Osteoarthritis of the Knee: Selected Treatments

Number: 0673

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.

Aetna considers arthroscopic debridement medically necessary for persons presenting with mild-to-moderate (Outerbridge classification I and II) osteoarthritis with knee pain plus mechanical symptoms due to loose bodies and/or meniscal tears.

Aetna considers arthroscopic partial meniscectomy medically necessary for traumatic meniscal tears. Aetna considers arthroscopic partial meniscectomy experimental and investigational for degenerative meniscal tears.

Aetna considers the following interventions experimental and investigational because the effectiveness of these approaches has not been established:

- Arthroscopic debridement for persons with osteoarthritis presenting with knee pain only or with severe osteoarthritis (Outerbridge classification III or IV)
- Arthroscopic lavage
- Balneotherapy

Policy History

Last Review
06/17/2020

Effective: 09/26/2003

Next Review: 07/10/2020

Review History

Definitions

Additional Information

Clinical Policy Bulletin
Notes
• Bone marrow aspirate concentrate
• Combination of high tibial osteotomy and autologous bone marrow derived cell implantation
• Cryotherapy (e.g., llovera cryoneurolysis)
• Extracorporeal shock wave therapy
• Intra-articular injections of autologous conditioned serum
• Patellar denervation
• Percutaneous autologous fat injections
• Percutaneous calcium phosphate injections
• Stem cell therapy (e.g., intra-articular injections of adipose tissue-derived stem cells, bone marrow-derived mononuclear cell, infra-patellar fat pad-derived mesenchymal stem cell or pre-cartilaginous stem cells)

Aetna considers extended-release triamcinolone acetonide injectable suspension (Zilretta) not medically necessary because it has not demonstrated a significant improvement in osteoarthritis pain compared with the immediate-release formulation of triamcinolone acetonide.

Notes:

*The most commonly used instrument to classify the severity of osteoarthritis in study patients was the Outerbridge scale. The Outerbridge scale classifies the articular degeneration of the knee by compartment in four grades. Grade I refers to softening or blistering of the articular cartilage. Grade II describes fragmentation or fissuring in an area less than 1 cm, while those with an area greater than 1 cm are considered Grade III. Finally, Grade IV refers to cartilage erosion down to the bone.

See also

CPB 0009 - Orthopedic Casts, Braces and Splints
(../1_99/0009.html)
, CPB 0179 - Viscosupplementation (../100_199/0179.html),

Notes:
Background

Osteoarthritis (OA) is a non-inflammatory degenerative joint disease that occurs mainly in middle-aged and older individuals. Osteoarthritis of the knee occurs when the elastoviscous properties of the synovial fluid in the knee joint becomes diminished, resulting in less protection and shock absorption. Osteoarthritis of the knee is often characterized by pain that frequently requires medical and/or surgical intervention. In general, the pain associated with OA develops gradually, although sudden onset is also possible. The joint may become stiff and swollen, making it difficult to bend or straighten the knee. Pain and swelling are worse in the morning or after a period of inactivity. Pain may also increase after activities such as walking, stair climbing or kneeling. The pain may often cause a feeling of weakness in the knee,
resulting in a "locking" or "buckling". Many arthritic patients note that changes in the weather also affect the degree of pain from arthritis.

Based on the criteria of the American College of Rheumatology (Altman et al, 1986), a diagnosis of OA of the knee can be rendered if patients experience knee pain and at least 5 of the following:

- Bony enlargement
- Bony tenderness
- Crepitus (noisy, grating sound) on active motion
- Erythrocyte sedimentation rate (ESR) less than 40 mm/hr
- Less than 30 minutes of morning stiffness
- No palpable warmth of synovium
- Over 50 years of age
- Rheumatoid factor less than 1:40 titer (agglutination method)
- Synovial fluid signs.

The severity of OA is often described according to the Outerbridge scale, which classifies the articular degeneration of the knee by compartment in 4 grades: (i) Grade I refers to softening or blistering of the articular cartilage, (ii) Grade II describes fragmentation or fissuring in an area less than 1 cm, (iii) Grade III describes fragmentation or fissuring in an area greater than 1 cm, and (iv) Grade IV refers to cartilage erosion down to the bone.

Treatment of mild symptomatic OA entails patient education, non-pharmacological approaches such as exercises, lifestyle modifications, and use of supportive devices, as well as pharmacotherapies including non-opioid oral and topical analgesics. In patients who are unresponsive to this regimen, the use of non-steroidal anti-inflammatory drugs (NSAIDs) is appropriate. Intra-articular injections of steroids or viscosupplementation may be used for patients who fail
conservative management. Patients with severe symptomatic OA of the knee may require surgical intervention, e.g., arthroscopic surgery, osteotomy, abrasion arthroplasty, subchondral penetration procedures, and laser/thermal chondroplasty.

Arthroscopy involves direct visualization of the joint by a videofiberoptic device. Arthroscopic lavage and/or debridement is often recommended when medical therapy fails to reduce osteoarthritic knee pain and improve functioning. Lavage entails either large or small volume saline irrigation of the knee. Debridement covers many types of arthroscopic surgery and may include but is not limited to variable amounts of the following treatments: partial synovectomy, decompression and resection of plicae/adipose tissue, partial meniscectomy, chondroplasty, loose body removal, and/or osteophyte removal. In clinical practice, debridement is generally performed with low volume lavage or washout. The available evidence supporting the use of arthroscopic surgery for the treatment of symptomatic OA of the knee is largely retrospective and lacks validated health-related quality-of-life measures. In this regard, the reports by Baumgaertner and colleagues (1990), Ogilvie-Harris and Fitsialos (1991), Yang and Nisonson (1995), as well as Jackson and Dieterichs (2003) were case series studies, while that by Fond et al (2002) was a cohort observational study.

In contrast, findings of many randomized controlled studies indicate that arthroscopic lavage and/or debridement did not result in pain relief and improvement of functioning. Gibson et al (1992) studied the effect of arthroscopic lavage and debridement of the osteoarthritic knee. A total of 20 patients were randomly assigned to receive (i) lavage, or (ii) debridement. The primary outcome was objective evaluation of thigh muscle function in the affected quadriceps compared to that of the non-affected quadriceps before and after operation. There was some improvement in quadriceps...
isokinetic torque at 6 and 12 weeks after joint lavage but not after debridement. However, neither method significantly relieved patients' symptoms.

In a multi-center, randomized, controlled study, Ravaud et al (1999) assessed the effectiveness of joint lavage and intra-articular steroid injection, alone and in combination, in the treatment of patients with symptomatic knee OA. A total of 98 patients were randomly assigned to 4 treatment groups: (i) intra-articular placebo (1.5 ml of 0.9 % normal saline), (ii) intra-articular corticosteroids (3.75 mg of cortivazol in 1.5 ml), (iii) joint lavage and intra-articular placebo, and (iv) joint lavage and intra-articular corticosteroid. Outcome measures including severity of pain (100-mm visual analog scale [VAS]), global status (100-mm VAS), and Lequesne's functional index were evaluated at baseline, week 1, week 4, week 12, and week 24. There was no interaction between steroid injection and joint lavage. Patients who had undergone joint lavage had significantly improved pain VAS scores at week 24 (p < 0.020). In contrast, corticosteroid injection had no long-term effect (p < 0.313); corticosteroid injection was associated with a decrease in pain only at week 1 (p < 0.003) and week 4 (p < 0.020). However, there was no significant improvement in function at week 4 regardless of the assigned treatment as indexed by Lequesne's functional index.

In a multi-center, randomized, controlled study, Kalunian and associates (2000) examined if visually-guided arthroscopic irrigation is an effective therapeutic intervention in patients with early knee OA. A total of 90 patients were randomly assigned in a double-blind fashion to receive (i) arthroscopic irrigation with 3,000 ml of saline (treatment group), or (ii) the minimal amount of irrigation (250 ml) needed to perform arthroscopy (placebo group). The primary outcome variable was aggregate Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score. The study did not demonstrate an effect of irrigation on arthritis severity as
measured by aggregate WOMAC scores, the primary outcome variable. The mean change in aggregate WOMAC score at 12 months was 15.5 (95% confidence interval [CI]: 7.7 to 23.4) for the full irrigation group compared to 8.9 (95% CI: 4.9 to 13.0) for the minimal irrigation group (p < 0.10).

In a prospective, randomized, placebo-controlled trial to determine whether a placebo effect might play a role in arthroscopic treatment of OA of the knee (Moseley et al, 1996), 5 subjects were randomized to a placebo arthroscopy group, 3 subjects were randomized to an arthroscopic lavage group, and 2 subjects were randomized to a standard arthroscopic debridement group. Patients who received the placebo surgery reported decreased frequency, intensity, and duration of knee pain. They also thought that the procedure was worthwhile and would recommend it to family and friends. Thus, there may be a significant placebo effect for arthroscopic treatment of osteoarthritis of the knee. The authors concluded that a larger study is needed to evaluate fully the effectiveness of an arthroscopic procedure for this condition. Recent evidence published in the New England Journal of Medicine (Moseley et al, 2002) confirms this earlier finding that arthroscopic lavage and/or debridement in patients with OA of the knee without other specific indications is no better than placebo surgery.

Moseley and colleagues (2002) carried out a randomized, placebo-controlled study to examine the effectiveness of arthroscopy for OA of the knee. A total of 180 patients with knee OA were randomly assigned to receive (i) arthroscopic debridement, (ii) arthroscopic lavage, or (iii) placebo surgery. Patients in the placebo group received skin incisions and underwent a simulated debridement without insertion of the arthroscope. Patients and assessors of outcome were blinded to the treatment-group assignment. Outcomes were assessed at multiple points over a 24-month period with the use of 5 self-reported scores — 3 on scales for pain and 2 on
scales for function -- and 1 objective test of walking and stair climbing. A total of 165 patients completed the trial. At no point did either of the intervention groups report less pain or better function than the placebo group. For example, mean (+/- standard deviation [SD]) scores on the Knee-Specific Pain Scale (range of 0 to 100, with higher scores indicating more severe pain) were similar in the placebo, lavage, and debridement groups: 48.9 +/- 21.9, 54.8 +/- 19.8, and 51.7 +/- 22.4, respectively, at 1 year (p < 0.14 for the comparison between placebo and lavage; p < 0.51 for the comparison between placebo and debridement) and 51.6 +/- 23.7, 53.7 +/- 23.7, and 51.4 +/- 23.2, respectively, at 2 years (p < 0.64 and p < 0.96, respectively). Furthermore, the 95% CIs for the differences between the placebo group and the intervention groups exclude any clinically meaningful difference. These researchers concluded that for patients with OA of the knee, the outcomes after arthroscopic lavage or arthroscopic debridement were no better than those after a placebo procedure.

In view of the findings of Moseley and associates, advocates of arthroscopic lavage and debridement suggest that maybe these procedures are effective in subgroups of patients with knee OA including those at the early stages of OA, those with normal alignment as well as those with mechanical symptoms. However, Moseley and co-workers stated that they have performed an extensive subgroup analysis and did not find any differences to support the claim that outcomes of arthroscopic surgery for OA of the knee may be related to the severity of arthritis or alignment (Wray et al, 2002).

In a sham-controlled, randomized, double-blinded study, Bradley et al (2002) evaluated the effectiveness of tidal irrigation (TI) in comparison with a well-matched sham irrigation (SI) procedure as a treatment for OA of the knee. A total of 180 patients with knee OA were randomized to receive TI or SI, with clinical follow-up over the ensuing 12 months. The primary outcomes of interest were changes in pain and
function, as measured by the WOMAC. Patients and the nurse assessor were blinded, and success of blinding was assessed. Although the study groups were otherwise comparable, the baseline WOMAC pain and physical functioning scores were higher (worse) in the SI group. After adjustment for baseline, there were no differences between the effects of SI and TI. Blinding was successful with approximately 90% of SI and TI patients stating that they had received the TI procedure. The authors concluded that the improvement of these patients with knee OA following TI was due to a placebo effect.

Dervin and colleagues (2003) prospectively evaluated a cohort of patients (n = 126) with OA of the knee who were selected for arthroscopic debridement and determined which clinical criteria favor a sustained improvement in health-related quality of life after 2 years of follow-up. These researchers found that the prospectively evaluated quality-of-life benefit from arthroscopic debridement of the osteoarthritic knee is less than that reported in previous retrospective surveys on satisfaction. Additionally, clinical variables were only partially helpful for predicting a successful result after arthroscopic debridement.

The American College of Rheumatology (ACR) (2000) guidelines on OA of the hip and knee has concluded that “[n]o well-controlled trials of arthroscopic debridement with or without arthroplasty have been conducted, and the utility of this intervention for the treatment of knee osteoarthritis is unproven.” The ACR guidelines state that routine arthroscopic lavage with or without debridement should not be routinely recommended to patients with knee OA who have failed medical therapy. Arthroscopic removal of debris may, however, be useful for relief of pain and improvement in joint function in patients with mechanical symptoms due to loose bodies and meniscal tears. However, further studies in these types of patients are needed.
An assessment of arthroscopic lavage for knee osteoarthritis conducted by the Wessex Institute for Health Research and Development (Algood, 2002) summarized the evidence on arthroscopic lavage and debridement for osteoarthritis: "We found evidence from one good quality RCT [randomized controlled trial] that arthroscopic debridement or lavage did not improve patient reported pain and function at 2 years compared with sham arthroscopy for men with osteoarthritis of the knee. Two other, weaker, RCTs found that debridement and lavage did not improve symptoms compared with non-arthroscopic lavage. Another RCT found that arthroscopic lavage with 3,000 ml saline slightly improved pain compared with arthroscopic lavage with 250 ml saline. Another RCT found that arthroscopic debridement improved pain relief compared with arthroscopic lavage in people with isolated degenerative disease on the medial femoral condyle. We found no evidence that arthroscopic debridement or lavage improves symptoms compared with non-arthroscopic treatments."

In the Patient-Oriented Evidence that Matters (POEMs) of the Journal of Family Practice, Bailey (2002) stated that arthroscopy does not provide any benefit over sham surgery in reducing pain or physical functioning of patients with knee OA. In the Interpreting Key Trials section of the Cleveland clinic Journal of Medicine, Bernstein and Quach (2003) stated that the value of arthroscopy in treating patients with arthritic joints must be proved. Furthermore, in the American College of Physicians Journal Club, Gillespie (2003) stated that the study by Moseley et al (2002) made a case for questioning the value of arthroscopic lavage and debridement in active men younger than 65 years of age with OA of the knee. In addition, the Centers for Medicare and Medicaid Services (2003) will be issuing a national non-coverage determination stating that arthroscopic lavage alone is not reasonable and necessary for patients with OA of the knee; and that arthroscopic
debridement is not reasonable and necessary for patients presenting with knee pain only or with severe OA (Outerbridge classification III or IV).

An assessment of arthroscopic lavage and debridement by the Medical Advisory Secretariat of the Ontario Ministry of Health and Long-term Care (2005) concluded: “Arthroscopic debridement of the knee has thus far only been found to be effective for medial compartmental OA. All other indications should be reviewed with a view to reducing arthroscopic debridement as an effective therapy. Arthroscopic lavage of the knee is not indicated for any stage of OA. There is very poor quality evidence on the effectiveness of debridement with partial meniscectomy in the case of meniscal tears in OA of the knee.”

A randomized study by Kirkley et al (2008) published in the New England Journal of Medicine found that arthroscopic lavage and debridement for OA of the knee provided no additional benefit to optimized physical and medical therapy. The investigators conducted a single-center, randomized, controlled trial of arthroscopic surgery in patients with moderate-to-severe OA of the knee. Patients were randomly assigned to surgical lavage and arthroscopic debridement together with optimized physical and medical therapy or to treatment with physical and medical therapy alone. The primary outcome was the total Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score at 2 years of follow-up. Secondary outcomes included the Short Form-36 (SF-36) Physical Component Summary score. Of the 92 patients assigned to surgery, 6 did not undergo surgery. Of the 86 patients assigned to control treatment, all received only physical and medical therapy. After 2 years, there were no statistically significant differences in WOMAC scores or the SF-36 Physical Component Summary scores for the surgery group as compared with the control group. Analyses of WOMAC scores at interim visits and other secondary outcomes also failed to show superiority of surgery.
An accompanying study published in the *New England Journal of Medicine* found that incidental meniscal findings on magnetic resonance imaging (MRI) of the knee are common in the general population and increase with increasing age (Englund et al, 2008). MRI of the knee is often performed in patients who have knee symptoms of unclear cause. When meniscal tears are found, it is commonly assumed that the symptoms are attributable to them. However, there is a paucity of data regarding the prevalence of meniscal damage in the general population and the association of meniscal tears with knee symptoms and with radiographical evidence of osteoarthritis. Englund et al (2008) studied persons from Framingham, Massachusetts, who were drawn from census-tract data and random-digit telephone dialing. Subjects were 50 to 90 years of age and ambulatory; selection was not made on the basis of knee or other joint problems. The investigators assessed the integrity of the menisci in the right knee on 1.5-tesla MRI scans obtained from 991 subjects (57 % of whom were women). Symptoms involving the right knee were evaluated by questionnaire. The investigators found that the prevalence of a meniscal tear or of meniscal destruction in the right knee as detected on MRI ranged from 19 % among women 50 to 59 years of age to 56 % among men 70 to 90 years of age; prevalences were not materially lower when subjects who had had previous knee surgery were excluded. Among persons with radiographical evidence of OA, the prevalence of a meniscal tear was 63 % among those with knee pain, aching, or stiffness on most days and 60 % among those without these symptoms. The corresponding prevalences among persons without radiographical evidence of OA were 32 % and 23 %. Sixty-one percent of the subjects who had meniscal tears in their knees had not had any pain, aching, or stiffness during the previous month.

An accompanying editorial by Marx (2008) in the *New England Journal of Medicine* concluded that the study by Kirkley et al (2008), combined with other evidence, indicates that OA of the knee (in the absence of a history and physical examination...
suggesting meniscal or other findings) is not an indication for arthroscopic surgery and indeed has been associated with inferior outcomes after arthroscopic knee surgery. The editorialist stated, however, that OA is not a contraindication to arthroscopic surgery, and arthroscopic surgery remains appropriate in patients with arthritis in specific situations in which OA is not believed to be the primary cause of pain.

In a systematic review of outcomes of 3 treatments for OA of the knee: (i) intra-articular viscosupplementation, (ii) oral glucosamine, chondroitin or the combination, and (iii) arthroscopic lavage or debridement, Samson et al (2007) concluded that these 3 interventions are widely used in the treatment of OA of the knee, yet the best available evidence does not clearly demonstrate clinical benefit. Uncertainty regarding clinical benefit can be resolved only by rigorous, multi-center randomized controlled trials. Furthermore, a Cochrane review on arthroscopic debridement for knee OA, Laupattarakasem et al (2008) concluded that there is "gold" level evidence that arthroscopic debridement has no benefit for undiscriminated OA (mechanical or inflammatory causes).

In a review on surgical options for patients with OA of the knee, Lützner and colleagues (2009) stated that surgical treatments for knee OA include arthroscopy, osteotomy and knee arthroplasty; determining which of these procedures is most appropriate will depend on several factors, including the location and severity of OA damage, patient characteristics and risk factors. Arthroscopic lavage and debridement do not alter disease progression, and should not be used as a routine treatment for the osteoarthritic knee.

The American Association of Orthopaedic Surgeons’ clinical practice guideline on the treatment of OA of the knee (AAOS, 2008) does not recommend performing arthroscopy with debridement or lavage. Furthermore, it does not recommend performing needle lavage. Also, a recent Agency for
Healthcare Research and Quality's (AHRQ, 2009) report summarized the evidence on the safety and effectiveness of 3 treatments for OA of the knee: (i) use of the supplements glucosamine hydrochloride, chondroitin sulfate, or combination of both; (ii) viscosupplementation; and (iii) arthroscopic lavage and debridement of the knee joint. The evidence evaluated comes mainly from comparisons of each therapeutic approach with a placebo. The AHRQ guideline concluded that glucosamine and chondroitin, viscosupplementation, as well as arthroscopic lavage with or without debridement do not lead to clinically meaningful improvement.

In a Cochrane review, Reichenbach and colleagues (2010) compared joint lavage with sham intervention, placebo or non-intervention control in terms of effects on pain, function and safety outcomes in patients with knee OAs. These investigators searched CENTRAL, MEDLINE, EMBASE, and CINAHL up to August 3, 2009, checked conference proceedings, reference lists, and contacted authors. They included studies if they were randomized or quasi-randomized trials that compared arthroscopic and non-arthroscopic joint lavage with a control intervention in patients with OA of the knee. Two independent review authors extracted data using standardised forms. They contacted investigators to obtain missing outcome information, and calculated standardized mean differences (SMDs) for pain and function, and risk ratios for safety outcomes. They combined trials using inverse-variance random-effects meta-analysis. These researchers included 7 trials with 567 patients; 3 trials examined arthroscopic joint lavage, 2 non-arthroscopic joint lavage and 2 tidal irrigation. The methodological quality and the quality of reporting was poor and these investigators identified a moderate-to-large degree of heterogeneity among the trials ($I^2 = 65\%$). They found little evidence for a benefit of joint lavage in terms of pain relief at 3 months (SMD -0.11, 95% CI: -0.42 to 0.21), corresponding to
a difference in pain scores between joint lavage and control of 0.3 cm on a 10-cm VAS. Results for improvement in function at 3 months were similar (SMD -0.10, 95 % CI: -0.30 to 0.11), corresponding to a difference in function scores between joint lavage and control of 0.2 cm on a WOMAC disability sub-scale from 0 to 10. For pain, estimates of effect sizes varied to some degree depending on the type of lavage, but this variation was likely to be explained by differences in the credibility of control interventions: trials using sham interventions to closely mimic the process of joint lavage showed a null-effect. Reporting on adverse events and drop-out rates was unsatisfactory, and they were unable to draw conclusions for these secondary outcomes. The authors concluded that joint lavage does not result in a relevant benefit for patients with knee OA in terms of pain relief or improvement of function.

Ronn et al (2011) noted that OA of the knee is common, and the chances of suffering from OA increase with age. Its treatment should be initially non-operative and requires both pharmacological and non-pharmacological treatment modalities. If conservative therapy fails, surgery should be considered. Surgical treatments for knee OA include arthroscopy, cartilage repair, osteotomy, and knee arthroplasty. Determining which of these procedures is most appropriate depends on several factors, including the location, stage of OA, co-morbidities on the one side and patients suffering on the other side. Arthroscopic lavage and debridement is often carried out, but does not alter disease progression. If OA is limited to one compartment, unicompartmental knee arthroplasty or unloading osteotomy can be considered. They are recommended in young and active patients in regard to the risks and limited durability of total knee replacement. Total arthroplasty of the knee is a common and safe method in the elderly patients with advanced knee OA.

The effectiveness of arthroscopic partial meniscectomy for torn
meniscus is unknown. Arthroscopic partial meniscectomy is performed in patients with symptomatic osteoarthritis of the knee who also have primary signs and symptoms of a torn meniscus. Guidelines from the AAOS stated: "We are unable to recommend for or against arthroscopic partial meniscectomy in patients with osteoarthritis of the knee with a torn meniscus". The AAOS identified only a single study of arthroscopic partial meniscectomy that met criteria for inclusion in their analysis. The study, by Herrlin et al (2007), compared arthroscopic partial meniscectomy followed by supervised exercise to supervised exercise alone and measured Knee injury and Osteoarthritis Outcome Score (KOOS) pain, symptoms, activities of daily life, sports/recreation, and quality of life subscales scores as outcomes. The study was downgraded from moderate- to low-strength because 40% of patients declined participation and the arthroscopic group had non-homogeneous preoperative KOOS scores. The authors reported no significant treatment benefits of meniscectomy using any of the outcomes at 8 weeks and 6 months. Since there was only one low-strength study, the AAOS recommendation was graded inconclusive.

Additional studies of arthroscopic partial meniscectomy have been published since the AAOS guideline that have found no benefit to arthroscopic partial meniscectomy for torn meniscus. Sihvonen and colleagues (2013) conducted a multi-center, randomized, double-blind, sham-controlled trial in 146 patients 35 to 65 years of age who had knee symptoms consistent with a degenerative medial meniscus tear and no knee osteoarthritis. Patients were randomly assigned to arthroscopic partial meniscectomy or sham surgery. The primary outcomes were changes in the Lysholm and Western Ontario Meniscus Evaluation Tool (WOMET) scores (each ranging from 0 to 100, with lower scores indicating more severe symptoms) and in knee pain after exercise (rated on a scale from 0 to 10, with 0 denoting no pain) at 12 months after the procedure. The investigators reported that, in the intention-to-treat analysis, there were no significant between-
group differences in the change from baseline to 12 months in any primary outcome. The mean changes (improvements) in the primary outcome measures were as follows: Lysholm score, 21.7 points in the partial-meniscectomy group as compared with 23.3 points in the sham-surgery group (between-group difference, -1.6 points; 95 % CI: -7.2 to 4.0); WOMET score, 24.6 and 27.1 points, respectively (between-group difference, -2.5 points; 95 % CI: -9.2 to 4.1); and score for knee pain after exercise, 3.1 and 3.3 points, respectively (between-group difference, -0.1; 95 % CI: -0.9 to 0.7). The investigators reported that there were no significant differences between groups in the number of patients who required subsequent knee surgery (2 in the partial-meniscectomy group and 5 in the sham-surgery group) or serious adverse events (1 and 0, respectively).

Katz et al (2013) conducted a multi-center, randomized, controlled trial involving symptomatic patients 45 years of age or older with a meniscal tear and evidence of mild-to-moderate osteoarthritis on imaging. The investigators randomly assigned 351 patients to surgery and post-operative physical therapy or to a standardized physical-therapy regimen (with the option to cross-over to surgery at the discretion of the patient and surgeon). The patients were evaluated at 6 and 12 months. The primary outcome was the difference between the groups with respect to the change in the WOMAC physical-function score (ranging from 0 to 100, with higher scores indicating more severe symptoms) 6 months after randomization. In the intention-to-treat analysis, the mean improvement in the WOMAC score after 6 months was 20.9 points (95 % CI: 17.9 to 23.9) in the surgical group and 18.5 (95 % CI: 15.6 to 21.5) in the physical-therapy group (mean difference, 2.4 points; 95 % CI: -1.8 to 6.5). At 6 months, 51 active participants in the study who were assigned to physical therapy alone (30 %) had undergone surgery, and 9 patients assigned to surgery (6 %) had not undergone surgery. The
results at 12 months were similar to those at 6 months. The frequency of adverse events did not differ significantly between the groups.

Patello-Femoral Replacement (Arthroplasty)

Lonner (2007) stated that patella-femoral arthroplasty (PFA) can be an effective intermediate treatment for the patient with isolated arthritis of the anterior compartment of the knee. In the absence of patellar mal-alignment, results were optimized when an implant with sound geometric features was used, the prosthesis was appropriately aligned, and the soft tissues were balanced. Although previous prosthesis designs resulted in a relatively high prevalence of failure because of PF mal-tracking, PF catching, and anterior knee pain (AKP), newer prosthesis designs showed promise in reducing the prevalence of PF dysfunction. Progressive tibio-femoral cartilage degeneration was another so-called failure mechanism; such progressive degeneration underscored the importance of restricting the procedure to patients who do not have tibio-femoral chondromalacia. Because long-term failure as a result of tibio-femoral degeneration may occur in approximately 25% of patients, PFA may be considered an intermediate procedure for select patients with PF arthritis.

Ackroyd et al (2007) reported the mid-term results of a new PFA for established isolated PF arthritis. These researchers reviewed the experience of 109 consecutive PF resurfacing arthroplasties in 85 patients who were followed-up for at least 5 years. The 5-year survival rate, with revision as the endpoint, was 95.8% (95% Cl: 91.8% to 99.8%). There were no cases of loosening of the prosthesis. At 5 years the median Bristol pain score improved from 15 of 40 points (interquartile range [IQR] of 5 to 20) pre-operatively, to 35 (IQR of 20 to 40), the median Melbourne score from 10 of 30 points (IQR of 6 to 15) to 25 (IQR of 20 to 29), and the median Oxford score from 18 of 48 points (IQR of 13 to 24) to 39 (IQR of 24 to 45). Successful results, judged on a Bristol pain score of at least 20
at 5 years, occurred in 80% (66) of knees. The main complication was radiological progression of arthritis, which occurred in 25 patients (28%) and emphasized the importance of the careful selection of patients. The authors concluded that these results gave increased confidence in the use of PFA. However, this study only provided mid-term results (5 years); and radiological progression of arthritis occurred in 28% of patients; long-term results are needed.

Luring et al (2011) stated that isolated OA of the PF joint occurs in 9% of patients over 40 years of age and women are more often affected. Options of treatment were varied and not sufficiently justified by the literature. These investigators performed a literature research with keywords in the field of femoro-patellar OA in the relevant databases. Studies were categorized into different treatment options and analyzed. There are almost no Level I studies comparing the different treatment options. In the literature there are indications that relief of pain can be achieved by conservative treatment, arthroscopic surgery, cartilage conserving surgery and isolated arthroplasty. The authors concluded that in view of the fact that there are almost no prospective RCTs, none of the options for treatment can be highly recommended. They stated that there is still no gold standard for the treatment of isolated patella-femoral OA.

Davies (2013) noted that unicompartmental PFAs are uncommon; however numbers are increasing and there are a variety of new prostheses available. The Femoro-Patella Vialla (FPV, Wright Medical, UK) device was the second most commonly used PF unicompartmental prosthesis in the 2012 British National Joint Register. There are however no published outcomes data for this device. In this study, a total of 52 consecutive cases were studied prospectively using Oxford Knee Score and American Knee Society (AKS) Scores pre-operatively and at follow-up to a minimum of 2 years. Overall, Oxford Knee Scores improved from 30 points pre-operatively (36.6%) to 19 points (60%) at 1-year. American
Knee Society Knee scores improved from 51 points pre-operatively to 81 points at 1-year. Functional scores improved from 42 points pre-operatively to 70 points at 1-year. Moreover, 13 (25 %) patients had an excellent outcome with pain abolished and near normal knee function; 11 (21 %) patients gained very little improvement and scored their knees similar or worse to their pre-operative state. There were no infective or thrombo-embolic complications. Seven cases have been revised to a total knee replacement (TKR) for on-going pain in 6 cases and progression of arthritis in the tibio-femoral compartments in 1 case. The patellar button was found to be very poorly fixed in all cases that were revised. The authors concluded that early results with the FPV prosthesis showed that successful outcomes can be achieved; however the results were unpredictable and a significant minority of patients had on-going symptoms that they found unacceptable. They stated that the early revision rate was high in this series.

Al-Hadithy et al (2014) stated that isolated PF joint OA affects approximately 10 % of patients aged over 40 years and treatment remains controversial. The FPV PF joint replacement has been shown to restore functional kinematics of the knee close to normal. Despite its increasing popularity in recent years, there are no studies evaluating the mid-term results with an objective scoring assessment. These investigators reported the clinical and radiological outcomes of FPV PF joint replacement in patients with isolated PF arthritis. Between 2006 and 2012, these researchers performed 53 consecutive FPV PFAs in 41 patients with isolated PF joint OA. The mean follow-up was 3 years. Mean Oxford Knee Scores improved from 19.7 to 37.7 at latest follow-up. The progression of tibio-femoral OA was seen 12 % of knees. Two knees required revision to TKR at 7 months post-operatively, which these investigators attributed to poor patient selection. There were no cases of mal-tracking patellae, and no lateral releases were performed. The authors concluded that these findings suggested the FPV PFI prosthesis provided good pain
relief and survivorship with no significant mal-tracking patellae. This was a relatively small study (n = 41 patients) with mid-term results. These findings need to be validated by well-designed studies with larger sample size and long-term follow-up.

Lustig (2014) noted that PFA remains controversial, primarily due to the high failure rates reported with early implants. Several case series have been published over the years, which described the results with various 1st- and 2nd-generation implants. These researchers summarized results published up to now and identified common themes for implants, surgical techniques, and indications. First-generation resurfacing implants had relatively high failure rates in the medium-term. Second-generation implants, with femoral cuts based on total knee arthroplasty (TKA) designs, have yielded more promising medium-term results. The surgical indications were quite specific and must be chosen carefully to minimize poor results. Short-term complications were generally related to patellar mal-tracking, while long-term complications were generally related to progression of OA in the tibio-femoral joint. Implant loosening and polyethylene wear were rare. The author concluded that recent improvements in implant design and surgical techniques have resulted in better short- and medium-term results; however, more work is needed to evaluate the long-term outcomes of modern implant designs.

King et al (2015) reported the incidence of patellar fracture after PFA and determined associated factors as well as outcomes of patients with and without this complication. A total of 77 knees in 59 patients with minimum 2-year follow-up were included. Seven (9.1%) patients experienced a patellar fracture at a mean of 34 (range of 16 to 64) months post-operatively. All were treated non-operatively. Lower body mass index (BMI; p = 0.03), change in patellar thickness (p < 0.001), amount of bone resected (p = 0.001), and larger trochlear component size (p = 0.01) were associated with a greater incidence of fracture. Fewer fractures occurred when
the post-operative patellar height exceeded the pre-operatively measured height. No statistically significant differences were found in outcome scores between groups at mean 4-year follow-up. It should be noted that a fair amount of fractures at mid-term; and it is unclear if the incidence would increase at long-term.

Dy et al (2012) concluded that patients who undergo PFA rather than TKA are more likely to experience complications and require re-operation or revision, however, subgroup analysis suggested a relation to implant design. There was no significant difference in re-operation, revision, pain, or mechanical complications between 2G-PFA and TKA. Level of Evidence = III.

Lonner et al (2013) noted that PFA has a long record of use in the treatment of isolated patellofemoral arthritis, with outcomes influenced by patient selection, surgical technique, and trochlear implant design. The trochlear components have evolved from inlay-style to onlay-style designs, which have reduced the incidence of patellar instability. Minimizing the risk of patellar instability with onlay-design PFAs has enhanced mid-term and long-term results and leaves progressive tibiofemoral arthritis as the primary failure mechanism beyond 10 to 15 years. Moreover, the authors stated that several studies have reported successful results of TKA for isolated anterior compartment arthritis, with good mid-term results in up to 90% of patients. One retrospective study compared outcomes in 45 patients undergoing PFA or TKA at mean of 2.5 years of follow-up. They found similar Knee Society and pain scores, but the PFA group had significantly higher activity scores. However, high-quality comparisons of PFA to other treatments, including TKA, for isolated patellofemoral arthritis have not been reported to-date. One ongoing RCT is currently evaluating PFA compared with TKA in this scenario and is expected to report results in 2013.
Kazarian et al (2016) reviewed the clinical and radiographic outcomes of a consecutive series of patients who underwent PFA using a modern onlay-style trochlear design and all-polyethylene patellar component. An additional goal of the study was to elucidate, for the first time, the extent to which patients were satisfied with their implant and whether expectations were met after undergoing PFA. These researchers identified a consecutive series of 70 knees (53 patients) treated with primary isolated PFA between October 2007 and May 2012. For the clinical outcomes analysis, these investigators included patients with a minimum follow-up of 2 years and available pre-operative original Knee Society scores. At an average 4.9 years of follow-up, the mean ROM and Knee Society Knee and Function scores improved significantly, and less than 4% of patients required revision arthroplasty. There was no radiographic evidence of component loosening or wear. Despite these improvements, new Knee Society scores indicated that fewer than 2/3 of patients were satisfied or had their expectations met. Dissatisfied patients and those whose expectations were not met had significantly lower Mental Health scores according to the Short Form-36 following PFA. The authors concluded that despite the clinical and radiographic success of this implant, patient satisfaction remained low, which may be partially explained by poor mental health.

The authors stated that this study had several drawbacks. These researchers did not have complete data for all patients, which may have impacted the results and skewed the data. Because the study took place before the conception, validation, and publication of the new KSS, these investigators did not have pre-operative new KSS data for their patients and were, therefore, unable to fully compare pre-operative and post-operative discretionary and functional activity levels. The authors were prospectively tracking these data as of 2012 when they began using the new KSS in their practice to further elucidate the value of PFA. An additional drawback of this study was that there was no control group with isolated
patellofemoral arthritis treated with TKA. By comparing the results of this control to satisfaction results after TKA from published studies, they could determine if dissatisfaction after surgical intervention for patellofemoral arthritis was due to the unique OA pattern of this disease or due to the PFA procedure itself, as well as whether patients with isolated patellofemoral arthritis would be any more satisfied if treated with TKA. Finally, future studies could more closely analyze post-operative function of the patellofemoral joint by using assessments of stair ascending and descending as well as patellofemoral scoring measures.

Konan and Haddad (2016) concluded that the study showed good mid-term results (mean of 7.1 years; range of 5 to 11 years) for Avon PFJ system in post-traumatic patella-femoral joint osteoarthritis (PFJOA) in a relatively young patient cohort (n = 47; average age of 57 years. The authors stated that this study had several drawbacks. This study reported a consecutive series of patients who presented to the senior author and were diagnosed with isolated PFJOA on history, examination, and radiographic findings. Patients with any evidence of tibio-femoral OA were not included in this study. There was no comparison group. However, these researchers had only 2 revisions in this cohort and no loss to follow-up in the first 5 years. It was possible that careful selection of patients had resulted in only 1 of the study patients showing progression of tibio-femoral OA or revision. This was a relatively small (n = 47) study with mid-term follow-up (7.1 years).

van der List et al (2017) noted that historically poor results of PFA were reported in the setting of isolated patellofemoral osteoarthritis (PFOA). In order to lower PFA failure rates, it is important to identify failure modes using a standardized method. In this systematic review, PFA failure modes were assessed and compared in early versus late failures and older versus recent studies. Databases of PubMed, Embase and Cochrane and annual registries were searched for studies.
reporting PFA failures. Failure modes in studies with mean follow-up of less than 5 years were classified as early failures while greater than 5 years were classified late failures. Cohorts started before 2000 were classified as older studies and started after 2000 as recent studies. A total of 39 cohort studies (10 level II and 29 level III or IV studies) and 3 registries were included with overall low quality of studies (GRADE criteria). A total of 938 PFA failures were included and were caused by OA progression (38 %), pain (16 %), aseptic loosening (14 %) and patellar mal-tracking (10 %). Pain was responsible for most early failures (31 %), while OA progression was most common in late failures (46 %). In older studies, OA progression was more commonly reported as failure mode than in more recent studies (53 % versus 39 %, p = 0.005). The authors concluded that this level IV systematic review with low quality of studies identified OA progression and pain as major failure modes. Reviewing these studies, appropriate patient selection could prevent PFA failures in select cases. Moreover, these researchers stated that future studies assessing the role of PFA in isolated PFOA are needed.

Pisanu et al (2017) noted that PFOA can be associated with anterior knee pain, stiffness, and functional impairment. Some authors reported that PFOA affects approximately 9 % of patients older than 40 years with a greater prevalence in women. Etiology of PFOA is multi-factorial and is related to the presence of abnormal stresses at the PF joint due to knee- and patient-related factors. The need for a joint preserving treatment by isolated replacement of the injured compartment of the knee led to the development of PFA. When a correct PF replacement is performed, PFA preserves physiologic tibio-femoral joint, thus allowing patients for a rapid recovery with a high satisfaction. The outcomes for PFA were quite variable with a trend toward good-to-excellent results, mainly owing to the improvement in surgical techniques, patient selection, and implant design. The development of the 2nd generation of PFA improved the outcomes, which was attributed to the
different trochlear designs. Recently, encouraging results have been provided by the association of PFA and unicompartmental knee arthroplasty (UKA). In many studies, the main cause of PFA failure is progression of tibio-femoral OA. The authors concluded that PFA has shown to be a viable option for the treatment of isolated PFOA. The ideal candidate for a PFA is a middle-aged woman with PFOA not responsive to the conservative treatment and without significant malalignment or tibio-femoral OA. Modern PFA design onlay style, strict patient selection, and improvement in surgical techniques have produced satisfactory results in the past decades in short- to mid-term follow-up, with 10-years of survivorship of almost 90%. The main cause of failure of 2nd-generation PFA is progression of tibio-femoral OA. However, the introduction of the association of PFA and UKA may reduce the need for revision to TKA due to tibio-femoral OA progression. These researchers stated that despite the good mid-term outcomes after PFA, future research is needed to evaluate the long-term results of the 2nd-generation PFA, and eventually, the efficacy of combination of PFA and UKA in comparison with TKA.

Odgaard et al (2018) stated that controversy exists over the surgical treatment for severe PFOA. These investigators compared the outcome of PFA with TKA in a blinded RCT. In the first 2 years after surgery: Does the overall gain in quality of life (QOL) differ between the implants based on the area under the curve of patient-reported outcomes (PROs) versus time? Do patients obtain a better QOL at specific points in time after PFA than after TKA? Do patients get a better range of movement (ROM) after PFA than after TKA? Does PFA result in more complications than TKA? Patients were eligible if they had debilitating symptoms and isolated patellofemoral disease. A total of 100 patients were included from 2007 to 2014 and were randomized to PFA or TKA (blinded for the 1st year; blinded to patient, therapists, primary care physicians, etc.; quasi-blinded to assessor). Patients were observed for 4 clinical follow-ups and completed 6 sets of questionnaires.
during the first 2 post-operative years. SF-36 bodily pain was the primary outcome. Other outcomes were ROM, PROs (SF-36, Oxford Knee Score [OKS], Knee injury and Osteoarthritis Outcome Score [KOOS]) as well as complications and revisions; 4 % (2 of 50) of patients died within the first 2 years in the PFA group (none in the TKA group), and 2 % (1 of 50) became ill and declined further participation after 1 year in the PFA group (none in the TKA group). The mean age at inclusion was 64 years (SD 8.9), and 77 % (77 of 100) were women. The area under the curve (AUC) up to 2 years for SF-36 bodily pain of patients undergoing PFA and those undergoing TKA was 9.2 (SD 4.3) and 6.5 (SD 4.5) months, respectively (p = 0.008). The SF-36 physical functioning, KOOS symptoms, and OKS also showed a better AUC up to 2 years for PFA compared with TKA (6.6 [SD 4.8] versus 4.2 [SD 4.3] months, p = 0.028; 5.6 [SD 4.1] versus 2.8 [SD 4.5] months, p = 0.006; 7.5 [SD 2.7] versus 5.0 [SD 3.6] months, p = 0.001; respectively). The SF-36 bodily pain improvement at 6 months for patients undergoing PFA and those undergoing TKA was 38 (SD 24) and 27 (SD 23), respectively (p = 0.041), and at 2 years, the improvement was 39 (SD 24) and 33 (SD 22), respectively (p = 0.199). The KOOS symptoms improvement at 6 months for patients undergoing PFA and those undergoing TKA was 24 (SD 20) and 7 (SD 21), respectively (p < 0.001), and at 2 years, the improvement was 27 (SD 19) and 17 (SD 21), respectively (p = 0.023). Improvements from baseline for KOOS pain, SF-36 physical functioning, and OKS also differed in favor of PFA at 6 months, whereas only KOOS symptoms showed a difference between the groups at 2 years. No PRO dimension showed a difference in favor of TKA. At 4 months, 1 year, and 2 years, the ROM change from baseline for patients undergoing PFA and those undergoing TKA was (-7° [SD 13°] versus -18° [SD 14°], p < 0.001; -4° [SD 15°] versus -11° [SD 12°], p = 0.011; and -3° [SD 12°] versus -10° [SD 12°], p = 0.010). There was no difference in the number of complications. During the first 2 post-operative years, there were 2 revisions in patients undergoing PFA (1 to a new PFA and 1 to a TKA). The
authors concluded that patients undergoing PFA obtained a better overall knee-specific QOL than patients undergoing TKA throughout the first 2 years after operation for isolated PFOA. At 2 years, only KOOS function differed between patients undergoing PFA and those undergoing TKA, whereas other PRO dimensions did not show a difference between groups. The observations could be explained by patients undergoing PFA recovering faster than patients undergoing TKA and the functional outcome being better for patients undergoing PFA up to 9 months. Patients undergoing PFA regain their pre-operative ROM, whereas patients undergoing TKA at 2 years have lost 10° of ROM. These researchers found no differences in complications. Moreover, the authors stated that TKA historically has been preferred over PFA as the surgical treatment of choice for patients with severe and isolated patellofemoral arthritis, and register data have been used in support of this practice. However, data with contemporary PFA implants suggested that it may represent a durable solution and perhaps one that has advantages over TKA, but to the authors' knowledge, this has not been evaluated in a randomized trial. They noted that based on the 2-year results of this blinded randomized study, they suggested that PFA rather than TKA should be performed in cases of debilitating isolated PFOA. Patients undergoing PFA enjoy a higher knee-related QOL and ROM than patients undergoing TKA during the first 2 post-operative years. The results challenge register data, and if the results remain favorable over longer term follow-up, they should result in a shift in implant selection from TKA to PFA in patients with isolated patellofemoral arthritis.

This study had several drawbacks. It reported on the 2-year results only, because data for longer follow-up are incomplete. If one of the groups should show unwanted results as the follow-up period increases, any change will have to be balanced against any advantages or disadvantages observed earlier. The authors found it reasonable to use the AUC (the integral) of the PROs as an overall measure of the health benefit obtained by the patient. It was difficult to achieve
perfect double-blinding in a surgical trial. However, they believed that the distribution of patients' guesses about which implant they may have had demonstrated that the patient blinding was effective. It was difficult to ascertain if the assessor blinding was effective, but the authors had no reason to suspect that the assessors obtained information about the implants before completing case forms at follow-up appointments.

Choudhury et al (2018) stated that PFOA affects 32 % men and 36 % women over the age of 60 years and is associated with anterior knee pain, stiffness, and poor mobility; PFA is a bone-sparing treatment for isolated PFOA. These investigators examined the relationship between patient-related outcome measures (PROMs) and measurements obtained from gait analysis before and after PFA. There are currently no studies relating to gait analysis and PFA available in the literature. These investigators addressed the question: Does PFA improve PROMs and restore normal gait? A prospective cohort study was conducted of 10 patients known to have isolated PFOA who had undergone PFA compared to a gender- and age-matched control group. The patients were also asked to complete questionnaires (Oxford knee score (OKS), EQ-5D-5 L) before surgery and 1 year after surgery. Gait analysis was done on an instrumented treadmill comparing Ground reaction force parameters between the control and pre and post-operative PFA patients. The average age 60 (49 to 69) years with a female to male ratio of 9:1. Patient and healthy subjects were matched for age and gender, with no significant difference in body mass index (BMI). Post-op PFA improvement in gait could be seen in ground reaction force at 6.5 km/h. Base support difference between control and pre-op group was statistically significant both on the flat \( p = 0.0001 \) and uphill \( p = 0.429 \) (5 % inclination) and \( p = 0.0062 \) (10 % inclination). Uphill gait at 15 % showed post-operative gait improvements. PROMS response rate was 70 % (7/10) pre-operative and 60 % (6/10) post-operative. EQ-5D-5 L scores reflected patient health
state was better post-operatively. The authors concluded that this study found that gait analysis provided an objective measure of functional gait and reflected by significant improvement in QOL of patients post-PFA. Current literature discusses positive outcomes in relation to physiological gait patterns, normalized gait analysis parameters and PROMs in TKA. Literature lacks studies relating to gait-analysis and PFA. Valuable information provided by this study highlighted that PFA has a beneficial outcome reflected by PROMs and improvement in vertical ground reaction force and gait uphill. These researchers stated that further research and studies are needed to examine how care-providers may use gait-analysis as part of patient care plans for PFOA patients. This was a small (n = 10) study with short-term follow-up (1 year); these preliminary findings need to be validated by well-designed studies.

Strickland et al (2018) described current indications, implants, economic benefits, comparison to TKA, and functional and patient-reported outcomes of PFA. Modern onlay implants and improved patient selection have allowed for recent improvements in short- and long-term outcomes after patellofemoral joint replacement surgery. Patellofemoral arthroplasty has become an increasingly utilized technique for the successful treatment of isolated patellofemoral arthritis. Advances in patient selection, implant design, and surgical technique have resulted in improved performance and longevity of these implants. The authors concluded that although short- and mid-term data for modern PFA appear promising, future studies assessing the long-term results of new designs and technologies of PFA as well as comparison studies to TKA are needed to evaluate patient outcomes and implant performance.

Godshaw and associates (2018) stated that patellofemoral arthritis is a common cause of anterior knee pain and limits flexion-related activities of daily living and exercise. While frequently present in bi-compartmental and tri-compartmental
OA, patellofemoral arthritis could occur in isolation; and PFA as a therapeutic option is gaining in popularity, especially with new implant designs. These researchers reported a case in which new inlay implants were used to resurface the patellofemoral joint in a patient with contralateral compromise secondary to a previous below-knee amputation. A 37-year-old woman with a contralateral right below-knee amputation and progressive left patellofemoral arthritis had failed multiple conservative treatment modalities. She underwent isolated PFA using an inlay-designed implant. The patient was followed for 2 years post-operatively. She noticed an immediate increase in her knee ROM and her pain scores improved; 2 years post-operatively, she demonstrated drastic improvement in all outcome measures: International Knee Documentation Committee score (16.1 to 88.5), Lysholm Knee Scoring Scale (22 to 100), Knee Injury and Osteoarthritis Outcome Score (KOOS) Symptoms (7.14 to 96.43), KOOS Pain (2.78 to 100), KOOS Activities of Daily Living (0 to 100), KOOS Sports (0 to 100), and KOOS Quality of Life (12.5 to 93.75). The authors concluded that inlay PFA is a valid therapeutic option for isolated patellofemoral arthritis. Successful results could be attained with this procedure after failure of conservative measures in patients with limited or no evidence of tibio-femoral arthritis. Moreover, these researchers stated that despite the superiority of PFA, the long-term follow-up literature for this design is limited, and thus further studies are needed to fully explore its benefits and efficacy.

Ajnin et al (2018) stated that the Femoro Patella Vialli FPV is a 2nd-generation PFA implant. It is the 2nd most commonly used patellofemoral implant in the National Joint Registry of England and Wales. This was the 1st published mid-term outcome series for this prosthesis. These investigators reviewed the outcomes for all patients who had PFA. Primary outcome was the intention to revise the implant; secondary outcome measures were Oxford and Kujala outcome scores. A total of 43 FPV patellofemoral joint prostheses were
implanted in 32 patients at the authors’ institution between April 2004 and December 2012. Mean follow-up was 65 (30 to 119) months. Only 1 patient was lost to follow-up. At final follow-up the mean flexion was 110° (85° to 130°); 5 of 43 knees required revision to a TKA because of progressive tibio-femoral OA. Revisions were carried out after a mean of 56 months (30 to 109). There was no radiographic loosening in any case. The most recent functional assessment showed that the mean Oxford Knee score (OKS) has improved from 18 (5 to 35) pre-operatively to 29 (9 to 45) and the Kujala score from 35 (5 to 74) pre-operatively to 58 (18 to 91). The authors concluded that mid-term results with FPV prosthesis demonstrated that moderate outcomes could be achieved; PFA may be used to delay TKA; but judicious patient selection to identify truly isolated PFOA is needed. Chondral lesion in weight bearing area can lead to early implant failure. The main cause of failure was progressive tibio-femoral OA. Long-term follow-up data are needed to ascertain the safety and effectiveness of this device/procedure’s long-term performance.

van Engen et al (2018 2019) noted that patellar tendon shortening may occur following patellofemoral joint replacement (PFJR). These investigators hypothesized that patellar tendon shortening results in unfavorable PROs. These researchers examined the effect of patellar tendon shortening following PFJR on PROs. In this sub-study of a prospective cohort study, a total of 108 patients with isolated PFOA underwent 124 PFJRs. They measured both patellar tendon length and length of the patella on pre-operative radiographs, and on radiographs acquired at 8 weeks and at 1 year post-operative. More than 10 % decrease in patellar tendon length relative to the pre-operative patellar tendon length was defined as patellar tendon shortening. Clinical outcomes were assessed using the knee-specific KOOS questionnaire (Knee Injury and Osteoarthritis Outcome Score). Repeated measures ANOVA was used to analyze for differences in change from baseline KOOS subscales between
patients with and patients without patellar tendon shortening. A complete series of standardized pre-operative, 8 weeks and 1 year post-operative radiographs was available for 87 knees in 82 patients. At 8 weeks, 16 of 87 knees (18%) showed patellar tendon length shortening, and 27 of 87 knees (31%) at 1 year. The authors found no statistically significant relation between patellar tendon length shortening and change from baseline KOOS subscales at 1 year follow-up (pain p = 0.29, symptoms p = 0.56, ADL p = 0.23, sport or recreation p = 0.22, knee-related QoL p = 0.15). The authors concluded that patellar tendon length shortening following PFJR occurred in 31% of knees at 1 year, and did not result in inferior PROs. This study provided only short-term follow-up (1 year) data.

Bunyoz et al (2019) noted that due to inconsistent results and high failure rates, TKA is more often used to treat isolated PFOA despite the theoretical advantage of PFA. It is perceived that 2nd-generation PFA may have improved the outcomes of surgery. In this systematic review, these investigators compared outcomes of 2nd-generation PFA and TKA by assessment of PROMs. A systematic search was made in PubMed, Medline, Embase, Cinahl, Web of Science, Cochrane Library and MeSH to identify studies using 2nd-generation PFA implants or TKA for treatment of PFOA. Only studies using the American Knee Society (AKSS), the Oxford Knee Score (OKS) or the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) to report on PROMs were included. The post-operative weighted mean AKSS knee scores were 88.6 in the 2nd-generation PFA group and 91.8 in the TKA group. The post-operative weighted mean AKSS function score was 79.5 in the 2nd-generation PFA group and 86.4 in the TKA group. There was no significant difference in the mean AKSS knee or function scores between the 2nd-generation PFA group and the TKA group. The post-operative weighted mean OKS score was 36.7 and the post-operative weighted mean WOMAC score was 24.4. The revision rate was higher in the 2nd-generation PFA group (113 revisions [8.4%]) than in the TKA group (3
revisions [1.3%]). Progression of OA was most commonly noted as the reason for revision of PFA, and it was noted in 60 cases [53.1%]; this was followed by pain in 33 cases [29.2%]. The authors concluded that excellent post-operative weighted mean AKSS knee scores were found in both the 2nd-generation PFA group and in the TKA group, suggesting that both surgical options could result in a satisfying patient-reported outcome. Higher revision rates in the 2nd-generation PFA studies may in part be due to challenges related to patient selection. Based on evaluation of PROMs, the use of 2nd-generation PFA appeared to be an equal option to TKA for the treatment of isolated PFOA in appropriately selected patients. Hopefully, this can be considered by physicians in their daily clinical work. Level of Evidence = IV.

These researchers stated that this systematic review was limited by the lack of availability of the individual patients’ PROM outcome in the included studies; thus, inaccuracy was introduced to the reporting of data as weighted means. Furthermore, there were few studies reporting the use of TKA to treat isolated PFOA, and in general, the number of patients in all the studies were low. Finally, the low level of evidence in studies included a considerable risk of selection bias in the studies, which must be accounted for in the interpretation of results. In the future, there is a need of more prospective, RCTs or comparative studies to bring forward higher level evidence in the comparison of 2nd generation PFA with TKA for treatment of isolated PFOA. In addition, evidence considering the long-term prognosis for younger patients who would be expected to outlive the typical lifespan of a TKA is limited and should be further investigated.

Joseph, et al. (2020) reported on a pragmatic, single-center, double-blind randomized clinical trial that was conducted in a UK National Health Service (NHS) teaching hospital to evaluate whether there is a difference in functional knee scores, quality-of-life outcome assessments, and complications at one-year after intervention between total knee
arthroplasty (TKA) and patellofemoral arthroplasty (PFA) in patients with severe isolated patellofemoral arthritis. The parallel, two-arm, superiority trial was powered at 80%, and involved 64 patients with severe isolated patellofemoral arthritis. The primary outcome measure was the functional section of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score at 12 months. Secondary outcomes were the full 24-item WOMAC, Oxford Knee Score (OKS), American Knee Society Score (AKSS), EuroQol five dimension (EQ-5D) quality-of-life score, the University of California, Los Angeles (UCLA) Physical Activity Rating Scale, and complication rates collected at three, six, and 12 months. For longer-term follow-up, OKS, EQ-5D, and self-reported satisfaction score were collected at 24 and 60 months. Among 64 patients who were randomized, five patients did not receive the allocated intervention, three withdrew, and one declined the intervention. There were no statistically significant differences in the patients' WOMAC function score at 12 months (adjusted mean difference, -1.2 (95% confidence interval -9.19 to 6.80); p = 0.765). There were no clinically significant differences in the secondary outcomes. Complication rates were comparable (superficial surgical site infections, four in the PFA group versus five in the TKA group). There were no statistically significant differences in the patients' OKS score at 24 and 60 months or self-reported satisfaction score or pain-free years. The investigators concluded that, among patients with severe isolated patellofemoral arthritis, this study found similar functional outcome at 12 months and mid-term in the use of PFA compared with TKA.

Patellar Denervation

van Jonbergen et al (2014) noted that they have previously shown that in the absence of patellar resurfacing the use of electrocautery around the margin of the patella improved the 1-year clinical outcome of TKR. In this prospective, randomized study, these researchers compared the mean 3.7
year (1.1 to 4.2) clinical outcomes of 300 TKRs performed with and without electrocautery of the patellar rim -- this was an update of a previous report. The overall prevalence of AKP was 32% (95% CI: 26 to 39), and 26% (95% CI: 18 to 35) in the intervention group compared with 38% (95% CI: 29 to 48) in the control group (chi-squared test; p = 0.06). The overall prevalence of AKP remained unchanged between the 1-year and 3.7-year follow-up (chi-squared test; p = 0.12). The mean total WOMAC and the AKS knee and function scores at 3.7 years' follow-up were similar in the intervention and control groups (repeated measures analysis of variance p = 0.43, p = 0.09 and p = 0.59, respectively). There were no complications. A total of 10 patients (intervention group, n = 3; control group, n = 7) required secondary patellar resurfacing after the 1st year. The authors concluded that the findings of this study suggested that the improved clinical outcome with electrocautery denervation compared with no electrocautery was not maintained at a mean of 3.7 years' follow-up.

Handel et al (2014) determined possible differences in the mid-term results of TKA in patients treated with and without denervation of the patella. This study included 80 TKR in 71 patients who were treated with TKR, either with (n = 40) or without (n = 40) simultaneous denervation of the patella out of a total population with 122 knee replacements in 100 patients. Comparability of both groups was achieved by applying matching criteria. All patients were reviewed by isokinetic tests, physical and radiological examination. The mean follow-up time was 2.2 years. The mean hospital for special surgery (HSS) score revealed no statistically significant differences between both groups (with denervation 77.9 ± 11.1 and without denervation 77.8 ± 11.0, p = 0.976). The isokinetic torque measurements with low angle velocity (60°/s) indicated slightly higher values during extension (60.2 ± 32.2 Nm versus 55.8 ± 25.2 Nm, p = 0.497) and flexion (52.4 ± 28.3 Nm versus 46.1 ± 22.3 Nm, p = 0.272) movements of the affected knee joint. However, the differences did not reach statistical significance. At high angle velocity (180°/s) no differences could be found.
between both groups. No cases of post-operative necrosis of the patella were observed. Anterior knee pain after denervation was reported in 6 cases (15%) compared to 10 cases (25%) in patients who were treated without denervation (p = 0.402). The authors concluded that no statistically significant differences could be found between patients with and without denervation of the patella for TKA.

Pulavarti et al (2014) randomized 126 consecutive patients undergoing primary TKA into 2 groups: Group 1 -- patella denervation (n = 63) and Group 2 -- no patella denervation (n = 63). Assessment was performed pre-operatively and at 3, 12 and 24 months post-operatively. Average follow-up of patients was 26.5 months for denervation group and 26.3 months for no denervation group (p = 0.84). Pain scores for AKP were significantly better in the denervation group at 3 months but not at 12 and 24 months. Patient satisfaction was higher in the denervation group. Flexion range was higher in the denervation group at 3, 12 and 24 months review (p < 0.01). However, the authors noted that there were no statistically significant differences with other validated knee scores.

Cheng et al (2014) stated that the impact of patellar denervation with electrocautery in TKA on post-operative outcomes has been under debate. These researchers conducted a meta-analysis and systematic review to compare the benefits and risks of circum-patellar electrocautery with those of non-electrocautery in primary TKAs. Comparative studies and RCTs were identified by conducting an electronic search of articles dated up to September 2012 in PubMed, EMBASE, Scopus, and the Cochrane databases. A total of 6 studies that focus on a total of 849 knees were analyzed. A random-effects model was conducted using the inverse-variance method for continuous variables and the Mantel-Haenszel method for dichotomous variables. There was no significant difference in the incidence of AKP between the electrocautery and non-electrocautery groups. In term of patellar score and Knee Society Score (KSS), circum-patellar
electrocautery improved clinical outcomes compared with non-electrocautery in TKAs. The statistical differences were in favor of the electrocautery group; but have minimal clinical significance. In addition, the overall complications indicated no statistical significance between the 2 groups. The authors concluded that the findings of this study showed no strong evidence either for or against electrocautery compared with non-electrocautery in TKAs.

In a meta-analysis, Li and colleagues (2014) examined if patellar denervation with electrocautery after TKA could reduce the post-operative AKP. A total of 5 RCTs with 572 patients and 657 knees were eligible for this meta-analysis. The results showed that patellar denervation with electrocautery was associated with less AKP, lower VAS, higher patellar scores and better Knee Function Score (KFS) compared with no patellar denervation. Complications did not differ significantly between the 2 groups. The authors concluded that the existing evidence indicated that patellar denervation with electrocautery may be a better approach, as it improved both AKP and knee function after TKA. Moreover, they stated that future multi-center RCTs with large sample sizes are needed to verify these findings.

Arirachakaran et al (2015) conducted a systematic review and network meta-analysis of RCTs with the aim of comparing relevant clinical outcomes between patellar denervation, resurfacing and non-resurfacing. A database search was performed using PubMed and Scopus search engines; RCTs or quasi-experimental designs comparing clinical outcomes between treatments by a search of articles dated from inception to October 23, 2012. Unstandardized mean difference (UMD) and random effects methods were applied for pooling continuous and dichotomous outcomes, respectively. A longitudinal mixed regression model was used for network meta-analysis to indirectly compare treatment effects; 18 of 315 studies identified were eligible. Compared with patellar non-resurfacing, patellar denervation had a UMD
that displayed a significant improvement in symptoms with values in pain VAS and KSS of -0.6 [95 % CI: -1.13 to -0.25] and 2.55 (95 % CI: 0.43 to 4.68), respectively. The UMD in VAS, KSS, and KFS in patellar resurfacing showed no significant improvement in symptoms when compared to non-resurfacing. Patients who underwent surgery with patellar resurfacing had a lower re-operation rates with pooled relative risks (RRs) of 0.69 (95 % CI: 0.50 to 0.94) when compared to non-resurfacing. The network meta-analysis suggested a benefit of borderline significance for patellar denervation with a pooled RR of 0.63 (95 % CI: 0.38 to 1.03), showing that there is a lower chance of AKP when compared to non-resurfacing. Patellar resurfacing also displayed a significantly lower chance of re-operation with a pooled RR of 0.68 (95 % CI: 0.50 to 0.92) when compared to non-resurfacing. Multiple active treatment comparisons indicated that patellar denervation resulted in greater improvement in KFS than patellar resurfacing. The authors concluded that the findings of this review suggested that either patellar denervation or patellar resurfacing may be selected for the management of the PF component in TKR. They noted that patellar denervation may help improve post-operative knee function, but does not improve pain when compared to patellar resurfacing.

Kwon et al (2015) stated that there is controversy over the need for electrocauterization of the patella in non-resurfacing TKA. In a prospective RCT, these researchers examined if this procedure is beneficial. A total of 50 patients who underwent electrocautery were compared with 50 patients who did not undergo this procedure. These investigators determined cartilage status, pre-operative and post-operative AKS score, the WOMAC and the PF scores for a minimum of 5 years. The 2 groups did not differ significantly in demographics, intra-operative cartilage status, or pre-operative or post-operative outcomes. No complications were detected in either group. The authors concluded that they found no benefits of electrocautery of the patella in patellar non-resurfacing TKA up to 5 years.
Cryotherapy

The American Academy of Orthopaedic Surgeons (AAOS)'s evidence-based clinical practice guideline on "Surgical management of osteoarthritis of the knee" (2015) noted that cryotherapy is one of the interventions that were considered but not recommended.

Intra-Articular Injection Triamcinolone Acetonide Extended-Release (Zilretta)

In a randomized, blinded, placebo-controlled clinical trial, Henriksen et al (2015) evaluated the clinical benefits of an intra-articular corticosteroid injection given before exercise therapy in patients with OA of the knee. The participants had radiographic confirmation of clinical OA of the knee, clinical signs of localized inflammation in the knee, and knee pain during walking (score greater than 4 on a scale of 0 to 10). Subjects were randomly allocated (1:1) to an intra-articular 1-ml injection of the knee with methylprednisolone acetate (Depo-Medrol), 40 mg/ml, dissolved in 4 ml of lidocaine hydrochloride (10 mg/ml) (corticosteroid group) or a 1-ml isotonic saline injection mixed with 4 ml of lidocaine hydrochloride (10 mg/ml) (placebo group). Two weeks after the injections, all participants started a 12-week supervised exercise program. The primary outcome was change in the Pain subscale of the KOOS questionnaire (range of 0 to 100; higher scores indicate greater improvement) at week 14. Secondary outcomes included the remaining KOOS subscales and objective measures of physical function and inflammation. Outcomes were measured at baseline, week 2 (exercise start), week 14 (exercise stop), and week 26 (follow-up). A total of 100 patients were randomized to the corticosteroid group (n = 50) or the placebo group (n = 50); 45 and 44 patients, respectively, completed the trial. The mean (SE) changes in the KOOS Pain subscale score at week 14 were 13.6 (1.8) and 14.8 (1.8) points in the corticosteroid and placebo groups, respectively, corresponding to a statistically insignificant mean
difference of 1.2 points (95% CI: -3.8 to 6.2; p = 0.64). These researchers found no statistically significant group differences in any of the secondary outcomes at any time-point. The authors concluded that no additional benefit resulted from adding an intra-articular injection of 40 mg of corticosteroid before exercise in patients with painful OA of the knee. They stated that further research is needed to establish optimal and potentially synergistic combinations of conservative treatments.

Zilretta is an extended release form triamcinolone acetonide (Kenalog-40 injection) and is FDA-approved for the treatment of osteoarthritis pain of the knee. Zilretta is dosed as a single 32 mg intra-articular injection. The labeling states that the efficacy and safety of repeat administration have not been evaluated (Flexion, 2017). Zilretta is not interchangeable with other formulations of triamcinolone acetonide. The labeling states that Zilretta is not suitable for use in small joints, such as the hand. The labeling states that the efficacy and safety of Zilretta for management of osteoarthritis pain of shoulder and hip have not been evaluated.

The labeling states that, in the pivotal study for FDA approval, Zilretta demonstrated a statistically significant reduction in pain intensity at the primary endpoint versus placebo (Flexion, 2017). However, in a secondary exploratory analysis, statistical significance was not demonstrated between the Zilretta and the active control (immediate-release triamcinolone acetonide) treatment groups for the change from baseline at Week 12 in weekly mean Average Daily Pain intensity scores (see Conaghan, et al., below).

Conaghan et al (2018) stated intra-articular corticosteroids relieve osteoarthritis pain, but rapid systemic absorption limits efficacy. FX006 (Zilretta), a novel, microsphere-based, extended-release triamcinolone acetonide (TA) formulation, prolongs TA joint residence and reduces systemic exposure compared with standard TA crystalline suspension (TAs). The
authors assessed symptomatic benefits and safety of FX006 compared with saline-solution placebo and TAs. In this Phase-3, multicenter, double-blinded, 24-week study, adults ≥40 years of age with knee osteoarthritis (Kellgren-Lawrence grade 2 or 3) and average-daily-pain (ADP)-intensity scores of ≥5 and ≤9 (0 to 10 numeric rating scale) were centrally randomized (1:1:1) to a single intra-articular injection of FX006 (32 mg), saline-solution placebo, or TAs (40 mg). The primary end point was change from baseline to week 12 in weekly mean ADP-intensity scores for FX006 compared with saline-solution placebo. Secondary end points were area-under-effect (AUE) curves of the change in weekly mean ADP-intensity scores from baseline to week 12 for FX006 compared with saline-solution placebo, AUE curves of the change in weekly mean ADP-intensity scores from baseline to week 12 for FX006 compared with TAs, change in weekly mean ADP-intensity scores from baseline to week 12 for FX006 compared with TAs, and AUE curves of the change in weekly mean ADP-intensity scores from baseline to week 24 for FX006 compared with saline-solution placebo. Exploratory end points included week-12 changes in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Knee Injury and Osteoarthritis Outcome Score Quality of Life (KOOS-QOL) subscale scores for FX006 compared with saline-solution placebo and TAs. Adverse events were elicited at each inpatient visit. The primary end point was met. Among 484 treated patients (n = 161 for FX006, n = 162 for saline-solution placebo, and n = 161 for TAs), FX006 provided significant week-12 improvement in ADP intensity compared with that observed for saline-solution placebo (least-squares mean change from baseline: -3.12 versus -2.14; p < 0.0001) indicating ~50% improvement. FX006 afforded improvements over saline-solution placebo for all secondary and exploratory end points (p < 0.05). Improvements in osteoarthritis pain were not significant for FX006 compared with TAs using the ADP-based secondary measures. Exploratory analyses of WOMAC-A, B, and C and KOOS-QOL subscales favored FX006 (p ≤ 0.05). Adverse events were generally mild,
occurring at similar frequencies across treatments. The authors concluded that FX006 provided significant, clinically meaningful pain reduction compared with saline-solution placebo at week 12 (primary end point).

In a phase IIb study, Conaghan et al (2018) compared the analgesic benefits of 2 FX006 (Zilretta) doses with saline placebo injection. Participants with knee OA (Kellgren/Lawrence grade 2 to 3) and average daily pain (ADP) intensity greater than or equal to 5 to less than or equal to 9 (on a 0 to 10 Numerical Rating Scale [NRS]) were randomized (1:1:1) to receive single intra-articular (IA) injections of FX006 32 mg (n = 104) or 16 mg (n = 102) or saline placebo (n = 100). The primary end-point was the least squares mean (LSM) change from baseline to week 12 in weekly mean ADP intensity scores for FX006 32 mg versus saline placebo. The investigators reported that the primary end-point was not met (LSM change at week 12 -3.1 with FX006 32 mg versus -2.5 with saline placebo; LSM difference [95 % CI]: −0.58 [−1.22 to 0.07]) (p = 0.08). However, improvements in ADP intensity were significantly greater with FX006 32-mg than saline placebo at weeks 1 to 11 and week 13. Improvements in ADP intensity were significantly greater with FX006 16-mg versus saline placebo at weeks 1 to 9. A dose-response effect in duration of maximal analgesic effect was evident (13 weeks with 32-mg versus 9 weeks with 16-mg), with FX006 32-mg providing increased therapeutic benefit relative to FX006 16-mg. All treatments were well-tolerated. The investigators concluded that, although the primary end-point was not met, their findings indicated a prolonged reduction in symptoms with FX006 with an evident dose response and a safety profile similar to saline placebo.

Bodick et al (2015) stated IA corticosteroids are a mainstay in the treatment of knee osteoarthritis, and in clinical trials, they demonstrate a large initial analgesic effect that wanes over one to four weeks with the rapid efflux of drug from the joint. The present study was undertaken to determine if FX006, an
extended-release formulation of triamcinolone acetonide, can provide pain relief that is superior to the current standard of care, immediate-release triamcinolone acetonide. In this Phase-2, double-blind, multicenter study, 228 patients with moderate to severe knee osteoarthritis pain were randomized to a single intra-articular injection of FX006 (containing 10, 40, or 60 mg of triamcinolone acetonide) or 40 mg of immediate-release triamcinolone acetonide. Data on the mean daily pain on the 11-point Numeric Rating Scale were collected over twelve weeks; the primary efficacy end point was the change from baseline to each of eight, ten, and twelve weeks in the weekly mean of the mean daily pain intensity scores analyzed with a longitudinal mixed-effects model. The 10-mg dose of FX006 produced pain relief that was improved relative to immediate-release triamcinolone acetonide at two through twelve weeks, although the difference in pain relief was not significant ($p \geq 0.05$). The 40-mg dose of FX006 produced pain relief that was improved at two through twelve weeks and was significantly superior to immediate-release triamcinolone acetonide at five to ten weeks ($p < 0.05$ at each time point). At the 40-mg dose of FX006, prespecified secondary analyses, including responder analyses and all Western Ontario and McMaster Universities subscales, were significantly superior ($p < 0.05$) to immediate-release triamcinolone acetonide at eight weeks, and the time-weighted mean pain relief (assessed with mean daily pain intensity scores) was significantly superior to immediate-release triamcinolone acetonide over one to twelve weeks ($p = 0.04$). The 60-mg dose did not provide additional improvement relative to the 40-mg dose. Adverse events were generally mild and similar across all treatments. The authors concluded that intra-articular injection of FX006, an extended-release formulation of triamcinolone acetonide, provided a clinically relevant improvement in pain relief in patients with knee osteoarthritis relative to immediate-release triamcinolone acetonide, the current standard of care.

Russell et al (2018) compared blood glucose levels following intra-articular injection of triamcinolone acetonide extended-
release (TA-ER) versus standard triamcinolone acetonide crystalline suspension (TAc) in patients with knee OA and co-morbid type 2 diabetes. In this double-blind, randomized, parallel-group, phase-II study (NCT02762370), 33 patients with knee OA (ACR criteria) and type 2 diabetes mellitus (HbA1c 6.5 to 9.0 % [48 to 75 mmol/mol]; 1 to 2 oral hypoglycemic agents) were treated with IA TA-ER (32-mg n = 18) or TAc 40-mg (n = 15). Continuous glucose monitoring-measured glucose (CGMG) was assessed from 1 week pre-injection through 2 weeks post-injection. End-points included change in average daily CGMG from baseline (days -3 to -1) to days 1 to 3 post-injection (CGMG days 1 to 3) (primary) and percent time average hourly CGMG levels remained in prespecified glycemic ranges. The change CGMG days 1 to 3 was significantly lower following TA-ER versus TAc (14.7 versus 33.9 mg/dL, least-squares-mean-difference [95 % CI]: -19.2 [-38.0 to -0.4]; \( p = 0.0452 \)). The clinical significance of this difference in this transient difference in average daily CGMG levels between TA-ER and TAc was unknown. The percentage of time over days 1 to 3 that CGMG was in the target glycemic range (70 to 180 mg/dL) was numerically greater for TA-ER (63.3%) versus TAc (49.7%), and that CGMG was greater than 180 mg/dL was lower for TA-ER (34.5 %) versus TAc (49.9 %) (statistical significance of these differences not tested). Non-glycemic AEs were mild and comparable between groups.

In an open-label, single-arm, phase III-b clinical trial, Spitzer and colleagues (2019) examined the safety and efficacy of repeat administration of TA-ER in patients with symptomatic knee OA, including those with advanced radiographic severity. Subjects aged greater than or equal to 40 years received the 1st intra-articular TA-ER injection on day 1. Patients received the 2nd injection timed to the response to the 1st injection (at either week 12, 16, 20, or 24). Patients who received 2 injections were evaluated every 4 weeks for 52 weeks. Safety was evaluated via treatment-emergent AEs and any change at 52 weeks in index-knee radiographs.
(chondrolysis, osteonecrosis, insufficiency fractures, subchondral bone changes). Exploratory efficacy end-points included WOMAC-A (pain), -B (stiffness), -C (function), and KOOS-Quality of Life (KOOS-QoL) after each injection. Initiative in Methods, Measurements and Pain Assessment in Clinical Trials (IMMPACT) criteria were used to determine moderate and substantial treatment response. A total of 208 patients were enrolled and received the 1st injection of TA-ER; 179 (86.1 %) received the 2nd injection (median time to 2nd injection: 16.6 weeks). Both injections were well-tolerated, with no unexpected AEs or significant radiographic changes at week 52. The magnitude and duration of clinical benefit following the 1st and 2nd injections were similar, and most patients reported a substantial (greater than or equal to 50 %) analgesic response after both doses. The authors concluded that repeat administration of TA-ER using a flexible dosing schedule timed to patient response was well-tolerated, with no radiographic evidence of cartilage impact. Both injections resulted in similar improvements in OA symptoms across a broad spectrum of disease severity reflective of that observed in clinical practice.

The authors stated that this study had several drawbacks. Although the 52-week follow-up period and radiographic assessment provided useful data on the safety of repeat TA-ER injections, a longer study duration, additional administrations of TA-ER, and MRI would be useful for assessing certain safety parameters such as changes in the elements of joint structure. In this study, subjects were limited to 2 injections of TA-ER. Additional administration of TA-ER would have provided more data and may have improved subject retention; 25 subjects discontinued treatment due to pain recurrence sometime following the 2nd injection. All discontinuations due to pain recurrence occurred greater than 12 weeks after the 2nd injection, indicating that those subjects had responded to the 2nd injection. Allowing a 3rd administration of TA-ER may have reduced the number of discontinuations. In addition, as with any open-label, single-
arm study, there was potential for bias; however, this was mitigated with respect to the radiographic data by time-blinding the independent radiologists. While inclusion of a placebo-arm would have been optimal, the high discontinuation rate expected for subjects randomized to placebo who would have been prohibited from receiving other treatment for their knee OA for 1 year (including IA corticosteroids in any joint, any other IA intervention in the index knee, and opiates) precluded this. Despite these drawbacks, this study allowed for evaluation of exploratory safety and efficacy of TA-ER repeat administration under circumstances more closely approximating “real-world” conditions than previous clinical trials.

Langworthy and co-workers (2019) stated that in a phase-III RCT, a single IA injection of TA-ER in patients with unilateral or bilateral knee OA demonstrated substantial improvement in pain and symptoms. Bilateral knee pain has emerged as a confounding factor in clinical trials when evaluating the effect of a single IA injection. Furthermore, unilateral disease is frequently first to emerge in active military personnel secondary to prior traumatic joint injury. In a post-hoc analysis, these researchers examined the safety and efficacy of TA-ER in a subgroup of subjects with unilateral knee OA. Subjects greater than or equal to 40 years of age with symptomatic knee OA were randomized to a single IA injection of TA-ER (32-mg), TA crystalline suspension (TAc; 40 mg), or saline-placebo. Average daily pain (ADP)-intensity and rescue medication use were collected at each of weeks 1 to 24 post-injection; WOMAC-A (pain), WOMAC-B (stiffness), WOMAC-C (function), and KOOS-QoL were collected at weeks 4, 8, 12, 16, 20, and 24 post-injection; AEs were assessed throughout the study. Subjects with unilateral knee OA were selected for this analysis. Of 170 subjects with unilateral OA (TA-ER, n=51; saline-placebo, n=60; TAc, n=59), 42 % were men and 89 % were white; TA-ER significantly (p < 0.05) improved ADP-intensity versus saline-placebo (weeks 1 to 24) and TAc (weeks 4 to 21); TA-ER significantly (p < 0.05) improved
WOMAC-A versus saline-placebo (all time-points) and TAc's (weeks 4, 8, 12, 24). Consistent outcomes were observed for rescue medication, WOMAC-B, WOMAC-C, and KOOS-QoL; AEs were similar in frequency/type across treatments. The authors concluded that TA-ER provided 5 to 6 months' pain relief that consistently exceeded saline-placebo and TAc's, suggesting that intraarticularly injected TA-ER into the affected knee may be an effective non-opioid therapeutic option.

Although the subjects included in this analysis did not fully represent the diverse demographics of active service members, the substantial unmet medical need in the military population suggested that TA-ER may be an important therapeutic option; prospective studies of TA-ER outcomes in a military-specific population are needed.

The authors stated that drawbacks of this post-hoc subgroup analysis included the relatively small unilateral knee OA sample sizes and the selection of subjects based on self-reported unilateral pain without confirmation of unilateral OA using X-ray evaluation of the contralateral knee. In addition, the age, sex, and racial distribution of the subjects in this study did not correlate with the demographics of the active duty military population. Although the active duty force is composed of 84.1% men, only 37.3% of subjects who received TA-ER in this analysis were men. Similarly, the population in this study was 11.2% non-white, whereas approximately 1/3 of active duty members identify as a racial minority. In addition, the average age of subjects receiving TA-ER (60 years) may be older than military members seeking treatment for OA given the increased incidence of OA in younger age groups for military members compared with the general population.

Paik and colleagues (2019) noted that triamcinolone acetonide extended-release (ER) 32-mg (Zilretta) is approved for the management of OA pain of the knee and is administered as a single, 5-ml IA injection. Although the therapeutic effects from IA corticosteroids are typically short-lived, triamcinolone
Acetonide ER is formulated in poly (lactic-co-glycolic acid) (PLGA) microspheres that slowly release triamcinolone acetonide in the synovium, enabling their prolonged presence in the joint. This reduces systemic exposure and lessens corticosteroid-related systemic AEs, such as blood glucose elevations. In a 24-week, randomized, phase-III clinical trial, triamcinolone acetonide ER 32-mg significantly improved mean average daily pain intensity in patients with knee OA relative to placebo, and pain, stiffness and physical function (according to WOMAC criteria) relative to placebo and triamcinolone acetonide crystalline suspension (CS). Triamcinolone acetonide ER was generally well-tolerated, with a tolerability profile similar to that of triamcinolone acetonide CS and placebo. Findings from a single-arm, phase-IIIb clinical trial indicated that a repeat administration of triamcinolone acetonide ER may be similarly effective to an initial injection without having deleterious effects on cartilage or other aspects of joint structure. The authors concluded that triamcinolone acetonide ER expands the therapeutic options available for the management of OA pain of the knee. Moreover, these researchers stated that further investigation into the tolerability and efficacy of repeat administration of triamcinolone acetonide ER would be of interest, namely with longer-term and/or placebo-controlled studies.

Kivitz and associates (2019) noted that in randomized controlled knee osteoarthritis (OAK) trials (NCT01487161, NCT02116972, NCT02357459), IA TA-ER demonstrated substantial, prolonged analgesia versus saline-placebo and TACs as assessed by patient-reported pain scales. This pooled analysis examined the impact of TA-ER on rescue medication use. Patients (n = 798) with OAK (ACR criteria; Kellgren-Lawrence grade 2/3) and baseline average daily pain intensity score of greater than or equal to 5 to less than or equal to 9 (0 to 10 numeric rating scale [NRS]) received a single IA injection of TA-ER (n = 324), saline-placebo (n = 262), or TACs (n = 212). Acetaminophen/paracetamol tablets were provided to treat uncontrolled pain (knee or otherwise).
Rescue medication consumption was monitored through a daily diary; pill counts were confirmed at the clinical site. Differences in rescue medication use were measured by least-squares mean (LSM) differences, number of rescue medication tablets used per day, and in area under the effect (AUE) curves of rescue medication tablets used per week. The overall number of rescue medication tablets used per day through week 24 was significantly less ($p \leq 0.05$) for TA-ER versus saline-placebo (LSM difference, -0.43) and TAc (0.24). Rescue medication use was significantly ($p \leq 0.05$) lower following TA-ER versus saline-placebo across weeks 1 to 12 (AUE weeks 1 to 12; LSM difference, -24.5) and weeks 1 to 24 (AUE weeks 1 to 24; -51.6) and versus TAc across weeks 1 to 12 (AUE weeks 1 to 12; -21.1). The authors concluded that in patients with painful OAK, reduced rescue medication use may be a potential benefit of TA-ER and further supports its analgesic efficacy. Moreover, these researchers stated that additional research is needed to examine if TA-ER impacts the use of other common oral analgesics (NSAIDs, opioids) for patients with OAK.

The authors stated that this analysis was limited by its pooled retrospective nature. This resulted in differences in the number of patients receiving each treatment because of differences in individual study designs and durations. Furthermore, the allowance to use rescue medication for any worsening pain, not limited to OA knee pain, may have confounded the results; however, given the fact that these were large randomized trials, the impact of this potential confounder was considered to be minimal.

Percutaneous Calcium Phosphate Injections

Chatterjee et al (2015) noted that injury to sub-chondral bone is associated with knee pain and OA. A percutaneous calcium phosphate injection is a novel approach in which sub-chondral bone marrow edema lesions are percutaneously injected with calcium phosphate. In theory, calcium phosphate provides
structural support while it is gradually replaced by bone. However, little clinical evidence supports the effectiveness of percutaneous calcium phosphate injections. These researchers asked: (i) Does percutaneous calcium phosphate injection improve validated patient-reported outcome measures? (ii) What proportion of patients experience failure of treatment (defined as a low score on the Tegner Lysholm Knee Scoring Scale)? And (iii) Is there a relationship between outcome and age, sex, BMI, and pre-operative grade of OA? Between September 2012 and January 2014, these investigators treated 33 patients with percutaneous calcium phosphate injections; 25 satisfied this study inclusion criteria; of those, 3 were lost to follow-up and 22 (88%; 13 men, 9 women) with a median age of 53.5 years (range of 38 to 70) were available for retrospective chart review and telephone evaluation at a minimum of 6 months (median of 12 months; range of 6 to 24). The general indications for this procedure were the presence of sub-chondral bone marrow edema lesions observed on MR images involving weight-bearing regions of the knee associated with localized pain on weight-bearing and palpation and failure to respond to conservative therapy (greater than 3 months). Patients with pain secondary to extensive non-degenerative meniscal tears with a flipped displaced component at the level of bone marrow edema lesions, or with mechanical axis deviation greater than 8° were excluded. All patients had Grades III or IV chondral lesions (modified Outerbridge grading system for chondromalacia) overlying MRI-identified sub-chondral bone marrow edema lesions. Percutaneous calcium phosphate injection was performed on the medial tibial condyle (15 patients), the medial femoral condyle (5 patients), and the lateral femoral condyle (2 patients). Concomitant partial meniscectomy was performed in 18 patients. Pre-operative and post-operative scores from the KOOS and the Tegner Lysholm Knee Scoring Scale were analyzed. For patients available for follow-up, the outcome scores improved after treatment. The KOOS
improved from a mean of 39.5 ± 21.8 to 71.3 ± 23 (95% CI: 18.6 to 45.2; p < 0.001) and the Tegner and Lysholm score from 48 ± 15.1 to 77.5 ± 20.6 (95% CI: 18.8 to 40.2; p < 0.001). However, 7 of the 22 patients had poor clinical outcomes as assessed by the Tegner Lysholm Knee Scoring Scale, whereas 3 had fair results, 5 had good results, and 7 had excellent results. The post-operative Tegner Lysholm score was inversely related to the pre-operative Kellgren-Lawrence OA grade (R(2) = 0.292; F (1.20) = 9.645; p = 0.006). These researchers found no relationship between outcome scores and age, sex, or BMI. The authors concluded that in a study that would have been expected to present a best-case analysis (short-term follow-up, loss to follow-up of patients with potentially unsatisfactory results, and use of invasive co-treatments including arthroscopic debridement), the authors found that percutaneous calcium phosphate injection in patients with symptomatic bone marrow edema lesions of the knee and advanced OA yielded poor results in a concerning proportion of patients. Based on these results, these investigators advised against the use of percutaneous calcium phosphate injections for patients with advanced osteoarthritic changes.

Arthroscopic Meniscal Surgery

In a comparative, prospective, cohort study, Thorlund and co-workers (2017) compared patient reported outcomes from before surgery to 52 weeks after surgery between individuals undergoing arthroscopic partial meniscectomy (APM) for traumatic meniscal tears and those for degenerative meniscal tears. This study was performed in 4 public orthopedic departments in the Region of Southern Denmark; subject were recruited between February 1, 2013 and January 31, 2014, and at 1 of the original 4 hospitals from February 1, 2014 to January 31, 2015. Subjects were selected from Knee Arthroscopy Cohort Southern Denmark, aged 18 to 55 years, and undergoing APM for a traumatic or degenerative meniscal tear (defined by a combination of age and symptom onset).
Both participant groups underwent APM for a meniscal tear, with operating surgeons recording relevant information on knee pathology. Patient reported outcomes were recorded via online questionnaires. Primary outcome was the average between-group difference in change on 4 of 5 subscales of the KOOS. The 4 subscales covered pain, symptoms, sport and recreational function, and quality of life (KOOS4). A 95% CI excluding differences greater than 10 KOOS points between groups was interpreted as absence of a clinically meaningful difference. Analyses adjusted for age, sex, and BMI. A total of 397 eligible adults (42% women) with a traumatic or degenerative meniscal tear (n = 141, mean age of 38.7 years (SD 10.9); n = 256, 46.6 years (6.4); respectively) were included in the main analysis. At 52 weeks after APM, 55 (14%) patients were lost to follow-up. Statistically, participants with degenerative meniscal tears had a significantly larger improvement in KOOS4 scores than those with traumatic tears (adjusted between-group difference -5.1 (95% CI: -8.9 to -1.3); p = 0.008). In the analysis including KOOS4 score at all time-points, a significant time-by-group interaction was observed in both the unadjusted (p = 0.025) and adjusted analysis (p = 0.024), indicating better self-reported outcomes in participants with degenerative tears. However, the difference between groups was at no time-point considered clinically meaningful. The authors concluded that these results questioned the current tenet that patients with traumatic meniscal tears experience greater improvements in patient reported outcomes after APM than patients with degenerative tears.

Tornbjerg and colleagues (2017) stated that the relationship between meniscal tears and other joint pathologies with patient-reported symptoms is not clear. These researchers investigated associations between structural knee pathologies identified at surgery with pre-operative knee pain and function in patients undergoing arthroscopic meniscal surgery. This study included 443 patients from the Knee Arthroscopy Cohort Southern Denmark (KACS), a prospective cohort following
patients 18 years or older undergoing arthroscopic meniscal surgery at 4 hospitals between February 1, 2013 and January 31, 2014. Patient-reported outcomes, including the KOOS, were obtained by online questionnaires prior to surgery. Knee pathology was assessed by the operating surgeons using a modified version of the International Society of Arthroscopy, Knee Surgery and Orthopedic Sports Medicine (ISAKOS) classification of meniscal tears questionnaire, supplemented with information extracted from surgery reports. Following hypothesis-driven pre-selection of candidate variables, backward elimination regressions were performed to investigate associations between patient-reported outcomes and structural knee pathologies. Regression models only explained a small proportion of the variability in self-reported pain and function (adjusted $R^2 = 0.10$ to 0.12) and this association was mainly driven by age, gender and BMI. The authors concluded that specific meniscal pathology and other structural joint pathologies found at meniscal surgery were not associated with pre-operative self-reported pain and function in patients with meniscal tears questioning inferences made about a direct relationship between these. They stated that these findings questioned the role of arthroscopic surgery to address structural pathology as a means to improve patient-reported outcomes in patients having surgery for a meniscal tear.

Monk and associates (2017) stated that arthroscopic surgery of the knee is one of the most frequently performed orthopedic procedures; 1/3 of these procedures are performed for meniscal injuries. It is essential that this commonly performed surgery be supported by robust evidence. In a systematic review, these investigators compared the effectiveness of arthroscopic surgery for meniscal injuries in all populations. These researchers carried out an online search for RCTs and systematic reviews (SRs) that compared therapeutic options for meniscal injury. The following databases (inception to April 2015) were included in the search: CENTRAL; Medline; Embase; NHS Evidence; National Guideline Clearing House,
Database of Abstracts of Reviews of Effects, Health Technology Assessment; ISRCTN; Clinicaltrials.gov; WHO trials platform. Only studies whose participants were selected on the basis of meniscal injury were included; no restrictions were placed on patient demographics. Two independent reviewers applied AMSTAR (A Measurement Tool to Assess Systematic Reviews) criteria for SRs and the Cochrane Collaboration risk-of-bias tool for RCTs. A total of 9 RCTs and 8 SRs were included in the review. No difference was found between arthroscopic meniscal debridement compared with non-operative management as a 1st-line treatment strategy for patients with knee pain and a degenerative meniscal tear (MD: Knee injury and Osteoarthritis Outcome Score, 1.6 [95 % CI: -2.2 to 5.2], pain VAS, -0.06 [95 % CI: -0.28 to 0.15]). Some evidence was found to indicate that patients with resistant mechanical symptoms who initially fail non-operative management may benefit from meniscal debridement. No studies compared meniscal repair with meniscectomy or non-operative management. Initial evidence suggested that meniscal transplant might be favorable in certain patient groups. The authors concluded that further evidence is needed to determine which patient groups have good outcomes from each intervention. Given the current widespread use of arthroscopic meniscal surgeries, more research is needed to support evidence-based practice in meniscal surgery in order to reduce the numbers of ineffective interventions and support potentially beneficial surgery.

In a multi-center, participant-blinded and outcome assessor-blinded RCT, Sihvonen and colleagues (2018) examined if APM is superior to placebo surgery in the treatment of patients with degenerative tear of the medial meniscus. This trial included a total of 146 adults, aged 35 to 65 years, with knee symptoms consistent with degenerative medial meniscus tear and no knee osteoarthritis; they were randomized to APM or placebo surgery. The primary outcome was the between-group difference in the change from baseline in the WOMET and Lysholm knee scores and knee pain after exercise at 24
months after surgery. Secondary outcomes included the frequency of un-blinding of the treatment-group allocation, participants' satisfaction, impression of change, return to normal activities, the incidence of serious adverse events (SAEs) and the presence of meniscal symptoms in clinical examination. Two subgroup analyses, assessing the outcome on those with mechanical symptoms and those with unstable meniscus tears, were also carried out. In the intention-to-treat analysis, there were no significant between-group differences in the mean changes from baseline to 24 months in WOMET score: 27.3 in the APM group as compared with 31.6 in the placebo-surgery group (between-group difference, -4.3; 95 % CI: -11.3 to 2.6); Lysholm knee score: 23.1 and 26.3, respectively (-3.2; 95 % CI: -8.9 to 2.4) or knee pain after exercise, 3.5 and 3.9, respectively (-0.4; 95 % CI: -1.3 to 0.5). There were no statistically significant differences between the 2 groups in any of the secondary outcomes or within the analyzed subgroups. The authors concluded that in this 2-year follow-up of patients without knee osteoarthritis but with symptoms of a degenerative medial meniscus tear, the outcomes after APM were no better than those after placebo surgery. No evidence could be found to support the prevailing ideas that patients with presence of mechanical symptoms or certain meniscus tear characteristics or those who have failed initial conservative treatment are more likely to benefit from APM. Moreover, they stated that given the mounting evidence, anyone still advocating APMs should promptly launch methodologically rigorous, practical, real-world trial(s) embedded in the flow of practice to prove that APM truly works in the asserted subgroups of patients.

Commenting on the afore-mentioned study by Sihvonen et al (2018), Coblyn (2018) stated that “Researchers reported in 2014 that, in a randomized trial of 146 patients (age range, 35-65) with knee pain and non-traumatic meniscal tears without osteoarthritis, those who underwent arthroscopic partial meniscectomies showed no benefit after 1 year compared with those who underwent sham procedures. Both groups showed
marked improvement in knee pain-related scores, and no significant differences were observed between groups in secondary outcomes (NEJM JW Gen Med Feb 15 2014 and N Engl J Med 2013; 369:2515). Now, the same investigators report a 2-year follow-up. After 2 years of follow-up, no differences between groups were noted in any of the standardized knee pain scores. In addition, all secondary outcome scores were similar, including in subgroups of patients with mechanical symptoms and certain meniscus tear characteristics. This paper extends the conclusion reported earlier: No significant difference in outcomes was found between meniscectomy and a sham procedure among patients with knee pain and meniscal tears without osteoarthritis. Time and physical therapy should remain the initial treatments for patients like these”.

In a multi-center, participant-blinded and outcome assessor-blinded, placebo-surgery RCT, Sihvonen et al (2018) examined if APM is superior to placebo surgery in the treatment of patients with degenerative tear of the medial meniscus. This trial involved 146 adults, aged 35 to 65 years, with knee symptoms consistent with degenerative medial meniscus tear and no knee OA. Subjects were randomized to APM or placebo surgery. The primary outcome was the between-group difference in the change from baseline in the Western Ontario Meniscal Evaluation Tool (WOMET) and Lysholm knee scores and knee pain after exercise at 24 months after surgery. Secondary outcomes included the frequency of unblinding of the treatment-group allocation, participants’ satisfaction, impression of change, return to normal activities, the incidence of SAEs and the presence of meniscal symptoms in clinical examination. Two subgroup analyses, assessing the outcome on those with mechanical symptoms and those with unstable meniscus tears, were also carried out. In the intention-to-treat (ITT) analysis, there were no significant between-group differences in the mean changes from baseline to 24 months in WOMET score: 27.3 in the APM group as compared with 31.6 in the placebo-surgery group.
between-group difference, -4.3; 95% CI: -11.3 to 2.6); Lysholm knee score: 23.1 and 26.3, respectively (-3.2; -8.9 to 2.4) or knee pain after exercise, 3.5 and 3.9, respectively (-0.4; -1.3 to 0.5). There were no statistically significant differences between the 2 groups in any of the secondary outcomes or within the analyzed subgroups. The authors concluded that in this 2-year follow-up of patients without knee OA but with symptoms of a degenerative medial meniscus tear, the outcomes after APM were no better than those after placebo surgery. No evidence could be found to support the prevailing ideas that patients with presence of mechanical symptoms or certain meniscus tear characteristics or those who have failed initial conservative treatment are more likely to benefit from APM. These investigators stated that these findings supported the evolving consensus that degenerative meniscus tear represents an (early) sign of knee OA, rather than a clinical entity on its own, and accordingly, caution should be exercised in referring patients with knee pain and suspicion of a degenerative meniscal tear to MRI examination or APM, even after a failed attempt of conservative treatment.

Lizaur-Utrilla and colleagues (2019) noted that there is controversy regarding the benefit of APM for degenerative lesions in middle-aged patients. In a cohort study, these researchers compared satisfaction with APM between middle-aged patients with no or mild knee OA and a degenerative meniscal tear and those with a traumatic tear. A comparative prospective study at 5 years of middle-aged patients (45 to 60 years old) with no or mild OA undergoing APM for degenerative (n = 115) or traumatic (n = 143) tears was conducted. Patient satisfaction was measured by a 5-point Likert scale and functional outcomes by the KOOS and WOMAC. Uni-variate and multi-variate regression analyses were used to identify factors correlating with patient-reported satisfaction at 5 years post-operatively. Baseline patient characteristics were not different between groups. At the 5-year evaluation, the satisfaction rate in the traumatic and degenerative groups was 68.5% versus 71.3%, respectively.
Patient satisfaction was significantly associated with functional outcomes ($r = 0.69; p = 0.024$). In the degenerative group, 43 patients (37.4%) had OA progression to K-L grade 2 or 3, but only 24 patients (20.8%) had a symptomatic knee at final follow-up. Multi-variate regression analysis for patient dissatisfaction at 5-year follow-up showed the following significant independent factors: female sex (odds ratio [OR], 1.6 [95% CI: 1.1 to 2.3]; $p = 0.018$), BMI greater than 30 kg/m² (OR, 2.6 [95% CI: 1.7 to 4.9]; $p = 0.035$), lateral meniscal tears (OR, 0.6 [95% CI: 0.1 to 0.9]; $p = 0.039$), and OA progression to K-L grade greater than or equal to 2 at final follow-up (OR, 1.4 [95% CI: 1.2 to 2.6]; $p = 0.014$). At the final evaluation, there were no significant differences between groups in pain scores ($p = 0.648$), WOMAC scores ($p = 0.083$), or KOOS-4 scores ($p = 0.187$). Likewise, there were no significant differences in the KOOS sub-scores for pain ($p = 0.144$), symptoms ($p = 0.097$), or sports/recreation ($p = 0.150$). Although the degenerative group had significantly higher sub-scores for activities of daily living ($p = 0.001$) and quality of life (QOL; $p = 0.004$), the differences were considered not clinically meaningful. The authors concluded that there were no meaningful differences in patient satisfaction or clinical outcomes between patients with traumatic and degenerative tears and no or mild OA.

Predictors of dissatisfaction with APM were female sex, obesity, and lateral meniscal tears. These investigators stated that these findings suggested that APM was an effective medium-term option to relieve pain and recover function in middle-aged patients with degenerative meniscal tears, without obvious OA, and with failed prior physical therapy.

Level of evidence = II.

Karpinski et al (2019) performed a systematic review of prospective RCTs comparing arthroscopic treatment for knee OA with either other therapeutic interventions or sham treatment. A systematic search for RCT about arthroscopic treatment (AT) for knee OA was performed according to the PRISMA guidelines. Arthroscopic treatment included
procedures such as lavage, debridement and partial meniscectomy of the knee. Data source was PubMed central. A total of 14 articles were included; 5 studies compared interventional AT with either sham surgery, lavage or diagnostic arthroscopy; 9 trials compared AT with another active intervention (exercise, steroid injection, hyaluronic acid injection). In 10 trials, the clinical scores improved after arthroscopic treatment of knee OA in comparison to the baseline. In 7 trials, there was a significant difference in the final clinical outcome with higher scores for patients after arthroscopic OA treatment in comparison to a control group. In 4 trials, the ITT analysis revealed no significant difference between arthroscopic OA treatment and the control group. In 1 of those trials, which compared APM with exercise, the cross-over rate from exercise to AT was 34.9%. The clinical scores of cross-over patients improved after APM. In 1 study, the subgroup analysis revealed that patients with tears of the anterior 2/3 of the medial meniscus or any lateral meniscus tear had a higher probability of improvement after arthroscopic surgery than did patients with other intra-articular pathology. There was no difference in the side effects between patients with AT and the control group. Despite acceptable scores in the methodological quality assessment, significant flaws could be found in all studies. These flaws included bad description of the exact surgical technique or poor control of post-operative use of NSAID. The authors concluded that results of RCTs comparing AT with other therapeutic options were heterogeneous; AT in OA patients is not useless because there is evidence that a subgroup of patients with non-traumatic flap tears of the medial meniscus or patients with crystal arthropathy benefit from arthroscopy. These researchers stated that the results of these randomized studies, however, should be interpreted with care because in many studies, the use of other therapeutic variables such as pain killers or NSAIDs was not controlled or reported.
In a systematic review and meta-analysis, Abram et al (2019) evaluated the benefit of APM in adults with a meniscal tear and knee pain in 3 defined populations (taking account of the comparison intervention): (A) all patients (any type of meniscal tear with or without radiographic OA); (B) patients with any type of meniscal tear in a non-OA knee; and (C) patients with an unstable meniscal tear in a non-OA knee. These investigators carried out a search of Medline, Embase, CENTRAL, Scopus, Web of Science, Clinicaltrials.gov and ISRCTN was performed, unlimited by language or publication date (inception to October 18, 2018); (RCTs performed in adults with meniscal tears, comparing APM versus (i) non-surgical intervention; (ii) pharmacological intervention; (iii) surgical intervention; and (iv) no intervention were selected for analysis. A total of 10 trials were identified: 7 compared with non-surgery, 1 pharmacological and 2 surgical. Findings were limited by small sample size, small number of trials and cross-over of participants to APM from comparator interventions. In group A (all patients) receiving APM versus non-surgical intervention (physiotherapy), at 6 to 12 months, there was a small mean improvement in knee pain (SMD 0.22 [95 % CI: 0.03 to 0.40]; 5 trials, 943 patients; I² 48 %; Grading of Recommendations Assessment, Development and Evaluation [GRADE]: low), knee-specific QOL (SMD 0.43 [95 % CI: 0.10 to 0.75]; 3 trials, 350 patients; I² 56 %; GRADE: low) and knee function (SMD 0.18 [95 % CI: 0.04 to 0.33]; 6 trials, 1,050 patients; I² 27 %; GRADE: low). When the analysis was restricted to people without OA (group B), there was a small-to-moderate improvement in knee pain (SMD 0.35 [95 % CI: 0.04 to 0.66]; 3 trials, 402 patients; I² 58 %; GRADE: very low), knee-specific QOL (SMD 0.59 [95 % CI: 0.11 to 1.07]; 2 trials, 244 patients; I² 71 %; GRADE: low) and knee function (SMD 0.30 [95 % CI: 0.06 to 0.53]; 4 trials, 507 patients; I² 44 %; GRADE: very low). There was no improvement in knee pain, function or QOL in patients receiving APM compared with placebo surgery at 6 to 12 months in group A or B (pain: SMD 0.08 [95 % CI: -0.24 to 0.41]; 1 trial, 146 patients; GRADE: low; function: SMD -0.08 [95 % CI: -0.41 to 0.24]; 1 trial, 146
patients; GRADE: high; QOL: SMD 0.05 [95% CI: -0.27 to 0.38]; 1 trial; 146 patients; GRADE: high). No trials were identified for people in group C. The authors concluded that performing APM in all patients with knee pain and a meniscal tear is not appropriate, and surgical treatment should not be considered the 1st-line intervention. There may, however, be a small-to-moderate benefit from APM compared with physiotherapy for patients without OA. No trial has been limited to patients failing non-operative treatment or patients with an unstable meniscal tear in a non-arthritic joint; research is needed to establish the value of APM in this population.

Balneotherapy for the Treatment of Osteoarthritis of the Knee

In a meta-analysis, Matsumoto and colleagues (2017) examined the effect of balneotherapy on relieving pain and stiffness and improving physical function, compared to controls, among patients with knee OA. These investigators searched electronic databases for eligible studies published from 2004 to December 31, 2016, with language restrictions of English or Japanese. They screened publications in Medline, Embase, Cochrane library, and the Japan Medical Abstracts Society Database using two approaches, MeSH terms and free words. Studies that examined the effect of balneotherapy for treating knee OA of a greater than or equal to 2-week duration were included; WOMAC scores were used as the outcome measure. A total of 102 publications were assessed according to the exclusion criteria of the study; 8 clinical trial studies, which comprised a total of 359 cases and 375 controls, were included in this meta-analysis. The meta-analysis analyzed improvement in WOMAC score at the final follow-up visit, which varied from 2 to 12 months post-intervention. This meta-analysis indicated that balneotherapy was clinically effective in relieving pain and stiffness, and improving function, as assessed by WOMAC score, compared to controls. However, there was high heterogeneity (88 to 93%). The authors concluded that it is possible that
Balneotherapy may reduce pain and stiffness, and improve function, in individuals with knee OA, although the quality of current publications contributed to the heterogeneity observed in this meta-analysis.

Furthermore, UpToDate reviews on “Management of knee osteoarthritis” (Deveza and Bennell, 2018a) and “Management of moderate to severe knee osteoarthritis” (Deveza and Bennell, 2018b) do not mention balneotherapy as a therapeutic option.

Bone Marrow Aspirate Concentrate

Shapiro and colleagues (2017) hypothesized that bone marrow aspirate concentrate (BMAC) is feasible, safe, and effective for the treatment of pain due to mild-to-moderate degenerative joint disease of the knee. In this prospective, single-blind, placebo-controlled trial, a total of 25 patients with bilateral knee pain from bilateral OA were randomized to receive BMAC into 1 knee and saline placebo into the other. A total of 52 ml of bone marrow was aspirated from the iliac crests and concentrated in an automated centrifuge. The resulting BMAC was combined with platelet-poor plasma for an injection into the arthritic knee and was compared with a saline injection into the contralateral knee, thereby utilizing each patient as his or her own control. Safety outcomes, pain relief, and function as measured by Osteoarthritis Research Society International (OARSI) measures and the VAS score were tracked initially at 1 week, 3 months, and 6 months after the procedure. There were no serious adverse events from the BMAC procedure; OARSI Intermittent and Constant Osteoarthritis Pain and VAS pain scores in both knees decreased significantly from baseline at 1 week, 3 months, and 6 months (p ≤ 0.019 for all). Pain relief, although dramatic, did not differ significantly between treated knees (p > 0.09 for all). The authors concluded that early results showed that BMAC is safe to use and is a reliable and viable cellular product. Study patients experienced a similar relief of pain in
both BMAC- and saline-treated arthritic knees. They stated that further study is needed to determine the mechanisms of action, duration of efficacy, optimal frequency of treatments, and regenerative potential.

Combination of High Tibial Osteotomy and Autologous Bone Marrow Derived Cell Implantation

Cavallo and colleagues (2018) stated that high tibial osteotomy (HTO) is a recommended treatment for medial compartment knee OA. Newer cartilage regenerative procedures may add benefits to the results of HTO. In this prospective study, these researchers examined the safety and also results of HTO associated with autologous bone marrow derived cells (BMDC) implantation in relatively young and middle aged active individuals with early OA of the knee. A total of 24 patients (mean age of 47.9 years) with varus knee and symptomatic medial compartment OA were treated with medial opening-wedge HTO in conjunction with implantation of BMDC into the chondral lesions. The clinical outcomes were assessed by IKDC, KOOS, VAS, and Tegner scores. The radiographic studies were performed pre-operatively and at follow-ups. No major complications were seen during the operations and post-operative follow-ups. All clinical scores were significantly improved for the IKDC score (from 32.7 ± 15 to 64 ± 21) (p < 0.005), KOOS score (from 30 ± 11 to 68 ± 19) (p < 0.005), VAS (from 7.5 to 3) and Tegner score (from 1.2 to 2.1) (p < 0.004). The authors concluded that HTO in conjunction with BMDC implantation is a safe and feasible treatment and is associated with good results in short-term follow-up for early medial compartment OA in varus knees. Level of evidence: IV.

The authors stated that drawbacks of this preliminary study were the lack of control group, short-term follow-up (2 to 3 years), absence of second look arthroscopy and histological
assessment of the regenerated cartilage. They stated that further RCTs are needed to confirm the clinical advantage of this procedure in early osteoarthritic patients.

Extracorporeal Shock Wave Therapy

Kang and colleagues (2018) noted that bone marrow edema (BME) represents a reversible but highly painful finding in MRI of patients with knee OA. In a retrospective study, these researchers evaluated the efficacy of extracorporeal shock wave therapy (ESWT) on painful BME in OA of the knee. This study focused on people who had early-to-mid stage OA with knee pain and MRI findings of BME. Patients who underwent ESWT or prescribed alendronate treatment in the authors’ department were analyzed. Knee pain and function were measured using the VAS for pain and the WOMAC, respectively. The degree of BME was measured with MRI scans. A total of 126 patients who received ESWT treatment (Group A, n=82) or alendronate treatment (Group B, n=44) were included. All patients were followed-up clinically and radiographically for a minimum of 12 months. The mean follow-up was 23.5 months (range of 12 to 38 months). The VAS and WOMAC score decreased more significantly after treatment in Group A than that in Group B (p < 0.01) within 3 months. In 6-month MRI follow-ups, there was higher incidence of distinct reduction and complete regression of BME of the affected knee in Group A than that in Group B (p < 0.01). The authors concluded that ESWT is an effective, reliable, and non-invasive treatment in patients with painful BME in OA of the knee followed by a rapid normalization of the MRI appearance. It has the potential to shorten the natural course of this disease. Moreover, they stated that multi-center RCTs with long-term outcomes are needed to validate this conclusion.

The authors stated that this study had several drawback. The mechanisms and indications of ESWT have not been very clear. The indications are mainly based on the supported
literatures and previous clinical observation. This study was limited by virtue of the retrospective analysis. There was no randomized and blinded control group with conservative treatment in this study. Intravenous prostacyclin could achieve a reduction in BME, with a considerable improvement of painful symptoms, by improving tissue blood supply in a variety of situations through multiple mechanisms, such as vasodilatation and inhibition of platelet aggregation. It is that pain relief and rapid regression of BME due to the action of prostacyclin in reducing capillary permeability and dilating vessels. Based on this, all patients in both groups were treated with combined alprostadil in this study. The functional improvement in the knee was assessed subjectively using the VAS and functional scores, but no objective measures were utilized. The follow-up time was relatively short (23.5 months). This study was only a pilot clinical study.

Intra-Articular Injections of Autologous Conditioned Serum

Zarringam and colleagues (2018) stated that Orthokin is an intra-articular autologous conditioned serum (ACS). Its use might have a beneficial biological effect on pain and function of OA in the knee. However, earlier studies lack any consensus on its clinical application and disease-modifying effect. In a prospective, cohort study, these investigators examined the long-term effect of Orthokin injection treatment on prevention of surgical treatment for end-stage knee OA. Patients of the previously published Orthokin cohort were contacted to examine if any intra-articular surgical intervention or osteotomy of the studied knee had taken place during the past decade. A log-rank test was performed to evaluate the differences in the survival distribution for the 2 types of intervention: Orthokin versus placebo. The survival distributions for the 2 interventions were not statistically significantly different, \( \chi^2(1) = 2.069, p = 0.150 \). After 7.5 ± 3.9 years, 46.3% of the placebo and 40.3% of the Orthokin group had been treated surgically. The authors concluded that the use of Orthokin in
knee OA patients did not result in a delay regarding surgical treatment. The intra-articular use of Orthokin did not appear to prevent or delay surgical intervention at 10 years after treatment for end-stage knee OA.

Per cutaneous Autologous Fat Injections

In a case-series study, Adriani and colleagues (2017) evaluated the safety and efficacy of autologous aspirated and purified fat tissue injected percutaneously into the knee joint for the treatment of symptomatic OA. These researchers reviewed 30 patients, who received an autologous percutaneous fat injection for the treatment of knee OA from January 2012 to March 2015. Mean patients' age was 63.3 ± 5.3 years (range of 50 to 80 years); BMI was 25.1 ± 1.7. Clinical evaluation was based on pain VAS and WOMAC score for functional and subjective assessment. These investigators also noted the adverse reactions and the consumption of NSAIDs in the post-treatment period. All patients reported improvements with respect to pain: average VAS was 7.7 ± 1.2 at baseline, 5.2 ± 0.2 at 1-month follow-up, and 4.3 ± 1 at 3-month follow-up. A slight deterioration (5.0 ± 1.1) was evidenced at 1 year. Total WOMAC score was 89.9 ± 1.7 at baseline, 66.3 ± 1 at 1 month, 68.6 ± 1.7 at 3 months, and 73.2 ± 1.8 at 12 months of follow-up. The authors concluded that these preliminary findings suggested that percutaneous autologous fat injections are a valid therapeutic option for knee OA. Level of Evidence = IV. This was a small case-series study (n =30) with short-term follow-up (1 year). These preliminary findings need to be validated by well-designed studies with long-term follow-up.

Stem Cell Therapy

In a cases-control study, Koh and Choi (2012) examined if isolated mesenchymal stem cells (MSCs) derived from the infra-patellar fat pad could effectively improve clinical results when percutaneously injected into arthritic knees. A total of
25 stem cell injections combined with arthroscopic debridement were administered to patients with knee OA. A mean of 1.89 × 10⁶ stem cells were prepared with approximately 3.0 ml of platelet-rich plasma (PRP) and injected in the selected knees of patients in the study group. The mean Lysholm, Tegner activity scale, and VAS scores of patients in the study group improved significantly by the last follow-up visit. No major adverse events related to the injections were observed during the treatment and follow-up periods. The results were compared between the study and control groups, in which the patients had undergone arthroscopic debridement and PRP injection without stem cells. Although the pre-operative mean Lysholm, Tegner activity scale, and VAS scores of the study group were significantly poorer than those of the control group, the clinical results at the last follow-up visit were similar and not significantly different between the 2 groups. The authors concluded that the short-term results of this study are encouraging and show that infra-patellar fat pad-derived MSC therapy with intra-articular injections is safe, and provides assistance in reducing pain and improving function in patients with knee OA. These preliminary findings need to be validated by well-designed studies.

Mei and associates (2017) stated that MSC-based cell therapy is a promising avenue for OA treatment. These researchers evaluated the efficacy of intra-articular injections of culture-expanded allogenic adipose tissue-derived stem cells (ADSCs) for the treatment of anterior cruciate ligament transection (ACLT)-induced rat OA model. The paracrine effects of major histocompatibility complex (MHC)-unmatched ADSCs on chondrocytes were investigated in-vitro. Rats were divided into an OA group that underwent ACLT surgery and a sham-operated group that did not undergo ACLT surgery. Four weeks after surgery mild OA was induced in the OA group. Subsequently, the OA rats were randomly divided into ADSC and control groups. A single dose of 1 × 10⁶ ADSCs suspended in 60 μL phosphate-buffered saline (PBS) was
intra-articularly injected into the rats of the ADSC group. The control group received only 60 μL PBS. Progression of OA was evaluated macroscopically and histologically at 8 and 12 weeks after surgery. ADSC treatment did not cause any adverse local or systemic reactions. The degeneration of articular cartilage was significantly weaker in the ADSC group compared to that in the control group at both 8 and 12 weeks. Chondrocytes were co-cultured with MHC-unmatched ADSCs in trans-wells to assess the paracrine effects of ADSCs on chondrocytes. Co-culture with ADSCs counteracted the IL-1β-induced mRNA up-regulation of the extracellular matrix-degrading enzymes MMP-3 and MMP-13 and the pro-inflammatory cytokines TNF-α and IL-6 in chondrocytes. Importantly, ADSCs increased the expression of the anti-inflammatory cytokine IL-10 in chondrocytes. The authors concluded that the findings of this study indicated that the intra-articular injection of culture-expanded allogenic ADSCs attenuated cartilage degeneration in an experimental rat OA model without inducing any adverse reactions; MHC-unmatched ADSCs protected chondrocytes from inflammatory factor-induced damage. The paracrine effects of ADSCs on OA chondrocytes are at least part of the mechanism by which ADSCs exert their therapeutic activity. Moreover, they stated that further studies are needed to validate this hypothesis.

Fan and colleagues (2018) examined the effect and mechanism of pre-cartilaginous stem cells (PSCs) engraftment-inducing tissue repair in a knee OA rat model. Knee OA model was constructed in Sprague Dawley (SD) rats by partial removal of the medial meniscus of the right knee; PSCs were engrafted by injecting PSCs into the right knee cavity. At 4 and 8 weeks after model construction, the serum levels of interleukine (IL)-1β, tumor necrosis factor (TNF)-α, and IL-6 were assessed using enzyme-linked immunosorbent assay (ELISA). Hematoxylin-eosin (HE) staining was performed to assess the histopathology of synovial membrane and cartilage. Western blot analysis was used to assess Notch1, Bcl-2 and Bax levels in the articular cartilage. At 4
and 8 weeks, OA rats demonstrated significantly higher IL-1β, TNF-α, and IL-6 levels than normal rats (p < 0.05), whereas PSCs treatment prominently attenuated IL-1β up-regulation (p < 0.05). In OA rats, the number of chondrocytes dramatically decreased over time in OA rats, with disruption of chondrocytes organization and cell layers. PSCs alleviated the deterioration of cartilage, as evidenced by the relatively smooth articular surface, distinct tidemark and clear cell layers. The model and treatment groups demonstrated substantially higher Notch1 expression. The Bcl-2/Bax value in the OA rats was lower than the control group, while PSCs treatment led to increase in Bcl-2/Bax value. The authors concluded that PSCs treatment down-regulated the expression of inflammatory cytokines, alleviating OA in the knee of rats. Notch1 signaling pathway plays an important role in this ameliorating effect of PSCs treatment. These findings need to be validated in well-designed studies with human subjects.

In a case-series study, Goncars and associates (2019) evaluated the main symptoms of knee OA and tissue structure changes after a single-dose bone marrow-derived mononuclear cell (BM MNC) intra-articular injection. Patients with knee OA Kellgren Lawrence (K-L) grade II and III received 1 injection of BM MNC. The clinical results were analyzed with the KOOS and KSS before, 3, 6, and 12 months after injection. Radiological evaluation was performed with a calibrated X-ray and MRI before and 6 to 7 months post-injection. A total of 34 knees were treated with BM MNC injections. Mean (± SD) age of patient group was 53.96 ± 14.15 years; there were 16 men, 16 women, KL grade II, 16; KL grade III, 18. The average injected count of BM MNCs was 45.56 ± 34.94 × 10⁶ cells. At the end-point of 12 months, 65% of patients still had minimal perceptible clinical improvement of the KOOS total score. The mean improvement of KOOS total score was +15.3 and of the KSS knee score was +21.45 and the function subscale +27.08 (p < 0.05) points. The Whole Organ Magnetic Resonance Imaging Score (WORMS) improved from 44.31 to 42.93 points (p < 0.05). No adverse
effects after the BM-MNC injection were observed. The authors concluded that single-dose BM MNC partially reduced clinical signs of the knee OA stage II/III and in some cases, decreased degenerative changes in the joint building tissue over 12-month period. This was a small case-series study (n = 34 knees) with short-term follow-ups (12 months). These preliminary findings need to be validated by well-designed studies with long-term follow-up.

Appendix

Zilretta is administered as a 32 mg single intra-articular injection in the knee. Zilretta is not interchangeable with other formulations of injectable triamcinolone acetonide.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
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<tbody>
<tr>
<td></td>
<td>Arthroscopic debridement:</td>
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<tr>
<td></td>
<td>CPT codes covered if selection criteria are met:</td>
</tr>
<tr>
<td>29874</td>
<td>Arthroscopy, knee, surgical; for removal of loose body or foreign body (eg, osteochondritis dissecans fragmentation, chondral fragmentation)</td>
</tr>
<tr>
<td></td>
<td>HCPCS codes covered if selection criteria are met:</td>
</tr>
<tr>
<td>G0289</td>
<td>Arthroscopy, knee, surgical, for removal of loose body, foreign body, debridement/shaving of articular cartilage (chondroplasty) at the time of other surgical knee arthroscopy in a different compartment of the same knee</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>ICD-10 codes covered if selection criteria are met:</td>
</tr>
<tr>
<td></td>
<td>M17.0 - M17.9 Osteoarthritis of knee</td>
</tr>
<tr>
<td></td>
<td>M23.000 - M23.369 Derangement of meniscus due to old tear or injury</td>
</tr>
<tr>
<td></td>
<td>M25.561 - M25.569 Pain in knee</td>
</tr>
<tr>
<td></td>
<td>M25.661 - M25.669 Stiffness of knee, not elsewhere classified</td>
</tr>
<tr>
<td></td>
<td>Q68.6 Discoid meniscus</td>
</tr>
<tr>
<td></td>
<td><strong>Arthroscopic partial meniscectomy:</strong></td>
</tr>
<tr>
<td></td>
<td>CPT codes covered if selection criteria are met:</td>
</tr>
<tr>
<td>29880</td>
<td>Arthroscopy, knee, surgical; with meniscectomy (medial AND lateral, including any meniscal shaving) including debridement/shaving of articular cartilage (chondroplasty), same or separate compartment(s), when performed</td>
</tr>
<tr>
<td>29881</td>
<td>with meniscectomy (medial OR lateral, including any meniscal shaving) including debridement/shaving of articular cartilage (chondroplasty), same or separate compartment(s), when performed</td>
</tr>
<tr>
<td></td>
<td>CPT codes not covered for indications listed in the CPB (not all-inclusive):</td>
</tr>
<tr>
<td></td>
<td><strong>Balneotherapy - no specific code:</strong></td>
</tr>
<tr>
<td>0101T</td>
<td>Extracorporeal shock wave involving musculoskeletal system, not otherwise specified, high energy</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>----------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>0565T</td>
<td>Autologous cellular implant derived from adipose tissue for the treatment of osteoarthritis of the knees; tissue harvesting and cellular implant creation</td>
</tr>
<tr>
<td>0566T</td>
<td>Injection of cellular implant into knee joint including ultrasound guidance, unilateral</td>
</tr>
<tr>
<td>15876 -</td>
<td>Suction assisted lipectomy [for percutaneous autologous fat injections]</td>
</tr>
<tr>
<td>15879</td>
<td></td>
</tr>
<tr>
<td>20610 -</td>
<td>Arthrocentesis, aspiration and/or injection; major joint or bursa (eg, shoulder, hip, knee joint, subacromial bursa) [bone marrow aspirate concentrate] [intra-articular injections of autologous conditioned serum]</td>
</tr>
<tr>
<td>20611</td>
<td></td>
</tr>
<tr>
<td>27457</td>
<td>Osteotomy, proximal tibia, including fibular excision or osteotomy (includes correction of genu varus [bowleg] or genu valgus [knock-knee]); after epiphyseal closure [Combination of high tibial osteotomy and autologous bone marrow derived cell implantation]</td>
</tr>
<tr>
<td>29870</td>
<td>Arthroscopy, knee, diagnostic, with or without synovial biopsy (separate procedure)</td>
</tr>
<tr>
<td>29871</td>
<td>for infection, lavage and drainage [not covered for arthroscopic lavage]</td>
</tr>
<tr>
<td>29875</td>
<td>Synovectomy, limited (eg, plica or shelf resection) (separate procedure) [not covered for patellar denervation]</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>----------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>29877</td>
<td>debridement/shaving of articular cartilage (chondroplasty) [not covered for arthroscopic debridement for persons with osteoarthritis presenting with knee pain only or with severe osteoarthritis (Outerbridge classification III or IV*)]</td>
</tr>
<tr>
<td>30286</td>
<td>Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous [Stem cell therapy]</td>
</tr>
<tr>
<td>38232</td>
<td>Bone marrow harvesting for transplantation; autologous [Combination of high tibial osteotomy and autologous bone marrow derived cell implantation] [bone marrow aspirate concentrate]</td>
</tr>
<tr>
<td>38241</td>
<td>Hematopoietic progenitor cell (HPC); autologous transplantation [Combination of high tibial osteotomy and autologous bone marrow derived cell implantation] [Stem cell therapy]</td>
</tr>
<tr>
<td>96372</td>
<td>Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular [for percutaneous autologous fat injections]</td>
</tr>
</tbody>
</table>

Other CPT codes related to the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>27437</td>
<td>Arthroplasty, patella; without prosthesis</td>
</tr>
<tr>
<td>27438</td>
<td>with prosthesis</td>
</tr>
</tbody>
</table>

HCPCS codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J3304</td>
<td>Injection, triamcinolone acetonide, preservative-free, extended-release, microsphere formulation, 1 mg</td>
</tr>
</tbody>
</table>

Other HCPCS codes related to the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1776</td>
<td>Joint device (implantable)</td>
</tr>
</tbody>
</table>
### ICD-10 codes covered if selection criteria are met:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>S83.200A</td>
<td>Tear of meniscus, current injury</td>
</tr>
<tr>
<td>S83.289S</td>
<td></td>
</tr>
</tbody>
</table>

### ICD-10 codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M23.200</td>
<td>Derangement of meniscus due to old tear or injury</td>
</tr>
<tr>
<td>M23.269</td>
<td></td>
</tr>
<tr>
<td>M25.561</td>
<td>Pain in knee</td>
</tr>
<tr>
<td>M25.569</td>
<td></td>
</tr>
<tr>
<td>M25.661</td>
<td>Stiffness of knee, not elsewhere classified</td>
</tr>
<tr>
<td>M25.669</td>
<td></td>
</tr>
</tbody>
</table>

The above policy is based on the following references:


21. Gibson JN, White MD, Chapman VM, Strachan RK. Arthroscopic lavage and debridement for

22. Gillespie WJ. Arthroscopic surgery was not effective for relieving pain or improving function in osteoarthritis of the knee. ACP J Club. 2003;138(2):49.


47. Stuart MJ, Lubowitz JH. What, if any, are the indications for arthroscopic debridement of the osteoarthritic knee? Arthroscopy. 2006;22(3):238-239.


Patellar Denervation

1. Arirachakaran A, Sangkaew C, Kongtharvonskul J. Patellofemoral resurfacing and patellar denervation in


Patellofemoral Replacement (Arthroplasty)


Miscellaneous Interventions


AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0673 Osteoarthritis of the Knee: Selected Treatments

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania  revised 06/11/2020