndrome. *Australian Journal of Science and Medicine in Sport.* 1991;23(3):81-3.
1990. Martens M, Libbrecht P, Burssens A. Surgical treatment of the iliotibial band friction syndrome. *Am J Sports Med.* 1989;17(5):651-4.
1991. Orava S, Leppilahti J, Karpakka J. Operative treatment of typical overuse injuries in sport. *Ann Chir Gynaecol.* 1991;80(2):208-11.
1992. Newell SG. Overuse injuries to the knee in runners. *Phys Sportmed.* 1984;1281-92.
1993. Brosseau L, Casimiro L, Milne S, et al. Deep transverse friction massage for treating tendinitis. *Cochrane Database Syst Rev.* 2002(4):CD003528.
1994. Noble HB, Hajek MR, Porter M. Diagnosis and treatment of iliotibial band tightness in runners. *Phys Sportmed.* 1982;10(4):67-74.
1995. Calabrese LH, Rooney TW. The use of nonsteroidal anti-inflammatory drugs in sports. *Phys Sports Med.* 1986;1489-97.
1996. Clyman B. Role of non-steroidal anti-inflammatory drugs in sports medicine. *Sports Med.* 1986;3(4):342-6.
1997. Bischoff C, Prusaczyk W, Sopchick T, Pratt N, Goforth H. Comparison of phonophoresis and knee immobilization in treating iliotibial band syndrome. *Sports Medicine, Training, and Rehabilitation.* 1995;6(1):1-6.
1998. Gunter P, Schwellnus MP. Local corticosteroid injection in iliotibial band friction syndrome in runners: a randomised controlled trial. *Br J Sports Med.* 2004;38(3):269-72; discussion 72.
1999. Schache AG, Wrigley TV, Baker R, Pandy MG. Biomechanical response to hamstring muscle strain injury. *Gait Posture.* 2009;29(2):332-8.
2000. Heiderscheidt BC, Hoerth DM, Chumanov ES, Swanson SC, Thelen BJ, Thelen DG. Identifying the time of occurrence of a hamstring strain injury during treadmill running: a case study. *Clin Biomech (Bristol, Avon).* 2005;20(10):1072-8.
2001. Askling C, Karlsson J, Thorstensson A. Hamstring injury occurrence in elite soccer players after preseason strength training with eccentric overload. *Scand J Med Sci Sports.* 2003;13(4):244-50.
2002. Sherry MA, Best TM. A comparison of 2 rehabilitation programs in the treatment of acute hamstring strains. *J Orthop Sports Phys Ther.* 2004;34(3):116-25.

2003. Engebretsen AH, Myklebust G, Holme I, Engebretsen L, Bahr R. Prevention of injuries among male soccer players: a prospective, randomized intervention study targeting players with previous injuries or reduced function. *Am J Sports Med.* 2008;36(6):1052-60.
2004. Holmich P, Uhrskou P, Ulnits L, et al. Effectiveness of active physical training as treatment for long-standing adductor-related groin pain in athletes: randomised trial. *Lancet.* 1999;353(9151):439-43.
2005. Hartig DE, Henderson JM. Increasing hamstring flexibility decreases lower extremity overuse injuries in military basic trainees. *Am J Sports Med.* 1999;27(2):173-6.
2006. Edson CJ. Conservative and postoperative rehabilitation of isolated and combined injuries of the medial collateral ligament. *Sports Med Arthrosc.* 2006;14(2):105-10.
2007. American Medical Association. Standard nomenclature of athletic injuries. American Medical Association; 1966.
2008. Odensten M, Hamberg P, Nordin M, Lysholm J, Gillquist J. Surgical or conservative treatment of the acutely torn anterior cruciate ligament. A randomized study with short-term follow-up observations. *Clin Orthop Relat Res.* 1985(198):87-93.
2009. Frobell RB, Roos EM, Roos HP, Ranstam J, Lohmander LS. A randomized trial of treatment for acute anterior cruciate ligament tears. *N Engl J Med.* 2010;363(4):331-42.
2010. Kannus P, Jarvinen M. Knee ligament injuries in adolescents. Eight year follow-up of conservative management. *J Bone Joint Surg Br.* 1988;70(5):772-6.
2011. Hastings DE. The non-operative management of collateral ligament injuries of the knee joint. *Clin Orthop Relat Res.* 1980(147):22-8.
2012. Gardiner JC, Weiss JA, Rosenberg TD. Strain in the human medial collateral ligament during valgus loading of the knee. *Clin Orthop Relat Res.* 2001(391):266-74.
2013. Mahler P, Mahler F, Duruz H, Ramazzina M, Liguori V, Mautone G. Double-blind, randomized, controlled study on the efficacy and safety of a novel diclofenac epolamine gel formulated with lecithin for the treatment of sprains, strains and contusions. *Drugs Exp Clin Res.* 2003;29(1):45-52.
2014. Duncan JJ, Farr JE. Comparison of diclofenac sodium and aspirin in the treatment of acute sports injuries. *Am J Sports Med.* 1988;16(6):656-9.
2015. Frahm E, Elsasser U, Kammereit A. Topical treatment of acute sprains. *Br J Clin Pract.* 1993;47(6):321-2.
2016. Abasolo L, Carmona L, Hernandez-Garcia C, et al. Musculoskeletal work disability for clinicians: time course and effectiveness of a specialized intervention program by diagnosis. *Arthritis Rheum.* 2007;57(2):335-42.
2017. Hughes DL, Crosby AC. Treatment of knee sprains: modified Robert Jones or elastic support bandage? *J Accid Emerg Med.* 1995;12(2):115-8.
2018. Hubscher M, Zech A, Pfeifer K, Hansel F, Vogt L, Banzer W. Neuromuscular training for sports injury prevention: a systematic review. *Med Sci Sports Exerc.* 2010;42(3):413-21.
2019. Emery CA, Meeuwisse WH. The effectiveness of a neuromuscular prevention strategy to reduce injuries in youth soccer: a cluster-randomised controlled trial. *Br J Sports Med.* 2010;44(8):555-62.
2020. Ekstrand J, Gillquist J, Liljedahl SO. Prevention of soccer injuries. Supervision by doctor and physiotherapist. *Am J Sports Med.* 1983;11(3):116-20.
2021. Caraffa A, Cerulli G, Progetti M, Aisa G, Rizzo A. Prevention of anterior cruciate ligament injuries in soccer. A prospective controlled study of proprioceptive training. *Knee Surg Sports Traumatol Arthrosc.* 1996;4(1):19-21.
2022. O'Sullivan K, Murray E, Sainsbury D. The effect of warm-up, static stretching and dynamic stretching on hamstring flexibility in previously injured subjects. *BMC Musculoskelet Disord.* 2009;1037.
2023. Beynon BD, Johnson RJ, Fleming BC, et al. The effect of functional knee bracing on the anterior cruciate ligament in the weightbearing and nonweightbearing knee. *Am J Sports Med.* 1997;25(3):353-9.
2024. Cawley PW, France EP, Paulos LE. The current state of functional knee bracing research. A review of the literature. *Am J Sports Med.* 1991;19(3):226-33.
2025. Coughlin L, Oliver J, Berretta G. Knee bracing and anterolateral rotatory instability. *Am J Sports Med.* 1987;15(2):161-3.
2026. France EP, Cawley PW, Paulos LE. Choosing functional knee braces. *Clin Sports Med.* 1990;9(4):743-50.
2027. Liu SH, Mirzayan R. Current review. Functional knee bracing. *Clin Orthop Relat Res.* 1995(317):273-81.
2028. Nelson KA. The use of knee braces during rehabilitation. *Clin Sports Med.* 1990;9(4):799-811.

2029. Styf J. The effects of functional knee bracing on muscle function and performance. *Sports Med.* 1999;28(2):77-81.
2030. Vailas JC, Pink M. Biomechanical effects of functional knee bracing. Practical implications. *Sports Med.* 1993;15(3):210-8.
2031. Wright RW, Fetzner GB. Bracing after ACL reconstruction: a systematic review. *Clin Orthop Relat Res.* 2007;455:162-8.
2032. Jonsson H, Riklund-Ahlstrom K, Lind J. Positive pivot shift after ACL reconstruction predicts later osteoarthritis: 63 patients followed 5-9 years after surgery. *Acta Orthop Scand.* 2004;75(5):594-9.
2033. Birmingham TB, Bryant DM, Giffin JR, et al. A randomized controlled trial comparing the effectiveness of functional knee brace and neoprene sleeve use after anterior cruciate ligament reconstruction. *Am J Sports Med.* 2008;36(4):648-55.
2034. Wright RW, Preston E, Fleming BC, et al. A systematic review of anterior cruciate ligament reconstruction rehabilitation: part I: continuous passive motion, early weight bearing, postoperative bracing, and home-based rehabilitation. *J Knee Surg.* 2008;21(3):217-24.
2035. Hiemstra LA, Heard SM, Sasyniuk TM, Buchko GL, Reed JG, Monteleone BJ. Knee immobilization for pain control after a hamstring tendon anterior cruciate ligament reconstruction: a randomized clinical trial. *Am J Sports Med.* 2009;37(1):56-64.
2036. Brandsson S, Faxen E, Kartus J, Eriksson BI, Karlsson J. Is a knee brace advantageous after anterior cruciate ligament surgery? A prospective, randomised study with a two-year follow-up. *Scand J Med Sci Sports.* 2001;11(2):110-4.
2037. Feller J, Bartlett J, Chapman S, Delahunt M. Use of an extension-assisting brace following anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 1997;5(1):6-9.
2038. Harilainen A, Sandelin J. Post-operative use of knee brace in bone and tendon bone patellar tendon anterior cruciate ligament reconstruction: 5-year follow-up results of a randomized prospective study. 2006:14-8.
2039. Henriksson M, Rockborn P, Good L. Range of motion training in brace vs. plaster immobilization after anterior cruciate ligament reconstruction: a prospective randomized comparison with a 2-year follow-up. *Scand J Med Sci Sports.* 2002;12(2):73-80.
2040. Ito Y, Deie M, Adachi N, et al. A prospective study of 3-day versus 2-week immobilization period after anterior cruciate ligament reconstruction. *Knee.* 2007;14(1):34-8.
2041. McDevitt ER, Taylor DC, Miller MD, et al. Functional bracing after anterior cruciate ligament reconstruction: a prospective, randomized, multicenter study. *Am J Sports Med.* 2004;32(8):1887-92.
2042. Risberg MA, Holm I, Steen H, Eriksson J, Ekeland A. The effect of knee bracing after anterior cruciate ligament reconstruction. A prospective, randomized study with two years' follow-up. *Am J Sports Med.* 1999;27(1):76-83.
2043. Wu GK, Ng GY, Mak AF. Effects of knee bracing on the sensorimotor function of subjects with anterior cruciate ligament reconstruction. *Am J Sports Med.* 2001;29(5):641-5.
2044. Swirtun LR, Jansson A, Renstrom P. The effects of a functional knee brace during early treatment of patients with a nonoperated acute anterior cruciate ligament tear: a prospective randomized study. *Clin J Sport Med.* 2005;15(5):299-304.
2045. Andersson C, Odensten M, Gillquist J. Knee function after surgical or nonsurgical treatment of acute rupture of the anterior cruciate ligament: a randomized study with a long-term follow-up period. *Clin Orthop Relat Res.* 1991(264):255-63.
2046. Andersson C, Odensten M, Good L, Gillquist J. Surgical or non-surgical treatment of acute rupture of the anterior cruciate ligament. A randomized study with long-term follow-up. *J Bone Joint Surg Am.* 1989;71(7):965-74.
2047. Grant JA, Mohtadi NG, Maitland ME, Zernicke RF. Comparison of home versus physical therapy-supervised rehabilitation programs after anterior cruciate ligament reconstruction: a randomized clinical trial. *Am J Sports Med.* 2005;33(9):1288-97.
2048. Meunier A, Odensten M, Good L. Long-term results after primary repair or non-surgical treatment of anterior cruciate ligament rupture: a randomized study with a 15-year follow-up. *Scand J Med Sci Sports.* 2007;17(3):230-7.

2049. Risberg MA, Holm I. The long-term effect of 2 postoperative rehabilitation programs after anterior cruciate ligament reconstruction: a randomized controlled clinical trial with 2 years of follow-up. *Am J Sports Med.* 2009;37(10):1958-66.
2050. Segawa H, Omori G, Koga Y. Long-term results of non-operative treatment of anterior cruciate ligament injury. *Knee.* 2001;8(1):5-11.
2051. Shaw T, Williams MT, Chipchase LS. Do early quadriceps exercises affect the outcome of ACL reconstruction? A randomised controlled trial. *Aust J Physiother.* 2005;51(1):9-17.
2052. Risberg MA, Holm I, Myklebust G, Engebretsen L. Neuromuscular training versus strength training during first 6 months after anterior cruciate ligament reconstruction: a randomized clinical trial. *Phys Ther.* 2007;87(6):737-50.
2053. Heijne A, Werner S. Early versus late start of open kinetic chain quadriceps exercises after ACL reconstruction with patellar tendon or hamstring grafts: a prospective randomized outcome study. *Knee Surg Sports Traumatol Arthrosc.* 2007;15(4):402-14.
2054. Morrissey MC, Drechsler WI, Morrissey D, Knight PR, Armstrong PW, McAuliffe TB. Effects of distally fixated versus nondistally fixated leg extensor resistance training on knee pain in the early period after anterior cruciate ligament reconstruction. *Phys Ther.* 2002;82(1):35-43.
2055. Beynon BD, Johnson RJ, Fleming BC, et al. Anterior cruciate ligament replacement: comparison of bone-patellar tendon-bone grafts with two-strand hamstring grafts. A prospective, randomized study. *J Bone Joint Surg Am.* 2002;84-A(9):1503-13.
2056. Beard DJ, Dodd CA. Home or supervised rehabilitation following anterior cruciate ligament reconstruction: a randomized controlled trial. *J Orthop Sports Phys Ther.* 1998;27(2):134-43.
2057. Fischer DA, Tewes DP, Boyd JL, Smith JP, Quick DC. Home based rehabilitation for anterior cruciate ligament reconstruction. *Clin Orthop Relat Res.* 1998(347):194-9.
2058. Schenck RC, Jr., Blaschak MJ, Lance ED, Turturro TC, Holmes CF. A prospective outcome study of rehabilitation programs and anterior cruciate ligament reconstruction. *Arthroscopy.* 1997;13(3):285-90.
2059. Revenas ASA, Johansson A, Leppert J. A randomized study of two physiotherapeutic approaches after knee ligament reconstruction. *Advances in Physiotherapy.* 2009;1130-41.
2060. Zatterstrom R, Friden T, Lindstrand A, Moritz U. Rehabilitation following acute anterior cruciate ligament injuries--a 12-month follow-up of a randomized clinical trial. *Scand J Med Sci Sports.* 2000;10(3):156-63.
2061. Bynum EB, Barrack RL, Alexander AH. Open versus closed chain kinetic exercises after anterior cruciate ligament reconstruction. A prospective randomized study. *Am J Sports Med.* 1995;23(4):401-6.
2062. Cooper RL, Taylor NF, Feller JA. A randomised controlled trial of proprioceptive and balance training after surgical reconstruction of the anterior cruciate ligament. *Res Sports Med.* 2005;13(3):217-30.
2063. Hooper DM, Morrissey MC, Drechsler W, Morrissey D, King J. Open and closed kinetic chain exercises in the early period after anterior cruciate ligament reconstruction. Improvements in level walking, stair ascent, and stair descent. *Am J Sports Med.* 2001;29(2):167-74.
2064. Morrissey MC, Hudson ZL, Drechsler WI, Coutts FJ, King JB, McAuliffe TB. Correlates of knee laxity change in early rehabilitation after anterior cruciate ligament reconstruction. *Int J Sports Med.* 2000;21(7):529-35.
2065. Perry MC, Morrissey MC, King JB, Morrissey D, Earnshaw P. Effects of closed versus open kinetic chain knee extensor resistance training on knee laxity and leg function in patients during the 8- to 14-week post-operative period after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2005;13(5):357-69.
2066. Fitzgerald GK, Axe MJ, Snyder-Mackler L. The efficacy of perturbation training in nonoperative anterior cruciate ligament rehabilitation programs for physical active individuals. *Phys Ther.* 2000;80(2):128-40.
2067. Hartigan E, Axe MJ, Snyder-Mackler L. Perturbation training prior to ACL reconstruction improves gait asymmetries in non-copers. *J Orthop Res.* 2009;27(6):724-9.
2068. Hartigan EH, Axe MJ, Snyder-Mackler L. Time line for noncopers to pass return-to-sports criteria after anterior cruciate ligament reconstruction. *J Orthop Sports Phys Ther.* 2010;40(3):141-54.
2069. Noyes FR, Mangine RE, Barber S. Early knee motion after open and arthroscopic anterior cruciate ligament reconstruction. *Am J Sports Med.* 1987;15(2):149-60.
2070. Olivier N, Weissland T, Berthoin S, et al. Effect of one-leg cycling aerobic training in amateur soccer players after anterior cruciate ligament reconstruction. *Am J Phys Med Rehabil.* 2009;88(5):362-8.

2071. Sekir U, Gur H, Akova B. Early versus late start of isokinetic hamstring-strengthening exercise after anterior cruciate ligament reconstruction with patellar tendon graft. *Am J Sports Med.* 2010;38(3):492-500.
2072. Cabaud HE, Feagin JA, Rodkey WG. Acute anterior cruciate ligament injury and augmented repair. Experimental studies. *Am J Sports Med.* 1980;8(6):395-401.
2073. Chick RP, Collins HR, Rubin BD, et al. The pes anserinus transfer. A long-term follow-up. *J Bone Joint Surg Am.* 1981;63(9):1449-52.
2074. Clancy WG, Jr., Ray JM, Zoltan DJ. Acute tears of the anterior cruciate ligament. Surgical versus conservative treatment. *J Bone Joint Surg Am.* 1988;70(10):1483-8.
2075. Feagin JA, Jr., Curl WW. Isolated tear of the anterior cruciate ligament: 5-year follow-up study. *Am J Sports Med.* 1976;4(3):95-100.
2076. Ishibashi Y, Tsuda E, Yamamoto Y, Tsukada H, Toh S. Navigation evaluation of the pivot-shift phenomenon during double-bundle anterior cruciate ligament reconstruction: is the posterolateral bundle more important? *Arthroscopy.* 2009;25(5):488-95.
2077. Lysholm J, Gillquist J. Evaluation of knee ligament surgery results with special emphasis on use of a scoring scale. *Am J Sports Med.* 1982;10(3):150-4.
2078. O'Donoghue DH. An analysis of end results of surgical treatment of major injuries to the ligaments of the knee. *J Bone Joint Surg Am.* 1955;37-A(1):1-13; passim.
2079. Sandberg R, Balkfors B. Partial rupture of the anterior cruciate ligament. Natural course. *Clin Orthop Relat Res.* 1987(220):176-8.
2080. Harilainen A, Sandelin J. A prospective comparison of 3 hamstring ACL fixation devices--Rigidfix, BioScrew, and Intrafix--randomized into 4 groups with 2 years of follow-up. *Am J Sports Med.* 2009;37(4):699-706.
2081. Benedetto KP, Fellingner M, Lim TE, Passler JM, Schoen JL, Willems WJ. A new bioabsorbable interference screw: preliminary results of a prospective, multicenter, randomized clinical trial. *Arthroscopy.* 2000;16(1):41-8.
2082. Arneja S, Froese W, MacDonald P. Augmentation of femoral fixation in hamstring anterior cruciate ligament reconstruction with a bioabsorbable bead: a prospective single-blind randomized clinical trial. *Am J Sports Med.* 2004;32(1):159-63.
2083. Myers P, Logan M, Stokes A, Boyd K, Watts M. Bioabsorbable Versus Titanium Interference Screws With Hamstring Autograft in Anterior Cruciate Ligament Reconstruction: A Prospective Randomized Trial With 2-Year Follow-up. *Arthroscopy: The Journal of Arthroscopic & Related Surgery.* 2008;24(7):817-23.
2084. Moisala AS, Jarvela T, Paakkala A, Paakkala T, Kannus P, Jarvinen M. Comparison of the bioabsorbable and metal screw fixation after ACL reconstruction with a hamstring autograft in MRI and clinical outcome: a prospective randomized study. *Knee Surg Sports Traumatol Arthrosc.* 2008;16(12):1080-6.
2085. Drogset JO, Grontvedt T, Jessen V, Tegnander A, Mollnes TE, Bergh K. Comparison of in vitro and in vivo complement activation by metal and bioabsorbable screws used in anterior cruciate ligament reconstruction. *Arthroscopy.* 2006;22(5):489-96.
2086. Rose T, Hepp P, Venus J, Stockmar C, Josten C, Lill H. Prospective randomized clinical comparison of femoral transfixation versus bioscrew fixation in hamstring tendon ACL reconstruction--a preliminary report. *Knee Surgery, Sports Traumatology, Arthroscopy.* 2006;14(8):730-8.
2087. Fink C, Benedetto KP, Hackl W, Hoser C, Freund MC, Rieger M. Bioabsorbable polyglyconate interference screw fixation in anterior cruciate ligament reconstruction: A prospective computed tomography-controlled study. *Arthroscopy: The Journal of Arthroscopic & Related Surgery.* 2000;16(5):491-8.
2088. Harilainen A, Sandelin J, Jansson KA. Cross-pin femoral fixation versus metal interference screw fixation in anterior cruciate ligament reconstruction with hamstring tendons: Results of a controlled prospective randomized study with 2-year follow-up. *Arthroscopy: The Journal of Arthroscopic & Related Surgery.* 2005;21(1):25-33.
2089. Nicholas SJ, Tyler TF, McHugh MP, Gleim GW. The effect on leg strength of tourniquet use during anterior cruciate ligament reconstruction: A prospective randomized study. *Arthroscopy.* 2001;17(6):603-7.
2090. Mariani PP, Camillieri G, Margheritini F. Transcondylar screw fixation in anterior cruciate ligament reconstruction. *Arthroscopy: The Journal of Arthroscopic & Related Surgery.* 2001;17(7):717-23.

2091. Ejerhed L, Kartus J, Koehler K, Sernert N, Brandsson S, Karlsson J. Preconditioning patellar tendon autografts in arthroscopic anterior cruciate ligament reconstruction: a prospective randomized study. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2001;9(1):6-11.
2092. Engebretsen L, Benum P, Fasting O, Molster A, Strand T. A prospective, randomized study of three surgical techniques for treatment of acute ruptures of the anterior cruciate ligament. *Am J Sports Med*. 1990;18(6):585-90.
2093. Gohil S, Annear PO, Bredahl W. Anterior cruciate ligament reconstruction using autologous double hamstrings: a comparison of standard versus minimal debridement techniques using MRI to assess revascularisation: A RANDOMISED PROSPECTIVE STUDY WITH A ONE-YEAR FOLLOW-UP. 2007:1165-71.
2094. Grondvedt T. Comparison between two techniques for surgical repair of the acutely torn anterior cruciate ligament. A prospective, randomized follow-up study of 48 patients. *Scand J Med Sci Sports*. 1995;5(3):358-63.
2095. Hollis R, West H, Greis P, Brown N, Burks R. Autologous bone effects on femoral tunnel widening in hamstring anterior cruciate ligament reconstruction. *J Knee Surg*. 2009;22(2):114-9.
2096. Jepsen CF, Lundberg-Jensen AK, Faunoe P. Does the Position of the Femoral Tunnel Affect the Laxity or Clinical Outcome of the Anterior Cruciate Ligament-Reconstructed Knee? A Clinical, Prospective, Randomized, Double-Blind Study. *Arthroscopy: The Journal of Arthroscopic & Related Surgery*. 2007;23(12):1326-33.
2097. Thuresson P, Sandberg R, Johansson O, Balkfors B, Westlin N. Anterior cruciate ligament reconstruction with the patellar tendon--augmentation or not? A 2-year follow-up of 82 patients. *Scand J Med Sci Sports*. 1996;6(4):247-54.
2098. Cameron SE, Wilson W, St Pierre P. A prospective, randomized comparison of open vs arthroscopically assisted ACL reconstruction. *Orthopedics*. 1995;18(3):249-52.
2099. Dahlstedt L, Dalen N, Jonsson U. Goretex prosthetic ligament vs. Kennedy ligament augmentation device in anterior cruciate ligament reconstruction. A prospective randomized 3-year follow-up of 41 cases. *Acta Orthop Scand*. 1990;61(3):217-24.
2100. Gerich TG, Lattermann C, Fremerey RW, Zeichen J, Lobenhoffer HP. One- versus two-incision technique for anterior cruciate ligament reconstruction with patellar tendon graft. Results on early rehabilitation and stability. *Knee Surg Sports Traumatol Arthrosc*. 1997;5(4):213-6.
2101. Gobbi A, Francisco R. Factors affecting return to sports after anterior cruciate ligament reconstruction with patellar tendon and hamstring graft: a prospective clinical investigation. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2006;14(10):1021-8.
2102. Basad E, Ishaque B, Bachmann G, Sturz H, Steinmeyer J. Matrix-induced autologous chondrocyte implantation versus microfracture in the treatment of cartilage defects of the knee: a 2-year randomised study. *Knee Surg Sports Traumatol Arthrosc*. 2010;18(4):519-27.
2103. Cerullo G, Puddu G, Gianni E, Damiani A, Pigozzi F. Anterior cruciate ligament patellar tendon reconstruction: it is probably better to leave the tendon defect open! *Knee Surg Sports Traumatol Arthrosc*. 1995;3(1):14-7.
2104. Chouteau J, Benareau I, Testa R, Fessy MH, Lerat JL, Moyon B. Comparative study of knee anterior cruciate ligament reconstruction with or without fluoroscopic assistance: a prospective study of 73 cases. *Arch Orthop Trauma Surg*. 2008;128(9):945-50.
2105. Robert H, Es-Sayeh J. The role of periosteal flap in the prevention of femoral widening in anterior cruciate ligament reconstruction using hamstring tendons. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2004;12(1):30-5.
2106. Zeifang F, Oberle D, Nierhoff C, Richter W, Moradi B, Schmitt H. Autologous chondrocyte implantation using the original periosteum-cover technique versus matrix-associated autologous chondrocyte implantation: a randomized clinical trial. *Am J Sports Med*. 2010;38(5):924-33.
2107. Petruskevicius J, Nielsen S, Kaalund S, Knudsen PR, Overgaard S. No effect of Osteoset, a bone graft substitute, on bone healing in humans: a prospective randomized double-blind study. *Acta Orthop Scand*. 2002;73(5):575-8.
2108. Aglietti P, Buzzi R, Bassi PB. Arthroscopic partial meniscectomy in the anterior cruciate deficient knee. *Am J Sports Med*. 1988;16(6):597-602.

2109. Andersson C, Gillquist J. Treatment of acute isolated and combined ruptures of the anterior cruciate ligament. A long-term follow-up study. *Am J Sports Med.* 1992;20(1):7-12.
2110. Hazel WA, Jr., Rand JA, Morrey BF. Results of meniscectomy in the knee with anterior cruciate ligament deficiency. *Clin Orthop Relat Res.* 1993(292):232-8.
2111. Neyret P, Donell ST, Dejour H. Results of partial meniscectomy related to the state of the anterior cruciate ligament. Review at 20 to 35 years. *J Bone Joint Surg Br.* 1993;75(1):36-40.
2112. Wickiewicz TL. Meniscal injuries in the cruciate-deficient knee. *Clin Sports Med.* 1990;9(3):681-94.
2113. Meighan AA, Keating JF, Will E. Outcome after reconstruction of the anterior cruciate ligament in athletic patients. A comparison of early versus delayed surgery. *J Bone Joint Surg Br.* 2003;85(4):521-4.
2114. Ahlden M, Kartus J, Ejerhed L, Karlsson J, Sernert N. Knee laxity measurements after anterior cruciate ligament reconstruction, using either bone-patellar-tendon-bone or hamstring tendon autografts, with special emphasis on comparison over time. *Knee Surg Sports Traumatol Arthrosc.* 2009;17(9):1117-24.
2115. Yasuda K, Kondo E, Ichiyama H, Tanabe Y, Tohyama H. Clinical Evaluation of Anatomic Double-Bundle Anterior Cruciate Ligament Reconstruction Procedure Using Hamstring Tendon Grafts: Comparisons Among 3 Different Procedures. *Arthroscopy: The Journal of Arthroscopic & Related Surgery.* 2006;22(3):240-51.
2116. Anderson AF, Snyder RB, Lipscomb AB, Jr. Anterior cruciate ligament reconstruction. A prospective randomized study of three surgical methods. *Am J Sports Med.* 2001;29(3):272-9.
2117. Eriksson K, Anderberg P, Hamberg P, Olerud P, Wredmark T. There are differences in early morbidity after ACL reconstruction when comparing patellar tendon and semitendinosus tendon graft. A prospective randomized study of 107 patients. *Scand J Med Sci Sports.* 2001;11(3):170-7.
2118. Feller JA, Webster KE, Gavin B. Early post-operative morbidity following anterior cruciate ligament reconstruction: patellar tendon versus hamstring graft. *Knee Surgery, Sports Traumatology, Arthroscopy.* 2001;9(5):260-6.
2119. Laxdal G, Kartus J, Hansson L, Heidvall M, Ejerhed L, Karlsson J. A prospective randomized comparison of bone-patellar tendon-bone and hamstring grafts for anterior cruciate ligament reconstruction. *Arthroscopy: The Journal of Arthroscopic & Related Surgery.* 2005;21(1):34-42.
2120. Zaffagnini S, Marcacci M, Lo Presti M, Giordano G, Iacono F, Neri M. Prospective and randomized evaluation of ACL reconstruction with three techniques: a clinical and radiographic evaluation at 5 years follow-up. *Knee Surgery, Sports Traumatology, Arthroscopy.* 2006;14(11):1060-9.
2121. Pigozzi F, Di Salvo V, Parisi A, et al. Isokinetic evaluation of anterior cruciate ligament reconstruction: quadriceps tendon versus patellar tendon. *J Sports Med Phys Fitness.* 2004;44(3):288-93.
2122. Pinczewski LA, Lyman J, Salmon LJ, Russell VJ, Roe J, Linklater J. A 10-Year Comparison of Anterior Cruciate Ligament Reconstructions With Hamstring Tendon and Patellar Tendon Autograft. 2007:564-74.
2123. Liden M, Ejerhed L, Sernert N, Laxdal G, Kartus J. Patellar tendon or semitendinosus tendon autografts for anterior cruciate ligament reconstruction: a prospective, randomized study with a 7-Year follow-up. *Am J Sports Med.* 2007;35(5):740-8.
2124. Webster KE, Feller JA, Hameister KA. Bone tunnel enlargement following anterior cruciate ligament reconstruction: a randomised comparison of hamstring and patellar tendon grafts with 2-year follow-up. *Knee Surg Sports Traumatol Arthrosc.* 2001;9(2):86-91.
2125. Carter TR, Edinger S. Isokinetic Evaluation of Anterior Cruciate Ligament Reconstruction: Hamstring Versus Patellar Tendon. *Arthroscopy: The Journal of Arthroscopic & Related Surgery.* 1999;15(2):169-72.
2126. Harilainen A, Linko E, Sandelin J. Randomized prospective study of ACL reconstruction with interference screw fixation in patellar tendon autografts versus femoral metal plate suspension and tibial post fixation in hamstring tendon autografts: 5-year clinical and radiological follow-up. *Knee Surgery, Sports Traumatology, Arthroscopy.* 2006;14(6):517-28.
2127. Sastre S, Popescu D, Nunez M, Pomes J, Tomas X, Peidro L. Double-bundle versus single-bundle ACL reconstruction using the horizontal femoral position: a prospective, randomized study. *Knee Surg Sports Traumatol Arthrosc.* 2010;18(1):32-6.
2128. Järvelä T, Moisala A-S, Paakkala T, Paakkala A. Tunnel Enlargement After Double-Bundle Anterior Cruciate Ligament Reconstruction: A Prospective, Randomized Study. *Arthroscopy: The Journal of Arthroscopic & Related Surgery.* 2008;24(12):1349-57.

2129. Kanaya A, Ochi M, Deie M, Adachi N, Nishimori M, Nakamae A. Intraoperative evaluation of anteroposterior and rotational stabilities in anterior cruciate ligament reconstruction: lower femoral tunnel placed single-bundle versus double-bundle reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2009;17(8):907-13.
2130. Streich N, Friedrich K, Gotterbarm T, Schmitt H. Reconstruction of the ACL with a semitendinosus tendon graft: a prospective randomized single blinded comparison of double-bundle versus single-bundle technique in male athletes. *Knee Surgery, Sports Traumatology, Arthroscopy.* 2008;16(3):232-8.
2131. Siebold R, Dehler C, Ellert T. Prospective Randomized Comparison of Double-Bundle Versus Single-Bundle Anterior Cruciate Ligament Reconstruction. *Arthroscopy: The Journal of Arthroscopic & Related Surgery.* 2008;24(2):137-45.
2132. Yagi M, Kuroda R, Nagamune K, Yoshiya S, Kurosaka M. Double-bundle ACL reconstruction can improve rotational stability. *Clin Orthop Relat Res.* 2007;454:100-7.
2133. Muneta T, Koga H, Mochizuki T, et al. A prospective randomized study of 4-strand semitendinosus tendon anterior cruciate ligament reconstruction comparing single-bundle and double-bundle techniques. *Arthroscopy.* 2007;23(6):618-28.
2134. Zhao J, He Y, Wang J. Double-Bundle Anterior Cruciate Ligament Reconstruction: Four Versus Eight Strands of Hamstring Tendon Graft. *Arthroscopy: The Journal of Arthroscopic & Related Surgery.* 2007;23(7):766-70.
2135. Sun K, Tian S, Zhang J, Xia C, Zhang C, Yu T. Anterior cruciate ligament reconstruction with BPTB autograft, irradiated versus non-irradiated allograft: a prospective randomized clinical study. *Knee Surgery, Sports Traumatology, Arthroscopy.* 2009;17(5):464-74.
2136. Sun K, Tian SQ, Zhang JH, Xia CS, Zhang CL, Yu TB. ACL reconstruction with BPTB autograft and irradiated fresh frozen allograft. *J Zhejiang Univ Sci B.* 2009;10(4):306-16.
2137. Sun K, Tian SQ, Zhang JH, Xia CS, Zhang CL, Yu TB. Anterior cruciate ligament reconstruction with bone-patellar tendon-bone autograft versus allograft. *Arthroscopy.* 2009;25(7):750-9.
2138. Engstrom B, Wredmark T, Westblad P. Patellar tendon or Leeds-Keio graft in the surgical treatment of anterior cruciate ligament ruptures. Intermediate results. *Clin Orthop Relat Res.* 1993(295):190-7.
2139. Beattie KA, Boulous P, Pui M, et al. Abnormalities identified in the knees of asymptomatic volunteers using peripheral magnetic resonance imaging. *Osteoarthritis Cartilage.* 2005;13(3):181-6.
2140. Jerosch J, Castro WH, Assheuer J. Age-related magnetic resonance imaging morphology of the menisci in asymptomatic individuals. *Arch Orthop Trauma Surg.* 1996;115(3-4):199-202.
2141. LaPrade RF, Burnett QM, 2nd, Veenstra MA, Hodgman CG. The prevalence of abnormal magnetic resonance imaging findings in asymptomatic knees. With correlation of magnetic resonance imaging to arthroscopic findings in symptomatic knees. *Am J Sports Med.* 1994;22(6):739-45.
2142. Scholten RJ, Deville WL, Opstelten W, Bijl D, van der Plas CG, Bouter LM. The accuracy of physical diagnostic tests for assessing meniscal lesions of the knee: a meta-analysis. *J Fam Pract.* 2001;50(11):938-44.
2143. Eren OT. The accuracy of joint line tenderness by physical examination in the diagnosis of meniscal tears. *Arthroscopy.* 2003;19(8):850-4.
2144. Hegedus EJ, Cook C, Hasselblad V, Goode A, McCrory DC. Physical examination tests for assessing a torn meniscus in the knee: a systematic review with meta-analysis. *J Orthop Sports Phys Ther.* 2007;37(9):541-50.
2145. Miller GK. A prospective study comparing the accuracy of the clinical diagnosis of meniscus tear with magnetic resonance imaging and its effect on clinical outcome. *Arthroscopy.* 1996;12(4):406-13.
2146. Muellner T, Weinstabl R, Schabus R, Vecsei V, Kainberger F. The diagnosis of meniscal tears in athletes. A comparison of clinical and magnetic resonance imaging investigations. *Am J Sports Med.* 1997;25(1):7-12.
2147. Anderson MW. MR imaging of the meniscus. *Radiol Clin North Am.* 2002;40(5):1081-94.
2148. Aydingoz U, Firat AK, Atay OA, Doral MN. MR imaging of meniscal bucket-handle tears: a review of signs and their relation to arthroscopic classification. *Eur Radiol.* 2003;13(3):618-25.
2149. Boxheimer L, Lutz AM, Zanetti M, et al. Characteristics of displaceable and nondisplaceable meniscal tears at kinematic MR imaging of the knee. *Radiology.* 2006;238(1):221-31.
2150. Burk DL, Jr., Mitchell DG, Rifkin MD, Vinitski S. Recent advances in magnetic resonance imaging of the knee. *Radiol Clin North Am.* 1990;28(2):379-93.

2151. De Smet AA, Blankenbaker DG, Kijowski R, Graf BK, Shinki K. MR diagnosis of posterior root tears of the lateral meniscus using arthroscopy as the reference standard. *AJR Am J Roentgenol.* 2009;192(2):480-6.
2152. Fox MG. MR imaging of the meniscus: review, current trends, and clinical implications. *Radiol Clin North Am.* 2007;45(6):1033-53, vii.
2153. Harper KW, Helms CA, Lambert HS, 3rd, Higgins LD. Radial meniscal tears: significance, incidence, and MR appearance. *AJR Am J Roentgenol.* 2005;185(6):1429-34.
2154. Helms CA. The meniscus: recent advances in MR imaging of the knee. *AJR Am J Roentgenol.* 2002;179(5):1115-22.
2155. Hollingworth W, Todd CJ, Bell MI, et al. The diagnostic and therapeutic impact of MRI: an observational multi-centre study. *Clin Radiol.* 2000;55(11):825-31.
2156. Huysse WC, Verstraete KL, Verdonk PC, Verdonk R. Meniscus imaging. *Semin Musculoskelet Radiol.* 2008;12(4):318-33.
2157. Jones AO, Houang MT, Low RS, Wood DG. Medial meniscus posterior root attachment injury and degeneration: MRI findings. *Australas Radiol.* 2006;50(4):306-13.
2158. Jung JY, Yoon YC, Kwon JW, Ahn JH, Choe BK. Diagnosis of internal derangement of the knee at 3.0-T MR imaging: 3D isotropic intermediate-weighted versus 2D sequences. *Radiology.* 2009;253(3):780-7.
2159. Karantanas AH, Zibis AH, Papanikolaou N. Comparison of echo planar imaging, gradient echo and fast spin echo MR scans of knee menisci. *Comput Med Imaging Graph.* 2000;24(5):309-16.
2160. Kaushik S, Erickson JK, Palmer WE, Winalski CS, Kilpatrick SJ, Weissman BN. Effect of chondrocalcinosis on the MR imaging of knee menisci. *AJR Am J Roentgenol.* 2001;177(4):905-9.
2161. Ludman CN, Hough DO, Cooper TG, Gottschalk A. Silent meniscal abnormalities in athletes: magnetic resonance imaging of asymptomatic competitive gymnasts. *Br J Sports Med.* 1999;33(6):414-6.
2162. Lyle NJ, Sampson MA, Barrett DS. MRI of intermittent meniscal dislocation in the knee. *Br J Radiol.* 2009;82(977):374-9.
2163. Magee T. MR findings of meniscal extrusion correlated with arthroscopy. *J Magn Reson Imaging.* 2008;28(2):466-70.
2164. Magee T, Shapiro M, Williams D. Prevalence of meniscal radial tears of the knee revealed by MRI after surgery. *AJR Am J Roentgenol.* 2004;182(4):931-6.
2165. Magee T, Williams D. Detection of meniscal tears and marrow lesions using coronal MRI. *AJR Am J Roentgenol.* 2004;183(5):1469-73.
2166. Makdissi M, Eriksson KO, Morris HG, Young DA. MRI-negative bucket-handle tears of the lateral meniscus in athletes: a case series. *Knee Surg Sports Traumatol Arthrosc.* 2006;14(10):1012-6.
2167. Manco LG, Berlow ME. Meniscal tears--comparison of arthrography, CT, and MRI. *Crit Rev Diagn Imaging.* 1989;29(2):151-79.
2168. Manco LG, Lozman J, Coleman ND, Kavanaugh JH, Bilfield BS, Dougherty J. Noninvasive evaluation of knee meniscal tears: preliminary comparison of MR imaging and CT. *Radiology.* 1987;163(3):727-30.
2169. McGlade CT. Magnetic resonance imaging of the meniscus. *Clin Sports Med.* 1990;9(3):551-9.
2170. Mesgarzadeh M, Moyer R, Leder DS, et al. MR imaging of the knee: expanded classification and pitfalls to interpretation of meniscal tears. *Radiographics.* 1993;13(3):489-500.
2171. Nourissat G, Beaufile P, Charrois O, et al. Magnetic resonance imaging as a tool to predict reparability of longitudinal full-thickness meniscus lesions. *Knee Surg Sports Traumatol Arthrosc.* 2008;16(5):482-6.
2172. Oei EH, Nikken JJ, Verstijnen AC, Ginai AZ, Myriam Hunink MG. MR imaging of the menisci and cruciate ligaments: a systematic review. *Radiology.* 2003;226(3):837-48.
2173. Rauscher I, Stahl R, Cheng J, et al. Meniscal measurements of T1rho and T2 at MR imaging in healthy subjects and patients with osteoarthritis. *Radiology.* 2008;249(2):591-600.
2174. Ryzewicz M, Peterson B, Siparsky PN, Bartz RL. The diagnosis of meniscus tears: the role of MRI and clinical examination. *Clin Orthop Relat Res.* 2007;455:123-33.
2175. Tyson LL, Daughters TC, Jr., Ryu RK, Crues JV, 3rd. MRI appearance of meniscal cysts. *Skeletal Radiol.* 1995;24(6):421-4.
2176. Vance K, Meredick R, Schweitzer ME, Lubowitz JH. Magnetic resonance imaging of the postoperative meniscus. *Arthroscopy.* 2009;25(5):522-30.

2177. Vande Berg BC, Malghem J, Poilvache P, Maldague B, Lecouvet FE. Meniscal tears with fragments displaced in notch and recesses of knee: MR imaging with arthroscopic comparison. *Radiology*. 2005;234(3):842-50.
2178. Kocabey Y, Tetik O, Isbell WM, Atay OA, Johnson DL. The value of clinical examination versus magnetic resonance imaging in the diagnosis of meniscal tears and anterior cruciate ligament rupture. *Arthroscopy*. 2004;20(7):696-700.
2179. Rose NE, Gold SM. A comparison of accuracy between clinical examination and magnetic resonance imaging in the diagnosis of meniscal and anterior cruciate ligament tears. *Arthroscopy*. 1996;12(4):398-405.
2180. Brealey S, DAMASK Trial Team. Influence of magnetic resonance of the knee on GPs' decisions: a randomised trial. *Br J Gen Pract*. 2007;57(541):622-9.
2181. Ben-Galim P, Steinberg EL, Amir H, Ash N, Dekel S, Arbel R. Accuracy of magnetic resonance imaging of the knee and unjustified surgery. *Clin Orthop Relat Res*. 2006;447:100-4.
2182. Casser HR, Sohn C, Kiekenbeck A. Current evaluation of sonography of the meniscus. Results of a comparative study of sonographic and arthroscopic findings. *Arch Orthop Trauma Surg*. 1990;109(3):150-4.
2183. De Flaviis L, Scaglione P, Nessi R, Albisetti W. Ultrasound in degenerative cystic meniscal disease of the knee. *Skeletal Radiol*. 1990;19(6):441-5.
2184. Sandhu MS, Dhillon MS, Katariya S, Gopal V, Nagi ON. High resolution sonography for analysis of meniscal injuries. *J Indian Med Assoc*. 2007;105(1):49-50, 2.
2185. Shetty AA, Tindall AJ, James KD, Relwani J, Fernando KW. Accuracy of hand-held ultrasound scanning in detecting meniscal tears. *J Bone Joint Surg Br*. 2008;90(8):1045-8.
2186. Azzoni R, Cabitza P. Is there a role for sonography in the diagnosis of tears of the knee menisci? *J Clin Ultrasound*. 2002;30(8):472-6.
2187. Manco LG, Berlow ME, Czajka J, Alfred R. Bucket-handle tears of the meniscus: appearance at CT. *Radiology*. 1988;168(3):709-12.
2188. Lee W, Kim HS, Kim SJ, et al. CT arthrography and virtual arthroscopy in the diagnosis of the anterior cruciate ligament and meniscal abnormalities of the knee joint. *Korean J Radiol*. 2004;5(1):47-54.
2189. Vande Berg BC, Lecouvet FE, Poilvache P, Dubuc JE, Maldague B, Malghem J. Anterior cruciate ligament tears and associated meniscal lesions: assessment at dual-detector spiral CT arthrography. *Radiology*. 2002;223(2):403-9.
2190. Coulier B. Direct 3D imaging of the knee menisci during 16-row multislice CT arthrography. *JBR-BTR*. 2006;89(6):291-7.
2191. Collier BD, Johnson RP, Carrera GF, et al. Chronic knee pain assessed by SPECT: comparison with other modalities. *Radiology*. 1985;157(3):795-802.
2192. Grevitt MP, Taylor M, Churchill M, Allen P, Ryan PJ, Fogelman I. SPECT imaging in the diagnosis of meniscal tears. *J R Soc Med*. 1993;86(11):639-41.
2193. Yildirim M, GURSOY R, Varoglu E, Oztasyonar Y, S. C. 99mTc-MDP bone SPECT in evaluation of the knee in asymptomatic soccer players. *Br J Sports Med*. 2004;38(1):15-8.
2194. So Y, Chung JK, Seong SC, et al. Usefulness of 99Tcm-MDP knee SPET for pre-arthroscopic evaluation of patients with internal derangements of the knee. *Nucl Med Commun*. 2000;21(1):103-9.
2195. Westrich G, Schaefer S, Walcott-Sapp S, Lyman S. Randomized prospective evaluation of adjuvant hyaluronic acid therapy administered after knee arthroscopy. *Am J Orthop (Belle Mead NJ)*. 2009;38(12):612-6.
2196. Barber FA. Accelerated rehabilitation for meniscus repairs. *Arthroscopy*. 1994;10(2):206-10.
2197. Shelbourne KD, Patel DV, Adsit WS, Porter DA. Rehabilitation after meniscal repair. *Clin Sports Med*. 1996;15(3):595-612.
2198. Wheatley WB, Krome J, Martin DF. Rehabilitation programmes following arthroscopic meniscectomy in athletes. *Sports Med*. 1996;21(6):447-56.
2199. Herrlin S, Hallander M, Wange P, Weidenhielm L, Werner S. Arthroscopic or conservative treatment of degenerative medial meniscal tears: a prospective randomised trial. *Knee Surg Sports Traumatol Arthrosc*. 2007;15(4):393-401.
2200. Karumo I. Intensive physical therapy after meniscectomy. *Ann Chir Gynaecol*. 1977;66(1):41-6.

2201. Goodwin PC, Morrissey MC, Omar RZ, Brown M, Southall K, McAuliffe TB. Effectiveness of supervised physical therapy in the early period after arthroscopic partial meniscectomy. *Phys Ther.* 2003;83(6):520-35.
2202. Vervest AM, Maurer CA, Schambergen TG, de Bie RA, Bulstra SK. Effectiveness of physiotherapy after meniscectomy. *Knee Surg Sports Traumatol Arthrosc.* 1999;7(6):360-4.
2203. Kelln BM, Ingersoll CD, Saliba S, Miller MD, Hertel J. Effect of early active range of motion rehabilitation on outcome measures after partial meniscectomy. *Knee Surg Sports Traumatol Arthrosc.* 2009;17(6):607-16.
2204. Ericsson YB, Dahlberg LE, Roos EM. Effects of functional exercise training on performance and muscle strength after meniscectomy: a randomized trial. *Scand J Med Sci Sports.* 2009;19(2):156-65.
2205. Petersen MM, Olsen C, Lauritzen JB, Lund B, Hede A. Late changes in bone mineral density of the proximal tibia following total or partial medial meniscectomy. A randomized study. *J Orthop Res.* 1996;14(1):16-21.
2206. Hamberg P, Gillquist J, Lysholm J. A comparison between arthroscopic meniscectomy and modified open meniscectomy. A prospective randomised study with emphasis on postoperative rehabilitation. *J Bone Joint Surg Br.* 1984;66(2):189-92.
2207. Thorblad J, Ekstrand J, Hamberg P, Gillquist J. Muscle rehabilitation after arthroscopic meniscectomy with or without tourniquet control. A preliminary randomized study. *Am J Sports Med.* 1985;13(2):133-5.
2208. Barber FA, Iwasko NG. Treatment of grade III femoral chondral lesions: mechanical chondroplasty versus monopolar radiofrequency probe. *Arthroscopy.* 2006;22(12):1312-7.
2209. Dobner JJ, Nitz AJ. Postmeniscectomy tourniquet palsy and functional sequelae. *Am J Sports Med.* 1982;10(4):211-4.
2210. Bryant D, Dill J, Litchfield R, et al. Effectiveness of bioabsorbable arrows compared with inside-out suturing for vertical, reparable meniscal lesions: a randomized clinical trial. *Am J Sports Med.* 2007;35(6):889-96.
2211. Hantes ME, Zachos VC, Varitimidis SE, Dailiana ZH, Karachalios T, Malizos KN. Arthroscopic meniscal repair: a comparative study between three different surgical techniques. *Knee Surg Sports Traumatol Arthrosc.* 2006;14(12):1232-7.
2212. Albrecht-Olsen P, Kristensen G, Burgaard P, Joergensen U, Toerholm C. The arrow versus horizontal suture in arthroscopic meniscus repair. A prospective randomized study with arthroscopic evaluation. *Knee Surg Sports Traumatol Arthrosc.* 1999;7(5):268-73.
2213. Howell SM, Kuznik K, Hull ML, Siston RA. Results of an initial experience with custom-fit positioning total knee arthroplasty in a series of 48 patients. *Orthopedics.* 2008;31(9):857-63.
2214. Andersson-Molina H, Karlsson H, Rockborn P. Arthroscopic partial and total meniscectomy: A long-term follow-up study with matched controls. *Arthroscopy.* 2002;18(2):183-9.
2215. Awbrey BJ. Arthroscopic management of meniscal injuries. *Curr Opin Rheumatol.* 1993;5(3):309-16.
2216. Bergstrom R, Hamberg P, Lysholm J, Gillquist J. Comparison of open and endoscopic meniscectomy. *Clin Orthop Relat Res.* 1984(184):133-6.
2217. Chatain F, Adeleine P, Chambat P, Neyret P. A comparative study of medial versus lateral arthroscopic partial meniscectomy on stable knees: 10-year minimum follow-up. *Arthroscopy.* 2003;19(8):842-9.
2218. Del Pizzo W, Fox JM. Results of arthroscopic meniscectomy. *Clin Sports Med.* 1990;9(3):633-9.
2219. Fabricant PD, Jokl P. Surgical outcomes after arthroscopic partial meniscectomy. *J Am Acad Orthop Surg.* 2007;15(11):647-53.
2220. Farnig E, Sherman O. Meniscal repair devices: a clinical and biomechanical literature review. *Arthroscopy.* 2004;20(3):273-86.
2221. Graf B, Jensen K, Orwin J, Duck H, Hagen P, Keene J. The effect of tourniquet use on postoperative strength recovery after arthroscopic meniscectomy. *Orthopedics.* 1996;19(6):497-500.
2222. Grana WA, Connor S, Hollingsworth S. Partial arthroscopic meniscectomy: a preliminary report. *Clin Orthop Relat Res.* 1982(164):78-83.
2223. Greis PE, Bardana DD, Holmstrom MC, Burks RT. Meniscal injury: I. Basic science and evaluation. *J Am Acad Orthop Surg.* 2002;10(3):168-76.
2224. Greis PE, Holmstrom MC, Bardana DD, Burks RT. Meniscal injury: II. Management. *J Am Acad Orthop Surg.* 2002;10(3):177-87.
2225. Heckmann TP, Barber-Westin SD, Noyes FR. Meniscal repair and transplantation: indications, techniques, rehabilitation, and clinical outcome. *J Orthop Sports Phys Ther.* 2006;36(10):795-814.

2226. Ireland J, Trickey EL, Stoker DJ. Arthroscopy and arthrography of the knee: a critical review. *J Bone Joint Surg Br.* 1980;62-B(1):3-6.
2227. Koenig JH, Ranawat AS, Umans HR, Difelice GS. Meniscal root tears: diagnosis and treatment. *Arthroscopy.* 2009;25(9):1025-32.
2228. Pearse EO, Craig DM. Partial meniscectomy in the presence of severe osteoarthritis does not hasten the symptomatic progression of osteoarthritis. *Arthroscopy.* 2003;19(9):963-8.
2229. Pettrone FA. Meniscectomy: arthrotomy versus arthroscopy. *Am J Sports Med.* 1982;10(6):355-9.
2230. Polousky JD, Hedman TP, Vangness CT, Jr. Electrosurgical methods for arthroscopic meniscectomy: A review of the literature. *Arthroscopy.* 2000;16(8):813-21.
2231. Rangger C, Kathrein A, Klestil T, Glotzer W. Partial meniscectomy and osteoarthritis. Implications for treatment of athletes. *Sports Med.* 1997;23(1):61-8.
2232. Shelbourne KD, Carr DR. Meniscal repair compared with meniscectomy for bucket-handle medial meniscal tears in anterior cruciate ligament-reconstructed knees. *Am J Sports Med.* 2003;31(5):718-23.
2233. Siparsky P, Ryzewicz M, Peterson B, Bartz R. Arthroscopic treatment of osteoarthritis of the knee: are there any evidence-based indications? *Clin Orthop Relat Res.* 2007;455:107-12.
2234. St Pierre RK, Sones PJ, Fleming LL. Arthroscopy and arthrography of the knee: a comparison study. *South Med J.* 1981;74(11):1322-8.
2235. Steenbrugge F, Verdonk R, Hurel C, Verstraete K. Arthroscopic meniscus repair: inside-out technique vs. Biofix meniscus arrow. *Knee Surg Sports Traumatol Arthrosc.* 2004;12(1):43-9.
2236. Venkatachalam S, Godsiff SP, Harding ML. Review of the clinical results of arthroscopic meniscal repair. *Knee.* 2001;8(2):129-33.
2237. Northmore-Ball MD, Dandy DJ, Jackson RW. Arthroscopic, open partial, and total meniscectomy. A comparative study. *J Bone Joint Surg Br.* 1983;65(4):400-4.
2238. McGinity JB, Geuss LF, Marvin RA. Partial or total meniscectomy: a comparative analysis. *J Bone Joint Surg Am.* 1977;59(6):763-6.
2239. Lanzer WL, Komenda G. Changes in articular cartilage after meniscectomy. *Clin Orthop Relat Res.* 1990(252):41-8.
2240. McDermott ID, Amis AA. The consequences of meniscectomy. *J Bone Joint Surg Br.* 2006;88(12):1549-56.
2241. Meredith DS, Losina E, Mahomed NN, Wright J, Katz JN. Factors predicting functional and radiographic outcomes after arthroscopic partial meniscectomy: a review of the literature. *Arthroscopy.* 2005;21(2):211-23.
2242. Paxton ES, Stock MV, Brophy RH. Meniscal repair versus partial meniscectomy: a systematic review comparing reoperation rates and clinical outcomes. *Arthroscopy.* 2011;27(9):1275-88.
2243. Grant JA, Wilde J, Miller BS, Bedi A. Comparison of inside-out and all-inside techniques for the repair of isolated meniscal tears: a systematic review. *Am J Sports Med.* 2012;40(2):459-68.
2244. Lozano J, Li X, Link TM, Safran M, Majumdar S, Ma CB. Detection of posttraumatic cartilage injury using quantitative T1rho magnetic resonance imaging. A report of two cases with arthroscopic findings. *J Bone Joint Surg Am.* 2006;88(6):1349-52.
2245. Ramappa M, Anand S, Jennings A. Total knee replacement following high tibial osteotomy versus total knee replacement without high tibial osteotomy: a systematic review and meta analysis. *Arch Orthop Trauma Surg.* 2013;133(11):1587-93.
2246. Centeno CJ, Busse D, Kisiday J, Keohan C, Freeman M, Karli D. Regeneration of meniscus cartilage in a knee treated with percutaneously implanted autologous mesenchymal stem cells. *Med Hypotheses.* 2008;71(6):900-8.
2247. Marsano A, Vunjak-Novakovic G, Martin I. Towards tissue engineering of meniscus substitutes: selection of cell source and culture environment. *Conf Proc IEEE Eng Med Biol Soc.* 2006;13656-8.
2248. Marsano A, Wendt D, Raiteri R, et al. Use of hydrodynamic forces to engineer cartilaginous tissues resembling the non-uniform structure and function of meniscus. *Biomaterials.* 2006;27(35):5927-34.
2249. Cameron JC, Saha S. Meniscal allograft transplantation for unicompartmental arthritis of the knee. *Clin Orthop Relat Res.* 1997(337):164-71.
2250. Garrett JC. Osteochondral allografts. *Instr Course Lect.* 1993;42:355-8.
2251. Garrett JC, Steensen RN. Meniscal transplantation in the human knee: a preliminary report. *Arthroscopy.* 1991;7(1):57-62.

2252. Goble EM, Verdonk R, Kohn D. Arthroscopic and open surgical techniques for meniscus replacement--meniscal allograft transplantation and tendon autograft transplantation. *Scand J Med Sci Sports*. 1999;9(3):168-76.
2253. Graf KW, Jr., Sekiya JK, Wojtys EM. Long-term results after combined medial meniscal allograft transplantation and anterior cruciate ligament reconstruction: minimum 8.5-year follow-up study. *Arthroscopy*. 2004;20(2):129-40.
2254. Khetia EA, McKeon BP. Meniscal allografts: biomechanics and techniques. *Sports Med Arthrosc*. 2007;15(3):114-20.
2255. McDermott ID. What tissue bankers should know about the use of allograft meniscus in orthopaedics. *Cell Tissue Bank*. 2010;11(1):75-85.
2256. Milachowski KA, Weismeier K, Wirth CJ. Homologous meniscus transplantation. Experimental and clinical results. *Int Orthop*. 1989;13(1):1-11.
2257. Noyes FR, Barber-Westin SD, Rankin M. Meniscal transplantation in symptomatic patients less than fifty years old. *J Bone Joint Surg Am*. 2004;86-A(7):1392-404.
2258. Packer JD, Rodeo SA. Meniscal allograft transplantation. *Clin Sports Med*. 2009;28(2):259-83, viii.
2259. Peters G, Wirth CJ. The current state of meniscal allograft transplantation and replacement. *Knee*. 2003;10(1):19-31.
2260. Rath E, Richmond JC, Yassir W, Albright JD, Gundogan F. Meniscal allograft transplantation. Two- to eight-year results. *Am J Sports Med*. 2001;29(4):410-4.
2261. Rijk PC. Meniscal allograft transplantation--part II: alternative treatments, effects on articular cartilage, and future directions. *Arthroscopy*. 2004;20(8):851-9.
2262. Rijk PC. Meniscal allograft transplantation--part I: background, results, graft selection and preservation, and surgical considerations. *Arthroscopy*. 2004;20(7):728-43.
2263. Rodeo SA. Meniscal allografts--where do we stand? *Am J Sports Med*. 2001;29(2):246-61.
2264. Rue JP, Yanke AB, Busam ML, McNickle AG, Cole BJ. Prospective evaluation of concurrent meniscus transplantation and articular cartilage repair: minimum 2-year follow-up. *Am J Sports Med*. 2008;36(9):1770-8.
2265. Ryu RK, Dunbar VW, Morse GG. Meniscal allograft replacement: a 1-year to 6-year experience. *Arthroscopy*. 2002;18(9):989-94.
2266. Sekiya JK, Giffin JR, Irrgang JJ, Fu FH, Harner CD. Clinical outcomes after combined meniscal allograft transplantation and anterior cruciate ligament reconstruction. *Am J Sports Med*. 2003;31(6):896-906.
2267. Sohn DH, Toth AP. Meniscus transplantation: current concepts. *J Knee Surg*. 2008;21(2):163-72.
2268. Stollsteimer GT, Shelton WR, Dukes A, Bomboy AL. Meniscal allograft transplantation: a 1- to 5-year follow-up of 22 patients. *Arthroscopy*. 2000;16(4):343-7.
2269. van Arkel ER, de Boer HH. Human meniscal transplantation. Preliminary results at 2 to 5-year follow-up. *J Bone Joint Surg Br*. 1995;77(4):589-95.
2270. van Arkel ER, de Boer HH. Survival analysis of human meniscal transplantations. *J Bone Joint Surg Br*. 2002;84(2):227-31.
2271. Veltri DM, Warren RF, Wickiewicz TL, O'Brien SJ. Current status of allograft meniscal transplantation. *Clin Orthop Relat Res*. 1994(303):44-55.
2272. Verdonk PC, Demurie A, Almqvist KF, Veys EM, Verbruggen G, Verdonk R. Transplantation of viable meniscal allograft. Survivorship analysis and clinical outcome of one hundred cases. *J Bone Joint Surg Am*. 2005;87(4):715-24.
2273. Wirth CJ, Peters G, Milachowski KA, Weismeier KG, Kohn D. Long-term results of meniscal allograft transplantation. *Am J Sports Med*. 2002;30(2):174-81.
2274. Yoldas EA, Sekiya JK, Irrgang JJ, Fu FH, Harner CD. Arthroscopically assisted meniscal allograft transplantation with and without combined anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc*. 2003;11(3):173-82.
2275. Rodkey WG, DeHaven KE, Montgomery WH, 3rd, et al. Comparison of the collagen meniscus implant with partial meniscectomy. A prospective randomized trial. *J Bone Joint Surg Am*. 2008;90(7):1413-26.
2276. van Tienen TG, Hannink G, Buma P. Meniscus replacement using synthetic materials. *Clin Sports Med*. 2009;28(1):143-56.

2277. Sihvonen R, Paavola M, Malmivaara A, et al. Arthroscopic partial meniscectomy versus sham surgery for a degenerative meniscal tear. *N Engl J Med*. 2013;369(26):2515-24.
2278. Spahn G, Kahl E, Muckley T, Hofmann GO, Klinger HM. Arthroscopic knee chondroplasty using a bipolar radiofrequency-based device compared to mechanical shaver: results of a prospective, randomized, controlled study. *Knee Surg Sports Traumatol Arthrosc*. 2008;16(6):565-73.
2279. Hede A, Hejgaard N, Larsen E. Partial or total open meniscectomy? A prospective, randomized study. *Int Orthop*. 1986;10(2):105-8.
2280. Hede A, Larsen E, Sandberg H. Partial versus total meniscectomy. A prospective, randomised study with long-term follow-up. *J Bone Joint Surg Br*. 1992;74(1):118-21.
2281. Hede A, Larsen E, Sandberg H. The long term outcome of open total and partial meniscectomy related to the quantity and site of the meniscus removed. *Int Orthop*. 1992;16(2):122-5.
2282. Perdue PS, Jr., Hummer CD, 3rd, Colosimo AJ, Heidt RS, Jr., Dormer SG. Meniscal repair: outcomes and clinical follow-up. *Arthroscopy*. 1996;12(6):694-8.
2283. Barrett GR, Field MH, Treacy SH, Ruff CG. Clinical results of meniscus repair in patients 40 years and older. *Arthroscopy*. 1998;14(8):824-9.
2284. Boyd KT, Myers PT. Meniscus preservation; rationale, repair techniques and results. *Knee*. 2003;10(1):1-11.
2285. Noyes FR, Barber-Westin SD. Arthroscopic repair of meniscus tears extending into the avascular zone with or without anterior cruciate ligament reconstruction in patients 40 years of age and older. *Arthroscopy*. 2000;16(8):822-9.
2286. Jarvela S, Sihvonen R, Sirkeoja H, Jarvela T. All-inside meniscal repair with bioabsorbable meniscal screws or with bioabsorbable meniscus arrows: a prospective, randomized clinical study with 2-year results. *Am J Sports Med*. 2010;38(11):2211-7.
2287. Biedert RM. Treatment of intrasubstance meniscal lesions: a randomized prospective study of four different methods. *Knee Surg Sports Traumatol Arthrosc*. 2000;8(2):104-8.
2288. Grifka J, Boenke S, Schreiner C, Lohnert J. Significance of laser treatment in arthroscopic therapy of degenerative gonarthrosis. A prospective, randomised clinical study and experimental research. *Knee Surg Sports Traumatol Arthrosc*. 1994;2(2):88-93.
2289. Krebs DE. Clinical electromyographic feedback following meniscectomy. A multiple regression experimental analysis. *Phys Ther*. 1981;61(7):1017-21.
2290. Kirnap M, Calis M, Turgut AO, Halici M, Tuncel M. The efficacy of EMG-biofeedback training on quadriceps muscle strength in patients after arthroscopic meniscectomy. *N Z Med J*. 2005;118(1224):U1704.
2291. Shell D, Perkins R, Cosgarea A. Septic olecranon bursitis: recognition and treatment. *J Am Board Fam Pract*. 1995;8(3):217-20.
2292. Cardone DA, Tallia AF. Diagnostic and therapeutic injection of the elbow region. *Am Fam Physician*. 2002;66(11):2097-100.
2293. Butcher J, Salzman K, Lillegard W. Lower extremity bursitis. *Am Fam Physician*. 1996;53(7):2317-24.
2294. Salzman K, Lillegard WA, Butcher JD. Upper extremity bursitis. *Am Fam Physician*. 1997;56(7):1797-806.
2295. Gendernalik JD, Sechriest VF, 2nd. Prepatellar septic bursitis: a case report of skin necrosis associated with open bursectomy. *Mil Med*. 2009;174(6):666-9.
2296. Ho G, Jr., Tice AD. Comparison of nonseptic and septic bursitis. Further observations on the treatment of septic bursitis. *Arch Intern Med*. 1979;139(11):1269-73.
2297. Pien F, Ching D, Kim E. Septic bursitis: experience in a community practice. *Orthopedics*. 1991;14(9):981-4.
2298. Kosmoliaptsis V, Soni R. Tophaceous gout mass distending the prepatellar bursa. *J Clin Rheumatol*. 2007;13(6):359.
2299. Wittich CM, Ficalora RD, Mason TG, Beckman TJ. Musculoskeletal injection. *Mayo Clin Proc*. 2009;84(9):831-6; quiz 7.
2300. Kerr DR. Prepatellar and olecranon arthroscopic bursectomy. *Clin Sports Med*. 1993;12(1):137-42.
2301. Kerr DR, Carpenter CW. Arthroscopic resection of olecranon and prepatellar bursae. *Arthroscopy*. 1990;6(2):86-8.
2302. Hennrikus WL, Champa JR, Mack GR. Treating septic prepatellar bursitis. *West J Med*. 1989;151(3):331-2.

2303. McAfee JH, Smith DL. Olecranon and prepatellar bursitis. Diagnosis and treatment. *West J Med.* 1988;149(5):607-10.
2304. Wilson-MacDonald J. Management and outcome of infective prepatellar bursitis. *Postgrad Med J.* 1987;63(744):851-3.
2305. Collado H, Fredericson M. Patellofemoral pain syndrome. *Clin Sports Med.* 2010;29(3):379-98.
2306. Redziniak DE, Diduch DR, Mihalko WM, et al. Patellar instability. *Instr Course Lect.* 2010;59:195-206.
2307. Tanamas SK, Teichtahl AJ, Wluka AE, et al. The associations between indices of patellofemoral geometry and knee pain and patella cartilage volume: a cross-sectional study. *BMC Musculoskelet Disord.* 2010;11;87.
2308. Collins N, Crossley K, Beller E, Darnell R, McPoil T, Vicenzino B. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: randomised clinical trial. *Bmj.* 2008;337a1735.
2309. Creedon F, Lewis T. Are Open (OKC) or Closed Kinetic Chain (CKC) exercises most effective in the treatment of patello femoral pain? 2008.
2310. Crossley K, Bennell K, Green S, Cowan S, McConnell J. Physical therapy for patellofemoral pain: a randomized, double-blinded, placebo-controlled trial. *Am J Sports Med.* 2002;30(6):857-65.
2311. McMullen W, Roncarati A, Koval P. Static and isokinetic treatments of chondromalacia patella: a comparative investigation. *J Orthop Sports Phys Ther.* 1990;12(6):256-66.
2312. Stiene HA, Brosky T, Reinking MF, Nyland J, Mason MB. A comparison of closed kinetic chain and isokinetic joint isolation exercise in patients with patellofemoral dysfunction. *J Orthop Sports Phys Ther.* 1996;24(3):136-41.
2313. Vicenzino B, Collins N, Crossley K, Beller E, Darnell R, McPoil T. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: a randomised clinical trial. *BMC Musculoskelet Disord.* 2008;927.
2314. Wang C, Schmid CH, Hibberd PL, et al. Tai Chi for treating knee osteoarthritis: designing a long-term follow up randomized controlled trial. *BMC Musculoskelet Disord.* 2008;9108.
2315. Kettunen JA, Harilainen A, Sandelin J, et al. Knee arthroscopy and exercise versus exercise only for chronic patellofemoral pain syndrome: a randomized controlled trial. *BMC Med.* 2007;538.
2316. Bahr R, Fossan B, Loken S, Engebretsen L. Surgical treatment compared with eccentric training for patellar tendinopathy (Jumper's Knee). A randomized, controlled trial. *J Bone Joint Surg Am.* 2006;88(8):1689-98.
2317. Cannell LJ, Taunton JE, Clement DB, Smith C, Khan KM. A randomised clinical trial of the efficacy of drop squats or leg extension/leg curl exercises to treat clinically diagnosed jumper's knee in athletes: pilot study. *Br J Sports Med.* 2001;35(1):60-4.
2318. Crossley KM, Cowan SM, McConnell J, Bennell KL. Physical therapy improves knee flexion during stair ambulation in patellofemoral pain. *Med Sci Sports Exerc.* 2005;37(2):176-83.
2319. Herrington L, Al-Sherhi A. A controlled trial of weight-bearing versus non-weight-bearing exercises for patellofemoral pain. *J Orthop Sports Phys Ther.* 2007;37(4):155-60.
2320. Nakagawa TH, Muniz TB, Baldon Rde M, Dias Maciel C, de Menezes Reiff RB, Serrao FV. The effect of additional strengthening of hip abductor and lateral rotator muscles in patellofemoral pain syndrome: a randomized controlled pilot study. *Clin Rehabil.* 2008;22(12):1051-60.
2321. Quilty B, Tucker M, Campbell R, Dieppe P. Physiotherapy, including quadriceps exercises and patellar taping, for knee osteoarthritis with predominant patello-femoral joint involvement: randomized controlled trial. *J Rheumatol.* 2003;30(6):1311-7.
2322. Song CY, Lin YF, Wei TC, Lin DH, Yen TY, Jan MH. Surplus value of hip adduction in leg-press exercise in patients with patellofemoral pain syndrome: a randomized controlled trial. *Phys Ther.* 2009;89(5):409-18.
2323. Visnes H, Hoksrud A, Cook J, Bahr R. No effect of eccentric training on jumper's knee in volleyball players during the competitive season: a randomized clinical trial. *Clin J Sport Med.* 2005;15(4):227-34.
2324. Avraham F, Aviv S, Ya'akobi P, et al. The efficacy of treatment of different intervention programs for patellofemoral pain syndrome--a single blinded randomized clinical trial. Pilot study. *ScientificWorldJournal.* 2007;71256-62.
2325. Bakhtiary AH, Fatemi E. Open versus closed kinetic chain exercises for patellar chondromalacia. *Br J Sports Med.* 2008;42(2):99-102; discussion
2326. Roush MB, Sevier TL, Wilson JK, et al. Anterior knee pain: a clinical comparison of rehabilitation methods. *Clin J Sport Med.* 2000;10(1):22-8.

2327. Witvrouw E, Cambier D, Danneels L, et al. The effect of exercise regimens on reflex response time of the vasti muscles in patients with anterior knee pain: a prospective randomized intervention study. *Scand J Med Sci Sports*. 2003;13(4):251-8.
2328. Witvrouw E, Danneels L, Van Tiggelen D, Willems TM, Cambier D. Open versus closed kinetic chain exercises in patellofemoral pain: a 5-year prospective randomized study. *Am J Sports Med*. 2004;32(5):1122-30.
2329. Witvrouw E, Lysens R, Bellemans J, Peers K, Vanderstraeten G. Open versus closed kinetic chain exercises for patellofemoral pain. A prospective, randomized study. *Am J Sports Med*. 2000;28(5):687-94.
2330. Young MA, Cook JL, Purdam CR, Kiss ZS, Alfredson H. Eccentric decline squat protocol offers superior results at 12 months compared with traditional eccentric protocol for patellar tendinopathy in volleyball players. *Br J Sports Med*. 2005;39(2):102-5.
2331. Jonsson P, Alfredson H. Superior results with eccentric compared to concentric quadriceps training in patients with jumper's knee: a prospective randomised study. *Br J Sports Med*. 2005;39(11):847-50.
2332. Crossley K, Bennell K, Green S, McConnell J. A systematic review of physical interventions for patellofemoral pain syndrome. *Clin J Sport Med*. 2001;11(2):103-10.
2333. van Linschoten R, van Middelkoop M, Berger MY, et al. Supervised exercise therapy versus usual care for patellofemoral pain syndrome: an open label randomised controlled trial. *Bmj*. 2009;339b4074.
2334. van Linschoten R, van Middelkoop M, Berger MY, et al. The PEX study – Exercise therapy for patellofemoral pain syndrome: design of a randomized clinical trial in general practice and sports medicine [ISRCTN83938749]. *BMC Musculoskeletal Disorders*. 2006;7(31).
2335. Syme G, Rowe P, Martin D, Daly G. Disability in patients with chronic patellofemoral pain syndrome: a randomised controlled trial of VMO selective training versus general quadriceps strengthening. *Man Ther*. 2009;14(3):252-63.
2336. Lun VM, Wiley JP, Meeuwisse WH, Yanagawa TL. Effectiveness of patellar bracing for treatment of patellofemoral pain syndrome. *Clin J Sport Med*. 2005;15(4):235-40.
2337. Cowan SM, Bennell KL, Crossley KM, Hodges PW, McConnell J. Physical therapy alters recruitment of the vasti in patellofemoral pain syndrome. *Med Sci Sports Exerc*. 2002;34(12):1879-85.
2338. Colon VF, Mangine R, McKnight C, Kues J. The pogo stick in rehabilitating patients with patellofemoral chondrosis. *J Rehabil*. 1988;54(1):73-7.
2339. Thomee R. A comprehensive treatment approach for patellofemoral pain syndrome in young women. *Phys Ther*. 1997;77(12):1690-703.
2340. Callaghan MJ, Selfe J, McHenry A, Oldham JA. Effects of patellar taping on knee joint proprioception in patients with patellofemoral pain syndrome. *Man Ther*. 2008;13(3):192-9.
2341. Crossley K, Cowan SM, Bennell KL, McConnell J. Patellar taping: is clinical success supported by scientific evidence? *Man Ther*. 2000;5(3):142-50.
2342. Warden SJ, Hinman RS, Watson MA, Jr., Avin KG, Bialocerowski AE, Crossley KM. Patellar taping and bracing for the treatment of chronic knee pain: a systematic review and meta-analysis. *Arthritis Rheum*. 2008;59(1):73-83.
2343. Hinman RS, Crossley KM, McConnell J, Bennell KL. Efficacy of knee tape in the management of osteoarthritis of the knee: blinded randomised controlled trial. *Bmj*. 2003;327(7407):135.
2344. Clark DI, Downing N, Mitchell J, Coulson L, Syzpyt EP, Doherty M. Physiotherapy for anterior knee pain: a randomised controlled trial. *Ann Rheum Dis*. 2000;59(9):700-4.
2345. Kowall MG, Kolk G, Nuber GW, Cassisi JE, Stern SH. Patellar taping in the treatment of patellofemoral pain. A prospective randomized study. *Am J Sports Med*. 1996;24(1):61-6.
2346. Whittingham M, Palmer S, Macmillan F. Effects of taping on pain and function in patellofemoral pain syndrome: a randomized controlled trial. *J Orthop Sports Phys Ther*. 2004;34(9):504-10.
2347. Cowan SM, Bennell KL, Hodges PW. Therapeutic patellar taping changes the timing of vasti muscle activation in people with patellofemoral pain syndrome. *Clin J Sport Med*. 2002;12(6):339-47.
2348. Cushnaghan J, McCarthy C, Dieppe P. Taping the patella medially: a new treatment for osteoarthritis of the knee joint? *Bmj*. 1994;308(6931):753-5.
2349. Ryan CG, Rowe PJ. An electromyographical study to investigate the effects of patellar taping on the vastus medialis/vastus lateralis ratio in asymptomatic participants. *Physiother Theory Pract*. 2006;22(6):309-15.

2350. D'Hondt N E, Struijs PA, Kerkhoffs GM, et al. Orthotic devices for treating patellofemoral pain syndrome. *Cochrane Database Syst Rev*. 2002(2):CD002267.
2351. Wang CJ. Management of patellofemoral arthrosis in middle-aged patients. *Chang Gung Med J*. 2001;24(11):672-80.
2352. Van Tiggelen D, Witvrouw E, Roget P, Cambier D, Danneels L, Verdonk R. Effect of bracing on the prevention of anterior knee pain--a prospective randomized study. *Knee Surg Sports Traumatol Arthrosc*. 2004;12(5):434-9.
2353. Finestone A, Radin EL, Lev B, Shlamkovitch N, Wiener M, Milgrom C. Treatment of overuse patellofemoral pain. Prospective randomized controlled clinical trial in a military setting. *Clin Orthop Relat Res*. 1993(293):208-10.
2354. Miller MD, Hinkin DT, Wisnowski JW. The efficacy of orthotics for anterior knee pain in military trainees. A preliminary report. *Am J Knee Surg*. 1997;10(1):10-3.
2355. Timm KE. Randomized controlled trial of Protonics on patellar pain, position, and function. *Med Sci Sports Exerc*. 1998;30(5):665-70.
2356. Bily W, Trimmel L, Modlin M, Kaider A, Kern H. Training program and additional electric muscle stimulation for patellofemoral pain syndrome: a pilot study. *Arch Phys Med Rehabil*. 2008;89(7):1230-6.
2357. Suter E, McMorland G, Herzog W, Bray R. Decrease in quadriceps inhibition after sacroiliac joint manipulation in patients with anterior knee pain. *J Manipulative Physiol Ther*. 1999;22(3):149-53.
2358. Jensen R, Gothesen O, Liseth K, Baerheim A. Acupuncture treatment of patellofemoral pain syndrome. *J Altern Complement Med*. 1999;5(6):521-7.
2359. Yip SL, Ng GY. Biofeedback supplementation to physiotherapy exercise programme for rehabilitation of patellofemoral pain syndrome: a randomized controlled pilot study. *Clin Rehabil*. 2006;20(12):1050-7.
2360. Dursun N, Dursun E, Kilic Z. Electromyographic biofeedback-controlled exercise versus conservative care for patellofemoral pain syndrome. *Arch Phys Med Rehabil*. 2001;82(12):1692-5.
2361. Ng GY, Zhang AQ, Li CK. Biofeedback exercise improved the EMG activity ratio of the medial and lateral vasti muscles in subjects with patellofemoral pain syndrome. *J Electromyogr Kinesiol*. 2008;18(1):128-33.
2362. Capasso G, Testa V, Maffulli, Bifulco G. Aprotinin, corticosteroids and normosaline in the management of patellar tendinopathy in athletes: a prospective randomized study. *Sports Exerc Injury*. 1997;3:111-5.
2363. Edwards SG, Calandruccio JH. Autologous blood injections for refractory lateral epicondylitis. *J Hand Surg Am*. 2003;28(2):272-8.
2364. Mishra A, Pavelko T. Treatment of chronic elbow tendinosis with buffered platelet-rich plasma. *Am J Sports Med*. 2006;34(11):1774-8.
2365. Sanchez M, Anitua E, Azofra J, Andia I, Padilla S, Mujika I. Comparison of surgically repaired Achilles tendon tears using platelet-rich fibrin matrices. *Am J Sports Med*. 2007;35:245-51.
2366. Sanchez M, Anitua E, Orive G, Mujika I, Andia I. Platelet-rich therapies in the treatment of orthopaedic sport injuries. *Sports Med*. 2009;39(5):345-54.
2367. Hall MP, Band PA, Meislin RJ, Jazrawi LM, Cardone DA. Platelet-rich plasma: current concepts and application in sports medicine. *J Am Acad Orthop Surg*. 2009;17(10):602-8.
2368. Foster TE, Puskas BL, Mandelbaum BR, Gerhardt MB, Rodeo SA. Platelet-rich plasma: from basic science to clinical applications. *Am J Sports Med*. 2009;37(11):2259-72.
2369. Chang KV, Hung CY, Aliwarga F, Wang TG, Han DS, Chen WS. Comparative effectiveness of platelet-rich plasma injections for treating knee joint cartilage degenerative pathology: a systematic review and meta-analysis. *Arch Phys Med Rehabil*. 2014;95(3):562-75.
2370. Dold AP, Zywiell MG, Taylor DW, Dwyer T, Theodoropoulos J. Platelet-rich plasma in the management of articular cartilage pathology: a systematic review. *Clin J Sport Med*. 2014;24(1):31-43.
2371. Khoshbin A, Leroux T, Wasserstein D, et al. The efficacy of platelet-rich plasma in the treatment of symptomatic knee osteoarthritis: a systematic review with quantitative synthesis. *Arthroscopy*. 2013;29(12):2037-48.
2372. Dragoo JL, Wasterlain AS, Braun HJ, Nead KT. Platelet-rich plasma as a treatment for patellar tendinopathy: a double-blind, randomized controlled trial. *Am J Sports Med*. 2014;42(3):610-8.
2373. Smith J, Sellon JL. Comparing PRP injections with ESWT for athletes with chronic patellar tendinopathy. *Clin J Sport Med*. 2014;24(1):88-9.

2374. Vetrano M, Castorina A, Vulpiani MC, Baldini R, Pavan A, Ferretti A. Platelet-rich plasma versus focused shock waves in the treatment of jumper's knee in athletes. *Am J Sports Med.* 2013;41(4):795-803.
2375. Clarke AW, Alyas F, Morris T, Robertson CJ, Bell J, Connell DA. Skin-derived tenocyte-like cells for the treatment of patellar tendinopathy. *Am J Sports Med.* 2011;39(3):614-23.
2376. de Almeida A, Demange M, Sobrado M, Rodrigues M, Pedrinelli A, Hernandez A. Patellar tendon healing with platelet-rich plasma: a prospective randomized controlled trial. *Am J Sports Med.* 2012;40(6):1282-8.
2377. Hoksrud A, Ohberg L, Alfredson H, Bahr R. Ultrasound-guided sclerosis of neovessels in painful chronic patellar tendinopathy: a randomized controlled trial. *Am J Sports Med.* 2006;34(11):1738-46.
2378. Kannus P, Natri A, Niittymaki S, Jarvinen M. Effect of intraarticular glycosaminoglycan polysulfate treatment on patellofemoral pain syndrome. A prospective, randomized double-blind trial comparing glycosaminoglycan polysulfate with placebo and quadriceps muscle exercises. *Arthritis Rheum.* 1992;35(9):1053-61.
2379. McShane JM, Shah VN, Nazarian LN. Sonographically guided percutaneous needle tenotomy for treatment of common extensor tendinosis in the elbow: is a corticosteroid necessary? *J Ultrasound Med.* 2008;27(8):1137-44.
2380. Harniman E, Carette S, Kennedy C, Beaton D. Extracorporeal shock wave therapy for calcific and noncalcific tendonitis of the rotator cuff: a systematic review. *J Hand Ther.* 2004;17(2):132-51.
2381. Loew M, Daecke W, Kusnierczak D, Rahmzadeh M, Ewerbeck V. Shock-wave therapy is effective for chronic calcifying tendinitis of the shoulder. *J Bone Joint Surg Br.* 1999;81(5):863-7.
2382. Mouzopoulos G, Stamatakos M, Mouzopoulos D, Tzurbakis M. Extracorporeal shock wave treatment for shoulder calcific tendonitis: a systematic review. *Skeletal Radiol.* 2007;36(9):803-11.
2383. Rompe JD, Krischek O, Eysel P, Hopf C, Jage J. [Results of extracorporeal shock-wave application in lateral elbow tendopathy]. *Schmerz.* 1998;12(2):105-11.
2384. Rompe JD, Zoellner J, Nafe B. Shock wave therapy versus conventional surgery in the treatment of calcifying tendinitis of the shoulder. *Clin Orthop Relat Res.* 2001(387):72-82.
2385. Sems A, Dimeff R, Iannotti JP. Extracorporeal shock wave therapy in the treatment of chronic tendinopathies. *J Am Acad Orthop Surg.* 2006;14(4):195-204.
2386. Wang CJ, Ko JY, Chan YS, Weng LH, Hsu SL. Extracorporeal shockwave for chronic patellar tendinopathy. *Am J Sports Med.* 2007;35(6):972-8.
2387. Ceder LC, Larson RL. Z-plasty lateral retinacular release for the treatment of patellar compression syndrome. *Clin Orthop Relat Res.* 1979(144):110-3.
2388. Ficat P. [Disorders of the patellar gliding balance]. *Chir Narzadow Ruchu Ortop Pol.* 1977;42(2):169-76.
2389. Fu FH, Maday MG. Arthroscopic lateral release and the lateral patellar compression syndrome. *Orthop Clin North Am.* 1992;23(4):601-12.
2390. Fulkerson J, Shea K. Current concepts review: Disorders of patellofemoral alignment. *J Bone Joint Surg Am.* 1990;72A1424-9.
2391. Fulkerson JP. Patellofemoral Pain Disorders: Evaluation and Management. *J Am Acad Orthop Surg.* 1994;2(2):124-32.
2392. Fulkerson JP, Becker GJ, Meaney JA, Miranda M, Folcik MA. Anteromedial tibial tubercle transfer without bone graft. *Am J Sports Med.* 1990;18(5):490-6; discussion 6-7.
2393. Henry JE, Pflum FA, Jr. Arthroscopic proximal patella realignment and stabilization. *Arthroscopy.* 1995;11(4):424-5.
2394. Hughston JC, Walsh WM. Proximal and distal reconstruction of the extensor mechanism for patellar subluxation *Clin Orthopaed Related Res.* 1979;144:36-42.
2395. Kettelkamp DB. Management of patellar malalignment. *J Bone Joint Surg Am.* 1981;63(8):1344-8.
2396. Larson RL, Cabaud HE, Slocum DB, James SL, Keenan T, Hutchinson T. The patellar compression syndrome: surgical treatment by lateral retinacular release. *Clin Orthop Relat Res.* 1978(134):158-67.
2397. McGinty JB, McCarthy JC. Endoscopic lateral retinacular release: a preliminary report. *Clin Orthop Relat Res.* 1981(158):120-5.
2398. Dehaven KE, Dolan WA, Mayer PJ. Chondromalacia patellae in athletes. Clinical presentation and conservative management. *Am J Sports Med.* 1979;7(1):5-11.
2399. Betz R, Magill 3rd J, Lonergan R. The percutaneous lateral retinacular release. *Am J Sports Med.* 1987;15:77-82.

2400. Chen SC, Ramanathan EB. The treatment of patellar instability by lateral release. *J Bone Joint Surg Br.* 1984;66(3):344-8.
2401. Dandy DJ, Desai SS. The results of arthroscopic lateral release of the extensor mechanism for recurrent dislocation of the patella after 8 years. *Arthroscopy.* 1994;10(5):540-5.
2402. Metcalf RW. An arthroscopic method for lateral release of subluxating or dislocating patella. *Clin Orthop Relat Res.* 1982(167):9-18.
2403. Sherman OH, Fox JM, Sperling H, et al. Patellar instability: treatment by arthroscopic electrosurgical lateral release. *Arthroscopy.* 1987;3(3):152-60.
2404. Woods GW, Elkousy HA, O'Connor DP. Arthroscopic release of the vastus lateralis tendon for recurrent patellar dislocation. *Am J Sports Med.* 2006;34(5):824-31.
2405. Abraham E, Washington E, Huang TL. Insall proximal realignment for disorders of the patella. *Clin Orthop Relat Res.* 1989(248):61-5.
2406. Brief LP. Lateral patellar instability: treatment with a combined open-arthroscopic approach. *Arthroscopy.* 1993;9(6):617-23.
2407. Myers P, Williams A, Dodds R, Bulow J. The three-in-one proximal and distal soft tissue patellar realignment procedure. Results, and its place in the management of patellofemoral instability. *Am J Sports Med.* 1999;27(5):575-9.
2408. Ricchetti ET, Mehta S, Sennett BJ, Huffman GR. Comparison of lateral release versus lateral release with medial soft-tissue realignment for the treatment of recurrent patellar instability: a systematic review. *Arthroscopy.* 2007;23(5):463-8.
2409. Scuderi G, Cuomo F, Scott WN. Lateral release and proximal realignment for patellar subluxation and dislocation. A long-term follow-up. *J Bone Joint Surg Am.* 1988;70(6):856-61.
2410. Insall JN. Patella pain syndromes and chondromalacia patellae. *Instr Course Lect.* 1981;30:342-56.
2411. Zeichen J, Lobenhoffer P, Gerich T, Tscherne H, Bosch U. Medium-term results of the operative treatment of recurrent patellar dislocation by Insall proximal realignment. *Knee Surg Sports Traumatol Arthrosc.* 1999;7(3):173-6.
2412. Fernandez-Fairen M, Querales V, Jakowlew A, Murcia A, Ballester J. Tantalum is a good bone graft substitute in tibial tubercle advancement. *Clin Orthop Relat Res.* 2010;468(5):1284-95.
2413. O'Neill DB. Open lateral retinacular lengthening compared with arthroscopic release. A prospective, randomized outcome study. *J Bone Joint Surg Am.* 1997;79(12):1759-69.
2414. Camanho GL, Viegas Ade C, Bitar AC, Demange MK, Hernandez AJ. Conservative versus surgical treatment for repair of the medial patellofemoral ligament in acute dislocations of the patella. *Arthroscopy.* 2009;25(6):620-5.
2415. Harris JS, Sinnott PL, Holland JP, et al. Methodology to update the practice recommendations in the American College of Occupational and Environmental Medicine's Occupational Medicine Practice Guidelines, second edition. *J Occup Environ Med.* 2008;50(3):282-95.
2416. Railhac, J.J., et al., Effect of 12 months treatment with chondroitin sulfate on cartilage volume in knee osteoarthritis patients: a randomized, double-blind, placebo-controlled pilot study using MRI. *Clin Rheumatol*, 2012. 31(9): p. 1347-57.
2417. Kwok, C.K., et al., Effect of oral glucosamine on joint structure in individuals with chronic knee pain: a randomized, placebo-controlled clinical trial. *Arthritis Rheumatol*, 2014. 66(4): p. 930-9.
2418. Durmus, D., et al., Assessment of the effect of glucosamine sulfate and exercise on knee cartilage using magnetic resonance imaging in patients with knee osteoarthritis: a randomized controlled clinical trial. *J Back Musculoskelet Rehabil*, 2012. 25(4): p. 275-84.
2419. Fransen, M., et al., *Glucosamine and chondroitin for knee osteoarthritis: a double-blind randomised placebo-controlled clinical trial evaluating single and combination regimens.* *Ann Rheum Dis*, 2015. 74(5): p. 851-8.
2420. Hochberg, M.C., et al., *Combined chondroitin sulfate and glucosamine for painful knee osteoarthritis: a multicentre, randomised, double-blind, non-inferiority trial versus celecoxib.* *Ann Rheum Dis*, 2016. 75(1): p. 37-44.
2421. Joshi Jubert, N., et al., *Platelet-rich plasma injections for advanced knee osteoarthritis: a prospective, randomized, double-blinded clinical trial.* *Orthopaedic journal of sports medicine*, 2017. 5(2): p. 2325967116689386.

2422. Uslu Guvend, E., et al., Comparison of efficiency between corticosteroid and platelet rich plasma injection therapies in patients with knee osteoarthritis. *Arch Rheumatol*. 2018, **33**(3): p. 273–281.
2423. Patel, S., et al., Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial. *Am J Sports Med*. 2013 Feb;41(2):356-64.
2424. Smith, P.A., Intra-articular autologous conditioned plasma injections provide safe and efficacious treatment for knee osteoarthritis: an FDA-sanctioned, randomized, double-blind, placebo-controlled clinical trial. *The American journal of sports medicine*, 2016. 44(4): p. 884-891.
2425. Yu, W., et al., Clinical therapy of hyaluronic acid combined with platelet-rich plasma for the treatment of knee osteoarthritis. *Experimental and therapeutic medicine*, 2018. 16(3): p. 2119-2125.
2426. Gobbi, A., D. Lad, and G. Karnatzikos, The effects of repeated intra-articular PRP injections on clinical outcomes of early osteoarthritis of the knee. *Knee Surgery, Sports Traumatology, Arthroscopy*, 2015. 23(8): p. 2170-2177.
2427. Buendía-López, D., M. Medina-Quirós, and M.Á.F.-V. Marín, Clinical and radiographic comparison of a single LP-PRP injection, a single hyaluronic acid injection and daily NSAID administration with a 52-week follow-up: a randomized controlled trial. *Journal of Orthopaedics and Traumatology*, 2018. 19(1): p. 3.
2428. Lisi, C., et al., Treatment of knee osteoarthritis: platelet-derived growth factors vs. hyaluronic acid. A randomized controlled trial. *Clin Rehabil*, 2018. 32(3): p. 330-339.
2429. Baltzer, A.W., et al., Autologous conditioned serum (Orthokine) is an effective treatment for knee osteoarthritis. *Osteoarthritis Cartilage*, 2009. 17(2): p. 152-60.
2430. Lin, K.-Y., et al., Intra-articular Injection of Platelet-Rich Plasma Is Superior to Hyaluronic Acid or Saline Solution in the Treatment of Mild to Moderate Knee Osteoarthritis: A Randomized, Double-Blind, Triple-Parallel, Placebo-Controlled Clinical Trial. *Arthroscopy: The Journal of Arthroscopic & Related Surgery*, 2019. 35(1): p. 106-117.
2431. Wang, S.Z., et al., Intra-articular, single-shot co-injection of hyaluronic acid and corticosteroids in knee osteoarthritis: A randomized controlled trial. *Experimental and therapeutic medicine*, 2018. 16(3): p. 1928-1934.
2432. Görmeli, G., et al., Multiple PRP injections are more effective than single injections and hyaluronic acid in knees with early osteoarthritis: a randomized, double-blind, placebo-controlled trial. *Knee Surgery, Sports Traumatology, Arthroscopy*, 2017. 25(3): p. 958-965.
2433. Wu, Y.-T., et al., Effects of platelet-rich plasma on pain and muscle strength in patients with knee osteoarthritis. *American journal of physical medicine & rehabilitation*, 2018. 97(4): p. 248-254.
2434. Louis, M.L., et al., Growth factors levels determine efficacy of platelets rich plasma injection in knee osteoarthritis: a randomized double blind noninferiority trial compared with viscosupplementation. *Arthroscopy: The Journal of Arthroscopic & Related Surgery*, 2018. 34(5): p. 1530-1540. e2.
2435. Aggarwal, A.K., V. Shashikanth, and N. Marwaha, Platelet-rich plasma prevents blood loss and pain and enhances early functional outcome after total knee arthroplasty: a prospective randomised controlled study. *International orthopaedics*, 2014. 38(2): p. 387-395.
2436. Duif, C., et al., Does intraoperative application of leukocyte-poor platelet-rich plasma during arthroscopy for knee degeneration affect postoperative pain, function and quality of life? A 12-month randomized controlled double-blind trial. *Archives of orthopaedic and trauma surgery*, 2015. 135(7): p. 971-977.
2437. Bastos, R., et al., Intra-articular injections of expanded mesenchymal stem cells with and without addition of platelet-rich plasma are safe and effective for knee osteoarthritis. *Knee Surgery, Sports Traumatology, Arthroscopy*, 2018. 26(11): p. 3342-3350.
2438. Vangsness, C.T., Jr., et al., Adult human mesenchymal stem cells delivered via intra-articular injection to the knee following partial medial meniscectomy: a randomized, double-blind, controlled study. *J Bone Joint Surg Am*, 2014. 96(2): p. 90-8.
2439. Bastos, R., et al., Intra-articular injections of expanded mesenchymal stem cells with and without addition of platelet-rich plasma are safe and effective for knee osteoarthritis. *Knee Surgery, Sports Traumatology, Arthroscopy*, 2018. 26(11): p. 3342-3350.
2440. Lamo-Espinosa, J.M., et al., Intra-articular injection of two different doses of autologous bone marrow mesenchymal stem cells versus hyaluronic acid in the treatment of knee osteoarthritis: multicenter randomized controlled clinical trial (phase I/II). *J Transl Med*, 2016. 14(1): p. 246.

2441. Lamo-Espinosa, J.M., et al., Intra-articular injection of two different doses of autologous bone marrow mesenchymal stem cells versus hyaluronic acid in the treatment of knee osteoarthritis: long-term follow up of a multicenter randomized controlled clinical trial (phase I/II). *Journal of translational medicine*, 2018. 16(1): p. 213.
2442. Yang, L., J. Zhang, and G. Wang, The effect of sodium hyaluronate treating knee osteoarthritis on synovial fluid interleukin -1beta and clinical treatment mechanism. *Pak J Pharm Sci*, 2015. 28(1 Suppl): p. 407-10.
2443. Giombini, A., et al., Comparison between intrarticular injection of hyaluronic acid, oxygen ozone, and the combination of both in the treatment of knee osteoarthrosis. *Journal of biological regulators and homeostatic agents*, 2016. 30(2): p. 621-625.
2444. Martin Martin, L.S., et al., A double blind randomized active-controlled clinical trial on the intra-articular use of Md-Knee versus sodium hyaluronate in patients with knee osteoarthritis ("Joint"). *BMC Musculoskelet Disord*, 2016. 17: p. 94.
2445. Montanez-Heredia, E., et al., Intra-Articular Injections of Platelet-Rich Plasma versus Hyaluronic Acid in the Treatment of Osteoarthritic Knee Pain: A Randomized Clinical Trial in the Context of the Spanish National Health Care System. *Int J Mol Sci*, 2016. 17(7).
2446. Henrotin, Y., et al., Reduction of the serum levels of a specific biomarker of cartilage degradation (Coll2-1) by hyaluronic acid (KARTILAGE® CROSS) compared to placebo in painful knee osteoarthritis patients: the EPIKART study, a pilot prospective comparative randomized double blind trial. *BMC musculoskeletal disorders*, 2017. 18(1): p. 222.
2447. Arden, N.K., et al., A randomized saline-controlled trial of NASHA hyaluronic acid for knee osteoarthritis. *Current medical research and opinion*, 2014. 30(2): p. 279-286.
2448. van der Weegen, W., et al., No difference between intra-articular injection of hyaluronic acid and placebo for mild to moderate knee osteoarthritis: a randomized, controlled, double-blind trial. *J Arthroplasty*, 2015. 30(5): p. 754-7.
2449. Petterson, S.C., et al., Improved function from progressive strengthening interventions after total knee arthroplasty: a randomized clinical trial with an imbedded prospective cohort. *Arthritis Rheum*, 2009. 61(2): p. 174-83.
2450. McAlindon, T.E., et al., Effect of Intra-articular Triamcinolone vs Saline on Knee Cartilage Volume and Pain in Patients With Knee Osteoarthritis: A Randomized Clinical Trial. *Jama*, 2017. 317(19): p. 1967-1975.
2451. Arendt-Nielsen, L., et al., Intra-articular onabotulinumtoxinA in osteoarthritis knee pain: effect on human mechanistic pain biomarkers and clinical pain. *Scandinavian journal of rheumatology*, 2017. 46(4): p. 303-316.
2452. Hsieh, L.F., et al., Effects of Botulinum Toxin Landmark-Guided Intra-articular Injection in Subjects With Knee Osteoarthritis. *Pm r*, 2016. 8(12): p. 1127-1135.
2453. Bao, X., et al., Effect of Therapeutic Exercise on Knee Osteoarthritis After Intra-Articular Injection of Botulinum Toxin Type A, Hyaluronate or Saline: A Randomized Controlled Trial. *Journal of rehabilitation medicine*, 2018. 50(6): p. 534-541.
2454. Boon, A.J., et al., Efficacy of intra-articular botulinum toxin type A in painful knee osteoarthritis: a pilot study. *PM&R*, 2010. 2(4): p. 268-276.
2455. Singh, J.A., M.L. Mahowald, and S. Noorbaloochi, Intraarticular botulinum toxin A for refractory painful total knee arthroplasty: a randomized controlled trial. *J Rheumatol*, 2010. 37(11): p. 2377-86.
2456. Singer, B.J., et al., Treatment of refractory anterior knee pain using botulinum toxin type A (Dysport) injection to the distal vastus lateralis muscle: a randomised placebo controlled crossover trial. *Br J Sports Med*, 2011. 45(8): p. 640-5.
2457. Vermesan, D., et al., Arthroscopic debridement compared to intra-articular steroids in treating degenerative medial meniscal tears. *Eur Rev Med Pharmacol Sci*. 2013 Dec;17(23):3192-6.
2458. Malliaropoulos, N., et al., Low-level laser therapy in meniscal pathology: a double-blinded placebo-controlled trial. *Lasers in medical science*, 2013. 28(4): p. 1183-1188.2459.
2459. Hudson, R., et al., Innovative treatment of clinically diagnosed meniscal tears: a randomized sham-controlled trial of the Mulligan concept 'squeeze' technique. *Journal of Manual & Manipulative Therapy*, 2018: p. 1-10.
2460. Kaminski, R., et al., Short-Term Outcomes of Percutaneous Trephination with a Platelet Rich Plasma Intrameniscal Injection for the Repair of Degenerative Meniscal Lesions. A Prospective, Randomized,

- Double-Blind, Parallel-Group, Placebo-Controlled Study. *International journal of molecular sciences*, 2019. 20(4): p. 856.
2461. Sihvonen, R., et al., Arthroscopic partial meniscectomy versus placebo surgery for a degenerative meniscus tear: a 2-year follow-up of the randomised controlled trial. *Annals of the rheumatic diseases*, 2018. 77(2): p. 188-195.
2462. Yim, J.H., A comparative study of meniscectomy and nonoperative treatment for degenerative horizontal tears of the medial meniscus. *Am J Sports Med*. 2013 Jul;41(7):1565-70.
2463. Resteghini P, K.T., Mughal S, Sivardeen Z, Double-Blind Randomized Controlled Trial: Injection of Autologous Blood in the Treatment of Chronic Patella Tendinopathy-A Pilot Study. *Clin J Sport Med*, 2016. 26(1): p. 17-23.
2464. Kaux JF, B.O., Croisier JL, Forthomme B, Le Goff C, Crielaard JM, One-year follow-up of platelet-rich plasma infiltration to treat chronic proximal patellar tendinopathies. *Acta Orthop Belg*, 2015. 81(2): p. 251-256.
2465. Zayni R, T.M., Fayard JM, Hager JP, Carrillon Y, Clechet J, Gadea F, Archbold P, Sonnery Cottet B, Platelet-rich plasma as a treatment for chronic patellar tendinopathy: comparison of a single versus two consecutive injections. *Muscles Ligaments Tendons J*, 2015. 5(2): p. 92-98.
2466. Zwerver, J., et al., No effect of extracorporeal shockwave therapy on patellar tendinopathy in jumping athletes during the competitive season: a randomized clinical trial. *Am J Sports Med*. 2011 Jun;39(6):1191-9.
2467. Thijs, K.M., et al., Effectiveness of Shockwave Treatment Combined With Eccentric Training for Patellar Tendinopathy: A Double-Blinded Randomized Study. *Clin J Sport Med*. 2017 Mar;27(2):89-96.
2468. van der Worp, H., ESWT for tendinopathy: technology and clinical implications. *Knee Surg Sports Traumatol Arthrosc*. 2013 Jun;21(6):1451-8.
2469. Bagnato, G.L., et al., Pulsed electromagnetic fields in knee osteoarthritis: a double blind, placebo-controlled, randomized clinical trial. *Rheumatology (Oxford)*. 2016 Apr;55(4):755-62.
2470. Rahimzadeh, P., et al., The effects of injecting intra-articular platelet-rich plasma or prolotherapy on pain score and function in knee osteoarthritis. *Clin Interv Aging*. 2018 Jan 4;13:73-79.
2471. Frobell, R.B., et al. Treatment for acute anterior cruciate ligament tear: five year outcome of randomised trial. *BMJ*. 2013 Jan 24;346:f232.
2472. Popma, J.W., et al. Comparison of 2 Dosages of Intraarticular Triamcinolone for the Treatment of Knee Arthritis: Results of a 12-week Randomized Controlled Clinical Trial. *J Rheumatol*. 2015 Oct;42(10):1865-8.
2473. Conaghan, P.G., et al. Brief Report: A Phase IIb Trial of a Novel Extended-Release Microsphere Formulation of Triamcinolone Acetonide for Intraarticular Injection in Knee Osteoarthritis. *Arthritis Rheumatol*. 2018 Feb;70(2):204-211.
2474. Bodick, N., et al. An intra-articular, extended-release formulation of triamcinolone acetonide prolongs and amplifies analgesic effect in patients with osteoarthritis of the knee: a randomized clinical trial. *J Bone Joint Surg Am*. 2015 Jun 3;97(11):877-88.
2475. Bradley, J.D., et al. Tidal irrigation as treatment for knee osteoarthritis: a sham-controlled, randomized, double-blinded evaluation. *Arthritis Rheum*. 2002 Jan;46(1):100-8.