Osteoarthritis and Cartilage Open 5 (2023) 100332

Contents lists available at ScienceDirect

Osteoarthritis and Cartilage Open

journal homepage: www.elsevier.com/journals/osteoarthritis-and-cartilage-open/2665-9131

Evaluation of disease burden, patient journey, unmet diagnosis and treatment needs of patients with HIP and knee osteoarthritis in Turkey: A study through Delphi Methodology

Hasan Fatih Çay [a,*], Ayşen Akıncı [b], Lale Altan [c], Şebnem Ataman [d], Semih Aydoğdu [e], Demirhan Dıraçoğlu [f], Hakan Genç [g], Simin Hepgüler [h], Ayşegül Ketenci [f], Kadriye Öneş [i], Meltem Uyar [j], Salih Gümrü [k], Başak Hacıbedel [l], Kerem Helvacıoğlu [l], Ayşe Ölmez [k], Tiraje Tuncer [m]

[a] Department of Rheumatology, Antalya Training and Research Hospital, University of Health Sciences, Antalya, Turkey
[b] Department of Physical Medicine and Rehabilitation, Hacettepe University Medical School, Ankara, Turkey
[c] Department of Physical Medicine and Rehabilitation, Uludağ University Medical School, Bursa, Turkey
[d] Department of Rheumatology, Ankara University Medical School, Ankara, Turkey
[e] Department of Orthopaedic Surgery, School of Medicine, Ege University, İzmir, Turkey
[f] Department of Physical Medicine and Rehabilitation, İstanbul Faculty of Medicine, İstanbul University, İstanbul, Turkey
[g] Department of Physical Medicine and Rehabilitation, University of Health Sciences, Ankara Training and Research Hospital, Ankara, Turkey
[h] Department of Physical Medicine and Rehabilitation, School of Medicine, Ege University, İzmir, Turkey
[i] Department of Physical Medicine and Rehabilitation, İstanbul Physical Medicine and Rehabilitation Training and Research Hospital, University of Health Sciences, İstanbul, Turkey
[j] Department of Anaesthesiology and Reanimation, Pain Clinic, Ege University, İzmir, Turkey
[k] Department of Medical Affairs, Pfizer, Istanbul, Turkey
[l] Health Economics and Outcomes Research Department, Pfizer, Istanbul, Turkey
[m] Division of Rheumatology, Department of Physical Medicine and Rehabilitation, Akdeniz University School of Medicine, Antalya, Turkey

ARTICLE INFO

Handling Editor: Professor H Madry

Keywords:
osteoarthritis
disease burden
diagnosis
severity
treatment response
arthroplasty

ABSTRACT

Objective: To get information-driven insights from expert physicians regarding multiple aspects of the patient journey in knee and hip OA and establish a consensus for future studies and decision tree models in Turkey.
Design: 157 questions were asked in total during this three-round modified Delphi-method panel to 10 physical medicine and rehabilitation specialists (2 have rheumatology and 3 have algology subspeciality), one orthopaedic surgeon and one algology specialist from anaesthesia specialty background. A consensus was achieved when 80% of the panel members agreed with an item. Contradictions between different disciplines were accepted as a non-consensus factor.
Results: Panellists agreed that American College of Rheumatology classification criteria is mostly sufficient to provide an OA diagnosis in clinical practice, OA patients with ≥5 Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain or physical function score can be defined as moderate-to-severe OA if they have an additional ≥2 Kellgren-Lawrence (KL) score, a minimum improvement of 30% from baseline in WOMAC pain or function subscales or in PGA score can be accepted as moderate treatment response where ≥50% improvement from baseline in those scores as substantial response. Panellists stated that arthroplasty procedures need to be delayed as long as possible, but this delay should not jeopardize a beneficial and successful operation.
Conclusions: These findings show that there is a significant disease burden, unmet treatment needs for patients with moderate-to-severe OA in Turkey from experts' perspective. Therefore, an updated systematic approach and decision tree models are needed to be implemented.

* Corresponding author. Professor Doctor Hasan Fatih Çay, Address: , Tel.: +90 532 250 91 47
E-mail addresses: drhfatih.cay@gmail.com (H.F. Çay), aysenakinci@gmail.com (A. Akıncı), lalealtan@gmail.com (L. Altan), ataman.sebnem@gmail.com (Ş. Ataman), semih.aydogdu@ege.edu.tr (S. Aydoğdu), demirhan1@yahoo.com (D. Dıraçoğlu), hakangenc06@hotmail.com (H. Genç), simin.hepguler@gmail.com (S. Hepgüler), draysegulketenci@gmail.com (A. Ketenci), kadriyeones@yahoo.com (K. Öneş), meltemuyar@gmail.com (M. Uyar), salih.gumru@pfizer.com (S. Gümrü), basak.hacibedel@pfizer.com (B. Hacıbedel), kerem.helvacioglu@pfizer.com (K. Helvacıoğlu), ayse.olmez@pfizer.com (A. Ölmez), heratt@gmail.com (T. Tuncer).

https://doi.org/10.1016/j.ocarto.2022.100332
Received 3 April 2022; Received in revised form 3 November 2022; Accepted 20 December 2022

1. Introduction

Osteoarthritis (OA), which represents the most common form of arthritis, is the leading cause of disability globally, particularly when the knee and hip joints are involved [1–5]. The pain experienced in knee OA is well-recognized to typically transition from intermittent weight-bearing pain to more persistent, chronic pain [6]. A recent meta-analysis estimated that approximately 654.1 million individuals aged ≥40 years had knee OA in 2020 worldwide [7]. The prevalence of OA is increasing owing to the increasing age of populations in developed and developing countries as well as an increase in risk factors that may lead to OA, particularly obesity and sedentary lifestyle [8]. A previous study published in 2011 reported that OA accounted for 3% of all diseases in Turkey [9]. Another study from Turkey confirmed that OA was the most common diagnosis in patients aged >65 years who were attending a physical medicine and rehabilitation (PMR) outpatient clinic [10].

Local clinical guidance, patient preferences, and economic factors are all considered during the decision-making process; consequently, disease management in OA differs across and within countries. Several regional epidemiological and cross-sectional retrospective studies have addressed the burden and clinical management of knee and hip OA; nonetheless, few studies have evaluated these topics from the perspective of physicians in different country settings. The present study aimed to update our understanding of this disease in Turkey by obtaining information-driven insights from expert physicians regarding the current disease burden, clinical management, and multiple aspects of the journey of patients with knee and hip OA in Turkey and, consequently, to establish a consensus.

2. Methods

2.1. Study design

The modified Delphi method panel comprised three rounds and was conducted over a 6-month period (between December 10, 2020 and May 08, 2021). The Delphi method aims to achieve mutual decisions and consensus on several issues among experts when only limited data are available or the available body of information in relevant fields is scarce [11,12]. The classical Delphi technique serves as a forum for achieving consensus among homogeneous groups of experts, whereas the variant modified Delphi technique includes a combination of the Delphi method with other methods (e.g., scenario writing) to develop relevant arguments and expose underlying reasons for different opinions regarding a specific issue. Additionally, the modified Delphi technique is described as a modification of the classical Delphi technique that combines it with, for instance, the employment of a focus group, interviews, or review results to develop the first round [11–13]. For the present study, we preferred the modified version because the subjects in the discussion were significantly broad and the use of only repetitive surveys with the same questions would not be sufficient to draw a conclusion or provide a take-away message concerning a given subject matter. Our modified method consisted of semi-structured interviews, a literature review, repeated online surveys, and face-to-face discussions to transform expert opinions into a consensus-based group decision. In this modified context, the panel was implemented in five steps, as shown in Fig. 1.

2.2. Development of questions and evaluation of answers

Before reviewing the relevant literature and preparing the first-round questionnaire, an independent consultant conducted one-to-one semi-

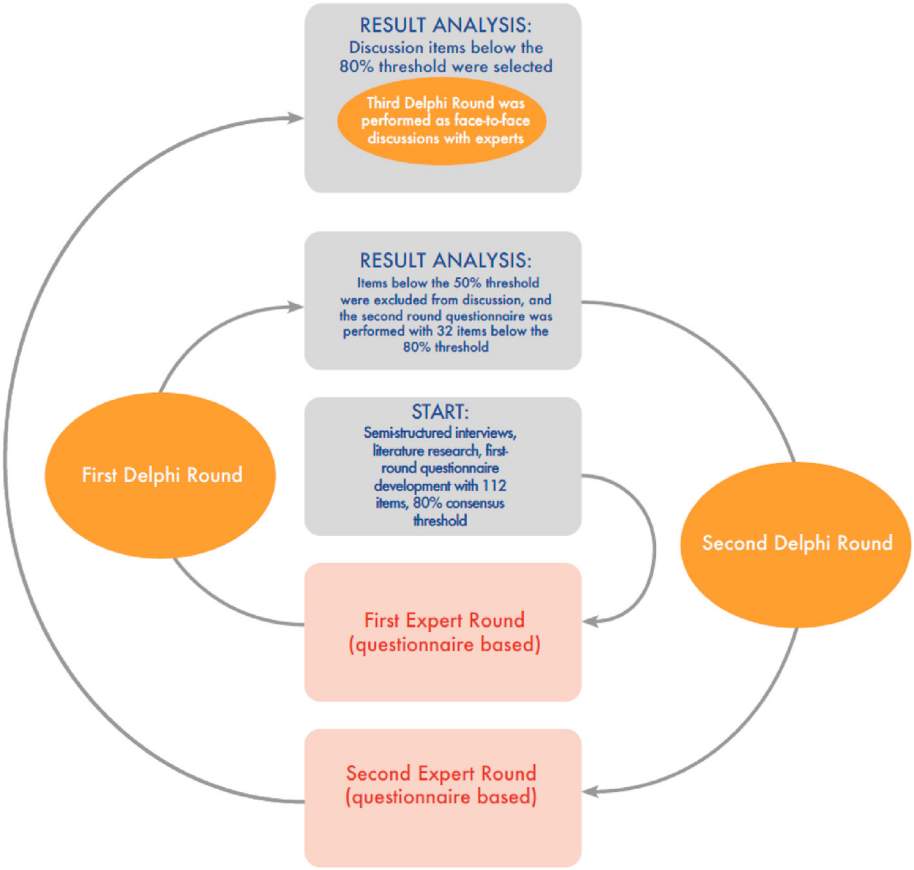

Fig. 1. Delphi process.

structured interviews with each panelist. Subsequently, a systematic literature review was performed to prepare the first-round questions based on the interview outcomes. Available literature published between 2010 and 2021 was searched online in MEDLINE (via the PubMed interface), Web of Science, Google Scholar, and EMBASE databases using Medical Subject Headings terms (MEDLINE), EMBASE terms, and free-text words. The search terms were as follows: "osteoarthritis," "prevalence," "burden," "disability," "hip," "knee," "diagnosis," "severity," "treatment," "response to treatment," "arthroplasty," "total hip replacement," and "total knee replacement." As further selection criteria, evidence-based recommendations and care pathways were highlighted. Additionally, the relevant guidelines from 2010 to 2021 were systematically reviewed. The main topics to be investigated in the study questionnaire were then pooled; the same independent consultant prepared the survey questions in order to avoid participation bias among panelists.

A total of 157 questions were asked during the two-round online survey. The respondents' opinions were collected using an electronic questionnaire. Open- and closed-ended questions were prepared to explore the perspective of panelists on the available literature, including the latest guidelines, observations on the journey of patients with OA in clinical practice, perception on OA disease burden, and disease awareness in Turkey. A 5-point Likert scale was used to seek consensus on statements based on the literature and experience. A consensus, joint observation, or common perception was achieved when 80% of the participants selected the same answer or strongly agreed/agreed (or strongly disagreed/disagreed) with a statement. Statements with <50% agreement were excluded from the Delphi rounds and were not repeated. The questions asked in the second round of this study were either the same questions from the first round or questions that were rephrased based on the participants' feedback in the first round. Contradictions between different disciplines were considered a non-consensus factor.

2.3. Participants and the Delphi process

At the beginning of the project, two academic specialists in PMR (one of whom with a subspecialty in rheumatology) formed a study coordination committee. Both study coordinators were board members of a national OA-related academic association who had previously led national guideline developments on these subjects and had published articles on OA. The study coordinators supervised the study design and conduct. These two committee members selected the candidate study participants according to their specific interests and extensive experience in OA. The chosen participants were academic specialists in PMR ($n = 8$, one of whom with a subspecialty in rheumatology, excluding the study coordination committee members), orthopedics ($n = 1$, with a special interest in arthroplasty), and algology ($n = 1$); all participating academic specialists were working in the university and at research and training hospitals and had ≥20 years of experience in OA. Each panelist either was a board member of an academic association who contributed to the development of guidelines on the subject or had published articles on OA. These 12 experts shared their opinions and experience through semi-structured interviews and answered online survey questions in two rounds. One of the coordinators also supervised the data analysis after the first round and did not participate in the second round of the survey to avoid potential bias. After evaluating the two-round online survey results, all panel members, including study coordinators, came together in a face-to-face meeting (the third round). During this face-to-face meeting, the panelists reviewed all statements that achieved consensus. The panelists amended some of the consensus statements by mutual agreement to be in line with the latest scientific evidence. Additionally, during this face-to-face meeting, the panelists had the opportunity to discuss the non-consensus statements from the second round and managed to arrive at a consensus on some non-consensus statements after amending their phrasing. Overall, all 12 panelists were involved in the final manuscript development and validation.

3. Results

Each participant answered 157 questions in total. Consensus was achieved on 71 out of 142 statements. The lowest consensus percentage was observed in the "treatment" section, whereas the highest percentage was attained in the "disease severity" section. As for the remaining 15 observation and perception questions, there was consensus on nearly all questions (Table 1). Online survey results and notes from face-to-face discussions with ≥80% agreement are presented under five headings—namely, diagnosis and patient journey; disease severity; comorbidities; treatment and response to treatment; and disease burden and unmet needs.

3.1. Diagnosis and patient journey

Consensus was achieved on 16 out of 37 statements in this section (Table 2). In particular, full agreement on clinical diagnosis, positioning of radiographic imaging, and patient journey statements was achieved. Blood tests, synovial fluid analysis, ultrasonography, and magnetic resonance imaging (MRI) were helpful in distinguishing OA from other conditions based on different aspects of structural damage in OA. The most common observation in Turkey was the absence of a defined referral system for patients with OA, which delayed timely access to effective treatments, deteriorated the rational use of medications, and impaired the sufficient use of healthcare services for patients with OA. Additionally, all panelists agreed that the availability of most OA treatments (mainly nonsteroidal anti-inflammatory drugs [NSAIDs]) over the counter had significantly deteriorated the rational use of medications in Turkey.

3.2. Disease severity

This section had the highest observed number of consensus. Full agreement on eight statements was achieved (Table 3). The panelists agreed that disease severity assessment in OA at the time of diagnosis might provide guidance for an adequate treatment plan and offer proper evaluation of treatment response. There was a consensus on the definition of OA disease severity—that is, moderate-to-severe OA could be defined as a Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain or physical function score of ≥5 with an additional

Table 1
Summary of results.

Sections	Total number of questions in each section	Total number of consensus[a] in each section, *n* (%)
Statements		
A. Diagnosis and patient journey	37	16 (43)
B. Disease severity	16	11 (68)
C. Comorbidities	19	12 (63)
D. Treatment and response to treatment	43	18 (41)
F. Disease burden and unmet needs	27	14 (51)
Joint observation and common perception		
Sections	*Total number of questions in each section*	*Total number of consensus[a] in each section*
1. Diagnosis and patient journey	*5*	*4*
2. Disease severity	*2*	*2*
3. Comorbidities	*3*	*3*
4. Disease burden and unmet needs	*5*	*5*

[a] A consensus, joint observation, or common perception was achieved when 80% of the participants selected the same answer or strongly agreed/agreed (or strongly disagreed/disagreed) with a statement.

Table 2
Results regarding diagnosis and patient journey.

Statements	Consensus[a] (%)
OA is a clinical diagnosis.	83.3
The American College of Rheumatology diagnostic criteria are sufficient to diagnose OA.	100
Radiographic findings can support OA diagnosis.	100
Radiography is not sufficiently sensitive to detect the early stages of OA.	100
Baseline radiographic findings at the time of the first OA diagnosis provide a reference point for the assessment of disease progression.	83.3
The KL score system is a sufficient assessment tool to support OA diagnosis based on radiographic findings.	91.6
The absence of joint space narrowing, subchondral cyst, subchondral sclerosis, and osteophyte formation on radiographic findings require the involvement of other diagnostic tools and methods.	83.3
Blood tests are helpful in distinguishing OA from other conditions (such as rheumatoid arthritis) when clinical findings are not clear enough to diagnose OA.	83.3
Synovial fluid analysis is helpful in distinguishing OA from other conditions (such as gout disease and infection) when clinical findings are not clear enough to diagnose OA.	83.3
Ultrasound is helpful in assessing joint effusion, synovitis, osteophytes, cartilage loss, meniscus, and enthesopathy.	100
MRI is a sufficient tool for detecting rapidly progressing OA in the early stage and OA that cannot be diagnosed using clinical and radiographic findings.	83.3
OA can usually be diagnosed in primary care without a specialist referral or a need for further investigation.	83.3
Patients with mild OA can be treated by primary care physicians.	100
Defining a referral pathway will contribute to the timely management of patients with OA and provide better access to more suitable treatments.	100
OA requires a multidisciplinary (primary care, PMR, rheumatology, and orthopedics) approach to long-term treatment and follow-up management.	100
Pain, including its duration, location, intensity, nature (mechanical or inflammatory), and aggravating or alleviating factors, should be assessed at each stage of OA, starting from its diagnosis.	100
Joint observations[a]	*%*
The current absence of a defined referral system for patients with OA delays timely access to effective treatments in Turkey.	*91.6*
The current absence of a defined referral system for patients with OA deteriorates the rational use of medications in Turkey.	*100*
The current absence of a defined referral system for patients with OA impairs the sufficient use of healthcare services in Turkey.	*100*
The availability of most OA treatments (mainly NSAIDs) over the counter without a prescription significantly deteriorates the rational use of medications in Turkey and increases the possibility of side effects, development of new comorbidities, and aggravation of previous comorbidities.	*100*

Abbreviations: OA, osteoarthritis; KL, Kellgren–Lawrence; MRI, magnetic resonance imaging.
[a] A consensus, joint observation, or common perception was achieved when 80% of the participants selected the same answer or strongly agreed/agreed (or strongly disagreed/disagreed) with a statement.

Table 3
Results regarding OA disease severity and assessment approaches.

Statements	Consensus[a] (%)
Disease severity assessment in OA at the time of diagnosis may provide guidance for an adequate treatment plan and offer proper evaluation of treatment response.	100
None of the available severity assessment tools are objective or sufficient to assess disease severity in OA.	100
Discordance between symptoms (pain, functional decline) and structural (radiographic) changes may be observed in patients with OA.	100
Baseline radiological severity assessment with the KL score at the time of diagnosis can be useful in providing a reference point for the assessment of disease progression.	100
The WOMAC is usually a sufficient assessment tool for evaluating symptomatic and functional disease severity in OA.	91.6
Compared with the VAS, the WOMAC provides a more detailed and sensitive evaluation with its multiple parameters while assessing the complaints of patients with OA.	83.3
The VAS is less sufficient in assessing pain and functional limitations based on activity levels than the WOMAC.	100
The use of systems that allow for patients' self-assessment of disease severity provides an ideal treatment approach by combining the perspectives of both patients and physicians in OA management.	83.3
Patients with OA with a WOMAC pain or physical function score of $\geq$5 can be considered to have moderate-to-severe OA if they have an additional KL score of $\geq$2.	100
Physicians' clinical judgment is supported by severity scoring systems but not limited by their outcomes.	100
Radiological and symptomatic disease severity in patients with OA should be assessed at the time of diagnosis and regularly assessed during the treatment period using standardized indexes.	100
Joint observations[a]	*%*
Radiological severity scores (e.g., KL score) of patients with OA are usually not recorded in daily practice in Turkey, except in clinical trials.	100
Symptomatic severity scores (e.g., WOMAC score, VAS score, PGA score) of patients with OA are usually not recorded in daily practice in Turkey, except in clinical trials.	100

Abbreviations: OA, osteoarthritis; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; VAS, visual analog scale; KL, Kellgren–Lawrence; PGA, patient global assessment.
[a] A consensus, joint observation, or common perception was achieved when 80% of the participants selected the same answer or strongly agreed/agreed (or strongly disagreed/disagreed) with a statement.

Kellgren–Lawrence (KL) score of $\geq$2. During face-to-face discussions, the panelist also reached a consensus on the notion that while physicians' clinical judgment could be supported by severity scores/indexes, such judgment was not limited by the scoring results. The common observation with full consensus in this section was that radiological severity scores (e.g., KL score) and symptomatic severity scores (e.g., WOMAC score, visual analog scale [VAS] score, patient global assessment [PGA] score) of patients with OA were usually not recorded in daily practice in Turkey, except in clinical trials.

3.3. Comorbidities

The panelists achieved full agreement on the notion that individuals with OA had significantly more coexisting chronic conditions and a higher risk of developing new chronic conditions. Additionally, the panelists reached full consensus on several statements regarding comorbidities in patients with OA; for example, individuals with OA should be queried about their coexisting conditions, medication history, and accompanying risk factors, both at the time of diagnosis and during

the treatment period. The most common observation was the lack of comorbidity index use in daily practice in Turkey to predict the clinical prognosis of patients with OA (Table 4).

3.4. Treatment and response to treatment

This section had the lowest observed number of consensus (Table 5). Full agreement was achieved with respect to the differing benefits of treatments in the heterogeneous OA population, controversial evidence on the effectiveness of OA treatments (except for major surgical interventions) against pathological and radiological disease progression, and suitable patient profiles for arthroplasty. As stated by the panelists, the lack of evidence to support the effectiveness of OA treatments (except for major surgical interventions), absence of studies comparing treatments, and heterogeneous profile of patients with OA posed a barrier to the establishment of standardized treatment regimens for OA. Additionally, the panelists reached a consensus on statements claiming that "Arthroplasty should be recommended for patients with moderate-to-

Table 4
Results regarding OA-related comorbidities.

Statements	Consensus[a] %
Individuals with OA have significantly more coexisting chronic conditions than those without OA.	100
Individuals with OA have a significantly higher risk of developing new chronic conditions than those without OA.	100
Individuals with OA have a significantly higher risk of mortality regarding their comorbidities.	83.3
OA-related pain also contributes to the development of cardiovascular disease, diabetes mellitus, and obesity by limiting an individual's physical activity.	91.6
Individuals with OA have limited pain treatment options due to their coexisting conditions and an increased risk of new chronic conditions, as compared with those without OA.	91.6
Individuals with OA have limited NSAID options due to their coexisting conditions and an increased risk of new chronic conditions, as compared with those without OA.	91.6
Individuals with moderate-to-severe OA have significantly more coexisting chronic conditions and limited treatment options for these comorbidities, as compared with those with mild OA.	83.3
Existing comorbidities and additional risk factors in patients with OA should be assessed and recorded at the time of diagnosis and regularly assessed during the treatment period.	100
Individuals with OA should be queried about their medication history related to their coexisting chronic conditions, and this information should be accordingly recorded.	100
Chronic conditions that may be triggered by the common side effects of OA treatments should also be regularly queried during the treatment period.	100
Comorbidity indexes for predicting clinical prognosis should be considered during the decision-making for treatment in patients with OA.	83.3
Comorbidity indexes for predicting clinical prognosis should be considered when planning surgery for patients with OA.	91.6
Joint observations[a]	%
Coexisting chronic conditions of patients with OA are not usually recorded at the time of diagnosis in daily practice in Turkey.	83.3
Newly developing or aggravated comorbidities in patients with OA are not usually queried in detail or typically recorded on a regular basis during the treatment period in daily practice in Turkey.	83.3
Comorbidity indexes for predicting clinical prognosis are rarely used in patients with OA in daily practice in Turkey.	100

Abbreviations: OA, osteoarthritis;
[a] A consensus, joint observation, or common perception was achieved when 80% of the participants selected the same answer or strongly agreed/agreed (or strongly disagreed/disagreed) with a statement.

Table 5
Results regarding treatment and response to treatments.

Treatment statements	Consensus[a] (%)
With such a heterogeneous patient population, patients with OA do not equally benefit from the same treatments, and treatment durations can greatly differ.	100
Evidence supporting the effectiveness of OA treatments (except for major surgical interventions) against pathological and radiological disease progression remains controversial.	100
The heterogeneous profile of patients with OA poses a barrier to the establishment of standardized treatment regimens.	83.3
A lack of studies comparing OA treatments poses a barrier to the establishment of standardized treatment regimens.	83.3
As with any major operation, arthroplasty can be associated with major postoperative medical complications and mortality, mainly depending on patients' existing comorbidities.	91.6
Patients with OA should be informed of all other available treatments indicated for OA before undergoing arthroplasty.	100
Arthroplasty should be recommended for patients with moderate-to-severe OA who have experienced inadequate response to other available treatments and who have no barriers (comorbidities, etc.) to a major surgery.	100
Although arthroplasty should be delayed as much as possible, a patient's age and health performance should also be considered to ensure that this delay will not reduce the benefits of arthroplasty or will not take the patient's surgical chance away.	91.6
Response-to-treatment statements	(%)
None of the available assessment tools are objective or sufficient to assess the treatment response in OA.	100
Moderate treatment response can be defined as ≥30% improvement from baseline in either the WOMAC pain or physical function score.	100
Substantial treatment response can be defined as ≥50% improvement from baseline in either the WOMAC pain or physical function score.	100
Moderate treatment response can be defined as ≥30% improvement from baseline in the PGA score.	100
Substantial treatment response can be defined as ≥50% improvement from baseline in the PGA score.	100
In patients with OA, ≥50% worsening of symptoms and/or findings over 3 months from baseline may be an indicator of rapid disease progression.	100
In patients with OA, ≥2 mm of annual joint space narrowing from baseline may be an indicator of rapid disease progression.	100
In patients with OA, assessment of treatment response should be performed by comparing the pre- and post-treatment symptoms.	100
In patients with OA, standardized disease severity indexes/scores should be used to assess the treatment response.	83.3
MRI can be a guiding tool for choosing a new treatment for patients with OA who do not sufficiently respond to treatments or show progression despite treatment.	83.3

Abbreviations: OA, osteoarthritis; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; VAS, visual analog scale; KL, Kellgren–Lawrence; PGA, patient global assessment; MRI, magnetic resonance imaging.
[a] A consensus, joint observation, or common perception was achieved when 80% of the participants selected the same answer or strongly agreed/agreed (or strongly disagreed/disagreed) with a statement.

severe OA who have experienced inadequate response to other available treatments and who have no barriers (comorbidities, etc.) to a major surgery," "Patients with OA should be informed of all other available treatments indicated for OA before undergoing arthroplasty," and "Although arthroplasty should be delayed as much as possible, a patient's age and health performance should also be considered to ensure that this delay will not reduce the benefits of arthroplasty or will not take the patient's surgical chance away." Panelists agreed on some of the definitions of response to treatment. In particular, moderate treatment response could be defined as ≥30% improvement from baseline in either the WOMAC pain or physical function score or PGA score, whereas substantial treatment response could be defined as ≥50% improvement from baseline in either the WOMAC pain or physical function score or PGA score.

3.5. Disease burden and unmet needs

Consensus was achieved on 14 out of 27 statements in this section (Table 6). The panelists reached full consensus on the notion that individuals with moderate-to-severe OA had significantly poorer health-related quality of life, significantly more work and productivity impairment, and greater long-term medication consumption than those without OA. Furthermore, the panelists described OA as a debilitating and disabling disease. Current treatments were not deemed to be sufficient by the panelists to meet the therapeutic needs of patients with moderate-to-severe OA. Additionally, consensus was reached on the notion that there were significant unmet needs for treatment options that might aid in delaying surgery to later years in life among patients with OA who experienced inadequate treatment response or intolerance to available treatments, who had barriers that could interfere with the benefits of arthroplasty (comorbidity, active infection, etc.), and who exhibited inadequate clinical improvement after arthroplasty. Moreover, the panelists agreed on the common observation that awareness about disease burden, including OA-related impairment and disability, was lacking in Turkey.

4. Discussion

The present study explored the disease management and treatment journey of patients with moderate-to-severe OA from the perspective of treating physicians in Turkey. The panelists agreed that assessments of disease severity and response to treatment in patients with OA were significantly lacking in Turkish clinical practice. Additionally, the panelists highlighted that current treatment approaches and available treatments did not meet the needs of patients with moderate-to-severe OA. The broader discussion points of our findings are presented below:

4.1. Diagnosis and assessment of disease stage/severity

All panelists agreed that clinical diagnosis of OA could usually be accomplished by using the American College of Rheumatology diagnostic criteria. Nevertheless, despite the lack of sensitivity in the early stages of the disease, for which MRI is more sensitive, radiographic findings are useful in supporting the diagnosis. OA diagnosis and severity assessment are not always straightforward, as there are no definitive diagnostic tests or biomarkers for assessing the severity of this condition. Therefore, clinicians worldwide rely on patients' self-reported status, in addition to clinical and radiological assessments of disease parameters, which may be subjective and difficult to standardize [14]. Despite cost concerns, a lack of clarity with respect to its diagnostic performance, and little standardization regarding its interpretation, MRI is increasingly being used to facilitate diagnostic decisions in clinical practice based on a growing body of evidence on OA [15]. Therefore, further studies are necessary to be conducted to justify the rationale for the use of MRI and other methods such as synovial fluid analysis, ultrasound, and blood tests for early disease detection and differentiation of OA from other conditions.

The panelists agreed that disease severity assessment in OA at the time of diagnosis might provide guidance for an adequate treatment plan and offer proper evaluation of treatment response. However, none of the available severity assessment tools were objective or sufficient to assess

Table 6
Results regarding disease burden and unmet needs.

Disease burden statements	Consensus[a] %
Individuals with moderate-to-severe OA have a significantly poorer sleep quality than those without OA.	91.6
Individuals with moderate-to-severe OA have significantly more depression and anxiety than those without OA.	91.6
Individuals with moderate-to-severe OA have a significantly poorer health-related quality of life than those without OA.	100
Individuals with moderate-to-severe OA have significantly less social engagement than those without OA.	91.6
Moderate-to-severe OA causes significant work and productivity impairment.	100
Patients with moderate-to-severe OA retire earlier than those without OA.	100
The rate of referral to an outpatient healthcare provider is significantly increased in patients with moderate-to-severe OA, compared with those with mild OA.	100
Individuals with moderate-to-severe OA have significantly higher major surgery rates than those with mild OA.	83.3
Individuals with moderate-to-severe OA have significantly greater long-term medication consumption than those with mild OA.	100
Moderate-to-severe OA is a debilitating or disabling disease.	100
Indexes of health-related quality of life will contribute to suitable treatment selection and treatment response evaluation.	100
Unmet need statements	**%**
There is a significant unmet need for treatment options that may aid in delaying surgery to later years in life in patients with OA who experience inadequate treatment response or intolerance to available treatments.	100
Despite the availability of pharmacological and complementary treatments, significant unmet needs for treatment still remain in patients with OA who have barriers to arthroplasty (comorbidity, active infection, etc.).	100
There is a significant unmet need for treatment in patients with OA who show inadequate clinical improvement after arthroplasty.	100
Joint observations[a]	*%*
Indexes of health-related quality of life are not usually used to assess patients with OA in Turkey.	100
The establishment of easy-to-use decision tree models is needed at each level of healthcare provision in Turkey, which would support the OA diagnosis pathway and treatment management.	100
Easy-to-use additional parameters need to be embedded in the current patient recording systems with universal access to allow physicians to assess and follow up patients with OA, regardless of the healthcare provider visited each time.	100
There is insufficient awareness about the total disease burden of OA in Turkey.	100
There is insufficient awareness of OA-related impairment and disability in Turkey.	83.3

Abbreviation: OA, osteoarthritis.

[a] A consensus, joint observation, or common perception was achieved when 80% of the participants selected the same answer or strongly agreed/agreed (or strongly disagreed/disagreed) with a statement.

disease severity in OA, and all panelists agreed that a WOMAC pain or physical function score of ≥5 with an additional KL score of ≥2 could be considered to be indicative of moderate-to-severe OA. The most common approaches employed for pain assessment in knee and hip OA are the VAS or numerical rating scale (NRS) for pain-intensity assessment, WOMAC pain subscale, and Knee Injury and Osteoarthritis Outcome Score [16-21]. The WOMAC score can also be used for hip OA, in which the Hip Disability and Osteoarthritis Outcome Score is specific for hip OA. A meta-analysis suggested that different patient-reported outcome measures of pain severity generally had comparable responsiveness to treatment, with the single-item pain assessment with the VAS or NRS resulting in effect estimates comparable to those of the WOMAC pain subscale; however, their mean standardized effect sizes were lower [19]. Despite the substantial benefits of disease severity assessment with respect to pain and physical function, the regular use of time-consuming scoring systems can be challenging in busy outpatient clinics. Nonetheless, choosing a treatment alternative on the basis of the patients' instant comments regarding pain/physical limitations only without a baseline evaluation and regular assessment using validated scoring systems during OA treatment will not be rational or scientifically appropriate.

Although some observational studies from different countries have investigated the journey of patients with OA, most of these studies did not examine how patients with OA were diagnosed or how their disease severity and response to treatment was assessed [22, 23]. Additionally, there exist few studies designed to establish a consensus on disease management, including diagnosis; however, all of them are nearly a true reflection of the current guidelines and do not provide an additional discussion point [24,25].

4.2. Treatment

In the present study, barriers to the establishment of standardized treatment regimens for OA were identified as follows: a lack of evidence to support the effectiveness of OA treatments (except for major surgical interventions), absence of studies comparing treatments, and heterogeneous profile of patients with OA. The panelists agreed that all patients should be informed of all other available treatments indicated for OA before undergoing arthroplasty and that arthroplasty should be delayed as much as possible. However, they also added that a patient's age and health performance should be considered to ensure that this delay would not reduce the benefits of arthroplasty or take the patient's surgical chance away. Current treatments, including arthroplasty, were not deemed to be sufficient by the panelists to meet the therapeutic needs of patients with moderate-to-severe OA. Joint replacement proves to be an effective treatment option for advanced-stage hip and knee OA and relieves pain in the majority of patients; however, 10–40% continue to experience moderate-to-severe persistent pain after surgery, and joint replacements tend to wear out after a certain amount of time [26-33].

Despite the availability of evidence-based treatment guidelines for OA, the recommended indication criteria fall short of guiding decision-making regarding the timing of total hip arthroplasty and total knee arthroplasty, and large gaps in overall disease management remain [34]. Consequently, a significant number of patients with OA remain inadequately treated. This unmet need for OA treatment imposes a considerable burden on the society, with large cost implications consequent to work and productivity impairment as well as early retirement [35-38].

4.3. Disease burden

All panelists from different disciplines agreed that hip and knee OA had a significant negative impact on patients' quality of life in terms of depression and anxiety, work and productivity impairment, disability, utilization of healthcare resources, and long-term medication consumption. They also claimed that there was insufficient awareness of the total disease burden of OA in Turkey. Moreover, the panelists highlighted the significant burden of comorbidities in patients with OA, which significantly contributed to increased mortality and treatment limitations, as compared with those in individuals without OA. Current evidence confirms that hip and knee OA usually leads to joint dysfunction and hypomobility, which may complicate other pathologies, such as diabetes mellitus and cardiopathy, and increase mortality in other comorbidities [39,40]. The presence of multiple chronic conditions causes higher mortality rates with increased hospitalization, impaired physical and mental health, and worse disease outcomes, leading to poorer quality of life [41-43]. The morbidity burden of OA is well-documented by global organizations and developed countries; however, no studies have investigated the impact of hip and knee OA on patients' lives, especially in terms of morbidity, mortality, and disability. According to the 2019 World Health Organization Global Burden of Disease Study, OA was the 15th leading cause of years lived with disability (YLDs) worldwide and was responsible for 2% of the total global YLDs. While YLDs for OA have been reported to be lower in middle sociodemographic index (SDI) regions than in high SDI countries (approximately 525 vs. 220 YLDs per 100,000 population), the rate of change in YLDs has been far greater in middle SDI countries than in high SDI countries (89% vs. 48%) since 1990 [1,2]. The French Disability-Health Survey revealed that individuals with OA were almost twice as limited as those without OA with respect to walking (adjusted odds ratio, 1.9; 95% CI, 1.7–2.2) and carrying objects (adjusted odds ratio, 1.7; 95% CI, 1.5–2.0) [40]. OA was the main contributor to limitations in activities, with 22% of difficulties in walking, 18.6% of difficulties in carrying objects, and 12.8% of difficulties in dressing being attributable to OA in France. OA was also a contributor to the need for human assistance (9.2% of the need for help from immediate family, 11.8% of help from health professionals, and 8.9% of health service delivery attributable to OA) [44]. Nüesch et al. and Hawker et al. reported excess all-cause mortality with OA in their population cohorts [39, 45]. These data may not be transposable to other settings because the built environment, social determinants, and access to healthcare influence the disparate disease burden of OA, particularly in lower- and middle-income countries [46-48]. Only two studies from Turkey reported that OA accounted for 3% of all diseases, and OA was the most common diagnosis in patients aged >65 years who were attending a PMR outpatient clinic [9,10]. Therefore, more national studies examining the disease burden are required to better assess the needs of local populations.

4.4. Patients' overall journey

In this study, the panelists underlined the absence of an established referral system in Turkey for patients with OA, which impaired the sufficient use of healthcare services, delayed the diagnosis and timely access to effective treatments, and worsened the rational use of medications in patients with OA. Additionally, the availability of most OA treatments (mainly NSAIDs) was also claimed to worsen the rational use of medications in Turkey. OA diagnosis in Turkey is mostly achieved by PMR, orthopedic, or rheumatology specialists in secondary or tertiary clinics, regardless of the disease stage. There is no mandatory referral system from primary care to hospitals, and patients are generally free to consult whomever they think is related to their condition. Evidence suggests that the management of patients presenting with OA in developed countries is also not in line with published guidance; many patients consulting with peripheral joint pain reported that the problem may be dismissed, and core treatments are not routinely offered early on in the course of their condition [49-50]. The disconnect between general practitioners, specialists, and community services for OA care has also been reported to result in incomplete, conflicting, or inaccurate information [50].

5. Conclusion

This study revealed the significant disease burden and unmet needs for treatment among patients with moderate-to-severe OA in Turkey. None of the consensus contradicted with the current evidence. Based on

the findings of this study, our panel suggests that general practitioners in Turkey should be trained and updated regularly in OA diagnosis and that patients with OA should be consistently supported and referred to specialist clinics at the earliest. Additionally, we believe that there is a need for an update in current patient recording systems and easy-to-use decision tree models at each level of healthcare provision in Turkey, which would support the OA diagnosis pathway and treatment management. Further multidisciplinary expert panels that include general practitioners and specialists in PMR, orthopedics, and rheumatology endorsed by their official societies will surely contribute to the design of a better referral system and to the optimum management of patients with OA.

Strengths, limitations and implications for further studies

The present study has all the limitations arising from the nature of the Delphi method. Limited numbers of experts and different rates of representation from physical medicine and rehabilitation, rheumatology, orthopedics and algology clinics result in a limitation with regard to reflecting the approaches and insights of all disciplines at an ideal level. The absence of OA patients in this panel could also be seen as a limitation in terms of reflecting their perception on the disease burden and unmet treatment needs. However, this Delphi method study allowed a broad and systematic exploration of clinical, diagnostic, and follow-up approaches in patients with OA based on the qualified opinions of experts in Turkey in a limited period of time. Outputs under each topic and each limitation of this study can be used as reference points to trigger and establish further, more focused and more populated consensus studies not only in Turkey but also in other developing countries.

Contributions

Dr Hasan Fatih Çay and Dr Tiraje Tuncer acted as study coordinators, supervised the design and conduct of the study. Dr Hasan Fatih Çay also took responsibility for the integrity of the work as a whole. All authors except Pfizer employees reviewed and amended the achieved consensus together. All authors were involved in the final manuscript development and validation.

Role of the funding source

Project management and technical support was provided by Remedium Consulting Group and funded by Pfizer. Author Pfizer employees did not have any involvement in the achieved consensus nor the decision for journal submission.

Declaration of Competing Interest

HFC received honorarium from MSD, Celltrion, Amgen. LA received honorarium from Pfizer, Abbvie, MSD, Exeltis, Sanovel, Lilly, Gensenta, Menarini, Nobel, Kocak. S. Ataman received honorarium from Abbvie, UCB and Novartis. SA, SH acted in advisory board of Pfizer. DD recevied honorarium from Santa Farma, Menarini, Exeltis, Sandoz and Expanscience. HG received honorarium from Pfizer and Menarini. AK recevied honorarium from Abbott, Abdi Ibrahim and Pfizer. MU received honorarium from Pfizer. BH is an employee and holding stock options of Pfizer. AO, SG and KH are employees of Pfizer.

Acknowledgements

Project management, interview with panelists, panel moderation and analysis of the results, submission secretaria are provided by Dr Ayse Özlem Yilmaz, Dr Deniz Okur and Dr Ferda Kiziltas at Remedium Consulting Group.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ocarto.2022.100332.

References

1 GBD 2015 DALYs, HALE Collaborators, Global, regional, and national disability-adjusted life-years (DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015, Lancet 388 (2016) P1603–P1658. X1.
2 Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2019 (GBD 2019) results. 2020. http://ghdx.healthdata.org/gbd- results-tool (accessed November 2, 2020).
3 Y1. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2019 (GBD 2019) results. Osteoarthritis —level 3 cause. 2020. http://www.healthdata.org/results/gbd_summaries/2019/osteoarthritis- level-3-cause (accessed November 2, 2020).
4 L. Murphy, T.A. Schwartz, C.G. Helmick, J.B. Renner, G. Tudor, G. Koch, et al., Lifetime risk of symptomatic knee osteoarthritis, Arthritis Rheum 59 (2008) 1207–1213.
5 L.B. Murphy, C.G. Helmick, T.A. Schwartz, J.B. Renner, G. Tudor, G.G. Koch, et al., One in four people may develop symptomatic hip osteoarthritis in his or her lifetime, Osteoarthritis Cartilage 18 (2010) 1372–1379.
6 T. Neogi, The epidemiology and impact of pain in osteoarthritis, Osteoarthritis Cartilage 21 (9) (2013) 1145–1153.
7 A. Cui, H. Li, D. Wang, et al., Global, Regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies, EClinicalMedicine (29-30) (2020), 100587.
8 Clémence Palazzo, Christelle Nguyen, Marie-Martine Lefevre-Colau, François Rannou, Serge Poiraudeau, Risk factors and burden of osteoarthritis, Annals of Physical and Rehabilitation Medicine 59 (3) (2016) 134–138.
9 Türkiye Hastalık Yükü çalışması 2004. TC Sağlık Bakanlığı, Refik Saydam Hıfzıssıhha Merkezi Başkanlığı, Hıfzıssıhha Mektebi Müdürlüğü. Aydoğdu Ofset Matbaacılık San. ve Tic. Ltd. Şti Matbaası, in: N. Ünüvar, S. Mollahaliloğlu, N. Yardım (Eds.), Sağlık Bakanlığı Yayın 701 (2007) 1–71.
10 Seçkin, P. Borman, H. Bodur, Fizik Tedavi ve Rehabilitasyon polikliniğine başvuran yaşlıların tanısal dağılımı, Turkish Journal of Geriatrics 2 (2) (1999) 57–60.
11 F. Hasson, S. Keeney, Enhancing rigour in the Delphi technique research, Technol Forecast Soc Change 78 (9) (2011) 1695–1704.
12 E.A. Holey, J.L. Feeley, J. Dixon, V.J. Whittaker, An exploration of the use of simple statistics to measure consensus and stability in Delphi studies, BMC Med Res Methodol 7 (52) (2007) 1–10.
13 A. Strasser, Delphi Method Variants in Information Systems Research: Taxonomy Development and Application, The Electronic Journal of Business Research Methods 15 (2) (2017) 120–133.
14 K.D. Allen, P.F. Choong, A.M. Davis, et al., Models for appropriate care across the disease continuum, Best Pract Res Clin Rheumatol 30 (2016) 503–535.
15 D.J. Hunter, N. Arden, P.G. Conaghan, et al., Definition of osteoarthritis on MRI: results of a Delphi exercise, Osteoarthritis Cartilage 19 (8) (2011) 963–969.
16 L.W. Stitt, Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee, J Rheumatol 15 (1988) 1833–1840.
17 E.M. Roos, L.S. Lohmander, The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis, Health Qual Life Outcomes 1 (2003) 64.
18 G.A. Hawker, S. Mian, T. Kendzerska, M. French, Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent And Constant Osteoarthritis Pain (ICOAP), Arthritis Care Res (Hoboken) 63 (2011) S240–S252.
19 R.H. Dworkin, S. Peirce-Sandner, D.C. Turk, M.P. McDermott, A. Gibofsky, L.S. Simon, et al., Outcome measures in placebo-controlled trials of osteoarthritis: responsiveness to treatment effects in the REPORT database, Osteoarthritis Cartilage 19 (2011) 483–492.
20 T. Pham, D. van der Heijde, R.D. Altman, J.J. Anderson, N. Bellamy, M. Hochberg, et al., OMERACT-OARSI initiative: Osteoarthritis Research Society International set of responder criteria for osteoarthritis clinical trials revisited, Osteoarthritis Cartilage 12 (2004) 389–399.
21 M. Klassbo, E. Larsson, E. Mannevik, Hip disability and osteoarthritis outcome score. An extension of the Western Ontario and McMaster Universities Osteoarthritis Index, Scand J Rheumatol 32 (2003) 46–51.
22 A.V. Edenbaugh, G. Oderda, V.C. Lee, J. Moller, D. Brixner, S. Kennedy, et al., The patient journey in knee osteoarthritis-variations in diagnosis, patient characteristics, and treatment by physician specialty, Osteoarthritis and Cartilage 29 (1) (2021) 281–282.
23 J.A. Wallis, N.F. Taylor, S. Bunzli, N. Shields, Experience of living with knee osteoarthritis: a systematic review of qualitative studies, BMJ Open 9 (2019), e030060.
24 S.S. Yeap, S.R. Abu Amin, H. Baharuddin, et al., A Malaysian Delphi consensus on managing knee osteoarthritis, BMC Musculoskelet Disord 22 (2022) 514.
25 M. Porcheret, J. Grime, C. Main, et al., Developing a model osteoarthritis consultation: a Delphi consensus exercise, BMC Musculoskelet Disord 14 (2013) 25.

26 O. Ethgen, O. Bruyere, F. Richy, C. Dardennes, J.Y. Reginster, Health-related quality of life in total hip and total knee arthroplasty. A qualitative and systematic review of the literature, J Bone Joint Surg Am 86 (2004) 963–974.
27 F. Şahin, S.G. Beyaz, N. Karakuş, M.E. İnanmaz, Total Knee Arthroplasty Postsurgical Chronic Pain, Neuropathic Pain, and the Prevalence of Neuropathic Symptoms: A Prospective Observational Study in Turkey, J Pain Res 14 (2021) 1315–1321.
28 D.B. Larsen, M. Laursen, R.R. Edwards, O. Simonsen, L. Arendt-Nielsen, K.K. Petersen, The Combination of Preoperative Pain, Conditioned Pain Modulation, and Pain Catastrophizing Predicts Postoperative Pain 12 Months After Total Knee Arthroplasty, Pain Med 25;22 (7) (2021) 1583–1590.
29 K. Maeda, M. Sonohata, M. Kitajima, S. Kawano, M. Mawatari, Risk Factors of Neuropathic Pain after Total Hip Arthroplasty, Hip Pelvis 30 (4) (2018) 226–232.
30 D.A. Rice, M.T. Kluger, P.J. McNair, G.N. Lewis, A.A. Somogyi, R. Borotkanics, D.T. Barratt, M. Walker, Persistent postoperative pain after total knee arthroplasty: a prospective cohort study of potential risk factors, Br J Anaesth 121 (4) (2018) 804–812.
31 M. Fitzsimmons, E. Carr, L. Woodhouse, G.P. Bostick, Development and Persistence of Suspected Neuropathic Pain After Total Knee Arthroplasty in Individuals with Osteoarthritis, PM R 10 (9) (2018) 903–909.
32 A. Baldini, L. Castellani, F. Traverso, A. Balatri, G. Balato, V. Franceschini, The difficult primary total knee arthroplasty: a review, Bone Jt J 97-B (10 Suppl A) (2015) 30–39.
33 Mheen, M.G.J. Gademan, S.N. Hofstede, T.P.M. Vliet Vlieland, et al., Indication criteria for total hip or knee arthroplasty in osteoarthritis: a state-of-the-science overview, BMC Musculoskelet Disord 17 (2016) 463.
34 J. Hermans, M.A. Koopmanschap, S.M. Bierma-Zeinstra, J.H. van Linge, J.A. Verhaar, M. Reijman, et al., Productivity costs and medical costs among working patients with knee osteoarthritis, Arthritis Care Res (Hoboken). 64 (6) (2012) 853e61.
35 D.J. Hunter, D. Schofield, E. Callander, The individual and socioeconomic impact of osteoarthritis, Nat Rev Rheumatol 10 (2014) 437e41.
36 C. Le Pen, C. Reygrobellet, I. Gerentes, Financial cost of osteoarthritis in France. The "COART" France study, Jt Bone Spine 72 (6) (2005) 567e70.
37 S.R. Kingsbury, H.J. Gross, G. Isherwood, P.G. Conaghan, Osteoarthritis in Europe: impact on health status, work productivity and use of pharmacotherapies in five European countries, Rheumatology (Oxford) 53 (5) (2014) 937e47.
38 B. Sharif, R. Garner, D. Hennessy, C. Sanmartin, W.M. Flanagan, D.A. Marshall, Productivity costs of work loss associated with osteoarthritis in Canada from 2010 to 2031, Osteoarthritis Cartilage 25 (2) (2017) 249e58.
39 E. Nuesch, P. Dieppe, S. Reichenbach, et al., All cause and disease specific mortality in patients with knee or hip osteoarthritis: population-based cohort study, BMJ 342 (2011) d1165.
40 A. Ryan, E. Wallace, P. O'Hara, S.M. Smith, Multimorbidity and functional decline in community-dwelling adults: a systematic review, Health Qual Life Outcomes 13 (2015) 168.
41 M. Fortin, L. Lapointe, C. Hudon, A. Vanasse, A.L. Ntetu, D. Maltais, Multimorbidity and quality of life in primary care: a systematic review, Health Qual Life Outcomes 2 (2004) 51.
42 K.W. Chan, H.Y. Ngai, K.K. Ip, K.H. Lam, W.W. Lai, Co-morbidities of patients with knee osteoarthritis, Hong Kong Med J 15 (2009) 168–172.
43 U. Kadam, K. Jordan, P. Croft, Clinical comorbidity in patients with osteoarthritis: a case-control study of general practice consulters in England and Wales, Ann Rheum Dis 63 (2004) 408–414.
44 C. Palazzo, J.-F. Ravaud, A. Papelard, P. Ravaud, S. Poiraudeau, The burden of musculoskeletal conditions, PLoS ONE 9 (2014), e90633.
45 G.A. Hawker, R. Croxford, A.S. Bierman, P.J. Harvey, B. Ravi, I. Stanaitis, et al., All-cause mortality and serious cardiovascular events in people with hip and knee osteoarthritis: a population-based cohort study, PLoS ONE 7;9 (3) (2014), e91286.
46 P.A. Parmelee, T.L. Harralson, J.A. McPherron, J. DeCoster, H.R. Schumacher, Pain,disability, and depression in osteoarthritis: effects of race and sex, J Aging Health 24 (2012) 168–187.
47 Y.M. Golightly, K.L. Dominick, Racial variations in self-reported osteoarthritis symptom severity among veterans, Aging Clin Exp Res 17 (2005) 264–269.
48 M.L. Luong, R.J. Cleveland, K.A. Nyrop, L.F. Callahan, Social determinants and osteoarthritis outcomes, Aging Health 8 (2012) 413–437.
49 S.A. Ali, K.E. Walsh, M. Kloseck, Patient perspectives on improving osteoarthritis management in urban and rural communities, J Pain Res 11 (2018) 417–425.
50 O. Chassany, F. Boureau, F. Liard, P. Bertin, A. Serrie, P. Ferran, Effects of training on general practitioners' management of pain in osteoarthritis: a randomized multicenter study, J Rheumatol 33 (9) (2006) 1827–1834.