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Albert Szent-Györgyi Medical School

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Quality of life and pain management of patients with hip and knee osteoarthritis

PhD Thesis

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List of publications

Original publications directly related to the Ph.D. thesis:

I. **Mezey, GA.**, Máté, Z., Paulik, E. Factors Influencing Pain Management of Patients with Osteoarthritis: A Cross-Sectional Study. Journal of Clinical Medicine. 11(5):1352 (2022). https://doi.org/10.3390/jcm11051352

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II. **Mezey GA.**, Paulik, E., Máté, Z. Effect of osteoarthritis and its surgical treatment on patients' quality of life: a longitudinal study. BMC Musculoskeletal Disorders 24(1):537 (2023).

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2. **Mezey, GA.**, Máté, Z., Paulik, E. The 'wear and tear' of the public health sector: the under-recognized burden of osteoarthritis on the quality of life. International Conference on Chronic Diseases and 6th Savez Conference: Chronic Diseases and Integrated Care: Rethinking Health and Welfare Systems. Book of Abstracts p. 4. Kosice, Slovakia, 24-25 October 2019

3. **Mezey, GA.**, Máté, Z., Paulik, E. Pain management and consequential gastrointestinal risks in patients with osteoarthritis. NKE Conference XIV, Hungary. 26-27 August 2021. Népegészségügy, 98: 2 pp 285-285 Paper P/9. (2021)

Abstracts not related to the thesis:

1. **Mezey, GA.,** Paulik, E. Phone hygiene - the missing step in infection control. In: EUGLOH Annual Student Research Conference: Book of Abstracts pp 57-57, 28-30 September 2020 (Online)

List of abbreviations

ACR	American College of Rheumatology
ANOVA	Analysis of variance
BMI	Body mass index
CI	Confidence interval
COVID-19	Coronavirus disease 2019
COX-2	selective cyclooxygenase-2
DMOAD	Disease modifying osteoarthritis drug
EULAR	European League Against Rheumatism
GDP	Gross Domestic Product
GERD	Gastroesophageal reflux disease
GI	Gastrointestinal
HRQOL	Health-related quality of life
IBM SPSS	IBM's Statistical Package for the Social Sciences
IQR	Interquartile range
MCID	Minimal clinically important difference
MSM	Methylsulfonylmethane
NCH	Northern-Central Hungary
NGP	Northern Great Plain
NH	Northern Hungary
NRS	Numeric rating scale
NSAID	Non-steroidal anti-inflammatory drug
OA	Osteoarthritis
OARSI	Osteoarthritis Research Society International
OMERACT	Outcome Measures in Rheumatoid Arthritis Clinical Trials
OR	Odds ratio
OTC	Over-the-counter (medication)
QOL	Quality of life
ROM	Range of motion
SCH	Southern-Central Hungary
SD	Standard deviation
SGP	Southern Great Plain

ST	Southern Transdanubia
THA	Total hip arthroplasty
TJA	Total joint arthroplasty
TKA	Total knee arthroplasty
WCH	Western-Central Hungary
WT	Western Transdanubia
VAS	Visual analogue scale
WHO	World Health Organization
WHOQOL	World Health Organization Quality of Life instrument
WHOQOL-BREF	World Health Organization Quality of Life Brief Version
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index
YLD	Years lived with disability

1. Introduction

Osteoarthritis (OA) is a complex disease defined by the Subcommittee on Osteoarthritis of the American College of Rheumatology (ACR) Diagnostic and Therapeutic Criteria Committee as "A heterogeneous group of conditions that lead to joint symptoms and signs which are associated with defective integrity of articular cartilage, in addition to related changes in the underlying bone at the joint margins"[1]. Articular cartilage is the smooth cartilage at the end of long bones and within the intervertebral discs. It provides a low friction surface for articulation while being able to transmit heavy loads. Although the half-life of the collagen within the cartilage is long, it heals very slowly if at all, even with minor injuries. Although the cartilage has the most notable changes, the entire joint is affected, including the synovium, joint ligaments, and subchondral bone [2]. Clinically, OA is characterized by joint pain, joint stiffness, gait abnormalities, variable degrees of functional impairment and local inflammation [3].

From 1990 to 2019, the disability-adjusted life year of hip OA increased from 0.46 million to 1.04 million, reflecting a total increase of 126.97% [4]. As stated in the Global Health Estimates 2000–2019 study, OA was the 17th leading cause of total years lived with disability (YLD), with 1.8% of YLDs in 2000, but by 2019, it had become the 13th leading cause of YLDs at a global level with 2.3% of YLDs [5]; becoming the third-most rapidly rising condition associated with disability behind diabetes and dementia. Globally, 595 million people had osteoarthritis in 2020, equal to 7.6% of the global population, and an increase of 132.2% in total cases since 1990. Compared with 2020, cases of osteoarthritis are projected to increase 74.9% for knee, 48.6% for hand, 78.6% for hip, and 95.1% for other types of osteoarthritis by 2050 [6]. It is expected to become a major healthcare concern as the population ages, obesity rates rise, and more people adopt the Western lifestyle [7]. Arthritis has a profound economic burden. In 2013, the total US arthritis-attributable medical care costs and earnings losses among adults with arthritis were USD 303.5 billion which was 1% of the 2013 US Gross Domestic Product (GDP) [8]. OA was the second most-costly health condition treated at US hospitals and the most expensive condition for which privately insured patients were hospitalized in 2013 accounting for over USD 6.2 billion in hospital costs [9].

Certain factors have been shown to be associated with a greater risk of developing OA [10]. Some of these risk factors for OA are modifiable or preventable, such as obesity, certain occupations that place repetitive stress on a particular joint, metabolic disease (i.e. diabetes), endocrine disorders and a history of other rheumatic diseases such as rheumatoid arthritis, gout, and, to a certain extent, bone deformities. Potentially modifiable risk factors for

OA include joint trauma, sports injuries, joint malalignment and quadriceps weakness. Major risk factors such as age, gender and genetics are non-modifiable. Critical risk factors for OA are age, as the risk of developing most types of arthritis increases with it, and gender, as most types of arthritis are more common in women and 60% of all people with arthritis are women [11].

In the absence of disease modifying OA drugs (DMOADs) personalized therapy should include lifestyle evaluation, physical therapy and rehabilitation. Even if structure modifying drugs for OA are on the horizon, it will take decades before we have epidemiological data on efficacy. Therefore, as we eagerly anticipate the development of novel DMOADs it would be prudent to focus on OA prevention rather than treatment [12].

1.1 The ACR's classification system of osteoarthritis

The classification system of the ACR separates patients with OA into 2 categories: 1) those with no known prior event or disease related to the OA (idiopathic); and 2) those with known events or disease associated with OA (secondary). The system takes into account that all OA may be secondary to a yet undiscovered disease; hence, the term "idiopathic OA" is used instead of the term "primary OA". Table 1 details the different manifestation of OA, recognising that it may involve virtually any joint [1]. Twin-pair and family segregation studies have revealed that idiopathic OA has a major genetic component and that environmental factors play a significant role in disease expression. Regarding secondary OA, two main types of hip morphology have been identified as potential risk factors for hip OA: hip dysplasia (an undercoverage of the acetabulum relative to the femoral head) and hip morphology associated with femoroacetabular impingement syndrome [13]. The incidence of clinical neonatal hip instability at birth ranges from 0.4 in Africans to 61.7 in Polish Caucasians per 1000 live births [14]. In order to delay the onset of OA for patients born with hip dysplasia, early treatment is required to stimulate normal joint development by the use of dynamic brace (Pavlik harness), spica casting, or in more severe cases an extensive open surgical reduction with possible femoral and pelvic osteotomies [15]. Congenital deformities of the hip have been screened in Hungary since 1958 and as required by law (51/1997, XII. Decree No 18 of the Minister for National Welfare on health services for the prevention and early detection of diseases and certification of screening tests under compulsory health insurance), is currently done between 0-4 days after birth, and every month in the first 4 months [16]. Between 1999 and 2021 the number of infants diagnosed with congenital hip deformity increased by 465% [17].

Table 1 American College of Rheumatology's classification system for subsets of osteoarthritis

I. Idiopathic
a. Localized
i. Hands: e.g., Heberden's and Bouchard's nodes
ii. Feet: e.g., hallux valgus, contracted toes
iii. Knee: medial/lateral/patellofemoral compartment
iv. Hip: eccentric/concentric/diffuse (coxae senilis)
v. Spine: apophyseal/intervertebral/spondylosis/ligamentous
vi. Other sites: e.g. shoulder, ankle, wrist, sacroiliac
b. Generalized: includes 3 or more areas listed above
i. Small (peripheral) and spine
ii. Large (central) and spine
iii. Mixed (peripheral and central) and spine
II. Secondary
a. Post-traumatic
b. Congenital or developmental diseases
i. Localized
1. Hip diseases: e.g., congenital hip dislocation, shallow acetabulum
2. Mechanical and local factors: e.g., obesity, extreme valgus/varus deformity, hypermobility syndromes, scoliosis
ii. Generalized
1. Bone dysplasias: e.g., epiphyseal dysplasia, spondylo-apophy seal dysplasia
2. Metabolic diseases: e.g., hemochromatosis, Gaucher's disease, Ehlers-Danlos disease
c. Calcium deposition disease
d. Other bone and joint disorders: e.g., avascular necrosis, rheumatoid arthritis, gouty arthritis, septic arthritis, Paget's disease, osteopetrosis, osteochondritis
i. Endocrine diseases: e.g., acromegaly, hypothyroidism, hyperparathyroidism
ii. Neuropathic arthropathy (Charcot joints)
iii. Miscellaneous: e.g., frostbite, Kashin-Beck disease
e. Other diseases: e.g., Caisson disease

Source: Altman, R., et al., 1986, p. 1040 [1]

1.2 Joint replacement surgery

Joint replacement surgery (also known as arthroplasty or total joint arthroplasty, TJA) is a surgical procedure, when certain parts of a damaged joint are removed and replaced with artificial implants in order to relieve pain and improve function. Although most commonly performed to treat arthritis, it may also be used to treat traumas, bone tumours, deformities and other conditions. The most common joints replaced are the hip and knee.

1.2.1 Hip replacement surgery

The hip joint is a ball and socket joint, where the proximal end of the femur ("ball") fits into the acetabulum ("socket") in the pelvis. Of the hip replacement surgeries, total hip arthroplasty (THA) is the most common, while in rarer circumstances, hip resurfacing or even partial hip replacement may be used.

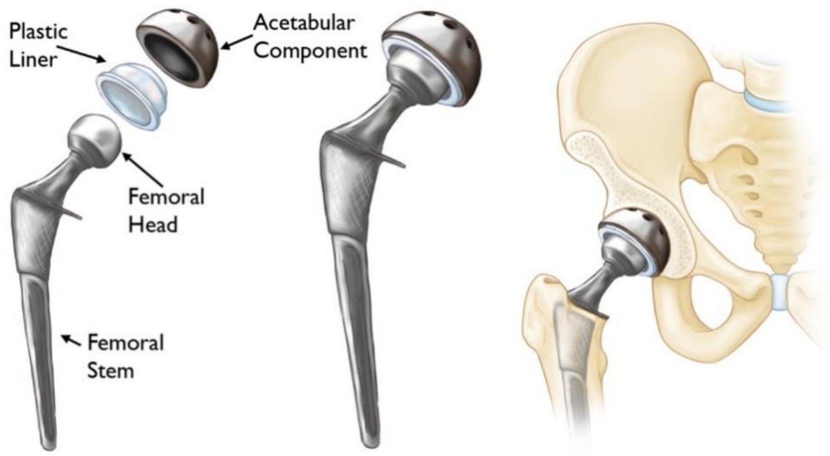


Figure 1. The individual components used in a total hip replacement (Left). The components merged into an implant (Centre). The implant as it fits into the hip (Right). AAOS. Total Hip Replacement. [18]

To begin the operation, the orthopaedic surgeon will make an incision on skin of the hip. Two of the most commonly used approaches are the anterolateral (most commonly used in Hungary) and the posterior approaches (more frequently used in the US). Separating the muscles and ligaments, the surgeon exposes the joint capsule. Then the femoral head is dislocated from the acetabulum. Damaged cartilage and bone will be removed from the acetabulum. By using surgical cement, a cup, called the acetabular component, is secured in place (Figure 1). A rounded acetabular insert/liner is put inside the acetabular cup. The insert may be ceramic or plastic and will facilitate smooth movement within the new joint. Then the surgeon prepares the femur and inserts the metal stem, called the femoral component, into the medullary cavity of the femur, securing it with cement for older patients [19]. A temporary prosthetic ball is attached to the top of the femoral stem. This ball is size-matched to the new acetabulum cup and insert. The surgeon will insert a temporary ball into the new socket and move the hip around, checking to make sure the joint has ease of motion and does not dislocate. After this, the trial component is exchange with the final ball. After repositioning the femoral component into the acetabular component, the surgeon tests the movement of the new hip joint and confirms its location with an X-ray. Finally, the joint capsule is closed, the muscles are repaired, a drain is placed in to help the drainage of excess fluids and the incision is closed [20].

1.2.2 Knee replacement surgeries

The knee joint is the largest joint in the human body. From a biomechanical view, it is a hinge joint, meaning it allows the leg to extend and bend back and forth with minimal side-to-side motion. The joint is formed where the distal end of the femur meets with the proximal end of the tibia, and the posterior surface of the patella.

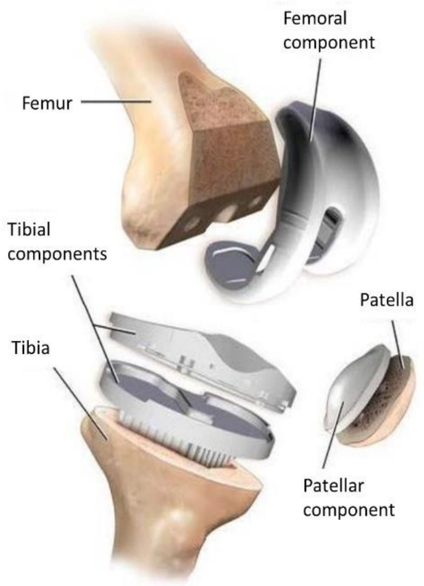


Figure 2. The individual components used in total knee arthroplasty. AAHKS. [21]

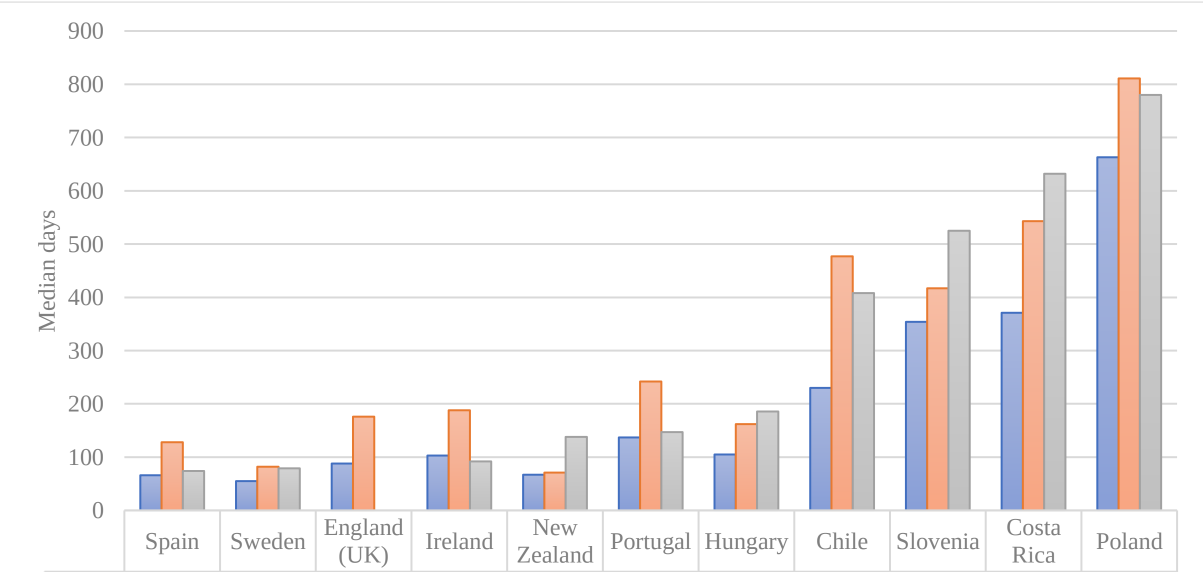
For shock absorption and stabilising purposes, two, semicircular cartilage pads known as menisci are located between the femur and the tibia, further stabilised by four ligaments.

Based on the extent of the tissue damage, surgeons can perform a partial or unicompartmental knee replacement, where only one damaged compartment of the knee is replaced, or a total knee arthroplasty (TKA), where the entire joint is replaced with artificial surfaces.

First, the surgeon makes an incision down the centre of the knee and then cuts through deeper tissue, including the quadriceps tendon, flips over the kneecap to access the femur and tibia. Using a bone saw the surgeon removes the damaged areas at the distal end of the femur and the proximal end of the tibia. With the help of a metal jig or computer assistance, each bone is reshaped to exactly fit its new prosthesis. The back of the patella may be resurfaced as well, with an optional polyethylene component attached to it. Components are attached to the femur, tibia, and – if applicable – the patella (Figure 2). Typically, these components are affixed using fast-drying bone cement, though cementless components also exist. A flexible cushion, usually made of polyethylene, is attached on top of the new tibia surfaces. This spacer acts as a shock absorber between the two new prosthetic surfaces. The leg is flexed and extended to test the fit of the components and the new knee's range of motion. Finally, the surgeon straightens the knee, repairs any deep tissue that was cut during surgery and then closes the incision [22].

1.3. Waiting list

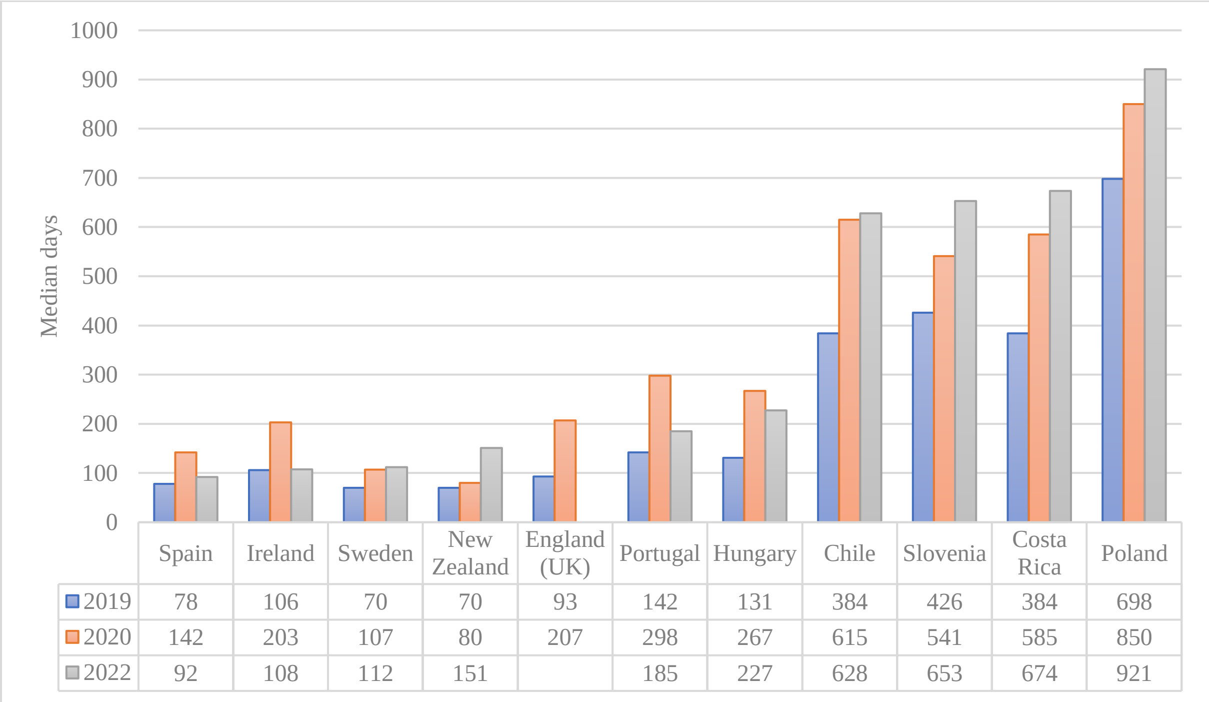
Many countries' healthcare systems had been reorganised in response to the pandemic, which meant a significant decrease in elective surgeries (such as TJA) and consequently increased waiting list [23]. Just before the COVID-19-pandemic, waiting time for THA, already varied from 55 median days in Sweden to 105 in Hungary up to 663 in Poland (Figure 3); while with TKA, it varied from 70 median days for Sweden to 131 in Hungary and even 698 in Poland (Figure 4) [24]. A steady increase could be detected globally in 2020. Many countries had taken actions to address the backlogs, and a decrease could be detected in countries such as Spain, Ireland and Portugal for both surgeries. Similarly to other countries, Hungarian patients also experienced the longer waiting time, but by the first half of 2024, the average national waiting time for knee surgery was 170 median days (mean 227), while hip surgery wait time dropped to 17 median days (mean 112) according to the National Health Insurance Fund of Hungary [25,26]. However, differences between regions within the country are significant (Figure 5) [25,26]. The waiting time for TKA varies from mean 217 days in Southern-Central Hungary to mean 384 days in Western Transdanubia, the latter region having the longest waiting list for THA as well with mean 194 days, compared to the Southern Great Plain with its mean 44 days.



	Spain	Sweden	England (UK)	Ireland	New Zealand	Portugal	Hungary	Chile	Slovenia	Costa Rica	Poland
2019	66	55	88	103	67	137	105	230	354	371	663
2020	128	82	176	188	71	242	162	477	417	543	811
2022	74	79		92	138	147	186	408	525	632	780

Figure 3 Waiting time (median days) for hip replacement surgery in OECD countries

Source: OECD Health Statistics 2024, StatLink 2 https://stat.link/w0dbuh



	Spain	Ireland	Sweden	New Zealand	England (UK)	Portugal	Hungary	Chile	Slovenia	Costa Rica	Poland
2019	78	106	70	70	93	142	131	384	426	384	698
2020	142	203	107	80	207	298	267	615	541	585	850
2022	92	108	112	151		185	227	628	653	674	921

Figure 4 Waiting time (median days) for knee replacement surgery in OECD countries

Source: OECD Health Statistics 2023, StatLink 2 https://stat.link/40q36v

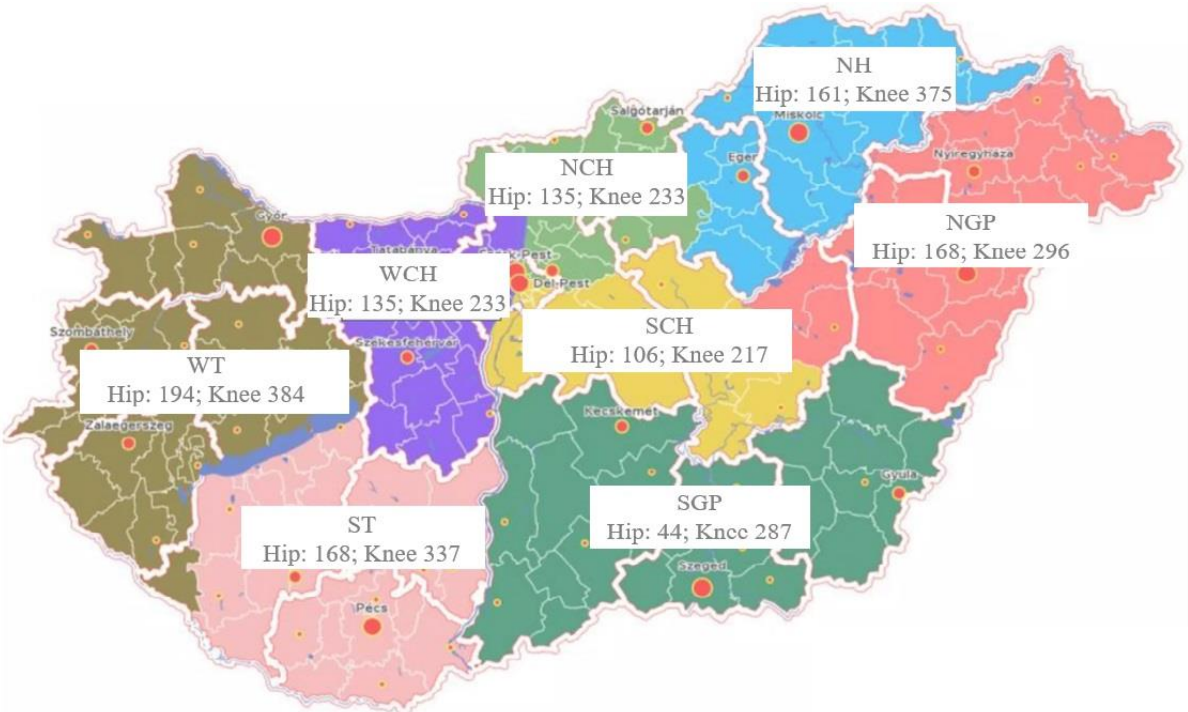


Figure 5 Mean number of days on hip and knee replacement surgery waiting list in the first half of 2024 in Hungary

The 8 regions of Hungary devided by health service area: [WT] Western Transdanubia, [ST] Southern Transdanubia, [WCH] Western-Central Hungary, [NCH] Northern-Central Hungary, [SCH] Southern-Central Hungary, [SGP] Southern Great Plain, [NH] Northern Hungary, [NGP] Northern Great Plain.
Source: https://jogviszony.neak.gov.hu/varolista_pub/varolistak-teteles-lekerdezese/?ocsk=O20
https://jogviszony.neak.gov.hu/varolista_pub/varolistak-teteles-lekerdezese/?ocsk=O22

1.4. Quality of life

The World Health Organization (WHO) explains quality of life (QOL) as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns [27]. Common facets of QOL include personal health (physical, mental, and spiritual), relationships, education status, work environment, social status, wealth, a sense of security and safety, freedom, autonomy in decision-making, social-belonging and their physical surroundings. The pain and decreased mobility caused by OA affects social connectedness, relationships, and emotional well-being, thus reducing multiple aspects of QOL [28]. Furthermore, OA has been shown to be significantly associated with deteriorated mental health [29,30].

Health is consistently regarded as an important aspect of QOL. Health-related QOL (HRQOL) aims to measure QOL components impacted by certain diseases and effectiveness of treatment. Therefore, studies on HRQOL may evaluate the quality and outcome of health care provided or may identify applicative items [31]. Analysis of QOL data can also identify subgroups, can help guide interventions to improve the situation of those with poor perceived health and avert more serious consequences [32]. Patients with chronic pain associated with musculoskeletal disorders have some of the poorest HRQOL ahead of neurological, renal, and cardiovascular diseases, with severe restrictions in their work and ordinary activities of daily living [33].

The WHO has developed a generic measure of QOL (WHOQOL-100) that encompasses general, physical, psychological, social, and environmental aspects through 100 items, making it ideal for measuring a broad range of factors, thus giving a more complete picture of the individual’s life and wellbeing [34]. As the WHOQOL-100 may be too lengthy for practical use, the abbreviated version of the WHOQOL assessment tool (WHOQOL-BREF) was developed, where one item from each facet of the WHOQOL-100 has been included with the addition of one question regarding overall QOL and one about general health. Reis et al. (2014) have used the WHOQOL-BREF when reporting on how significant knee pain in elderly women with knee OA affected their balance and overall QOL compared to elderly women with no OA [35]. This decline in QOL has been supported by the study of Cavalcante et al. (2015) as well [36], and even younger patients (<50 years) have reported a poorer QOL because of OA [37].

THA and TKA are regarded as one of the most successful operations in medicine as a whole [18], leading to statistically significant improvement in QOL by 4% after 6 weeks and 13% after 6 months [38]. Post-surgical improvements in pain and function have been shown to extend over years, but examining the whole spectrum of QOL might give a more in-depth understanding of outcomes relevant for the individual [39].

While the measuring of generic QOL is advantageous when assessing the overall burden of a given health problem, disease-specific measures of QOL have the advantage of being frequently more responsive and clinically useful than generic measures by measuring the frequency and severity of specific symptoms [40]. Since its initial validation [41], the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) has become a popular patient reported outcome measure used for evaluation of hip and knee OA. It has been used extensively in research studies [42-44] and clinical trials [45-47] and has been recognized by the Outcome Measures in Rheumatoid Arthritis Clinical Trials group (OMERACT) and Osteoarthritis Research Society International (OARSI) [48,49]. It can be also used to classify patient satisfaction after total knee arthroplasty as proved by Walker et al. (2018), where four levels of patient satisfaction were defined by the grades in the WOMAC scores. Three threshold values were identified: >75 points on total WOMAC scores predicted very satisfied from satisfied patients, >56 points predicted satisfied from dissatisfied and >43 points predicted dissatisfied from very dissatisfied patients. One year following TKA, 67.5% of patients were very satisfied, 22.2% satisfied, 7.4% dissatisfied and 2.9% very dissatisfied with their surgery [50].

1.5 Pain management

OA remains a relatively unaddressed public health concern compared to such chronic diseases as cancer, diabetes, and heart disease. There is a certain level of complacency and a fallacy that joint pains are an inevitable part of aging. The degradation of articular cartilage is often seen as a condition to be tolerated, not managed [51]. As many people do not recognise their joint pain as a disease, they often do not consult a health professional for its management. They treat their joint pain at a symptomatic level with over-the-counter (OTC) pain medications, similarly to a headache or lower back pain. The popularity of non-steroidal anti-inflammatory drugs (NSAIDs) can be seen worldwide. In 2024, the revenue generated in the OTC Analgesics market amounts to USD 33.05 billion globally, USD 8.45 billion in Europe and USD 7,243 million in the United States. Worldwide, the demand for analgesics in the OTC Pharmaceuticals market is projected to grow at an annual rate of 5.61% between 2024 and 2029, with countries like the United States and Japan leading the way in consumption, while in Germany there is a growing demand for natural and herbal analgesics [52,53].

A serious problem is that this practice is contrary to major clinical guidelines, which generally agree on a combination of non-pharmacological and pharmacological therapies. The ACR deems non-pharmacological therapies as the “cornerstone of OA management”, which should be maintained throughout the course of the disease, and stresses that pharmacological therapies should function as add-on therapy to non-pharmacological treatment [54]. The European League Against Rheumatism (EULAR) recommends the use of topical NSAIDs and capsaicin as alternatives to oral analgesics or in combination with them [55].

Regarding oral analgesics, paracetamol was favoured previously by major clinical guidelines, recommending it to be the first choice in managing mild-to-moderate OA-related pain [54,56-59], while recently both NSAIDs and paracetamol are considered to be appropriate for treatment, though now a more conservative dosing for the latter is advised due to the increased risk of adverse events [60]. Beyond their burden on the cardiovascular system, it is widely accepted that regular use of NSAIDs increases the risk of interstitial nephritis, atrial fibrillation, and severe gastrointestinal (GI) complications, including ulceration, bleeding, and perforation, by 2 to 4 times [61]. This fact is further aggravated by the increasing number of people who are opting for self-medication with OTC medications, without consulting a doctor, often under the influence of advertisements.

Major and Vincze (2010) contacted 4536 specialists (pharmacists, pharmaceutical assistants, and pharmacy managers) to investigate the Hungarian patients’ habit of buying OTC medications. Their results show that 58.2% of patients buying OTC medications in pharmacies are usually self-reliant in self-medication, but they have little knowledge about these drugs [62]. When researching consumer awareness and knowledge regarding use NSAIDs in Italy, Montuori et al. (2024) found that more than 20% of participants ignored the chances of potential side effects, but those with higher level of education were more aware of the appropriate use of NSAIDs [63]. Meanwhile in Australia, Mullan et al. (2017) reported that almost a third of ibuprofen users couldn't correctly identify the maximum daily dose and fewer than half recognised potential side effects of ibuprofen [64]. The fact that the knowledge of the general population regarding the harmful adverse effects of NSAIDs needed to be improved was also highlighted by Almohamed et al. (2023) of Saudi Arabia, who found a significant association between the female gender, lower levels of education, and a higher frequency of repeated use of analgesics [65]. A national study in the United States, conducted by Kaufman et al. (2018), showed that most users did not recognize that the products they were taking were NSAIDs, 11% exceeded the maximum daily dose of ibuprofen, 4% of other NSAIDs, and on 9.1% users exceeded the NSAID usage days [66].

The combination of OA patients' needs for analgesics, the risk of concomitant use of multiple NSAIDs, and patients' tendency for self-medication practices emphasizes the need for healthcare professionals to understand osteoarthritic patients' health behaviour. Unfortunately, many times the attending physicians have no detailed data on what their patients use to alleviate their pain and in what quantities do they take OTC painkillers, a problem we wish to solve.

2. Objectives

With its rapid rising and significant effect on QOL, OA continues to be a major health concern. The available treatments for managing the pain associated with OA have adverse effects that are not insignificant. One of the more common being NSAIDs, which are wildly known for their GI adverse effects such as peptic ulcer.

The overall aim of the study is to give a detailed analysis of the QOL and pain management of OA patients of the Southern Great Plain Region of Hungary.

Three primary objectives were:

I. To measure OA's effects on the QOL of the patients as accurately as possible using validated questionnaires already routinely used in international practice. Information regarding both general and disease-specific QOL needed to be collected to get a well-rounded picture. As a definitive treatment and major surgical intervention, TKA and THA are expected to significantly increase the QOL, and so a repeated assessment was carried out in the postoperative study.
   a. A secondary objective was to explore the factors that might alter how surgery affects QOL.
   b. Another secondary objective was to investigate hip dysplasia patients' experiences, if they could be considered a vulnerable sub-group among OA patients.

II. To investigate pain caused by the disease and its impact on QOL, and the OA patients' habits of pain management and the explanatory factors of various ways of self-treatment.
   a. A secondary objective was to estimate the risk of developing a drug-related GI complication.

III. To identify the modifiable factors or actions on which preventive recommendations can be made.

3. Materials and methods

3.1. Study design and participants

A longitudinal study was performed by the Department of Public Health, University of Szeged, based on data collected from August 2019 to September 2020 (preoperative data collection), and from March 2021 to November 2021 (postoperative data collection). Figure 6 demonstrates the phases of our study with the recruitment sources, timelines, baseline and follow up numbers.

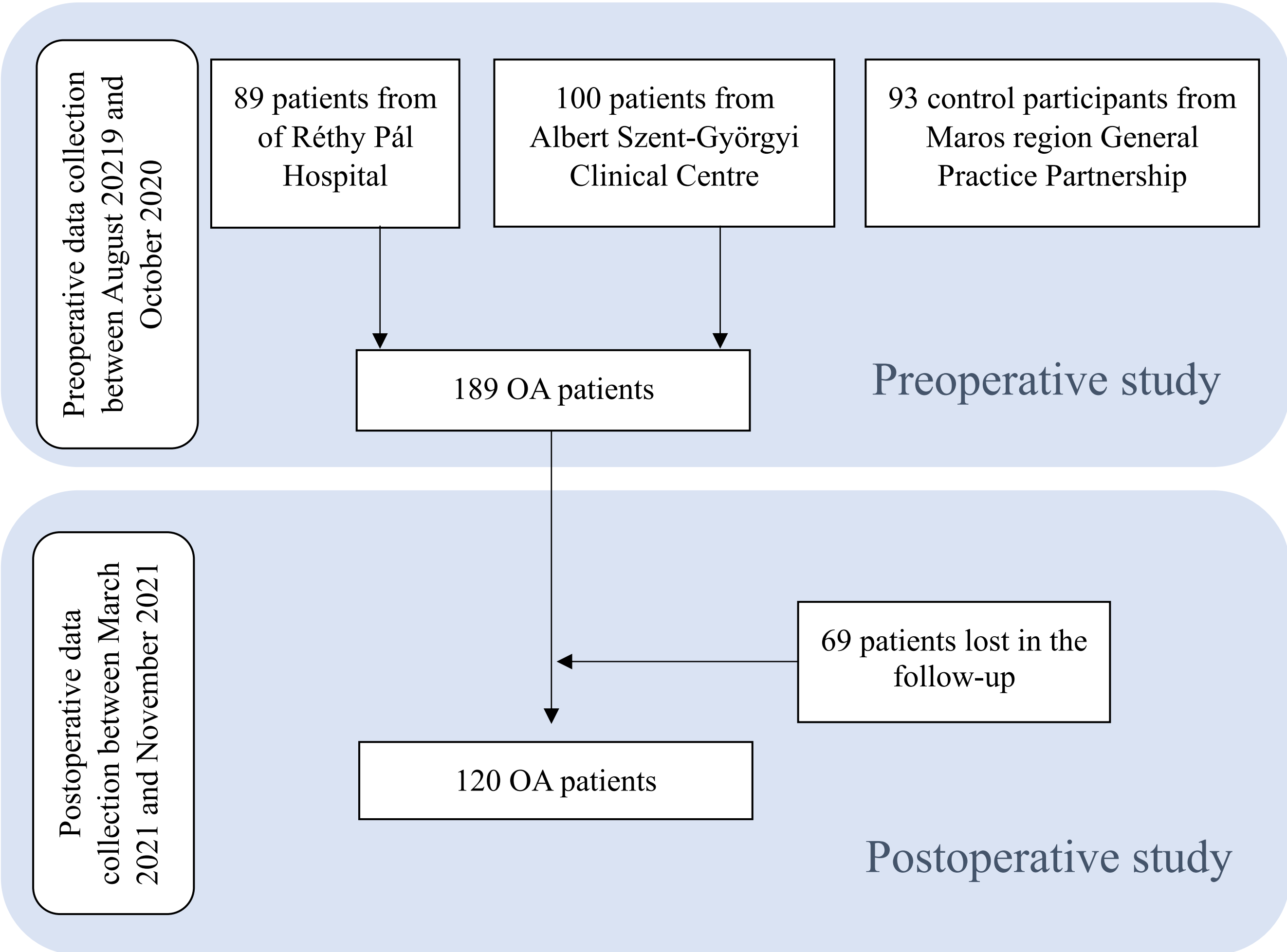


Figure 6 Flow diagram describing the recruitment and progress of participants

The population consisted of the group of OA patients undergoing surgery at the Department of Orthopaedics, Albert Szent-Györgyi Clinical Centre, University of Szeged (Szeged, Hungary) (n=100) and at the Orthopaedic Ward of Réthy Pál Hospital of Békés County Central Hospital (Békéscsaba, Hungary) (n=89); and a control group from the Maros region General Practice Partnership (n=93).

Patients with knee or hip OA scheduled for TJA were involved, while patients receiving unicompartmental knee arthroplasty were excluded. No other exclusion criteria were set. Patients were involved on a voluntary basis where participation was offered for all eligible patients consecutively with every subject standing an equal chance of being included to reduce selection bias.

3.2. Data collection

Data collection was carried out with the use of a paper and pencil questionnaire 24 hours prior to surgery. Patients filled out the self-administered questionnaire in their rooms after being informed about the study and signing the informed consent form. To assess the surgery's effect on QOL, postoperative data collection was carried out one year after surgery. Due to coronavirus disease 2019 (COVID-19) lockdown, the questionnaires were sent and returned by post, as well as participants were also able to fill out the online version. This one year waiting period was chosen as to make sure the patients made full recovery after surgery including wound healing and physiotherapist-directed rehabilitation.

Participants of the control group filled out the questionnaire at the general practitioners' office at the same period of time when the patient group filled out the preoperative form. The exclusion criteria for participants of the control group were the presence of hip or knee OA or previous TJA.

The questionnaire comprised three basic sections: 1, sociodemographic data (age, gender, etc.); 2, QOL measuring tools (WHOQOL-BREF, WOMAC); 3, pain management (pharmacological and non-pharmacological).

3.2.1. Sociodemographic and anthropometric data

Based on their age, participants were divided into two groups split at the age of 65 as that is the age of retirement in Hungary, making this grouping suitable to assess the effect of the disease and the treatment on both the economically active and inactive population.

The level of education was considered as 'low' if the participants had no high school diploma, 'middle' if they had one, and 'high' if they had a college or university degree.

Based on job profile, participants whose job was physically demanding (e.g. manual labour) formed the "manual" group, while those with intellectual work (e.g. desk jobs) formed the "non-manual" group.

After calculating the body mass index (BMI) (weight in kilograms divided by height squared in meters), the participants were grouped, based on the WHO recommendation, as underweight (BMI below 18.5 kg/m^2), normal (BMI 18.5 kg/m^2 to 24.9 kg/m^2), overweight (25.0 kg/m^2 to 29.9 kg/m^2) and obese (over 30.0 kg/m^2) [67].

3.2.2. Quality of life measures

General QOL was measured by the validated Hungarian version of WHOQOL-BREF, which measures QOL with 26 questions through 4 domains: 1, *physical health* (activities of daily living, dependence on medicinal substances and medical aids, energy and fatigue, mobility, pain and discomfort, sleep and rest, work capacity); 2, *psychological health* (bodily image and appearance, negative feelings, positive feelings, self-esteem, spirituality/religion/personal beliefs, thinking, learning, memory and concentration); 3, *social relationships* (personal relationships, social support, sexual activity); 4, *environment* (financial resources, freedom, physical safety and security, health and social care: accessibility and quality, home environment, opportunities for acquiring new information and skills, participation in and opportunities for recreation/leisure activities, physical environment, transport). There are also two separate introductory questions which ask specifically about 1, the individual's overall perception of their health and 2, the individual's overall perception of their QOL. The answers were measured by a 5-point Likert scale. In accordance with the instructions of the WHOQOL-BREF manual, domain scores were calculated and then converted to a 0-100 scale, this way it became comparable with the scores used in the WHOQOL-100. The results of the two separate questions were left untransformed. The higher score represented better QOL [68].

In order to assess the disease-specific QOL, we used the validated Hungarian version of the WOMAC Index Version 3.1 numeric rating scale (NRS) [69], which covers 3 dimensions through 24 items: *pain* (5 items) during walking, going up/down the stairs, lying in bed, sitting, and standing upright; *stiffness* (2 items) after waking up and later in the day; and *function* (17 items) going up/down the stairs, rising from sitting, standing, bending, walking, getting in/out of a car, shopping, putting on/taking off socks, rising from bed, lying in bed, getting in/out of the bathtub, sitting, getting on/off toilet, performing heavy domestic duties or light domestic duties. All items were assessed by using a 1-10 NRS, (1=no pain/stiffness/difficulty to 10=extreme pain/stiffness/difficulty) totalling 24–240, where higher scores indicated increased pain and decrease function. The results of the individual domains as well as the total score were later standardised to a 0–100 scale. The WOMAC questionnaire was chosen for this study for its good reported internal consistency, excellent test–retest reliability, and experts' involvement in development [70].

3.2.3. Pain management and related risk

To investigate pain management, the name, dose, and frequency of use of OTC and prescription-only medications were recorded. We only took into account regular medication use, that is, painkillers that participants used at least once a week. Based on these data, the following categories were made: total painkiller use (regular use of any type of painkiller), regular use of OTC oral NSAID, regular use of topical NSAID (cream/gel/patch), regular use of oral prescription medication, regular use of per os opioid-containing medication, and regular use of non-pharmacological methods. We also enquired about steroid and hyaluronic acid intra-articular injections and the corresponding patient satisfaction.

In order to explore drug-related GI risks, based on the LOGICA study we have taken into account the following risk factors: age >60, anticoagulant use, ulcer, dyspepsia or gastroesophageal reflux disease (GERD) in medical history, use of two NSAIDs, a high dose of one NSAID or the concomitant use of NSAIDs and anticoagulant. The dose of a medication was considered high if it reached or passed the recommended daily intake, that is: ibuprofen >1800 mg/day, naproxen ≥1000 mg/day, diclofenac ≥150 mg/day, aceclofenac ≥100 mg/day, niflumic acid ≥750 mg/day, meloxicam ≥15 mg/day, piroxicam ≥20 mg/day, and nimesulide ≥200 mg/day [71].

Then patients were classified into three GI categories. Patients at low GI risk were considered to be those without any of the aforementioned risk factors. Patients at moderate GI risk included patients with at least one GI risk factor. Patients at high GI risk were considered to be those with either a GI bleeding history, concomitant use of NSAIDs and anticoagulants or the presence of three of the risk factors described for moderate GI risk.

We also examined non-pharmacological pain management techniques (e.g., physiotherapy, therapeutic massage, cold wraps, etc.). In this context, "physiotherapy" describes manual therapy and exercise therapy guided by a professional physiotherapist in order to build muscle strength and improve ROM, while "exercising" includes basic warm-up and stretching exercises carried out by the patients in their homes, typically once a day in the morning to ease the joint stiffness they acquired during sleep. "Massage" specifically refers to massages carried out by the patients themselves. The term "cold wraps" includes chilled gel packs as well as towels soaked in cold water. Finally, participants were asked about their use of supplements for bone and cartilage health.

3.2.4. Supplementary questions and data

In order to get a more detailed picture of patients' condition, the questionnaire was expanded with supplementary questions regarding:

- for how long their hip/knee had been hurting
- what patients think caused their illness
- if their job and weight played a part in their condition
- congenital abnormality of the musculoskeletal system
- previous joint injury
- sporting habits
- use of walking aid
- previous administration of intra-articular hyaluronic acid and/or steroid injections and their satisfaction with the injections (1-10 scale)
- previous joint replacement surgeries
- satisfaction with the outcome of current surgery (1-10 scale)

Patients' documentations were checked for:

- pre- and postoperative range of motion (ROM)
- extension deficit after surgery
- subjective limb shortening after surgery
- pre- and postoperative muscle strength
- pre- and postoperative pain scale (Visual analogue scale, VAS: 1-10)
- flexion design of the prosthesis (conventional or high-flexion)
- use of cement
- surgical complications
- start of rehabilitation after surgery

Preoperative ROM and muscle strength was evaluated by orthopaedic surgeons on the last follow-up before hospital admission, while postoperative evaluation was done by physiotherapist 5-6 days after surgery, before hospital discharge.

1.3 Statistical analyses

Data analysis was carried out with IBM SPSS (Statistical Package for the Social Sciences) version 27 (SPSS Inc., Chicago, IL, USA). Descriptive statistics including frequency, percentage, mean, median, standard deviation (SD), and interquartile range (IQR) were performed to describe the study sample. After normality testing, age did not follow a normal distribution, as OA predominantly affects the older generation.

QOL measures: As the outcome measures had non-normal distribution, a Mann-Whitney U test was conducted to compare the baseline scores of patients and the control group, while Wilcoxon tests were carried out to assess the difference of the preoperative and postoperative QOL outcome measures. To explore the role of independent variables in the results, subgroups were made based on gender, age, affected joint, BMI categories, work profile, level of education and the presence of a comorbidity. Sub-group analyses were carried out using mixed-design two-way repeated measures analysis of variance (ANOVA). Statistical significance was set at $p<0.05$.

Pain management measures: In preoperative data, association between categorical data was evaluated with a Chi-square test, and with one-way ANOVA for continuous data. To assess the change of painkiller use before and after surgery, McNemar test was carried out. Multivariable binary logistic regression analyses using the forward stepwise method were applied to determine the explanatory factors for analgesic use. The independent variables entered into the model were: gender, age group, level of education, job profile, affected joint, BMI category, and WOMAC total score. P-values for covariates to be included in the model were set at 0.05. Odds ratios (OR) and 95% confidence intervals (95% CI) were calculated, and statistical significance was set at $p <0.05$.

Joint kinetics and pain measures: the changes in the joints' ROM and muscles strength were evaluated by paired-sample T-test, while pain measured on the visual analogue scale were recorded 3 times and assessed by repeated measure ANOVA. Statistical significance was set at $p<0.05$.

3.4. Ethical approval

The study was approved by the Human Investigations Review Board of University of Szeged, Albert Szent-Györgyi Clinical Centre, Hungary (ID: 4059) and conducted in accordance with the Declaration of Helsinki. All subjects were informed about the aim and attributes of the study and provided written informed consent before filling out the questionnaire.

4. Results

4.1. Preoperative study

4.1.1. Demography

The baseline characteristics of the patients (n = 189) and control individuals (n= 93) are shown in Table 2. The median age was 68 years (IQR=62, 74) and 64 years (IQR=58, 69) respectively, and the majority of participants were women, 70.4% and 74.2%.

Table 2 Baseline characteristics of study participants

Characteristics		
	Patient	Control
	n (%)	n (%)
Gender		
Men	56 (29.6)	24 (25.8)
Women	133 (70.4)	69 (74.2)
Age groups		
<65 years	65 (34.4)	47 (50.5)
≥65 years	124 (65.6)	46 (49.5)
Level of education		
Lower	82 (43.4)	54 (58.0)
Middle	69 (36.5)	26 (28.0)
Higher	38 (20.1)	13 (14.0)
Job profile		
Manual	97 (51.3)	60 (60.0)
Non-manual	92 (48.7)	30 (30.0)
Affected joint		
Hip	92 (48.7)	n.a.
Knee	97 (51.3)	n.a.
BMI categories (kg/m^2)		
<18.5	0	1 (1.1)
18.5–24.9	28 (14.8)	19 (21.1)
25.0–29.9	53 (28.1)	32 (35.6)
≥30.0	108 (57.1)	38 (42.2)

BMI: body mass index, n.a.: not applicable

Of our OA patient sample nearly half of them had hip (48.7%) OA, and more than half (57.1%) were obese, a slightly higher percentage compared to the control group (42.2%) (Table 2). 30 patients had been diagnosed with osteoporosis, but only 50% of them were taking medication because of it. 18 patients were suffering from GERD. Due to OA associated problems 58% of patients used some kind of walking aid.

Majority of patients (58.7%) came for their first, 27% for their second, 9.5% for their third, 2% for fourth, 1% for fifth operation, while 1-1 patient for their sixth and seventh one. Regarding waiting times, 29.8% waited less than a year, 36.2% between 1-5 years, 16.5% between 5-10 years and 17.6% for more than 10 years. When asked about the reason of this time, 54 patients reported the waiting list as a cause, of which 11 cases had longer waiting time due to the COVID-19 pandemic temporary surgical stoppage; seven patients were delayed by their workplace, three waited for their retirement, five postponed the procedure out of fear, two due to comorbidity and another two patients required a special prosthesis to be ordered.

As OA patients spend a considerable amount of time in pain often facing difficulties in everyday tasks, we asked them, if they consider themselves ill. Only 49.5% of patients listed arthritis as a current health problem, 26.3% only mentioned other chronic conditions such as hypertension or diabetes and 24.2% said that they are not suffering from any type of disease.

4.1.2. Risk factors

In an open-ended question we asked the participant, what was the cause of their disease. The majority (19%) wrote their job, while 6.9% wrote congenital problem, 3.2% sports, 2.1% injury, 1.6% other musculoskeletal disease and 1.1% wrote their age. This was followed up by two targeted questions on how much do they think their job and weight contributed to the development of their disease (Table 3).

Table 3 Patients opinion on their job's and weight's effect on the disease

Effect of:	**job n=184 (%)**	**weight n=119 (%)**
Significant	87 (47.3)	20 (16.8)
Moderate	45 (24.4)	30 (25.2)
Lesser	11 (6.0)	33 (27.7)
No effect	20 (10.9)	36 (30.3)
Cannot judge	21 (11.4)	0

Competitive sport is known for being taxing on the joints, 24 OA patients reported playing competitive sport in their past for an average of 12.3 years (2-40 years), handball being the most common (6 patients). 9% of OA patients reported congenital disease, of which 7.4% were hip dysplasia, while 18.5% reported previous injury to the joint that will be operated on.

4.1.3. Preoperative QOL assessment

4.1.3.1. General QOL (WHOQOL-BREF)

In case of general QOL, compared to the control group, OA patients reported a significantly lower QOL only in the *physical health domain* (Table 4). Detailed preoperative results of the questionnaire can be found in Supplementary Table 1.

Table 4 General quality of life outcomes of control participants and patients with osteoarthritis

WHOQOL-BREF						
Domains		n	Mean Rank	SE	U	p Value
Physical health	Control	93	173.83	639.57	5782.00	**<0.001**
	OA	189	125.59			
Psychological	Control	93	144.34	637.61	8524.50	0.679
	OA	189	140.10			
Social relationships	Control	93	154.72	638.98	7559.00	0.054
	OA	189	134.99			
Environment	Control	93	152.60	638.18	7756.00	0.106
	OA	189	136.04			

WHOQOL-BREF: World Health Organization Quality of Life Brief Version, OA: osteoarthritis, SE: standard error, U: Mann-Whitney U test. Significant *p*-value is highlighted in bold.

Analyses within the OA patient group revealed that patients with manual jobs reported a significantly lower QOL in the *physical health* and *psychological domain* (p=0.002). Hip OA patients also reported a decrease in the *physical health domain* (p=0.002) compared to knee OA patients. In case of 65+ year-patient, the decrease in QOL appeared in the *social relationships domain* (p<0.001), while BMI had no association with the perceived QOL.

4.1.3.2. Disease-specific QOL (WOMAC)

Compared to the control group, OA patients reported a significantly lower disease specific QOL in all domains (Table 5). When assessing the relationship between the patients' job, age group and BMI, we found that OA patients with manual job reported a significantly higher level of *pain* (p=0.004) and decreased *physical function* (p=0.021) and overall state (p<0.01) on the WOMAC scale compared to OA patients with non-manual jobs. Patients of the 65+ age group reported worse joint *stiffness* (p<0.05); while BMI had no effect on the disease specific QOL. Hip OA patient reported a generally worse QOL compared to knee OA patients, significantly so in *physical function* and overall score (p<0.05). Detailed preoperative results of the questionnaire can be found in Supplementary Table 3.

Table 5 Disease-specific quality of life outcomes of control participants and patients with osteoarthritis

			WOMAC			
Domains		n	Mean Rank	SE	U	p Value
Pain	Control	93	85.46	643.59	14000.50	**<0.001**
	OA	189	169.08			
Stiffness	Control	93	97.95	642.57	12838.50	**<0.001**
	OA	189	162.93			
Physical function	Control	93	81.68	643.80	14352.00	**<0.001**
	OA	189	170.94			
Total score	Control	93	81.16	643.81	14400.50	**<0.001**
	OA	189	171.19			

OA: osteoarthritis, SE: standard error, U: Mann-Whitney U test, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index. Significant *p*-values are highlighted in bold.

4.1.4. Assessment of pain management

Of the patients, 6.9% used neither pharmacological nor non-pharmacological methods to alleviate their pain, not even occasionally.

4.1.4.1. Pharmacological pain management carried out by patients

The active ingredients of oral pain medications and the number of participants taking them are represented in Table 6. Diclofenac was the most frequently used drug, followed by ibuprofen and tramadol. Medications with paracetamol and selective cyclooxygenase-2 (COX-2) blockers were taken by nine patients (4.8%) and one (0.5%) patient, respectively. A total of 24 participants (12.7%) took 2 different types of oral analgesic, while nine (4.8%) and two patients (1.1%) took 3 or 4 different types, respectively. Also, 34 patients (18%) took high doses of painkillers regularly. Diclofenac was the most favoured with 15 patients reaching the recommended daily dose. A total of 38.1% of patients used prescription medication regularly. Diclofenac was the most frequently used active ingredient among topical analgesics as well. A total of 29.1% of patients used topical analgesics, all of which had diclofenac as an active ingredient.

While assessing the differences between knee and hip OA patients, knee patients were found to have significantly higher BMI ($p < 0.01$). There were no differences between the two groups' demographic characteristics. Even though hip OA patients reported significantly worse HRQOL in the WOMAC total score (mean ± SD: 152.76 ± 41.23) than knee OA patients (139.62 ± 45.12) ($p = 0.038$), they were less likely to regularly use NSAIDs, either in tablet or cream form (42.2%), than were knee patients (59.8%), (p = 0. 017). Knee OA patients were significantly more likely to use topical analgesics ($p = 0.013$) and had a greater tendency to use non-pharmacological methods of pain management.

Table 6 Frequency of oral pain medication used by osteoarthritis patients before surgery and by our control individuals, listed by active ingredients.

Medication		
	OA Patients	**Control**
	n (%)	n (%)
NSAIDs		
Diclofenac	74 (39.2)	21 (22.6)
Ibuprofen	42 (22.2)	21 (22.6)
Aceclofenac	12 (6.3)	16 (17.2)
Acemetacin	10 (5.3)	1 (1.1)
Naproxen	9 (4.8)	2 (2.2)
Nimesulide	4 (2.1)	7 (7.5)
Piroxicam	3 (1.6)	0
Aspirin	3 (1.6)	0
Meloxicam	1 (0.5)	0
Niflumic acid	1 (0.5)	0
Lornoxicam	1 (0.5)	0
Coxibs		
Etoricoxib	1 (0.5)	0
Opioids		
Tramadol	13 (6.9)	7 (7.5)
Paracetamol	2 (1.0)	2 (2.2)
Combinations		
Tramadol + paracetamol	6 (3.2)	7 (7.5)
Tramadol + dexketoprofen	1 (0.5)	0
Paracetamol + codeine phosphate	1 (0.5)	0

OA: osteoarthritis, NSAID: non-steroidal anti-inflammatory drug.

4.1.4.2. Non-pharmacological pain management carried out by patients

The majority of patients (65.1%) practiced a non-pharmacological method to mitigate their pain, with 7.4% using these methods exclusively. Exercise, massages, and cold packs were the most favoured. 18.5% used a topical herbal cream with comfrey extract. Only seven patients took part in physiotherapy, and of them, only two reported it as a regular (two times per week) activity (Table 7). As another mean to support the joints, 55% of patient took supplements for bone and cartilage health daily, most frequently glucosamine sulfate (31.7%), Vitamin D3 (26.5%), calcium (23.8%), chondroitin sulfate (15.3%), magnesium (9%), methylsulfonylmethane (MSM) (8.5%), hyaluronic acid (2.1%) and Vitamin K2 (1.6%).

Table 7 The different modes of pain management and their frequencies used by osteoarthritis patients before surgery and by our control individuals

Form of Treatment		
	OA Patients (n=189)	**Control (n=93)**
	n (%)	n (%)
Pharmacological methods	148 (78.3)	65 (69.9)
Total painkiller use	95 (50.3)	45 (48.4)
Regular OTC oral NSAID	44 (23.3)	12 (12.9)
Topical NSAID cream/gel/patch	55 (29.1)	19 (20.4)
Prescription medication	72 (38.1)	64 (68.8)
Oral opioid-containing medication	18 (9.5)	12 (12.9)
Topical herbal cream	35 (18.5)	14 (15.1)
Non-pharmacological methods	124 (65.6)	67 (72)
Exercising	59 (31.2)	43 (46.2)
Massage	55 (29.1)	35 37.6)
Cold packs	49 (25.9)	10 (10.6)
Warm bath	20 (10.6)	12 (12.9)
Physiotherapy	7 (3.7)	4 (4.3)
Kinesio tape	6 (3.2)	4 (4.3)
Magnetic band/patch	2 (1.1)	0

OA: osteoarthritis, OTC: over the counter, NSAID: non-steroidal anti-inflammatory drug.

4.1.4.3. Pharmacological pain management carried out by physicians

Awaiting surgery, 50 patients (26.5%) were administered intra-articular hyaluronic acid and 27 patients (14.3%) were administered intra-articular steroid injections. When asked about their effectiveness in a 1-10 scale, patient satisfaction on average was 4.74 (SD 2.97) with hyaluronic acid and 5.59 (SD 3.40) with steroid injections. There was no significant difference between the satisfaction scores of the two types of injections.

4.1.5. Assessment of influencing factors

When calculating associations between the different pain management methods and patient characteristics, manual labour showed the most connections to painkiller use both with oral ($p=0.011$) and topical ($p=0.030$) NSAIDs and overall analgesic use ($p=0.016$). Knee OA suggested an even stronger association with overall ($p=0.007$) and topical ($p=0.013$) NSAID use, the latter indicating connection to the BMI as well (Table 8).

To identify the most important predictor variables and examine the probability of painkiller use if certain characteristics are present, a series of the stepwise logistic regression analyses were carried out (Tables 9-13). Regarding factors associated with non-pharmacological pain management, female patients showed a greater willingness to mitigate their pain in such ways. Variables associated with stress on the joint such as manual labour and higher WOMAC score, showed a greater likelihood of medication use, however in the case of BMI, a higher value in fact suggested a bigger chance for topical analgesic use, but patients with higher BMIs were less likely to take OTC NSAIDs, compared to participants with normal BMI. Knee OA patients were more than twice as likely to regularly use painkillers or topical analgesics compared to hip OA patients. As shown in Table 12, WOMAC Score results showed that patients with poorer physical function and/or higher pain level were more likely to take prescription medications, each point increases the chance of taking medicine by 1.3%.

Table 8 Associations between different pain management methods and patients' characteristics.

	All painkillers ***n*** **(%)**	**OTC NSAIDs** ***n*** **(%)**	**Prescript. painkillers** ***n*** **(%)**	**Topical NSAIDs** ***n*** **(%)**	**Opioid** ***n*** **(%)**	**Non-pharma** ***n*** **(%)**
Gender [a]	$p = 0.186$	$p = 0.443$	$p = 0.662$	$p = 0.649$	$p = 0.070$	**$p < 0.001$**
Men	24 (42.9)	11 (19.6)	20 (35.7)	15 (26.8)	2 (3.6)	27 (48.2)
Women	71 (53.4)	33 (24.8)	52 (39.1)	40 (30.1)	16 (12.0)	97 (72.9)
Age group [a]	$p = 0.609$	$p = 0.256$	$p = 0.181$	$p = 0.098$	$p = 0.673$	$p = 0.160$
<65 years	31 (47.7)	12 (18.5)	29 (44.6)	51 (78.5)	7 (10.8)	47 (72.3)
≥65 years	64 (51.6)	32 (25.8)	43 (34.7)	83 (66.9)	11 (8.9)	77 (62.1)
Level of education [a]	$p = 0.368$	$p = 0.385$	$p = 0.213$	$p = 0.251$	$p = 0.949$	$p = 0.086$
Low	46 (56.1)	23 (28.0)	37 (45.1)	29 (35.4)	8 (9.8)	47 (57.3)
Middle	32 (46.4)	13 (18.8)	22 (31.9)	17 (24.6)	6 (8.7)	48 (69.6)
High	17 (44.7)	8 (21.1)	13 (34.2)	9 (23.7)	4 (10.5)	29 (76.3)
Job profile [a]	**$p = 0.016$**	**$p = 0.011$**	$p = 0.225$	**$p = 0.030$**	$p = 0.171$	$p = 0.615$
Manual	57 (58.8)	30 (30.9)	41 (42.3)	35 (36.1)	12 (12.4)	62 (63.9)
Non-manual	38 (41.3)	14 (15.2)	31 (33.7)	20 (21.7)	6 (6.5)	62 (67.4)
Affected joint [a]	**$p = 0.007$**	$p = 0.625$	$p = 0.558$	**$p = 0.013$**	$p = 0.539$	$p = 0.101$
Hip	37 (40.2)	20 (21.7)	37 (40.2)	19 (20.7)	8 (8.2)	55 (59.8)
Knee	58 (59.8)	24 (24.7)	35 (36.1)	36 (37.1)	10 (10.9)	69 (71.1)
BMI categ. [a]	$p = 0.955$	$p = 0.056$	$p = 0.854$	**$p = 0.034$**	$p = 0.280$	$p = 0.104$
18.5–24.9 kg/m^2	14 (51.9)	11 (40.7)	10 (35.7)	4 (14.8)	2 (7.4)	21 (75.0)
25.0–29.9 kg/m^2	26 (49.1)	9 (17.0)	19 (35.8)	22 (41.5)	8 (15.1)	39 (73.6)
≥30.0 kg/m^2	55 (51.4)	24 (22.4)	43 (39.8)	29 (27.1)	8 (7.5)	64 (59.3)
WOMAC total score [b]	$p = 0.531$	$p = 0.077$	**$p < 0.001$**	$p = 0.351$	**$p = 0.041$**	$p = 0.086$
Users	148.00 ± 42.39	156.20 ± 44.17	160.72 ± 37.70	150.65 ± 36.69	166.00 ± 31.55	149.96 ± 43.39
Non-users	144.01 ± 45.03	142.92 ± 43.17	136.97 ± 44.74	144.11 ± 46.20	143.91 ± 44.28	138.49 ± 43.52

p values: [a] results of chi-square tests; [b] results of one-way ANOVA, comparing users of a given treatment with non-users. OTC: over the counter, NSAID: non-steroidal anti-inflammatory drug, Prescript. painkillers: prescription painkillers, Non-pharma: non-pharmacological methods, BMI categ: body mass index categories, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index. Significant *p*-values are highlighted in bold.

Table 9 Forward stepwise logistic regression analysis of factors associated with non-pharmacological pain management (last step).

Variable	OR (95% CI)	*p* Value
Gender (women)	2.894 (1.513–5.537)	**0.001**

OR: odds ratio, 95%; CI: confidence interval, 95%. Variables not entered in the model: age group, level of education, job profile, affected joint, BMI, WOMAC Total Score.

Table 10 Forward stepwise logistic regression analysis of factors associated with regular painkillers use (last step).

Variable	OR (95% CI)	*p* Value
Job profile (manual)	2.253 (1.231–4.121)	**0.008**
Affected joint (knee)	2.440 (1.334–4.464)	**0.004**

Variables not entered into the model: gender, age group, level of education, BMI, WOMAC Total Score. OR: odds ratio, 95% CI: confidence interval, 95%.

Table 11 Forward stepwise logistic regression analysis of factors associated with regular use of OTC NSAIDs (last step).

Variable	OR (95% CI)	*p* Value
Job profile (manual)	2.637 (1.270–5.479)	**0.009**
BMI categories		
25.0–29.9 kg/m^2	0.274 (0.093–0.806)	**0.019**
≥30.0 kg/m^2	0.387 (0.154–0.971)	**0.043**

Variables not entered in the model: gender, age group, level of education, affected joint, BMI reference category: 18.5–24.9 kg/m^2, WOMAC Total Score. OR: odds ratio, 95%; CI: confidence interval, 95%; OTC: over the counter; NSAID: non-steroidal anti-inflammatory drug; BMI: body mass index.

Table 12 Forward stepwise logistic regression analysis of factors associated with regular use of prescription medication (last step).

Variable	OR (95% CI)	*p* Value
WOMAC Total Score (continuous)	1.013 (1.006–1.021)	**<0.001**

Variables not entered into the model: gender, age group, level of education, affected joint, BMI. OR: odds ratio, 95%; CI: confidence interval, 95%; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

Table 13 Forward stepwise logistic regression analysis of factors associated with regular use of topical analgesic (last step).

Variable	**OR (95% CI)**	***p* Value**
Job profile (manual)	2.346 (1.183–4.651)	**0.015**
Affected joint (knee)	2.870 (1.403–5.871)	**0.004**
BMI categories		
25.0–29.9 kg/m^2	4.261 (1.232–14.746)	**0.022**
≥30.0 kg/m^2	1.656 (0.503–5.447)	**0.407**

Variables not entered in the model: gender, age group, level of education, WOMAC Total Score, BMI reference category: 18.5–24.9 kg/m^2. OR: odds ratio, 95%; CI: confidence interval, 95%; BMI: body mass index.

4.1.6. Assessment of drug-related GI risks

After assessing our population for possible GI risk, participants were put into 3 risk categories as shown on Table 14. OA patients were significantly more likely to be in a higher GI risk category compared to the control participants (p=0.002). However, we found that a significant number of participants was considered at moderate risk solely because of their age, thus an assessment was carried out excluding age as a risk factor, and putting more emphasis on the risk posed by medications. After the exclusion of age, this difference was even more significant (p=0.0004). Only 34.2% of responders reported taking either proton pump inhibitors or histamine H2-receptor antagonist.

Table 14 Number of patients in GI risk categories including and not including age as risk factor

	Low risk	**Moderate risk**	**High risk**	**Total**	**p Value**
Including age as a risk factor					**0.002**
Control	22	69	2	93	
OA patient	25	139	25	189	
Not including age as a risk factor					**<0.001**
Control	79	14	0	93	
OA patient	116	61	12	189	

OA: osteoarthritis, GI: gastrointestinal. Significant *p*-values, highlighted in bold. OA patients significantly higher likelihood to be in a higher GI risk category was calculated by Chi-square test. (Control n = 93; OA patients n = 189).

4.1.7. Surgery descriptives and preoperative joint status

Of the 189 surgeries, 92 were performed on hip joint, of which 22% were cemented and 78% uncemented. Of the 97 TKAs, in 12% of cases a high-flexion prosthesis was used. Two patients needed blood transfusion due to intraoperative blood loss, and in 94% of cases serosanguineous drainage from the wound was reported. Bacteria in the drainage, fever and dislocation was reported one time each. Reoperation was required in four cases: three for haematoma evacuation and one for repeated dislocation where the femoral component was changed. Leg length discrepancy was reported in two cases to the extent of 1 and 2 cm shortening, while 10 cm extension deficit was recorded in two cases. All patients received prophylactic antibiotic treatment. In the early rehabilitation framework, all patient received physiotherapy typically on the first postoperative day, on average, knee OA patient started on 1.3 days and hip patients 1.2 days after surgery.

ROM of a given joint is suitable indicator of the probability of disability. Only about half of knee OA patients had the necessary ROM for going up and down the stairs and standing up from a sitting position, a task that only 11% of hip OA patient had the needed ROM for (Table 15).

Table 15 Required ROM of knee and hip joint for everyday activities and the percentage of patients with the necessary ROM

Activity	Required ROM of knee[a], (% of knee OA patients)	Required ROM of hip[b], (% of hip OA patients)
Walking	67 (96)	50 (94)
Ascending stairs	99 (48)	68 (80)
Descending stairs	97 (50)	52 (92)
Sit to stand	99 (48)	103 (11)

ROM: range of motion, OA: osteoarthritis. Four daily activities, and the necessary flexion angle of the hip and knee joint in degrees that a patient needs to achieve in order to carry out said activity. ROM acquired from data from literature. The percentage of OA patients possessing the needed ROM in brackets [a] measured by Rowe et al [72], [b] measured by Sah [73].

4.1.8. Patients with hip dysplasia

Of the hip dysplasia patients (n=14), all were women with an average of 59.5 years (range: 40-80), and an average BMI of 29.8. Regarding their physical strain, four worked manual labour, three used to practice sport competitively (athletics; handball and running; ping pong and swimming). When comparing to the other hip OA patients, they were significantly younger (on average 10 years, $p<0.01$), half of them waited more, then 10 years for surgery, and yet needed more surgery done: five patients came for their first surgery, six for their second and one patient each for their third, fourth and fifth.

Supplementary questions were asked in order to gain a more in-depth view of this group. When asked about if they had a follow-up by a professional after their initial treatment, only one patient reported a follow up, one was advised how not to move the affected joint, one was advised on weight control and two were advised against a vaginal delivery in future pregnancies, further guidance was not noted. We asked them on their opinion on how could be the QOL of people with dysplasia improved. Continuous and personalised physiotherapy were to most frequent answer, regular follow up visits every year or every other year. The possibility of earlier surgery was noted as the patient stated "there is no need to wait for complete deterioration". One patient noted that her orthopaedic surgeon advised against vaginal delivery, but since according to her gynaecologist, her dysplasia would not affect the delivery, she gave birth vaginally, after which she found that the state of her hips started declining rapidly. A patient whose child was also born with dysplasia wished, that parents should be informed after the birth of their baby about the avoidance of contact sport or dances with heavy footwork, as well as about the recommendations for physiotherapy and regular swimming in case of hip dysplasia.

From the OA population, nine reported having a child born with dysplasia, typically treated with Pavlik harness, but only one mentioned any life-style advise given by their doctor.

4.2. Postoperative study

One year after surgery, we repeated the patient assessments. During follow-up, 69 patients failed to return the questionnaire, and so the postoperative study population consisted of 120 OA patients (Figure 6).

4.2.1. Postoperative QOL

4.2.1.1. General QOL (WHOQOL-BREF)

Detailed postoperative results of the questionnaire filled out by the 120 participants still in the study can be found in Supplementary Table 2. The introductory questions of WHOQOL-BREF demonstrated patients reporting a significant increase of the perceived QOL, where score increased from 3.30±0.84 to 3.58±0.69 (p=0.002) and of satisfaction with their health, the score of which rose from 3.03±0.84 to 3.31±0.70 (p=0.001) after surgery. QOL outcome results indicated that the patients had significantly better QOL compared to their previous state in the *physical health* and *social relationship domain*. On the other hand, the improvement in the *psychological domain* was negligible, which can be attributed to the fact that the baseline values of that domain were better than those of the other domains (Table 16).

Table 16 Pre- and postoperative results of the general QOL assessment

	WHOQOL-BREF		
	Preoperative data	**Postoperative data**	***p* Value**
	mean±SD	mean±SD	
Physical health domain	46.51±15.53	61.04±16.70	**<0.001**
Psychological domain	63.99±14.97	64.40±15.14	0.762
Social relationships domain	54.59±21.87	59.58±16.79	**0.012**
Environment domain	64.93±15.52	65.88±13.85	0.494

WHOQOL-BREF: World Health Organization Quality of Life Brief Version, SD: standard deviation. Significant *p*-values, highlighted in bold, *p*-values were determined using paired-samples *t*-test. (Preoperative sample, n = 189; postoperative sample, n = 120).

While all patients reported a significant increase of QOL in the WHOQOL-BREF *physical health domain*, sub-group analysis (Table 17) showed that younger patients (<65 years) reported significantly better outcomes compared to older ones (p=0.022). Patients in the manual job group reported significantly greater increase in the *physical* (p=0.008), and *psychological domains* (p=0.003) compared to the non-manual group. Regardless of the patients' gender, age, level of education, job profile, BMI, affected joint, or the presence of other diseases, a significantly better QOL scores were achieved in the *physical health* (p<0.001) and *social relationships domains* (ranging from p=0.033 to p=0.010) after the surgery.

Table 17. Sub-group analysis for preoperative and postoperative results of the general quality of life assessment

	WHOQOL-BREF											
	Physical health			Psychological			Social relationships			Environment		
	Preoperative	Postoperative	Sig.	Preoperative	Postoperative	Sig.	Preoperative	Postoperative	Sig.	Preoperative	Postoperative	Sig.
	mean±SD	mean±SD		mean±SD	mean±SD		mean±SD	mean±SD		mean±SD	mean±SD	
Gender			**$p_c<0.001$**			$p_c=0.77$			**$p_c=0.033$**			$p_c=0.459$
Male	45.92±15.04	64.49±17.02	$p_i=0.121$	66.68±14.51	67.11±15.57	$p_i=0.99$	56.46±21.84	59.95±16.34	$p_i=0.610$	65.46±14.65	67.00±14.55	$p_i=0.772$
Female	46.77±15.82	59.51±16.42		62.80±15.10	63.19±14.88		53.76±21.96	59.41±17.09		64.70±15.98	65.37±13.58	
Age groups			**$p_c<0.001$**			$p_c=0.548$			$p_c=0.102$			$p_c=0.477$
<65	44.87±16.62	66.13±15.91	**$p_i=0.022$**	65.97±16.21	67.97±15.42	$p_i=0.487$	62.94±22.47	63.87±16.43	$p_i=0.222$	67.45±14.68	68.84±11.83	**$p_i=0.036$**
≥65	47.08±15.19	59.27±16.68		63.30±14.55	63.16±14.92		51.69±21.01	58.08±2.59		64.06±15.79	64.84±14.40	
Level of education			**$p_c<0.001$**			$p_c=0.900$			**$p_c=0.024$**			$p_c=0.528$
Lower	42.45±13.15	59.59±15.74		61.32±13.57	63.95±14.72		51.30±20.23	58.77±16.63		63.98±15.96	64.98±13.66	
Middle	49.09±15.68	60.60±17.20	$p_i=0.371$	63.27±2.27	63.18±15.58	$p_i=0.387$	54.00±19.22	59.73±16.15	$p_i=0.351$	63.29±14.40	64.53±12.68	$p_i=0.973$
Higher	48.52±2.68	63.74±17.48		68.84±2.69	66.81±15.28		60.13±26.81	60.48±18.38		68.68±16.33	69.10±15.57	
Job profile			**$p_c<0.001$**			$p_c=0.541$			**$p_c=0.010$**			$p_c=0.446$
Manual	41.44±13.93	61.02±16.50	**$p_i=0.008$**	60.83±13.50	65.56±13.74	**$p_i=0.003$**	51.98±20.90	58.43±17.57	$p_i=0.500$	62.91±15.15	65.11±14.18	$p_i=0.408$
Non-manual	50.65±15.64	61.06±16.98		66.58±2.50	63.45±16.23		56.73±22.56	60.52±16.21		66.59±15.74	66.50±13.65	
Affected joint			**$p_c<0.001$**			$p_c=0.852$			**$p_c=0.014$**			$p_c=0.504$
Knee	50.75±15.64	61.45±17.78	**$p_i=0.038$**	66.52±15.63	64.37±15.28	$p_i=0.075$	56.71±22.59	60.50±17.54	$p_i=0.568$	65.70±17.11	66.38±13.78	$p_i=0.859$
Hip	42.80±14.56	60.69±15.81		61.78±14.13	64.42±15.13		52.73±21.21	58.77±16.20		64.27±14.10	65.44±14.00	
Comorbidity			**$p_c<0.001$**			$p_c=0.884$			$p_c=0.099$			$p_c=0.721$
Reported	42.00±14.36	55.10±15.73	$p_i=0.636$	62.20±12.79	60.70±16.37	$p_i=0.414$	56.67±19.93	57.93±15.44	$p_i=0.273$	65.93±12.01	62.37±15.19	$p_i=0.057$
Not reported	48.01±15.69	63.02±16.62		64.59±15.65	65.63±14.59		53.90±22.54	60.12±17.27		64.60±16.58	67.04±13.25	
BMI category			**$p_c<0.001$**			$p_c=0.467$			**$p_c=0.014$**			$p_c=0.960$
18.5–24.9	44.12±15.96	62.18±18.03		59.71±11.27	61.18±17.26		53.65±21.15	61.06±14.58		67.12±9.69	64.06±10.46	
25.0–29.9	46.97±16.23	63.22±16.91	$p_i=0.479$	64.47±14.39	67.89±14.23	$p_i=0.262$	53.44±22.47	59.17±19.11	$p_i=0.816$	66.92±16.37	68.72±16.26	$p_i=0.497$
≥30.0	46.87±15.23	59.58±16.35		64.82±16.06	63.34±14.93		55.45±22.01	59.42±16.20		63.31±16.23	64.81±13.13	

p_c: p value for the entire group's change e.g. gender and physical health; p_i: p value of sub-group interaction, e.g. male vs female and physical health. P-values were determined using mixed-design two-way repeated measures ANOVA. Significant p-values, highlighted in bold.

4.2.1.2. Disease-specific QOL (WOMAC)

Disease-specific QOL outcome results indicated that overall, patients gained significantly better QOL in all domains of the WOMAC score (Table 18). Detailed postoperative results of the questionnaire can be found in Supplementary Table 4.

Table 18 Pre- and postoperative results of the disease-specific QOL assessment

	WOMAC		
Domain	**Preoperative data**	**Postoperative data**	***p* Value**
	mean±SD	mean±SD	
Pain	57.03±21.87	28.09±20.87	**<0.001**
Stiffness	59.08±21.28	29.71±22.59	**<0.001**
Physical function	61.26±18.06	34.01±20.61	**<0.001**
Total score	60.19±17.57	32.39±19.84	**<0.001**

WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index SD: standard deviation. Significant *p*-values, highlighted in bold, were determined using paired-samples *t*-test. (Preoperative sample, n = 189; postoperative sample, n = 120).

In the sub-group analysis (Table 19), participants from the younger age-group (<65) reported significant decrease in joint *stiffness* (p=0.005), and overall, a better disease-specific QOL (p=0.05). Patients in the manual group reported significantly greater increase in *physical function* (p=0.037) and overall score (p=0.024) compared to the non-manual group. Patients with hip OA seemed to gain the most out of their operation as they reported better outcome in the WOMAC *pain* (p=0.019), *stiffness* (p=0.010), *physical function domains* (p=0.011) and total score (p=0.007) compared to knee OA patients. Participants who reported no comorbidities had significant decrease of joint *stiffness* compared to comorbid patients (p=0.010). Regarding the connection of BMI and QOL, normal weight and overweight patients reported a significant decrease in their *pain* compared to obese patients (p=0.017). Among knee OA patients, the model of the prosthesis (high-flexion or conventional) had no effect on the HRQOL.

Total WOMAC score indicated significantly better disease-specific QOL after the surgery in all subgroups, regardless of the patients' gender, level of education, BMI category or the presence of other diseases (p<0.001).

Table 19. Sub-group analysis for preoperative and postoperative results of the disease-specific quality of life assessment

	WOMAC											
	Pain			**Stiffness**			**Physical function**			**Total score**		
	Preoperative	Postoperative	Sig.	Preoperative	Postoperative	Sig.	Preoperative	Postoperative	Sig.	Preoperative	Postoperative	Sig.
	mean±SD	mean±SD		mean±SD	mean±SD		mean±SD	mean±SD		mean±SD	mean±SD	
Gender			**$p_c<0.001$**			**$p_c<0.001$**			**$p_c<0.001$**			**$p_c<0.001$**
Male	55.56±22.97	26.67±20.87	$p_i=0.988$	61.62±21.64	27.16±20.09	$p_i=0.228$	60.91±17.49	32.80±22.13	$p_i=0.813$	59.98±17.56	30.84±21.23	$p_i=0.714$
Female	57.70±21.47	28.73±20.97		57.93±21.15	30.85±23.66		61.42±18.41	34.56±20.02		60.28±17.68	33.08±19.28	
Age groups			**$p_c<0.001$**			**$p_c<0.001$**			**$p_c<0.001$**			**$p_c<0.001$**
<65	58.65±19.97	24.39±19.13	$p_i=0.244$	65.97±20.22	23.39±18.64	**$p_i=0.005$**	63.45±16.85	28.18±17.08	$p_i=0.050$	62.66±16.40	26.99±16.70	**$p_i=0.050$**
≥65	56.45±22.61	29.44±21.42		56.65±21.23	31.93±23.52		60.50±18.49	36.05±21.42		59.29±17.97	34.34±20.54	
Level of education			**$p_c<0.001$**			**$p_c<0.001$**			**$p_c<0.001$**			**$p_c<0.001$**
Lower	63.81±24.16	31.19±22.05		63.98±24.63	32.61±25.71		68.60±17.35	38.26±21.16		67.40±17.96	35.75±21.02	
Middle	52.82±19.16	26.14±20.17	$p_i=0.604$	55.67±18.11	27.44±20.77	$p_i=0.866$	59.24±14.47	32.16±20.05	$p_i=0.514$	57.37±14.22	30.58±18.90	$p_i=0.445$
Higher	53.73±20.56	26.60±20.37		57.00±19.68	28.83±20.50		53.78±20.29	30.66±20.26		54.31±18.66	30.39±19.54	
Job profile			**$p_c<0.001$**			**$p_c<0.001$**			**$p_c<0.001$**			**$p_c<0.001$**
Manual	62.12±23.82	28.35±20.41	$p_i=0.114$	63.80±23.63	29.26±23.16	$p_i=0.096$	67.81±15.71	34.99±19.79	**$p_i=0.037$**	66.42±16.70	32.56±19.37	**$p_i=0.024$**
Non-manual	52.91±19.37	27.88±21.40		55.15±18.39	30.08±22.28		55.90±18.18	33.22±21.37		55.20±16.74	32.25±20.35	
Affected joint			**$p_c<0.001$**			**$p_c<0.001$**			**$p_c<0.001$**			**$p_c<0.001$**
Knee	56.48±23.07	34.41±23.54	**$p_i=0.019$**	58.04±20.51	36.95±25.11	**$p_i=0.010$**	59.84±17.84	39.14±23.44	**$p_i=0.011$**	58.85±17.57	37.96±22.78	**$p_i=0.007$**
Hip	57.52±20.95	22.58±16.55		60.00±22.07	23.25±17.94		62.50±18.29	29.53±16.71		61.37±17.62	27.45±15.36	
Comorbidity			**$p_c<0.001$**			**$p_c<0.001$**			**$p_c<0.001$**			**$p_c<0.001$**
Reported	59.93±20.47	36.97±25.09	$p_i=0.209$	54.14±21.38	37.59±27.21	**$p_i=0.010$**	61.98±18.73	39.63±23.21	$p_i=0.245$	61.38±17.85	39.87±22.49	$p_i=0.136$
Not reported	56.07±22.34	25.13±18.50		60.67±21.12	27.17±20.42		61.02±17.93	32.14±19.45		59.79±17.56	29.92±18.36	
BMI category			**$p_c<0.001$**			**$p_c<0.001$**			**$p_c<0.001$**			**$p_c<0.001$**
18.5–24.9	66.11±19.35	22.82±17.90		55.00±21.29	25.88±20.93		58.27±22.96	28.27±15.23		59.63±20.13	26.94±15.46	
25.0–29.9	55.06±22.94	20.75±14.96	**$p_i=0.017$**	61.43±19.95	22.71±17.63	$p_i=0.088$	61.68±16.20	27.84±17.83	$p_i=0.127$	60.29±16.77	25.44±15.42	$p_i=0.074$
≥30.0	55.67±21.69	32.93±22.79		58.88±22.08	34.33±24.38		61.79±17.84	38.79±22.11		60.27±17.54	37.20±21.52	

p_c: p value for the entire group's change e.g. gender and pain; p_i: p value of sub-group interaction, e.g. male vs female and pain. P-values were determined using mixed-design two-way repeated measures ANOVA. Significant p-values, highlighted in bold.

4.2.2. Changes in pain management

After the surgery, patients reported a considerable, in many categories significant decrease in their analgesic medication consumption (Table 20). Only 10 patients kept taking oral NSAID on a regular basis. Regarding GI risk, nine patients could be considered at moderate risk and one at high risk when age was considered a risk factor, however, excluding age, five patients were regarded as low and five as a moderate chance for GI complication. Regular use of either proton pump inhibitors or histamine H2-receptor antagonist decreased from 34.2% to 30%. After surgery 50% of responders took supplements for bone and cartilage health daily.

Table 20 Changes in the use of different pain management methods used by osteoarthritis patients before and after surgery

	n (%)		
	Preoperative	**Postoperative**	***p* Value**
Total painkiller use	60 (50.8)	35 (29.2)	**<0.001**
Regular OTC oral NSAID	27 (23.3)	10 (8.3)	**0.005**
Topical NSAID cream/gel/patch	37 (30.8)	15 (12.5)	**0.001**
Prescription medication	47 (39.2)	16 (13.3)	**<0.001**
Oral opioid-containing medication	8 (6.7)	5 (4.2)	0.549
Topical herbal cream	25 (20.8)	10 (8.3)	**0.009**
Non-pharmacological methods	76 (64.2)	83 (69,2)	0.381

OTC: over the counter, NSAID: non-steroidal anti-inflammatory drug. Significant *p*-values, highlighted in bold, P-values were determined using paired-samples *t*-test. Preoperative sample, n = 189; postoperative sample, n = 120.

4.2.3. Surgical outcomes

When patients were asked to rate their satisfaction with their surgery on a scale of 1-10, an average of 8 points (SD=3) was recorded. Using a visual analogue scale (VAS), pain was measured three times, prior to surgery, directly after surgery and one year after surgery, mean VAS results were 8.16, 3.39 and 2.54 respectively. Patients reported a significant decrease in their pain overall ($p<0.001$), with the biggest improvement noted between the first and second measures, while the improvement between the second and third measures was also significant, although for a lesser extent ($p<0.01$). Changes in joint kinetics are depicted in Table 21. After surgery, a significant increase in flexion muscle strength, active flexion angle and ROM was measured for both knee OA and hip OA groups, but also a significant extension deficit. Hip OA patients were recorded a significant increase in passive flexion as well in contrast with the decrease in ROM of knee patients. ROM in the frontal plane (abduction-addiction) also increased significantly for hip OA patients.

Table 21 ROM and muscle strength of OA patients before and after surgery

	Hip OA mean degree±SD			
	Healthy joint	**Preoperative**	**Postoperative**	***p* Value**
ROM (flexion-extension)	140	82.10±19.13	89.03±2.84	**0.005**
Passive flexion	130-140	78.13±19.50	89.69±1.77	**0.002**
Active flexion	110-120	55.76±10.54	88.48±3.64	**<0.001**
Extension	10-15	9.03±7.79	0.65±2.50	**<0.001**
Abduction	30-45	14.56±4.98	29.12±5.96	**<0.001**
Adduction	20-30	1.43±3.78	4.29±4.50	0.321
External Rotation	40-50	2.86±7.56	2.86±5.67	1.000
Internal Rotation	30-40	1.43±3.78	0.29±0.76	0.476
Flexion Muscle Strength	5/5	2.92±0.28	3.69±0.48	**<0.001**
Extension Muscle Strength	5/5	2.77±0.44	3.77±0.44	*
Abduction Muscle Strength	5/5	2.08±0.29	3.08±0.29	*

	Knee OA mean degree±SD			
	Healthy joint	**Preoperative**	**Postoperative**	***p* Value**
ROM (flexion-extension) knee	145	95.56±15.75	90.09±5.18	**0.009**
Passive flexion	120-150	92.50±10.76	90.36±1.89	0.297
Active flexion	120-135	57.67±19.36	88.50±5.44	**<0.001**
Extension	5-10	10.58±15.12	1.54±3.09	**0.005**
Flexion Muscle Strength	5/5	2.67±0.49	3.53±0.52	**0.001**
Extension Muscle Strength	5/5	2.60±0.51	3.60±0.51	*

*The correlation and t cannot be computed because the standard error of the difference is 0
ROM: range of motion, OA: osteoarthritis.
Significant *p*-values, highlighted in bold, p-values were determined using paired-samples *t*-test. Preoperative sample, n = 189; postoperative sample, n = 120.

5. Discussion

The aim of our study was to examine the effects of OA on the patients' QOL, how they manage their pain and if their pain management is in line with recommendations. We evaluated what sociodemographic and lifestyle factors could be associated with how patients rate their QOL or which pain management method they use. After a one year waiting period, ensuring that patients had the time to heal and go through rehabilitation, we surveyed our participants again to examine the surgery's effect on both QOL and a possibly reduced need for painkillers. Lastly, we explore in which levels of prevention could our results be used.

5.1. QOL outcomes

One of our major aims was to investigate the general and disease-specific QOL of osteoarthritic patients before and after surgery, and whether surgery would result in significant improvement. As reported by Yildiz et al. (2010), domains related to physical health status show relatively lower scores as compared with psychological components in patients before surgery [74]; this result is consistent with our results.

In case of general QOL, OA patients reported a significantly lower QOL in the *physical health domain* compared to the control group, and a borderline significance was detected in the *social relationships domain*, which can be associated with a decrease of social interactions that stems from pain and disability, which has a more significant impact on the elderly population. A significant negative correlation with pain and social domain was recognised by Wojcieszek et al. (2022) as well [75]. After the surgery, patients' perceived QOL improved significantly, as well as their satisfaction with their health. Our results indicated statistically significant improvement in all domains concerning physical functions in the patient population as well as in the domain of *social relationships*, indicating a restored social connectedness. The improvement in the *psychological domain* was negligible except for patients with a manual job, which can be attributed to the known beneficial health effects of returning to work [76]. While all patients reported a significant increase of QOL in the WHOQOL-BREF *physical health domain*, younger patients and those with manual jobs reported the most gains.

Generic measures might reveal effects of the surgery in the long run, but disease-specific measures are considered to be more accurate for assessing immediate effects, as observed by Neuprez et al. [77].

In this study, we investigated the possible role of independent variables in the disease-specific disability functional assessment performed using the WOMAC questionnaire. According to our results, patients with hip OA seemed to gain the most out of their operation, as they reported better outcome in the WOMAC *pain*, *stiffness*, *physical function domains* and total score compared to knee OA patients. A similarly significant improvement was measured among patients of the working age group (<65 years) compared to the older patients and with manual jobs compared to non-manual workers. As the latter group is heavily exposed to the degeneration of cartilage because of their profession, it is a significant achievement that they can benefit from the surgery to this extent. The success of the surgery among the working age population indicates that many of them may be able to return to their job actively, thus decreasing the economic burden of OA.

Our results regarding the effect of the surgery on QOL outcomes are consistent with other studies. Papakostidou et al. (2012) found that after TKA, all groups of patients showed a statistically significant improvement in WOMAC domains between the pre- and the 12-month postoperative assessments, and there have been no significant differences in WOMAC domains in age, BMI, education and gender [78].

On the contrary, other studies have shown opposite results regarding the effect of gender and BMI. In a pooled analysis of 1783 knee and 2400 hip OA patients, Hofstede et al. (2018) have reported that being female or having higher BMI are associated with lower postoperative HRQOL and functioning and more pain [79]. Alkan et al. (2014) have also found that WOMAC pain scores are higher in female patients; however, we found no difference between the two genders either before or after surgery [80]. It has been reported that over 50% of the patients who required TKA for end-stage OA are obese [81], a ratio that we experienced as well. However, we saw no difference in improvement by BMI category either in the generic or in the disease specific QOL.

Even though the success of joint replacement surgery is indisputable, additional therapies have been shown to boost its efficacy. The results of a study by Desmeules et al. (2013) suggest that the prehabilitation programme not only can alter the physical decline caused by OA, but it can help participants to improve their level of function before surgery as well, which is an important achievement in view of the fact that preoperative physical function is a major determinant of postoperative physical function [82,83].

Although we did not detect a significant difference of QOL outcomes between patients with hip dysplasia and the rest of the hip OA population, that fact that dysplasia patients were significantly younger and went under a higher number of surgeries indicates the risk this joint abnormality represents. There was though a significantly better QOL domain, where hip dysplasia patients reported a better score, which was the *social relationship domain* of the WHOQOL-BREF, but we attributed this to the younger age of the members of the group. When patients with dysplasia were asked for their opinion on how to prevent the early onset of OA, on participant voiced her concern about what effect pregnancy and the birthing process may have on their joints and vice a versa. Hip dysplasia by itself is not associated with increased difficulty with normal delivery. With hip dysplasia the socket itself is shallow, but the internal borders of the pelvis have normal size and shape and so, it is very uncommon for hip dysplasia or hip dysplasia surgery to be a problem for delivery [84].

5.2. Pain management

Another major aim was to investigate osteoarthritic patients' habits of pain management and to examine the explanatory factors of various ways of self-treatment. OA is a disease for which pain is a main characteristic. Accordingly, patients in the current study utilized a wide variety of pain management technics. The majority of patients practiced a non-pharmacological method, with women in particular favouring it, while pharmacological methods were chosen by patients doing manual labour. Although more weight puts more strain on the joint, contrary to expectations, patients with higher BMI were less likely to take OTC NSAIDs.

A total of 23.3% of patients took OTC NSAIDs regularly. This is in line with the results (26.5%) from the 2011 Five European Countries National Health and Wellness Survey, as reported by Kingsbury et al. (2014) [85]. Our results for prescription medication use (38.1%) and paracetamol (1.0%) were comfortably within the range of the survey's result of 33.0–53.2% and 0–6.0%, respectively. On the other hand, we experienced two major differences. On average, the use of opioid medications and COX-2 inhibitors was higher in the participating countries (France, Germany, Italy, Spain, and the UK) with 35.6% and 6.6%, compared to our results, 6.9% and 0.5%, respectively [86]. This infrequent use of paracetamol can be seen throughout Europe, barring the Nordic countries, where it is highly favoured. Results showing that diclofenac and ibuprofen were the most-used active ingredients by our sample also correspond with results from European and Asian countries [86-88]. A total of 38.1% of patients used prescription medication; we can only hope that this fraction of the patient population was under the care of a specialist. It is, however, obviously important to assess also those who take NSAIDs on their own accord since the lack of professional supervision increases the chance of the complications that arise from self-medication, either by drug abuse or lack of mucosa protection. Medicines preferred by patients are a cause for concern, with diclofenac being the most popular but COX-2 inhibitors being neglected, as a study by Massó González et al. (2010) showed that the relative risk of upper GI bleeding/perforation was 4.50 for traditional NSAIDs, and 3.98 for diclofenac specifically, but only 1.88 for coxibs [89].

The distribution of active ingredients indicates that patients tend to use well-known pain medications even if their side effect profiles are less desirable. But questions arise even in case of professionally recommended medications, as some guidelines warn against the use of the previously favoured paracetamol, recommending it only conditionally, and stressing the importance of personalised therapies [90]. Knee OA patients were significantly more likely to use topical analgesics, which on one hand can be attributed to the fact that the knee joint is easier to reach and the active ingredients absorbed through the skin reach the site of pain more efficiently, but also knee OA patients had significantly higher BMIs compared to hip OA patients, and as the influencing factor assessment showed, patients with higher BMIs were over four times more likely to use topical analgesics compared to those with normal BMIs. Since hip OA patient with higher BMIs did not use more topical painkillers compared to those with lower BMIs, it seems that the fact that the knee joint is affected contributes more to the use of topical painkillers than BMI. The fact that only 29.1% of patients used topical analgesics is also a possible indicator that many patients managed their pain by themselves, even though professional guidelines (e.g., that of the ACR) favour topical drugs over oral medication as a way to decrease harmful GI side-effects [91]. It would be worth paying particular attention to hip OA patients who seem to prefer oral painkillers.

The importance of using topical analgesics cannot be overemphasised, given the advanced age of our patients, the high risk of co-morbidities, and the additional drug use associated with these conditions involving the risk of potential drug interactions. Beyond the well-known GI side effects caused by NSAIDs, with diclofenac being the most favoured OTC painkiller, the possibility of adverse cardiovascular events must not be over-looked. Schmidt et al. (2018) found that people taking diclofenac had a 20% increased rate for a major adverse cardiovascular event, such as a myocardial infarction, compared to patients taking paracetamol, and 30% compared to those who took naproxen [92].

Our study also showed high prevalence of the use of non-pharmacological techniques, which is fortunate, although typically limited to herbal creams, cold compressions, and in one case, warm baths, as Hungary has a long history of balneotherapy [93]. Although pain management methods that could be carried out by the patients themselves seem to be popular, unfortunately the prevalence of professionally guided physiotherapy was low compared to other studies [88,94]. Although 31.2% of patients reported doing exercise, it was practiced as a way of weight management. As 57.1% of patients were over-weight and BMI was identified in this study as a risk factor, we wish to emphasise the systematic integration of weight management into the OA therapy course because obesity is suggested to be the main modifiable risk factor of OA [95]. A comprehensive and individualised plan for management of OA should therefore include educational, behavioural, psychosocial, and physical interventions, as well as topical, oral, and intraarticular medications [86]. We also wish to highlight the importance of preoperative physiotherapy. Unfortunately, patients are not routinely referred to physiotherapy within a year before surgery, even though studies showed that among patients who received preoperative physiotherapy a significant improvement was found for active and passive rotation, pain, daily functioning, vitality, psychological health, and social life [96].

For both hip and knee OA, the core treatments are exercise, education, mechanical interventions, and weight loss [97]. Given how few of our patients do exercise or receive physiotherapy, the question arises as to how much information patients have about non-pharmacological therapies. Because of this, we would like to encourage both general practitioners and specialists to recommend the following techniques to their patients taking their current condition into account. Manual therapy [98,99], transcutaneous electrical nerve stimulation, [100,101] and knee braces [102,103] are proven to reduce pain, the latter having the additional benefit of reducing knee instability, and they can also be effective when there is a valgus or varus deformity. To compensate for decreased muscular strength, resistance [104] and neuromuscular exercise [105] have been shown to be effective. Specifically for patients with hip OA, Nordic walking was found to build muscle strength and has been shown to be effective for weight loss, thus providing further benefits for OA patients [106,107].

In order to help patients maintain their exercise programmes, group-mediated cognitive behavioural physical activity intervention is advised [108].

By postponing non-urgent elective surgery during the COVID-19 pandemic, waiting times increased and the number of operations decreased. Compared to 2019, the median number of days on the waiting list before surgery increased by 88 days for TKA and by 58 days for THA in 2020 [109]. In this situation, a further increase in self-medication by patients can be expected; thus, the responsibility of general practitioners in pain management has increased significantly. It is highly important that physicians are up to date on their new OA patients' pain management habits so as to monitor habitual painkiller use and for their long-time patients to keep them updated with the current guidelines. The National Health Service Greater Glasgow and Clyde's Guidelines for the management of chronic non-malignant pain intends to assist healthcare professionals in the choice of disease-specific treatments focusing on supporting self-management through five steps: Initial Assessment, Formulating a Pain Management Plan, Self-Management Strategies, Pharmacological Management Strategies, and Follow-up and Annual Referral if Indicated [110].

Regarding the surgeries, our data shows a high satisfaction rate and an overall success indicated by not only the significant increase in QOL, but the considerable decrease in painkiller consumption, which fortunately was also followed by the reduced GI risk. The improvement in muscle strength and ROM was detectable right after surgery, barring the angel of extension for both joints, which can be expected as oedema and haematoma frequently appear after the intervention, as well as the joints are in a 20° flexion angle resting position post-surgery.

5.3. Prevention

Although, many patients and even some health-care providers tend to treat OA in a very passive way by waiting till the affected joint necessitates replacement surgery, all levels of prevention can be utilized to a certain degree.

As OA has various modifiable risk factors, takes a long period of time to manifest and its symptoms worsens gradually, there are ample opportunities for primary prevention. With the lack of approved DMOADs, our focus should be on preventing the onset and slowing down the disease progression by tackling modifiable risk factors. Based on our results and literature data, the most important risk factors that should be managed are: 1) obesity, 2) physically taxing jobs and 3) impaired muscle function.

While addressing obesity in osteoarthritis, healthy diet and physical activity is paramount (keeping sport injury prevention in mind). It is important to consider that weight gain is typically accelerated during early adulthood [111], and that interventions for weight reduction have been more successful at an individual level and less so at the population level [112]. Patients working physically demanding jobs are more likely to suffer from OA, but occupation should be considered as a semi-modifiable risk factor, as not all phases of these works can be automated. Despite this, through occupational health services workers should receive education on both joint-friendly techniques they could use during work and injury prevention. The problem of impaired muscle function can be managed by regular exercise in general and with prehabilitation when the patients are preparing for surgery, although it should be noted that prehabilitative physiotherapy is not available at every hospital.

Regarding secondary prevention, OA is not typically known to be screened similarly to other disease such as cancer, however, screening and treatment of hip dysplasia is critical in reducing the risk of the later development of OA.

Tertiary prevention methods can be utilized in order to limit or delay complications. Based on our results concerning patients' habit of self-medication and risks arising from it, it is clear that OA patients need guidance on safe pain management methods, which presents an opportunity to improve patient education.

Beyond academic research, we wished for the patients to benefit from this study, and so a series of patient information material is under development, which will be available at GP's and specialists' offices as well, which hopefully will benefit the Hungarian OA patients despite the fact that so far Hungary has no national action plan in contrast with countries such as Australia [113] and the US [114].

5.4. Limitations of study

As data collection was carried out by self-administered questionnaires, inaccuracies in patients' memories have the potential to distort our data. Although this study was carried out in two different health centres, findings may not be generalizable to the overall population since the population was not very large, only representing part of the country, and only consisting of severe OA patients. The limitations of our study are consistent with the nature of observational studies and the bias on patient selection, for which we tried to correct by selecting a large number of participants from two different counties of the country and enrolling consecutive patients.

6. Summary and conclusion

I. In comparison to the control group, OA patients reported a significantly decreased QOL in all facets of physical health and functions, and a considerably lower score in the *social relationships domain*, indicating how reduced mobility can affect interpersonal connections, especially among the elderly population. Patients with hip OA or working manual jobs were the most affected. Postoperative QOL outcome results indicated a significant improvement in physical functions and social relationships in the study population.

   a. According to our results, patients with hip OA, manual jobs and of the working age group seemed to gain the most out of their operation, suggesting that many of them may be able to return to their job actively, thus decreasing the economic burden of OA. Even though obesity is a major risk factor, BMI had no effect on the disease specific QOL in this study.

   b. Compared to the other hip OA patients, participants with hip dysplasia were significantly younger, and had more hip surgery in their history, despite that, only one patient indicated regular follow-up with a specialist. As hip dysplasia shortens the time for OA to develop, these patients must be treated as vulnerable population, receiving regular consultancy.

II. Patients tended to use well-known pain medications even if their side effect profiles were less desirable. While knee OA patients favoured topical analgesics, hip OA patients seemed to prefer oral painkillers. Women favoured non-pharmacological techniques, while pharmacological methods were chosen by patients doing manual labour. After the surgery, patients reported a considerable decrease in their analgesic medication consumption.

   a. Prior to operation, OA patients were significantly more likely to be in a higher GI risk category compared to the control participants, but the decrease of analgesic consumption after surgery was followed by the decrease of risk of developing a drug-related GI complication.

III. In order for patients to benefit from this study, a series of patient information material is under development, which will be available at GP's and specialists' offices as well, which hopefully will benefit the Hungarian OA patients.

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9. Supplementary materials

Supplementary Table 1. Descriptive statistics of the preoperative WHOQOL-BREF results

	Domain	n	Min.	Max.	Mean	SD
1. How would you rate your quality of life?	n.a.	189	1	5	3.25	0.90
2. How satisfied are you with your health?	n.a.	189	1	5	2.98	0.86
3. To what extent do you feel that (physical) pain prevents you from doing what you need to do?	Phys	189	1	5	3.68	0.80
4. How much do you need any medical treatment to function in your daily life?	Phys	189	1	5	2.65	1.11
5. How much do you enjoy life?	Psy	184	1	5	3.28	0.93
6. To what extent do you feel your life to be meaningful?	Psy	186	1	5	3.62	0.86
7. How well are you able to concentrate?	Psy	188	2	5	3.70	0.66
8. How safe do you feel in your daily life?	Env	188	1	5	3.45	0.80
9. How healthy is your physical environment?	Env	186	1	5	3.60	0.81
10. Do you have enough energy for everyday life?	Phys	188	1	5	3.42	0.91
11. Are you able to accept your bodily appearance?	Psy	189	1	5	3.71	0.99
12. Have you enough money to meet your needs?	Env	172	1	5	3.40	1.07
13. How available to you is the information that you need in your day-to-day life?	Env	187	1	5	4.05	0.98
14. To what extent do you have the opportunity for leisure activities?	Env	188	1	5	3.20	1.21
15. How well are you able to get around?	Phys	189	1	5	2.36	0.97
16. How satisfied are you with your sleep?	Phys	186	1	5	3.02	1.09
17. How satisfied are you with your ability to perform your daily living activities?	Phys	186	1	5	3.26	0.85
18. How satisfied are you with your capacity for work?	Phys	188	1	5	2.81	0.96
19. How satisfied are you with yourself?	Psy	188	1	5	3.35	0.85
20. How satisfied are you with your personal relationships?	Soc	187	1	5	3.91	0.78
21. How satisfied are you with your sex life?	Soc	111	1	5	3.17	1.26
22. How satisfied are you with the support you get from your friends?	Soc	182	1	5	3.88	0.87
23. How satisfied are you with the conditions of your living place?	Env	187	1	5	3.87	0.85
24. How satisfied are you with your access to health services?	Env	189	1	5	3.48	1.02
25. How satisfied are you with your transport?	Env	189	1	5	3.42	1.12
26. How often do you have negative feelings such as blue mood, despair, anxiety, depression?	Psy	189	1	5	2.37	0.95

Domains (Phys: Physical health, Psy: Psychological health, Env: Environment, Soc: Social relationships), n.a.: not applicable, the two introductory questions are not part of either domain

Supplementary Table 2. Descriptive statistics of the postoperative WHOQOL-BREF results

	Domain	n	Min.	Max.	Mean	SD
1. How would you rate your quality of life?	n.a.	120	2	5	3.58	0.69
2. How satisfied are you with your health?	n.a.	120	2	5	3.31	0.70
3. To what extent do you feel that (physical) pain prevents you from doing what you need to do?	Phys	120	1	4	2.73	0.91
4. How much do you need any medical treatment to function in your daily life?	Phys	120	1	4	1.89	0.95
5. How much do you enjoy life?	Psy	120	1	5	3.33	0.77
6. To what extent do you feel your life to be meaningful?	Psy	120	1	5	3.47	0.93
7. How well are you able to concentrate?	Psy	120	2	5	3.66	0.70
8. How safe do you feel in your daily life?	Env	120	2	5	3.38	0.70
9. How healthy is your physical environment?	Env	119	2	5	3.55	0.71
10. Do you have enough energy for everyday life?	Phys	120	2	5	3.58	0.85
11. Are you able to accept your bodily appearance?	Psy	120	1	5	3.80	0.95
12. Have you enough money to meet your needs?	Env	119	2	5	3.51	0.92
13. How available to you is the information that you need in your day-to-day life?	Env	120	2	5	4.14	0.85
14. To what extent do you have the opportunity for leisure activities?	Env	120	1	5	3.36	1.13
15. How well are you able to get around?	Phys	119	1	5	3.30	1.05
16. How satisfied are you with your sleep?	Phys	120	1	5	3.23	0.97
17. How satisfied are you with your ability to perform your daily living activities?	Phys	120	1	5	3.37	0.78
18. How satisfied are you with your capacity for work?	Phys	120	1	5	3.13	0.90
19. How satisfied are you with yourself?	Psy	120	1	5	3.47	0.78
20. How satisfied are you with your personal relationships?	Soc	120	2	5	3.84	0.70
21. How satisfied are you with your sex life?	Soc	114	1	5	2.87	1.08
22. How satisfied are you with the support you get from your friends?	Soc	119	1	5	3.62	0.92
23. How satisfied are you with the conditions of your living place?	Env	120	2	5	3.85	0.72
24. How satisfied are you with your access to health services?	Env	120	1	5	3.25	1.06
25. How satisfied are you with your transport?	Env	120	1	5	3.57	1.03
26. How often do you have negative feelings such as blue mood, despair, anxiety, depression?	Psy	120	1	5	2.28	0.85

Domains (Phys: Physical health, Psy: Psychological health, Env: Environment, Soc: Social relationships), n.a.: not applicable, the two introductory questions are not part of either domain

Supplementary Table 3. Descriptive statistics of the pre-operative WOMAC results

	n	Min.	Max.	Mean	SD
1.Pain – walking	189	1	10	5.94	2.66
2. Pain – stair climbing	189	1	10	6.68	2.86
3. Pain – at night in bed	189	1	10	5.25	2.92
4. Pain – sitting or lying	189	1	10	4.81	2.85
5. Pain – standing upright	189	1	10	6.55	2.80
1. Stiffness in the morning	189	1	10	6.24	2.47
2. Stiffness during the day	189	1	10	5.72	2.45
1. Difficulty – descending stairs	189	1	10	6.51	2.80
2. Difficulty – ascending stairs	189	1	10	6.86	2.64
3. Difficulty – rising from sitting	189	1	10	6.54	2.27
4. Difficulty – standing	189	1	10	6.65	2.54
5. Difficulty – bending forward	189	1	10	5.58	2.69
6. Difficulty – walking in the flat	189	1	10	5.31	2.46
7. Difficulty – getting in/out of car	189	1	10	6.77	2.39
8. Difficulty – going shopping	189	1	10	6.52	2.94
9. Difficulty – putting on socks	189	1	10	6.70	2.84
10. Difficulty – rising from bed	189	1	10	5.98	2.46
11. Difficulty – taking off socks	189	1	10	6.40	2.72
12. Difficulty – lying in bed	189	1	10	4.71	2.85
13. Difficulty – getting in/out of bathtub	189	1	10	6.58	3.17
14. Difficulty - sitting	189	1	10	4.78	2.65
15. Difficulty – getting on/off toilet	189	1	10	5.75	2.60
16. Difficulty – performing heavy domestic duties	189	1	10	7.67	2.62
17. Difficulty – performing light domestic duties	189	1	10	5.51	2.37

Supplementary Table 4. Descriptive statistics of the postoperative WOMAC results

	n	Min.	Max.	Mean	SD
1.Pain – walking	117	1	9	2.58	2.18
2. Pain – stair climbing	117	1	10	3.31	2.69
3. Pain – at night in bed	118	1	9	2.39	2.08
4. Pain – sitting or lying	118	1	9	2.41	2.10
5. Pain – standing upright	119	1	10	3.53	2.80
1. Stiffness in the morning	119	1	10	3.23	2.54
2. Stiffness during the day	119	1	9	2.71	2.16
1. Difficulty – descending stairs	119	1	10	3.37	2.54
2. Difficulty – ascending stairs	119	1	10	3.58	2.56
3. Difficulty – rising from sitting	119	1	10	3.54	2.51
4. Difficulty – standing	119	1	10	3.83	2.85
5. Difficulty – bending forward	119	1	10	3.21	2.46
6. Difficulty – walking in the flat	119	1	10	2.58	2.18
7. Difficulty – getting in/out of car	119	1	10	3.67	2.46
8. Difficulty – going shopping	119	1	10	3.55	2.64
9. Difficulty – putting on socks	119	1	10	4.29	2.82
10. Difficulty – rising from bed	119	1	10	2.87	2.22
11. Difficulty – taking off socks	118	1	10	3.87	2.69
12. Difficulty – lying in bed	118	1	9	2.22	2.08
13. Difficulty – getting in/out of bathtub	119	1	10	4.62	3.21
14. Difficulty - sitting	118	1	8	2.44	1.91
15. Difficulty – getting on/off toilet	119	1	10	2.97	2.17
16. Difficulty – performing heavy domestic duties	119	1	10	4.95	3.10
17. Difficulty – performing light domestic duties	118	1	10	2.85	2.20

APPENDICES

I.

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Article

Factors Influencing Pain Management of Patients with Osteoarthritis: A Cross-Sectional Study

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Abstract: Background: Osteoarthritis (OA) is a complex disease associated with chronic pain. Many patients treat their joint pain at a symptomatic level with over-the-counter (OTC) pain medications, often without the knowledge of their physicians. The aim of this study was to provide physicians with data about osteoarthritic patients' habits of pain management and to examine the explanatory factors of various ways of self-treatment. Methods: A cross-sectional study involving 189 patients with hip or knee OA and scheduled for joint replacement surgery was carried out. Participants filled out a self-administered questionnaire consisting of the Western Ontario and McMaster Universities Osteoarthritis Index and questions about their methods of alleviating pain. Results: 2.6% of patients did not use anything to alleviate their pain, while 63% practiced a non-pharmacological method. Diclofenac was the most frequently used drug, followed by ibuprofen. Profession had the greatest impact on medication habits; patients doing manual work were significantly more likely to take OTC non-steroidal anti-inflammatory drugs and use topical analgesics. Conclusions: Patients utilized a wide variety of pain management techniques. They seemed to use well-known painkillers, even if their side effects were less desirable. Such patients require comprehensive pain management, including educational and behavioural interventions, complemented by topical and oral medication.

Keywords: self-medication; knee osteoarthritis; hip osteoarthritis; WOMAC

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1. Introduction

Osteoarthritis (OA) is a complex disease defined by the American College of Rheumatology (ACR) as "A heterogeneous group of conditions that lead to joint symptoms and signs which are associated with defective integrity of articular cartilage" [1]. Clinically, OA is characterized by joint pain, joint stiffness, gait abnormalities, and variable degrees of functional impairment [2]. Patients with chronic pain associated with musculoskeletal disorders have some of the poorest health-related quality of life (HRQoL) ahead of neurological, renal, and cardiovascular diseases, with severe restrictions in their work and ordinary activities of daily living [3].

As stated in the Global Health Estimates 2000–2019 study, OA was the 17th leading cause of total years lived with disability (YLD), with 1.8% of YLDs in 2000, but by 2019, it had become the 13th leading cause of YLDs at a global level with 2.3% of YLDs [4]; becoming the third-most rapidly rising condition associated with disability behind diabetes and dementia. Global prevalence of hip and knee OA is approaching 5% [5], and by 2030, it is predicted to reach 30% [6]. It is expected to become a major healthcare concern as the population ages, obesity rates rise, and more people adopt the Western lifestyle [7].

OA remains a relatively unaddressed public health concern compared to such chronic diseases as cancer, diabetes, and heart disease. There is a certain level of complacency and a fallacy that joint pains are an inevitable part of aging. The degradation of articular cartilage is often seen as a condition to be tolerated, not managed [8]. As many people do not recognise their joint pain as a disease, they often do not consult a health professional for its management. They treat their joint pain at a symptomatic level with over-the-counter (OTC) pain medications, similarly to a headache or lower back pain. A serious problem is that this practice is contrary to major clinical guidelines, which generally agree on a combination of non-pharmacological and pharmacological therapies. The ACR deems non-pharmacological therapies as the "cornerstone of OA management", which should be maintained throughout the course of the disease, and stresses that pharmacological therapies should function as add-on therapy to non-pharmacological treatment [9]. The European League Against Rheumatism recommends the use of topical non-steroidal anti-inflammatory drugs (NSAIDs) and capsaicin as alternatives to oral analgesics or in combination with them [10].

Regarding oral analgesics, paracetamol was favoured previously by major clinical guidelines, recommending it to be the first choice in managing mild-to-moderate OA-related pain [9,11–14], while recently both NSAIDs and paracetamol are considered to be appropriate for treatment, though now a more conservative dosing for the latter is advised due to the increased risk of adverse events [15]. Beyond their burden on the cardiovascular system, it is widely accepted that regular use of NSAIDs increases the risk of interstitial nephritis, atrial fibrillation, and severe GI complications, including ulceration, bleeding, and perforation, by 2 to 4 times [16]. This fact is further aggravated by the increasing number of people who are opting for self-medication with OTC medications, without consulting a doctor, often under the influence of advertisements. Major and Vincze contacted 4536 specialists (pharmacists, pharmaceutical assistants, and pharmacy managers) to investigate the Hungarian patients' habit of buying OTC medications. Their results show that 58.2% of patients buying OTC medications in pharmacies are usually self-reliant in self-medication, but they have little knowledge about these drugs [17].

The combination of OA patients' needs for analgesics, the risk of concomitant use of multiple NSAIDs, and patients' tendency for self-medication practices emphasizes the need for healthcare professionals to understand osteoarthritic patients' health behaviour. Unfortunately, many times the attending physicians have no detailed data on what their patients use to alleviate their pain and in what quantities do they take OTC painkillers, a problem we wish to solve.

The aim of this study was to investigate osteoarthritic patients' habits of pain management (both pharmacological and non-pharmacological) and to examine the explanatory factors of various ways of treatment.

2. Materials and Methods

2.1. Study Design and Participants

A cross-sectional study was performed by the Department of Public Health, University of Szeged, based on data collected at the Department of Orthopaedics, Albert Szent-Györgyi Health Care Centre, University of Szeged (Szeged, Hungary) and at the Orthopaedic Ward of Réthy Pál Hospital of Békés County Central Hospital (Békéscsaba, Hungary) from August 2019 to September 2020.

2.2. Inclusion and Exclusion Criteria

Only patients awaiting total knee or hip surgery were included, while patients receiving unicondylar knee arthroplasty were excluded. No other exclusion criteria were set, and participation was offered for all eligible patients in order to have the full list of eligible subjects, with every subject standing an equal chance of being included to reduce selection bias.

2.3. Data Collection

Data collection was carried out with the use of a paper and pencil questionnaire 24 h prior to surgery. Patients with knee or hip OA scheduled for joint replacement surgery were involved on a voluntary basis. Patients filled out the self-administered questionnaire in their rooms after receiving a detailed briefing and signing the informed consent form.

2.4. Variables

The questionnaire comprised three basic sections: 1, pain management; 2, measures of pain and functionality by WOMAC; 3, sociodemographic data (age, gender, etc.).

2.4.1. Dependent Variables

To investigate pain management, the name, dose, and frequency of use of OTC and prescription-only medications were recorded. We only took into account regular medication use, that is, painkillers that participants used at least once a week. Based on these data, the following categories were made: total painkiller use (regular use of any type of painkiller), regular use of OTC oral NSAID, regular use of topical NSAID (cream/gel/patch), regular use of oral prescription medication, regular use of per os opioid-containing medication, and regular use of non-pharmacological methods. The dose of a medication was considered high if it reached or passed the recommended daily intake, that is: ibuprofen > 1800 mg/day, naproxen ≥ 1000 mg/day, diclofenac ≥ 150 mg/day, aceclofenac ≥ 100 mg/day, niflumic acid ≥ 750 mg/day, meloxicam ≥ 15 mg/day, piroxicam ≥ 20 mg/day, and nimesulide ≥ 200 mg/day [18].

We also examined non-pharmacological pain management techniques (e.g., physiotherapy, therapeutic massage, cold wraps, etc.). In this context, "physiotherapy" describes manual therapy and exercise therapy guided by a professional physiotherapist in order to build muscle strength and improve range of motion, while "exercising" includes basic warm-up and stretching exercises carried out by the patients in their homes, typically once a day in the morning to ease the joint stiffness they acquired during sleep. "Massage" specifically refers to massages carried out by the patients themselves. The term "cold wraps" includes chilled gel packs as well as towels soaked in cold water.

2.4.2. Independent Variables

Pain and functionality were measured by the validated Hungarian version of the disease-specific Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), which contains 24 items, covering 3 dimensions: pain (5 items) during walking, using stairs, in bed, sitting or lying, and standing upright; stiffness (2 items) after waking up and later in the day; and function (17 items) using stairs, rising from sitting, standing, bending, walking, getting in/out of a car, shopping, putting on/taking off socks, rising from bed, lying in bed, getting in/out of bathtub, sitting, getting on/off toilet, heavy domestic duties, and light domestic duties. All items were scored on a scale of 1–10, totalling 24–240, where higher scores indicated increased pain and decreased function [19,20].

The WOMAC questionnaire was chosen for this study for its good reported internal consistency, excellent test–retest reliability, and experts' involvement in development [21].

Regarding level of education, participants without a high school diploma were considered as 'low', with a high school diploma as 'middle', and with college and university diploma as 'high' level. Job profile was considered manual if the person's job was physically demanding (e.g., manual labour), and non-manual if it was intellectual work (e.g., office environment). Body mass index (BMI) was calculated as weight in kilograms divided by height squared in meters. Based on the World Health Organization recommendations, patients with BMIs below 18.5 kg/m^2 were categorised as underweight, those with BMIs between 18.5 kg/m^2 and 24.9 kg/m^2 as normal, BMIs between 25.0 kg/m^2 and 29.9 kg/m^2 as overweight, and anyone with a BMI over 30.0 as obese [22].

2.5. Statistical Analysis

Data analysis was carried out with IBM SPSS (Statistical Package for the Social Sciences) version 27 (SPSS Inc., Chicago, IL, USA). Descriptive statistics including frequency, percentage, mean, median, standard deviation (SD), and interquartile range (IQR) were performed to describe the study sample. After normality testing, the only variable not following a normal distribution was age, as OA predominantly affects the older generation. Association between categorical data was evaluated with a Chi-square test, and with one-way ANOVA for continuous data. Multivariable binary logistic regression analyses using the forward stepwise method were applied to determine the explanatory factors for analgesic use. The independent variables entered into the model were: gender, age group, level of education, job profile, affected joint, BMI category, and WOMAC total score. p-values for covariates to be included in the model were set at 0.05. Odds ratios (OR) and 95% confidence intervals (95% CI) were calculated, and statistical significance was set at $p < 0.05$.

3. Results

3.1. Characteristics of Patients

The baseline characteristics of the patients (n = 189) are shown in Table 1. The median age was 68 years (IQR: 12 years), and the majority of patients were women (70.1%). Nearly half of them had hip (48.7%) OA, and more than half (57.1%) were obese.

Table 1. Baseline characteristics of patients.

Characteristics	*n* (%)
Gender	
Men	56 (29.6)
Women	133 (70.4)
Age groups	
<65 years	65 (34.4)
≥65 years	124 (65.6)
Level of education	
Lower	82 (43.4)
Middle	69 (36.5)
Higher	38 (20.1)
Job profile	
Manual	97 (51.3)
Non-manual	92 (48.7)
Affected joint	
Hip	92 (48.7)
Knee	97 (51.3)
BMI categories (kg/m^2)	
18.5–24.9	28 (14.8)
25.0–29.9	53 (28.1)
≥30.0	108 (57.1)
WOMAC Index	mean ± SD
Pain	29.23 ± 11.00
Stiffness	11.96 ± 4.47
Physical function	104.83 ± 31.91
Total score	146.02 ± 43.65

3.2. Characteristics of Treatment

Of the patients, 6.9% used neither pharmacological nor non-pharmacological methods to alleviate their pain, not even occasionally.

3.2.1. Pharmacological Pain Management

The active ingredients of oral pain medications and the number of participants taking them are represented in Table 2. Diclofenac was the most frequently used drug, followed by ibuprofen and tramadol. Medications with paracetamol and selective cyclooxygenase-2 (COX-2) blockers were taken by 9 patients (4.8%) and 1 (0.5%) patient, respectively. A total of 24 participants (12.7%) took 2 different types of oral analgesic, while 9 (4.8%) and 2 patients (1.1%) took 3 or 4 different types, respectively. Also, 34 patients (18%) took high doses of painkillers regularly. Diclofenac was the most favoured with 15 patients reaching the recommended daily dose. A total of 38.1% of patients used prescription medication regularly.

Table 2. Active ingredients of oral medications.

Medication	*n* (%)
NSAIDs	
Diclofenac	74 (39.2)
Ibuprofen	42 (22.2)
Aceclofenac	12 (6.3)
Acemetacin	10 (5.3)
Naproxen	9 (4.8)
Nimesulide	4 (2.1)
Piroxicam	3 (1.6)
Aspirin	3 (1.6)
Meloxicam	1 (0.5)
Niflumic acid	1 (0.5)
Lornoxicam	1 (0.5)
Coxibs	
Etoricoxib	1 (0.5)
Opioids	
Tramadol	13 (6.9)
Combinations	
Tramadol + paracetamol	6 (3.2)
Tramadol + dexketoprofen	1 (0.5)
Paracetamol + codeine phosphate	1 (0.5)
Paracetamol	2 (1.0)

3.2.2. Non-Pharmacological Pain Management

The majority of patients (65.1%) practiced a non-pharmacological method to mitigate their pain, with 7.4% using these methods exclusively. Exercise, massages, and cold packs were the most favoured. A total of 29.1% used topical analgesics, all of which had diclofenac as an active ingredient, while 18.5% used a topical herbal cream with comfrey extract. Only 7 patients took part in physiotherapy, and of them, only 2 reported it as a regular (two times per week) activity (Table 3).

Table 3. The occurrence of different treatment forms.

Form of Treatment	*n* (%)
Total painkiller use	95 (50.3)
Regular OTC oral NSAID	44 (23.3)
Topical NSAID cream/gel/patch	55 (29.1)
Prescription medication	72 (38.1)
Per os opioid-containing medication	18 (9.5)
Topical herbal cream	35 (18.5)
Non-pharmacological methods	124 (65.6)
Exercising	59 (31.2)
Massage	55 (29.1)
Cold packs	49 (25.9)
Warm bath	20 (10.6)
Physiotherapy	7 (3.7)
Kinesio tape	6 (3.2)
Magnetic band/patch	2 (1.1)

OTC: over the counter, NSAID: non-steroidal anti-inflammatory drug.

While assessing the differences between knee and hip OA patients, knee patients were found to have significantly higher BMI ($\chi = 10.12$, $p < 0.01$), but there were no other differences between the two groups' demographic characteristics. Even though hip OA patients reported significantly worse HRQoL in the WOMAC total score (mean ± SD: 152.76 ± 41.23) than knee OA patients (139.62 ± 45.12) (p = 0.038), they were less likely to regularly use NSAIDs, either in tablet or cream form (42.2%), than were knee patients (59.8%), (χ^2 = 5.72, p = 0.017).

Knee OA patients were significantly more likely to use topical analgesics (χ^2 = 6.20, p = 0.013) and had a greater tendency to use non-pharmacological methods of pain management.

3.3. Assessment of Influencing Factors

Table 4 demonstrates the associations between different treatment forms and patients' characteristics.

Table 4. Associations between different treatment forms and patients' characteristics.

	All Painkillers n (%)	OTC NSAIDs n (%)	Prescription Painkillers n (%)	Topical NSAIDs n (%)	Opioid n (%)	Non-Pharma n (%)
Gender [a]	p = 0.186	p = 0.443	p = 0.662	p = 0.649	p = 0.070	p < 0.001
Men	24 (42.9)	11 (19.6)	20 (35.7)	15 (26.8)	2 (3.6)	27 (48.2)
Women	71 (53.4)	33 (24.8)	52 (39.1)	40 (30.1)	16 (12.0)	97 (72.9)
Age group [a]	p = 0.609	p = 0.256	p = 0.181	p = 0.098	p = 0.673	p = 0.160
<65 years	31 (47.7)	12 (18.5)	29 (44.6)	51 (78.5)	7 (10.8)	47 (72.3)
≥65 years	64 (51.6)	32 (25.8)	43 (34.7)	83 (66.9)	11 (8.9)	77 (62.1)
Level of education [a]	p = 0.368	p = 0.385	p = 0.213	p = 0.251	p = 0.949	p = 0.086
Low	46 (56.1)	23 (28.0)	37 (45.1)	29 (35.4)	8 (9.8)	47 (57.3)
Middle	32 (46.4)	13 (18.8)	22 (31.9)	17 (24.6)	6 (8.7)	48 (69.6)
High	17 (44.7)	8 (21.1)	13 (34.2)	9 (23.7)	4 (10.5)	29 (76.3)
Job profile [a]	p = 0.016	p = 0.011	p = 0.225	p = 0.030	p = 0.171	p = 0.615
Manual	57 (58.8)	30 (30.9)	41 (42.3)	35 (36.1)	12 (12.4)	62 (63.9)
Non-manual	38 (41.3)	14 (15.2)	31 (33.7)	20 (21.7)	6 (6.5)	62 (67.4)
Affected joint [a]	p = 0.007	p = 0.625	p = 0.558	p = 0.013	p = 0.539	p = 0.101
Hip	37 (40.2)	20 (21.7)	37 (40.2)	19 (20.7)	8 (8.2)	55 (59.8)
Knee	58 (59.8)	24 (24.7)	35 (36.1)	36 (37.1)	10 (10.9)	69 (71.1)
BMI categories [a]	p = 0.955	p = 0.056	p = 0.854	p = 0.034	p = 0.280	p = 0.104
18.5–24.9 kg/m^2	14 (51.9)	11 (40.7)	10 (35.7)	4 (14.8)	2 (7.4)	21 (75.0)
25.0–29.9 kg/m^2	26 (49.1)	9 (17.0)	19 (35.8)	22 (41.5)	8 (15.1)	39 (73.6)
≥30.0 kg/m^2	55 (51.4)	24 (22.4)	43 (39.8)	29 (27.1)	8 (7.5)	64 (59.3)
WOMAC total score [b]	p = 0.531	p = 0.077	p < 0.001	p = 0.351	p = 0.041	p = 0.086
Users	148.00 ± 42.39	156.20 ± 44.17	160.72 ± 37.70	150.65 ± 36.69	166.00 ± 31.55	149.96 ± 43.39
Non-users	144.01 ± 45.03	142.92 ± 43.17	136.97 ± 44.74	144.11 ± 46.20	143.91 ± 44.28	138.49 ± 43.52

p values: [a] results of chi-square tests; [b] results of one-way ANOVA, comparing users of a given treatment with non-users. Non-pharma: non-pharmacological methods, BMI: body mass index, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

Results of the stepwise logistic regression analysis showed that manual work had the greatest impact on medication habits; patients with physically demanding jobs were significantly more likely to take painkillers in general, OTC NSAIDs, and topical analgesics. Degeneration of the knee joint specifically seems to be connected to manual work, as such patients were similarly more likely to use painkillers in general and topical analgesics. As shown in Table 4, WOMAC Score results showed that patients with poorer physical function and/or higher pain level were more likely to take prescription medications, each point increases the chance of taking medicine by 1.3.

All variables related to stress on the joint showed a greater likelihood of medication use except BMI, in the case of which, a higher value in fact suggested a bigger chance for topical analgesic use, but patients with higher BMIs were less likely to take OTC NSAIDs, compared to participants with normal BMIs. Regarding factors associated with non-pharmacological pain management, female patients showed a greater willingness to mitigate their pain in such ways (Tables 5–9).

Table 5. Forward stepwise logistic regression analysis of factors associated with regular painkillers use (last step).

Variable	OR (95% CI)	*p* Value
Job profile (manual)	2.253 (1.231–4.121)	0.008
Affected joint (knee)	2.440 (1.334–4.464)	0.004

Variables not entered into the model: gender, age group, level of education, BMI, WOMAC Total Score. OR: odds ratio, 95% CI: confidence interval, 95%; BMI: body mass index.

Table 6. Forward stepwise logistic regression analysis of factors associated with regular use of OTC NSAIDs (last step).

Variable	OR (95% CI)	*p* Value
Job profile (manual)	2.637 (1.270–5.479)	0.009
BMI categories		
25.0–29.9 kg/m^2	0.274 (0.093–0.806)	0.019
$\geq$30.0 kg/m^2	0.387 (0.154–0.971)	0.043

BMI reference category: 18.5–24.9 kg/m^2. Variables not entered in the model: gender, age group, level of education, affected joint, WOMAC Total Score. OR: odds ratio, 95%; CI: confidence interval, 95%; OTC: over the counter; NSAID: non-steroidal anti-inflammatory drug; BMI: body mass index.

Table 7. Forward stepwise logistic regression analysis of factors associated with regular use of prescription medication (last step).

Variable	OR (95% CI)	*p* Value
WOMAC Total Score (continuous)	1.013 (1.006–1.021)	$<$0.001

Variables not entered into the model: gender, age group, level of education, affected joint, BMI. OR: odds ratio, 95%; CI: confidence interval, 95%; BMI: body mass index.

Table 8. Forward stepwise logistic regression analysis of factors associated with regular use of topical analgesic (last step).

Variable	OR (95% CI)	*p* Value
Job profile (manual)	2.346 (1.183–4.651)	0.015
Affected joint (knee)	2.870 (1.403–5.871)	0.004
BMI categories		
25.0–29.9 kg/m^2	4.261 (1.232–14.746)	0.022
$\geq$30.0 kg/m^2	1.656 (0.503–5.447)	0.407

BMI reference category: 18.5–24.9 kg/m^2. OR: odds ratio, 95%; CI: confidence interval, 95%; BMI: body mass index. Variables not entered in the model: gender, age group, level of education, WOMAC Total Score.

Table 9. Forward stepwise logistic regression analysis of factors associated with non-pharmacological pain management (last step).

Variable	OR (95% CI)	*p* Value
Gender (women)	2.894 (1.513–5.537)	0.001

OR: odds ratio, 95%; CI: confidence interval, 95%. Variables not entered in the model: age group, level of education, job profile, affected joint, BMI, WOMAC Total Score.

4. Discussion

In this study, we aimed to investigate osteoarthritic patients' habits of pain management and to examine the explanatory factors of various ways of self-treatment. OA is a disease for which pain is a main characteristic. Accordingly, patients in the current study utilized a wide variety of pain management technics. The majority of patients practiced a non-pharmacological method, with women in particular favouring it, while pharmacological methods were chosen by patients doing manual labour. Although more weight puts more strain on the joint, contrary to expectations, patients with higher BMI were less likely to take OTC NSAIDs.

A total of 23.3% of patients took OTC NSAIDs regularly. This is in line with the results (26.5%) from the 2011 Five European Countries National Health and Wellness Survey, as reported by Kingsbury et al. Our results for prescription medication use (38.1%) and paracetamol (1.0%) were comfortably within the range of the survey's result of 33.0–53.2% and 0–6.0%, respectively. On the other hand, we experienced two major differences. On average, the use of opioid medications and COX-2 inhibitors was higher in the participating countries (France, Germany, Italy, Spain, and the UK) with 35.6% and 6.6%, compared to our results, 6.9% and 0.5%, respectively [23]. This infrequent use of paracetamol can be seen throughout Europe, barring the Nordic countries, where it is highly favoured [24]. Results showing that diclofenac and ibuprofen were the most-used active ingredients by our sample also correspond with results from European and Asian countries [23–25]. A total of 38.1% of patients used prescription medication; we can only hope that this fraction of the patient population was under the care of a specialist. It is, however, obviously important to assess also those who take NSAIDs on their own accord since the lack of professional supervision increases the chance of the complications that arise from self-medication, either by drug abuse or lack of mucosa protection. Medicines preferred by patients are a cause for concern, with diclofenac being the most popular but COX-2 inhibitors being neglected, as a study by Massó González et al. showed that the relative risk of upper GI bleeding/perforation was 4.50 for traditional NSAIDs, and 3.98 for diclofenac specifically, but only 1.88 for coxibs [26].

The distribution of active ingredients indicates that patients tend to use well-known pain medications even if their side effect profiles are less desirable. But questions arise even in case of professionally recommended medications, as some guidelines warn against the use of the previously favoured paracetamol, recommending it only conditionally, and stressing the importance of personalised therapies [27]. Knee OA patients were significantly more likely to use topical analgesics, which on one hand can be attributed to the fact that the knee joint is easier to reach and the active ingredients absorbed through the skin reach the site of pain more efficiently, but also knee OA patients had significantly higher BMIs compared to hip OA patients, and as the influencing factor assessment showed, patients with higher BMIs were over four times more likely to use topical analgesics compared to those with normal BMIs. Since hip OA patient with higher BMIs did not use more topical painkillers compared to those with lower BMIs, it seems that the fact that the knee joint is affected contributes more to the use of topical painkillers than BMI. The fact that only 29.1% of patients used topical analgesics is also a possible indicator that many patients managed their pain by themselves, even though professional guidelines (e.g., that of the ACR) favour topical drugs over oral medication as a way to decrease harmful GI side-effects [28]. It would be worth paying particular attention to hip OA patients who seem to prefer oral painkillers.

The importance of using topical analgesics cannot be overemphasised, given the advanced age of our patients, the high risk of co-morbidities, and the additional drug use associated with these conditions involving the risk of potential drug interactions. Beyond the well-known GI side effects caused by NSAIDs, with diclofenac being the most favoured OTC painkiller, the possibility of adverse cardiovascular events must not be overlooked. Schmidt et al. found that people taking diclofenac had a 20% increased rate for a major adverse cardiovascular event, such as a myocardial infarction, compared to patients taking paracetamol, and 30% compared to those who took naproxen [29].

Our study also showed high prevalence of the use of non-pharmacological techniques, which is fortunate, although typically limited to herbal creams, cold compressions, and in one case, warm baths, as Hungary has a long history of balneotherapy [30]. Although pain management methods that could be carried out by the patients themselves seem to be popular, unfortunately the prevalence of professionally guided physiotherapy was low compared to other studies [25,31]. Although 31.2% of patients reported doing exercise, it was practiced as a way of weight management. As 57.1% of patients were overweight and BMI was identified in this study as a risk factor, we wish to emphasise the systematic integration of weight management into the OA therapy course because obesity is suggested to be the main modifiable risk factor of OA [32]. A comprehensive and individualised plan for management of OA should therefore include educational, behavioural, psychosocial, and physical interventions, as well as topical, oral, and intraarticular medications [23]. We also wish to highlight the importance of preoperative physiotherapy. Unfortunately, patients are not routinely referred to physiotherapy within a year before surgery, even though studies showed that among patients who received preoperative physiotherapy a significant improvement was found for active and passive rotation, pain, daily functioning, vitality, psychological health, and social life [33].

For both hip and knee OA, the core treatments are exercise, education, mechanical interventions, and weight loss [34]. Given how few of our patients do exercise or receive physiotherapy, the question arises as to how much information patients have about non-pharmacological therapies. Because of this, we would like to encourage both general practitioners and specialists to recommend the following techniques to their patients taking their current condition into account. Manual therapy [35], transcutaneous electrical nerve stimulation, [36] and knee braces [37] are proven to reduce pain, the latter having the additional benefit of reducing knee instability, and they can also be effective when there is a valgus or varus deformity. To compensate for decreased muscular strength, resistance [38] and neuromuscular exercise [39] have been shown to be effective. Specifically for patients with hip OA, Nordic walking was found to build muscle strength and has been shown to be effective for weight loss, thus providing further benefits for OA patients [40,41].

In order to help patients maintain their exercise programmes, group-mediated cognitive behavioural physical activity intervention is advised [42].

By postponing non-urgent elective surgery during the COVID-19 pandemic, waiting times increased and the number of operations decreased. Compared to 2019, the median number of days on the waiting list before surgery increased by 88 days for knee replacements and by 58 days for hip replacements in 2020 [43]. In this situation, a further increase in self-medication by patients can be expected; thus, the responsibility of general practitioners in pain management has increased significantly. It is highly important that physicians are up to date on their new OA patients' pain management habits so as to monitor habitual painkiller use and for their long-time patients to keep them updated with the current guidelines. The National Health Service Greater Glasgow and Clyde's Guidelines for the management of chronic non-malignant pain intends to assist healthcare professionals in the choice of disease-specific treatments focusing on supporting self-management through five steps: Initial Assessment, Formulating a Pain Management Plan, Self-Management Strategies, Pharmacological Management Strategies, and Follow-up and Annual Referral if Indicated [44].

As data collection was carried out by self-administered questionnaires, inaccuracies in patients' memories have the potential to distort our data. Although this study was carried out in two different health centres, findings may not be generalizable to the overall population since the population was not very large, only representing part of the country, and only consisting of severe OA patients. The limitations of our study are consistent with the nature of observational studies and the bias on patient selection, for which we tried to correct by selecting a large number of participants from two different counties of the country and enrolling consecutive patients. Also, the potential adverse effect of the NSAID use could not be determined because of a lack of data on such factors as antacid use. We wish to expand on this current study in the future by gathering information regarding the use of antacids to support risk assessment, and also the effect a successful replacement surgery has on the amount of medication patients take.

5. Conclusions

The use of NSAIDs in OA treatment, either planned by a medical professional or taken of the patients' own accord, is very high. Two-thirds of the population affected by OA are over 65 (which is the standard age of retirement in Hungary), which carries the risk of comorbidities and the parallel use of several medications, but a considerable fraction of OA patients is still active, for whom immediate and long-lasting pain management is both medically and financially important. Both general practitioners and specialists need to familiarise themselves with their patients' pain management habits and make a comprehensive and personalized plan for the management of OA patients.

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RESEARCH

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Effect of osteoarthritis and its surgical treatment on patients' quality of life: a longitudinal study

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Abstract

Background Osteoarthritis (OA) is one of the primary causes of pain and disability worldwide leading to patients having some of the worst health-related quality of life (QOL). The purpose of our study was to investigate the progression of the generic and disease-specific QOL of osteoarthritic patients going through total hip or knee replacement surgery and the factors that might alter the effect of surgery on QOL.

Methods A longitudinal study was performed based on data collected from 120 OA patients who filled in the short version of the WHO's generic measure of quality of life (WHOQOL-BREF) and the disease-specific Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) before and after surgery.

Results Domains related to physical health status showed relatively lower scores in patients before surgery. Patients reported a significant increase of QOL after surgery in the WHOQOL-BREF physical domain, especially if they were from the younger group (<65 years, $p=0.022$) or had a manual job ($p=0.008$). Disease-specific QOL outcome results indicate that overall patients gained significantly better QOL in all domains of the WOMAC score. Patients with hip OA seemed to have the most benefit of their operation as they reported better outcome in WOMAC pain ($p=0.019$), stiffness ($p=0.010$), physical function domains ($p=0.011$) and total score ($p=0.007$) compared to knee OA patients.

Conclusion There was a statistically significant improvement in all domains concerning physical functions in the study population. Patients also reported significant improvement in the social relationship domain, which indicates that OA itself as well as its management might have a profound effect on patients' life beyond the reduction of their pain.

Keywords Osteoarthritis, Quality of life outcomes, Total hip replacement, Total knee replacement, WHOQOL-BREF, WOMAC

Background

Osteoarthritis (OA) is one of the primary causes of pain and disability worldwide. From 1990 to 2019, the disabilty-adjusted life year of hip osteoarthritis increased from 0.46 million to 1.04 million, reflecting a total increase of 126.97% [1]. The number of OA cases, increasing with age and obesity rates and showing female predominance reached 527.81 million cases globally in 2019; therefore, it remains a major public health concern [2, 3].

The pain and disability caused by OA are associated with articular cartilage degeneration and functional restrictions [4]. Resulting from the latter, OA also affects social connectedness, relationships, and emotional well-being, thus reducing multiple aspects of quality of life

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(QOL) [5]. Furthermore, knee OA has been shown to be significantly associated with deteriorated mental health [6].

Health is consistently regarded as an important aspect of QOL. Health-related QOL (HRQOL) aims to measure QOL components impacted by certain diseases and effectiveness of treatment. Therefore, studies on HRQOL may evaluate the quality and outcome of health care provided or may identify applicative items [7]. Analysis of QOL data can also identify subgroups, can help guide interventions to improve the situation of those with poor perceived health and avert more serious consequences [8]. Patients with chronic musculoskeletal pain have some of the worst HRQOL with severe restrictions in their work and daily living [9]. The WHO has developed a generic measure of QOL (WHOQOL) that encompasses general, physical, psychological, social, and environmental aspects, making it ideal for measuring a broad range of factors, thus giving a more complete picture of the individual's life and wellbeing [10]. Reis et al. have used the abbreviated version of the WHOQOL assessment tool (WHOQOL-BREF) when reporting on how significant knee pain in elderly women with knee OA affected their balance and overall QOL compared to elderly women with no OA [11]. This decline in QOL has been supported by the study of Cavalcante et al. as well [12], and even younger patients (<50 years) have reported a poorer QOL because of OA [13].

Hip and knee joint replacement surgery is regarded as one of the most successful operations in medicine as a whole [14], leading to statistically significant improvement in QOL by 4% after 6 weeks and 13% after 6 months [15]. Post-surgical improvements in pain and function have been shown to extend over years, but examining the whole spectrum of QOL might give a more in-depth understanding of outcomes relevant for the individual [16].

While measuring of generic QOL is advantageous when assessing the overall burden of a given health problem, disease-specific measures of QOL have the advantage of being frequently more responsive and clinically useful than generic measures by measuring the frequency and severity of specific symptoms [17]. Since its initial validation [18], the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) has become a popular patient reported outcome measure used for evaluation of hip and knee OA. It has been used extensively in research studies [19–21] and clinical trials [22–24] and has been recognized by the Outcome Measures in Rheumatoid Arthritis Clinical Trials group (OMERACT) and Osteoarthritis Research Society International (OARSI) [25, 26]. It also can also be used to classify patient satisfaction after total knee arthroplasty [27].

The aim of our study was to investigate the progression of the generic and disease-specific QOL of osteoarthritic patients undergoing total hip or knee replacement surgery, and the factors that might alter the effects of surgery effect on QOL.

Methods

Study design and participants.

This longitudinal study was performed based on data collected from OA patients at the Department of Orthopaedics, Albert Szent-Györgyi Clinical Centre, University of Szeged (Szeged, Hungary) and at the Orthopaedic Ward of Réthy Pál Hospital of Békés County Central Hospital (Békéscsaba, Hungary) between August 2019 and October 2020. The recruitment process is illustrated in Fig. 1. Patients with knee or hip OA scheduled for total joint replacement surgery were involved, while patients receiving unicondylar knee arthroplasty were excluded. No other exclusion criteria were set. Participation was offered to all eligible patients consecutively to reduce selection bias. The self-administered questionnaires were filled in by the patients 24 h prior to surgery. To assess the effect of the surgery effect on QOL, post-operative data collection was carried out one year after the surgery when the questionnaires were sent and returned by post because of the COVID lockdown.

Questionnaire

The questionnaire comprised sociodemographic data (e.g., age and gender) and QOL measuring tools.

Based on their age, participants were divided into two groups split at the age of 65 as that is the age of retirement in Hungary, making this grouping suitable to assess the effect of the disease and the treatment on both the economically active and inactive population. The level of education was considered 'low' if the participants had no high school degree, 'middle' if they had high school degree, and 'high' if they had a college or university degree. Based on job profile, participants whose job was physically demanding (e.g., manual labour) formed the "manual" group, while those with intellectual work (e.g., desk jobs) formed the "non-manual" group. After calculating the body mass index (BMI) (weight in kilograms divided by height squared in meters), the participants were grouped based on the WHO recommendation, as underweight (BMI below 18.5 kg/m^2), normal (BMI 18.5 kg/m^2 to 24.9 kg/m^2), overweight (25.0 kg/m^2 to 29.9 kg/m^2), and obese (over 30.0 kg/m^2) [28].

General QOL was measured by the validated Hungarian version of WHOQOL-BREF [29], which measures QOL with 26 questions in 4 domains: 1, Physical health (activities of daily living, dependence on medicinal substances and medical aids, energy and fatigue, mobility,

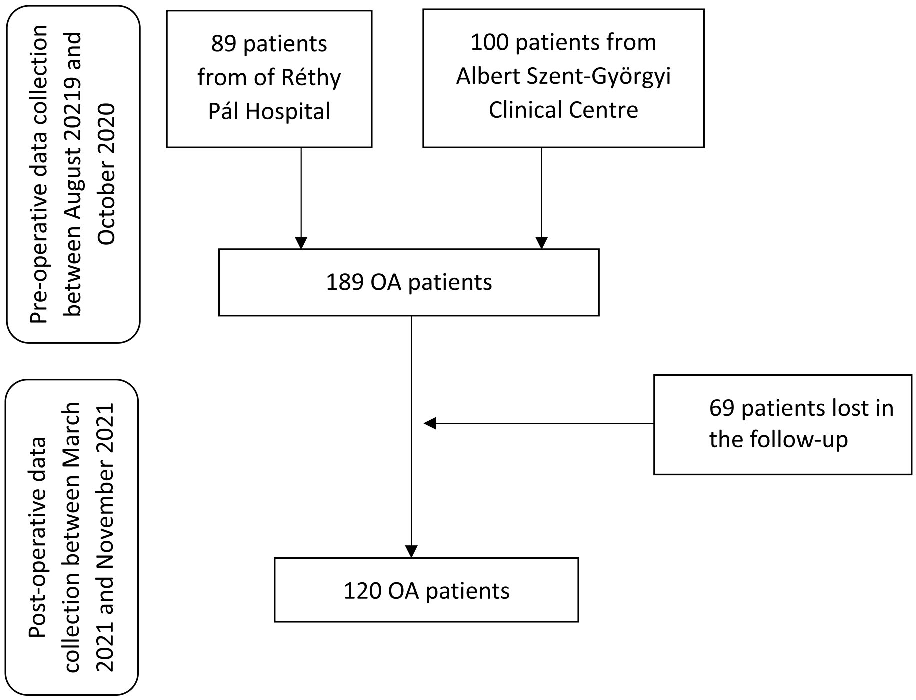

Fig. 1 Flow diagram describing recruitment and progress of participants to the follow-up study

pain and discomfort, sleep and rest, and work capacity); 2, Psychological health (bodily image and appearance, negative feelings, positive feelings, self-esteem, spirituality/religion/personal beliefs, thinking, learning, memory, and concentration); 3, Social relationships (personal relationships, social support, and sexual activity); 4, Environment (financial resources, freedom, physical safety and security, health and social care: accessibility and quality, home environment, opportunities for acquiring new information and skills, participation in and opportunities for recreation/leisure activities, physical environment, and transport). There are also two separate questions that are asked specifically about 1, the individual's overall perception of their own health and 2, the individual's overall perception of their QOL. The answers were measured by a 5-point Likert scale. In accordance with the instructions of the WHOQOL-BREF manual [30], domain scores were calculated and then converted to a 0–100 scale, whereas the results of the two separate questions were left untransformed. The higher score represented better QOL.

In order to assess the disease-specific QOL, we used the validated Hungarian version of the WOMAC [31] Index Version 3.1 numeric rating scale (NRS), which covers 3 dimensions through 24 items: Pain (5 items) during walking, going up/down the stairs, lying in bed, sitting, and standing upright; Stiffness (2 items) after waking up and later in the day; and Function (17 items) going up/down the stairs, rising from sitting, standing, bending, walking, getting in/out of a car, shopping, putting on/taking off socks, rising from bed, lying in bed, getting in/out of the bathtub, sitting, getting on/off toilet, performing heavy domestic duties or light domestic duties. All items were assessed by using a 1–10 NRS, (1 = no pain/stiffness/difficulty to 10 = extreme pain/stiffness/difficulty) totalling 24–240, where higher scores indicated increased pain and decrease function [32]. The results of the individual domains as well as the total score were later standardised to a 0–100 scale.

Statistical analysis

Data analysis was carried out using IBM SPSS (Statistical Package for the Social Sciences) version 27 (SPSS Inc., Chicago, IL, USA). Descriptive statistics including frequency, percentage, mean and standard deviation (SD) were performed to characterize the study sample. As the outcome measures had non-normal distribution, Wilcoxon tests were carried out to assess the difference of the QOL outcome measures pre- and post-surgery. To explore the role of independent variables in the results, subgroups were made based on gender, age, affected joint, BMI categories, work profile, level of education and the presence of a comorbidity. Subgroup analyses were carried out using mixed-design two-way repeated measures ANOVA. Statistical significance was set at $p < 0.05$.

Ethical consideration

The study was approved by the Regional and Institutional Review Board of Human Investigations in University of Szeged, Hungary (ID: 4059) and conducted in accordance with the Declaration of Helsinki. All subjects provided written informed consent before the questionnaire.

Results

Participants

The characteristics of the patients who we reached during the follow-up ($n=120$) are shown in Table 1. The mean age was 68.68 years and the majority (85.8%) of the participants was overweight or obese. More than two-thirds of the patients were women (69.2%).

Table 1 Characteristics of patients

Characteristics	*n (%)*
Gender	
Men	37 (30.8)
Women	83 (69.2)
Age groups	
< 65 years	31 (25.8)
≥ 65 years	89 (74.2)
Level of education	
Lower	44 (36.7)
Middle	45 (37.5)
Higher	31 (25.8)
Job profile	
Manual	54 (45.0)
Non-manual	66 (55.0)
Affected joint	
Hip	56 (46.7)
Knee	64 (53.3)
Comorbidity	
Reported	30 (25.0)
Not reported	90 (75.0)
BMI categories (kg/m^2)	
18.5–24.9	17 (14.2)
25.0–29.9	36 (30.0)
≥ 30.0	67 (55.8)

Quality of life outcomes

General QOL (WHOQOL-BREF)

The opening questions of WHOQOL-BREF demonstrated patients reporting a significant increase of the perceived QOL, where score increased from 3.30 ± 0.84 to 3.58 ± 0.69 ($p=0.002$) and of satisfaction with their health, the score of which rose from 3.03 ± 0.84 to 3.31 ± 0.70 ($p=0.001$) after surgery. QOL outcome results indicated that the patients had significantly better QOL compared to their previous state in the physical health and social relationship domain. On the other hand, the improvement in the psychological domain was negligible, which can be attributed to the fact that the baseline values of that domain were better than those of the other domains (Table 2).

While all patients reported a significant increase of QOL in the WHOQOL-BREF physical domain, subgroup analysis showed that younger patients (< 65 years) reported significantly better outcomes compared to older ones ($p=0.022$). Patients in the manual job group reported significantly greater increase in the physical ($p=0.008$), and psychological ($p=0.003$) domains compared to the non-manual group. Regardless of the patients' gender, age, level of education, job profile, BMI, affected joint or the presence of other diseases, a significantly better QOL scores were achieved in the physical health ($p<0.001$) and social relationships domains (from $p=0.033$ to $p<0.001$) after the surgery (Table 3) which is in accordance with the data in Table 2.

Disease-specific QOL (WOMAC)

Disease-specific QOL outcome results indicated that overall, patients gained significantly better QOL in all domains of the WOMAC score (Table 4).

In the sub-group analysis (Table 5), participants from the younger age-group (< 65) reported significant decrease in joint stiffness ($p=0.005$), and overall, a better disease-specific QOL ($p=0.05$). Patients in the

Table 2 Population results of the general QOL assessment

WHOQOL-BREF	Preoperative data mean ± SD	Postoperative data mean ± SD	
Physical health domain	46.51 ± 15.53	61.04 ± 16.70	p < 0.001
Psychological domain	63.99 ± 14.97	64.40 ± 15.14	p = 0.762
Social relationships domain	54.59 ± 21.87	59.58 ± 16.79	p = 0.012
Environment domain	64.93 ± 15.52	65.88 ± 13.85	p = 0.494

Table 3 Sub-group analysis results of the general QOL assessment

		WHOQOL-BREF											
		Physical health			**Psychological**			**Social relationships**			**Environment**		
		Preop	**Postop**	**Sig**	**Preop**	**Postop**	**Sig**	**Preop**	**Postop**	**Sig**	**Preop**	**Postop**	**Sig**
		mean ± SD	**mean ± SD**		**mean ± SD**	**mean ± SD**		**mean ± SD**	**mean ± SD**		**mean ± SD**	**mean ± SD**	
Gender				**$p_c < 0.001$**			$p_c = 0.77$			**$p_c = 0.033$**			$p_c = 0.459$
	Male	45.92 ± 15.04	64.49 ± 17.02	$p_i = 0.121$	66.68 ± 14.51	67.11 ± 15.57	$p_i = 0.99$	56.46 ± 21.84	59.95 ± 16.34	$p_i = 0.610$	65.46 ± 14.65	67.00 ± 14.55	$p_i = 0.772$
	Female	46.77 ± 15.82	59.51 ± 16.42		62.80 ± 15.10	63.19 ± 14.88		53.76 ± 21.96	59.41 ± 17.09		64.70 ± 15.98	65.37 ± 13.58	
Age groups				**$p_c < 0.001$**			$p_c = 0.548$			$p_c = 0.102$			$p_c = 0.477$
	< 65	44.87 ± 16.62	66.13 ± 15.91	**$p_i = 0.022$**	65.97 ± 16.21	67.97 ± 15.42	$p_i = 0.487$	62.94 ± 22.47	63.87 ± 16.43	$p_i = 0.222$	67.45 ± 14.68	68.84 ± 11.83	**$p_i = 0.036$**
	≥ 65	47.08 ± 15.19	59.27 ± 16.68		63.30 ± 14.55	63.16 ± 14.92		51.69 ± 21.01	58.08 ± 2.59		64.06 ± 15.79	64.84 ± 14.40	
Level of education				**$p_c < 0.001$**			$p_c = 0.900$			**$p_{c=}0.024$**			$p_c = 0.528$
	Lower	42.45 ± 13.15	59.59 ± 15.74	$p_i = 0.371$	61.32 ± 13.57	63.95 ± 14.72	$p_i = 0.387$	51.30 ± 20.23	58.77 ± 16.63	$p_i = 0.351$	63.98 ± 15.96	64.98 ± 13.66	$p_i = 0.973$
	Middle	49.09 ± 15.68	60.60 ± 17.20		63.27 ± 2.27	63.18 ± 15.58		54.00 ± 19.22	59.73 ± 16.15		63.29 ± 14.40	64.53 ± 12.68	
	Higher	48.52 ± 2.68	63.74 ± 17.48		68.84 ± 2.69	66.81 ± 15.28		60.13 ± 26.81	60.48 ± 18.38		68.68 ± 16.33	69.10 ± 15.57	
Job profile				**$p_c < 0.001$**			$p_c = 0.541$			**$p_c = 0.010$**			$p_c = 0.446$
	Manual	41.44 ± 13.93	61.02 ± 16.50	**$p_i = 0.008$**	60.83 ± 13.50	65.56 ± 13.74	**$p_i = 0.003$**	51.98 ± 20.90	58.43 ± 17.57	$p_i = 0.500$	62.91 ± 15.15	65.11 ± 14.18	$p_i = 0.408$
	Non-manual	50.65 ± 15.64	61.06 ± 16.98		66.58 ± 2.50	63.45 ± 16.23		56.73 ± 22.56	60.52 ± 16.21		66.59 ± 15.74	66.50 ± 13.65	
Affected joint				**$p_c < 0.001$**			$p_c = 0.852$			**$p_c = 0.014$**			$p_c = 0.504$
	Knee	50.75 ± 15.64	61.45 ± 17.78	**$p_i = 0.038$**	66.52 ± 15.63	64.37 ± 15.28	$p_i = 0.075$	56.71 ± 22.59	60.50 ± 17.54	$p_i = 0.568$	65.70 ± 17.11	66.38 ± 13.78	$p_i = 0.859$
	Hip	42.80 ± 14.56	60.69 ± 15.81		61.78 ± 14.13	64.42 ± 15.13		52.73 ± 21.21	58.77 ± 16.20		64.27 ± 14.10	65.44 ± 14.00	
Comorbidity				**$p_c < 0.001$**			$p_c = 0.884$			$p_c = 0.099$			$p_c = 0.721$
	Reported	42.00 ± 14.36	55.10 ± 15.73	$p_i = 0.636$	62.20 ± 12.79	60.70 ± 16.37	$p_i = 0.414$	56.67 ± 19.93	57.93 ± 15.44	$p_i = 0.273$	65.93 ± 12.01	62.37 ± 15.19	$p_i = 0.057$
	Not reported	48.01 ± 15.69	63.02 ± 16.62		64.59 ± 15.65	65.63 ± 14.59		53.90 ± 22.54	60.12 ± 17.27		64.60 ± 16.58	67.04 ± 13.25	
BMI(kg/m^2) category				**$p_c < 0.001$**			$p_c = 0.467$			**$p_c = 0.014$**			$p_c = 0.960$
	18.5–24.9	44.12 ± 15.96	62.18 ± 18.03	$p_i = 0.479$	59.71 ± 11.27	61.18 ± 17.26	$p_i = 0.262$	53.65 ± 21.15	61.06 ± 14.58	$p_i = 0.816$	67.12 ± 9.69	64.06 ± 10.46	$p_i = 0.497$
	25.0–29.9	46.97 ± 16.23	63.22 ± 16.91		64.47 ± 14.39	67.89 ± 14.23		53.44 ± 22.47	59.17 ± 19.11		66.92 ± 16.37	68.72 ± 16.26	
	≥ 30.0	46.87 ± 15.23	59.58 ± 16.35		64.82 ± 16.06	63.34 ± 14.93		55.45 ± 22.01	59.42 ± 16.20		63.31 ± 16.23	64.81 ± 13.13	

p_c: *p* value for both group's combined change; p_i: *p* value of group interaction

Table 4 Population results of the disease-specific QOL assessment

WOMAC			
Domain	**Preoperative data mean ± SD**	**Postoperative data mean ± SD**	
Pain	57.03 ± 21.87	28.09 ± 20.87	p < 0.001
Stiffness	59.08 ± 21.28	29.71 ± 22.59	p < 0.001
Physical function	61.26 ± 18.06	34.01 ± 20.61	p < 0.001
Total score	60.19 ± 17.57	32.39 ± 19.84	p < 0.001

manual group reported significantly greater increase in physical function ($p = 0.037$) and overall score ($p = 0.024$) compared to the non-manual group. Patients with hip OA seemed to gain the most out of their operation as they reported better outcome in the WOMAC pain ($p = 0.019$), stiffness ($p = 0.010$), physical function domains ($p = 0.011$) and total score ($p = 0.007$) compared to knee OA patients. Participants who reported no comorbidities had significant decrease of joint stiffness compared to comorbid patients ($p = 0.010$). Regarding the connection of BMI and QOL, normal weight and overweight patients reported a significant decrease in their pain compared to obese patients ($p = 0.017$).

Total WOMAC score indicated significantly better disease-specific QOL post-surgery in all subgroups, regardless of the patients' gender, level of education, BMI category or the presence of other diseases ($p < 0.001$).

MacKay et al. carried out a literary review of 13 articles assessing the minimal clinically important difference (MCID) of WOMAC in patients who underwent total hip or knee replacement, and reported a MCID between 8.3–41 and 9.7–34 for pain and function domain respectively. For knee replacement they reported a MCID between 13.3–36 and 1.8–33 for pain and function domain respectively [33].

If we accept the value of MCID as 8.3 for pain and 9.7 for function domain, 83.87% and 81.25% of our hip OA patients exceeded these values. If we also accept the lowest reported MCID values for knee OA patients, 66.67% and 76.79% of our knee patients exceeded these values respectively.

Discussion

In this study, we aimed to investigate the general and disease-specific QOL of osteoarthritic patients pre- and post-surgery, and whether surgery would result in significant improvement. Disease-specific measures are considered to be more accurate for assessing immediate effects, whereas generic measures might reveal effects of the surgery in the long run as observed by Neuprez et al. [34].

As reported by other studies, domains related to physical health status show relatively lower scores as compared with psychological components in patients before surgery [35]; this result is consistent with our results.

The results indicated statistically significant improvement in all domains concerning physical functions in the study population as well as in the domain of social relationships, the latter indicating the impact of the difficulty of getting around in one's environment.

In this study, we investigated the possible role of independent variables in the disease-specific disability functional assessment performed using the WOMAC questionnaire. According to our results, patients with hip OA seemed to gain the most out of their operation, as they reported better outcome in the WOMAC pain, stiffness, physical function domains and total score compared to knee OA patients. A similarly significant improvement was measured among participants of the working age group (< 65 years) compared to the older patients and with manual jobs compared to non-manual workers as shown in Table 5. As the latter group is heavily exposed to the degeneration of cartilage because of their profession, it is a significant achievement that they can benefit from the surgery to this extent. The success of the surgery among the working age population indicates that many of them may be able to return to their job actively, thus decreasing the economic burden of OA.

Our results regarding the effect of the surgery on QOL outcomes are consistent with other studies. Papakostidou et al. found that after TKA, all groups of patients showed a statistically significant improvement in WOMAC domains between the pre- and the 12-month post-operative assessments, and there have been no significant differences in WOMAC domains in age, BMI, education and gender [36].

On the contrary, other studies have shown opposite results regarding the effect of gender and BMI. In a pooled analysis of 1783 knee and 2400 hip OA patients, Hofstede et al. have reported that being female or having higher BMI are associated with lower postoperative HRQoL and functioning and more pain [37]. Alkan et al. [38] have also found that WOMAC pain scores are higher in female patients; however, we found no difference between the two genders either pre- nor post-surgery. It has been reported that over 50% of the patients who required total knee replacement for end-stage OA are obese [39], a ratio that we experienced as well. However, we saw no difference in improvement by BMI category either in the generic or in the disease specific QOL.

Even though the success of joint replacement surgery is indisputable, additional therapies have been shown to boost its efficacy. The results of a study by Desmeules et al. suggest that the prehabilitation programme not only can

Table 5 Sub-group results of the disease-specific QOL assessment

		WOMAC											
		Pain			Stiffness			Physical function			Total score		
		Preop	Postop	Sig	Preop	Postop	Sig	Preop	Postop	Sig	Preop	Postop	Sig
		mean ± SD	mean ± SD		mean ± SD	mean ± SD		mean ± SD	mean ± SD		mean ± SD	mean ± SD	
Gender				**$p_c < 0.001$**			**$p_c < 0.001$**			**$p_c < 0.001$**			**$p_c < 0.001$**
	Male	55.56 ± 22.97	26.67 ± 20.87	$p_i = 0.988$	61.62 ± 21.64	27.16 ± 20.09	$p_i = 0.228$	60.91 ± 17.49	32.80 ± 22.13	$p_i = 0.813$	59.98 ± 17.56	30.84 ± 21.23	$p_i = 0.714$
	Female	57.70 ± 21.47	28.73 ± 20.97		57.93 ± 21.15	30.85 ± 23.66		61.42 ± 18.41	34.56 ± 20.02		60.28 ± 17.68	33.08 ± 19.28	
Age groups				**$p_c < 0.001$**			**$p_c < 0.001$**			**$p_c < 0.001$**			**$p_c < 0.001$**
	< 65	58.65 ± 19.97	24.39 ± 19.13	$p_i = 0.244$	65.97 ± 20.22	23.39 ± 18.64	**$p_i = 0.005$**	63.45 ± 16.85	28.18 ± 17.08	$p_i = 0.050$	62.66 ± 16.40	26.99 ± 16.70	**$p_i = 0.050$**
	≥ 65	56.45 ± 22.61	29.44 ± 21.42		56.65 ± 21.23	31.93 ± 23.52		60.50 ± 18.49	36.05 ± 21.42		59.29 ± 17.97	34.34 ± 20.54	
Level of education				**$p_c < 0.001$**			**$p_c < 0.001$**			**$p_c < 0.001$**			**$p_c < 0.001$**
	Lower	63.81 ± 24.16	31.19 ± 22.05	$p_i = 0.604$	63.98 ± 24.63	32.61 ± 25.71	$p_i = 0.866$	68.60 ± 17.35	38.26 ± 21.16	$p_i = 0.514$	67.40 ± 17.96	35.75 ± 21.02	$p_i = 0.445$
	Middle	52.82 ± 19.16	26.14 ± 20.17		55.67 ± 18.11	27.44 ± 20.77		59.24 ± 14.47	32.16 ± 20.05		57.37 ± 14.22	30.58 ± 18.90	
	Higher	53.73 ± 20.56	26.60 ± 20.37		57.00 ± 19.68	28.83 ± 20.50		53.78 ± 20.29	30.66 ± 20.26		54.31 ± 18.66	30.39 ± 19.54	
Job profile				**$p_c < 0.001$**			**$p_c < 0.001$**			**$p_c < 0.001$**			**$p_c < 0.001$**
	Manual	62.12 ± 23.82	28.35 ± 20.41	$p_i = 0.114$	63.80 ± 23.63	29.26 ± 23.16	$p_i = 0.096$	67.81 ± 15.71	34.99 ± 19.79	**$p_i = 0.037$**	66.42 ± 16.70	32.56 ± 19.37	**$p_i = 0.024$**
	Non-manual	52.91 ± 19.37	27.88 ± 21.40		55.15 ± 18.39	30.08 ± 22.28		55.90 ± 18.18	33.22 ± 21.37		55.20 ± 16.74	32.25 ± 20.35	
Affected joint				**$p_c < 0.001$**			**$p_c < 0.001$**			**$p_c < 0.001$**			**$p_c < 0.001$**
	Knee	56.48 ± 23.07	34.41 ± 23.54	**$p_i = 0.019$**	58.04 ± 20.51	36.95 ± 25.11	**$p_i = 0.010$**	59.84 ± 17.84	39.14 ± 23.44	**$p_i = 0.011$**	58.85 ± 17.57	37.96 ± 22.78	**$p_i = 0.007$**
	Hip	57.52 ± 20.95	22.58 ± 16.55		60.00 ± 22.07	23.25 ± 17.94		62.50 ± 18.29	29.53 ± 16.71		61.37 ± 17.62	27.45 ± 15.36	
Comorbidity				**$p_c < 0.001$**			**$p_c < 0.001$**			**$p_c < 0.001$**			**$p_c < 0.001$**
	Reported	59.93 ± 20.47	36.97 ± 25.09	$p_i = 0.209$	54.14 ± 21.38	37.59 ± 27.21	**$p_i = 0.010$**	61.98 ± 18.73	39.63 ± 23.21	$p_i = 0.245$	61.38 ± 17.85	39.87 ± 22.49	$p_i = 0.136$
	Not reported	56.07 ± 22.34	25.13 ± 18.50		60.67 ± 21.12	27.17 ± 20.42		61.02 ± 17.93	32.14 ± 19.45		59.79 ± 17.56	29.92 ± 18.36	
BMI (kg/m^2) category				**$p_c < 0.001$**			**$p_c < 0.001$**			**$p_c < 0.001$**			**$p_c < 0.001$**
	18.5–24.9	66.11 ± 19.35	22.82 ± 17.90	**$p_i = 0.017$**	55.00 ± 21.29	25.88 ± 20.93	$p_i = 0.088$	58.27 ± 22.96	28.27 ± 15.23	$p_i = 0.127$	59.63 ± 20.13	26.94 ± 15.46	$p_i = 0.074$
	25.0–29.9	55.06 ± 22.94	20.75 ± 14.96		61.43 ± 19.95	22.71 ± 17.63		61.68 ± 16.20	27.84 ± 17.83		60.29 ± 16.77	25.44 ± 15.42	
	≥ 30.0	55.67 ± 21.69	32.93 ± 22.79		58.88 ± 22.08	34.33 ± 24.38		61.79 ± 17.84	38.79 ± 22.11		60.27 ± 17.54	37.20 ± 21.52	

p_c: *p* value for both group's combined change; p_i: *p* value of group interaction alter the physical decline caused by OA, but it can help participants to improve their level of function before surgery as well, which is an important achievement in view of the fact that preoperative physical function is a major determinant of postoperative physical function [40, 41].

Although several studies investigated QOL among patients with OA, the cornerstone of those were a disease-specific QOL instrument. To assess the general QOL, many studies chose the 36-Item Short Form Survey which do measure aspects that are linked to health and functional performance. However, WHOQOL-BREF has been shown to be a better fit for assessing global QOL and thus a better choice to gain a more comprehensive picture when investigating QOL, which we aimed to contribute the literature.

Conclusion

OA was proved to cause severe pain and disability regardless of the patients' socioeconomic and anthropometric characteristics. The results of the physical domain of the general QOL questionnaire were consistent with the results of the disease-specific measures, and thus proved to be sensitive to the physical symptoms caused by the disease. Total hip replacement is regarded as one of the most successful surgeries in medicine today, which is supported by the results of our disease-specific QOL assessment as well as by the physical health domain of the general QOL outcomes. This success was most pronounced in case of the active population and patients doing physical labour. The fact that patients reported a significant improvement in the social relationships domain may indicate that OA itself as well as its management has a profound effect on patients' life beyond the reduction of their pain.

Limitations

As data collection was carried out by self-administered questionnaires, inaccuracies in patients' memories have the potential to distort our data. The limitations of our study are consistent with the nature of observational studies and the bias on patient selection, for which we tried to correct by selecting a large number of participants from two different counties of the country and by enrolling them consecutively. Although this study was carried out in two different health centres, both of them were from the South-Eastern region of Hungary, and so findings may not be generalizable to the overall Hungarian population. Also, as the study population only consisted of patients with severe OA, we cannot extrapolate our results to patients with mild or moderate OA. Postoperative data collection was carried out after the local outbreak of the COVID-19 pandemic, which might alter the outcome data, especially that of the psychological domain.

Abbreviations

BMI	Body mass index
HRQOL	Health-related Quality of life
MCID	Minimal clinically important difference
OA	Osteoarthritis
OARSI	Osteoarthritis Research Society International
OMERACT	Outcome Measures in Rheumatoid Arthritis Clinical Trials group
QOL	Quality of life
SD	Standard deviation
SF-36	36-Item Short Form Survey
SPSS	Statistical Package for the Social Sciences
WHOQOL	World Health Organization Quality of life generic measurement tool
WHOQOL-BREF	26-Item World Health Organization Quality of Life questionnaire
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

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Authors' contributions

Conceptualization: GAM, EP and ZM; Methodology: EP; Data curation: GAM; Formal analysis: GAM and EP; Investigation: GAM; Project administration: EP; Validation, GAM, EP, and ZM; Visualization, EP and ZM; Writing—original draft preparation: GAM; Writing—review and editing: EP and ZM; Funding acquisition and resources: EP; Supervision: EP and ZM. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Regional and Institutional Review Board of Human Investigations in University of Szeged, Hungary (2019/4059). Written informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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