Evidence Portfolio – Chronic Conditions Subcommittee, Question 2

In individuals with osteoarthritis, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, (4) disease progression, and (5) pain?

a. Is there a dose-response relationship? If yes, what is the shape of the relationship?
b. Does the relationship vary by age, sex, race/ethnicity, socio-economic status, or weight status?
c. Does the relationship vary based on: frequency, duration, intensity, type (mode), or how physical activity is measured?

Sources of Evidence: Original Research, Existing Systematic Review, and Existing Meta-Analyses

Conclusion Statements and Grades

RISK OF CO-MORBID CONDITIONS

Insufficient evidence is available to determine whether a relationship exists between greater amounts of physical activity and comorbidities in individuals with osteoarthritis. **PAGAC Grade: Not assignable.**

PHYSICAL FUNCTION OR PAIN

Strong evidence demonstrates a relationship between greater amounts of physical activity with decreased pain and improved physical function in adults with osteoarthritis of the knee and hip. **PAGAC Grade: Strong**.

Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity with pain or physical function in individuals with osteoarthritis. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity with pain or physical function varies by age, sex, race/ethnicity, socioeconomic status, or body weight status in individuals with osteoarthritis. **PAGAC Grade: Not assignable**.

Limited evidence suggests that greater intensity or duration of aerobic and muscle-strengthening physical activity is related to improvement in pain and physical function in individuals with osteoarthritis of the knee and hip. **PAGAC Grade: Limited.**

HEALTH-RELATED QUALITY OF LIFE

Moderate evidence indicates a relationship between greater amounts of physical activity and improved health-related quality of life in individuals with osteoarthritis of the knee and hip. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether a dose-response relationship exists between physical activity and health-related quality of life in individuals with osteoarthritis. **PAGAC Grade: Not assignable.**

Insufficient evidence is available to determine whether the relationship between physical activity and health-related quality of life varies by age, sex, race/ethnicity, socioeconomic status, or body weight status in individuals with osteoarthritis. **PAGAC Grade: Not assignable**.

Insufficient evidence is available to determine whether the frequency, duration, intensity, or type (mode) of physical activity is related to health-related quality of life in individuals with osteoarthritis. **PAGAC Grade: Not assignable.**

DISEASE PROGRESSION

Moderate evidence indicates a relationship between physical activity and disease progression in individuals with osteoarthritis. Moderate evidence indicates that up to the range of 10,000 steps per day, ambulatory physical activity does not accelerate osteoarthritis of the knee. **PAGAC Grade: Moderate.**

Moderate evidence indicates a dose-response relationship between physical activity and disease progression in individuals with osteoarthritis. The relationship appears to be U-shaped. **PAGAC Grade: Moderate.**

Insufficient evidence is available to determine whether the relationship between physical activity and progression varies by age, sex, race/ethnicity, socioeconomic status, or body weight status in individuals with osteoarthritis. **PAGAC Grade: Not assignable**.

Insufficient evidence is available to determine whether the frequency, duration, intensity, or type (mode) of physical activity is related to progression in individuals with osteoarthritis. **PAGAC Grade: Not assignable.**

Description of the Evidence

An initial search for systematic reviews, meta-analyses, pooled analyses, and reports identified sufficient literature to answer four of the five health outcomes in the research question. The initial search for systematic reviews, meta-analyses, pooled analyses, and reports did not identify sufficient literature to answer the disease progression health outcome in the research question as determined by the Chronic Conditions Subcommittee. A supplementary search for original research was conducted to capture literature related to the disease progression health outcome.

PAIN

Existing Meta-Analyses

Overview

A total of 5 meta-analyses were included.[1-5] The reviews were published between 2014 and 2016 and included a range of 11 to 54 studies. The meta-analyses covered an extensive timeframe: inception to 2012,[5] inception to 2013,[4] inception to 2014,[2] and 1945 to April 2015.[1] Chang et al[3] did not report on the search timeframe.

Exposures

The meta-analyses examined a variety of physical activity interventions, including land-based therapeutic strength and aerobic exercises,[2, 4] aquatic activities,[1, 2] and tai chi.[3, 4] Juhl et al[5] examined single exercises or a combination of exercises, including aerobic, resistance, and performance training.

Outcomes

The included reviews[1-5] addressed pain as an outcome using a variety of scales (e.g., Western Ontario and McMaster's Osteoarthritis Index, Lequesne Osteoarthritis Index).

PHYSICAL FUNCTION

Existing Meta-Analyses

Overview

A total of 5 meta-analyses were included.[1, 3-6] These reviews were published between 2011 and 2016 and included a range of 11 to 54 studies. The meta-analyses covered an extensive timeframe: inception to 2010,[6] inception to 2012,[5] inception to 2013,[4] and 1945 to April 2015.[1] Chang et al[3] did not report on the search timeframe.

Exposures

The meta-analyses examined a variety of physical activity interventions, including land-based strength and aerobic exercises,[4, 6] aquatic activities,[1, 6] and tai chi.[3, 4, 6] Juhl et al[5] examined single exercises or a combination of exercises, including aerobic, resistance, and performance training.

Outcomes

The included reviews addressed physical function outcomes in a variety of ways, including perceived self-efficacy and cognitive and emotional impairment[3]; functional aerobic capacity[3, 6]; and disability and physical function measured using the Activities of Daily Living Scale, Western Ontario and McMaster's Osteoarthritis Index, or Global Disability Scores, among other tools.[1, 4, 5]

HEALTH-RELATED QUALITY OF LIFE

Existing Meta-Analyses

Overview

A total of 2 meta-analyses were included.[1, 4] The reviews were published in 2015 and 2016 and included a range of 13–54 studies. The 2 meta-analyses covered an extensive timeframe: from inception to 2013[4] and from 1945 to April 2015.[1]

Exposures

Fransen et al[4] examined a variety of land-based therapeutic exercises, including muscle strengthening, balance training, aerobic walking, cycling, and tai chi. Bartels et al[1] assessed various types of exercises (e.g., range of motion, strength, aerobics) performed in a therapeutic or heated indoor pool.

Outcomes

The included reviews addressed health-related quality of life as an outcome using a variety of scales.[1, 4]

DISEASE PROGRESSION

Existing Systematic Review and Meta-Analysis

Overview

A total of 2 existing reviews were included: 1 systematic review[7] and 1 meta-analysis.[8] The reviews were published in 2015 and 2016. The systematic review[7] included 49 studies published from inception to 2013. The meta-analysis included 3 studies published from inception to 2015.

Exposures

The meta-analysis[8] assessed self-reported running or jogging (including running-related sports such as triathlon and orienteering). The studies included in the systematic review[7] used low-impact therapeutic physical activity combining strengthening, stretching, and aerobic elements.

Outcomes

Timmins et al[8] used radiography, imaging, and questionnaires to examine diagnosis of knee osteoarthritis, radiographic markers of knee osteoarthritis, knee joint surgery for osteoarthritis, knee pain, and knee-associated disability. Quicke et al[7] assessed structural osteoarthritis imaging progression or progression to total knee replacement as outcomes.

Original Research

Overview

A total of 5 original research studies that examined the relationship between physical activity and disease progression were included as sources of evidence.[9-13] All studies were prospective cohorts and were published from 2013 to 2016.

The analytical sample size ranged from 100[11] to 2,073.[10] Of the 4 studies that reported location, 3 were conducted in the United States[10, 12, 13] and 1 was conducted in Tasmania.[9]

Exposure

The included studies examined self-reported[10-12] physical activity using the Physical Activity Scale for the Elderly (PASE), and measured steps objectively via accelerometer or pedometer.[9, 13]

Outcomes

All included studies examined osteoarthritis progression (e.g., knee structural change, cartilage loss) as the outcome.

Populations Analyzed

The table below lists the populations analyzed in each article.

Table 1. Populations Analyzed by All Sources of Evidence

	Age	Chronic Conditions	Other
Bartels, 2016	Older adults	Osteoarthritis	
Beumer, 2016	Adults	Osteoarthritis	
Chang, 2016	Adults	Osteoarthritis	
Dore, 2013	Age 50–80	Subjects with and without pre-existing knee abnormalities (56–58% with knee osteoarthritis)	
Escalante, 2011	Adults	Osteoarthritis	
Felson, 2013	Mean 61	With or at high risk of knee osteoarthritis	
Fransen, 2015	Adults	Osteoarthritis	
Juhl, 2014	52.2–73.8	Osteoarthritis	
Kwee, 2016	45–79	Osteoarthritis	
Lin, 2013	45–60		
Oiestad, 2015	50–79	Subjects at high risk or with osteoarthritis diagnosis (Kellgren and Lawrence grades <3)	
Quicke, 2016	Mean age >45	Osteoarthritis	Knee pain
Timmins, 2016	Adults	Osteoarthritis	

Existing Systematic Review and Meta-Analyses

Table 2. Existing Systematic Review and Meta-Analyses Individual Evidence Summary Tables

<table>
<tr><th colspan="2">Pain, Physical Function, and Health-Related Quality of Life</th></tr>
<tr><td colspan="2">Meta-Analysis
Citation: Bartels EM, Juhl CB, Christensen R, et al. Aquatic exercise for the treatment of knee and hip osteoarthritis. Cochrane Database Syst Rev. March 2016:Cd005523. doi:10.1002/14651858.CD005523.pub3.</td></tr>
<tr><td>Purpose: To evaluate the effects of aquatic exercise for people with knee or hip osteoarthritis, or both, compared to no intervention.</td><td rowspan="5">Abstract: BACKGROUND: Osteoarthritis is a chronic disease characterized by joint pain, tenderness, and limitation of movement. At present, no cure is available. Thus only treatment of the person's symptoms and treatment to prevent further development of the disease are possible. Clinical trials indicate that aquatic exercise may have advantages for people with osteoarthritis. This is an update of a published Cochrane review. OBJECTIVES: To evaluate the effects of aquatic exercise for people with knee or hip osteoarthritis, or both, compared to no intervention. SEARCH METHODS: We searched the following databases up to 28 April 2015: the Cochrane Central Register of Controlled Trials (CENTRAL; the Cochrane Library Issue 1, 2014), MEDLINE (from 1949), EMBASE (from 1980), CINAHL (from 1982), PEDro (Physiotherapy Evidence Database), and Web of Science (from 1945). There was no language restriction. SELECTION CRITERIA: Randomized controlled clinical trials of aquatic exercise compared to a control group (e.g. usual care, education, social attention, telephone call, waiting list for surgery) of participants with knee or hip osteoarthritis. DATA COLLECTION AND ANALYSIS: Two review authors independently selected trials for inclusion, extracted data and assessed risk of bias of the included trials. We analysed the pooled results using standardized mean difference (SMD) values. MAIN RESULTS: Nine new trials met the inclusion criteria and we excluded two earlier included trials. Thus the number of participants increased from 800 to 1190 and the number of included trials increased from six to 13. Most participants were female (75%), with an average age of 68 years and a body mass index (BMI) of 29.4. Osteoarthritis duration was 6.7 years, with a great variation of the included participants. The mean aquatic exercise duration was 12 weeks. We found 12 trials at low to unclear risk of bias for all domains except blinding of participants and personnel. They showed that aquatic exercise caused a small short term improvement compared to control in pain (SMD -0.31, 95% CI -0.47 to -0.15; 12 trials, 1076 participants) and disability (SMD -0.32, 95% CI -0.47 to -0.17; 12 trials, 1059 participants). Ten trials showed a small effect on quality of life (QoL) (SMD -0.25, 95% CI -0.49 to -0.01; 10 trials, 971 participants). These effects on pain and disability correspond to a five point lower (95% CI three to eight points lower) score on mean pain and mean disability compared to the control group (scale 0 to 100), and a seven point higher (95% CI 0 to 13 points higher) score on mean QoL compared with control group (scale 0 to 100). No included trials performed a radiographic evaluation. No serious adverse events were reported in the included trials with relation to aquatic exercise. AUTHORS' CONCLUSIONS: There is moderate quality evidence that aquatic</td></tr>
<tr><td>Timeframe: 1945–April 2015</td></tr>
<tr><td>Total # of Studies: 13</td></tr>
<tr><td>Exposure Definition: All types of exercises (e.g., range of motion, strength, aerobics) performed in a therapeutic/heated indoor pool. The mean length of the interventions was 12 weeks (range 6–20 weeks).
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Pain, disability, quality of life: measurement tools, e.g., Activities of Daily Living Scale, visual analog scale, short form health survey (SF 36/12/8), Western Ontario and McMaster Universities Arthritis Index (WOMAC) physical function subscale with a scale of 0–100.</td></tr>
</table>

Examine Cardiorespiratory Fitness as Outcome: No	exercise may have small, short-term, and clinically relevant effects on patient-reported pain, disability, and QoL in people with knee and hip OA. The conclusions of this review update does not change those of the previous published version of this Cochrane review.
Populations Analyzed: Older adults, Osteoarthritis	**Author-Stated Funding Source:** The Oak Foundation.

<table>
<tr><th colspan="2">Pain</th></tr>
<tr><td colspan="2">Meta-Analysis
Citation: Beumer L, Wong J, Warden SJ, Kemp JL, Foster P, Crossley KM. Effects of exercise and manual therapy on pain associated with hip osteoarthritis: a systematic review and meta-analysis. Br J Sports Med. 2016;50(8):458–463. doi:10.1136/bjsports-2015-095255.</td></tr>
<tr><td>Purpose: To examine the short-term, medium-term, and long-term efficacy of land-based and water-based exercise therapies and manual therapies in the reduction of pain in patients with hip osteoarthritis.</td><td rowspan="4">Abstract: AIM: To explore the effects of exercise (water-based or land-based) and/or manual therapies on pain in adults with clinically and/or radiographically diagnosed hip osteoarthritis (OA). METHODS: A systematic review and meta-analysis was performed, with patient reported pain assessed using a visual analogue scale (VAS) or the Western Ontario and McMaster Universities Arthritis Index (WOMAC) pain subscale. Data were grouped by follow-up time (0-3 months=short term; 4-12 months=medium term and; >12 months=long term), and standardised mean differences (SMD) with 95% CIs were used to establish intervention effect sizes. Study quality was assessed using modified PEDro scores. RESULTS: 19 trials were included. Four studies showed short-term benefits favouring water-based exercise over minimal control using the WOMAC pain subscale (SMD -0.53, 95% CI -0.96 to -0.10). Six studies supported a short-term benefit of land-based exercise compared to minimal control on VAS assessed pain (SMD -0.49, 95% CI -0.70 to -0.29). There were no medium (SMD -0.23, 95% CI -0.48 to 0.03) or long (SMD -0.22, 95% CI -0.51 to 0.06) term benefits of exercise therapy, or benefit of combining exercise therapy with manual therapy (SMD -0.38, 95% CI -0.88 to 0.13) when compared to minimal control. CONCLUSIONS: Best available evidence indicates that exercise therapy (whether land-based or water-based) is more effective than minimal control in managing pain associated with hip OA in the short term. Larger high-quality RCTs are needed to establish the effectiveness of exercise and manual therapies in the medium and long term.</td></tr>
<tr><td>Timeframe: Inception–July 2014</td></tr>
<tr><td>Total # of Studies: 19</td></tr>
<tr><td>Exposure Definition: Exercise or manual therapies. Exercise therapies were either land or water based. Intervention durations were <3 months, 4–12 months, and >12 months. Study and intervention characteristics were included in 2 appendices.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Pain: patient-reported, assessed using a visual analogue scale (VAS) or the Western Ontario and McMaster Universities Arthritis Index (WOMAC) pain subscale.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Adults, Osteoarthritis</td><td>Author-Stated Funding Source: No funding source used.</td></tr>
</table>

<table>
<tr><th colspan="2">Pain and Physical Function</th></tr>
<tr><td colspan="2">Meta-Analysis
Citation: Chang WD, Chen S, Lee CL, Lin HY, Lai PT. The effects of tai chi chuan on improving mind-body health for knee osteoarthritis patients: a systematic review and meta-analysis. Evid Based Complement Alternat Med. July 2016:1813979. doi:10.1155/2016/1813979.</td></tr>
<tr><td>Purpose: To conduct a meta-analysis and systematic review examining whether tai chi chuan could have mental and physical benefits for patients with knee osteoarthritis.</td><td rowspan="4">Abstract: Purpose. To conduct a meta-analysis and systematic review examining whether Tai Chi Chuan could have mental and physical benefits for patients with knee osteoarthritis. Methods. MEDLINE, PUBMED, EMBASE, and CINAHL databases were searched for relevant studies. Data of the studies were collected, and outcomes were classified using the International Classification of Functioning, Disability, and Health model. Effect sizes of the mental and physical components were determined, along with the recommendation grades of Philadelphia Panel Classification System for Tai Chi Chuan on knee osteoarthritis. Results. Eleven studies were selected and retrieved from the databases. The results of meta-analysis revealed that the effects of Tai Chi Chuan were observed for physical components in the body functions and structures domain. The effects favoring Tai Chi Chuan were observed in the physical component in the activities and participation domain. Insufficient data was included in the meta-analysis of the mental component. Conclusions. The review revealed that Tai Chi Chuan had beneficial outcomes for patients with knee osteoarthritis. The evidence-based results represented that it had small-to-moderate effects on body functions and structures, activities, and participation of physical component. However, there was insufficient evidence to support that Tai Chi Chuan had beneficial mental effect.</td></tr>
<tr><td>Timeframe: Not reported</td></tr>
<tr><td>Total # of Studies: 11</td></tr>
<tr><td>Exposure Definition: Tai chi chuan was the primary intervention exercise; 12–31 movements of Sun-style form and 10–24 movements of Yang-style form were adopted, and 40- to 65-minute training sessions of tai chi chuan class were conducted 1–4 times each week for 6–24 weeks.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Perceived self-efficacy, benefits, barriers, and emotional salience: 28-item motivation scale for health behaviors. Cognitive and emotional impairment: 60-point Center for Epidemiologic Studies Depression Index and 30-point mini-mental state examination. Severity of pain during knee movement: 10-point visual analog scale and 35-point knee pain scale of Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Knee muscle strength, endurance, and range of motion: isokinetic dynamometer and a goniometer. Cardiovascular functioning: 6-minute walk test, stair climb test, sit-to-stand test, and Timed Up and Go test.
Examine Cardiorespiratory Fitness as Outcome: Yes</td></tr>
<tr><td>Populations Analyzed: Adults, Osteoarthritis</td><td>Author-Stated Funding Source: China Medical University.</td></tr>
</table>

<table>
<tr><th colspan="2">Physical Function</th></tr>
<tr><td colspan="2">Meta-Analysis
Citation: Escalante Y, Garcia-Hermoso A, Saavedra JM. Effects of exercise on functional aerobic capacity in lower limb osteoarthritis: a systematic review. J Sci Med Sport. 2011;14(3):190–198. doi:10.1016/j.jsams.2010.10.004.</td></tr>
<tr><td>Purpose: To summarize evidence for the effectiveness and structure of exercise programs on functional aerobic capacity in patients with hip and knee osteoarthritis.</td><td rowspan="5">Abstract: Osteoarthritis (OA) is a degenerative joint disease. The reduced aerobic capacity of patients with lower limb osteoarthritis affects their independence in performing everyday activities. The purpose of this systematic review was to summarize evidence for the effectiveness and structure of exercise programs on functional aerobic capacity (ability to perform activities of daily living that require sustained aerobic metabolism) in patients with hip and knee osteoarthritis. A computerized search was made of seven databases. Effect sizes (ES) and 95% confidence intervals (CI) were calculated, and the heterogeneity of the studies was assessed using Cochran's Q statistic applied to the ES means. The 20 studies that satisfied the inclusion criteria were selected for analysis. These studies were grouped into five categories according to the characteristics of the exercise program: land-based interventions (strength programs, tai chi, aerobic programs, mixed exercise programs) and aquatic intervention (hydrotherapy). The functional aerobic capacity improved in tai chi programs (ES=0.66; 95% CI, 0.23-1.09), aerobic programs (ES=0.90; 95% CI, 0.70-1.10), and mixed programs (ES=0.47; 95% CI, -0.38-0.39). The conclusions were: (i) despite recommendations for the use of exercise programs for aerobic fitness in patients with hip and knee osteoarthritis, few randomized clinical trials have been conducted; (ii) the structure of the exercise programs (program content and duration, and session frequency and duration) is very heterogeneous; (iii) overall, exercise programs based on tai chi, aerobic, and mixed exercise seem to give better results than hydrotherapy programs, but without the differences being altogether clear.</td></tr>
<tr><td>Timeframe: Inception–August 2010</td></tr>
<tr><td>Total # of Studies: 20</td></tr>
<tr><td>Exposure Definition: Physical exercise, including land exercise (strength, tai chi, aerobic, mixed programs) and aquatic interventions; minimum program duration of 4 weeks.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Aerobic capacity: 6-minute walk test.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Adults, Osteoarthritis</td><td>Author-Stated Funding Source: Ministry of Education; Social European Funds and the Autonomous Government of Extremadura.</td></tr>
</table>

Pain, Physical Function, and Health-Related Quality of Life	
Meta-Analysis **Citation:** Fransen M, McConnell S, Harmer AR, Van der Esch M, Simic M, Bennell KL. Exercise for osteoarthritis of the knee: a Cochrane systematic review. *Br J Sports Med*. 2015;49(24):1554–1557. doi:10.1136/bjsports-2015-095424.	
Purpose: To determine whether land-based therapeutic exercise is beneficial for people with knee osteoarthritis in terms of reduced joint pain or improved physical function and quality of life.	**Abstract:** OBJECTIVE: To determine whether land-based therapeutic exercise is beneficial for people with knee osteoarthritis (OA) in terms of reduced joint pain or improved physical function and quality of life. METHODS: Five electronic databases were searched, up until May 2013. Randomised clinical trials comparing some form of land-based therapeutic exercise with a non-exercise control were selected. Three teams of two review authors independently extracted data and assessed risk of bias for each study. Standardised mean differences immediately after treatment and 2-6 months after cessation of formal treatment were separately pooled using a random effects model. RESULTS: In total, 54 studies were identified. Overall, 19 (35%) studies reported adequate random sequence generation, allocation concealment and adequately accounted for incomplete outcome data. However, research results may be vulnerable to selection, attrition and detection bias. Pooled results from 44 trials indicated that exercise significantly reduced pain (12 points/100; 95% CI 10 to 15) and improved physical function (10 points/100; 95% CI 8 to 13) to a moderate degree immediately after treatment, while evidence from 13 studies revealed that exercise significantly improved quality of life immediately after treatment with small effect (4 points/100; 95% CI 2 to 5). In addition, 12 studies provided 2-month to 6-month post-treatment sustainability data which showed significantly reduced knee pain (6 points/100; 95% CI 3 to 9) and 10 studies which showed improved physical function (3 points/100; 95% CI 1 to 5). CONCLUSIONS: Among people with knee osteoarthritis, land-based therapeutic exercise provides short-term benefit that is sustained for at least 2-6 months after cessation of formal treatment.
Timeframe: Inception–May 2013	
Total # of Studies: 54	
Exposure Definition: Land-based therapeutic exercises, which varied widely in the type, location, frequency, duration, and intensity of exercise. Examples of exercise programs include a multimodal intervention with manual therapy, upper limb and trunk muscle strengthening, and balance training. Aerobic walking, cycling, and tai chi were also used as interventions, which ranged from 1 day per week to 5 days per week. Sessions lasted 20–60 minutes. **Measures Steps:** No **Measures Bouts:** No **Examines HIIT:** No	
Outcomes Addressed: Pain, physical function, quality of life: Scales (e.g., Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC], global disability scores, global pain scores, Short Form 36, sickness impact profile, or Lequesne Osteroarthritis Index). **Examine Cardiorespiratory Fitness as Outcome:** No	
Populations Analyzed: Adults, Osteoarthritis	**Author-Stated Funding Source:** National Health and Medical Research Council, Australia.

<table>
<tr><th colspan="2">Pain and Physical Function</th></tr>
<tr><td colspan="2">Meta-Analysis
Citation: Juhl C, Christensen R, Roos EM, Zhang W, Lund H. Impact of exercise type and dose on pain and disability in knee osteoarthritis: a systematic review and meta-regression analysis of randomized controlled trials. Arthritis Rheumatol. 2014;66(3):622–636. doi:10.1002/art.38290.</td></tr>
<tr><td>Purpose: To analyze the effect of exercise therapy interventions in order to identify the optimal exercise program for reducing pain and disability in knee osteoarthritis among adults.</td><td rowspan="5">Abstract: OBJECTIVE: To identify the optimal exercise program, characterized by type and intensity of exercise, length of program, duration of individual supervised sessions, and number of sessions per week, for reducing pain and patient-reported disability in knee osteoarthritis (OA). METHODS: A systematic review and meta-analysis of randomized controlled trials were performed. Standardized mean differences (SMDs) were combined using a random-effects model. Study-level covariates were applied in meta-regression analyses in order to reduce between-study heterogeneity. RESULTS: Forty-eight trials were included. Similar effects in reducing pain were found for aerobic, resistance, and performance exercise (SMD 0.67, 0.62, and 0.48, respectively; P = 0.733). These single-type exercise programs were more efficacious than programs that included different exercise types (SMD 0.61 versus 0.16; P < 0.001). The effect of aerobic exercise on pain relief increased with an increased number of supervised sessions (slope 0.022 [95% confidence interval 0.002, 0.043]). More pain reduction occurred with quadriceps-specific exercise than with lower limb exercise (SMD 0.85 versus 0.39; P = 0.005) and when supervised exercise was performed at least 3 times a week (SMD 0.68 versus 0.41; P = 0.017). No impact of intensity, duration of individual sessions, or patient characteristics was found. Similar results were found for the effect on patient-reported disability. CONCLUSION: Optimal exercise programs for knee OA should have one aim and focus on improving aerobic capacity, quadriceps muscle strength, or lower extremity performance. For best results, the program should be supervised and carried out 3 times a week. Such programs have a similar effect regardless of patient characteristics, including radiographic severity and baseline pain.</td></tr>
<tr><td>Timeframe: Inception–May 2012</td></tr>
<tr><td>Total # of Studies: 48</td></tr>
<tr><td>Exposure Definition: Exercise programs classified as a single type of exercise (at least 75% of the exercise session, including warm-up and cooldown, involved one type of exercise) or as consisting of a combination of different types of exercise (several types of exercise with different aims were performed within the same session). Stratified analysis by type (aerobic, resistance, or performance) and amount of exercise (low: up to 12 sessions, intermediate: 13–24, large: >25 sessions).
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Pain. Disability.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Ages 52.2–73.8, Osteoarthritis</td><td>Author-Stated Funding Source: Health Insurance Foundation; Danish Physiotherapy Association; Oak Foundation.</td></tr>
</table>

<table>
<tr><th colspan="2">Progression</th></tr>
<tr><td colspan="2">Systematic Review
Citation: Quicke JG, Foster NE, Thomas MJ, Holden MA. Is long-term physical activity safe for older adults with knee pain? A systematic review. Osteoarthritis Cartilage. 2015;23(9):1445–1456. doi:10.1016/j.joca.2015.05.002.</td></tr>
<tr><td>Purpose: To synthesize existing literature from multiple safety-related outcome domains to determine whether long-term PA is safe for older adults with knee pain.</td><td rowspan="4">Abstract: OBJECTIVE: To determine whether long-term physical activity is safe for older adults with knee pain. DESIGN: A comprehensive systematic review and narrative synthesis of existing literature was conducted using multiple electronic databases from inception until May 2013. Two reviewers independently screened, checked data extraction and carried out quality assessment. Inclusion criteria for study designs were randomised controlled trials (RCTs), prospective cohort studies or case control studies, which included adults of mean age over 45 years old with knee pain or osteoarthritis (OA), undertaking physical activity over at least 3 months and which measured a safety related outcome (adverse events, pain, physical functioning, structural OA imaging progression or progression to total knee replacement (TKR)). RESULTS: Of the 8614 unique references identified, 49 studies were included in the review, comprising 48 RCTs and one case control study. RCTs varied in quality and included an array of low impact therapeutic exercise interventions of varying cardiovascular intensity. There was no evidence of serious adverse events, increases in pain, decreases in physical function, progression of structural OA on imaging or increased TKR at group level. The case control study concluded that increasing levels of regular physical activity was associated with lower risk of progression to TKR. CONCLUSIONS: Long-term therapeutic exercise lasting 3 to 30 months is safe for most older adults with knee pain. This evidence supports current clinical guideline recommendations. However, most studies investigated selected, consenting older adults carrying out low impact therapeutic exercise which may affect result generalizability. SYSTEMATIC REVIEW REGISTRATION: PROSPERO 2014:CRD42014006913.</td></tr>
<tr><td>Timeframe: Inception–May 2013</td></tr>
<tr><td>Total # of Studies: 49</td></tr>
<tr><td>Exposure Definition: PA type, intensity, and duration varied widely. All of the randomized controlled trials investigated therapeutic exercise PA and were considered low impact. “Mixed” exercise interventions combining strengthening, stretching, and aerobic elements were most common. Duration ranged from 3 months to 30 months, and frequency varied from 1 to 3 sessions/week.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Pain: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scale and numerical pain scales. Physical function: WOMAC function and various objective function tests. Measures of osteoarthritis progression from imaging of the tibiofemoral joint: Kellgren and Lawrence score, joint space width, joint space narrowing, osteoarthritis severity, and cartilage volume.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Mean age >45, Knee pain and/or a diagnosis of osteoarthritis</td><td>Author-Stated Funding Source: National Institute for Health Research, Arthritis Research (UK).</td></tr>
</table>

<table>
<tr><th colspan="2">Progression</th></tr>
<tr><td colspan="2">Meta-Analysis
Citation: Timmins KA, Leech RD, Batt ME, Edwards KL. Running and knee osteoarthritis: a systematic review and meta-analysis. Am J Sports Med. 2016;45(6):1447-1457. doi:10.1177/0363546516657531.</td></tr>
<tr><td>Purpose: To determine, from the published literature, the role of running in the development of knee osteoarthritis.</td><td rowspan="4">Abstract: BACKGROUND: Osteoarthritis (OA) is a chronic condition characterized by pain, impaired function, and reduced quality of life. A number of risk factors for knee OA have been identified, such as obesity, occupation, and injury. The association between knee OA and physical activity or particular sports such as running is less clear. Previous reviews, and the evidence that informs them, present contradictory or inconclusive findings. PURPOSE: This systematic review aimed to determine the association between running and the development of knee OA. STUDY DESIGN: Systematic review and meta-analysis. METHODS: Four electronic databases were searched, along with citations in eligible articles and reviews and the contents of recent journal issues. Two reviewers independently screened the titles and abstracts using prespecified eligibility criteria. Full-text articles were also independently assessed for eligibility. Eligible studies were those in which running or running-related sports (eg, triathlon or orienteering) were assessed as a risk factor for the onset or progression of knee OA in adults. Relevant outcomes included (1) diagnosis of knee OA, (2) radiographic markers of knee OA, (3) knee joint surgery for OA, (4) knee pain, and (5) knee-associated disability. Risk of bias was judged by use of the Newcastle-Ottawa scale. A random-effects meta-analysis was performed with case-control studies investigating arthroplasty. RESULTS: After de-duplication, the search returned 1322 records. Of these, 153 full-text articles were assessed; 25 were eligible, describing 15 studies: 11 cohort (6 retrospective) and 4 case-control studies. Findings of studies with a diagnostic OA outcome were mixed. Some radiographic differences were observed in runners, but only at baseline within some subgroups. Meta-analysis suggested a protective effect of running against surgery due to OA: pooled odds ratio 0.46 (95% CI, 0.30-0.71). The I2 was 0% (95% CI, 0%-73%). Evidence relating to symptomatic outcomes was sparse and inconclusive. CONCLUSION: With this evidence, it is not possible to determine the role of running in knee OA. Moderate- to low-quality evidence suggests no association with OA diagnosis, a positive association with OA diagnosis, and a negative association with knee OA surgery. Conflicting results may reflect methodological heterogeneity. More evidence from well-designed, prospective studies is needed to clarify the contradictions.</td></tr>
<tr><td>Timeframe: Inception–November 2015</td></tr>
<tr><td>Total # of Studies: 15 (3 in meta-analysis)</td></tr>
<tr><td>Exposure Definition: Any form of running or jogging (including running-related sports such as triathlon and orienteering) assessed by questionnaires.
Measures Steps: No
Measures Bouts: No
Examines HIIT: No</td></tr>
<tr><td>Outcomes Addressed: Radiographic and imaging markers of osteoarthritis (e.g., osteophytes, sclerosis, cartilage thickness, volume, or surface area). Knee arthroplasty: attained from registries. Knee pain and knee-associated disability: questionnaires.
Examine Cardiorespiratory Fitness as Outcome: No</td></tr>
<tr><td>Populations Analyzed: Adults, Osteoarthritis</td><td>Author-Stated Funding Source: Arthritis Research UK.</td></tr>
</table>

Table 3. Existing Systematic Review and Meta-Analyses Quality Assessment Chart

AMSTARExBP: SR/MA	Bartels, 2016	Beumer, 2016	Chang, 2016	Escalante, 2011	Fransen, 2015	Juhl, 2014	Quicke, 2015	Timmins, 2016
Review questions and inclusion/exclusion criteria delineated prior to executing search strategy.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Population variables defined and considered in methods.	No	No	No	Yes	No	Yes	No	No
Comprehensive literature search performed.	Yes	Yes	Partially Yes	Partially Yes	Yes	Yes	Yes	Yes
Duplicate study selection and data extraction performed.	Yes	No	No	No	Yes	No	Yes	Yes
Search strategy clearly described.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Relevant grey literature included in review.	Yes	Yes	No	No	Yes	Yes	Yes	No
List of studies (included and excluded) provided.	Yes	No	No	No	Yes	No	No	No
Characteristics of included studies provided.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
FITT defined and examined in relation to outcome effect sizes.	No	No	No	No	No	Yes	N/A	No
Scientific quality (risk of bias) of included studies assessed and documented.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Results depended on study quality, either overall, or in interaction with moderators.	No	No	No	Yes	Yes	Yes	No	No
Scientific quality used appropriately in formulating conclusions.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Data appropriately synthesized and if applicable, heterogeneity assessed.	Yes	Yes	Yes	Yes	Yes	Yes	N/A	Yes
Effect size index chosen justified, statistically.	Yes	Yes	Yes	Yes	Yes	Yes	N/A	Yes
Individual-level meta-analysis used.	No	No	No	No	No	No	N/A	No
Practical recommendations clearly addressed.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Likelihood of publication bias assessed.	No	No	Yes	No	No	Yes	No	No
Conflict of interest disclosed.	Yes	No	Yes	No	Yes	No	Yes	Yes

Original Research

Table 4. Original Research Individual Evidence Summary Tables

<table>
<tr><th colspan="2">Progression</th></tr>
<tr><td colspan="2">Original Research
Citation: Dore DA, Winzenberg TM, Ding C, et al. The association between objectively measured physical activity and knee structural change using MRI. Ann Rheum Dis. 2013;72(7):1170–1175. doi:10.1136/annrheumdis-2012-201691.</td></tr>
<tr><td colspan="2">Purpose: To examine the longitudinal association between objectively assessed PA and knee structural change using magnetic resonance imaging (MRI).</td></tr>
<tr><td>Study Design: Prospective cohort study</td><td rowspan="4">Abstract: OBJECTIVES: This study describes the longitudinal association between objectively assessed physical activity (PA) and knee structural change measured using MRI. METHODS: 405 community-dwelling adults aged 51-81 years were measured at baseline and approximately 2.7 years later. MRI of the right knee at baseline and follow-up was performed to evaluate bone marrow lesions (BMLs), meniscal pathology, cartilage defects, and cartilage volume. PA was assessed at baseline by pedometer (steps/day). RESULTS: Doing >/=10 000 steps/day was associated with BML increases (RR 1.97, 95% CI 1.19 to 3.27, p=0.009). Participants doing >/=10 000 steps/day had a 1.52 times (95% CI 1.05 to 2.20, p=0.027) greater risk of increasing meniscal pathology score, which increased to 2.49 (95% CI 1.05 to 3.93, p=0.002) in those with adverse meniscal pathology at baseline. Doing >/=10 000 steps/day was associated with a greater risk of increasing cartilage defect score in those with prevalent BMLs at baseline (RR 1.36, 95% CI 1.03 to 1.69, p=0.013). Steps/day was protective against volume loss in those with more baseline cartilage volume but led to increased cartilage loss in those with less baseline cartilage volume. (p=0.046 for interaction). CONCLUSIONS: PA was deleteriously associated with knee structural change, especially in those with pre-existing knee structural abnormalities. This suggests individuals with knee abnormalities should avoid doing >/=10 000 steps/day. Alternatives to weight-bearing activity may be needed in order to maintain PA levels required for other aspects of health.</td></tr>
<tr><td>Location: Tasmania</td></tr>
<tr><td>Sample: 405
Attrition Rate: 53.71%
Sample Power: Not reported</td></tr>
<tr><td>Exposure Measurement
Device-Measured: Pedometer, steps/day, averaged from two 7-day wear periods, 6 months apart. Measured continuously and dichotomized by <10,000 or ≥10,000 steps/day.
Measures Steps: Yes
Measures Bouts: No</td></tr>
<tr><td>Refers to Other Materials: Yes
Adverse Events Addressed:
Examine Cardiorespiratory Fitness as Outcome: No</td><td>Outcomes Examined: MRI at baseline and follow-up: bone marrow lesions, meniscal damage, cartilage defects, tibial plateau bone area. Knee injury and surgery questions. Presence of radiographic osteoarthritis, defined as any score ≥1 for joint space narrowing or osetophytes.</td></tr>
<tr><td>Populations Analyzed: Adults 50–80, Subjects with and without pre-existing knee abnormalities (56–58% with knee osteoarthritis).</td><td>Author-Stated Funding Source: National Health and Medical Research Council of Australia, Tasmanian Community Fund, Masonic Centenary Medical Research Foundation, Royal Hobart Hospital Research Foundation, Arthritis Foundation of Australia.</td></tr>
</table>

<table>
<tr><th colspan="2">Progression</th></tr>
<tr><td colspan="2">Original Research
Citation: Felson DT, Niu J, Yang T, et al. Physical activity, alignment and knee osteoarthritis: data from MOST and the OAI. Osteoarthritis Cartilage. 2013;21(6):789–795. doi:10.1016/j.joca.2013.03.001.</td></tr>
<tr><td colspan="2">Purpose: To determine the effect of PA on knee osteoarthritis development in persons without knee injury and according to knee alignment.</td></tr>
<tr><td>Study Design: Prospective cohort study</td><td rowspan="4">Abstract: OBJECTIVE: To determine the effect of physical activity on knee osteoarthritis (OA) development in persons without knee injury and according to knee alignment. DESIGN: We combined data from Multicenter Osteoarthritis (MOST) and Osteoarthritis Initiative (OAI), studies of persons with or at high risk of OA. Subjects had long limb and repeated posteroanterior knee radiographs and completed the physical activity survey for the elderly (PASE). We studied persons without radiographic OA and excluded knees with major injury and without long limb films. We followed subjects 30 months (in MOST) and 48 months (in OAI) for one of two incident outcomes: (1) symptomatic tibiofemoral OA (radiographic OA and knee pain), or (2) tibiofemoral narrowing. 'Active' persons were those with PASE score in the highest quartile by gender. We examined risk of OA in active group using logistic regression adjusting for age, gender, body mass index (BMI), Western Ontario and McMaster Arthritis Index (WOMAC) pain score, Kellgren and Lawrence (KL) grade (0 or 1), and study of origin. We also analyzed knees from malaligned and neutrally aligned limbs. RESULTS: The combined sample comprised 2,073 subjects (3,542 knees) with mean age 61 years. The cumulative incidence of symptomatic tibiofemoral OA was 1.12% in the active group vs 1.82% in the others (odds ratio (OR) among active group 0.6, 95% confidence interval (CI) 0.3, 1.3). Joint space narrowing occurred in 3.41% of knees in the active group vs 4.04% in the others (OR among active group 0.9 (95% CI 0.5, 1.5)). Results did not differ by alignment status. CONCLUSIONS: Physical activity in the highest quartile did not affect the risk of developing OA.</td></tr>
<tr><td>Location: United States</td></tr>
<tr><td>Sample: 2,073
Attrition Rate: 0.00%
Sample Power: Not reported</td></tr>
<tr><td>Exposure Measurement
Self-Reported: Physical Activity Scale for the Elderly, created quartiles of activity.
Measures Steps: No
Measures Bouts: No</td></tr>
<tr><td>Refers to Other Materials: Yes
Examine Cardiorespiratory Fitness as Outcome: No</td><td>Outcomes Examined: Disease progression: the new combination of frequent knee pain and radiographic osteoarthritis.</td></tr>
<tr><td>Populations Analyzed: Adults mean age 61, With or at high risk of knee osteoarthritis.</td><td>Author-Stated Funding Source: National Institutes of Health, Merck Research Laboratories, Novartis Pharmaceuticals Corporation, GlaxoSmithKline, Pfizer.</td></tr>
</table>

<table>
<tr><th colspan="2">Progression</th></tr>
<tr><td colspan="2">Original Research
Citation: Kwee RM, Wirth W, Hafezi-Nejad N, Zikria BA, Guermazi A, Demehri S. Role of physical activity in cartilage damage progression of subjects with baseline full-thickness cartilage defects in medial tibiofemoral compartment: data from the Osteoarthritis Initiative. Osteoarthritis Cartilage. 2016;24(11):1898–1904. doi:10.1016/j.joca.2016.06.009.</td></tr>
<tr><td colspan="2">Purpose: To assess the association between PA and cartilage damage progression in the medial tibiofemoral compartment, using 2-year follow-up magnetic resonance imaging (MRI) in subjects with subchondral bones at the central weight-bearing medial femur detected at baseline MRI examination.</td></tr>
<tr><td>Study Design: Prospective cohort study</td><td rowspan="4">Abstract: OBJECTIVE: To assess the association between physical activity and cartilage damage progression in medial tibiofemoral compartment (MTFC) using 2-year follow-up magnetic resonance imaging (MRI) in subjects with denuded areas of subchondral bone (dABs) at the central weight-bearing medial femur (cMF) at baseline MRI examination. METHODS: One hundred subjects from the Osteoarthritis Initiative (OAI) progression cohort with dABs at the cMF at 3T MRI at baseline (51% men; mean age 62.2 years, range 45-79) were included. Sagittal 3D dual-echo steady-state with water excitation images were used to assess 2-year MTFC cartilage change. Associations between 2-year average Physical Activity Scale for the Elderly (PASE) and 2-year MTFC cartilage change were assessed by linear regression analysis. Subgroup analyses were performed. RESULTS: No associations between PASE and 2-year MTFC cartilage change were observed in the entire cohort. Similarly, in the subgroup with cartilage loss during the 2 years, the non-refuted confidence intervals for the regression coefficients were tightly clustered around the null value (regression coefficients for: mean cMF.ThCtAB = -0.00059; 98.75% CI: -0.00130 to 0.00012), cMF.dAB% = 0.02176; 98.75% CI: -0.02514 to 0.06865, Mean MT.ThCtAB = -0.00013; 98.75% CI: -0.00064 to 0.00038, MT.dAB% = 0.02543; 98.75% CI: -0.01485 to 0.06571. CONCLUSION: In the entire group of subjects with dABs at the cMF at baseline, no association between physical activity and 2-year MTFC cartilage change was detected. Due to the limited sample size of our study, small-sized effects may not have been detected in our study.</td></tr>
<tr><td>Location: Not reported</td></tr>
<tr><td>Sample: 100
Attrition Rate: 0.79%
Sample Power: Yes</td></tr>
<tr><td>Exposure Measurement
Self-Reported: 7-day recall using the Physical Activity Scale for the Elderly.
Measures Steps: No
Measures Bouts: No</td></tr>
<tr><td>Refers to Other Materials: No
Examine Cardiorespiratory Fitness as Outcome: No</td><td>Outcomes Examined: Disease progression: Percentage of denuded areas of subchondral bone at the medial tibia, mean cartilage thickness over total subchondral bone area at the medial tibia, and mean cartilage thickness over total subchondral bone area at the central medial femur.</td></tr>
<tr><td>Populations Analyzed: Adults 45–79, Osteoarthritis</td><td>Author-Stated Funding Source: No funding source used.</td></tr>
</table>

<table>
<tr><th colspan="2">Progression</th></tr>
<tr><td colspan="2">Original Research
Citation: Lin W, Alizai H, Joseph GB, et al. Physical activity in relation to knee cartilage T2 progression measured with 3 T MRI over a period of 4 years: data from the Osteoarthritis Initiative. Osteoarthritis Cartilage. 2013;21(10):1558–1566. doi:10.1016/j.joca.2013.06.022.</td></tr>
<tr><td colspan="2">Purpose: To analyze the longitudinal association between PA levels and early degenerative cartilage changes in the knee, measured using T2 relaxation times over a period of 4 years in individuals without clinical or radiographic evidence of osteoarthritis.</td></tr>
<tr><td>Study Design: Prospective cohort study</td><td rowspan="4">Abstract: OBJECTIVE: The purpose of this study was to analyze the longitudinal association between physical activity levels and early degenerative cartilage changes in the knee, measured using T2 relaxation times over a period of 4 years in individuals without clinical or radiographic evidence of OA. DESIGN: Cartilage T2 was measured at baseline and after 2 and 4 years in 205 subjects aged 45-60 years from the Osteoarthritis Initiative (OAI) incidence and normal cohorts with no knee pain (Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score of zero), and a Kellgren Lawrence (KL) score of <2 at baseline. Physical activity was scored using the Physical Activity Scale for the Elderly (PASE) questionnaire, which was obtained yearly over 4 years. The relationship between physical activity and T2 was studied using a mixed model linear regression, including random effects, and adjusted for age, sex, and body mass index (BMI). RESULTS: T2 values for all PASE tertiles progressed over the 4-year period. T2 progression was increased in the highest tertile of physical activity compared to the mid-tertile at the medial tibia (MT) (P = 0.041), patella (Pat) (P = 0.019), and average T2 of all knee compartments combined (P = 0.033). Subjects with the lowest 15% PASE scores showed significantly higher T2 progression compared to the mid-level physical activity group at the lateral femur (LF) (P = 0.025), lateral tibia (LT) (P = 0.043), medial femur (MF) (P = 0.044), tibiofemoral compartment (P = 0.017), patellofemoral compartment (P = 0.016), lateral compartments (P = 0.003), and average of all compartments (P = 0.043). CONCLUSION: High and very low PASE scores were associated with greater progression of cartilage T2 measurements in asymptomatic, middle-aged individuals, suggesting accelerated cartilage matrix biochemical degeneration over time.</td></tr>
<tr><td>Location: United States</td></tr>
<tr><td>Sample: 205
Attrition Rate: 0.16%
Sample Power: Yes</td></tr>
<tr><td>Exposure Measurement
Self-Reported: Physical Activity Scale for the Elderly questionnaire, assessed over last 7 days; included household, occupational, and leisure time PA. Created tertiles for assessment.
Measures Steps: No
Measures Bouts: No</td></tr>
<tr><td>Refers to Other Materials: No
Examine Cardiorespiratory Fitness as Outcome: No</td><td>Outcomes Examined: T2 relaxation time (disease progression): assessed radiographically.</td></tr>
<tr><td>Populations Analyzed: Adults 45–60</td><td>Author-Stated Funding Source: National Institutes of Health, Osteoarthritis Initiative.</td></tr>
</table>

<table>
<tr><th colspan="2">Progression</th></tr>
<tr><td colspan="2">Original Research
Citation: Oiestad BE, Quinn E, White, et al. No association between daily walking and knee structural changes in people at risk of or with mild knee osteoarthritis. Prospective data from the Multicenter Osteoarthritis Study. J Rheumatol. 2015;42(9):1685–1693. doi:10.3899/jrheum.150071.</td></tr>
<tr><td colspan="2">Purpose: To examine the association of objectively measured daily walking with structural change 2 years later in people at risk of or with mild knee osteoarthritis.</td></tr>
<tr><td>Study Design: Prospective cohort study
Location: United States
Sample: 779
Attrition Rate: 0.74%
Sample Power: Not reported
Exposure Measurement
Self-Reported:
Device-Measured: Accelerometer, average steps/day. Steps were also divided into tertiles of low, moderate, and high levels of daily walking. Minutes per day of walking, with moderate-to-vigorous PA characterized as walking at a frequency of >100 steps/minute.
Measures Steps: Yes
Measures Bouts: No</td><td>Abstract: OBJECTIVE: We investigated the association between objectively measured daily walking and knee structural change, defined either as radiographic worsening or as cartilage loss, in people at risk of or with knee osteoarthritis (OA). METHODS: Participants from the Multicenter Osteoarthritis Study (MOST) with Kellgren-Lawrence grades 0-2 and daily walking (measured with the StepWatch) at the 60-month visit were included. Participants had fixed-flexion, weight-bearing radiographs and knee magnetic resonance images (MRI) at 60 and 84 months. Radiographic worsening was read in both knees using the Osteoarthritis Research Society International grading, and MRI were read for 1 knee using the Whole-Organ MRI Score semiquantitative scoring. OR and 95% CI were calculated comparing those in the middle tertile against the lowest and highest tertiles of daily walking using logistic regression models and generalized estimating equations. Data on walking with moderate to vigorous intensity (min with > 100 steps/min/day) were associated to structural change using multivariate and logistic regression models. RESULTS: The 1179 study participants (59% women) were 67.0 years old (+/- 7.6), with a mean (+/- SD) body mass index of 29.8 kg/m(2) (+/- 5.3) who walked 6981 (+/- 2630) steps/day. After adjusting for confounders, we found no significant associations between daily walking and radiographic worsening or cartilage loss. More time spent walking at a moderate to vigorous intensity was not associated with either radiographic worsening or cartilage loss. CONCLUSION: Results from the MOST study indicated no association between daily walking and structural changes over 2 years in the knees of people at risk of or with mild knee OA.</td></tr>
<tr><td>Refers to Other Materials: No
Adverse Events Addressed:
Examine Cardiorespiratory Fitness as Outcome: No</td><td>Outcomes Examined: Cartilage loss: Whole-Organ MRI Score (WORMS) measured by knee magnetic resonance images (MRIs). Radiographic worsening: standing posterior-anterior and lateral radiographs were taken using SynaFlexer graded according to the KL classification system (grade 0–4) (posteroanterior view), and the Osteoarthritis Research Society International (OARSI) atlas (posteroanterior and lateral view).</td></tr>
<tr><td>Populations Analyzed: Adults 50–79, Subjects at high risk of or with osteoarthritis diagnosis (Kellgren and Lawrence grades <3)</td><td>Author-Stated Funding Source: National Institutes of Health, National Institute on Aging.</td></tr>
</table>

Table 5. Original Research Bias Assessment Chart

	Dore, 2013	Felson, 2013	Kwee, 2016	Lin, 2013	Oiestad, 2015
(???) = Can't Determine					
Inclusion/exclusion criteria similar across study groups.	Yes	Yes	Yes	N/A	Yes
Strategy for recruiting or allocating participants similar across study groups.	Yes	Yes	Yes	N/A	Yes
Allocation sequence randomly generated.	N/A	N/A	N/A	N/A	N/A
Group allocation concealed (i.e., assignments could not be predicted).	N/A	N/A	N/A	N/A	N/A
Distribution of critical confounding factors similar across study groups at baseline, or analysis controlled for differences between groups.	Yes	Yes	Yes	Yes	Yes
Accounted for variations in execution of study from proposed protocol or research plan.	N/A	N/A	N/A	N/A	N/A
Adherence to study protocols similar across study groups.	Yes	Yes	Yes	N/A	Yes
Investigators accounted for unintended concurrent exposures that were differentially experienced by study groups and might bias results.	No	N/A	N/A	N/A	No
Participants blinded to their intervention or exposure status.	N/A	N/A	N/A	N/A	N/A
Investigators blinded to participants' intervention or exposure status.	N/A	N/A	N/A	N/A	N/A
Outcome assessors blinded to participants' intervention or exposure status.	N/A	N/A	N/A	N/A	N/A
Valid and reliable measures used consistently across study groups to assess inclusion/exclusion criteria, exposures, outcomes, and confounders.	Yes	Yes	Yes	Yes	Yes
Length of follow-up similar across study groups.	Yes	Yes	Yes	Yes	Yes
In cases of high or differential loss to follow-up, impact assessed through sensitivity analysis or other adjustment.	No	N/A	No	???	Yes
Other sources of bias taken into account in design and/or analysis of study through matching or other statistical adjustment.	Yes	Yes	Yes	Yes	Yes
Adequate statistical methods used to assess primary outcomes.	Yes	Yes	Yes	Yes	Yes

Appendices

Appendix A: Analytical Framework

Topic Area
Chronic Conditions

Systematic Review Question

In individuals with osteoarthritis, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, (4) disease progression, and (5) pain?

a. Is there a dose-response relationship? If yes, what is the shape of the relationship?
b. Does the relationship vary by age, sex, race/ethnicity, socio-economic status, or weight status?
c. Does the relationship vary based on: frequency, duration, intensity, type (mode), or how physical activity is measured?

Population
Individuals of all ages with osteoarthritis

Intervention/Exposure
All types and intensities of physical activity

Comparison
Individuals with osteoarthritis who participate in varying levels of physical activity

Endpoint Health Outcomes

- Risk of co-morbid conditions
- Physical function
- Health-related quality of life
- Disease progression
- Pain

Key Definitions

- Risk of co-morbid conditions: The chance of having one or more additional conditions.
- Physical function: "Physical function" and "physical functioning" are regarded as synonyms that refer to: "the ability of a person to move around and to perform types of physical activity."
  - For example, measures of physical function include measures of ability to walk (e.g., usually gait speed), run, climb stairs, carry groceries, sweep the floor, stand up, and bathe oneself.
  - As measures of behavioral abilities, physical function measures do not include:
    - Physiologic measures, including measures of physiologic capacity (e.g., maximal lung capacities, maximal aerobic capacity, maximal muscle strength, bone density).
    - Measures of the environment or of the host-environmental interaction (e.g., disability accommodation).
    - Measures of what a person usually does (e.g., physical activity level) (as opposed to what a person is capable of doing).
- Health-related quality of life: "Health-related quality of life (HRQOL) is a multi-dimensional concept that includes domains related to physical, mental, emotional, and social functioning." Source: HealthyPeople.gov https://www.healthypeople.gov/2020/topics-objectives/topic/health-related-quality-of-life-well-being
- Disease progression: A change or worsening of a disease over time.

Appendix B: Final Search Strategy

Search Strategy: PubMed (Systematic Reviews, Meta-Analyses, Pooled Analyses, and High-Quality Reports)

Database: PubMed; Date of Search: 2/7/17; 271 results

Set	Search Terms
Limit: Language	(English[lang])
Limit: Exclude animal only	NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))
Limit: Publication Date (Systematic Reviews/Meta-Analyses)	AND ("2011/01/01"[PDAT] : "3000/12/31"[PDAT])
Limit: Publication Type Include (Systematic Reviews/Meta-Analyses)	AND (systematic[sb] OR meta-analysis[pt] OR "systematic review"[tiab] OR "systematic literature review"[tiab] OR metaanalysis[tiab] OR "meta analysis"[tiab] OR metanalyses[tiab] OR "meta analyses"[tiab] OR "pooled analysis"[tiab] OR "pooled analyses"[tiab] OR "pooled data"[tiab])
Limit: Publication Type Exclude (Systematic Reviews/Meta-Analyses)	NOT ("comment"[Publication Type] OR "editorial"[Publication Type])
Osteoarthritis	AND (("Osteoarthritis"[mh] OR "Osteoarthritis"[tiab] OR "Degenerative joint disease"[tiab] OR "Osteoarthritic"[tiab] OR "Osteophytosis"[tiab]) OR (("Degenerative Arthritides"[tiab] OR "Degenerative Arthritis"[tiab] OR "Osteoarthritides"[tiab] OR "Osteoarthroses"[tiab] OR "Osteoarthrosis"[tiab] OR "Osteoarthrosis Deformans"[tiab] OR "Wear and tear arthritis"[tiab]) NOT medline[sb]))
Physical Activity	AND ("Aerobic activities"[tiab] OR "Aerobic activity"[tiab] OR "Cardiovascular activities"[tiab] OR "Cardiovascular activity"[tiab] OR "Endurance activities"[tiab] OR "Endurance activity"[tiab] OR "Exercise"[mh] OR "Exercise"[tiab] OR "Functional training"[tiab] OR "leisure-time physical activity"[tiab] OR "Lifestyle activities"[tiab] OR "Lifestyle activity"[tiab] OR "muscle stretching exercises"[mh] OR "Physical activity"[tiab] OR "Physical conditioning"[tiab] OR "Qi gong"[tiab] OR "Recreational activities"[tiab] OR "Recreational activity"[tiab] OR "Resistance training"[tiab] OR "strength training"[tiab] OR "Tai chi"[tiab] OR "Tai ji"[mh] OR "Tai ji"[tiab] OR "Walk"[tiab] OR "Walking"[tiab] OR "Yoga"[mh] OR "Yoga"[tiab] OR "Free living activities"[tiab] OR "Free living activity"[tiab] OR "Sedentary"[tiab] OR "Sedentary lifestyle"[mh])

Search Strategy: CINAHL (Systematic Reviews, Meta-Analyses, Pooled Analyses, and High-Quality Reports)

Database: CINAHL; Date of Search: 2/7/17; 13 results
Terms searched in title or abstract

Set	Search Terms
Limits	2011-present English language Peer reviewed Exclude Medline records Human
Limit: Publication Type Include (Systematic Reviews/Meta-Analyses)	(“systematic review” OR “systematic literature review” OR "metaanalysis" OR "meta analysis" OR metanalyses OR "meta analyses" OR "pooled analysis" OR “pooled analyses” OR "pooled data")
Physical Activity	("Aerobic activities" OR "Aerobic activity" OR "Cardiovascular activities" OR "Cardiovascular activity" OR "Endurance activities" OR "Endurance activity" OR "Exercise" OR "Functional training" OR "leisure-time physical activity" OR "Lifestyle activities" OR "Lifestyle activity" OR "muscle stretching exercises" OR "Physical activity" OR "Physical conditioning" OR "Qi gong" OR "Recreational activities" OR "Recreational activity" OR "Resistance training" OR "strength training" OR "Tai chi" OR "Tai ji" OR "Walk" OR "Walking" OR "Yoga" OR “Free living activities” OR “Free living activity” OR “Sedentary”)
Osteoarthritis	AND ("Osteoarthritis" OR "Osteoarthritis" OR "Degenerative joint disease" OR "Degenerative Arthritides" OR "Degenerative Arthritis" OR "Osteoarthritic" OR "Osteoarthritides" OR "Osteoarthroses" OR "Osteoarthrosis" OR "Osteoarthrosis Deformans" OR "Osteophytosis" OR "Wear and tear arthritis")

Search Strategy: Cochrane (Systematic Reviews, Meta-Analyses, Pooled Analyses, and High-Quality Reports)

Database: Cochrane; Date of Search: 2/7/17; 50 results
Terms searched in title, abstract, or keywords

Set	Search Terms
Limits	2011-present Word variations not searched Cochrane Reviews (Reviews) and Other Reviews
Physical Activity	AND ("Aerobic activities" OR "Aerobic activity" OR "Cardiovascular activities" OR "Cardiovascular activity" OR "Endurance activities" OR "Endurance activity" OR "Exercise" OR "Functional training" OR "leisure-time physical activity" OR "Lifestyle activities" OR "Lifestyle activity" OR "muscle stretching exercises" OR "Physical activity" OR "Physical conditioning" OR "Qi gong" OR "Recreational activities" OR "Recreational activity" OR "Resistance training" OR "strength training" OR "Tai chi" OR "Tai ji" OR "Walk" OR "Walking" OR "Yoga" OR “Free living activities” OR “Free living activity” OR “Sedentary”)
Osteoarthritis	AND ("Osteoarthritis" OR "Osteoarthritis" OR "Degenerative joint disease" OR "Degenerative Arthritides" OR "Degenerative Arthritis" OR "Osteoarthritic" OR "Osteoarthritides" OR "Osteoarthroses" OR "Osteoarthrosis" OR "Osteoarthrosis Deformans" OR "Osteophytosis" OR "Wear and tear arthritis")

Search Strategy: PubMed (Original Research)

Database: PubMed; Date of Search: 6/26/17; 301 results

Set	Search Terms
Limit: Language	(English[lang])
Limit: Exclude animal only	NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh]))
Limit: Publication Date (Original)	AND ("2006/01/01"[PDAT] : "3000/12/31"[PDAT])
Limit: Publication Type Exclude (Original)	NOT (“comment”[Publication Type] OR “editorial”[Publication Type] OR “review”[Publication Type] OR systematic[sb] OR "meta-analysis"[publication type] OR “systematic review”[tiab] OR “systematic literature review”[tiab] OR metaanalysis[tiab] OR "meta analysis"[tiab] OR metanalyses[tiab] OR "meta analyses"[tiab] OR "pooled analysis"[tiab] OR “pooled analyses”[tiab] OR "pooled data"[tiab])
Osteoarthritis	AND (("Osteoarthritis"[mh] OR "Osteoarthritis"[tiab] OR "Degenerative joint disease"[tiab] OR "Osteoarthritic"[tiab] OR "Osteophytosis"[tiab]) OR (("Degenerative Arthritides"[tiab] OR "Degenerative Arthritis"[tiab] OR "Osteoarthritides"[tiab] OR "Osteoarthroses"[tiab] OR "Osteoarthrosis"[tiab] OR "Osteoarthrosis Deformans"[tiab] OR "Wear and tear arthritis"[tiab]) NOT medline[sb]))
Physical Activity	AND ("Aerobic activities"[tiab] OR "Aerobic activity"[tiab] OR "Cardiovascular activities"[tiab] OR "Cardiovascular activity"[tiab] OR "Endurance activities"[tiab] OR "Endurance activity"[tiab] OR "Exercise"[mh] OR "Exercise"[tiab] OR "Functional training"[tiab] OR "leisure-time physical activity"[tiab] OR "Lifestyle activities"[tiab] OR "Lifestyle activity"[tiab] OR "muscle stretching exercises"[mh] OR "Physical activity"[tiab] OR "Physical conditioning"[tiab] OR "Qi gong"[tiab] OR "Recreational activities"[tiab] OR "Recreational activity"[tiab] OR "Resistance training"[tiab] OR "strength training"[tiab] OR "Tai chi"[tiab] OR "Tai ji"[mh] OR "Tai ji"[tiab] OR "Walk"[tiab] OR "Walking"[tiab] OR "Yoga"[mh] OR "Yoga"[tiab] OR “Free living activities”[tiab] OR “Free living activity”[tiab] OR “Sedentary”[tiab] OR "Sedentary lifestyle"[mh])
Progression	AND ("Disease Progression"[mh] OR "Progression"[tiab] OR "Progressive OA"[tiab] OR "Progressive Osteoarthritis"[tiab] OR "Acceleration"[tiab] OR "Progresses"[tiab] OR "Progressive disease"[tiab])

Search Strategy: CINAHL (Original)

Database: CINAHL; Date of Search: 6/26/17; 15 results
Terms searched in title or abstract

Set	Search Terms
Limits	2006-present English language Peer reviewed Exclude Medline records Human
Limit: Publication Type Exclude (Original)	(“systematic review” OR “systematic literature review” OR "metaanalysis" OR "meta analysis" OR metanalyses OR "meta analyses" OR "pooled analysis" OR “pooled analyses” OR "pooled data")
Physical Activity	("Aerobic activities" OR "Aerobic activity" OR "Cardiovascular activities" OR "Cardiovascular activity" OR "Endurance activities" OR "Endurance activity" OR "Exercise" OR "Functional training" OR "leisure-time physical activity" OR "Lifestyle activities" OR "Lifestyle activity" OR "muscle stretching exercises" OR "Physical activity" OR "Physical conditioning" OR "Qi gong" OR "Recreational activities" OR "Recreational activity" OR "Resistance training" OR "strength training" OR "Tai chi" OR "Tai ji" OR "Walk" OR "Walking" OR "Yoga" OR “Free living activities” OR “Free living activity” OR “Sedentary”)
Osteoarthritis	AND ("Osteoarthritis" OR "Osteoarthritis" OR "Degenerative joint disease" OR "Degenerative Arthritides" OR "Degenerative Arthritis" OR "Osteoarthritic" OR "Osteoarthritides" OR "Osteoarthroses" OR "Osteoarthrosis" OR "Osteoarthrosis Deformans" OR "Osteophytosis" OR "Wear and tear arthritis")
Progression	AND ("Progression" OR "Progressive OA" OR "Progressive Osteoarthritis" OR "Acceleration" OR "Progresses" OR "Progressive disease" OR "Accelerated development of" OR "Acceleration of knee" OR "Acceleration of hip" OR "Acceleration of spine")

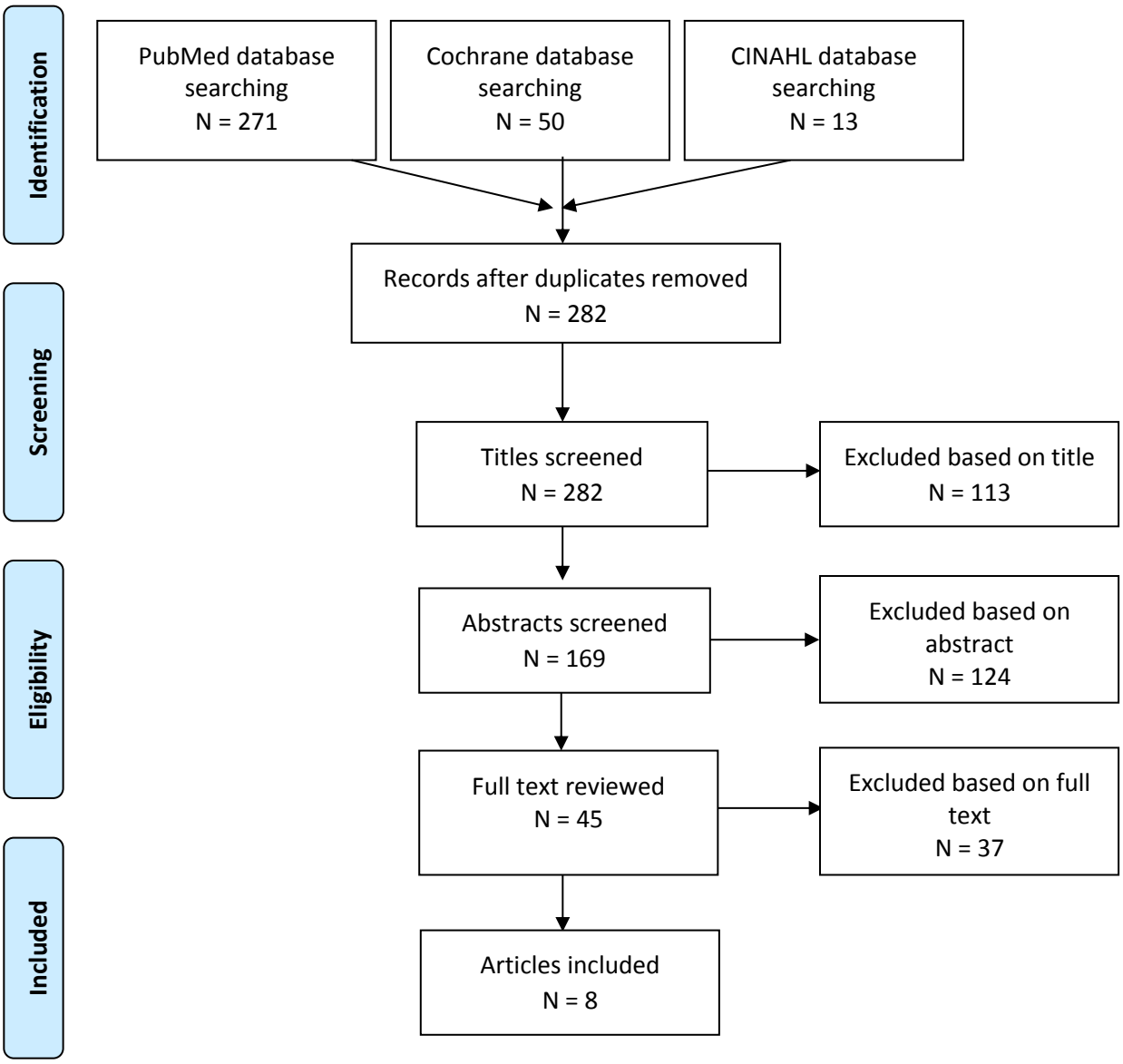
Search Strategy: Cochrane (Original Research)

Database: Cochrane; Date of Search: 6-26/17; 114 results
Terms searched in title, abstract, or keywords

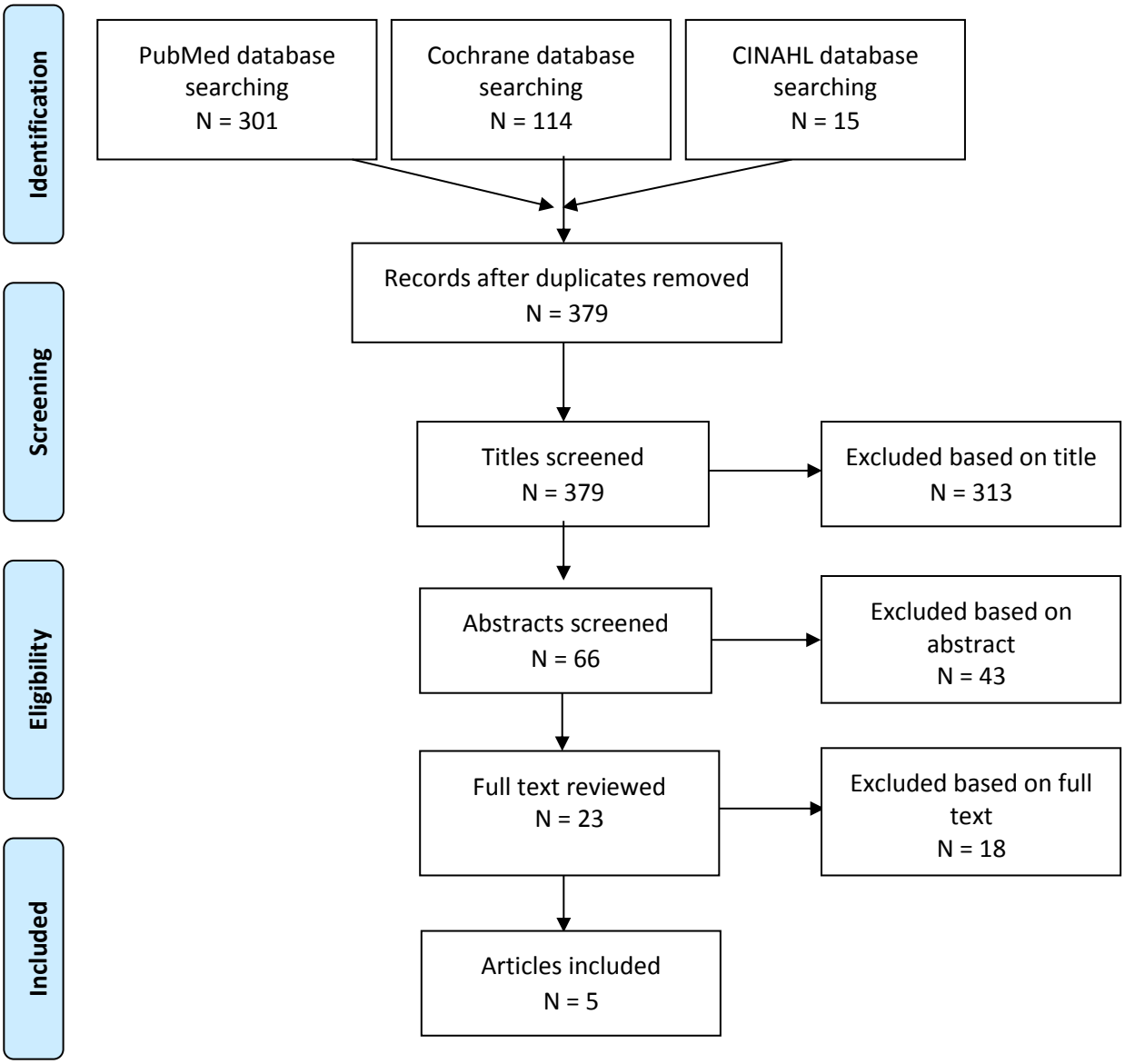
Set	Search Terms
Limits	2006-present Word variations not searched Trials
Physical Activity	("Aerobic activities" OR "Aerobic activity" OR "Cardiovascular activities" OR "Cardiovascular activity" OR "Endurance activities" OR "Endurance activity" OR "Exercise" OR "Functional training" OR "leisure-time physical activity" OR "Lifestyle activities" OR "Lifestyle activity" OR "muscle stretching exercises" OR "Physical activity" OR "Physical conditioning" OR "Qi gong" OR "Recreational activities" OR "Recreational activity" OR "Resistance training" OR "strength training" OR "Tai chi" OR "Tai ji" OR "Walk" OR "Walking" OR "Yoga" OR “Free living activities” OR “Free living activity” OR “Sedentary”)
Osteoarthritis	AND ("Osteoarthritis" OR "Osteoarthritis" OR "Degenerative joint disease" OR "Degenerative Arthritides" OR "Degenerative Arthritis" OR "Osteoarthritic" OR "Osteoarthritides" OR "Osteoarthroses" OR "Osteoarthrosis" OR "Osteoarthrosis Deformans" OR "Osteophytosis" OR "Wear and tear arthritis")
Progression	AND ("Progression" OR "Progressive OA" OR "Progressive Osteoarthritis" OR "Acceleration" OR "Progresses" OR "Progressive disease" OR "Accelerated development of" OR "Acceleration of knee" OR "Acceleration of hip" OR "Acceleration of spine")

Appendix C: Literature Tree

Existing Systematic Reviews, Meta-Analyses, Pooled Analyses, and Reports Literature Tree



Original Research Literature Tree



Appendix D: Inclusion/Exclusion Criteria

Chronic Conditions Subcommittee
Q2. In individuals with osteoarthritis, what is the relationship between physical activity and (1) risk of co-morbid conditions, (2) physical function, (3) health-related quality of life, (4) disease progression, and (5) pain?

a. Is there a dose-response relationship? If yes, what is the shape of the relationship?
b. Does the relationship vary by age, sex, race/ethnicity, socio-economic status, or weight status?
c. Is the relationship based on: frequency, duration, intensity, type (mode), or how physical activity is measured?

Category	Inclusion/Exclusion Criteria	Notes/Rationale
Publication Language	**Include:** • Studies published with full text in English	
Publication Status	**Include:** • Studies published in peer-reviewed journals • Reports determined to have appropriate suitability and quality by PAGAC **Exclude:** • Grey literature, including unpublished data, manuscripts, abstracts, conference proceedings	
Research Type	**Include:** • Original research • Meta-analyses • Systematic reviews • Reports determined to have appropriate suitability and quality by PAGAC	
Study Subjects	**Include:** • Human subjects	
Age of Study Subjects	**Include:** • People of all ages	
Health Status of Study Subjects	**Include:** • Studies of people with osteoarthritis **Exclude:** • Studies that include osteoarthritis as part of the study sample, but do not analyze results separately for osteoarthritis only	
Date of Publication	**Include:** • Systematic reviews, meta-analyses, pooled analyses, and reports published from 2011 to 2017 • Original research published from 2006 to 2017	
Study Design	**Include:** • Systematic reviews • Meta-analyses	

	• Pooled analyses • PAGAC-approved reports **Exclude:** • Randomized controlled trials • Prospective cohort studies • Narrative reviews • Commentaries • Editorials • Non-randomized controlled trials • Retrospective cohort studies • Case-control studies • Cross-sectional studies • Before-and-after studies	
Intervention/ Exposure	**Include studies in which the exposure or intervention is:** • All types and intensities of physical activity **Exclude:** • Studies that do not include physical activity • Studies of multimodal interventions that do not present data on physical activity alone • Studies of a single, acute session of exercise • Studies of a disease-specific therapeutic exercise delivered by a medical professional (e.g., physical therapist) • Studies with measures of physical fitness as the exposure	
Outcome	**Systematic Review, Meta-Analysis, Pooled Analysis, and Report Criteria:** **Include studies in which the outcome is:** • Risk of co-morbid conditions • Physical function • Health-related quality of life • Disease progression • Pain **Original Research Criteria:** **Include studies in which the outcome is:** • Disease progression	

Appendix E: Rationale for Exclusion at Abstract or Full-Text Triage for Existing Systematic Reviews, Meta-Analyses, Pooled Analyses, and Reports

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Abdulla A, Adams N, Bone M, et al. Guidance on the management of pain in older people. *Age Ageing*. 2013;42(suppl 1):i1-57. doi:10.1093/ageing/afs200.			X		X	
Anwer S, Alghadir A, Brismee JM. Effect of home exercise program in patients with knee osteoarthritis: a systematic review and meta-analysis. *J Geriatr Phys Ther.* 2016;39(1):38–48. doi:10.1519/JPT.0000000000000045.				X		
Anwer S, Alghadir A, Zafar H, Al-Eisa E. Effect of whole body vibration training on quadriceps muscle strength in individuals with knee osteoarthritis: a systematic review and meta-analysis. *Physiotherapy.* 2016;102(2):145-151. doi:10.1016/j.physio.2015.10.004.				X		
Arbesman M, Mosley LJ. Systematic review of occupation- and activity-based health management and maintenance interventions for community-dwelling older adults. *Am J Occup Ther.* 2012;66(3):277-283. doi:10.5014/ajot.2012.003327.				X		
Arnold JB, Walters JL, Ferrar KE. Does physical activity increase after total hip or knee arthroplasty for osteoarthritis? A systematic review. *J Orthop Sports Phys Ther*. 2016;46(6):431-442. doi:10.2519/jospt.2016.6449.	X				X	
Barker AL, Talevski J, Morello RT, Brand CA, Rahmann AE, Urquhart DM. Effectiveness of aquatic exercise for musculoskeletal conditions: a meta-analysis. *Arch Phys Med Rehabil*. 2014;95(9):1776-1786. doi:10.1016/j.apmr.2014.04.005.						X
Bartels EM, Juhl CB, Christensen R, et al. Aquatic exercise for the treatment of knee and hip osteoarthritis. *Cochrane Database Syst Rev.* 2016;(3):CD005523. doi:10.1002/14651858.CD005523.pub3.						X

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Batterham SI, Heywood S, Keating JL. Systematic review and meta-analysis comparing land and aquatic exercise for people with hip or knee arthritis on function, mobility and other health outcomes. *BMC Musculoskelet Disord*. June 2011;12:123. doi:10.1186/1471-2474-12-123.		X				
Beaudreuil J, Coudreuse JM, Guyen N, et al. An algorithm to improve knee orthosis prescription for osteoarthritis patients. *Ann Phys Rehabil Med*. Sept 2016;59s:e156.	X					
Beckwée D, Vaes P, Cnudde M, Swinnen E, Bautmans I. Osteoarthritis of the knee: why does exercise work? A qualitative study of the literature. *Ageing Res Rev*. 2013;12(1):226-236. doi:10.1016/j.arr.2012.09.005.			X			
Bennell KL, Buchbinder R, Hinman RS. Physical therapies in the management of osteoarthritis: current state of the evidence. *Curr Opin Rheumatol*. 2015;27(3):304-311. doi:10.1097/BOR.0000000000000160.				X		
Bennell KL, Hall M, Hinman RS. Osteoarthritis year in review 2015: rehabilitation and outcomes. *Osteoarthritis Cartilage.* 2016;24(1):58-70. doi:10.1016/j.joca.2015.07.028.				X		
Bennell KL, Hinman RS. A review of the clinical evidence for exercise in osteoarthritis of the hip and knee. *J Sci Med Sport*. 2011;14(1):4-9. doi:10.1016/j.jsams.2010.08.002.				X		
Bertozzi L, Valdes K, Vanti C, Negrini S, Pillastrini P, Villafañe JH. Investigation of the effect of conservative interventions in thumb carpometacarpal osteoarthritis: systematic review and meta-analysis. *Disabil Rehabil*. 2015;37(22):2025-2043. doi:10.3109/09638288.2014.996299.				X		
Brand E, Nyland J, Henzman C, McGinnis M. Arthritis self-efficacy scale scores in knee osteoarthritis: a systematic review and meta-analysis comparing arthritis self-management education with or without exercise. *J Orthop Sports Phys Ther*. 2013;43(12):895-910. doi:10.2519/jospt.2013.4471.				X		

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Brosseau L, Macleay L, Welch V, Tugwell P, Wells GA. WITHDRAWN: Intensity of exercise for the treatment of osteoarthritis. *Cochrane Database Syst Rev*. 2013;(2):Cd004259. doi:10.1002/14651858.CD004259.pub2.			X			
Brosseau L, Wells GA, Pugh AG, et al. Ottawa Panel evidence-based clinical practice guidelines for therapeutic exercise in the management of hip osteoarthritis. *Clin Rehabil*. 2016;30(10):935-946. doi:10.1177/0269215515606198.			X			
Brosseau L, Wells GA, Tugwell P, et al. Ottawa Panel evidence-based clinical practice guidelines for the management of osteoarthritis in adults who are obese or overweight. *Phys Ther*. 2011;91(6):843-861. doi:10.2522/ptj.20100104.			X			
Bruyere O, Cooper C, Pelletier JP, et al. An algorithm recommendation for the management of knee osteoarthritis in Europe and internationally: a report from a task force of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). *Semin Arthritis Rheum*. 2014;44(3):253-263. doi:10.1016/j.semarthrit.2014.05.014.			X			
Bruyn GA, Naredo E, Damjanov N, et al. An OMERACT reliability exercise of inflammatory and structural abnormalities in patients with knee osteoarthritis using ultrasound assessment. *Ann Rheum Dis*. 2016;75(5):842-846. doi:10.1136/annrheumdis-2014-206774.				X		
Button K, Roos PE, Spasić I, Adamson P, van Deursen RW. The clinical effectiveness of self-care interventions with an exercise component to manage knee conditions: a systematic review. *Knee*. 2015;22(5):360-371. doi:10.1016/j.knee.2015.05.003.				X		

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Cattano NM, Driban JB, Cameron KL, Sitler MR. Impact of physical activity and mechanical loading on biomarkers typically used in osteoarthritis assessment: current concepts and knowledge gaps. *Ther Adv Musculoskelet Dis*. 2017;9(1):11-21. doi:10.1177/1759720X16670613.	X					
Chang WJ, Bennell KL, Hodges PW, Hinman RS, Liston MB, Schabrun SM. Combined exercise and transcranial direct current stimulation intervention for knee osteoarthritis: protocol for a pilot randomised controlled trial. *BMJ Open*. 2015;5(8):e008482. doi:10.1136/bmjopen-2015-008482.			X			
Chang WD, Chen S, Lee CL, Lin HY, Lai PT. The effects of tai chi chuan on improving mind-body health for knee osteoarthritis patients: a systematic review and meta-analysis. *Evid Based Complement Alternat Med.* 2016:1813979. doi:10.1155/2016/1813979.	X					
Chapple CM, Nicholson H, Baxter GD, Abbott JH. Patient characteristics that predict progression of knee osteoarthritis: a systematic review of prognostic studies. *Arthritis Care Res (Hoboken).* 2011;63(8):1115-1125. doi:10.1002/acr.20492.				X		
Chen YW, Hunt MA, Campbell KL, Peill K, Reid WD. The effect of tai chi on four chronic conditions–cancer, osteoarthritis, heart failure and chronic obstructive pulmonary disease: a systematic review and meta-analyses. *Br J Sports Med*. 2016;50(7):397-407. doi:10.1136/bjsports-2014-094388.		X				
Chen WH, Liu XX, Tong PJ, et al. Diagnosis and management of knee osteoarthritis: Chinese medicine expert consensus (2015). *Chin J Integr Med*. 2016;22(2):150-153. doi:10.1007/s11655-015-2432-7.			X			
Corbett MS, Rice SJ, Madurasinghe V, et al. Acupuncture and other physical treatments for the relief of pain due to osteoarthritis of the knee: network meta-analysis. *Osteoarthritis Cartilage*. 2013;21(9):1290-1298. doi:10.1016/j.joca.2013.05.007.				X		

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Coudeyre E, Jegu AG, Giustanini M, Marrel JP, Edouard P, Pereira B. Isokinetic muscle strengthening for knee osteoarthritis: a systematic review of randomized controlled trials with meta-analysis. *Ann Phys Rehabil Med.* 2016;59(3):207-215. doi:10.1016/j.rehab.2016.01.013.				X		
Cramer H, Lauche R, Langhorst J, Dobos G. Yoga for rheumatic diseases: a systematic review. *Rheumatology (Oxford)*. 2013;52(11):2025-2030. doi:10.1093/rheumatology/ket264.		X				
Davis AM. Osteoarthritis year in review: rehabilitation and outcomes. *Osteoarthritis Cartilage.* 2012;20(3):201-206. doi:10.1016/j.joca.2012.01.006.				X		
Davis AM, MacKay C. Osteoarthritis year in review: outcome of rehabilitation. *Osteoarthritis Cartilage*. 2013;21(10):1414-1424. doi:10.1016/j.joca.2013.08.013.				X		
de Rooij M, van der Leeden M, Heymans MW, et al. Course and predictors of pain and physical functioning in patients with hip osteoarthritis: systematic review and meta-analysis. *J Rehabil Med*. 2016;48(3):245-252. doi:10.2340/16501977-2057.	X					
de Rooij M, van der Leeden M, Heymans MW, et al. Prognosis of pain and physical functioning in patients with knee osteoarthritis: a systematic review and meta-analysis. *Arthritis Care Res (Hoboken)*. 2016;68(4):481-492. doi:10.1002/acr.22693.				X		
Desveaux L, Beauchamp M, Goldstein R, Brooks D. Community-based exercise programs as a strategy to optimize function in chronic disease: a systematic review. *Med Care*. 2014;52(3):216-226. doi:10.1097/MLR.0000000000000065.		X				
Di Monaco M, Castiglioni C. Which type of exercise therapy is effective after hip arthroplasty? A systematic review of randomized controlled trials. *Eur J Phys Rehabil Med*. 2013;49(6):893-907, quiz 921-923.				X		

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Dobson F, Bennell KL, French SD, et al. Barriers and facilitators to exercise participation in people with hip and/or knee osteoarthritis: synthesis of the literature using behavior change theory. *Am J Phys Med Rehabil*. 2016;95(5):372-389. doi:10.1097/PHM.0000000000000448.				X		
Duan-Porter W, Goldstein K, McDuffie J, et al. *Mapping the evidence: sex effects in high-impact conditions for women veterans – Depression, Diabetes, and Chronic Pain.* VA Evidence-Based Synthesis Program Reports. Washington, DC: Department of Veterans Affairs; 2015.						X
Duan-Porter W, Goldstein KM, McDuffie JR, et al. Reporting of sex effects by systematic reviews on interventions for depression, diabetes, and chronic pain. *Ann Intern Med*. 2016;165(3):184-193. doi:10.7326/M15-2877.				X		
Duncan KJ, Chopp-Hurley JN, Maly MR. A systematic review to evaluate exercise for anterior cruciate ligament injuries: does this approach reduce the incidence of knee osteoarthritis? *Open Access Rheumatol*. 2016;8:1-16. doi:10.2147/OARRR.S81673.		X				
Fernandes L, Hagen KB, Bijlsma JW, et al. EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis. *Ann Rheum Dis*. 2013;72(7):1125-1135. doi:10.1136/annrheumdis-2012-202745.			X			
Ferreira GE, Robinson CC, Wiebusch M, Viero CC, da Rosa LH, Silva MF. The effect of exercise therapy on knee adduction moment in individuals with knee osteoarthritis: a systematic review. *Clin Biomech (Bristol, Avon).* 2015;30(6):521-527. doi:10.1016/j.clinbiomech.2015.03.028.	X					
Field T. Knee osteoarthritis pain in the elderly can be reduced by massage therapy, yoga and tai chi: a review. *Complement Ther Clin Pract*. Feb 2016;22:87-92. doi:10.1016/j.ctcp.2016.01.001.				X		

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Finney A, Healey E, Jordan JL, Ryan S, Dziedzic KS. Multidisciplinary approaches to managing osteoarthritis in multiple joint sites: a systematic review. *BMC Musculoskelet Disord.* July 2016;17:266. doi:10.1186/s12891-016-1125-5.				X		
Florez-García M, García-Pérez F, Curbelo R, et al. Efficacy and safety of home-based exercises versus individualized supervised outpatient physical therapy programs after total knee arthroplasty: a systematic review and meta-analysis. *Knee Surg Sports Traumatol Arthrosc*. July 2016. doi:10.1007/s00167-016-4231-x.				X	X	
Fransen M, McConnell S, Harmer AR, Van der Esch M, Simic M, Bennell KL. Exercise for osteoarthritis of the knee. *Cochrane Database Syst Rev*. 2015;(1)CD004376. doi:10.1002/14651858.CD004376.pub3.						X
Fransen M, McConnell S, Hernandez-Molina G, Reichenbach S. Exercise for osteoarthritis of the hip. *Cochrane Database Syst Rev.* 2014;(4):Cd007912. doi:10.1002/14651858.CD007912.pub2.						X
Gaught AM, Carneiro KA. Evidence for determining the exercise prescription in patients with osteoarthritis. *Phys Sportsmed*. 2013;41(1):58-65. doi:10.3810/psm.2013.02.2000.			X			
Geneen LJ, Moore RA, Clarke C, Martin D, Colvin LA, Smith BH. Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews. *Cochrane Database Syst Rev*. April 2017;1:CD011279. doi:10.1002/14651858.CD011279.pub3.		X				
Golightly YM, Allen KD, Caine DJ. A comprehensive review of the effectiveness of different exercise programs for patients with osteoarthritis. *Phys Sportsmed*. 2012;40(4):52–65. doi:10.3810/psm.2012.11.1988.			X			

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Gouttebarge V, Inklaar H, Frings-Dresen MH. Risk and consequences of osteoarthritis after a professional football career: a systematic review of the recent literature. *J Sports Med Phys Fitness*. 2014;54(4):494-504.				X		
Hagen KB, Dagfinrud H, Moe RH. Exercise therapy for bone and muscle health: an overview of systematic reviews. *BMC Med*. Dec 2012;10:167. doi:10.1186/1741-7015-10-167.		X				
Hagen KB, Smedslund G, Østerås N, Jamtvedt G. Quality of community-based osteoarthritis care: a systematic review and meta-analysis. *Arthritis Care Res (Hoboken).* 2016;68(10):1443-1452. doi:10.1002/acr.22891.				X		
Hall A, Copsey B, Richmond H, et al. Effectiveness of tai chi for chronic musculoskeletal pain conditions: updated systematic review and meta-analysis. *Phys Ther*. 2016;97(2):227-238. doi:10.2522/ptj.20160246.		X				
Hawker GA, Mian S, Bednis K, Stanaitis I. Osteoarthritis year 2010 in review: non-pharmacologic therapy. *Osteoarthritis Cartilage*. 2011;19(4):366-374. doi:10.1016/j.joca.2011.01.021.			X			
Henriksen M, Creaby MW, Lund H, Juhl C, Christensen R. Is there a causal link between knee loading and knee osteoarthritis progression? A systematic review and meta-analysis of cohort studies and randomised trials. *BMJ Open*. 2014;4(7):e005368. doi:10.1136/bmjopen-2014-005368.				X		
Henriksen M, Hansen JB, Klokker L, Bliddal H, Christensen R. Comparable effects of exercise and analgesics for pain secondary to knee osteoarthritis: a meta-analysis of trials included in Cochrane systematic reviews. *J Comp Eff Res.* 2016;5(4):417–431. doi:10.2217/cer-2016-0007.						X
Hochberg MC, Altman RD, April KT,, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res (Hoboken)*. 2012;64(4):465-474.			X		X	

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Hung CY, Hsiao MY, Chang KV, Han DS, Wang TG. Comparative effectiveness of dextrose prolotherapy versus control injections and exercise in the management of osteoarthritis pain: a systematic review and meta-analysis. *J Pain Res.* 2016;9:847-857. doi:10.2147/JPR.S118669.				X		
Iwamoto J, Sato Y, Takeda T, Matsumoto H. Effectiveness of exercise for osteoarthritis of the knee: a review of the literature. *World J Orthop*. 2011;2(5):37-42. doi:10.5312/wjo.v2.i5.37.			X			
Jackson KA, Glyn-Jones S, Batt ME, et al. Assessing risk factors for early hip osteoarthritis in activity-related hip pain: a Delphi study. *BMJ Open*. 2015;5(9):e007609. doi:10.1136/bmjopen-2015-007609.			X			
Jansen MJ, Viechtbauer W, Lenssen AF, Hendriks EJ, de Bie RA. Strength training alone, exercise therapy alone, and exercise therapy with passive manual mobilisation each reduce pain and disability in people with knee osteoarthritis: a systematic review. J Physiother. 2011;57(1):11–20. doi:10.1016/S1836-9553(11)70002-9.						X
Jansons PS, Haines TP, O'Brien L. Interventions to achieve ongoing exercise adherence for adults with chronic health conditions who have completed a supervised exercise program: Systematic review and meta-analysis. *Clin Rehabil*. 2017;31(4):465-477. doi:10.1177/0269215516653995.	X				X	
Jaramillo A, Welch VA, Ueffing E, et al. Prevention and self-management interventions are top priorities for osteoarthritis systematic reviews. *J Clin Epidemiol*. 2013;66(5):503-510.e4. doi:10.1016/j.jclinepi.2012.06.017.	X				X	
Jigami H, Sato D, Tsubaki A, et al. Effects of weekly and fortnightly therapeutic exercise on physical function and health-related quality of life in individuals with hip osteoarthritis. *J Orthop Sci*. 2012;17(6):737-744. doi:10.1007/s00776-012-0292-y.			X			

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Jones BQ, Covey CJ, Sineath MH Jr. Nonsurgical management of knee pain in adults. *Am Fam Physician*. 2015;92(10):875-883.			X			
Juhl C, Lund H, Roos EM, Zhang W, Christensen R. A hierarchy of patient-reported outcomes for meta-analysis of knee osteoarthritis trials: empirical evidence from a survey of high impact journals. *Arthritis.* 2012:136245. doi:10.1155/2012/136245.	X			X		
Kamioka H, Tsutani K, Mutoh Y, et al. A systematic review of nonrandomized controlled trials on the curative effects of aquatic exercise. *Int J Gen Med*. March 2011;4:239-260. doi:10.2147/IJGM.S17384.		X				
Kan L, Zhang J, Yang Y, Wang P. The effects of yoga on pain, mobility, and quality of life in patients with knee osteoarthritis: a systematic review. *Evid Based Complement Alternat Med*. Sept 2016:6016532. doi:10.1155/2016/6016532.						X
Kang JW, Lee MS, Posadzki P, Ernst E. T'ai chi for the treatment of osteoarthritis: a systematic review and meta-analysis. *BMJ Open*. 2011;1(1):e000035. doi:10.1136/bmjopen-2010-000035.						X
Kelley GA, Kelley KS, Hootman JM, Jones DL. Effects of community-deliverable exercise on pain and physical function in adults with arthritis and other rheumatic diseases: a meta-analysis. *Arthritis Care Res (Hoboken).* 2011;63(1):79-93. doi:10.1002/acr.20347.		X				
Kelley GA, Kelley KS, Hootman JM. Effects of exercise on depression in adults with arthritis: a systematic review with meta-analysis of randomized controlled trials. *Arthritis Res Ther.* Feb 2015;17:21. doi:10.1186/s13075-015-0533-5.	X					
Kelley GA, Kelley KS. Effects of exercise on depressive symptoms in adults with arthritis and other rheumatic disease: a systematic review of meta-analyses. *BMC Musculoskelet Disord*. April 2014;15:121. doi:10.1186/1471-2474-15-121.						X

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Kelley GA, Kelley KS. Exercise reduces depressive symptoms in adults with arthritis: evidential value. *World J Rheumatol*. 2016;6(2):23-29. doi:10.5499/WJR.v6.i2.23.		X				
Keysor JJ, Brembs A. Exercise: necessary but not sufficient for improving function and preventing disability? *Curr Opin Rheumatol*. 2011;23(2):211-218. doi:10.1097/BOR.0b013e3283432c41.		X				
Khalaj N, Abu Osman NA, Mokhtar AH, et al. Effect of exercise and gait retraining on knee adduction moment in people with knee osteoarthritis. *Proc Inst Mech Eng H*. 2014;228(2):190-199. doi:10.1177/0954411914521155.	X					
Khoja SS, Susko AM, Josbeno DA, Piva SR, Fitzgerald GK. Comparing physical activity programs for managing osteoarthritis in overweight or obese patients. *J Comp Eff Res*. 2014;3(3):283-299. doi:10.2217/cer.14.15.			X			
Kirkendall DT, Garrett WE Jr. Management of the retired athlete with osteoarthritis of the knee. *Cartilage*. 2012;3(suppl 1):69s-76s. doi:10.1177/1947603511408287.				X		
Kjeken I, Grotle M, Hagen KB, Østerås N. Development of an evidence-based exercise programme for people with hand osteoarthritis. *Scand J Occup Ther*. 2015;22(2):103-116. doi:10.3109/11038128.2014.941394.			X			
Kjeken I. Occupational therapy-based and evidence-supported recommendations for assessment and exercises in hand osteoarthritis. *Scand J Occup Ther*. 2011;18(4):265-281. doi:10.3109/11038128.2010.514942.			X			
Kjeken I, Smedslund G, Moe RH, Slatkowsky-Christensen B, Uhlig T, Hagen KB. Systematic review of design and effects of splints and exercise programs in hand osteoarthritis. *Arthritis Care Res (Hoboken).* 2011;63(6):834-848. doi:10.1002/acr.20427.				X		
Kong LJ, Lauche R, Klose P, et al. Tai chi for chronic pain conditions: a systematic review and meta-analysis of randomized controlled trials. *Sci Rep*. April 2016;6:25325. doi:10.1038/srep25325.						X

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Krauss I, Steinhilber B, Haupt G, Miller R, Grau S, Janssen P. Efficacy of conservative treatment regimes for hip osteoarthritis--evaluation of the therapeutic exercise regime "Hip School": a protocol for a randomised, controlled trial. *BMC Musculoskelet Disord*. Nov 2011;12:270. doi:10.1186/1471-2474-12-270.			X			
Kristensen J, Franklyn-Miller A. Resistance training in musculoskeletal rehabilitation: a systematic review. *Br J Sports Med*. 2012;46(10):719-726. doi:10.1136/bjsm.2010.079376.		X				
Kroon FP, van der Burg LR, Buchbinder R, Osborne RH, Johnston RV, Pitt V. Self-management education programmes for osteoarthritis. *Cochrane Database Syst Rev*. 2014;(1):CD008963. doi:10.1002/14651858.CD008963.pub2.				X		
Larmer PJ, Reay ND, Aubert ER, Kersten P. Systematic review of guidelines for the physical management of osteoarthritis. *Arch Phys Med Rehabil*. 2014;95(2):375-389. doi:10.1016/j.apmr.2013.10.011.			X			
Lauche R, Langhorst J, Dobos G, Cramer H. A systematic review and meta-analysis of tai chi for osteoarthritis of the knee. *Complement Ther Med*. 2013;21(4):396-406. doi:10.1016/j.ctim.2013.06.001.						X
Lee MS, Ernst E. Systematic reviews of t'ai chi: an overview. *Br J Sports Med*. 2012;46(10):713-718. doi:10.1136/bjsm.2010.080622.			X			
Lefèvre-Colau MM, Nguyen C, Haddad R, et al. Is physical activity, practiced as recommended for health benefit, a risk factor for osteoarthritis? *Ann Phys Rehabil Med*. 2016;59(3):196-206. doi:10.1016/j.rehab.2016.02.007.	X		X		X	
Li CS, Ayeni OR, Sprague S, Truong V, Bhandari M. Conservative treatments, surgical treatments, and the KineSpring® Knee Implant system for knee osteoarthritis: a systematic review. *J Long Term Eff Med Implants*. 2013;23(2-3):105-149.				X		

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Li X, Wang XQ, Chen BL, Huang LY, Liu Y. Erratum to "Whole-body vibration exercise for knee osteoarthritis: a systematic review and meta-analysis". *Evid Based Complement Alternat Med*. Nov 2015:636435. doi:10.1155/2015/636435.				X		
Li X, Wang XQ, Chen BL, Huang LY, Liu Y. Whole-body vibration exercise for knee osteoarthritis: a systematic review and meta-analysis. *Evid Based Complement Alternat Med*. Aug 2015:758147. doi:10.1155/2015/758147.				X		
Lim AY, Doherty M. What of guidelines for osteoarthritis? *Int J Rheum Dis*. 2011;14(2):136-144. doi:10.1111/j.1756-185X.2011.01609.x.			X			
Li Y, Su Y, Chen S, et al. The effects of resistance exercise in patients with knee osteoarthritis: a systematic review and meta-analysis. *Clin Rehabil*. 2016;30(10):947–959. doi:10.1177/0269215515610039.						X
Loew L, Brosseau L, Wells GA, et al. Ottawa panel evidence-based clinical practice guidelines for aerobic walking programs in the management of osteoarthritis. *Arch Phys Med Rehabil*. 2012;93(7):1269-1285. doi:10.1016/j.apmr.2012.01.024.			X			
Lowe CJ, Davies L, Sackley CM, Barker KL. Effectiveness of land-based physiotherapy exercise following hospital discharge following hip arthroplasty for osteoarthritis: an updated systematic review. *Physiotherapy*. 2015;101(3):252-265. doi:10.1016/j.physio.2014.12.003.				X		
Lu M, Su Y, Zhang Y, et al. Effectiveness of aquatic exercise for treatment of knee osteoarthritis: systematic review and meta-analysis. *Z Rheumatol*. 2015;74(6):543-552. doi:10.1007/s00393-014-1559-9.						X
Maly MR, Robbins SM. Osteoarthritis year in review 2014: rehabilitation and outcomes. *Osteoarthritis Cartilage*. 2014;22(12):1958-1988. doi:10.1016/j.joca.2014.08.011.				X		

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Mat S, Tan MP, Kamaruzzaman SB, Ng CT. Physical therapies for improving balance and reducing falls risk in osteoarthritis of the knee: a systematic review. *Age Ageing.* 2015;44(1):16-24. doi:10.1093/ageing/afu112.				X		
Mattos F, Leite N, Pitta A, Bento PC. Effects of aquatic exercise on muscle strength and functional performance of individuals with osteoarthritis: a systematic review. *Rev Bras Reumatol Engl Ed*. 2016;56(6):530-542. doi:10.1016/j.rbre.2016.09.003.				X		
McAlindon TE, Bannuru RR, Sullivan MC, et al. OARSI guidelines for the non-surgical management of knee osteoarthritis. *Osteoarthritis Cartilage*. 2014;22(3):363-388. doi:10.1016/j.joca.2014.01.003.			X			
McWilliams DF, Leeb BF, Muthuri SG, Doherty M, Zhang W. Occupational risk factors for osteoarthritis of the knee: a meta-analysis. *Osteoarthritis Cartilage*. 2011;19(7):829-839. doi:10.1016/j.joca.2011.02.016.		X				
Meneses SR, Goode AP, Nelson AE, et al. Clinical algorithms to aid osteoarthritis guideline dissemination. *Osteoarthritis Cartilage*. 2016;24(9):1487-1499. doi:10.1016/j.joca.2016.04.004.				X		
Mills K, Hunt MA, Leigh R, Ferber R. A systematic review and meta-analysis of lower limb neuromuscular alterations associated with knee osteoarthritis during level walking. *Clin Biomech (Bristol, Avon)*. 2013;28(7):713-724. doi:10.1016/j.clinbiomech.2013.07.008.				X		
Monticone M, Frizziero A, Rovere G, et al. Hyaluronic acid intra-articular injection and exercise therapy: effects on pain and disability in subjects affected by lower limb joints osteoarthritis. A systematic review by the Italian Society of Physical and Rehabilitation Medicine (SIMFER). *Eur J Phys Rehabil Med*. 2016;52(3):389-399.				X		
Moyer RF, Ratneswaran A, Beier F, Birmingham TB. Osteoarthritis year in review 2014: mechanics—basic and clinical studies in osteoarthritis. *Osteoarthritis Cartilage*. 2014;22(12):1989-2002. doi:10.1016/j.joca.2014.06.034.				X		

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Nahin RL, Boineau R, Khalsa PS, Stussman BJ, Weber WJ. Evidence-based evaluation of complementary health approaches for pain management in the United States. *Mayo Clin Proc*. 2016;91(9):1292-1306. doi:10.1016/j.mayocp.2016.06.007.			X			
Nelson AE, Allen KD, Golightly YM, Goode AP, Jordan JM. A systematic review of recommendations and guidelines for the management of osteoarthritis: the chronic osteoarthritis management initiative of the U.S. bone and joint initiative. *Semin Arthritis Rheum*. 2014;43(6):701-712. doi:10.1016/j.semarthrit.2013.11.012.	X					
Nguyen C, Lefèvre-Colau MM, Poiraudeau S, Rannou F. Rehabilitation (exercise and strength training) and osteoarthritis: a critical narrative review. *Ann Phys Rehabil Med*. 2016;59(3):190-195. doi:10.1016/j.rehab.2016.02.010.			X			
Nicolson PJA, Bennell KL, Dobson FL, Van Ginckel A, Holden MA, Hinman RS. Interventions to increase adherence to therapeutic exercise in older adults with low back pain and/or hip/knee osteoarthritis: a systematic review and meta-analysis. *Br J Sports Med.* 2017;51(10):791-799. doi:10.1136/bjsports-2016-096458.	X					
O'Connor SR, Tully MA, Ryan B, et al. Walking exercise for chronic musculoskeletal pain: systematic review and meta-analysis. *Arch Phys Med Rehabil*. 2015;96(4):724-734.e3. doi:10.1016/j.apmr.2014.12.003.		X				
Oliveira CB, Franco MR, Maher CG, et al. Physical activity interventions for increasing objectively measured physical activity levels in patients with chronic musculoskeletal pain: a systematic review. *Arthritis Care Res (Hoboken).* 2016;68(12):1832-1842. doi:10.1002/acr.22919.	X				X	
Østerås N, Kjeken I, Smedslund G, et al. Exercise for hand osteoarthritis. *Cochrane Database Syst Rev.* Jan 2017;1:Cd010388. doi:10.1002/14651858.CD010388.pub2.		X				

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Papavasiliou KA, Kenanidis E, Potoupnis ME, Kapetanou A, Sayegh FE. Participation in athletic activities may be associated with later development of hip and knee osteoarthritis. *Phys Sportsmed*. 2011;39(4):51-59. doi:10.3810/psm.2011.11.1939.			X			
Pedersen BK, Saltin B. Exercise as medicine—evidence for prescribing exercise as therapy in 26 different chronic diseases. *Scand J Med Sci Sports*. 2015;25(suppl 3):1-72. doi:10.1111/sms.12581.		X				
Porcheret M, Grime J, Main C, Dziedzic K. Developing a model osteoarthritis consultation: a Delphi consensus exercise. *BMC Musculoskelet Disord*. Jan 2013;14:25. doi:10.1186/1471-2474-14-25.			X			
Pozzi F, Snyder-Mackler L, Zeni J. Physical exercise after knee arthroplasty: a systematic review of controlled trials. *Eur J Phys Rehabil Med.* 2013;49(6):877-892.				X	X	
Quintrec JL, Verlhac B, Cadet C, et al. Physical exercise and weight loss for hip and knee osteoarthritis in very old patients: a systematic review of the literature. *Open Rheumatol J*. 2014;8:89-95. doi:10.2174/1874312901408010089.				X		
Regnaux JP, Lefevre-Colau MM, Trinquart L, et al. High-intensity versus low-intensity physical activity or exercise in people with hip or knee osteoarthritis. *Cochrane Database Syst Rev.* 2015;(10):Cd010203. doi:10.1002/14651858.CD010203.pub2.				X		
Richmond SA, Fukuchi RK, Ezzat A, Schneider K, Schneider G, Emery CA. Are joint injury, sport activity, physical activity, obesity, or occupational activities predictors for osteoarthritis? A systematic review. *J Orthop Sports Phys Ther*. 2013;43(8):515-B19. doi:10.2519/jospt.2013.4796.				X		
Ringdahl E, Pandit S. Treatment of knee osteoarthritis. *Am Fam Physician*. 2011;83(11):1287-1292.			X			

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Romeo A, Parazza S, Boschi M, Nava T, Vanti C. Manual therapy and therapeutic exercise in the treatment of osteoarthritis of the hip: a systematic review. *Reumatismo*. 2013;65(2):63-74. doi:10.4081/reumatismo.2013.63.						X
Roos EM, Juhl CB. Osteoarthritis 2012 year in review: rehabilitation and outcomes. *Osteoarthritis Cartilage*. 2012;20(12):1477-1483. doi:10.1016/j.joca.2012.08.028.				X		
Runhaar J, Luijsterburg P, Dekker J, Bierma-Zeinstra SM. Identifying potential working mechanisms behind the positive effects of exercise therapy on pain and function in osteoarthritis; a systematic review. *Osteoarthritis Cartilage*. 2015;23(7):1071-1082. doi:10.1016/j.joca.2014.12.027.	X					
Sampath KK, Mani R, Miyamori T, Tumilty S. The effects of manual therapy or exercise therapy or both in people with hip osteoarthritis: a systematic review and meta-analysis. Clin Rehabil. 2016;30(12):1141–1155. doi:10.1177/0269215515622670.						X
Sharma M. Yoga as an alternative and complementary approach for arthritis: a systematic review. *J Evid Based Complementary Altern Med*. 2014;19(1):51-58. doi:10.1177/2156587213499918.						X
Shengelia R, Parker SJ, Ballin M, George T, Reid MC. Complementary therapies for osteoarthritis: are they effective? *Pain Manag Nurs*. 2013;14(4):e274-e288. doi:10.1016/j.pmn.2012.01.001.						X
Silva A, Serrão PR, Driusso P, Mattiello SM. The effects of therapeutic exercise on the balance of women with knee osteoarthritis: a systematic review. *Rev Bras Fisioter*. 2012;16(1):1-9.	X					
Sliepen M, Brandes M, Rosenbaum D. Current physical activity monitors in hip and knee osteoarthritis – A review. *Arthritis Care Res (Hoboken).* Dec 2016. doi:10.1002/acr.23170.				X		
Smith TO, King JJ, Hing CB. The effectiveness of proprioceptive-based exercise for osteoarthritis of the knee: a systematic review and meta-analysis. *Rheumatol Int*. 2012;32(11):3339-3351. doi:10.1007/s00296-012-2480-7.				X		

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Smith T, Kirby E, Davies L. A systematic review to determine the optimal type and dosage of land-based exercises for treating knee osteoarthritis. *Physical Therapy Reviews.* 2014;19(2):105-113. doi:10.1179/1743288X13Y.0000000108.						X
Solloway MR, Taylor SL, Shekelle PG, et al. An evidence map of the effect of tai chi on health outcomes. *Syst Rev.* 2016;5(1):126. doi:10.1186/s13643-016-0300-y.		X				
Stubbs B, Hurley M, Smith T. What are the factors that influence physical activity participation in adults with knee and hip osteoarthritis? A systematic review of physical activity correlates. *Clin Rehabil*. 2015;29(1):80-94. doi:10.1177/0269215514538069.	X				X	
Tanaka R, Ozawa J, Kito N, Moriyama H. Does exercise therapy improve the health-related quality of life of people with knee osteoarthritis? A systematic review and meta-analysis of randomized controlled trials. *J Phys Ther Sci.* 2015;27(10):3309–3314. doi:10.1589/jpts.27.3309.						X
Tanaka R, Ozawa J, Kito N, Moriyama H. Effect of the frequency and duration of land-based therapeutic exercise on pain relief for people with knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. *J Phys Ther Sci.* 2014;26(7):969–975.						X
Tanaka R, Ozawa J, Kito N, Moriyama H. Effects of exercise therapy on walking ability in individuals with knee osteoarthritis: a systematic review and meta-analysis of randomised controlled trials. *Clin Rehabil*. 2016;30(1):36-52. doi:10.1177/0269215515570098.	X					
Tanaka R, Ozawa J, Kito N, Moriyama H. Efficacy of strengthening or aerobic exercise on pain relief in people with knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. *Clin Rehabil*. 2013;27(12):1059–1071. doi:10.1177/0269215513488898.						X

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Tanaka R, Ozawa J, Kito N, Yamasaki T, Moriyama H. Evidence of improvement in various impairments by exercise interventions in patients with knee osteoarthritis: a systematic review and meta-analysis of randomized clinical trials. *J Jpn Phys Ther Assoc*. 2013;16(1):7-21. doi:10.1298/jjpta.Vol16_003.	X					
Thorstensson CA, Garellick G, Rystedt H, Dahlberg LE. Better management of patients with osteoarthritis: development and nationwide implementation of an evidence-based supported osteoarthritis self-management programme. *Musculoskeletal Care.* 2015;13(2):67-75. doi:10.1002/msc.1085.			X			
Uthman OA, van der Windt DA, Jordan JL, et al. Exercise for lower limb osteoarthritis: systematic review incorporating trial sequential analysis and network meta-analysis. *BMJ*. Sept 2013;347:f5555. doi:10.1136/bmj.f5555.						X
Urquhart DM, Tobing JF, Hanna FS, et al. What is the effect of physical activity on the knee joint? A systematic review. *Med Sci Sports Exerc*. 2011;43(3):432-442. doi:10.1249/MSS.0b013e3181ef5bf8.						X
Veenhof C, Huisman PA, Barten JA, Takken T, Pisters MF. Factors associated with physical activity in patients with osteoarthritis of the hip or knee: a systematic review. *Osteoarthritis Cartilage*. 2012;20(1):6-12. doi:10.1016/j.joca.2011.10.006.	X					
Verhagen AP, Cardoso JR, Bierma-Zeinstra SM. Aquatic exercise & balneotherapy in musculoskeletal conditions. *Best Pract Res Clin Rheumatol*. 2012;26(3):335-343. doi:10.1016/j.berh.2012.05.008.			X			
Waller B, Ogonowska-Slodownik A, Vitor M, et al. Effect of therapeutic aquatic exercise on symptoms and function associated with lower limb osteoarthritis: systematic review with meta-analysis. *Phys Ther*. 2014;94(10):1383-1395. doi:10.2522/ptj.20130417.						X

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Wallis JA, Taylor NF. Pre-operative interventions (non-surgical and non-pharmacological) for patients with hip or knee osteoarthritis awaiting joint replacement surgery—a systematic review and meta-analysis. *Osteoarthritis Cartilage*. 2011;19(12):1381-1395. doi:10.1016/j.joca.2011.09.001.		X				
Wallis JA, Webster KE, Levinger P, Taylor NF. What proportion of people with hip and knee osteoarthritis meet physical activity guidelines? A systematic review and meta-analysis. *Osteoarthritis Cartilage*. 2013;21(11):1648-1659. doi:10.1016/j.joca.2013.08.003.	X				X	
Wang P, Yang X, Yang Y, et al. Effects of whole body vibration on pain, stiffness and physical functions in patients with knee osteoarthritis: a systematic review and meta-analysis. *Clin Rehabil*. 2015;29(10):939-951. doi:10.1177/0269215514564895.				X		
Ward L, Stebbings S, Cherkin D, Baxter GD. Components and reporting of yoga interventions for musculoskeletal conditions: a systematic review of randomised controlled trials. *Complement Ther Med*. 2014;22(5):909-919. doi:10.1016/j.ctim.2014.08.007.	X					
Ward L, Stebbings S, Cherkin D, Baxter GD. Yoga for functional ability, pain and psychosocial outcomes in musculoskeletal conditions: a systematic review and meta-analysis. *Musculoskeletal Care*. 2013;11(4):203-217. doi:10.1002/msc.1042.				X		
Williamson W, Kluzek S, Roberts N, et al. Behavioural physical activity interventions in participants with lower-limb osteoarthritis: a systematic review with meta-analysis. *BMJ Open*. 2015;5(8):e007642. doi:10.1136/bmjopen-2015-007642.	X				X	
Witjes S, Gouttebarge V, Kuijer PP, van Geenen RC, Poolman RW, Kerkhoffs GM. Return to sports and physical activity after total and unicondylar knee arthroplasty: a systematic review and meta-analysis. *Sports Med*. 2016;46(2):269-292. doi:10.1007/s40279-015-0421-9.	X			X		

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Witteveen AG, Hofstad CJ, Kerkhoffs GM. Hyaluronic acid and other conservative treatment options for osteoarthritis of the ankle. *Cochrane Database Syst Rev*. Oct 2015;(10):Cd010643. doi:10.1002/14651858.CD010643.pub2.		X				
Wood LR, Peat GM, Mullis R, Thomas E, Foster NE. Impairment-targeted exercises for older adults with knee pain: protocol for a proof-of-principle study. *BMC Musculoskelet Disord.* Jan 2011;12:2. doi:10.1186/1471-2474-12-2.			X			
Yan JH, Gu WJ, Sun J, Zhang WX, Li BW, Pan L. Efficacy of tai chi on pain, stiffness and function in patients with osteoarthritis: a meta-analysis. *PLoS One*. 2013;8(4):e61672. doi:10.1371/journal.pone.0061672.						X
Yang GY, Wang LQ, Ren J, et al. Evidence base of clinical studies on Tai Chi: a bibliometric analysis. *PLoS One*. 2015;10(3):e0120655. doi:10.1371/journal.pone.0120655.		X				
Ye J, Cai S, Zhong W, Cai S, Zheng Q. Effects of tai chi for patients with knee osteoarthritis: a systematic review. *J Phys Ther Sci*. 2014;26(7):1133-1137. doi:10.1589/jpts.26.1133.						X
Ye L, Kalichman L, Spittle A, Dobson F, Bennell K. Effects of rehabilitative interventions on pain, function and physical impairments in people with hand osteoarthritis: a systematic review. *Arthritis Res Ther*. 2011;13(1):R28. doi:10.1186/ar3254.		X				
Zacharias A, Green RA, Semciw AI, Kingsley MI, Pizzari T. Efficacy of rehabilitation programs for improving muscle strength in people with hip or knee osteoarthritis: a systematic review with meta-analysis. *Osteoarthritis Cartilage*. 2014;22(11):1752-1773. doi:10.1016/j.joca.2014.07.005.	X					
Zafar H, Alghadir A, Anwer S, Al-Eisa E. Therapeutic effects of whole-body vibration training in knee osteoarthritis: a systematic review and meta-analysis. *Arch Phys Med Rehabil*. 2015;96(8):1525-1532. doi:10.1016/j.apmr.2015.03.010.				X		

Citation	Outcome	Population	Study Design	Exposure	Not ideal fit for replacement of de novo search	Other
Zhang Y, Huang L, Su Y, Zhan Z, Li Y, Lai X. The effects of traditional Chinese exercise in treating knee osteoarthritis: a systematic review and meta-analysis. *PLoS One*. 2017;12(1):e0170237. doi:10.1371/journal.pone.0170237.						X

Rationale for Exclusion at Abstract or Full-Text Triage for Original Research

The table below lists the excluded articles with at least one reason for exclusion, but may not reflect all possible reasons.

Citation	Outcome	Population	Study Design	Exposure	Other
Ageberg E, Engström G, Gerhardsson de Verdier M, Rollof J, Roos EM, Lohmander LS. Effect of leisure time physical activity on severe knee or hip osteoarthritis leading to total joint replacement: a population-based prospective cohort study. *BMC Musculoskelet Disord*. May 2012;13:73. doi:10.1186/1471-2474-13-73.		X			
Ageberg E, Link A, Roos EM. Feasibility of neuromuscular training in patients with severe hip or knee OA: the individualized goal-based NEMEX-TJR training program. *BMC Musculoskelet Disord.* June 2010;11:126. doi:10.1186/1471-2474-11-126.	X				
Ageberg E, Nilsdotter A, Kosek E, Roos EM. Effects of neuromuscular training (NEMEX-TJR) on patient-reported outcomes and physical function in severe primary hip or knee osteoarthritis: a controlled before-and-after study. *BMC Musculoskelet Disord*. Aug 2013;14:232. doi:10.1186/1471-2474-14-232.				X	
Aguiar GC, Do Nascimento MR, De Miranda AS, Rocha NP, Teixeira AL, Scalzo PL. Effects of an exercise therapy protocol on inflammatory markers, perception of pain, and physical performance in individuals with knee osteoarthritis. *Rheumatol Int.* 2015;35(3):525-531. doi:10.1007/s00296-014-3148-2.			X		
Bennell KL, Hunt MA, Wrigley TV, et al. Hip strengthening reduces symptoms but not knee load in people with medial knee osteoarthritis and varus malalignment: a randomised controlled trial. *Osteoarthritis Cartilage*. 2010;18(5):621-628. doi:10.1016/j.joca.2010.01.010.					X
Bennell KL, Wrigley T, Kyriakides M, et al. Comparison of neuromuscular and quadriceps strengthening exercise in people with medial knee osteoarthritis and varus malalignment: randomised controlled trial. *Osteoarthritis Cartilage*. 2013;21:S273-S274. doi:10.1016/j.joca.2013.02.573.	X				

Citation	Outcome	Population	Study Design	Exposure	Other
Bennell KL, Kyriakides M, Metcalf B, et al. Neuromuscular versus quadriceps strengthening exercise in patients with medial knee osteoarthritis and varus malalignment: a randomized controlled trial. *Arthritis Rheumatol.* 2014;66(4):950-959. doi:10.1002/art.38317.	X				
Brakke R, Singh J, Sullivan W. Physical therapy in persons with osteoarthritis. *PM R.* 2012;4(suppl 5):S53-S58. doi:10.1016/j.pmrj.2012.02.017.			X		
Braun B, Parker D, Harvey L, Bissen J, Melko C, Xi M. Arthritis-friendly adaptations for weight management and physical activity promotion: two 12-month interventions. 134th Annual Meeting & Exposition; Nov 4 2006; Boston, MA. American Public Health Association; 2006.	X				
Burstein D. Tracking longitudinal changes in knee degeneration and repair. *J Bone Joint Surg Am*. 2009;91(suppl 1):51-53. doi:10.2106/JBJS.H.01412.				X	
Chakravarty EF, Hubert HB, Lingala VB, Zatarain E, Fries JF. Long distance running and knee osteoarthritis. A prospective study. *Am J Prev Med*. 2008;35(2):133-138. doi:10.1016/j.amepre.2008.03.032.		X			
Ciolac EG, Greve JM. Muscle strength and exercise intensity adaptation to resistance training in older women with knee osteoarthritis and total knee arthroplasty. *Clinics (Sao Paulo).* 2011;66(12):2079-2084.			X		
Constantinou M, Loureiro A, Carty C, Mills P, Barrett R. Hip joint mechanics during walking in individuals with mild-to-moderate hip osteoarthritis. *Gait Posture*. March 2017;53:162-167. doi:10.1016/j.gaitpost.2017.01.017.				X	
Desmeules F, Dionne CE, Belzile E, Bourbonnais R, Frémont P. Waiting for total knee replacement surgery: factors associated with pain, stiffness, function and quality of life. *BMC Musculoskelet Disord*. May 2009;10:52. doi:10.1186/1471-2474-10-52.				X	
Dunlop D. How lifestyle factors influence the development and progression of OA. *Osteoarthritis Cartilage*. 2014;22:S3-S4. doi:10.1016/j.joca.2014.02.023.			X		
Dunlop DD, Semanik P, Song J, et al. Moving to maintain function in knee osteoarthritis: evidence from the osteoarthritis initiative. *Arch Phys Med Rehabil*. 2010;91(5):714-721. doi:10.1016/j.apmr.2010.01.015.	X				
Dunlop DD, Song J, Semanik PA, et al. Objective physical activity measurement in the osteoarthritis initiative: are guidelines being met? *Arthritis Rheum.* 2011;63(11):3372-3382. doi:10.1002/art.30562.			X		

Citation	Outcome	Population	Study Design	Exposure	Other
Dunlop DD, Song J, Semanik PA, et al. Relation of physical activity time to incident disability in community dwelling adults with or at risk of knee arthritis: prospective cohort study. *BMJ*. April 2014;348:g2472. doi:10.1136/bmj.g2472.	X				
Durmus D, Alayli G, Bayrak IK, Canturk F. Assessment of the effect of glucosamine sulfate and exercise on knee cartilage using magnetic resonance imaging in patients with knee osteoarthritis: a randomized controlled clinical trial. *J Back Musculoskelet Rehabil*. 2012;25(4):275-284. doi:10.3233/BMR-2012-0336.			X		
Feinglass J, Song J, Semanik P, et al. Association of functional status with changes in physical activity: insights from a behavioral intervention for participants with arthritis. *Arch Phys Med Rehabil*. 2012;93(1):172-175. doi:10.1016/j.apmr.2011.06.037.				X	
Felson D, Niu J, Sack B, Aliabadi P, McCullough C, Nevitt MC. Progression of osteoarthritis as a state of inertia. *Ann Rheum Dis*. 2013;72(6):924-929. doi:10.1136/annrheumdis-2012-201575.				X	
Hirata S, Ono R, Yamada M, et al. Ambulatory physical activity, disease severity, and employment status in adult women with osteoarthritis of the hip. *J Rheumatol*. 2006;33(5):939-945.				X	
Holsgaard-Larsen A, Clausen B, Sondergaard J, Christensen R, Andriacchi TP, Roos E. The effect on knee-joint load of instruction in analgesic use compared with neuromuscular exercise in patients with early knee osteoarthritis—a randomized, single-blind, controlled trial. *Osteoarthritis Cartilage*. April 2016;24:S497-S498. doi:10.1016/j.joca.2016.01.912.					X
Hoogeboom TJ, den Broeder AA, de Bie RA, van den Ende CH. Longitudinal impact of joint pain comorbidity on quality of life and activity levels in knee osteoarthritis: data from the Osteoarthritis Initiative. *Rheumatology (Oxford).* 2013;52(3):543-546. doi:10.1093/rheumatology/kes314.				X	
Hunt MA, Pollock CL, Kraus VB, et al. Biomarkers of cartilage degradation and synthesis relevant to knee osteoarthritis: relationships with dynamic knee joint load and changes following exercise. *Osteoarthritis Cartilage*. April 2012;20:S83-S84. doi:10.1016/j.joca.2012.02.076.					X
Hunter DJ, Beavers DP, Eckstein F, et al. The Intensive Diet and Exercise for Arthritis (IDEA) trial: 18-month radiographic and MRI outcomes. *Osteoarthritis Cartilage*. 2015;23(7):1090-1098. doi:10.1016/j.joca.2015.03.034.			X		

Citation	Outcome	Population	Study Design	Exposure	Other
Hunter DJ, Beavers DP, Eckstein F, et al. The intensive diet and exercise for arthritis trial (IDEA): 18-month radiographic and MRI outcomes. *Arthritis Rheum*. 2012;64:S1070.			X		
Jegu AG, Pereira B, Andant N, Coudeyre E. Effect of eccentric isokinetic strengthening in the rehabilitation of patients with knee osteoarthritis: Isogo, a randomized trial. *Trials*. April 2014;15:106. doi:10.1186/1745-6215-15-106.	X				
Kean CO, Hinman RS, Wrigley TV, Lim BW, Bennell KL. Impact loading following quadriceps strength training in individuals with medial knee osteoarthritis and varus alignment. *Clin Biomech (Bristol, Avon).* Feb 2017;42:20-24. doi:10.1016/j.clinbiomech.2017.01.002.				X	
Kou U, Tohyama H, Chiba T, Ikoma K, Yasuda K. Long-term effects of video-based home exercise on clinical and radiographic outcomes in subject with knee osteoarthritis: a two-year randomized controlled trial. *Osteoarthritis Cartilage.* April 2013;21:S40. doi:10.1016/j.joca.2013.02.102.					X
Landsmeer ML, Runhaar J, van der Plas P, et al. Reducing progression of knee OA features assessed by MRI in overweight and obese women: secondary outcomes of a preventive RCT. *Osteoarthritis Cartilage*. 2016;24(6):982-990. doi:10.1016/j.joca.2015.12.016.				X	
Lange AK, Vanwanseele B, Foroughi N, et al. Resistive Exercise for Arthritic Cartilage Health (REACH): a randomized double-blind, sham-exercise controlled trial. *BMC Geriatr*. Jan 2009;9:1. doi:10.1186/1471-2318-9-1.			X		
Li LC, Lineker S, Cibere J, et al. Capitalizing on the teachable moment: osteoarthritis physical activity and exercise net for improving physical activity in early knee osteoarthritis. *JMIR Res Protoc*. 2013;2(1):e17. doi:10.2196/resprot.2553.			X		
Mikesky AE, Mazzuca SA, Brandt KD, Perkins SM, Damush T, Lane KA. Effects of strength training on the incidence and progression of knee osteoarthritis. *Arthritis Rheum*. 2006;55(5):690-699. doi:10.1002/art.22245.					X
Miller RH, Edwards WB, Brandon SC, Morton AM, Deluzio KJ. Why don't most runners get knee osteoarthritis? A case for per-unit-distance loads. *Med Sci Sports Exerc*. 2014;46(3):572-579. doi:10.1249/MSS.0000000000000135.				X	
Miyazaki T, Uchida K, Sato M, et al. Knee laxity after staircase exercise predicts radiographic disease progression in medial compartment knee osteoarthritis. *Arthritis Rheum*. 2012;64(12):3908-3916. doi:10.1002/art.34662.			X		

Citation	Outcome	Population	Study Design	Exposure	Other
Multanen J, Hakkinen A, Kujala U, et al. The effects of bone exercise on knee pain, stiffness and function among women with mild knee osteoarthritis: randomized, controlled trial. *Physiotherapy (United Kingdom)*. 2011;97:eS852-eS853.	X				
Neogi DS, Kumar A, Rijal L, Yadav CS, Jaiman A, Nag HL. Role of nonoperative treatment in managing degenerative tears of the medial meniscus posterior root. *J Orthop Traumatol*. 2013;14(3):193-199. doi:10.1007/s10195-013-0234-2.			X		
Ng NT, Heesch KC, Brown WJ. Efficacy of a progressive walking program and glucosamine sulphate supplementation on osteoarthritic symptoms of the hip and knee: a feasibility trial. *Arthritis Res Ther*. 2010;12(1):R25. doi:10.1186/ar2932.				X	
O'Hanlon MS, Siddiqi Q, Allen SL, Edwards KL. A randomised controlled trial to investigate walking 6,000 steps per day on pain and function in knee osteoarthritis progression: the walkout study. *Osteoarthritis Cartilage*. 2016;24:S486. doi:10.1016/j.joca.2016.01.891.				X	
Øiestad BE, White DK, Booton R, et al. Longitudinal course of physical function in people with symptomatic knee osteoarthritis: data from the Multicenter Osteoarthritis Study and the Osteoarthritis Initiative. *Arthritis Care Res (Hoboken).* 2016;68(3):325-331. doi:10.1002/acr.22674.				X	
Pisters MF, Veenhof C, van Dijk GM, Dekker J, CARPA Study Group. Avoidance of activity and limitations in activities in patients with osteoarthritis of the hip or knee: a 5 year follow-up study on the mediating role of reduced muscle strength. *Osteoarthritis Cartilage*. 2014;22(2):171-177. doi:10.1016/j.joca.2013.12.007.				X	
Quicke JG, Foster NE, Thomas MJ, Holden MA. Is long-term physical activity safe for older adults with knee pain? A systematic review. *Osteoarthritis Cartilage*. 2015;23(9):1445-56. doi:10.1016/j.joca.2015.05.002.					X
Rewald S, Mesters I, Emans PJ, Arts JJ, Lenssen AF, de Bie RA. Aquatic circuit training including aqua-cycling in patients with knee osteoarthritis: a feasibility study. *J Rehabil Med*. 2015;47(4):376-381. doi:10.2340/16501977-1937.	X				
Salli A, Sahin N, Baskent A, Ugurlu H. The effect of two exercise programs on various functional outcome measures in patients with osteoarthritis of the knee: a randomized controlled clinical trial. *Isokinet Exerc Sci*. 2010;18(4):201-209. doi:10.3233/IES-2010-0385.	X				

Citation	Outcome	Population	Study Design	Exposure	Other
Song J, Semanik P, Sharma L, et al. Assessing physical activity in persons with knee osteoarthritis using accelerometers: data from the osteoarthritis initiative. *Arthritis Care Res (Hoboken).* 2010;62(12):1724-1732. doi:10.1002/acr.20305.	X				
Srivastava RN, Avasthi V, Srivastava SR, Raj S. Does yoga improve pain, stiffness and physical disability in knee osteoarthritis? A randomize controlled clinical trial. *Osteoarthritis Cartilage*. April 2015;23:A167. doi:10.1016/j.joca.2015.02.930.				X	
Stensrud S, Roos EM, Risberg MA. A 12-week exercise therapy program in middle-aged patients with degenerative meniscus tears: a case series with 1-year follow-up. *J Orthop Sports Phys Ther*. 2012;42(11):919-931. doi:10.2519/jospt.2012.4165				X	
Tateuchi H, Koyama Y, Akiyama H, et al. Daily cumulative hip moment is associated with radiographic progression of secondary hip osteoarthritis. *Osteoarthritis Cartilage*. 2017;25(8):1291-1298. doi:10.1016/j.joca.2017.02.796.				X	
Thorp LE, Wimmer MA, Foucher KC, Sumner DR, Shakoor N, Block JA. The biomechanical effects of focused muscle training on medial knee loads in OA of the knee: a pilot, proof of concept study. *J Musculoskelet Neuronal Interact*. 2010;10(2):166-173.	X				
Tohyama H, Chiba T, Kou U, et al. Effects of video-based home exercise on clinical and radiographic outcomes in adults with knee osteoarthritis: a one-year randomized controlled trial. *Osteoarthritis Cartilage.* Sept 2011;19:S37. doi:10.1016/S1063-4584(11)60095-2.					X
Torry MR. Scientific and clinical advances leading to improved treatment of knee osteoarthritis. *Med Sci Sports Exerc*. 2008;40(2):191-192. doi:10.1249/mss.0b013e31815cb1eb.			X		
Uusi-Rasi K, Patil R, Karinkanta S, Tokola K, Kannus P, Sievänen H. Exercise training in treatment and rehabilitation of hip osteoarthritis: a 12-week pilot trial. *J Osteoporos*. Jan 2017:3905492. doi:10.1155/2017/3905492.			X		
Videman T, Battié MC, Ripatti S, Gill K, Manninen H, Kaprio J. Determinants of the progression in lumbar degeneration: a 5-year follow-up study of adult male monozygotic twins. *Spine (Phila Pa 1976)*. 2006;31(6):671-678. doi:10.1097/01.brs.0000202558.86309.ea.				X	
Vincent KR, Hamilton AS, Lomonaco C, et al. Poster 202 Progressive enhanced eccentric or concentric resistance exercise training for knee osteoarthritis: initial results on pain and function. *PM R*. 2012;4(10)(suppl):S188. doi:10.1016/j.pmrj.2012.09.629.	X				

Citation	Outcome	Population	Study Design	Exposure	Other
Vincent KR, Montero C, Vincent HK. Progressive enhanced eccentric or concentric resistance exercise training for knee osteoarthritis. *Osteoarthritis Cartilage*. 2013;21:S275-S276. doi:10.1016/j.joca.2013.02.577.	X				
Walter JP, D'Lima DD, Colwell CW Jr, Fregly BJ. Decreased knee adduction moment does not guarantee decreased medial contact force during gait. *J Orthop Res*. 2010;28(10):1348-1354. doi:10.1002/jor.21142.				X	
White DK, Zhang Y, Niu J, et al. Do worsening knee radiographs mean greater chances of severe functional limitation? *Arthritis Care Res (Hoboken)*. 2010;62(10):1433-1439. doi:10.1002/acr.20247.				X	
Wondrasch B, Aroen A, Rotterud JH, Hoysveen T, Bolstad K, Risberg MA. The feasibility of a 3-month active rehabilitation program for patients with knee full-thickness articular cartilage lesions: the Oslo Cartilage Active Rehabilitation and Education Study. *J Orthop Sports Phys Ther*. 2013;43(5):310-324. doi:10.2519/jospt.2013.4354.				X	
Yusuf E. Pharmacologic and non-pharmacologic treatment of osteoarthritis. *Curr Treatm Opt Rheumatol.* 2016;2(2):111-125.			X		
Zeni JA Jr, Higginson JS. Dynamic knee joint stiffness in subjects with a progressive increase in severity of knee osteoarthritis. *Clin Biomech (Bristol, Avon)*. 2009;24(4):366-371. doi:10.1016/j.clinbiomech.2009.01.005.	X				

References

1. Bartels EM, Juhl CB, Christensen R, et al. Aquatic exercise for the treatment of knee and hip osteoarthritis. *Cochrane Database Syst Rev*. 2016;Cd005523. doi:10.1002/14651858.CD005523.pub3.

2. Beumer L, Wong J, Warden SJ, Kemp JL, Foster P, Crossley KM. Effects of exercise and manual therapy on pain associated with hip osteoarthritis: a systematic review and meta-analysis. *Br J Sports Med*. 2016;50(8):458–463. doi:10.1136/bjsports-2015-095255.

3. Chang WD, Chen S, Lee CL, Lin HY, Lai PT. The effects of tai chi chuan on improving mind-body health for knee osteoarthritis patients: a systematic review and meta-analysis. *Evid Based Complement Alternat Med*. 2016;1813979. doi:10.1155/2016/1813979.

4. Fransen M, McConnell S, Harmer AR, Van der Esch M, Simic M, Bennell KL. Exercise for osteoarthritis of the knee: a Cochrane systematic review. *Br J Sports Med*. 2015;49(24):1554–1557. doi:10.1136/bjsports-2015-095424.

5. Juhl C, Christensen R, Roos EM, Zhang W, Lund H. Impact of exercise type and dose on pain and disability in knee osteoarthritis: a systematic review and meta-regression analysis of randomized controlled trials. *Arthritis Rheumatol*. 2014;66(3):622–636. doi:10.1002/art.38290.

6. Escalante Y, Garcia-Hermoso A, Saavedra JM. Effects of exercise on functional aerobic capacity in lower limb osteoarthritis: a systematic review. *J Sci Med Sport*. 2011;14(3):190–198. doi:10.1016/j.jsams.2010.10.004.

7. Quicke JG, Foster NE, Thomas MJ, Holden MA. Is long-term physical activity safe for older adults with knee pain? A systematic review. *Osteoarthritis Cartilage*. 2015;23(9):1445–1456. doi:10.1016/j.joca.2015.05.002.

8. Timmins KA, Leech RD, Batt ME, Edwards KL. Running and knee osteoarthritis: a systematic review and meta-analysis. *Am J Sports Med*. 2016;45(6):1447-1457. doi: 10.1177/0363546516657531.

9. Dore DA, Winzenberg TM, Ding C, et al. The association between objectively measured physical activity and knee structural change using MRI. *Ann Rheum Dis*. 2013;72(7):1170–1175. doi:10.1136/annrheumdis-2012-201691.

10. Felson DT, Niu J, Yang T, et al. Physical activity, alignment and knee osteoarthritis: data from MOST and the OAI. *Osteoarthritis Cartilage*. 2013;21(6):789–795. doi:10.1016/j.joca.2013.03.001.

11. Kwee RM, Wirth W, Hafezi-Nejad N, Zikria BA, Guermazi A, Demehri S. Role of physical activity in cartilage damage progression of subjects with baseline full-thickness cartilage defects in medial tibiofemoral compartment: data from the Osteoarthritis Initiative. *Osteoarthritis Cartilage*. 2016;24(11):1898–1904. doi:10.1016/j.joca.2016.06.009.

12. Lin W, Alizai H, Joseph GB, et al. Physical activity in relation to knee cartilage T2 progression measured with 3 T MRI over a period of 4 years: data from the Osteoarthritis Initiative. *Osteoarthritis Cartilage*. 2013;21(10):1558–1566. doi:10.1016/j.joca.2013.06.022.

13. Oiestad BE, Quinn E, White D, et al. No association between daily walking and knee structural changes in people at risk of or with mild knee osteoarthritis. Prospective data from the Multicenter Osteoarthritis Study. *J Rheumatol*. 2015;42(9):1685–1693. doi:10.3899/jrheum.150071.