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Physical activity for osteoarthritis: efficiency and review of recommandations

Camille Daste^{1,2,3}, Quentin Kirren^{1,2}, Joulnar Akoum⁴, Marie-Martine Lefèvre-Colau^{1,2,3,5}, François

Rannou^{1,2,4}, Christelle Nguyen^{1,2,4}

¹Université de Paris, Faculté de Santé, UFR de Médecine, 75006 Paris, France.

²AP-HP. Centre-Université de Paris, Hôpital Cochin, Service de Rééducation et de Réadaptation de

l'Appareil Locomoteur et des Pathologies du Rachis, 75014 Paris, France.

³INSERM UMR-S 1153, Centre de Recherche Épidémiologie et Statistique Paris (CRESS),

ECaMO Team, 75004 Paris, France.

⁴INSERM UMR-S 1124, Toxicité Environnementale, Cibles Thérapeutiques, Signalisation

Cellulaire et Biomarqueurs (T3S), Campus Saint-Germain-des-Prés, 75006 Paris, France.

⁵Institut Fédératif de Recherche sur le Handicap, 75013 Paris, France.

Corresponding author

Dr Christelle Nguyen,

AP-HP. Centre-Université de Paris, Hôpital Cochin

Rééducation et Réadaptation de l'Appareil Locomoteur et des Pathologies du Rachis

27, Rue du Faubourg Saint-Jacques 75014 Paris, FRANCE

Tel.: +33 1 58 41 29 45

Fax: +33 1 58 41 25 38

Email: christelle.nguyen2@aphp.fr

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Abstract

Physical activity is defined as movement of the body resulting from muscle contraction and

inducing energy expenditure. It can be adapted to a person's health status and have the objective of

maintaining or improving health status. The link between sedentary lifestyle and the severity of

symptoms in osteoarthritis is now well established, making adapted physical activity (APA) a first-

line targeted treatment in osteoarthritis, in order to fight against the effects of a sedentary lifestyle,

regardless of the phenotype or stage of the disease.

The latest recommendations from EULAR, ACR and OARSI consider APA, in the form of

structured exercise programmes for muscle strengthening, joint mobility, proprioception and

aerobic exercises, as the core treatment for people with osteoarthritis. The benefits of APA in

reducing pain and activity limitations in the short, mid and long terms in osteoarthritis, especially of

the lower limbs, has been demonstrated in high-level clinical trials and meta-analyses, with effect

sizes comparable to those observed with pharmacological treatments. In clinical practice, the

prescription of APA in people with osteoarthritis should be encouraged further. Particular attention

should also be paid to patients' adherence in the long term.

Keywords: Osteoarthritis; Exercise; Adapted Physical Activity; Rehabilitation; Pain.

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1. Introduction

a. Definitions (Figure 1)

Being sedentary is defined as a state of wakefulness with a low energy expenditure, specifically when sitting or lying down: i.e. less than 1.6 MET (Metabolic Equivalent of Task, corresponding to the ratio of the working metabolic rate relative to the resting metabolic rate) [1]. This is different to physical inactivity, which is defined as moderate to vigorous physical activity below a recommended threshold [2]. A sedentary lifestyle has deleterious health effects independent of physical inactivity [2]. In particular it is recognized as exacerbating all causes of mortality, and increasing the risk of cardiovascular and metabolic diseases, osteoporosis, anxiety, depression and some types of cancer [3]. As such, efforts to prevent the deleterious health effects of a sedentary lifestyle have become a public health priority in recent years [2]. Physical activity is defined as movement of the body and limbs, resulting from muscle contraction and inducing energy expenditure. It is one of the main therapeutic means of combatting the health effects of a sedentary lifestyle. It can be adapted to the state of health and the capabilities of people with specific needs and serve to stay healthy or improve health. This is called adapted physical activity (APA) [4]. Sport is a form of physical activity defined as an exercise category following a series of rules, which can be practised alone or in a group, for either leisure purposes or performance, in a competitive setting [5].

b. Osteoarthritis and sedentary lifestyle

Osteoarthritis is the most common musculoskeletal disorder. It causes joint pain and stiffness, impaired proprioception and muscle weakness, resulting in limited activity and participation [6]. Although the prevalence of osteoarthritis increases with age, it is not just an aging disease, but a

complex, multifactorial condition. A link between sedentary lifestyle, obesity, chronic inflammatory condition and symptomatic osteoarthritis has been demonstrated, associated with a dose-response relationship between the level of sedentariness and the severity of osteoarthritis symptoms [7]. Regular mechanical stress, such as that obtained during moderate to vigorous APA, is essential to maintain cartilage and muscle mass [8, 9]. However, not all types of mechanical stress lead to the same biological responses [10]. Articular chondrocytes, which are mechanosensitive cells, synthesize the extracellular matrix in response to moderate, cyclic mechanical stress. However, in vitro and in vivo experimental models show that overly intense mechanical stress can activate the pathways of apoptosis and promote cell loss [11]. These models have yet to be properly transposed to design specific exercise programmes and APA modelling should be further developed.

2. What are the current recommendations? (Table 1)

In 2013, the European League Against Rheumatism recommended APA, in the form of exercise, combined with weight control, appropriate footwear and walking aids, when needed, for non-pharmacological management of hip and knee osteoarthritis. Emphasis was placed on personalizing the exercise programme and the importance of therapeutic education to improve adherence, compliance and effectiveness [12]. The guidelines updated in 2018 place even greater importance on APA in the treatment of osteoarthritis [13].

In 2019 the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases recommended non-pharmacological treatments for core management of patients with symptomatic knee osteoarthritis, with APA in the form of strength training, stretching and aerobic activity the first-line treatment, along with therapeutic education and weight control [14].

The American College of Rheumatology recommends APA in the form of strength training,

proprioception and aerobic activity, both land and water-based, for first-line treatment of osteoarthritis of the hands and lower limbs, in conjunction with weight control and the prescription of braces and medication, if necessary [15].

The Osteoarthritis Research Society International has also placed APA at the heart of osteoarthritis management, regardless of the location, in combination with weight control and therapeutic education, before the use of braces, walking aids and drug therapy, which are suggested as adjunct treatments, to be adapted to the patient's comorbidities and biomechanics [16].

In short, all current international recommendations make non-pharmacological measures, including APA, the first-line treatment for osteoarthritis, regardless of the location and associated comorbidities. APA has been assessed in the form of specific and non-specific land and water-based exercises in structured programmes to improve joint mobility, strength, proprioception and aerobic capacity. Content and the delivery of exercise programmes still need to be explored. Currently there is no clear order of priority for the different types of exercise (strength, range of motion, proprioception, aerobic, land-based or water-based, specific or not), but a combination appears to be preferable. The choice should also be based on ease of access and patient preferences to improve adherence. There is no consensus on frequency, duration, intensity and whether exercises should be supervised or not and these should also be personalized. There is no 'one size fits all' exercise programme. APA in osteoarthritis and in chronic diseases in general should be encouraged in a prescription adapted to each patient, as would be the case for a drug, rather than simply urging the patient to "be active".

3. What is the level of evidence?

All national and international recommendations make APA the first-line treatment for osteoarthritis, with a high level of evidence and consensus among experts. They are based on several randomized controlled trials and meta-analyses demonstrating the safety and effectiveness of exercise on pain,

activity limitations and quality of life [17].

In knee osteoarthritis, the Cochrane group showed that land-based exercise reduced pain (musculoskeletal pain -0.49; 95% CI [-0.39 to -0.59]) and activity limitations (MSP -0.52; 95% CI [-0.39 to -0.64]) and improved quality of life (MSP 0.28; 95% CI [0.15 to 0.40]) in the short and long term. Water-based exercises had a beneficial effect on pain (MSP -0.31; 95% CI [-0.47 to -0.15]), activity limitations (MSP -0.32; 95% CI [-0.47 to -0.17]) and quality of life (MSP -0.25; 95% CI [-0.49 to -0.01]) in the short term [18]. A systematic review in 2016 also showed the effectiveness of specific muscle strengthening exercises on pain (MSP 1.218; 95% CI [0.899 to 1.54]) and on reducing activity limitations (MSP on the Lequesne index 1.61; 95% CI [0.40 to 2.81] and MSP on the WOMAC activity limitation score 0.58; 95% CI [0.04 to 1.11]) in the short and long term [8]. Lastly, a 2012 review showed the effectiveness of aerobic exercises on pain (MSP -0.21; 95% CI [-0.35 to -0.08]), activity limitation (MP on the WOMAC score -15.4; 95% CI [-24.8 to -5.92]) and quality of life (MSP -0.21; 95% CI [-0.37 to -0.04]) in the short term, of proprioceptive exercises on pain (MSP -0.71; 95% CI [-1.31 to -0.11]) and of non-specific exercise on activity limitations (MSP -0.44; 95% CI % [-0.88 to 0.00]) [19].

In hip OA, a 2014 Cochrane review analyzed the effectiveness of exercise, with a positive effect on pain and activity limitation (MSP -0.38; 95% CI [-0.55 to -0.20] and MSP -0.38; 95% CI [-0.54 to -0.05] respectively) in the short and long term, but no effect on quality of life (MSP -0.07; 95% CI [-0.23 to 0.36]) [20].

In osteoarthritis of the hands, a 2017 Cochrane review showed that exercise reduced pain (MSP - 0.27; 95% CI [-0.47 to -0.07]) and activity limitation (MSP -0.28; 95% CI [-0.58 to 0.02]) and improved finger mobility (MSP -0.36; 95% CI [-0.58 to -0.15]) in the short term [21].

No serious adverse reactions were reported. The exacerbation of pre-existing symptoms was reported inconsistently. This absence of serious adverse reactions should be an additional argument for prescribing APA in this non-life-threatening condition.

4. What should we do in practice?

a. A review of practices

A review of general practitioner practices in France shows only a small percentage (4% to 48.7%) prescribe APA, while 14% to 70% prescribe non-steroidal anti-inflammatory drugs, and up to 95.8% prescribe analgesics [22]. Physical exercise is recommended by European doctors (76/100 mm on a visual analogue scale) and the level of acceptability is considered high (88/100). This level is lower in France than in other European countries, and lower for certain specialists, such as orthopaedic surgeons, compared to physical medicine and rehabilitation specialists [23]. In short, despite unanimous recommendations and a high level of evidence for the benefits of APA in osteoarthritis, prescriptions are not always in line with recommendations. This could stem in part from clinical inertia, which is defined as "failure to implement or intensify treatment despite recommendations in force". Cottrell et al. reported that 87% of general practitioners encourage APA in osteoarthritis but only 11% prescribe it. APA is more frequently prescribed by general practitioners who believe in its benefits and are confident in their ability to encourage APA. External factors such as time constraints, access to a therapist, patient preferences or the severity of symptoms have little impact on this prescription [24].

b. Prescribing APA and the role of physiotherapists and APA teachers

In practice, when there are no contraindications, the doctor can prescribe advice and goals involving APA (walking, etc.), ROM/rehabilitation (physiotherapy) or prescribe APA on a specific form, which, after an assessment by an APA professional, allows referral to APA and/or health exercise programmes (i.e. exercise to stay healthy or improve health, supervised by APA professionals or trained sports instructors).

Physiotherapists are professionals providing prescribed physical therapy and their role is to assess, rehabilitate and educate patients through different techniques (massage, drainage, physiotherapy, ROM, muscle strengthening, exercise retraining and proprioceptive rehabilitation). APA teachers hold a university degree in sports science. They can help people with chronic diseases by teaching them physical and sports activities under suitable technical conditions for the purposes of rehabilitation, physical therapy and therapeutic education.

c. Encouraging APA

To encourage APA, it is first necessary to remove patients' concerns about the safety of exercising, the risk of exacerbating their osteoarthritis and about how to manage the possible worsening of pain [25]. It is also important to educate the patient simply, which can be incorporated into the consultation or programmes combining education and exercise. This helps explain the purpose of exercising and the beneficial effects on their health [26].

Next, it is important to set the goals of the APA with the patient. They must be specific, in other words understandable, precise and individualized based on age, motivation, the severity of the osteoarthritis, muscle strength and endurance, pain, aerobic capabilities, comorbidities, financial means and on the patient's current or past physical activities. It is important to focus on measurable, subjective goals, such as pain, activity limitations or quality of life, rather than on performance. Lastly, the goals set with the patient must be acceptable and realistic.

In practice, one example of APA to be encouraged is walking, which is effective in osteoarthritis of the lower limbs, is acceptable to patients and is easy to incorporate into their daily life [27]. Water-based APA can also be recommended as it is effective and tolerated more easily [18]. It also helps to focus on APA that will not be too much of a financial burden on the patient. The patient should be taught a small number of osteoarthritis exercises that are easy to memorize, only moderately vigorous, and that are short and repeated, rather than long exercises, if necessary prescribing pain-

relief measures before and after exercising, such as applying heat or cold, or even the use of technical aids (canes, walking sticks, etc.) [28]. Doctors must overcome their own and the patient's misconceptions (for example that weight-bearing APA is contraindicated in osteoarthritis of the lower limbs) and avoid moralizing.

d. Improving adherence

Treatment adherence guarantees effectiveness in the long term. However, it decreases over time, at a rate varying depending on the patient. In clinical practice, a number of factors can improve APA adherence in the medium and long term: ease of access to exercise programmes, support from family, friends and healthcare providers, exercising in a group, and help from healthcare providers including advice, instructions, encouragement and supervising exercises. In addition, it is important to monitor exercise and give the patient reminders to help them continue APA on their own and prevent the feeling of 'abandonment' often reported by patients after the supervised teaching and exercise phase ends. The use of digital tools, such as apps including education, exercises, goals, positive reinforcement and electronic reminders, or web-based intervention programmes, have shown encouraging results in improving APA adherence. The value of sending text message reminders is also being assessed [17, 29, 30]. As with programme content, there is no 'one-size-fits-all' combination of measures to improve adherence. They should be personalized based on the profile and preferences of the patient, and the experience of the teams. However, it would appear that positive biofeedback (e.g. self-efficacy) is a strategy shared by all these solutions.

Conclusion

APA, in particular structured programmes combining specific targeted exercises for muscle strengthening, improved joint mobility and proprioception, and non-specific exercises (aerobic endurance exercises), is the first-line treatment in osteoarthritis. Its benefit/risk ratio is greater than

that of drug therapy. APA is a targeted and precise treatment aimed at reducing both the associated risk factors (e.g. metabolic syndrome, excess weight, sarcopenia and chronic inflammation) and the symptoms bothering the patient the most (e.g. pain, joint stiffness and activity limitations). The efficacy of APA has been demonstrated in the treatment of osteoarthritis, especially OA of the lower limbs, by a number of studies and meta-analyses, with an excellent level of evidence. However, the most effective conditions (intensity, frequency, duration, repetition) have yet to be determined.

The importance of APA in the treatment of osteoarthritis has been confirmed in the latest national and international guidelines. To ensure that these guidelines are applied, particular attention should be paid to the feasibility of the prescribed treatment and the patient's adherence. To do this, it is important to decide on precise and individualized goals with the patient, reduce the burden of exercising, for example by limiting the number of exercises, focus on exercises that are easily accessible and inexpensive, and monitor exercises through supervised sessions and reminders.

References

- [1] Pate RR, O'Neill JR, Lobelo F. The evolving definition of "sedentary". Exercise and sport sciences reviews 2008;36(4):173-8.
- [2] Khan KM, Thompson AM, Blair SN, Sallis JF, Powell KE, Bull FC, et al. Sport and exercise as contributors to the health of nations. Lancet 2012;380(9836):59-64.
- [3] Paffenbarger RS, Jr., Hyde RT, Wing AL, Hsieh CC. Physical activity, all-cause mortality, and longevity of college alumni. The New England journal of medicine 1986;314(10):605-13.
- [4] Rouquette A, Badley EM, Falissard B, Dub T, Leplege A, Coste J. Moderators, mediators, and bidirectional relationships in the International Classification of Functioning, Disability and Health (ICF) framework: An empirical investigation using a longitudinal design and Structural Equation Modeling (SEM). Soc Sci Med 2015;135:133-42.
- [5] Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public health reports 1985;100(2):126-31.
- [6] Palazzo C, Nguyen C, Lefèvre-Colau MM, Rannou F, Poiraudeau S. Risk factors and burden of osteoarthritis. Annals of physical and rehabilitation medicine 2016;59(3):134-8.
- [7] Berenbaum F, Wallace IJ, Lieberman DE, Felson DT. Modern-day environmental factors in the pathogenesis of osteoarthritis. Nature reviews Rheumatology 2018;14(11):674-81.
- [8] Coudeyre E, Jegu AG, Giustanini M, Marrel JP, Edouard P, Pereira B. Isokinetic muscle strengthening for knee osteoarthritis: A systematic review of randomized controlled trials with meta-analysis. Annals of physical and rehabilitation medicine 2016;59(3):207-15.
- [9] Racunica TL, Teichtahl AJ, Wang Y, Wluka AE, English DR, Giles GG, et al. Effect of physical activity on articular knee joint structures in community-based adults. Arthritis and rheumatism 2007;57(7):1261-8.
- [10] Grad S, Eglin D, Alini M, Stoddart MJ. Physical stimulation of chondrogenic cells in vitro: a review. Clinical orthopaedics and related research 2011;469(10):2764-72.

- [11] Rannou F, Lee TS, Zhou RH, Chin J, Lotz JC, Mayoux-Benhamou MA, et al. Intervertebral disc degeneration: the role of the mitochondrial pathway in annulus fibrosus cell apoptosis induced by overload. The American journal of pathology 2004;164(3):915-24.
- [12] Fernandes L, Hagen KB, Bijlsma JW, Andreassen O, Christensen P, Conaghan PG, et al. EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis. Annals of the rheumatic diseases 2013;72(7):1125-35.
- [13] Rausch Osthoff AK, Niedermann K, Braun J, Adams J, Brodin N, Dagfinrud H, et al. 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. Annals of the rheumatic diseases 2018;77(9):1251-60.
- [14] Bruyère O, Honvo G, Veronese N, Arden NK, Branco J, Curtis EM, et al. An updated algorithm recommendation for the management of knee osteoarthritis from the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). Seminars in arthritis and rheumatism 2019;49(3):337-50.
- [15] Kolasinski SL, Neogi T, Hochberg MC, Oatis C, Guyatt G, Block J, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. Arthritis & rheumatology 2020;72(2):220-33.
- [16] Bannuru RR, Osani MC, Vaysbrot EE, Arden NK, Bennell K, Bierma-Zeinstra SMA, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarthritis and cartilage 2019;27(11):1578-89.
- [17] Nelligan RK, Hinman RS, Kasza J, Schwartz S, Kimp A, Atkins L, et al. Effect of a short message service (SMS) intervention on adherence to a physiotherapist-prescribed home exercise program for people with knee osteoarthritis and obesity: protocol for the ADHERE randomised controlled trial. BMC musculoskeletal disorders 2019;20(1):428.
- [18] Bartels EM, Juhl CB, Christensen R, Hagen KB, Danneskiold-Samsoe B, Dagfinrud H, et al. Aquatic exercise for the treatment of knee and hip osteoarthritis. The Cochrane database of systematic reviews 2016;3:CD005523.

- [19] Wang SY, Olson-Kellogg B, Shamliyan TA, Choi JY, Ramakrishnan R, Kane RL. Physical therapy interventions for knee pain secondary to osteoarthritis: a systematic review. Annals of internal medicine 2012;157(9):632-44.
- [20] Fransen M, McConnell S, Hernandez-Molina G, Reichenbach S. Exercise for osteoarthritis of the hip. The Cochrane database of systematic reviews 2014(4):CD007912.
- [21] Osteras N, Kjeken I, Smedslund G, Moe RH, Slatkowsky-Christensen B, Uhlig T, et al. Exercise for Hand Osteoarthritis: A Cochrane Systematic Review. The Journal of rheumatology 2017;44(12):1850-8.
- [22] Denoeud L, Mazières B, Payen-Champenois C, Ravaud P. First line treatment of knee osteoarthritis in outpatients in France: adherence to the EULAR 2000 recommendations and factors influencing adherence. Annals of the rheumatic diseases 2005;64(1):70-4.
- [23] Mazieres B. Level of acceptability of EULAR recommendations for the management of knee osteoarthritis by practitioners in different European countries. Annals of the Rheumatic Diseases. August 2005;64(8):1158-64.
- [24] Cottrell E, Foster NE, Porcheret M, Rathod T, Roddy E. GPs' attitudes, beliefs and behaviours regarding exercise for chronic knee pain: a questionnaire survey. BMJ open 2017;7(6):e014999.
- [25] Holden MA, Nicholls EE, Young J, Hay EM, Foster NE. Role of exercise for knee pain: what do older adults in the community think? Arthritis care & research 2012;64(10):1554-64.
- [26] Gay C, Chabaud A, Guilley E, Coudeyre E. Educating patients about the benefits of physical activity and exercise for their hip and knee osteoarthritis. Systematic literature review. Annals of physical and rehabilitation medicine 2016;59(3):174-83.
- [27] O'Connor SR, Tully MA, Ryan B, Bleakley CM, Baxter GD, Bradley JM, et al. Walking exercise for chronic musculoskeletal pain: systematic review and meta-analysis. Archives of physical medicine and rehabilitation 2015;96(4):724-34 e3.

- [28] Regnaux JP, Lefèvre-Colau MM, Trinquart L, Nguyen C, Boutron I, Brosseau L, et al. High-intensity versus low-intensity physical activity or exercise in people with hip or knee osteoarthritis. The Cochrane database of systematic reviews 2015(10):CD010203.
- [29] Schafer AGM, Zalpour C, von Piekartz H, Hall TM, Paelke V. The Efficacy of Electronic Health-Supported Home Exercise Interventions for Patients With Osteoarthritis of the Knee: Systematic Review. Journal of medical Internet research 2018;20(4):e152.
- [30] Bossen D, Veenhof C, Van Beek KE, Spreeuwenberg PM, Dekker J, De Bakker DH. Effectiveness of a web-based physical activity intervention in patients with knee and/or hip osteoarthritis: randomized controlled trial. Journal of medical Internet research 2013;15(11):e257.

Figure legend

Figure 1. Areas of physical activity, exercise and sport. According to Khan et al. [2].

Conflicts of interest

The authors declare that they have no conflicts of interest.

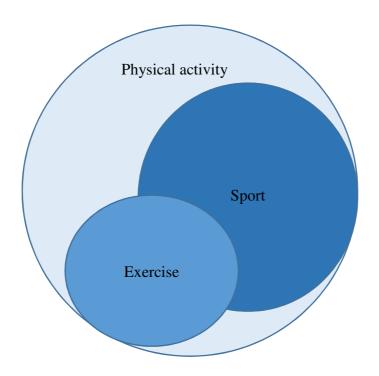


Table 1. Summary of the main current recommendations on the benefit of physical activity for osteoarthritis.

Recommendations	EULAR - 2018	ACR - 2019	OARSI - 2019	Level of evidence	Quality of evidence
Land-based exercise	-	Recommended	Recommended	Ia	Good
Water-based exercise	-	Recommended	Recommended	Ia	Good
Strength training	Recommended	Recommended	Recommended	Ia	Good
Active range of	Recommended	-	-		
motion exercise					
Aerobic activity	Recommended	Recommended	-	Ia	Good