

PICO SEARCH ASSIGNMENT WORKSHEET

Brief description of patient problem/setting (summarize the case very briefly)

A 57-year-old male with past medical history for hypertension, hyperlipidemia and BPH presents to outpatient clinic with chronic bilateral knee pain worsening over the past 2 years. He describes the pain as aching that worsens with prolonged walking. He reports occasional swelling of both knees and waking up feeling stiffness that would last 15-20 minutes. His previous Xray imaging of the knees show signs of narrowing of the joint space and some growth of bone spurs. Currently, he takes Tylenol but with little relief.

Search question: Clearly state the question (including outcomes or criteria to be tracked)

In adults with knee osteoarthritis, does exercise/physical therapy compared with NSAID therapy result in greater improvement in pain, physical function, and quality of life?

Question type: What kind of question is this?

Prevalence
Prognosis

Screening
 Treatment

Diagnosis
Harm

Assuming that the highest level of evidence to answer your question will be meta-analysis or systematic review, what other types of study might you include if these are not available (or if there is a much more current study of another type)? Please explain your choices.

If meta-analyses and systematic reviews are not available, I would include randomized controlled trials (RCTs), as they minimize bias and confounding variables through randomization and provide strong comparisons between physical therapy and NSAID pharmacotherapy for outcomes such as physical function and pain relief. I would also consider including more recent RCTs, as they may better reflect current medical recommendations and common clinical practices. If RCTs are limited or outdated, prospective cohort studies may also be helpful in tracking the effectiveness and long-term outcome of both interventions. Thus, cohort studies would be the next best level of evidence. I would avoid relying heavily on case reports or case series, as they do not provide strong comparative data and are more prone to bias.

PICO search terms:

P	I	C	O
Older adults	Physical therapy	NSAIDs	Pain relief/reduction
Knee osteoarthritis	Exercise therapy	Ibuprofen/Naproxen	Physical function
Degenerative joint knee disease	Physical rehabilitation	Anti-inflammatory medication	Mobility
			Efficacy
			Quality of life

Search tools and strategy used:

Database	Search terms used	# or results	Filters applied
PubMed	("knee osteoarthritis" OR "degenerative joint disease") AND ("physical therapy" OR "exercise") AND ("NSAIDs" OR "anti- inflammatory medications") AND ("pain relief) OR (physical function") OR ("mobility") OR ("life quality")	11	Last 10 years, full text, meta-analysis, randomized controlled trial, systematic review, English, MEDLINE
EBSCO	("knee osteoarthritis" OR "degenerative joint disease") AND ("physical therapy" OR "exercise") AND ("NSAIDs" OR "anti- inflammatory medications") AND ("pain relief) OR (physical function") OR ("mobility") OR ("treatment outcome") OR ("efficacy")	8	Past 10 years, English, Peer Reviewed, Academic Journal, Linked Full text
Google scholar	("knee osteoarthritis" OR "degenerative joint disease") AND ("physical therapy" OR "exercise") AND ("NSAIDs" OR "anti- inflammatory medications") AND ("pain relief) OR (physical function") OR ("mobility") OR ("treatment outcome") OR ("efficacy")	4,630	Time range: 2021- 2026, Review articles, sort by relevance

For this PICO question, I used the following databases: PubMed, EBSCO, and Google Scholar. In PubMed, I applied the search terms and filters listed above, which gave me 11 articles. For each

article, I read the title to gain a general understanding of each study's focus. Later, I read the abstracts of the articles that were relevant to my PICO question to better understand their objectives and findings. In the end, I chose two articles from PubMed: a systemic review and randomized controlled trial. In the EBSCO database, using the search terms and filters listed above gave me 8 articles. My approach to selecting articles was similar to the process I used for PubMed. There were a few duplicates of the ones I found on PubMed. Therefore, I decided not to select any additional articles from the EBSCO database, as they did not provide new evidence. In Google Scholar, the search resulted in 4,630 results after applying filters such as "sort by relevance" and limiting publication dates to the past five years. Since one of the filters was sort by relevance, I review the first 10 articles titles and abstracts. I focused on the finding articles that were systemic reviews, meta-analysis or randomized controlled trials. In the end, I selected two articles: a systemic review and meta-analysis and meta-analysis of randomized controlled trials.

Results found:

Article 1

Citation:

Weng Q, Goh SL, Wu J, Persson MSM, Wei J, Sarmanova A, Li X, Hall M, Doherty M, Jiang T, Zeng C, Lei G, Zhang W. Comparative efficacy of exercise therapy and oral non-steroidal anti-inflammatory drugs and paracetamol for knee or hip osteoarthritis: a network meta-analysis of randomised controlled trials. *Br J Sports Med.* 2023 Aug;57(15):990-996. doi: 10.1136/bjsports-2022-105898. Epub 2023 Jan 2. PMID: 36593092; PMCID: PMC10423468.

Type of article: Meta-analysis of randomized controlled trials

Abstract:

Objective: Clinical guidelines recommend exercise as a core treatment for knee or hip osteoarthritis (OA). However, how its analgesic effect compares to analgesics, for example, oral non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol—the most commonly used analgesics for OA—remains unknown.

Design: Network meta-analysis.

Data Sources: PubMed, Embase, Scopus, Cochrane Library, and Web of Science from database inception to January 2022.

Eligibility Criteria for Selecting Studies: Randomized controlled trials (RCTs) comparing exercise therapy with oral NSAIDs and paracetamol directly or indirectly in knee or hip OA.

Results: A total of $n = 152$ RCTs (17,431 participants) were included. For pain relief, there was no difference between exercise and oral NSAIDs and paracetamol at or nearest to 4 weeks (standardised mean difference [SMD] = -0.12, 95% credibility interval [CrI] -1.74 to 1.50; $n = 47$

RCTs), 8 weeks (SMD = 0.22, 95% CrI -0.05 to 0.49; n = 2 RCTs), and 24 weeks (SMD = 0.17, 95% CrI -0.77 to 1.12; n = 9 RCTs). Similarly, there was no difference between exercise and oral NSAIDs and paracetamol in functional improvement at or nearest to 4 weeks (SMD = 0.09, 95% CrI -1.69 to 1.85; n = 40 RCTs), 8 weeks (SMD = 0.06, 95% CrI -0.20 to 0.33; n = 2 RCTs), and 24 weeks (SMD = 0.05, 95% CrI -1.15 to 1.24; n = 9 RCTs).

Conclusions: Exercise has similar effects on pain and function to that of oral NSAIDs and paracetamol. Given its excellent safety profile, exercise should be given more prominence in clinical care, especially in older people with comorbidity or at higher risk of adverse events related to NSAIDs and paracetamol.

Key findings:

- Overall, exercise therapy is just as effective in pain management and physical function improvement for patients with knee or hip osteoarthritis compared to oral NSAIDs.
- One recent randomized controlled trial (n=94) reported that oral NSAIDs were more beneficial than exercise in people with knee OA (osteoarthritis) after 4 weeks of management
- Two other randomized controlled trials (n=141 and 142) compared 8 weeks of exercise and oral NSAIDs and found reduction in pain and improvement in function with no significant differences between the two groups.
- One randomized controlled trial (n=166) reports exercise as the more effective intervention than oral NSAIDs on knee OA pain over a 12-week period.
- Due to its safety profile, exercise therapy is a first-line treatment especially for older adults or those with multiple comorbidities because it avoids many adverse effects seen in long-term NSAID use such as gastrointestinal, renal and cardiovascular risks.
- Clinical guidelines recommend exercise as the core treatment for osteoarthritis either as stand-alone or part of a management plan with pharmacotherapy.

Why I chose this article: I chose this article because it evaluated the analgesic effects of exercise therapy/physical therapy on osteoarthritis pain compared with NSAID therapy. The study found that exercise therapy provided similar improvements in both pain and physical function when compared with NSAIDs. There were no significant differences in pain reduction or functional improvement between the two interventions. For my patient, who continues to experience chronic knee pain despite taking Tylenol, these findings suggest that exercise therapy may be a reasonable treatment option before initiating long-term NSAID therapy. Since many patients with osteoarthritis are older adults with multiple comorbidities and are often taking several medications already, exercise therapy may be more beneficial because it can provide similar symptom relief without the potential risks associated with chronic NSAID use. Additionally, the study found that exercise can be used as a stand-alone treatment while still providing comparable outcomes, which may be especially beneficial for patients dealing with polypharmacy.

Article 2

Citation:

Thorlund JB, Simic M, Pihl K, Berthelsen DB, Day R, Koes B, Juhl CB. Similar Effects of Exercise Therapy, Nonsteroidal Anti-inflammatory Drugs, and Opioids for Knee Osteoarthritis Pain: A Systematic Review with Network Meta-analysis. *J Orthop Sports Phys Ther.* 2022 Apr;52(4):207-216. doi: 10.2519/jospt.2022.10490. PMID: 35442752.

Type of article: Systematic review and meta-analysis

Abstract:

Objective: To compare the effectiveness of opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and exercise therapy for knee osteoarthritis pain.

Design: Systematic review with network meta-analysis.

Literature search: We searched the databases MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials from inception to April 15, 2021. Web of Science was used for citation tracking.

Study selection criteria: Randomized controlled trials comparing exercise therapy, NSAIDs, and opioids in any combination for knee osteoarthritis pain.

Data synthesis: Network meta-analysis comparing exercise therapy, NSAIDs, opioids, and placebo/control for knee osteoarthritis pain. Additional trials from previous reviews were included to create the external placebo/control anchor.

Results: We included 13 trials (1,398 patients) with direct comparisons, supplemented with data from 101 additional trials. The treatment effect of NSAIDs for knee osteoarthritis pain was similar to that of opioids (standardized mean difference [SMD], 0.02; 95% confidence interval [CI], -0.14 to 0.18; Grading of Recommendations, Assessment, Development and Evaluations [GRADE]: low certainty). Exercise therapy had a larger effect than NSAIDs (SMD, 0.54; 95% CI, 0.19 to 0.89; GRADE: very low certainty). No estimate could be made for exercise versus opioids due to the lack of studies. Exercise therapy ranked as the “best” intervention in the network meta-analysis, followed by NSAIDs, opioids, and placebo/control intervention (GRADE: low certainty).

Conclusion: Exercise therapy ranked as the best treatment for knee osteoarthritis pain, followed by NSAIDs and opioids. The difference between treatments was small and likely not clinically relevant, and the overall confidence in the ranking was low. The results highlight the limited evidence for comparative effectiveness between exercise therapy, NSAIDs, and opioids for knee osteoarthritis pain.

Key findings:

- Exercise therapy was ranked as the most effective treatment option and demonstrated greater osteoarthritis pain relief than topical/oral NSAID and opioid therapy.

- Despite physical therapy being most effective, quality of life utilization studies reports it being greatly under prescribed with NSAIDs being suggested more often by providers
- NSAID and opioids were found to provide similar levels of pain relief
- The study found no trials comparing exercise therapy to opioids. As a result, there was a no valid estimate of comparison between these two interventions.
- Patient may experience additional benefits besides pain reduction from exercise such as improved mobility and participation in physical activity. Many of the exercise interventions focused on improving muscle strength, mobility and knee function. Exercise therapy focused on quadricep and/or hamstring isokinetic exercises
- Exercise therapy provides pain relief without risk of opioid dependence or NSAID-related adverse effects.

Why I chose this article: This meta-analysis found that exercise therapy was ranked as the most effective intervention for osteoarthritis pain relief when compared with NSAIDs and opioids. In addition to pain relief, physical therapy offers other benefits such as improved mobility and increased participation in physical activities, which can ultimately improve a patient's overall quality of life. Although exercise therapy is recommended as a first-line treatment for osteoarthritis, it is often underutilized in clinical practice. This may be because pain medications can provide more immediate symptom relief, whereas an exercise program requires consistency, patient effort, and often guidance from a healthcare professional before meaningful results are seen. Nevertheless, therapeutic exercise not only helps reduce pain with a favorable safety profile but may also improve cardiovascular health, joint mobility, and long-term physical function. These findings are particularly relevant to my patient, who continues to experience chronic knee pain despite taking Tylenol, and suggest that physical therapy may provide benefits beyond symptom relief alone.

Article 3

Citation:

Chao J, Jing Z, Xuehua B, Peilei Y, Qi G. Effect of Systematic Exercise Rehabilitation on Patients With Knee Osteoarthritis: A Randomized Controlled Trial. *Cartilage*. 2021 Dec;13(1_suppl):1734S-1740S. doi: 10.1177/1947603520903443. Epub 2020 Feb 10. PMID: 32037857; PMCID: PMC8808852.

Type of article: Randomized controlled trial

Abstract:

Objectives: We aimed to compare the outcomes of exercise rehabilitation and conventional treatment in patients with knee osteoarthritis.

Methods: This trial included a total of 166 patients diagnosed with knee osteoarthritis; they were randomly divided into groups. The experimental group underwent systematic exercise rehabilitation, while the control group received naproxen ($n = 28$), diclofenac ($n = 27$), or

celecoxib ($n = 19$). Improvement in symptoms, knee function, and quality of life were compared. SPSS Statistics 24.0 was used for the data analysis.

Results: The mean age of patients was 56.0 ± 10.5 years, and the average follow-up time was 12 ± 2.3 weeks. No statistically significant differences were seen in age, body mass index, and sex ($P > 0.05$) between the groups. The average Western Ontario and MacMaster Universities (WOMAC) scores after treatment were 84.4 ± 15.2 , 108.3 ± 3.9 , 107.4 ± 5.4 , and 107 ± 6.0 in the exercise rehabilitation, diclofenac, naproxen, and celecoxib groups, respectively. The mean Lysholm scores were 60.3 ± 14.9 , 41.0 ± 0.1 , 43.5 ± 5.3 , and 41.7 ± 3.6 in the exercise rehabilitation, diclofenac, naproxen, and celecoxib groups, respectively. The mean SF-36 (Short Form-36 Survey) scores were 105.4 ± 21.5 , 82.5 ± 3.7 , 84.2 ± 3.5 , and 83.7 ± 5.0 in the exercise rehabilitation, naproxen, celecoxib, and diclofenac groups, respectively. The average ranges of knee motion were $125.0 \pm 6.2^\circ$, $116.4 \pm 1.4^\circ$, $114.7 \pm 1.1^\circ$, and $115.7 \pm 0.8^\circ$ after exercise rehabilitation, diclofenac, naproxen, and celecoxib treatments, respectively. These data presented statistical differences between the groups.

Conclusion: Exercise better improved symptoms and quality of life in patients with knee osteoarthritis over a 12-week follow-up period than that achieved with nonsteroidal anti-inflammatory drugs and COX-2 inhibitors.

Key findings:

- Patients who participated in the exercise rehabilitation program demonstrated significantly greater improvements in Lysholm knee scores compared with those treated with diclofenac. The exercise group achieved a Lysholm score of 77.3 ± 8.9 compared with 64.7 ± 8.1 in the diclofenac group.
- Exercise rehabilitation resulted in better quality-of-life outcomes than diclofenac therapy.
- Patients in the exercise group experienced improvements in muscle strength, flexibility, and aerobic conditioning, which contributed to better joint function. Exercise rehabilitation improved patients' ability to perform daily activities and participate in social activities compared with NSAID therapy.
- Functional improvements from exercise therapy were observed after 3 months and continued to increase with longer participation in the rehabilitation program 2 months later in a follow up.
- Inappropriate exercise programs/patterns can adversely affect the prognosis of knee OA. Treatment of knee OA requires appropriate type of exercises and intensity level

Why I chose this article: I chose this article because it directly compared exercise rehabilitation with commonly prescribed NSAIDs, including naproxen and diclofenac, in patients with knee osteoarthritis. The study found that patients who participated in exercise rehabilitation experienced greater improvements in pain, physical function, mobility, and quality of life than those receiving NSAID therapy. Additionally, exercise rehabilitation was associated with increased muscle strength, flexibility, and ability to perform daily activities. These findings are particularly relevant to my patient, who continues to experience chronic knee pain despite taking Tylenol and reports worsening symptoms with prolonged walking. Unlike Article 1, which found similar

outcomes between exercise therapy and NSAIDs, this study suggests that exercise rehabilitation may offer additional benefits beyond pain relief by improving overall function, mobility, and quality of life.

Foreign study considerations:

Cultural/social context:

This RCT study was conducted in China, where attitudes toward exercise, rehabilitation, and nonpharmacologic treatments may differ from those in the United States. Cultural beliefs and patient motivation may also influence participation and adherence to exercise programs. In addition, differences in physical activity levels, lifestyle factors, and body composition may affect treatment outcomes. Despite these differences, the benefits of exercise rehabilitation observed in this study are consistent with current osteoarthritis treatment recommendations used in the United States.

Economic context:

Healthcare systems and access to physical therapy services differ between China and the United States. The availability and cost of rehabilitation programs may influence how frequently patients utilize exercise therapy. However, both exercise therapy and NSAID therapy are commonly used treatments for knee osteoarthritis, making the findings relevant to clinical practice in the United States.

Language:

Although the study was conducted in China, it was published in English. Some patient-reported outcomes may have originally been collected in Chinese and later translated for publication, which may cause some minor differences in interpretation. However, the primary outcomes were evaluated with standardized measurements such as the WOMAC score, Lysholm score and SF-36 score. As a result, this reduces the likelihood of significant language-related bias.

Article 4

Citation:

Charlesworth J, Fitzpatrick J, Perera NKP, Orchard J. Osteoarthritis- a systematic review of long-term safety implications for osteoarthritis of the knee. BMC Musculoskelet Disord. 2019 Apr 9;20(1):151. doi: 10.1186/s12891-019-2525-0. PMID: 30961569; PMCID: PMC6454763.

Type of article: Systematic review

Abstract:

Background: There is no cure for knee osteoarthritis (KOA) and typically patients live approximately 30-years with the disease. Most common medical treatments result in short-term palliation of symptoms with little consideration of long-term risk. This systematic review aims to appraise the current evidence for the long-term (≥ 12 months) safety of common treatments for knee osteoarthritis (KOA).

Methods: Cochrane Database of Systematic Reviews, Medline and PubMed were systematically searched from 1990 to July 2017, inclusive. Inclusion criteria were 1) peer-reviewed publications investigating treatments for KOA referred to in the Australian Clinical Care Standard and/or Therapeutic Guidelines: Rheumatology 2) specifically addressing safety of the treatments 3) with ≥ 12 months of follow-up and 4) Downs and Black quality score ≥ 13 .

Results: Thirty-four studies fulfilled the inclusion criteria. Lifestyle modifications (moderate exercise and weight loss), paracetamol, glucosamine, Intraarticular Hyaluronic Acid (IAHA) and platelet-rich-plasma (PRP) injections have a low risk of harm and beneficial ≥ 12 month outcomes. Although Nonsteroidal Anti-inflammatory Drugs (NSAIDs) provide pain relief, they are associated with increased risk of medical complications. Cortisone injections are associated with radiological cartilage degeneration at > 12 months. Arthroscopy for degenerative meniscal tears in KOA leads to a 3-fold increase in total knee arthroplasty (TKA). TKA improves primary outcomes of KOA but has a low rate of significant medical complications.

Conclusions: Given the safety and effectiveness of lifestyle interventions such as weight loss and exercise, these should be advocated in all patients due to the low risk of harm. The use of NSAIDs should be minimized to avoid gastrointestinal complications. Treatment with opioids has a lack of evidence for use and a high risk of long-term harm. The use of IAHA and PRP may provide additional symptomatic benefit without the risk of harm. TKA is associated with significant medical complications but is justified by the efficacy of joint replacement in late-stage disease.

Key findings:

- Exercise interventions showed sustained benefits beyond initial treatment period
- Patients participating in exercise programs reported improved quality of life (QOL) AND daily functioning.
- Exercise has favorable long-term safety profile
- Weight loss combined with exercise provided additional symptom improvements
- NSAIDs provided symptom relief with the risk of gastrointestinal, cardiovascular and renal complications
- Exercise therapy was recommended as the core treatment plan regardless of disease severity

Why I chose this article: I chose this article because it examined the long-term management of knee osteoarthritis rather than focusing solely on short-term symptom relief. My patient has been experiencing chronic knee pain for the past 2 years, suggesting that she will likely require ongoing treatment rather than a temporary intervention. The review found that exercise programs provided sustained improvements in pain, mobility, and physical function while maintaining a favorable safety profile. In contrast, although NSAIDs can be effective for symptom relief, their long-term use may be associated with gastrointestinal, cardiovascular, and renal complications. This is especially important because my patient already has hypertension and hyperlipidemia, which may increase concern for some of the adverse effects associated with chronic NSAID use. I chose this article because it highlights that physical therapy is not only effective for improving symptoms but may also be a safer long-term treatment strategy for patients with chronic knee

osteoarthritis. These findings provide evidence that exercise therapy can offer lasting improvements in pain and function while reducing the risks associated with prolonged medication use.

Clinical bottom line:

Based on the articles reviewed, exercise therapy/physical therapy should be considered a first-line treatment option for this patient with chronic knee osteoarthritis. Overall, the evidence showed that exercise therapy provides similar, and in some studies greater, improvement in pain, physical function, mobility, and quality of life when compared with NSAID therapy. NSAIDs may still be helpful for short-term symptom relief, but they are not ideal as a long-term primary treatment, especially for patients with comorbidities such as hypertension and hyperlipidemia due to possible cardiovascular, renal, and gastrointestinal risks. For this patient, who has had bilateral knee pain for 2 years and only minimal relief with Tylenol, referral to physical therapy would be reasonable before relying on long-term NSAID therapy. Access to physical therapy (PT) can be a major barrier in treatment of osteoarthritis. Patients may have difficulty attending PT due to transportation issues, work schedules, insurance coverage, copays, or limited availability of nearby clinics. Health literacy may also affect whether patients understand that exercise therapy is a progressive and active treatment and not just a “one-time workout session.” Some patients may prefer medication because it provides faster relief and requires less time commitment. Because of this, management should include not only a PT referral, but also patient education, setting realistic goals, and a home exercise plan if outpatient PT is difficult to access. For this patient, the best approach would be to recommend supervised physical therapy if available and encourage low impact/intensity aerobic exercise and strengthening. NSAIDs should be reserved for short-term use when appropriate. This will balance effectiveness, safety, and social barriers that may affect compliance to the exercise program.