



MASTERCLASS

Knee osteoarthritis: key treatments and implications for physical therapy

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Received 16 March 2020; received in revised form 11 August 2020; accepted 19 August 2020

KEYWORDS

Arthritis;
Education;
Exercise;
Outcome measures;
Pain;
Weight loss

Abstract

Q2 **Background:** Knee osteoarthritis (OA) is a chronic progressive disease that imparts a substantial socioeconomic burden to society and healthcare systems. The prevalence of knee OA has dramatically risen in recent decades due to consistent increases in life expectancy and obesity worldwide. Patient education, physical exercise, and weight loss (for overweight or obese individuals) constitute the first-line knee OA treatment approach. However, less than 40% of patients with knee OA receive this kind of intervention. There is an unmet need for healthcare professionals treating individuals with knee OA to understand the current recommended treatment strategies to provide effective rehabilitation.

Objective: To guide physical therapists in their clinical decision making by summarizing the safest and most efficacious treatment options currently available, and by delineating the most traditional outcome measures used in clinical research for knee OA.

Conclusion: There is a need for healthcare providers to abandon low-quality and ineffective treatments and educate themselves and their patients about the current best evidence-based practices for knee OA.

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Introduction

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Q3 Life expectancy has increased globally over time; however, the growing burden of chronic diseases results in a large portion of society living longer, but in poorer health.¹ This scenario is indeed a reality for people suffering from one of the leading causes of chronic pain and disability

34 worldwide, knee osteoarthritis (OA).¹ The disease is ranked
35 as the 10th largest contributor to global years lived with
36 disabilities,² and its prevalence has more than doubled in
37 the last 10 years.^{1,3} In addition, medication intake, hospital
38 stays, and joint surgeries associated with managing knee
39 OA impose billions of dollars per year in costs to healthcare
40 systems.^{2,3}

41 The pathology of knee OA affects the whole joint, causing
42 synovial inflammation, cartilage damage, bone remodeling,
43 and osteophyte formation.⁴ Typical symptoms include pain,
44 muscle weakness, joint instability, brief morning stiffness,
45 crepitus, and functional limitations.⁴ Frequently, symptoms
46 are related to physical inactivity, which has been linked to
47 morbidity and mortality in the contemporary era and is a
48 significant contributor to the incidence of chronic diseases
49 worldwide.^{5,6} Methodologically rigorous international guidelines
50 strongly recommend non-pharmacological strategies as
51 the first line of treatment for knee OA.⁷⁻¹³ Exercise, patient
52 education, and weight loss – when needed – are the recom-
53 mended first-line strategies to manage symptoms of these
54 patients.⁷⁻¹³

55 There is high-quality evidence demonstrating the effec-
56 tiveness of education and exercise to improve function
57 in individuals with knee OA.^{8,13} Data from 9825 patients
58 with hip or knee OA showed that a 6-week combination
59 intervention comprising three sessions of patient education
60 delivered over the course of two weeks and 12 sessions of
61 neuromuscular exercise delivered twice per week had bene-
62 ficial effects on OA symptoms, physical function, medication
63 intake, and sick leave time.¹⁴ Furthermore, some beneficial
64 effects introduced by the interventions, including increased
65 physical activity and quality of life, were maintained after
66 one year. These results suggest that a combination of edu-
67 cation and exercise could result in long-term reductions in
68 the burden of knee OA and its costs to patients and the
69 healthcare system.

70 Although non-pharmacological strategies are of
71 paramount importance, less than 40% of patients with
72 knee OA receive this kind of treatment approach, indi-
73 cating that the uptake of evidence-based guidelines in
74 clinical practice and rehabilitation is still suboptimal.^{14,15}
75 Instead, pharmacological strategies remain dominant,
76 despite the fact that chronic use of many of these treat-
77 ments has been associated with severe adverse side
78 effects.^{16,17} The neglect of evidence-based strategies in
79 clinical practice applies to both clinicians and patients.
80 Factors such as the strong beliefs regarding old and
81 low-value treatments, the lack of knowledge regarding
82 current evidence, and a significant increase in the number
83 of current published guidelines are considered barriers
84 to the successful adoption of evidence-based clinical
85 practice.¹⁸⁻²⁰

86 A basic understanding of treatment strategies for knee
87 OA is necessary to target and improve rehabilitation. In this
88 article, we aim to provide updated information for physi-
89 cal therapists and show that exercise, weight maintenance,
90 and patient education are vital for the optimal treatment
91 of knee OA. We also aim to describe key outcome mea-
92 sures used in knee OA studies and to increase awareness
93 about useful tools for data collection for clinicians and
94 researchers.

Key treatments

Non-pharmacological strategies

95 Current clinical practice guidelines recommend education
96 and self-management, exercise, and weight loss (for over-
97 weight or obese patients) as the first-line treatments for
98 knee OA.⁷⁻¹³ We consider these strategies to be the core
99 of knee OA rehabilitation, because they have been proven
100 to effectively decrease pain and improve overall joint func-
101 tion and patient quality of life. In patients for whom knee
102 OA has a significant impact on ambulation or joint stability,
103 or for whom pain is severe, some guidelines strongly recom-
104 mend the use of tibiofemoral knee braces, canes or walkers,
105 orthopedic footwear, and other assistive technologies.^{12,13}

Patient education

108 Patient education plays an essential role in decision making,
109 disease self-management, and medication adherence
110 of individuals with knee OA.²¹ The negative impact of
111 the disease on the patients' self-esteem can be high, and
112 oftentimes, pain becomes a central aspect of their lives.
113 Misleading beliefs that OA is an incurable, progressive dis-
114 ease that is associated with specific causal factors can lead
115 patients to cut down on physical activities and adapt to
116 a restricted lifestyle with less spontaneity, which in many
117 cases results in a great feeling of loss and isolation associated
118 with a reduction in social relationships.²²⁻²⁴ There is an
119 urgent need to mitigate this negative impact, using proper
120 patient-education strategies to better manage the disease
121 and improve the concordance between patients' expecta-
122 tions and treatment outcomes. Overall, patient knowledge
123 about the disease is still inadequate. Although guidelines
124 organizations attempt to disseminate health information
125 targeting the general public, most patient education mate-
126 rials for people with knee OA are of fair quality and written
127 at inappropriate readability levels, frequently equal to, or
128 more complicated than the recommended level (7th to 8th
129 grade).^{25,26}

130 As healthcare providers, it is essential to develop a
131 clear understanding of the disease to direct patients toward
132 high-quality health information. However, before educating
133 patients with knee OA, it is crucial to understand how they
134 experience the disease. A systematic review of qualitative
135 studies highlighted the importance of considering patient
136 attitudes and experiences to plan and implement the best
137 treatment options for knee OA.²⁷ From the seven critical
138 themes that emerged, three call for attention: (1) "*The*
139 *perceived causes of knee osteoarthritis are multifactorial*
140 *and lead to structural damage to the knee and deteriora-*
141 *tion over time,*" where patients perceived knee OA as
142 a consequence of internal factors such as aging, working
143 occupation, family history, or external factors such as a
144 trauma or weather conditions; (2) "*Interactions with health*
145 *professionals can be positive or negative,*" where patients
146 related that positive interactions resulted in feeling listened
147 to and hopeful for the future, whereas negative interac-
148 tions were characterized by receiving less attention and less
149 information about the condition and treatment options; and
150 (3) "*Knee osteoarthritis leads to life adjustments,*" where

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some patients mentioned climbing fewer stairs, not carrying heavy things, looking for places to sit, and avoiding public transportation, while others reached a point where there was a profound feeling of loss because the disease led to giving up all enjoyable activities of daily living.

In a consensus statement reached by experts and patients with OA in 13 countries, 21 key messages were identified that should be communicated to patients.²⁸ The top 3 messages were related to (1) how regular physical activity and individualized exercise programs can reduce pain, prevent worsening, and improve daily function in OA; (2) the benefits of losing weight for overweight or obese patients, and the benefits of maintaining a healthy weight using diet changes and exercise; and (3) the fact that OA symptoms can often be significantly reduced without the need of undergoing a surgery. Other key messages pertained to disease knowledge (e.g., “*The symptoms of osteoarthritis can vary greatly from person to person*” and “*Osteoarthritis is not an inevitable part of getting older*”); medication intake (e.g., “*You should avoid the use of nonsteroidal anti-inflammatory drugs for your osteoarthritis over the long term*”); and about diagnostic methods (e.g., “*Joint damage on an X-ray does not indicate how much your osteoarthritis will affect you*”). These messages are fundamental to facilitate the translation of evidence into patient knowledge and to optimize the patient–clinician interaction, therefore providing insights into how to conduct education and improve decision-making for patients with knee OA.

Exercise

It is well-established that physical activity and exercise therapy reduce symptoms and improve physical function in individuals with knee OA.^{7–13} Literature shows that 150 min/week of moderate intensity aerobic exercise or 2 days/week of moderate-to-vigorous physical activity muscle-strengthening exercises are beneficial for individuals with preexisting knee OA. Translating these two activities into step counts, that would be approximately 7500 steps per day for aerobic exercises and 5750 steps per day for moderate-to-vigorous physical activity. In addition, there is more pain reduction when quadriceps-specific exercises were used compared to general lower-limb exercises and when supervised exercises were performed at least three times per week. However, the current recommendations suggesting one form of exercise over another are mainly based on expert opinion.

Irrespective of pain and function, a wide range of exercise options are available for knee OA.²⁹ To improve rehabilitation, physical therapists and other health care professionals should focus on patient-centered rehabilitation, considering patient’s preferences and access to exercise equipment. The National Institute for Health and Care Excellence (NICE)⁷ recommends strengthening exercises and aerobic fitness; the Osteoarthritis Research Society International (OARSI)⁸ recommends structured land-based exercise programs of two types: (1) strengthening and/or cardio and/or balance training/neuromuscular exercise or (2) mind-body exercise including Tai Chi or Yoga; the American College of Rheumatology (ACR)¹³ recommends aerobic, aquatic, and/or resistance exercises; the Ottawa

Panel^{9–11} recommends mind-body exercise (Hatha yoga, Tai Chi Qigong, sun style Tai Chi), strengthening exercise in isolation or combined with other types of exercise (coordination, balance, functional), and aerobic exercise in isolation or combined with strengthening exercise; and the European League Against Rheumatism (EULAR)¹² recommends pacing of activity and exercise in general for the management of knee OA.

There is high-quality evidence demonstrating the effectiveness and the clinically meaningful benefits of non-perioperative therapeutic exercise regimens to improve pain, physical function, and quality of life in individuals with knee OA.^{29,30} Moreover, these improvements are sustained for at least two to six months after the end of treatment. It is highly unlikely that new research on this area will change these conclusions.^{30,31} Therefore, there is no need to develop new trials to verify exercise effectiveness for knee OA. However, there is still a need to develop novel insights regarding treatment parameters used in rehabilitation programs, such as duration, frequency, modality (type), and intensity.³² The type and dosage of exercise, when prescribing a home-based exercise protocol, should be individualized, based on the clinical evaluation and the patient’s preferences.^{33,34}

Education plays a vital role when prescribing an exercise protocol. Most current exercise protocols are noticeably under-utilized by individuals with knee OA, mainly due to patient beliefs, socioeconomic barriers, fear of movement, lack of confidence, lack of time to insert the exercise routine in daily life, and early treatment pain aggravation.^{33–35} A survey with 123 physical therapists demonstrated that only 39% educated patients about the benefits of exercise for knee OA, 33% involved their patients in the development of the exercise program design, 28% managed to schedule follow-up appointments to review exercises and adherence, and 4% encouraged patients to keep going with exercises.³⁶ Prior to the beginning of an exercise protocol, patients need to clearly understand that pain/discomfort during the physical activity does not mean increased structural joint damage.³³ To optimize the effectiveness of exercise interventions, it is also essential to create strategies to increase adherence to exercise and overcome barriers, bearing in mind the environmental context and available resources of the patient.

Physical therapists can help patients with knee OA by fostering a positive therapeutic relationship. Some components of a positive therapeutic relationship may include increased relatability, supervision of exercise performance to promote success and confidence in self-management abilities of patients, use of group exercises, and follow-up telephone calls.³⁷ The top 5 behavior change techniques rated to be the most effective at increasing exercise adherence in patients with knee OA include: (1) review of progress in terms of pain and function at follow-up sessions, (2) development of a therapeutic plan which clearly states how often the patient will exercise and specifically what they will do, (3) development of specific and achievable goals related to the patient’s knee pain and function, (4) review, supervision, and correction of exercise techniques at subsequent treatment sessions, and (5) follow-up sessions more than 3 months after the initial session, to check on the exercises and progress the home-based protocol, if needed.³⁶ Other

strategies such as the use of booster sessions (i.e. returning to a therapist after an initial period of treatment to perform a new session focused on review and progression of the exercise therapy) and the use of graded behavioral exercises (i.e. an exercise routine that is gradually increased into daily living) also promoted adherence in individuals with knee OA.³⁵

279 Weight loss

280 Over one-third of the world's population is classified as over-
281 weight or obese and research shows that if the current
282 trends continue, more than 55% of the world population will
283 be classified as overweight or obese by 2030.^{38,39} Because
284 of its systemic effects on the body due to inflammatory and
285 metabolic changes, obesity and overweight are considered
286 primary risk factors related to chronic diseases, including
287 knee OA.^{40,41} Therefore, obesity presents a significant bur-
288 den to society and the public health system.³⁹

289 Weight change directly affects the risk of developing
290 knee OA.⁴² A reduction in weight of approximately 5.1 kg
291 decreases the risk of developing knee OA by more than 50%
292 in women with a baseline body mass index (BMI) higher than
293 25.0 kg/m².⁴² A meta-analysis showed that in adults with
294 mild to moderate knee OA and a mean BMI ranging from
295 33.6 to 36.4 kg/m², a weight reduction of 5%–10% can signif-
296 icantly improve pain, self-reported disability, and quality of
297 life. Results of the included studies demonstrated that diet
298 strategies such as meal replacements or the use of nutrition
299 powders, together with nutritional education and behavioral
300 therapy, can help individuals with knee OA to achieve weight
301 loss targets.⁴³

302 For individuals with knee OA, diet-only treatments have
303 not been shown to relieve pain; however, a combination of
304 diet and exercise has a moderate effect on this outcome.⁴⁴
305 Physical function, on the other hand, improved moderately
306 with both diet-only treatments and diet combined with exer-
307 cise. Patients who are classified as overweight should aim
308 for at least a 7.7% body weight loss to achieve a minimal
309 clinically important improvement in physical function.⁴⁵ In
310 addition, to lose weight, an intensive diet alone (loss of at
311 least 10% of baseline weight) is better than exercise alone
312 (aerobic and strengthening training). However, the combina-
313 tion of exercise and diet presents the best results for weight
314 loss.⁴⁶

315 Clearly, there is a dose-response relationship between
316 weight loss and symptom improvement in individuals with
317 knee OA.^{45,47–49} However, the maintenance of weight loss
318 in long-term rehabilitation remains a substantial challenge.
319 Successful strategies of weight maintenance are associated
320 with achieving an initial goal of weight loss, creating con-
321secutive weight goals, having a regular meal pattern that
322 includes breakfast and healthier eating, having a phys-
323 ically active lifestyle, and controlling over-eating through
324 self-monitoring behaviors. These strategies can be incor-
325 porated, when needed, in knee OA rehabilitation regimens
326 to improve goals and increase patients' overall satis-
327 faction with treatment. Other factors strongly associated with
328 weight maintenance include the presence of social support,
329 better coping strategies, higher self-efficacy, and overall
330 increased in psychological resiliency and stability.⁵⁰

In individuals with other chronic diseases, the contact
331 between patient and therapist seems to be a key factor for
332 weight loss.⁵¹ Furthermore, continuing contacts after the
333 end of the rehabilitation regimen appears to be effective,
334 regardless of whether the contact is face-to-face, through
335 telephone, or via email. Risk factors for regaining weight
336 include a range of eating behaviors that involve a lack of
337 restraint over food intake. These factors can include binge
338 eating disorder (i.e. recurrent episodes of eating large quan-
339 tities of food), eating as a reaction to emotions and stress,
340 and a general tendency toward passive reactions to prob-
341 lems.

342 Adjunct therapies

343 Several adjunct therapies are used as complements to core
344 knee OA treatments with the goal of maximizing outcomes
345 for patients. Thermal modalities, laser therapy, therapeu-
346 tic ultrasound, electrical stimulation, manual therapy
347 techniques, taping, acupuncture, among others, are some
348 interventions that are commonly used. For this article, we
349 will review some of the adjunct therapies most commonly
350 used by physical therapists in treating knee OA, providing
351 details about the quality of evidence and nature of the rec-
352 ommendation.

353 Thermal modalities

354 There is still a lack of evidence to support the use of ther-
355 mal modalities such as cold and heat in individuals with
356 knee OA.^{52,53} The overall quality of evidence for thermal
357 modalities is classified as very low by the OARSI guidelines
358 and as low by the ACR guidelines.^{8,13} Research shows that
359 patients with knee OA have individual preferences regard-
360 ing heat, cold, or contrast therapy to improve pain and
361 physical function status.⁵⁴ Women tend to prefer heat treat-
362 ments and generally respond with more improvements in
363 subjective quality of life and physical function to thermal
364 modalities. Conversely, men favor cold or contrast therapies
365 but were less likely to report benefits.^{54,55} In humans, the
366 use of cryotherapy was not superior to placebo to improve
367 pain, physical function, and quality of life in individuals
368 with knee OA.⁵⁶ Interestingly, clinical-like cryotherapy was
369 recently shown to improve not only gait and function, but
370 also to modulate the inflammatory process by reducing the
371 number of leukocytes and cytokines in the synovial fluid in
372 animal model with knee OA compared to placebo.⁵⁷

373 Laser, therapeutic ultrasound, and electrical 374 stimulation

375 The OARSI guidelines strongly recommended against the use
376 of laser therapy for knee OA, citing an implausible biological
377 mechanism and no efficacy, with a very low overall quality
378 of evidence.⁸ The potential mechanisms of pain relief by
379 laser therapy are due to the stimulus of tissue metabolism
380 and modulation of the inflammatory process. However, liter-
381 ature shows contrasting evidence regarding the use of laser
382 therapies, more specifically low-level laser therapy (LLLT),
383 in treating individuals with knee OA. A meta-analysis eval-

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5

385 uating the effectiveness of LLLT on symptoms and function
386 in patients with knee OA, showed no therapeutic benefit of
387 LLLT compared with placebo for patients.⁵⁸ A more recent
388 meta-analysis showed that LLLT seems to reduce pain and
389 disability in individuals with knee OA when compared to
390 placebo in randomized controlled trials.⁵⁹

391 Studies regarding therapeutic ultrasound, although
392 reporting beneficial effects of the therapy for knee OA, show
393 methodological limitations that hinder the evidence synthesis,
394 such as the inclusion of mixed interventions.^{60–64} Thus,
395 there is low quality of evidence to support the use of ther-
396 apeutic ultrasound for individuals with knee OA.⁸ However,
397 the ACR guidelines conditionally recommends its use (i.e.
398 the therapy is considered preference-sensitive to patients),
399 meaning that therapists need to give a complete and clear
400 explanation of benefits, harms, and burdens of the treat-
401 ment when presenting it as an option to a patient.¹³

402 Evidence for electrical stimulation shows that there is a
403 lack of adequate studies to support its use in patients with
404 knee OA.⁶⁵ OARSI guidelines corroborates this information
405 by presenting a very low quality of evidence for transcuta-
406 neous electrical stimulation.⁸ In addition, the ACR strongly
407 recommended against the use of transcutaneous electrical
408 stimulation in all patients with OA.¹³

409 Manual therapy techniques, taping, and 410 acupuncture

411 There is a low level of evidence to recommend the use of
412 manual therapy techniques for knee OA.^{8,13} Available tech-
413 niques encompass the use of manual lymphatic drainage,
414 massage, mobilization/manipulation, manual traction, and
415 passive range of motion. There is low level of evidence show-
416 ing that manual therapy techniques provide little additional
417 benefit when compared to exercise alone for managing knee
418 OA symptoms, and the ACR guidelines conditionally recom-
419 mended against its use.¹³

420 There is very low level of evidence to support the use
421 of taping for the management of knee OA.⁸ With a no effi-
422 cacy statement, the OARSI guidelines strongly recommends
423 against the use of the therapy.⁸ However, regarding Kine-
424 sio taping, the ACR guidelines conditionally recommends its
425 use.¹³

426 For traditional acupuncture with manual stimulation,
427 there is a low level of evidence to support the use of the
428 therapy for patients with knee OA.^{8,13} The ACR guidelines
429 conditionally recommended acupuncture.¹³ However, the
430 OARSI guidelines stated an implausible biological mechanism
431 and no efficacy for laser acupuncture and an unfavorable
432 efficacy with safety issues for electroacupuncture, strongly
433 recommending against and indicating a very low overall
434 quality of evidence to support the use of either therapy.⁸

435 There is still an unmet need for quality randomized
436 clinical trials regarding the majority of the adjunct ther-
437 apies described above. Additionally, for the majority of the
438 adjunct therapies, it remains to be seen whether comple-
439 mentary effects may be observed when they are combined
440 with a gold standard treatment for knee OA (e.g. the com-
441 plementary effects of cryotherapy when associated with an
442 exercise protocol).⁶⁶ Therefore, with the current evidence,
443 we recommend against the use of these therapies by physical

444 therapists in clinical practice. However, if the therapy is still
445 considered, we recommend it to be preference-sensitive to
446 patients, and therapists must give a complete and clear
447 explanation to patients regarding the evidence to support
448 the use of the therapy in knee OA.

449 Pharmacological strategies

450 For knee OA, local therapies are preferable as core pharma-
451 cological treatments. Appropriate monitoring of the patient
452 during a pharmacological treatment, especially for the
453 development of adverse effects, is also recommended.

454 Non-steroidal anti-inflammatory drugs (NSAIDs)

455 Due to minimal and mild adverse events, topical NSAIDs
456 are strongly recommended as first-line treatment in both
457 the OARSI⁸ and ACR¹³ guidelines. OARSI also recommends
458 the use of topical NSAIDs for patients with gastrointestinal
459 or cardiovascular comorbidities and patients with frailty.⁸
460 In addition to topical NSAIDs, the ACR guidelines strongly
461 recommends the use of oral NSAIDs and intraarticular gluco-
462 corticoid injections.¹³

463 Opioids

464 Opioids, another popular group of drugs that are frequently
465 considered as potent pain-relievers, should be heavily
466 discouraged.^{16,67,68} There is high-quality evidence demon-
467 strating that opioids have only small effects on pain and
468 physical function in individuals with knee OA.⁶⁹ Further-
469 more, when compared to placebo, patients that used opioids
470 had three to four times higher risks of serious adverse effects
471 and/or drop-out due to adverse events.

472 Nutraceuticals

473 Nutraceuticals, i.e. foods or food supplements thought
474 to have health benefits, are extremely popular in the
475 treatment of OA. Glucosamine and chondroitin sulfate,
476 nutraceuticals that are commonly used by patients with
477 knee OA, lack scientific evidence to support their use. Both
478 were strongly recommended against for the treatment of
479 knee OA by the ACR¹³ guidelines and classified as the lowest
480 level of recommendation by the OARSI guidelines.⁸ In addi-
481 tion, there are low efficacy and effect sizes of insufficient
482 clinical relevance, when comparing these supplements to
483 placebo.^{70–72}

484 Surgery

485 Surgery is typically a last resort for the management
486 of knee OA. Unfortunately, a vast majority of physicians
487 deviate from evidence-based practice regarding surgical
488 management of knee OA. From the variety of options avail-
489 able, arthroscopic knee surgery, specifically arthroscopic
490 joint lavage, is the most common procedure performed.^{4,73}
491 However, several high-quality studies have demonstrated
492 the low efficacy of arthroscopic surgery in terms of pain
493 relief and physical function improvement in individuals with

Table 1 Patient-reported measures and their psychometric properties for knee OA.

Outcome	Observations	Scoring	Psychometrics
Visual Analogue Scale (VAS)	The purpose of VAS is to measure pain. The scale is placed in front of the patient who is asked to rate their pain intensity according to a pre-determined period of time. VAS can be used before, during, or after physical function tests.	From 0 to 10 cm (0 – the complete absence of pain, and 10 – maximum intensity).	A pain reduction of 1.75 cm on the scale is the recommended MCID in OA research. ¹⁰³
Numeric Rating Scale (NRS)	The purpose of NRS is to represent a unidimensional measure of pain. Usually, it is a segmented numeric version of VAS, and it can be administered verbally (also by telephone) or graphically for self-competition. The scale is placed in front of the patient who is asked to rate their pain intensity according to a pre-determined period of time. NRS can be used before, during, or after physical function tests.	A 0–10-point numeric scale with 0 representing "no pain" and 10 representing "pain as bad as you can imagine"/"worst pain imaginable."	A pain reduction of 2 points on the scale is the recommended MCID in patients with chronic musculoskeletal pain. ¹⁰⁴
Western Ontario & McMaster Universities Osteoarthritis Questionnaire (WOMAC)	WOMAC is a self-report questionnaire designed to assess the problems experienced by individuals with lower limb OA in the past 72 h. It contains 24 specific questions divided into three domains: pain, stiffness, and physical function.	The score of each question ranges from 0 to 4. The total questionnaire score is 96, with high scores representing worse results.	An improvement greater than or equal to 12% from baseline is the recommended MCID in OA research. ¹⁰⁵
Knee Injury and Osteoarthritis Outcome Score (KOOS)	This self-report questionnaire assesses the problems experienced by people with lower limb OA in the prior week by measuring the quality of life and knee function. It contains 42 questions in 5 domains: pain, other symptoms, function in daily life, sports-related function and recreation, and knee-related quality of life.	The answers are standardized and scored from 0 to 4. The total score of the questionnaire is 168. High scores indicate worse results than low scores	A difference of 8–10 in the total score from baseline is the recommended MCID in OA research. ¹⁰⁶

Table 1 (Continued)

Outcome	Observations	Scoring	Psychometrics
Algofunctional indices for the knee or index of severity for knee disease (Lequesne Index)	This index is used specifically for the evaluation of pain, maximum walking distance, and the daily activities of patients with OA.	The 10-question questionnaire is scored on a 0-24-point scale. Lower scores indicate there is less functional impairment, and higher scores reflect the worst outcomes. The sum of the scores is classified as: little effect (1-4 points), moderate effect (5-7 points), severe effect (8-10 points), very severe effect (11-13 points) and extremely severe effect (greater than or equal to 14 points).	The MCID for the Lesquene Index is still not established in knee OA research.
Short Form-36 questionnaire (SF-36)	The short form questionnaire is intended to measure the patient's quality of life with 36 items referring to the past four weeks. It presents a multiple-choice scale that evaluates eight domains of life: Physical Functioning, Role Limitations due to Physical Problems, General Health Perceptions, Vitality, Social Functioning, Role Limitations due to Emotional Problems, General Mental Health and Health Transition.	The sum of the total value varies from 0 to 100, with higher indexes indicating a better quality of life. Each of the eight summed scores can be linearly transformed into a scale from 0 (negative health) to 100 (positive health) to provide a score for each subscale. Each subscale can be used independently.	A difference of 10 points is recommended as an MCID in OA research. ¹⁰⁷
Short Form-12 questionnaire (SF-12)	The short form questionnaire is intended to measure the patient's general physical and mental well-being, which is based upon the SF-36 score. It has two components, the physical component summary (PCS) and the mental component summary (MCS) scores.	Scores are reported on a scale of 1-100 with a higher score representing a better health status. The score is calculated independently for each component according to the responses recorded on Likert scales of six questions (each). Scores are converted into the validated score using a defined algorithm.	An improvement of 4.5 points for the physical component and 4.8 points for pain relief and function are established as MCID in OA research for patients after knee arthroplasty. ¹⁰⁸

Table 1 (Continued)

Outcome	Observations	Scoring	Psychometrics
Health Assessment Questionnaire (HAQ)	A self-administered questionnaire consisting of 20 detailed questions of people's daily activities divided into eight categories: dressing and activities related to taking care of appearance, getting up, eating, walking, hygiene, reaching, gripping, and daily life activities.	Each patient assesses the difficulty they face carrying out each activity on a scale from 0 to 3, where zero means no difficulty performing and three means unable to perform the activity. Increasing scores indicate worse functioning with 0 indicating no functional impairment and 3 indicating complete impairment.	The MCID for the HAQ questionnaire is still not established in knee OA research.

MCID, minimal clinically important difference; OA, osteoarthritis.

494 knee OA.⁷³⁻⁷⁵ The surgery also increases the chances of
 495 subsequent knee replacement surgery,^{76,77} and there are
 496 multiple harms associated with the procedure, including
 497 venous thrombosis, infection, pulmonary embolism, and in
 498 some cases, death.^{73,75} Clinical practice guidelines, includ-
 499 ing those published by the Journal of the American Academy
 500 of Orthopaedic Surgeons, strongly recommend against the
 501 use of arthroscopy in nearly all patients with degenerative
 502 knee disease.^{75,78}

503 Joint replacement is another popular surgery in indi-
 504 viduals with end-stage knee OA. It is a cost-effective
 505 treatment and should be considered when all non-surgical
 506 treatment options – used within a time-frame of 6-
 507 months – were unsuccessful.^{4,79} However, although joint
 508 replacement is a successful treatment for relieving many
 509 symptoms of individuals with knee OA, persistent pain
 510 after surgery is reported by some patients.⁸⁰ One in five
 511 patients who undergo total knee replacement is not satis-
 512 fied with the outcome.⁸¹ Predictors for poor outcomes after
 513 surgery include anxiety/depression, high patient expecta-
 514 tions for surgery, low 1-year WOMAC, pain at rest before
 515 surgery, and complications after surgery that necessitate
 516 readmission.^{81,82} Individuals with severe radiographic knee
 517 OA who have poor quality of life due to the disease are
 518 most likely to report considerable improvements in pain
 519 and function after knee replacement.⁸³ There is low- to
 520 moderate-quality of evidence showing that a period of 8
 521 weeks or more of exercise can improve functional outcomes
 522 and physical activity in individuals undergoing total knee
 523 replacement.⁸⁴

524 Key outcome measures

525 For researchers aiming to improve data collection in knee OA
 526 studies and for clinicians treating patients in clinical prac-
 527 tice, there are well-established core outcome measures that
 528 can be used to evaluate the domains of pain and physical
 529 function of patients.^{8,13,85-87} In Tables 1 and 2, we provide a
 530 comprehensive description of some of the critical subjective

531 and objective outcome measures used in knee OA stud-
 532 ies, respectively. In addition to the content provided in the
 533 tables, the following outcome measures were also classified
 534 as “important” (according to GRADE criteria) in evaluating
 535 the evidence that contributed to the OARSI guidelines: struc-
 536 tural progression of the disease measured by joint space
 537 narrowing, cartilage thickness, and cartilage volume; with-
 538 drawals due to adverse events, the total number of adverse
 539 events, serious adverse events, and other treatment-specific
 540 harms. Valid scales to measure self-efficacy and depression
 541 were also classified as important outcomes.^{8,88}

542 For physical function measures, it is crucial to understand
 543 that there is a clear distinction between patient-reported
 544 measures and performance-based measures. The first eval-
 545 uates what patients perceive they can do, and the latter
 546 reflects what they can do. Previous reports show that for
 547 individuals with knee OA, self-reported measures are not
 548 correlated with objective measures of physical function.⁸⁹⁻⁹⁴
 549 On the other hand, self-reported measures were related to
 550 pain, knee strength, and depression. Objective measures of
 551 physical function were correlated to functional self-efficacy
 552 (i.e. how confident an individual is to perform a physical
 553 task).⁹⁵ Both are different constructs and are complemen-
 554 tary, rather than competing, when assessing individuals
 555 with knee OA. Therefore, neither clinical researchers nor
 556 clinicians should substitute self-report outcome measures
 557 with performance-based measures, or vice versa. Instead,
 558 healthcare professionals treating knee OA should focus on
 559 collecting both types of outcome measures to obtain the
 560 most comprehensive assessment possible.

561 Future perspectives

562 Although research in OA has been documented for more than
 563 100 years, there are still no successful therapies to stop or
 564 reduce the progression of joint degeneration. However, with
 565 technological advancements, new approaches and therapies
 566 are emerging to aid these patients.

Table 2 Objective performance-based measures and their psychometric properties for knee OA.

Outcome	Observations	Scoring	Psychometrics
30-s Chair to Stand Test	A chair with no arms is placed against a wall to prevent oscillations. Patients sit in the middle of the chair, with their back straight, feet apart resting on the floor in line with their shoulders. The test requires to rise from a sitting to a standing position as many times as possible in 30 s.	The total number of repetitions.	An increase of 2–3 repetitions is recommended as the MCID in OA research. ⁸⁵
40 m (4 × 10 m) Fast Paced Walk Test	Administered at a distance of 10 m (marked by tapes), a cone is placed 2 m before the start and 2 m after the end of each marking. The participant is instructed to walk as quickly but as safely as possible the first 10 m (from the start mark), to turn around the cone and walk back the 10 m again, successively until completing the distance of 40 m.	Speed (m/s).	An increase of 0.2–0.3 m/s in the test is the recommended MCID in OA research. ⁸⁵
Stair Climb Test (SCT)	The participant is positioned in front of the stairs, and, at the therapist's signal, he/she has to climb the indicated steps (we use the 12-step SCT) and descend promptly, being able to use the handrail as a security instrument. We use 20 cm steps height, a handrail stair in an illuminated environment, free of traffic, or external distractions. Moreover, a pre-test was conducted to identify the need for safety measures.	The final score is calculated based on the time the participant takes to perform the test and is compared to the normative literature values available for the test.	A reduction of 5.5 s in the test is the recommended MCID in OA research. ⁸⁵
Timed-up and Go Test	This test assesses: balance moving from sitting to standing, stability in walking, and gait course changes without using compensatory strategies. The participant is asked to stand up from a chair, walk 3 m, turn around, return, and sit back in the chair.	The total time to complete the test.	For the MCID, a reduction of 0.8–1.4 s is recommended in OA research. ⁸⁵
6-Minute Walk Test	This test assesses the aerobic capacity and long-distance walking activity. In addition, it is used to assess endurance and dynamic balance when changing directions during the walking activity.	The maximum distance walked in 6 min	A small MCID of 20 m and a substantial MCID of 50 m have been estimated for the test in a sample of community-dwelling older adults with mobility dysfunction. ⁸⁷

MCID, minimal clinically important difference; OA, osteoarthritis.

567 Biomaterials such as scaffolds, hydrogels, microspheres, and nanofibers associated with cutting-edge advances in 568 cell-based approaches that focus primarily on cartilage 569 regeneration, hold promise in the regeneration of the OA 570 joint.⁹⁶ However, high-quality evidence is still scarce regarding 571 this topic. Computer technologies also hold promise 572 with respect to data mining (i.e. a process designed to 573 search databases for consistent patterns and/or systematic 574 relationships between variables) and machine learning 575 approaches (i.e. a statistical method of data analysis using 576 algorithms where a computer learns from a variety of 577 examples). These technologies can be used in tandem to 578 create patient-specific prediction models that analyze large 579 amounts of patient data to design and develop effective 580 and specific personalized therapeutic interventions for knee 581 OA. The use of such modeling techniques may also result in 582 substantial savings in medical resources and societal costs 583 by reducing the burden of the disease.⁹⁷ Moreover, these 584 technologies can help advance the fields of imaging, 585 electronic medical record keeping, genetic/genomic analysis, 586 and serum sample analysis, therefore facilitating the 587 stratification of relevant OA phenotypes.^{98,99}

588 Mobile health is another promising category that offers 589 an unprecedented opportunity to obtain real-world patient 590 data using a smartphone's capabilities and embedded 591 sensors, such as accelerometers, gyroscopes, magnetometers, 592 and barometers, among others.¹⁰⁰ These sensors, when 593 configured correctly, can be used to precisely monitor aspects 594 related to health, such as physical activity and function.¹⁰¹ 595 Through the development of specific algorithms, data from 596 these sensors can be processed and used to measure and 597 record movement patterns that are commonly assessed in 598 physical function tests. Researchers can collect and store 599 large quantities of objective clinical data, at multiple time 600 points, to help reduce patient's recall bias and to provide 601 more reliable and precise data about patients' fluctuation 602 in symptoms.^{101,102}

604 Conclusion

605 Osteoarthritis is one of the most frequent diseases worldwide. The burden to society and health care systems is 606 gradually increasing. It is our duty as healthcare professionals 607 to leverage our access to high-quality evidence to 608 increase the number of individuals receiving the appropriate 609 core non-pharmacological treatments for knee OA. By 610 doing so, we can increase the uptake of evidence-based 611 guidelines in clinical practice of physical therapy. Patient 612 education, exercise, and weight maintenance are vital for 613 the successful treatment of these patients.

615 Conflicts of interest

616 The authors declare no conflicts of interest.

617 Acknowledgements

618 L.O. Dantas is a Ph.D. researcher from the São Paulo 619 Research Foundation (FAPESP, Process number #2015/21422- 620 6).

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