

CZYŻEWSKI, Filip, BANYŚ, Filip, BOCHEN, Konrad, DUDEK, Stanisław, JASIŃSKI, Filip, ŁUKAWSKI, Artur, PASIERB, Karolina, SZAŁAJSKA, Julia, WIAK, Iga and WOJTACH, Klaudia. Approaches to Treating Knee Osteoarthritis: Surgery vs. Non-Surgery Treatment. *Quality in Sport.* 2024;29:55564. eISSN 2450-3118.
<https://dx.doi.org/10.12775/QS.2024.29.55564>
<https://apcz.umk.pl/QS/article/view/55564>

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.

Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).

Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.

Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

© The Authors 2024;

This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Toruń, Poland Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike. (<http://creativecommons.org/licenses/by-nc-sa/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.

The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 08.10.2024. Revised: 19.10.2024. Accepted: 23.10.2024. Published: 26.10.2024.

Approaches to Treating Knee Osteoarthritis: Surgery vs. Non-Surgery Treatment

Filip Czyżewski, Filip Banyś, Konrad Bochen, Stanisław Dudek, Filip Jasiński, Artur Łukawski, Karolina Pasierb, Julia Szałajska, Iga Wiak, Klaudia Wojtach

Filip Czyżewski, Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

<https://orcid.org/0009-0006-8556-6565>

czyzewskifilip@gmail.com

Filip Banyś, Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

<https://orcid.org/0009-0002-6231-0904>

filipbany607@gmail.com

Konrad Bochen, Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

<https://orcid.org/0009-0000-9757-0744>

konrad.bochen@gmail.com

Stanisław Dudek, Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

<https://orcid.org/0009-0002-3641-4865>

s077701@student.wum.edu.pl

Filip Jasiński, Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

<https://orcid.org/0009-0005-3327-255X>

filip.jasinski00@wp.pl

Artur Łukawski, Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

<https://orcid.org/0009-0006-6252-1655>

arturlukawski010120@op.pl

Karolina Pasierb, Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

<https://orcid.org/0009-0006-5806-3508>

k.pasierb36@gmail.com

Julia Szalajska, Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

<https://orcid.org/0009-0007-8866-5419>,

juliaszalajska.mail@gmail.com

Iga Wiak, Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

<https://orcid.org/0009-0003-6419-7287>

wiak.igakinga@gmail.com

Klaudia Wojtach, Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

<https://orcid.org/0009-0007-2220-0088>

klaudiaw2000@o2.pl

ABSTRACT

Introduction: Knee Osteoarthritis (KO) is a progressive, chronic disease that damage the joint cartilage of a knee and leads to a changes in a anatomy of the joint. Both surgical and non-surgical methods are used to treat the disease. In this study, we will compare the invasive vs non-invasive methods of KO treatment.

Objectives: The review and presentation of the current state of knowledge on Treating Knee Osteoarthritis, comparing surgery vs non-surgery methods.

Material and Methods: Review of the studies available on open access sources at PubMed, Google Scholar and National Library of Medicine.

Conclusions: Surgery approach for the Knee Osteoarthritis treatment are more durable, have better pain relief and treat casually the OA. Similar effects cannot be reached by non-surgery methods yet. However, there is a big promise in future studies about non-surgery methods, which can also raise a Quality of Life significantly and even avoid or postpone an operation in some groups of patients.

Keywords: Knee Osteoarthritis, Knee Joint, Osteoarthritis, Surgery.

STATE OF KNOWLEDGE

INTRODUCTION

Knee joint is the biggest synovial joint in humans. Its osteoarthritis is a main reason for a knee pain in adult humans. It can affect any of the soft parts among knee joint. Although we have wide spread options to heal that disease, none of them leads to the delay of the progression. Cartilage that builds a knee joint is sensitive to an erosion. Disappearance of the cartilage, chondrocyte loss and phenotypic transformation create an overview of this state. KO is a chronic disease; thus its symptoms are spread in the time and often it is not easy to observe its onset. Early symptoms usually consist of knee pain, especially during prolonged standing position and sport, stiffness of the knee and crackle sounds while flexion the leg occurs. Not to forget that functional changes play a mentioning-worth role in the KO. The whole geometry of the joint alter in time and lead to ongoing problems with i.e hip joint. The exact pathogenesis of KO is not yet known, but suggested mechanisms include inflammation of the knee, increase in metalloproteinases from MMP and ADAMTS families, that deplete proteoglycans. Diagnosis of KO is mainly by clinical symptoms in addition with radiological imaging. (1-3)

EPIDEMIOLOGY AND CHARACTERISTICS

Osteoarthritis is wide-spread disease that occurs in 10-15% of the population, above 60 years old, worldwide. In developed countries it affects 13% of women and 10% of men. The symptoms rarely are noticeable before 40 year of life, but its chronic and sneaky progress suggest that many of younger people have biochemical and radiological changes. Approximately 30% of adults have

radiological changes that may indicate KO. Positive prediction factors for KO are: obesity, muscle weakness, age and sitting lifestyle. Physical exercises (especially weight exercises), weight management and structured education about working position etc. are crucial to prevent and treat the symptoms of KO. Despite those recommendations sound easy, rarely patient are able to pursue all of them.(1, 4)

DIAGNOSIS

The proper diagnosis of KO should consist a deep history of a disease and well-imaged knee RTG. The results should be compared with Kellgren-Lawren Scale, Ahlback classification or knee osteoarthritis grading system (KGOS). The main goal of the differential diagnosis is to differentiate KO from rheumatoid arthritis or ankylosing spondylitis.(1, 5, 6)

ANATOMY AND ITS IMPLICATIONS

Knee joint is a hinge joint which has a wide range of motion in flexion (120-150 degrees) and extensions (5-10 degrees) movements and only 10 degrees internal rotation and 30-40 degrees external rotation. Knee joint is built with synovial cartilages. During lifetime cartilage gets thinner and loose its elasticity. The KO may influence any of the soft parts of a joint: Cartilages, synovial membrane , meniscus etc. Connected with unproper gait control and micro-damages it can result in inflammation, that induces KO.(7, 8)

TREATMENT APPROACHES

Currently we distinguish two basic differential criteria for a KO treatment. One is a surgery and second is non-surgery treatment, which includes physical therapy, stem cell therapy, pain management and interventional management as intra-articular corticosteroid injections and intra-articular hyaluronic acid injections. Aim of this study is to compare a surgery treatment to a non-surgery treatment, especially a physical therapy(9) (10)

SURGERY METHODS

Main goal of a surgery is to improve a quality of life, reduce pain and to avoid disability. Surgery is generally not a first-line treatment option but it is recommended when other options fail. We distinguish:

- 1. Total Knee Replacement Surgery (TKRS)**
- 1. TKRS comprise two plastic parts of prosthesis that are placed between tibia and femur. They imitate a natural joint surfaces and work perfectly well if surgery is optimally performed. TKRS is better, equal or worse in compare with physical therapy, because we must determine which effect is desired by a patient. Patients that undergo a TKRS have a better pain reduction and better quality of life according, than those who are treated only with physical therapy(11-13)**
- 2. Partial Knee Replacement Surgery (PKRS)**
- 2. This option is reserved for patients that only have a damage in smaller part of the knee joint i.e medial or lateral tibiofemoral**

compartment. Thus this operation requires tight incision only, it has less side effects and offer earlier discharge than TKRS.(14)

3. Knee arthroscopy (KA)

3. Not so ago the most popular way to treat KO. Minimization in its invasiveness is the biggest opportunity of this option. Currently we have no recommendations to prefer KA over TKRS.

4. Knee Osteotomy

4. This operation realigns a knee joint. It is a good alternative for patients with medial compartment of the knee deformity(15)

INTERVENTIONAL NON-SURGERY METHODS

1. Intra-Articular Corticosteroid Injection (IACI)

5. IACI has the biggest scientific support among many of those drugs, which were studied as intra-articular drugs. It shows also a greater efficacy than NSAIDS and other oral medications. Many of studies have shown that its efficiency in a long term treatment is worse than TKRS. IACI have a short duration (3 weeks-3 months) thus its real usefulness is very limited. Although it should be remembered that not every person is eligible for a TKRS, so IACI may help specific sort of patients.(16, 17)

2. Intra-Articular Hyaluronic Acid Injections (IAHAI)

6. It is a well-known substance with a high safety profile. However, recent studies have shown that its efficacy is not way better than Saline injections. That's one of the reasons, that its use is no longer in favor comparing to IACI. IAHAI are used only as a joint symptoms controller when IACI fail. (18, 19)

3. Intra-Articular Platelet-Rich Plasma Injections (PRP)

7. It appears to be a supreme over a IAHAI for a young adult patients, with a not fully developed OA. However this type of treatment doesn't have any indications as a first-line treatment.(20)

NON-INTERVENTIONAL PHARMACOLOGICAL METHODS

1. **Non-Steroidal Anti-Inflammatory Drugs (NSAID)**
 8. It is shown in multiple studies that NSAIDs have a good impact on symptoms control in all groups of probants. The most effective one is Diclofenac 150mg/day. Whereas oral NSAIDs are not recommended for a longer use, the local usage of gels and ointments have low possibility for cardiac, renal and gastric side-effects. Not to forget that NSAIDs offer only a symptomatic range of effects, so we should treat those as a part of bigger treatment solution. (21, 22)
2. **Paracetamol**
 9. Paracetamol has no anti-inflammatory action, it is not suggested by OARSI and metanalysis to use it as the only pharmacological approach. However paracetamol is considered as a safe and efficient analgetic when mixed with NSAIDs. Some local associations i.e Honk Kong LLOA stipulate that paracetamol is a main drug for a OA symptoms control.(2) (21)
3. **Opioids**
 10. They are generally not-recommended by OARSI as a pharmacological approach to a knee OA. Thus they show an excellent analgetic effects, they have a wide pallet of side-effects, which are not tolerated by patients. High risk of long-term opioid tolerance, addiction and withdrawal effects make them not relevant in OA control. Moreover they show no supremacy over an Intra-Articular injections when it comes to pain control.

4. Glucosamine

11. OARSI doesn't support the use of glucosamine in a knee OA. There is very little evidence for a glucosamine to be better than a placebo in pain and OA development control. Glucosamine is a diet supplement that is often sold as a joint function-improving medication. Smaller trials show even less evidence for a glucosamine than a commercial ones. (23, 24)

NON-INTERVENTIONAL AND NON-PHARMACOLOGICAL APPROACH

1. Education

12. It is a significant part of treatment approach. It helps patients with understanding their role in the whole process. It is a core first line treatment option with other non-interventional and non-pharmacological efforts. Whole counselling programs shouldn't be neglected as lifestyle changes are a must-have in this situation.

2. Weight loss

13. It is in a pair with an education first line treatment, which is a key to successful treatment. It is a common part of every association's guideline. It is also suggested for obese patients, who don't have any symptoms of the OA to lose their weight as a prevention. At the very beginning it is advised to change a lifestyle which means: changing diet, starting regular physical activity. Other parts of approach consist of adjusting a pharmacology for a patients, which means not only a better diabetes or blood lipids control, but also an anti-obesity

drugs. In high-stage of an obesity it is recommended to perform a gastric bypass surgery, gastric banding or gastrectomy. Weight loss reduce pain according to a different studies from 10 to 15% which is similar to a mild painkiller usage. Additionally weight loss comes with further positive changes in patients health.

3. Physical Exercise

14.Aerobic exercise, targeted strength exercise, stretching, improving flexibility – those are main recommendations. There are meant to strengthen muscles around knee joint, reduce pain, slower the changes in the joint. Patients who exercise have a 20-30% reduction in pain in comparison to those who don't train. Meta-analyses shown that the best sports are those, which have wide range of motion, strength compound and require aerobic exhaust. Tai chi and sports similar to it are highly recommended. Recently there is a boom for an aqua aerobic for treating OA, but it is evidenced, that it has a minor pain reduction function. Thus, its short-term efficacy is reliable. (25-27)

4. Biomechanical support

15.OARSI recommends a biomechanical support in many ways: walking canes, knee braces, foot orthoses. These equipment helps with reducing pain, stiffness and immobility of a patient. Unfortunately we are lack of evidence how sufficient is support of those to related topics. However ACR and OARSI indicate its helpfulness, but only in OA isolated to a knee, no a multi-joint OA. (28, 29)

COMPARISON BEETWEEN SURGERY AND NON-SURGERY METHODS

1. TKRS, PKRS with:

1.1 IACI

16.TKRS characterizes 85-90% reduction of pain and IACIs reduction in pain is still undefined by studies. TKRS works better in end stage OA, works faster than IACI (IACI needs 1-3 months to show its full power). TKRS offers a higher QoL for the next 15-20 years, which is far better than IACI, which needs to be repeated every 3-4 months. The only benefit of IACI over TKRS is shorter time of recovery after the procedure. Moreover TKRS doesn't damage the cartilage, what IACI does.(30)

1.2 IAHAI

17.it brings an ease in the pain only to 30-40% of patients and its effect last for 12 months, so it is better than IACI, but still worse than TKRS. However it is a good alternative for those, who can't undergo a surgery.(31)

1.3 PRP

18.PRP shows a longer duration of work than IACI or IAHAI, but also has a lowest grade of the evidence, although there is a big promise of positive results. It is okay to use it in mild to moderate OA. PRP in opposition to IAHAI and IACI repair a damaged cartilage and not only impacts on the symptoms.(32)

2. TKRS, PKRS with

2.1 Pharmacological approach (NSAIDs, Paracetamol, Glucosamine)

19.Only NSAIDS are ready to compete with TKRS when it comes to pain relief and improve in a mobility. They don't affect a reason of the OA, so we cannot use it with success without TKRS or other

intervention. Paracetamol and Glucosamine have very little scientific support and its use is still questionable. (33)

3. TKRS, PKRS with

3.1 Exercise

20. Those two represent different approaches to a KOA. TKRS in fact should be supported by physiotherapy. According to massive metanalyses physiotherapy can't replace TKRS. Exercises are suitable for patients in mild or moderate stage of KOA. The biggest advantage of TKRS over exercise is durability. Exercises show its benefits only when performed regularly and with care. Bad technic of exercises or lack of dedication can lead to no improvement. However, physical therapy is perfect option for those who have contraindications for the operation.(25, 34)

3.2 Weight loss

21. Weight loss is a significant change for a whole body health. Undoubtedly, it has worse impact on symptoms relief of OA than TKRS. Moreover it is fully dependent on determination of a patient, because studies show that lack of dedication and not sticking to a diet is a important reason, why weight loss is difficult to reach or maintain. However weight loss is supportive to TKRS, it benefits on general health of an individual, what makes it still worth.

4. Knee Arthroscopy with

4.1 IACI, IAHAI and PRP – it is shown that KA is not as good as thought in the past. American Academy of Orthopedic Surgeons doesn't include it as a first line of treatment. It is more invasive

than injections, costs more and we have burden of side effects. It summarizes as a worse treatment option than the injections.(35)

4.2 Exercise/ weight loss– like in KRS, we cannot switch operation to exercises/ weight loss so easily. Those are bind as a overall treatment approach. In opposition to KA, exercise and weight loss are well documented as a good resulting handling. (36)

5. Knee osteotomy (KO) with

5.1 IACAI, IAHAI, PRP – KO is a good option for patients with unilateral OA. It shows shorter durability of effects than KRS, approximately 10 years. It is lack of big metanalyses that compare KO to injections, so a further research is obligatory to take a conclusions.

5.2 Exercise/ weight loss – Knee Osteotomy and KRS are resemblant in this case – they should be supported by exercise and weight loss program but not substituted by it. (21)

DISCUSSION

Both surgery and non-surgery methods seem to be effective but in different type of patients. It is very hard to resolve a question which method is better. There is need and space for further studies on more specific groups of patients. It must be remembered that most non-surgery methods are no directly healing the knee, but slower the damage and relief the symptoms. However, there is bigger and bigger group of people, that can use non-surgery therapies without skipping a surgery. Authors think, that development of widely perceived fitness market improve the lifestyle of the patients, what means also improving KOA symptoms. Compliance of the treatment is also a huge problem when it comes to exercise and weight loss, so it is an obstacle, that many patients must face.

SUMMARY

Current state of knowledge spots TKRS and PKRS as a target treatment approach for most patients. We still don't have any evidence that non-invasive or invasive non-surgery methods are supreme over TKRS/PKRS. However, patients, who don't match the operation, can benefit from change of lifestyle and other pharmacological and non-pharmacological options. There is also a field for better understanding the OA and its mechanisms, since many of approaches seem experimental, not scientific based.

AUTHOR'S CONTRIBUTION

Conceptualization: F. Czyżewski; methodology: I. Wiak; F.Jasiński; software: K.Wojtach; check: F. Banyś, F. Czyżewski; formal analysis: K.Bochen, K.Pasierb, J.Szałajska; investigation: F.Czyżewski, A.Łukawski, I. Wiak; resources: S. Dudek, K. Wojtach, F.Banyś; data curation: K.Bochen; F.Jasiński; writing-rough preparation: F.Czyżewski, K. Pasierb, J.Szałajska; writing – review and editing: A.Łukawski, I.Wiak, S.Dudek; visualization: F.Banyś, A.Łukawski, K. Wojtach; supervision: F.Czyżewski, J.Szałajska; project administration: F.Czyżewski

FUNDING

This research received no external funding.

INSTITUTIONAL REVIEW BOARD STATEMENT

Not applicable.

INFORMED CONSENT STATEMENT

Not applicable.

ACKNOWLEDGMENTS

No acknowledgments.

CONFLICT OF INTERESTS

The authors declare no conflict of interest, that could be based on financial or commercial relationship.

REFERENCES:

1. Jang S, Lee K, Ju JH. Recent Updates of Diagnosis, Pathophysiology, and Treatment on Osteoarthritis of the Knee. *Int J Mol Sci.* 2021;22(5).
2. Kan HS, Chan PK, Chiu KY, Yan CH, Yeung SS, Ng YL, et al. Non-surgical treatment of knee osteoarthritis. *Hong Kong Med J.* 2019;25(2):127-33.
3. Hunter DJ, Nicolson PJA, Little CB, Robbins SR, Wang X, Bennell KL. Developing strategic priorities in osteoarthritis research: Proceedings and recommendations arising from the 2017 Australian Osteoarthritis Summit. *BMC Musculoskelet Disord.* 2019;20(1):74.
4. de Zwart AH, Dekker J, Lems W, Roorda LD, van der Esch M, van der Leeden M. Factors associated with upper leg muscle strength in knee osteoarthritis: A scoping review. *J Rehabil Med.* 2018;50(2):140-50.

5. Emmert D, Rasche T, Stieber C, Conrad R, Mucke M. [Knee pain - symptoms, diagnosis and therapy of osteoarthritis]. MMW Fortschr Med. 2018;160(15):58-64.
6. Clark GP. Treatment options for symptomatic knee osteoarthritis in adults. JAAPA. 2023;36(11):1-6.
7. Englund M. The role of the meniscus in osteoarthritis genesis. Rheum Dis Clin North Am. 2008;34(3):573-9.
8. Dieppe PA, Lohmander LS. Pathogenesis and management of pain in osteoarthritis. Lancet. 2005;365(9463):965-73.
9. Lubowitz JH, Brand JC, Rossi MJ. Nonoperative Management of Degenerative Meniscus Tears Is Worth a Try. Arthroscopy. 2020;36(2):327-8.
10. Katz JN, Brophy RH, Chaisson CE, de Chaves L, Cole BJ, Dahm DL, et al. Surgery versus physical therapy for a meniscal tear and osteoarthritis. N Engl J Med. 2013;368(18):1675-84.
11. Skou ST, Roos EM, Laursen MB, Rathleff MS, Arendt-Nielsen L, Simonsen O, et al. Criteria used when deciding on eligibility for total knee arthroplasty--Between thinking and doing. Knee. 2016;23(2):300-5.
12. Skou ST, Roos EM, Laursen MB, Rathleff MS, Arendt-Nielsen L, Simonsen O, et al. A Randomized, Controlled Trial of Total Knee Replacement. N Engl J Med. 2015;373(17):1597-606.
13. Nelson AE, Allen KD, Golightly YM, Goode AP, Jordan JM. A systematic review of recommendations and guidelines for the management of osteoarthritis: The chronic osteoarthritis management initiative of the U.S. bone and joint initiative. Semin Arthritis Rheum. 2014;43(6):701-12.
14. Rodriguez-Merchan EC, Gomez-Cardero P. Unicompartmental knee arthroplasty: Current indications, technical issues and results. EFORT Open Rev. 2018;3(6):363-73.
15. Liu X, Chen Z, Gao Y, Zhang J, Jin Z. High Tibial Osteotomy: Review of Techniques and Biomechanics. J Healthc Eng. 2019;2019:8363128.
16. McAlindon TE, LaValley MP, Harvey WF, Price LL, Driban JB, Zhang M, et al. Effect of Intra-articular Triamcinolone vs Saline on Knee Cartilage Volume and Pain in Patients With Knee Osteoarthritis: A Randomized Clinical Trial. JAMA. 2017;317(19):1967-75.
17. Guermazi A, Neogi T, Katz JN, Kwok CK, Conaghan PG, Felson DT, et al. Intra-articular Corticosteroid Injections for the Treatment of Hip and Knee Osteoarthritis-related Pain: Considerations and Controversies with a Focus on Imaging-Radiology Scientific Expert Panel. Radiology. 2020;297(3):503-12.
18. 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 Care Res (Hoboken). 2020;72(2):149-62.
19. McArthur BA, Dy CJ, Fabricant PD, Valle AG. Long term safety, efficacy, and patient acceptability of hyaluronic acid injection in patients with painful osteoarthritis of the knee. Patient Prefer Adherence. 2012;6:905-10.
20. . !!! INVALID CITATION !!! {}.
21. 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 Cartilage. 2019;27(11):1578-89.
22. da Costa BR, Reichenbach S, Keller N, Nartey L, Wandel S, Juni P, et al. Effectiveness of non-steroidal anti-inflammatory drugs for the treatment of pain in knee and hip osteoarthritis: a network meta-analysis. Lancet. 2017;390(10090):e21-e33.

23. Vincent HK, Heywood K, Connelly J, Hurley RW. Obesity and weight loss in the treatment and prevention of osteoarthritis. *PM R.* 2012;4(5 Suppl):S59-67.

24. Chmelo E, Nicklas B, Davis C, Miller GD, Legault C, Messier S. Physical activity and physical function in older adults with knee osteoarthritis. *J Phys Act Health.* 2013;10(6):777-83.

25. Fransen M, McConnell S, Harmer AR, Van der Esch M, Simic M, Bennell KL. Exercise for osteoarthritis of the knee: a Cochrane systematic review. *Br J Sports Med.* 2015;49(24):1554-7.

26. Jansen MJ, Viechtbauer W, Lenssen AF, Hendriks EJ, de Bie RA. Strength training alone, exercise therapy alone, and exercise therapy with passive manual mobilisation each reduce pain and disability in people with knee osteoarthritis: a systematic review. *J Physiother.* 2011;57(1):11-20.

27. 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. *Cochrane Database Syst Rev.* 2016;3(3):CD005523.

28. Raja K, Dewan N. Efficacy of knee braces and foot orthoses in conservative management of knee osteoarthritis: a systematic review. *Am J Phys Med Rehabil.* 2011;90(3):247-62.

29. Moyer RF, Birmingham TB, Bryant DM, Giffin JR, Marriott KA, Leitch KM. Biomechanical effects of valgus knee bracing: a systematic review and meta-analysis. *Osteoarthritis Cartilage.* 2015;23(2):178-88.

30. Price AJ, Alvand A, Troelsen A, Katz JN, Hooper G, Gray A, et al. Knee replacement. *Lancet.* 2018;392(10158):1672-82.

31. Jevsevar D, Donnelly P, Brown GA, Cummins DS. Viscosupplementation for Osteoarthritis of the Knee: A Systematic Review of the Evidence. *J Bone Joint Surg Am.* 2015;97(24):2047-60.

32. Laudy AB, Bakker EW, Rekers M, Moen MH. Efficacy of platelet-rich plasma injections in osteoarthritis of the knee: a systematic review and meta-analysis. *Br J Sports Med.* 2015;49(10):657-72.

33. Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden NK, et al. OARSI recommendations for the management of hip and knee osteoarthritis: part III: Changes in evidence following systematic cumulative update of research published through January 2009. *Osteoarthritis Cartilage.* 2010;18(4):476-99.

34. Skou ST, Roos EM, Simonsen O, Laursen MB, Rathleff MS, Arendt-Nielsen L, et al. The efficacy of non-surgical treatment on pain and sensitization in patients with knee osteoarthritis: a pre-defined ancillary analysis from a randomized controlled trial. *Osteoarthritis Cartilage.* 2016;24(1):108-16.

35. Moseley JB, O'Malley K, Petersen NJ, Menke TJ, Brody BA, Kuykendall DH, et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med.* 2002;347(2):81-8.

36. Bennell KL, Hinman RS, Metcalf BR, Buchbinder R, McConnell J, McColl G, et al. Efficacy of physiotherapy management of knee joint osteoarthritis: a randomised, double blind, placebo controlled trial. *Ann Rheum Dis.* 2005;64(6):906-12.