# Walking, running, and recreational sports for knee osteoarthritis: An overview of the evidence

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# Abstract

**Objective:** We provided an overview of narrative reviews, systematic reviews, and meta-analyses that summarize primary evidence of how physical activity (PA) relates to structural progression of knee osteoarthritis (OA). This overview can serve as a resource for healthcare providers when recommending PA to patients with, or at risk, for knee OA.

**Methods:** We searched the PubMED database for publications on "exercise" [MeSH Terms] and "knee osteoarthritis" [MeSH Terms]. We restricted our search to review articles, originally published in English, from 2005 to 2020. We then added several original studies to provide more detailed support of the findings of the review articles, based on the authors familiarity with the literature.

**Results:** We summarized the findings of 20 reviews and an additional 12 original studies. We found consistent evidence that common forms of PA (walking, running, and certain recreational sports) are not related to structural progression of knee OA, and can be safely recommended to patients with, or at risk, for knee OA.

**Conclusion:** Healthcare providers can refer to this overview of the evidence, as well as current PA guidelines, when recommending PA to their patients with, or at risk for, knee OA. Future studies can support PA guidelines that target preserving the structural integrity of the knees.

Keywords: Physical activity, exercise, running, osteoarthritis of the knee

#### Introduction

Knee osteoarthritis (OA) is a serious disease<sup>1</sup> characterized by structural breakdown of the knee joint. Globally, OA is the third fastest growing disease<sup>1</sup> and a leading cause of disability.<sup>2</sup> To address the growing burden of this disease, it is crucial that healthcare providers are able to recognize, and intervene on, key risk factors of knee OA.

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One such risk factor, whose role has remained unclear for some time, is physical activity (PA). PA is defined as "any bodily movement produced by skeletal muscle that results in energy expenditure."<sup>3</sup> Such movement may be structured (i.e., purposeful and repetitive, known as "exercise") or unstructured (e.g., house-hold activities, like cooking and gardening). While PA has many known health benefits, it is often associated with "wear and tear" on the knee joint.<sup>4</sup> Fortunately, our understanding of knee OA is evolving, as there is evidence that PA may not be harmful to the knee. That is, practice guidelines for the management of knee OA now recommend PA as a first-line intervention to improve pain and function.<sup>5–7</sup>

While pain and function are well-studied in the context of PA and knee OA, few studies examine how PA relates to structural progression of knee OA.<sup>8,9</sup> That is, healthcare providers know that recommending PA can improve pain and function in patients with knee OA but do *not* know how it affects the structural integrity of their patients' knees. This uncertainty serves as an important barrier to providers recommending PA.<sup>10,11</sup> and to patients increasing their PA.<sup>4,12,13</sup> Several studies over the last decade have attempted to address this gap in our understanding of knee OA. These studies are effectively summarized (qualitatively and/or quantitatively) through narrative reviews, systematic reviews (SRs), and meta-analyses; unfortunately, it may be cumbersome for healthcare providers to identify and synthesize existing reviews that are relevant to this clinical question.

Therefore, our objective was to provide a comprehensive overview of existing narrative reviews, SRs, and meta-analyses that examine how PA relates to structural progression of knee OA. We searched the PubMED database for reviews related to "exercise" [MeSH Terms] AND "knee osteoarthritis" [MeSH Terms] (Figure 1). Additional details about inclusion/exclusion of reviews can be found in the Supplementary

#### "exercise" [MeSH Terms] AND "knee osteoarthritis" [MeSH Terms] Reviews, Systematic Reviews, Meta-analyses 2005 - 2020Titles/abstracts reviewed: Excluded: n = 74 n = 114Not in knee OA, n = 10No structural outcomes, n = 59 Not originally published in English, n = 2Retrieved full text for detailed review: Duplicate, n = 3n = 40Excluded: n = 20Not in human subjects, n=1 No measures of physical activity, n=4 No structural outcomes, n = 12Duplicate, n=1 Unable to find full text, n=2 Included after detailed review: n = 20

Figure 1. Flow diagram depicting PubMed search strategy.

material. For SRs or narrative reviews with a qualitative synthesis and/or meta-analysis of original studies, we state their main results in Tables 1-3; for reviews that did not include a qualitative synthesis and/or meta-analysis of original studies, we state their main conclusions in Tables 1-3.

In the first section of this overview, we cite evidence as to how (and why) our understanding of PA and knee OA is evolving. In the next section, we describe general PA guidelines and then summarize the evidence for (1) walking, (2) running, and (3) recreational sports in three subsections. We added a fourth subsection to discuss how other risk factors (obesity, previous

# Main Points

- There is consistent evidence that common forms of PA (walking, running, and certain recreational sports) do not increase risk of structural progression of knee OA.
- Healthcare providers can refer to the WHO guidelines to provide a general PA recommendation to patients with, or at risk for, knee OA.
- Some patients may benefit from additional, specific recommendations that address other risk factors (obesity, previous knee injury, and other structural abnormalities) that relate to knee OA progression.
- Adults with (and without) knee OA could benefit from future studies that determine if meeting PA guidelines preserves the structural integrity of the knees.

knee injury, and other structural abnormalities) may impact PA recommendations for patients with, or at risk for, knee OA. In the final two sections of this overview, we provide suggestions for future research and highlight the need for PA guidelines that preserve the structural integrity of the knees.

# Then vs now: our evolving understanding of PA in knee OA

For years, it was a commonly held belief that engaging in PA-accelerated structural progression of knee OA.<sup>14</sup> Our understanding of knee OA was limited to gradual "wear and tear" of the knee joint, which could only be made worse by engaging in PA.<sup>15</sup> Fortunately, over the last few decades, our understanding of knee OA evolved. Numerous studies have demonstrated that PA improves pain and function in adults with knee OA<sup>5-7,9</sup>; now, PA is universally recommended as a first-line, nonpharmacological intervention for the management of knee OA.5-7 Unfortunately, a recent systematic umbrella review by Kraus et al.<sup>9</sup> concluded that there is much less evidence relating PA to structural outcomes in knee OA. This makes it difficult for providers<sup>16</sup> to refute patients' beliefs that PA causes "wear and tear."12,13

However, providers should be aware that available evidence consistently shows that many types of PA do not increase risk for structural progression of knee OA. That is, adults with, or at risk for, knee OA can regularly engage in PA without accelerating their OA. Systematic reviews by Bricca et al.<sup>17</sup> and Quicke et al.<sup>8</sup> examined structural outcomes following PA interventions in adults with knee OA and knee pain, respectively. Nearly, all PA interventions were weightbearing, land-based, and aerobic in nature, and all PA interventions involved a

structured exercise program at a moderate intensity for a minimum of 3 months. In the first review by Bricca et al.,<sup>17</sup> 13 out of 14 study comparisons revealed that PA had no effect (or a positive effect) on the structural integrity of knee cartilage. In the second review by Quicke et al.,<sup>8</sup> six out of seven studies concluded that PA did not increase risk of radiographic OA progression, and four out of four studies concluded that PA did not increase risk of knee replacement.

# Recommending PA for adults with knee OA

The World Health Organization (WHO) recommends that all adults engage in at least 150 minutes week<sup>-1</sup> of moderate intensity PA (e.g., brisk walking) or at least 75 minutes week<sup>-1</sup> of vigorous intensity PA (e.g., jogging or running).<sup>18</sup> These guidelines are echoed by the United States<sup>19</sup> and countries in the European Union.<sup>20</sup> Importantly, adults who meet these guidelines are not at increased risk for the development (i.e., incidence) of radiographic or symptomatic knee OA (hazard ratio [HR] = 1.2, 95% CI 0.9-1.8).<sup>21</sup>

It should be noted that the guidelines take a "one-size-fits-all" approach to recommending PA, whereby *all* adults (18+ years) are considered capable of meeting these guidelines. Below, we cite evidence that even adults with severe knee OA or symptoms, who walk with an assistive device or who are of older age, can safely engage in PA and meet PA guidelines.

First, adults with severe knee OA or symptoms can engage in PA without increasing their knee pain. A narrative review by Esser and Bailey<sup>16</sup> cited an original study by Mangione et al.,<sup>22</sup> in which adults with mild to severe knee OA were randomly assigned to either a low-intensity or high-intensity structured cycling program (25 minutes/session, three sessions/week over 10 weeks). Neither program increased acute pain per the visual analog scale, which was administered before and after each cycling session, and on a daily basis. In fact, both programs led to statistically significant reductions in knee pain over 10 weeks (P < .000).<sup>22</sup> Two additional studies by Wallis et al.<sup>23,24</sup> focused on adults with severe knee OA (Kellgren-Lawrence [KL] Grade IV) and randomly assigned them to either a structured walking program (walking at a moderate intensity for 70 minutes week<sup>-1</sup> over 12 weeks) or usual care (i.e., pain management). Those assigned to the walking program spent, on average, 18 more minutes per day in walking (95% CI 5-31 minutes) but had no greater knee pain than the usual care group (difference = 0.1, 95% Cl -0.7 to -1.0) per the Numeric Pain Rating Scale.<sup>23,24</sup>

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Table 1. Summary of Reviews That Examined General PA (Including Walking) and the Structural Progression of Knee OA						
Review Details	Measure(s) of Physical Activity	Measure(s) of Structural Progression of Knee OA	Main Results (Qualitative Synthesis or Meta-analysis) or Main Conclusions			
Kraus et al. <sup>9</sup> Systematic umbrella review Medicine & Sci- ence in Sports & Exercise	Self-reported PA via PASE questionnaire Steps/day via accelerometry	Knee replacement Progression of radio- graphic OA	<ul> <li>This umbrella review cited a meta-analysis by Timmins et al.<sup>49</sup></li> <li>that included 2, 172 adults from three case-control studies. The authors found that runners (who ran for 1 year up to a lifetime) had lower odds of knee replacement due to OA than nonrunners (pooled odds ratio [OR] = 0.46, P = .0004). See entry below for Timmins et al.<sup>49</sup></li> <li>This umbrella review also cited a systematic review by Quicke et al. that included 8,614 adults with knee pain and/or radiographic knee OA.</li> <li>Six out of seven RCTs found that adults who participated in a PA intervention (i.e., PA groups) had no greater risk for structural progression of OA than those who did not (i.e., non-PA groups)</li> <li>Four out of four RCTs found that adults in PA groups did not have more knee replacements than non-PA group (8 vs 10, respectively))</li> <li>A retrospective case-control study found that adults with high cumulative hours of recreational PA had lower odds of knee replacement than adults with a history of no regular PA (men: OR = 0.35, 95% CI 0.12-0.95 and women: OR = 0.56, 95% CI 0.30-0.93)</li> </ul>			
Bricca et al. <sup>17</sup> Systematic review British Journal of Sports Medicine	PA interventions last- ing a minimum of 3 months, most involving weight- bearing, land-based, aerobic, moderate intensity PA	Cartilage morphome- try (thickness and volume) Cartilage morphology (defects) Cartilage composition (glycosaminoglycan [GAG] content or T2 relaxation times)	This SR included 702 adults with or at risk for knee OA from nine RCTs. A total of 14 comparisons of MRI-based cartilage measures were made between PA and non-PA groups Ten out of 14 comparisons showed PA had no effect on cartilage Three comparisons showed PA had a positive effect on cartilage One comparison showed PA had a negative effect on cartilage			
Antony et al. <sup>41</sup> Narrative review Arthritis Research & Therapy	PA interventions including a 10-week moderate running program and 4- month moderate weight-bearing PA program Self-reported PA via questionnaire (recent and lifetime)	Cartilage volume Cartilage GAG content Incident radiographic OA	This narrative review focused on early life risk factors for knee OA including PA. The authors did not perform a qualitative syn- thesis of included studies The authors concluded that in children (9-18 years) and young adults (25 years), there is consistent evidence that moderate PA is beneficial to the knee joint later in life (based on cartilage volume, GAG content, BMLs); meanwhile, there is mixed evi- dence for the effects of vigorous PA			
Fransen et al. <sup>54</sup> Narrative review Best Practice & Research Clinical Rheumatology	Self-reported PA via questionnaire	Self-reported physician-diagnosed knee OA Radiographic OA Clinical knee OA Knee replacement	This narrative review included 10 "longitudinal cohort studies evaluating physical activity as a risk factor for symptomatic knee or hip OA (or joint replacement surgery)" Six out of seven studies found that self-reported PA was not related to incident symptomatic knee OA. For example, Barbour et al. found that meeting PA guidelines was not associ- ated with incident symptomatic knee OA (HR = 1.2, 95% CI 0.9-1.9). However, Martin et al. <sup>53</sup> found that women who were most active and obese had higher odds of incident knee OA (OR 1.8, 95% CI 1.5-2.2) One study found that self-reported walking was not related to incident knee pain Two studies found that moderate intensity PA or walking was not related to incident knee replacement			

Review Details	Measure(s) of Physical Activity	Measure(s) of Structural Progression of Knee OA	Main Results (Qualitative Synthesis or Meta-analysis) or Main Conclusions
Lim et al. <sup>53</sup> Systematic review Seminars in Arthritis and Rheumatism	Self-reported PA via questionnaire	Prevalent BMLs Incident BMLs	This SR included 533 adults, with or without knee OA, from three cross-sectional studies that examined how PA related to risk for BMLs. The authors highlighted the paucity of evidence regarding the relationship between PA and BMLs One study found that PA was not related to prevalent BMLs One study found that high PA (per the PASE questionnaire) was related to higher prevalence of BMLs (low PASE = 28%, middle PASE = 42%, and high PASE = 54%, P = .02) One study found that recreational walking frequency was protec- tive against BMLs 10 years later (OR = 0.6, 95% CI 0.3-0.98)
Jones et al. <sup>48</sup> Narrative review The Physician and Sportsmedicine	Self-reported PA via questionnaire Steps/day via accelerometry	Incident knee OA Cartilage volume Cartilage GAG content Cartilage defects BMLs Knee replacement	This narrative review focused on the effects of PA on structural outcomes measured via MRI. The authors did not perform a qualitative synthesis of included studies The authors concluded that the evidence most consistently indi- cates that PA has little effect on knee joint health. Furthermore, PA can be recommended to older adults without concern for structural deterioration, although there is still insufficient evi- dence for those with existing BMLs
Esser and Bailey <sup>16</sup> Narrative review Current Pain and Headache Reports	Self-reported PA via questionnaire PA interventions including walking, aerobic exercise, and cycling	Incident knee OA Number of osteophytes	This narrative review focused on addressing misconceptions that "health care providers and patients share" regarding PA and knee OA. The authors did not perform a qualitative synthe- sis of included studies The authors concluded that there is "overwhelming" evidence that light to moderate PA does not cause or accelerate knee OA. Furthermore, PA may protect against knee OA and should be recommended to all patients for its many benefits
Urquhart et al. <sup>40</sup> Systematic review Medicine & Sci- ence in Sports & Exercise	Self-reported PA via interview or questionnaire	Number of osteophytes Loss of joint space width Cartilage volume Cartilage defects	This SR included 9,582 adults, with and without knee OA, from 28 studies Five out of eight cross-sectional and case-control studies found that PA had no effect on structural (radiographic) progression of knee OA Eight out of 13 longitudinal studies found that PA had no effect on structural (radiographic) progression of knee OA Three out of four cross-sectional studies found that PA had no effect, or a beneficial effect, on knee cartilage based on MRI Three out of three longitudinal studies found that PA had no effect, or a beneficial effect, on knee cartilage based on MRI
Bennell and Hinman (2011) Narrative review Journal of Sci- ence and Medi- cine in Sport	PA interventions including a 12- month land-based strengthening program	Progression of radio- graphic OA	This narrative review focused on PA prescription to manage symptoms in patients with knee OA. The authors did not per- form a qualitative synthesis of included studies The authors concluded that few studies have evaluated the effects of PA on structural progression of knee OA, and "there is currently no evidence to show that PA can be disease-modifying"
Egan and Mentes <sup>28</sup> Narrative review Journal of Geron- tological Nursing	Self-reported PA via survey	Cartilage defects	This narrative review discussed several risk factors for knee OA and recommended nursing interventions for symptom manage- ment. The authors did not perform a qualitative synthesis of included studies The authors cited one original study by Racunica et al., <sup>38</sup> who found that vigorous PA was associated with improved integrity of knee joint structures in adults aged 50-79. The authors also cited one review by Ding et al., <sup>63</sup> who reported that women who walked regularly were less likely to show cartilage degeneration on MRI, and that regular exercise may be protec- tive against cartilage degeneration through maintenance of guadricens strength

Table 1. (continued)—Summary of Reviews That Examined General PA (Including Walking) and the Structural Progression of Knee OA

Review Details	Measure(s) of Physical Activity	Measure(s) of Structural Progression of Knee OA	Main Results (Qualitative Synthesis or Meta-analysis) or Main Conclusions
Bosomworth <sup>50</sup> Narrative review Canadian Family Physician	Self-reported PA, including walking, running, and sports PA interventions including walking and aerobic exercise	Incident radiographic OA	This narrative review focused on the effects of PA on the inci- dence and progression of knee OA. The author included 22 studies and performed a qualitative synthesis Fifteen out of 22 included studies (of various study designs) found that PA had no effect on structural progression of knee OA The authors concluded that the highest-quality evidence shows that PA at a moderate level, and especially running, is safe and does not accelerate the onset knee OA. Competitive sports par- ticipation in childhood and elite-level competition in adulthood may increase one's risk for OA, although this can also be attrib- uted to obesity, injury, occupational demands, and joint malalignment
Roddy et al. <sup>64</sup> Narrative review Rheumatology	PA interventions including an 18- month walking or strengthening program	Progression of radio- graphic OA	This narrative review was prepared by a multidisciplinary guide- line development group of 20 experts. They agreed upon 10 recommendations for the management of knee (or hip) OA and then summarized available evidence for each recommendation. Therefore, the authors did not perform a qualitative synthesis of included studies The ninth recommendation from the authors was as follows: "9. The effectiveness of exercise is independent of the presence or severity of radiographic findings." The authors concluded that evidence for this recommendation was very limited, but they cited one RCT by Fransen et al. <sup>54</sup> that found adults with lower loss of medial tibiofemoral joint space width were more likely to benefit from PA interventions (in terms of pain and function) than those with more severe loss of joint space width, which did not support the recommendation

Table 1. (continued)—Summary of Reviews That Examined General PA (Including Walking) and the Structural Progression of Knee OA

In addition, older adults with knee pain who use an assistive device can engage in walking (as a form of PA) without worsening pain or structural progression of knee OA.25 These adults can walk for 20 minutes  $day^{-1}$  (without a higher rate of falls) to minimize functional decline.<sup>26</sup> Furthermore, the PA guidelines also apply to adults who are considered "old-old" (75-84 years) or "oldest old" (85+ years). A large RCT by Pahor et al.<sup>27</sup> focused on adults in this age range (70-89 years) and randomly assigned them to either a structured PA program (walking at a moderate intensity for 150 minutes week $^{-1}$  plus strengthening, flexibility, and balance exercises) or an educational program. The PA program was protective against both incident (HR = 0.82, 95% CI 0.69-0.98) and persistent walking disability (HR = 0.72, 95% CI 0.57-0.91) over 2.6 years compared with the educational program and did not have a significantly higher rate of adverse events (HR = 1.08, 95% CI 0.98-1.20).

Thus, providers should recommend PA to all adults, so they can meet PA guidelines. This overview focuses on recommendations for three common forms of PA: (1) walking, (2) running, and (3) recreational sports. Recommending one form of PA over another should be largely based on patient preferences but should also consider the presence of certain risk factors (i.e., obesity, previous knee injury, and structural knee abnormalities) that independently contribute to the progression of knee OA.<sup>28</sup> We also provide a brief discussion as to how providers should recognize and address these other risk factors when recommending PA.

#### Walking

Walking is the most common form of PA among adults.<sup>29</sup> Walking is practical and accessible, as it requires only a comfortable pair of shoes.<sup>29</sup> Furthermore, brisk walking is a prime example of moderate intensity PA. "Brisk" walking generally refers to (1) a walking cadence of at least 100 steps min<sup>-1</sup>, (2) a walking pace of about 3 miles h<sup>-1</sup>, or (3) a walking pace of about 20 min mile<sup>-1.30</sup> That is, providers can recommend that patients go for a 30-minute brisk walk, 5 times week<sup>-1</sup>, to satisfy the WHO recommendation of at least 150 minutes week<sup>-1</sup> of moderate intensity PA. Reviews by Antony et al.<sup>41</sup> and Fransen et al.<sup>54</sup>

cited as an original study by Felson et al.<sup>31</sup> found that adults who were normal weight to overweight and reported walking at least 9 miles week $^{-1}$  (i.e., about 180 minutes week $^{-1}$ , which satisfies the WHO recommendation) did not have increased risk of joint space loss (OR = 0.95, 95% CI 0.62-1.45) or incident knee OA (OR = 1.10, 95% CI 0.73-1.66) over a 9-year period.<sup>31</sup> Reviews by Kraus et al.<sup>9</sup> and Fransen et al.<sup>54</sup> cited as original studies by Manninen et al.<sup>32</sup> and Ageberg et al.,<sup>33</sup> respectively, found that higher self-reported lifetime PA did not increase risk for knee replacement (men: OR = 0.35, 95% CI 0.12-0.95 and women: OR = 0.56, 95% Cl 0.30-0.93),<sup>32</sup> and higher leisuretime PA (including walking) was not associated with incident knee replacement.<sup>33</sup>

Alternatively, patients who use a pedometer or activity monitor can aim to walk a total of 10,000 steps day<sup>-1.34</sup> Reviews by Kraus et al.,<sup>9</sup> Esser and Bailey,<sup>16</sup> and Jones et al.<sup>48</sup> cited as original studies by Doré et al.<sup>35</sup> and Oiestad et al.<sup>36</sup> separately found that adults with mild to moderate knee OA who walked more than 10,000 steps day<sup>-1</sup> had no greater risk for worsening cartilage defects over 2 years

Table 2. Summary of Reviews That Examined Running and Structural Progression of Knee OA	

Review Details	Measure(s) of Physical Activity	Measure(s) of Structural Progression of Knee OA	Main Conclusion(s)
Gessel and Harrast <sup>43</sup> Narrative review Current Sports Medicine Reports	Self-reported running, categorized as: • Nonrunning • Low-dose, e.g., less than 25 mi week <sup>-1</sup> • High-dose, e.g., at least 25 mi week <sup>-1</sup>	Incident radiographic OA Progression of radio- graphic OA Incident symptomatic OA	This narrative review focused on the debate surrounding "whether or not running leads to the development of knee and hip osteoarthritis." The authors did not perform a quali- tative synthesis of included studies The authors concluded that low-dose running may protect against the onset and progression of knee OA, whereas higher-dose running may increase one's risk of developing OA in the lower extremities, although dosage remains chal- lenging to define The authors also included anecdotal evidence that health- care providers should talk to patients who want to start run- ning about (1) the importance of conditioning and cross- training, (2) possible modifications for adults who are obese, and (3) how to avoid and/or treat common running injuries
Castillo et al. <sup>44</sup> Narrative review American Journal of Physical Medicine & Rehabilitation	Self-reported running (12-24 mi week <sup>-1</sup> ) over a range of 32- 50 years	Loss of joint space width Progression of radio- graphic OA Number of osteophytes	This narrative review summarized evidence related to run- ning and risk for developing knee OA. The authors did not perform a qualitative synthesis of included studies The authors concluded that available evidence does not indicate a relationship between low- and moderate-level running and knee OA. Furthermore, competitive runners seem to demonstrate a higher risk of knee OA, but "competitive running" has been inconsistently defined
Alentorn-Geli et al. <sup>45</sup> Systematic review and meta-analysis Journal of Orthopaedic & Sports Physical Therapy	Self-reported running, categorized as: • Nonrunning • Recreational • Competitive, i.e., pro- fessional, elite, or ex- elite athletes	Incident radiographic OA Prevalent radiographic OA Progression of radio- graphic OA	This SR included 125,810 adults, with and without knee OA, from 25 studies that examined running and knee OA Eighteen out of 22 studies concluded that running was not related to increased risk of knee OA The authors performed a MA that included 114,829 adults from 17 studies. The meta-analysis showed that recrea- tional runners had lower odds of knee OA than control indi- viduals (pooled OR = 0.83, 95% CI 0.7-0.99). They also found that recreational runners had lower odds of knee OA than competitive runners (P = .005)
Miller <sup>46</sup> Narrative review Exercise and Sport Sci- ences Reviews	Self-reported running, categorized as: • Recreational, e.g., 10- 20 mi week <sup>-1</sup> • Competitive, e.g., $\geq$ 100 mi week <sup>-1</sup>	Incident radiographic OA Cartilage thickness Cartilage GAG content	This narrative review found that contrary to popular belief, runners are not at higher risk for developing knee OA. The author did not perform a qualitative synthesis of included studies The author offered two potential explanations as to why runners do not have higher risk for knee OA: (1) stresses on the knee joint during running are actually not very high, and (2) runners may have conditioned their cartilage to with- stand higher loads
Timmins et al. <sup>49</sup> Systematic review and meta-analysis American Journal of Sports Medicine	Self-reported running	Incident radiographic OA Progression of radio- graphic knee OA (based on osteophytes, carti- lage thickness/volume/ surface area, knee joint angle, and joint space width) Knee replacement	This SR included 8,753 adults with and without knee OA from 15 studies. A total of 19 statistical comparisons were made between runners and nonrunners Three out of five comparisons showed no differences in incident OA between runners and nonrunners ( $OR = 1.00$ , 95% CI 0.27-3.68). One comparison showed that male and female orienteers had no greater risk for incident OA than community controls ( $OR = 1.07$ , 95% CI 0.62-1.82 and OR = 0.91, 95% CI 0.34-2.45, respectively). One comparison showed that male elite orienteers had greater odds for incident OA than community controls ( $OR = 1.79$ , 95% CI 1.10-3.54)

Review Details	Measure(s) of Physical Activity	Measure(s) of Structural Progression of Knee OA	Main Conclusion(s)
			Twelve out of 14 comparisons showed no differences in pro- gression of radiographic OA between runners and nonrun- ners. One comparison showed a higher score of sclerosis in female runners compared to community controls (6.7 vs 5.1, $P < .05$ ) but not in male runners (5.5 vs 5.5). One com- parison showed a higher joint surface area in male triath- letes compared to controls (120 vs 110 cm <sup>2</sup> , $P < .01$ ) but not in female triathletes (95.2 vs 88.9 cm <sup>2</sup> ) The authors performed a MA for knee replacement. The MA included 2,172 adults from three case–control studies and found that runners (who ran for 1 year up to a lifetime) had lower odds of knee replacement due to OA than nonrunners (pooled OR = 0.46, $P = .0004$ )
Hansen et al. <sup>39</sup> Narrative review PM&R	Self-reported running	Prevalent radiographic OA Prevalent OA-related surgery Incident radiographic OA Progression of radio- graphic OA Cartilage thickness and volume	This narrative review summarized evidence related to run- ning and risk for developing knee OA. The authors did not perform a qualitative synthesis of included studies The authors concluded that low- and moderate-volume run- ning does not seem to increase risk of incident knee OA, and that the evidence regarding high-volume running is inconclusive. Furthermore, the authors commented that existing evidence suggests that older runners are generally healthier than nonrunners

Table 2.	(continued)—	-Summary of	f Reviews	That Exami	ned Running	and Structur	al Progression	of Knee O
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(Dore: RR = 1.06, P = .616; Oiestad: RR = 1.21, 95% CI 0.82-1.79).<sup>35,36</sup> However, it should be noted that while walking 10,000 steps day<sup>-1</sup> is likely to satisfy the WHO recommendation of 150 minutes week<sup>-1</sup> of moderate intensity PA, it is not guaranteed.<sup>37</sup>

In addition to consistent evidence that brisk walking does not play a role in the structural progression of knee OA, there is some evidence that it may be *beneficial* for the knee joint. Several reviews (nine out of 20) reported that adults who regularly engage in moderate intensity PA (e.g., brisk walking) had greater cartilage volume,<sup>38–40</sup> fewer cartilage defects,<sup>28,40</sup> and fewer bone marrow lesions (BMLs)<sup>38,41</sup> compared with sedentary controls. Even so, long-term preservation of the structural integrity of the knees is likely dependent on sustained engagement in moderate intensity PA over the course of a lifetime.<sup>42</sup>

#### Running

Running is another common form of PA that is growing in popularity.<sup>29</sup> Similar to walking, running requires little equipment and is highly accessible. Over the last decade, several reviews specifically addressed the misconception that running increases one's risk for knee OA (Table 2). For example, a review by Hansen et al.<sup>39</sup> identified the limitations of a few, older studies that posited a link between running and knee OA (e.g., small sample size, lack of a control group, and limited generalizability of findings).<sup>39</sup> Recent narrative reviews by Gessel and Harrast<sup>43</sup> and Castillo et al.,<sup>44</sup> as well as a systematic review by Alentorn-Geli et al.45 all provide consistent evidence that recreational running of 25 miles week<sup>-1</sup> ( $\sim$ 250 minutes week $^{-1}$ ) is not related to increased risk of structural progression of knee OA.43-45 In fact, Alentorn-Geli et al.45 performed a metaanalysis that showed recreational runners had both lower odds of knee OA than control individuals (pooled OR = 0.83, 95% CI 0.7-0.99), and lower prevalence of knee OA than competitive runners (P = .005).<sup>45</sup> In contrast, Miller<sup>46</sup> states that even elite-level runners (e.g., over 100 miles week<sup>-1</sup>) may not have higher risk of knee OA,<sup>46</sup> although he acknowledges that this is less conclusive and may only hold true for elite runners who remain uninjured.<sup>47</sup>

Narrative reviews by Jones et al.,<sup>48</sup> Hansen et al.,<sup>39</sup> and Urquhart et al.<sup>40</sup> presented evidence that running may also be *beneficial* for the knee joint.<sup>48</sup> Running seems to have consistently positive effects on knee cartilage<sup>39</sup> but not subchondral bone or osteophytes.<sup>40</sup> Additionally, a meta-analysis by Timmins et al.<sup>49</sup> summarized three case–control studies and concluded that runners had 54% lower odds (pooled OR = 0.46, *P* = .0004) of having a knee surgery due to OA when compared with nonrunners.<sup>49</sup>

In his narrative review, Bosomworth<sup>50</sup> proposed anecdotal recommendations for

patients who are runners vs nonrunners.<sup>50</sup> He advocated for patients who were already runners to be encouraged to continue running (so long as they also take measures to prevent injury<sup>47</sup>). Conversely, patients who are nonrunners can be encouraged to engage in walking, as there is more consistent evidence that walking is not harmful (and may be beneficial) to the knee joint.

#### Recreational sports

A narrative review by Lefe?vre-Colau et al.<sup>51</sup> concluded that recreational and elite-level sports participation were not consistently related to the progression of radiographic or symptomatic  $OA.^{\overline{5}1}$  However, the authors highlighted certain sports (e.g., gymnastics, martial arts, soccer, ball games, etc.) that seemed to increase risk for progression of knee OA, although these relationships may be confounded by risk of knee injury for a given sport. Similarly, a systematic review by Driban et al.<sup>47</sup> reported that elite-level participation in certain sports, including soccer, long-distance running, weightlifting, and wrestling, was associated with higher odds of knee OA (soccer: OR = 3.47, 95% CI 2.53-4.77, running: OR = 3.25, 95% CI 1.40-7.53, weightlifting: OR = 6.87, 95% CI 3.26-14.46, and wrestling: OR = 3.78, 95% CI 1.80-7.96),<sup>47</sup> although again these relationships may be confounded by risk of knee injury. Lefevre-Colau et al.<sup>51</sup> suggested that team and/or power sports have higher rates of injury than endurance sports (e.g.,

Table 3.         Summary of Reviews That Examined Recreational Sports and Stru	ctural Progression of Knee OA
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Review Details	Measure(s) of Physical Activity	Measure(s) of Structural Progression of Knee OA	Main Conclusion(s)
Lefevre-Colau et al. <sup>51</sup> Critical narrative review Annals of Physical and Rehabilitation Medicine	Self-reported PA via questionnaire	Self-reported physician- diagnosed knee OA	This narrative review evaluated how risk of knee OA is impacted by: (1) general PA, (2) rec- reational sports participation, (3) nonelite long- distance running, and (4) elite sports participation Seven out of 11 studies found that general PA
	activities via questionnaire		did not increase risk for knee OA; two of the four remaining studies found that general PA only increased risk for knee OA in men
		Radiographic knee OA	Three out of eight studies found that recrea- tional sports participation did not increase for knee OA; four of the five remaining studies found that sports participation only increased risk for knee OA for certain sports (e.g., gym- nastics, martial arts, soccer, ball games, etc.)
		Surgery due to knee OA	Four out of five studies found that nonelite long-distance running did not increase risk for knee OA; the remaining study found a higher number of osteophytes in female runners com- pared to controls (4.7 vs 2.3, $P < .01$ )
		Knee replacement	Three out of seven studies found that elite sports participation did not increase risk for knee OA
Driban et al. <sup>47</sup> Systematic review Journal of Athletic Training	Self-reported sports participation	Prevalent OA	This SR included 15,928 adults from 17 stud- ies. The authors performed a quantitative syn- thesis of included studies, with a total of 14 comparisons between exposed and nonex- posed groups after aggregating data by sport
		Loss of joint space width	A "significant" association exists between sport participation and prevalent OA for: Elite and nonelite soccer, elite long-distance run- ning, elite weightlifting, and elite wrestling (ORs ranged from 3.25 to 6.87, all were statis- tically significant)
			An "unclear but possible" association exists between sport participation and prevalent OA for: High School American football, elite throw- ing, elite handball, elite cross-country skiing, elite ice hockey, and elite orienteering (ORs ranged from 1.58 to 9.17, none were statisti-
			cally significant) An "unclear but unlikely" association exists between sport participation and prevalent OA for: elite basketball, elite boxing, elite shooting, and elite track and field (ORs ranged from 0.87 to 1.34 pope were statistically significant)
		Progression of radio- graphic OA	The authors presented data by Roos et al. <sup>57</sup> that showed uninjured controls/athletes had a lower prevalence of knee OA than injured controls/athletes (1.3-10.7% vs 12.5-33.3%), depending on the level of sports participation

long-distance running), which may explain why these two reviews have mixed findings regarding elite-level long-distance running and risk for knee OA.<sup>46</sup>

Thus, unlike walking and running, there are nuances to recommending participation in recreational sports. Namely, providers must weigh patient preferences against the risk for traumatic injury associated with a given sport (especially if the patient has previously been injured in that sport). Generally speaking, providers should encourage recreational sports participation so long as they also educate patients about practicing injury prevention.

# Considering other risk factors when recommending PA

We advocate that all patients with, or at risk for, knee OA should receive a PA recommendation. However, providers must consider other risk factors for knee OA progression, such as obesity, previous knee injury, and structural knee abnormalities, that are inherent to this patient population.

# Obesity

Obesity is a strong, independent risk factor for developing knee OA (risk ratio [RR] = 4.55, 95% Cl 2.90-7.13).<sup>52</sup> Thus, it is possible that

adults who are obese and increase their PA may be at risk for structural progression of knee OA. For example, a narrative review by Fransen et al.<sup>54</sup> cited as an original study by Martin et al.<sup>53</sup> found women who were obese and had the highest PA (unstructured) had higher odds of incident knee OA (OR 1.8, 95% CI 1.5-2.2).<sup>53</sup> This is not because PA itself is harmful; obesity is likely still the "driving force" behind their structural progression.<sup>54</sup> Fortunately, obesity is a modifiable risk factor that providers can address by encouraging weight loss.

Egan and Mentes<sup>28</sup> and Bosomworth<sup>50</sup> clarified that providers should not think of weight loss as a *prerequisite* for patients to engage in PA<sup>28,50</sup>; rather, patients can achieve weight loss *in conjunction with* PA, i.e., start exercising and eating a healthy diet at the same time.<sup>55</sup> Patients who are obese can engage in moderate intensity, low-impact PA such as brisk walking. Several reviews cited as the original study by Felson et al.<sup>31</sup> found adults who were obese could recreationally walk at least 6 miles week<sup>-1</sup> without increased risk of joint space loss (OR = 0.96, 95% CI 0.55-1.65) or incident knee OA (OR = 0.95, 95% CI 0.55-1.62) over a 9-year period.<sup>31</sup>

# Previous knee injury and other structural abnormalities

Several reviews<sup>41,46,47</sup> highlighted that previous knee injury is a strong, independent risk factor (and often a confounding factor) for developing knee OA (pooled OR = 4.20, 95%CI 3.11-5.66).<sup>56</sup> Furthermore, Driban et al.<sup>47</sup> presented the results of an original study by Roos et al.<sup>57</sup> that showed athletes/nonathletes with a previous knee injury consistently had greater odds of knee OA than athletes/nonathletes without a previous knee injury (12.5-33.3% vs 1.3-10.7%).<sup>57</sup> Thus, when recommending PA, a previous knee injury may alter the knee joints' response to PA.<sup>41,46,47</sup> As with obesity, the knee injury still likely acts as the "driving force" behind structural progression,<sup>16</sup> not PA itself. However, unlike obesity, a previous knee injury is nonmodifiable.

Reviews by Bennell and Hinman (2011),<sup>58</sup> Hansen et al.,<sup>39</sup> and Miller<sup>46</sup> suggest that providers should (1) recommend supervised PA, with monitoring of the patient's response to a gradual increase in PA<sup>46</sup> and (2) encourage the patient to allow adequate recovery time between bouts of PA.<sup>39</sup> These strategies are intended to minimize their risk of reinjury and/or exacerbation of a previous injury. Furthermore, a review by Lim et al.<sup>53</sup> suggests that these strategies also apply to patients with other structural abnormalities such as a meniscal pathology, BML, or significant varus or valgus frontal knee alignment.

# More studies are needed that examine PA and structural outcomes in knee OA Although more evidence has become available, a recent review by Kraus et al.<sup>9</sup> highlighted the continued need for high-quality studies to elucidate the effects of PA on the structural integrity of the knees.<sup>9</sup> First, future studies should leverage activity monitors for objective, accurate measurement of PA. Older studies that relied on self-report measures of PA (e.g., questionnaires) had mixed findings, including that PA could be harmful to the structural integrity of the knee joint.<sup>58</sup> In contrast, recent studies used objective measures of PA and found that PA had no effect on the

Second, studies should attempt to isolate the effects of joint injury from PA,<sup>48</sup> as joint injury alone increases risk for incident knee OA and rapid knee OA progression.<sup>59</sup> As well, studies should examine whether the consequences of a previous joint injury might be attenuated by regular engagement in moderate PA.<sup>42</sup>

knee joint.17

Third, future studies should consider the potential "U-shaped" relationship between PA and knee OA.<sup>9,43</sup> That is, adults with very low PA<sup>60</sup>, *as well as* adults with very high PA, may have the greatest risk for structural progression. Meanwhile, adults with moderate levels of PA may reside in the "sweet spot" and have the lowest risk for structural progression.<sup>16,42</sup>

Most studies fail to consider this "U-shaped" relationship when they select adults with low PA as their referent group. Instead, adults with moderate PA (i.e., the "sweet spot") may be a more appropriate referent (unexposed) group. By selecting those with moderate PA as the referent group, more studies can explore the consequences of low PA and formally test the existence of this "U-shaped" relationship. Interestingly, this "U-shaped" relationship is already supported by a meta-analysis of animal studies<sup>9</sup> and two recent cohort studies in humans.<sup>61,62</sup>

#### Future research should determine if meeting PA guidelines preserves the structural integrity of the knees

The WHO guidelines provide important PA targets for all adults, with and without knee OA. While there is unequivocal evidence that meeting these guidelines (1) promotes cardio-vascular and metabolic health and (2) preserves muscle and bone density, there is a need for evidence that shows meeting these guidelines can preserve the structural integrity of joints (including the knees). Current evidence only shows that meeting PA guidelines does not *worsen* knees<sup>21</sup>; while providers can use this knowledge to address patients' concerns about "wear and tear,"<sup>14</sup> there may be

greater incentives for adults to become active (i.e., PA actually *preserves* the knee joint). Once compelling evidence becomes available to show that PA prevents (or at least delays) the onset of knee OA,<sup>42</sup> it might encourage more adults to be active and benefit countless adults worldwide.

# Conclusion

To conclude, there is consistent evidence that common forms of PA (walking, running, and certain recreational sports) do not increase risk of structural progression of knee OA. These forms of PA may actually be beneficial to the knee joint, although more studies are needed to support this notion. Nevertheless, healthcare providers can refer to the WHO guidelines to provide a general PA recommendation to patients with, or at risk for knee OA. Providers can refer to this overview to make a more specific PA recommendation that considers how other risk factors (obesity, previous knee injury, or other structural abnormalities) relate to structural progression of knee OA.

There is still a need for high-quality studies that examine PA and structural outcomes in knee OA. These studies should elucidate how PA may be beneficial to the knee joint, thus providing additional incentive to adults who are not regularly active. As well, additional studies can support the notion that meeting PA guidelines preserves the knee joint, which, in turn, may reduce the global burden of knee OA.

# Supplementary material

We searched the PubMed database using the following search strategy: "exercise [MeSH Terms] AND osteoarthritis, knee [MeSH Terms]." MeSH is an acronym for "Medical Subject Headings" and refers the controlled vocabulary of the National Library of Medicine. Every article in PubMed is indexed using a set of MeSH terms.

A MeSH term is a heading that exists in a hierarchy; each MeSH term includes several related entry terms beneath it in the hierarchy. Thus, when a MeSH term is searched, PubMed retrieves citations that have been indexed with the MeSH term and/or its related entry terms. The MeSH term does not need to be the major topic of the citation but must be included in the set of terms used to index that citation.

For example, the MeSH term "exercise" retrieves citations that were indexed with the following terms: "acute exercise," "aerobic exercise," "exercise training," "exercise, aerobic," "exercise, isometric," "exercise, physical," "isometric exercise," and "physical activity." The MeSH term "osteoarthritis, knee" retrieves

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citations that were indexed with the following terms: "osteoarthritis of knee" and "osteoarthritis of the knee." Our search strategy, which combines "exercise" AND "osteoarthritis, knee", therefore retrieves citations that are relevant to both MeSH terms.

We restricted our PubMed search by "Article Type" to include only (1) meta-analyses, (2) reviews, and (3) systematic reviews. We also restricted our PubMed search to retrieve only citations that were originally published in English from 2005 to 2020.

First, we reviewed the abstract of each citation retrieved in the PubMed search (n = 114). We excluded a citation if the abstract clearly indicated: (1) the review did not include studies in adults with (or at risk for) knee OA, (2) the review did not mention a specific structural outcome of knee OA (e.g., radiographic or MRI measures), and/or (3) the review was not originally published in English or was a duplicate. Once we definitively excluded a citation based its abstract (n = 74), we did not search for a full-text version of that citation.

If we *did not* exclude a citation based on its abstract, we searched for and performed a detailed review of the full-text version of the citation. We excluded full-text versions of citations for the same three reasons listed above: (1) the review did not include studies in adults with (or at risk for) knee OA, (2) the review did not mention a specific measure of physical activity, or (3) the review did not mention a specific structural outcome of knee OA (e.g., radiographic or MRI measures).

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