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NEW PERSPECTIVES ON HEALTH-RELATED QUALITY OF LIFE ASSESSMENT IN PATIENTS WITH MUSCULOSKELETAL DISORDERS

PhD dissertation

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List of abbreviations

AI	Artificial intelligence
DALY	Disability-adjusted life year
GALI	Glocal Activity Limitation Indicator
eHEALS	eHealth Literacy Scale
HAQ-DI	Health Assessment Questionnaire Disability Index
HRQoL	Health-related quality of life
HTA	Health technology assessment
ICC	Intraclass correlation coefficient
ICECAP-A	ICEpop Capability measure for Adults
ICECAP-O	ICEpop Capability measure for Older people
IMD	Implantable medical device
MEHM	Minimum European Health Module
MSK	Musculoskeletal
MSK-HQ	Musculoskeletal Health Questionnaire
OMERACT	Outcome measurement in rheumatology
PRO	Patient-reported outcome
PROM	Patient-reported outcome measure
RCT	Randomised controlled Trial
QALY	Quality-adjusted life year
RA	Rheumatoid arthritis
SD	Standard deviation
SDM-Q-9	Shared Decision Making Questionnaire (9-item)

VAS	Visual Analogue Scale
WHO	World Health Organization
WHO-5	World Health Organization Five Well-Being Index
WTP	Willingness to pay
YLD	Years lived with disability

1 INTRODUCTION

The focus of my research is on musculoskeletal (MSK) disorders and specifically on the measurement of changes in quality of life associated with these disorders. The MSK disease area and research topic are fascinating to me for several reasons. Although the ageing society and the elderly are the primary people referred to as having MSK problems, these diseases increasingly affect young people as well. In the MSK field, we cannot think of a well-defined diagnosis as MSK diseases and therapeutic decisions often require a multi-disciplinary approach. Furthermore, MSK disorders also have a significant social and economic burden, both in terms of reduced work capacity and the need to care for patients with disabilities. In addition to family support, informal care, health and social care, innovative medical devices and technologies such as wearables and implantable devices or robotics are expected to play an increasingly important role in healthcare in the future.

1.1 Musculoskeletal health

According to the definition of the World Health Organisation, 'Musculoskeletal health refers to the performance of the locomotor system, comprising intact muscles, bones, joints and adjacent connective tissues. Musculoskeletal impairments comprise more than 150 different diseases/conditions that affect the system and are characterized by impairments in the muscles, bones, joints and adjacent connective tissues leading to temporary or lifelong limitations in functioning and participation.' (1)

1.1.1 The epidemiology of MSK diseases

The Global Burden of Disease survey in 2019 pointed out that approximately 1.7 billion people worldwide were living with an MSK disorder, with an overall prevalence that has been on a steadily increasing trend over the past decades, rising from 16.7% in 1990 to 20.4% in 2019. (2, 3) The prevalence increases with age, but MSK disorders also occur at younger ages, with adolescents and children being affected in addition to the elderly. (4, 5) Globally, the number of prevalent cases in the total population was highest for low back pain (7.6%), followed by osteoarthritis (7.1%), neck pain (3.0%%) and rheumatoid arthritis (RA; 0.3%). (3)

In 2019 (Hungarian Central Statistical Office), 32.0% of the Hungarian population aged 15 and over suffered from an MSK disorder, and this proportion increased with age,

reaching around 60.0% in the population aged 64 and over. (6) More women were affected in all age groups, and this gender gap increased with age, with 68.1% of women and 48.6% of men aged 64 and over suffering from an MSK disorder. The prevalence of chronic low back pain and arthritis was 19.8% and 15.2%, respectively, while RA or chronic arthritis affected 10.3%, chronic neck pain or cervical problems 8.4% and osteoporosis 5.6% of the population. (7)

1.1.2 The burden of musculoskeletal diseases

Musculoskeletal (MSK) disorders cause significant disease burden, ranking fifth worldwide in disability-adjusted life years (DALY; 5.9% of total DALYs) and first position in years lived with disability (YLD; 17.1% of total YLD). Among the MSK conditions listed in the Institute for Health Metrics and Evaluation (IHME) Viz Hub database, the highest disease burden in 2019 was observed for low back pain (7.4% of total YLDs), followed by osteoarthritis (2.2% of total YLDs), neck pain (2.6% of total YLDs) and RA (0.3% of total YLDs). (3) In addition to reduced mobility and functioning, MSK problems are also associated with increased mortality, which has been demonstrated in patients with osteoporotic bone fractures, RA, osteoarthritis and reduced mobility. (8-11)

In addition to their negative health effects, MSK disorders also have a significant impact on work capacity and productivity, resulting in a high social and economic burden. Therefore, they increase direct health expenditure, reduce the number of productive life years, increase absenteeism from work, and contribute to early retirement and reduced financial security. (12, 13) People with MSK problems also often need care, either from a professional (formal care) or from a relative or friend (informal care). (14, 15)

1.2 Health-related Quality of Life (HRQoL)

Quality of life can be defined as an individual's subjective impression and satisfaction with his or her own life and its quality, including his or her role, opportunities, goals and expectations. (16) In this sense, quality of life is a broad concept shaped by the combination of individual, social and environmental factors. In my thesis, the focus is on a specific area, namely health-related quality of life, which I will introduce in the next chapters.

1.2.1 The concept of HRQoL

Health-related quality of life (HRQoL) is a narrower understanding of the concept of quality of life, focusing solely on the impact of health and health status and thus considering only health-related factors as determinants of quality of life. (17) A number of models have been developed to describe and analyse it, using slightly different approaches, although there is no general consensus on its exact definition. (18) The most common and widely accepted understanding is that HRQoL is a subjective, dynamically changing characteristic of the individual, encompassing physical, social and psychological factors of well-being and functioning. (17) (Figure 1)

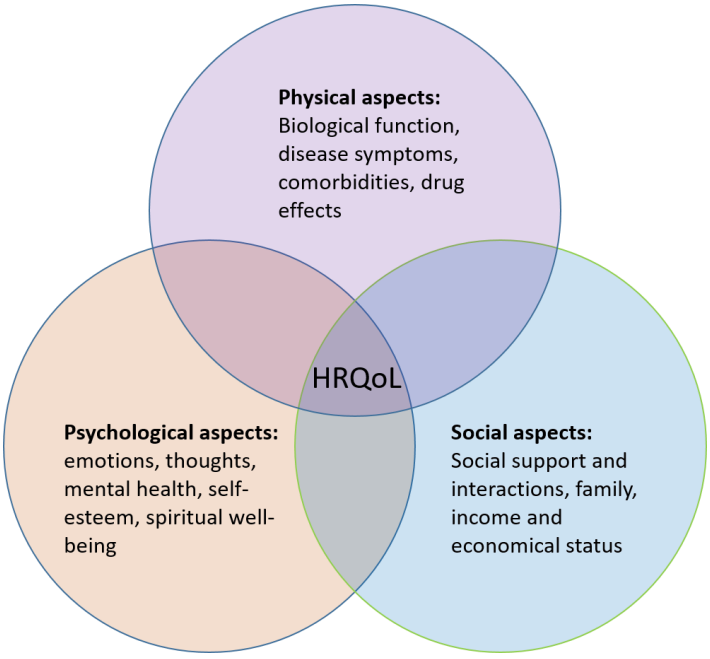

Figure 1: The general concept of Health-Related Quality of Life (HRQoL)

Modern patient-centred medicine places great emphasis on understanding and incorporating patients' opinions, experiences and preferences into healthcare. (19, 20) It is, therefore, necessary to introduce measures outside of routinely collected physiological indicators and diagnostic imaging that allow the assessment of subjective factors that patients consider relevant and perceptible. (21, 22) Such subjective outcomes include patients' self-reports about how they feel, how much pain they have, how they experience physical and psychosocial changes due to their illness, and how they evaluate their own life and its quality in the light of their health status. A year in poor health is usually considered not as valuable as a year in good health. Therefore, to measure the actual

outcome of a disease or an intervention, it is essential to assess the quality of the life years affected by the disease or gained with successful treatment (and sometimes, the disorder or treatment impacts only the HRQoL but not the length of life). This is particularly relevant for chronic conditions where patients may spend years or decades living with a disorder. (23-25)

1.2.2 The measurement of HRQoL

A number of instruments have been developed to measure HRQoL, distinguishing between general and disease-specific instruments based on their field of application. (26, 27) The former assesses the general dimensions of health and can, therefore, be used in any condition and the general population, making it possible to make comparisons across different diseases and match to counterparts from the general public. Hence, one of their main characteristics is their universal applicability, but at the same time, they are less sensitive to differences between health states. (27) Some examples of well-known and widely used general HRQoL measures are the 36-Item Short Form Health Survey (SF-36), the Nottingham Health Profile (NHP), the Assessment of Quality of Life - 6D (AQoL-6D) and the EQ-5D-3L and EQ-5D-5L questionnaires. (28-32)

In contrast, specific instruments are designed to measure disease-, condition- or function-specific aspects and their impact on HRQoL. In addition, there are also group-specific instruments designed to assess the health status of, for example, dermatological diseases (Dermatology Life Quality Index, DLQI), older people (Older people Quality of Life-7 domains, OQoL-7) or informal carers (Care-related Quality of Life instrument, CarerQol). (33-36) Their applicability is limited by their specificity, as they can only be used in certain conditions. However, they have a higher sensitivity, making them more suitable for assessing disease-specific problems and analyzing changes in the patient's (e.g., older people’s, informal caregiver’s) HRQoL. (27)

In practice, both general and disease-specific instruments have been used to measure HRQoL in MSK disorders. (37) For example, the EQ-5D, one of the most widely used general HRQoL questionnaires, was first validated in an MSK disease, namely in RA, but it is also used to assess HRQoL of patients with osteoarthritis and chronic back or neck pain. (38-42) In addition, disease-specific tools have been developed not only in RA (e.g., the Rheumatoid Arthritis-specific quality of life, RAQoL questionnaire), osteoarthritis

(e.g., the Osteoarthritis Knee and Hip Quality of Life questionnaire, OAKHQOL), but also in psoriatic arthritis (e.g., the Psoriatic Arthritis Quality of Life, PsAQoL questionnaire) and osteoporosis, for which a review identified nine different instruments. (43-46) However, a specific tool for the assessment of HRQoL in chronic back pain or neck pain is not yet available. (47, 48)

1.2.3 Standard health status and HRQoL measurement tools used in the Thesis

From the rich set of HRQoL measures available, I briefly present nine that I have used in empirical research, as well as other measures used in large international surveys.

1.2.3.1 Minimum European Health Module (MEHM)

The MEHM consists of three questions on self-perceived general health (very good, good, fair, bad, very bad), the presence of a long-standing (at least six months) illness or chronic morbidity (yes, no) and the presence of a long-standing (at least six months) activity limitation due to a health problem (not limited at all, limited but not severely, severely limited). (49)

1.2.3.2 EQ-5D-5L

The EQ-5D-5L was developed as a generic measure of HRQoL. It assesses five domains (mobility, self-care, usual activities, pain/discomfort, anxiety/depression). (31) In all domains, respondents can indicate on a 5-level Likert-scale how much problem they have on the day of completion. On the scale, 1 indicates the lowest (’no problems’), and 5 indicates the highest (’unable to’/’extreme’) level of problems. The scores given for each domain provide a health profile of the respondent. These profiles are combined with country-specific value sets to determine utility losses, from which the EQ-5D-5L index can be calculated. In our studies, the Hungarian value set was used (range -0.848-1, 1 means perfect health). (50) The EQ VAS is an additional item of the EQ-5D-5L that assesses self-reported health on a visual analogue scale (VAS) ranging from 0 to 100, representing worst to best imaginable health, respectively.

1.2.3.3 Health Assessment Questionnaire – Disability Index (HAQ-DI)

This questionnaire assesses the respondent’s functional ability for the past week with 20 items across eight domains (dressing, arising, eating, walking, hygiene, reach, grip, and common activities). (51) The level of difficulty can be indicated on a scale ranging from 0 (’without difficulty’) to 3 (’unable to do’). In addition, eighteen items are provided to indicate if any aid or device is required to do the activity mentioned in the domains. In

this study, the final score was calculated by taking the sum of the highest item scores in each domain and then dividing it by the number of domains (alternative scoring method – no correction for aids or devices). The resulting final score ranges from 0 to 3, with higher scores indicating worse functional ability.

1.2.3.4 Musculoskeletal Health Questionnaire (MSK-HQ)

The Musculoskeletal Health Questionnaire (MSK-HQ) was designed as a specific questionnaire that can be used across different MSK conditions. (52) It measures respondents' MSK-related health for the last two weeks. Respondents are asked 14 questions about their symptoms and HRQoL (items 1-11), their understanding of and confidence in managing their condition (items 12-13), and the overall impact of the symptoms (item 14). Responses can be given on a 5-level Likert-scale, where 0 indicates the worst and 4 the best condition. Individual scores given for each item are added together to get the final score (range: 0 – 56). The higher the final score, the better the respondent's MSK health. There is an additional item that assesses the number of days in the past week spent with physical activity, which is not taken into account when calculating the final score. Since its release, the tool has been validated in several healthcare settings and translated into different languages, and we developed and validated the Hungarian version (Chapter 4.1). (53, 54)

1.2.3.5 World Health Organisation-Five Well-Being Index (WHO-5)

The WHO-5 evaluates well-being in the past two weeks by asking five questions about the respondent's mental health. (55) Responses are given on a 6-level scale, ranging from 0 to 5, with higher scores indicating better condition. The sum of the item scores is multiplied by 4, resulting in a final score ranging from 0 to 100. The higher the final score, the better the mental well-being.

1.2.3.6 Happiness VAS

The respondent's current happiness was assessed using a visual analogue scale, ranging from 0 to 100, indicating 'completely unhappy' and 'completely happy', respectively.

1.2.3.7 ICECAP-A and ICECAP-O

The ICECAP measurement tools were developed to assess well-being with a focus on capability for use in economic evaluation. The ICECAP-A can be used for adults (18+ old), and the ICECAP-O among the elderly (65+ old). (56, 57) Both versions measure the level of capabilities with five items reflecting different aspects of life, which are

formulated differently for the ICECAP-A (attachment, stability, achievement, enjoyment, autonomy) and ICECAP-O (attachment, security, role, enjoyment, control). Response options are operationalized on a 4-level scale, with 1 indicating 'no capability' and 4 indicating 'full capability'. The index score is calculated by using country-specific value sets. In our study, the UK tariffs were used as the Hungarian value set was not available at the time of the analysis. (57, 58)

1.2.3.8 Electronic Health Literacy Scale (eHEALS)

The eHEALS scale measures the respondent's self-perceived knowledge and skills to find, understand, evaluate and use health-related electronic information. (59) It consists of eight statements focusing on four domains (with two statements in all domains): awareness, searching for information, evaluation of health resources, and utilisation. The level of agreement with each statement can be indicated on a 5-level scale (1 – 'strongly disagree'; 5 – 'strongly agree'). To get the final score (range: 8-40), the individual item scores are added together, with higher scores indicating better electronic health (eHealth) literacy. In the study, the validated Hungarian version of the scale was used. (60)

1.2.3.9 Shared Decision Making Questionnaire (SDM-Q-9)

The SDM-Q-9 has been developed to assess the extent to which a patient is involved in making health decisions that affect his/her own health. (61) The questionnaire starts with two open-ended questions on a recent health problem discussed with a healthcare provider and the subsequent decision. Then nine statements on different aspects of the decision making situation are given to the respondent, and the level of agreement with each can be indicated on a 6-level scale (0 – 'completely disagree'; 5 – 'completely agree'). The final score (range: 0 – 45) equals the sum of the scores given for each statement. The higher the final score, the greater the level of involvement in decision making. The validated Hungarian version of the questionnaire was used in this study. (62)

1.2.3.10 Other measures

In addition to the standard instruments described in this chapter, other study-specific measures were used (European Health Interview Survey questions, visual analogue scales to measure knowledge of implantable medical devices (IMDs), single question assessment of the impact of IMDs on HRQoL, hypothetical decision making situation and willingness-to-pay task for innovative digital health technologies), which are presented in the corresponding methods chapters.

1.2.4 The importance of HRQoL in different areas of decision making in healthcare

Both general and specific HRQoL measures are widely used to support regulatory, clinical, financial and health policy decisions. (63-69)

The marketing authorisation process of health technologies (medicines, medical devices, therapeutic and diagnostic procedures) includes the evaluation of their efficacy and safety. The use of patient-reported outcome measures (PROMs) in randomised clinical trials has become a standard that has also been proposed by regulatory authorities, recognising the importance of patient perspectives. (70-72) General preference-based HRQoL instruments such as the EQ-5D are widely used as secondary endpoints in clinical trials, for example, in RA, to measure health outcomes that patients consider relevant. (73) In addition, PROMs and HRQoL questionnaires are often used as primary, co-primary or surrogate endpoints in a number of trials, for example, in oncology or in chronic dermatological or MSK indications. (74-77)

There is also a growing emphasis on patient perspectives and HRQoL in therapeutic decision making, which is reflected in the recommendations of professional guidelines. (78, 79) For example, in its recommendations on the management of RA, the European Alliance of Associations for Rheumatology (EULAR) highlights the importance of PROs and the inclusion of patient perspectives in therapeutic decisions, which has been demonstrated to have a positive impact on medication adherence and satisfaction with therapy. (80-82)

HRQoL also plays a vital role in reimbursement decisions for new health technologies. In health economic analyses to inform health coverage decisions, the health gains associated with particular technologies are often expressed in a metric called quality-adjusted life year (QALY), in which the ‘Q’ is calculated using HRQoL. (83-85) Accordingly, both international Health Technology Assessment (HTA) organisations and the Hungarian Ministry of Human Capacities, in its guideline on economic evaluations in healthcare, recommend the use of QALY-based cost-utility analysis as the primary method for assessing the cost-effectiveness of new technologies. (86-88) In addition, the QALY can also be a valuable tool for informing resource allocation decisions, as it allows for a comprehensive assessment of different therapeutic areas. (84)

1.3 New perspectives and research gaps in the HRQoL assessment of musculoskeletal disorders

In the next chapters, I introduce five new perspectives from the past years in the HRQoL assessment of MSK disorders and point out research gaps that inspired my research aims.

1.3.1 New HRQoL assessment tools: combined measures, need for locally validated versions

Patient-centred care and informed decision making require knowledge of patients' conditions, disease activity, symptoms and HRQoL, as well as standardised, validated measures that allow these factors to be properly assessed. In response to these emerging needs, there has been considerable scientific activity in the field of outcome measurement. The Outcome Measures in Rheumatology (OMERACT) has been actively involved in the development and evaluation of new outcome measures since 1992 (89), but Hungary is also at the forefront of this work, not only in the Central and Eastern European region but also internationally. (90)

As a result, a great number of disease-specific measures have been developed (and adapted to Hungary) in the MSK field, and the applicability of generic questionnaires has been investigated in several well-defined MSK diagnoses (Chapter 1.2.2). However, for healthcare planning strategies, reimbursement and public health decisions, it is often needed to shift the focus from the individual patient level to a broader level, i.e., consider diseases as a joint group. Therefore, there is a growing demand for measurement tools that combine both disease symptoms and HRQoL and, in addition, can be applied to any diagnosis within a given disease group. (91, 92) This is particularly important in the field of MSK disorders, where the underlying causes can be very heterogeneous (e.g., arthritis, back pain), and different MSK problems may co-exist. (93) The new combined instruments are expected to measure all relevant aspects of MSK health and to be widely used in the MSK field to compare the health of patients with different problems. Such a comprehensive tool can be useful, for example, to evaluate and compare the effectiveness of physiotherapy in patients with different MSK problems (94, 95) or to compare the performance of different healthcare services aimed at MSK patients. (52, 96, 97)

To date, there are only a few disease group-specific measurement tools available in the MSK field that meet these requirements. An example is the Keele Musculoskeletal Patient Reported Outcome Measure (MSK-PROM), which was developed to monitor the health

status of patients across a wide range of MSK disorders. (98) The recently developed Musculoskeletal Health Questionnaire (MSK-HQ) was designed to assess patients' MSK-specific symptoms and HRQoL in different MSK conditions. (52) Since its first publication in 2016, it has been validated in a number of MSK patient groups and has been translated into several languages. (54) The performance and its growing popularity inspired us to make this tool available in Hungarian so that clinicians and healthcare decision-makers can comprehensively assess the condition of Hungarian MSK patients and make international comparisons.

1.3.2 New needs in epidemiology: musculoskeletal health of the population and of informal caregivers, prevalence of implantable medical devices

The medical field is constantly changing; new technologies are emerging due to technological advances, and, in parallel, decision-makers are faced with increasingly complex questions that can not be adequately addressed with traditional indicators, such as mortality and objective clinical indicators. (99) Over the past decades, HRQoL research has grown significantly, resulting in an increasing acceptance by physicians and researchers that, in addition to life expectancy, assessment of patient-reported outcomes (such as HRQoL) is necessary for the proper evaluation of medical and public health interventions. (100) As a result, HRQoL measurements have become a mandatory component not only of randomised controlled trials (RCTs), which form the basis for marketing authorisation, but also of epidemiological research, health services research and population surveys. (101)

As the importance of HRQoL measures grows, having country-specific population norms for already available tools is becoming increasingly important. Normative data show the average value and the distribution of a given characteristic, such as MSK health, in society and how this varies by socio-demographic subgroups. (102) Therefore, population norms can serve as a reference for objectively determining the health status of patients. (103) For example, these data can be used by health policymakers to examine disease burden in well-defined patient groups, map priorities between disease areas, and make international comparisons. (104) However, due to the scarcity of extensive population-based studies, population normative data are often unavailable or incomplete for many HRQoL measures. For example, a recent systematic review showed that in the Central and Eastern European region, the EQ-5D, one of the most widely used generic HRQoL

instruments, has been used in several studies across multiple disease areas. Yet, population norms were available in only three of the eight countries. (105) Researchers face an even more significant data gap in the case of more recently developed scales. The applicability of the MSK-HQ, described in the previous chapter, has been evaluated in several patient groups, but it has yet to be applied in a population survey. (54) This is how we became interested in the development of population normative data with the MSK-HQ measurement tool and also in the analyses of determining sociodemographic factors.

Identifying vulnerable subgroups within a population is a central issue in public health strategies, and MSK disorders are no exception. However, the group of informal caregivers living with MSK disorders has received less attention so far. Informal care refers to the care provided without remuneration to a family member or a close relative or friend who needs help in performing everyday activities due to a chronic illness, disability or other health problem. (106) Informal caregiving is often a time-consuming, stressful and demanding task, especially for those who suffer from physical or mental health problems. (107, 108) These affected caregivers typically have less time and energy to focus on their own health and have lower adherence to their therapy, putting them at increased risk of disease development. (109) There have been many informal care studies from the perspective of MSK patients being cared for, but only little attention has been paid to informal caregivers suffering from MSK problems. Therefore, our idea was to identify and study the subgroup of informal caregivers living with MSK health problems via epidemiological studies in order to have a first idea about the size of the problem and a basis for targeted social interventions.

In recent decades, there has been a strong focus on drug therapies for MSK diseases, but less attention has been paid to other health technologies, such as medical devices. (110) Consequently, epidemiological data are incomplete in this field; very little is known about the prevalence and characteristics of patients living with an IMD due to an MSK problem. At present, data on the prevalence of IMDs are primarily available only from single-centre observational studies or IMD-specific registries. (111-113) Therefore, we considered a population-based, descriptive epidemiological survey of IMDs to be a pioneering study at the international level.

1.3.3 New areas of HRQoL measurement: re-use of health-related data, well-being and happiness outcomes, advanced digital health technologies and medical devices

When assessing HRQoL, we are often faced with the problem that good quality, directly measured HRQoL data are partially or completely missing from the studies. In these cases, the question arises whether HRQoL data can be estimated based on available health information. According to recent reports, the volume of health data recorded in the United States reached 150 exabytes (150 billion gigabytes) in 2011 and is projected to increase by several orders of magnitude in the coming years. (114) In the European region, the Eurostat routinely collects data on health, including MSK health, through the European Health Interview Survey (EHIS), which is conducted every five years. In Hungary, the Hungarian Central Statistical Office is responsible for the organised collection and evaluation of EHIS. (6, 7) The EHIS includes questions such as 'Can you walk 500 metres on a flat terrain?' but does not involve the respondent's perspective (i.e., how much the limited walking ability bothers his life) that could be assessed with validated HRQoL measurement tools. (115) National health surveys and registers are also rich repositories of similar health information, but only very few collect any HRQoL data using validated tools. This accumulated body of information can be used for a deeper assessment of the relationship between widely available health statistics and HRQoL, as well as mapping between HRQoL measures. With this knowledge, HRQoL values can be estimated and used in HTA assessments to support health coverage and public health decisions, thus speeding up HRQoL-based decision making. (88) The Development of efficient and valuable solutions to use health statistics to estimate HRQoL data has caught our interest, and we commissioned research to investigate the relationship between MSK statistics of EHIS and the MSK-HQ measurement tool.

Recently, another new area of research has opened up, as there has been a growing demand from decision-makers for a comprehensive understanding of patients' conditions, perspectives and personal experiences that goes beyond the assessment of health-related factors alone. (116) There is, therefore, a need to extend the assessment of HRQoL to aspects such as happiness, satisfaction with life, mental and capability well-being, family effects, informal care, experiences with care, and preferences for different care settings (117) As a consequence, new measurement tools have emerged in recent years that allow these aspects to be measured in a standard, valid and reliable way. (117) ICECAP is a

family of instruments designed to assess the capability well-being of the adult population (ICECAP-A), older people (ICECAP-O), children (ICECAP-CYP)) and people in the end-of-life setting (ICECAP-SCM). (56, 57, 118-120) In addition, there has been progress towards combined measures of health status and well-being, such as the recently developed EQ-HWB. (121) Accordingly, there is a growing popularity of the well-being approach and the ICECAP measures, but there has been only limited research in the field of MSK disorders, so little is currently known about how patients' well-being relates to their MSK health. (122-124) Therefore, we thought we would shed light on the relevance of MSK health and HRQoL to the increasingly important well-being outcomes in decision making.

Another area of HRQoL measurement that is currently under intensive research is complex health technologies, including digital technologies and medical devices or wearables, which present a number of methodological challenges for HRQoL assessment. (125-127) This is particularly true for high-risk devices, such as implantable medical devices (IMDs), e.g. knee and hip replacement, bone fixation and spinal implants, where a full assessment of safety, efficacy (and economic impact) is required. (128) One common problem is that for these devices, the available evidence is often of poor quality and patient-relevant outcomes are rarely captured. For example, a systematic review found that for hip and knee replacement surgery, only 9% of the 151 studies identified between 1995 and 2021 were RCTs. (129) In addition, patient outcomes were rarely assessed, with only 40% of implants having some PRO data published during this period. (129) But a similarly low rate of published PRO data was observed among European HTA offices as well. In a large-scale European survey conducted in 2021, 18 out of 20 HTA offices indicated that methodological problems with the assessment of complex health technologies, including advanced surgical interventions, digital technologies and medical devices, were mainly due to a lack of adequate data, in particular HRQoL data. (130) A further major methodological challenge in the assessment of medical devices is that their real-life performance and effectiveness depend not only on the device itself but also on how it is used so that the skills, knowledge and experience of users with the device have a significant impact on expected health outcomes. (131, 132) Reflecting the difficulties associated with the evaluation of medical devices, major international HTA organisations have formulated their own recommendations. (133-135) The relevance and growing

importance of this topic is demonstrated by the roughly 100-fold increase in the number of annually published HTA reports on medical devices between 2000 and 2019. (110) Accordingly, we found it to be an important avenue for research to investigate the impact of IMDs on patients' HRQoL and its major influencing factors.

1.3.4 New aspects of patient involvement: shared decision making, electronic health (eHealth) literacy

Patients' role in healthcare is slowly changing as modern, patient-centred medicine places a strong emphasis on incorporating their perspectives and preferences into the treatment process. They are moving from a largely passive presence to becoming active participants in healthcare decisions. Accordingly, the patient's role is reinforced by clinical guidelines in many MSK conditions. For example, the EULAR guideline on the treatment of RA recommends among its overarching principles that treatment should be based on a joint decision between the rheumatologist and the patient. (82) Similarly, recommendations on the treatment of psoriatic arthritis and axial spondyloarthritis emphasise the importance of doctor-patient collaboration and shared decision making. (136, 137) However, how shared decision making should be made and how to measure the level of patient involvement is not elaborated upon and standardized. (138, 139) Furthermore, the measurement of shared decision making using standard, validated measures is in its infancy, and existing validated measures are little used or not used at all in the clinical practice. (139, 140) In addition, it is also not part of routine care (and not elaborated clinical guidelines) to assess patients' knowledge and awareness after they have been informed. This is a particularly important issue in the case of implantable medical devices (IMDs), where (unlike, for example, with biological therapies that are given under close clinical supervision) patients do not necessarily need to be regularly monitored after implantation (i.e. fixation of bone fractures with plates and screws). In these situations, patients have a great responsibility to wear their implant and to identify problems with the device that require medical intervention. In addition to knowledge and patient involvement, the growing uptake of electronic and digital technologies and devices has increased the focus on patients' eHealth literacy and its relationship with health outcomes, including HRQoL and patients' experiences of healthcare. (141-145) Therefore, we thought to investigate the level of shared decision making using a reliable and valid tool, the SDM-Q-9 questionnaire among individuals who have had a medical device

implantation, to assess their knowledge and eHealth literacy in parallel and analyse how these relates to clinical and HRQoL outcomes of IMDs.

1.3.5 New innovative digital health technologies: patients' preferences and acceptance of artificial intelligence-based health technologies

Advanced digital devices and AI-based technologies are becoming widely used in healthcare. In orthopaedic surgery, especially in joint replacement, a number of robot-assisted procedures have become available over the past two decades. (146) Available evidence suggests that, compared to traditional surgical procedures, these new technologies increase surgical accuracy, i.e., more accurate implant insertion and reduced limb length discrepancies have been observed in total hip replacement implantation. (147) However, it is currently unknown whether better accuracy is associated with improved health outcomes. For example, despite improved accuracy, no advantage in clinical efficacy has been observed for robot-assisted spine surgery and knee replacement implantation over conventional surgery. (148, 149) Robot-assisted systems are also widely used in rehabilitation and physiotherapy following MSK and neurological injuries, with encouraging results. (150-152) Artificial intelligence-based algorithms are now routinely used as part of imaging procedures in rheumatology, both for diagnosis and to aid therapeutic decisions. (153) A good example of this is the widespread use of AI-enhanced ultrasonography to automate tissue recognition, joint and muscle lesion detection and classification, which can help improve the accuracy and consistency of diagnostic assessments and improve the performance of the diagnostic workup. (154) In addition, the use of robotics has also emerged in other areas of healthcare, such as social care and elderly care, where encouraging results have been achieved. (155, 156)

Given their widespread use in healthcare, the question arises as to the acceptance of and preferences for advanced health technologies. As patients are gradually gaining a prominent role in healthcare (117), their attitudes towards therapies and interventions can have a profound impact on therapeutic decisions and affect health outcomes. (157-159) Many studies have been conducted among health workers, who are the first to encounter new technologies and play a key role in their adaptation, but little is known about the acceptance of advanced health technologies in the population. (160-163) Therefore, we have turned to research the preferences and attitudes of society (patients and potential future patients) and how these relate to socio-demographic characteristics, current health

status, HRQoL and eHealth literacy. These data can support developers in designing medical robots and AI technologies, endorse marketing and implementation strategies, as well as financial and health policy decisions.

2 OBJECTIVES

The conceptualisation of our empirical research and the formulation of the objectives were based on the five new perspectives of HRQoL assessment described above. We attempted to find answers to our research questions in 2 large population surveys, the second of which had two parts, resulting in a total of three studies.

In the first study, one of the aims was to develop and validate the Hungarian version of the recently developed international Musculoskeletal Health Questionnaire (MSK-HQ), thus making this combined measurement tool of MSK health and HRQoL available in Hungary. Regarding new areas of HRQoL measurement, we aimed to use the MSK-HQ to investigate the relationship between MSK health and statistical health data, standard HRQoL and well-being measures, thus creating new opportunities for better use of already available health data. Concerning new needs in epidemiology, the aim was to assess the population's MSK health with the MSK-HQ and to present population normative data. Also, we sought to assess the MSK health and HRQoL of informal caregivers, a largely unexplored social subgroup so far.

The second study was the first research module of the larger population survey mentioned above. As there is currently limited data on the prevalence of implantable medical devices (IMDs), including IMDs with MSK relevance, we aimed to fill this gap by obtaining detailed epidemiological data on IMDs among the general population. In addition, in terms of new areas of HRQoL measurement, we aimed to understand the impact of IMDs on patients' HRQoL, as there is also a need for more knowledge in this field. Concerning new aspects of patient involvement in medical decisions, we aimed to understand patients' perspectives by examining their awareness, eHealth literacy and experience of shared decision making and how these factors relate to the impact of IMDs on their lives.

In the third study, which was the second research module of the larger population survey mentioned above and focused on new innovative digital health technologies, we aimed to gain insight into the attitudes and preferences of the public towards robot-assisted surgery via the example of hip replacement surgery.

Our research goals and the two surveys are briefly summarised in Figure 2. Detailed study objectives of the surveys are listed in the next chapters.

2.1 Development and validation of the Hungarian version of the MSK-HQ and assessment of the musculoskeletal health of the population

- To develop and validate the Hungarian language version of the MSK-HQ measurement tool for Hungary and to assess its associations with routinely collected statistical MSK health data and other standard tools, including well-being measures (53, 54, 164, 165)
- To establish a population norm with the MSK-HQ measurement tool and investigate the MSK health by socio-demographic characteristics (53)
- To assess the MSK health and HRQoL of informal caregivers (53, 166, 167)

2.2 Living with implantable medical devices: focus on musculoskeletal patients

- To assess the epidemiology of IMDs among the general population (168-172)
- To assess the overall impact of IMDs on HRQoL (168, 170, 172)
- To assess patients' knowledge of IMDs, eHealth literacy, involvement in shared decision making and how these factors are associated with the impact of IMDs on HRQoL (168-174)

2.3 Social preferences and attitudes towards the use of artificial intelligence-based technologies in hip replacement surgery

- To assess stated preferences for robot-assisted hip replacement surgery, with special focus on the role of eHealth literacy of the population (175-177)
- To explore the strength of preferences for conventional and robot-assisted hip replacement surgery using the willingness to pay method and analyse its determinants, including the eHealth literacy of the individuals (175-177)

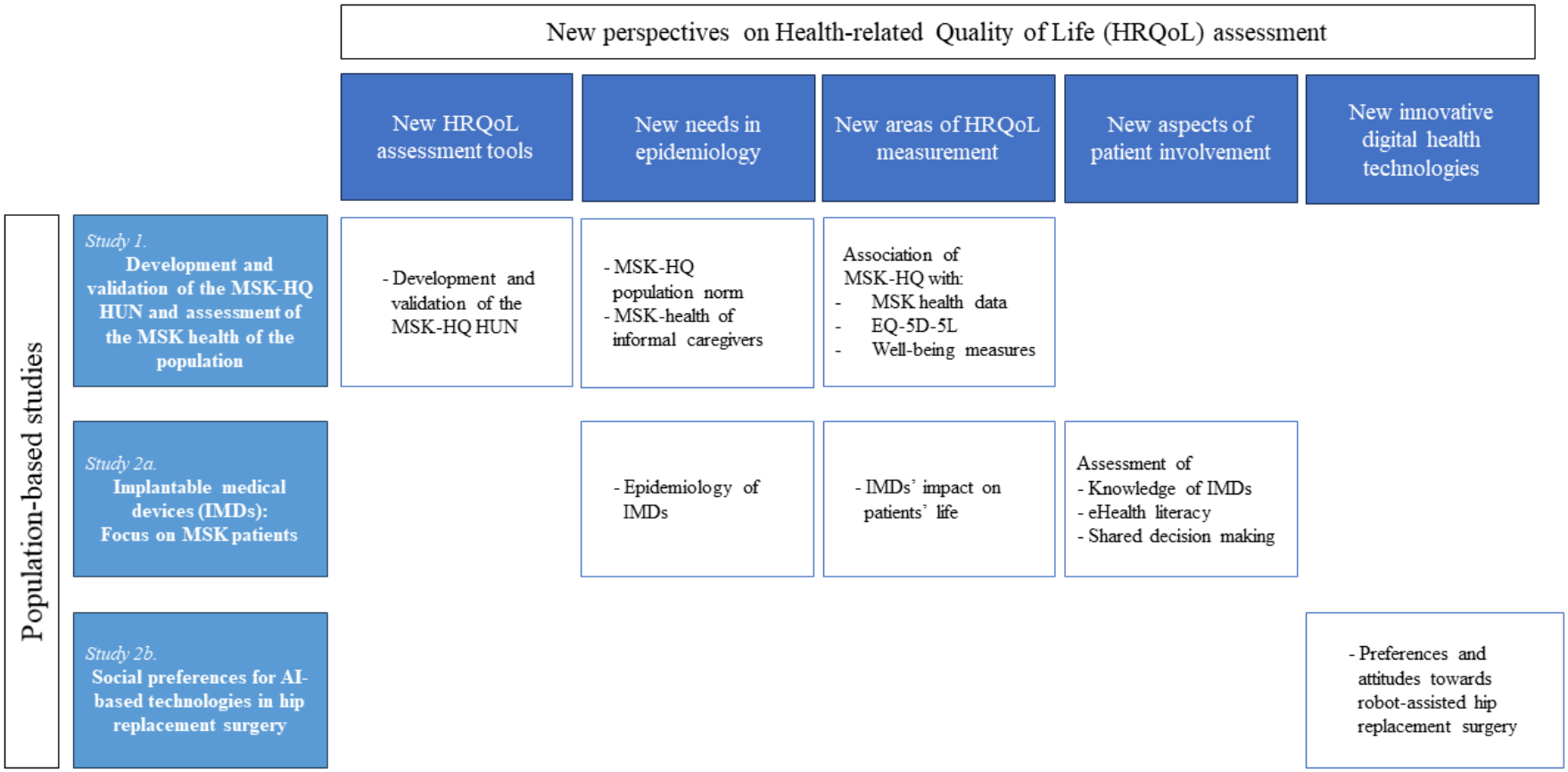

Figure 2: Overview of research objectives and studies included in the thesis

3 METHODS

In the following chapters, I introduce the three population studies that form the basis of my thesis.

3.1 Development and validation of the Hungarian version of the MSK-HQ and assessment of the musculoskeletal health of the population (Study 1)

We developed the Hungarian language version of the MSK-HQ according to the protocol of the developer (Oxford University Innovation). (178) Initial forward translations were carried out independently by three researchers, and after a thorough discussion, a consolidated Hungarian version was developed, which was then back-translated into English. After review by the developer, a second forward and back translation was carried out to address the issues identified. Finally, a pilot study involving five participants was conducted to examine interpretability, followed by proofreading and quality checks before acceptance of the final version. (54) We assessed the psychometric properties of the Hungarian MSK-HQ and the MSK health of the population in a larger study, the details of which I present in the following subchapters. (53)

3.1.1 Data collection and survey design

In 2020, an online cross-sectional study was carried out among the Hungarian general adult population. Participants were selected by quota sampling in order to obtain a representative sample in terms of sex, age, education and settlement type. Ethical approval was obtained from the Hungarian Medical Research Council (no. IV/565–5/2020/EKU). In the survey, socio-demographic characteristics, such as sex, age, education, type of settlement, marital status, number of household members, household income, and employment status were recorded. The occurrence of specific MSK problems (walking difficulties, problems with low back, back or neck, and osteoarthritis of the knee or the hip) was surveyed using the questions of the European Health Interview Survey (EHIS). (179) Respondents were also asked whether they had used healthcare services (general practitioner or specialist visits in the last three months or hospital admission in the last year), needed informal care due to MSK problems, or provided informal care for someone having physical or mental health problems, or problems due to ageing. After completing the survey, a randomly selected subsample (N=50) repeated the MSK-HQ in order to assess its test-retest reliability. (53)

3.1.2 Standard measurement tools

Participants' MSK health was assessed with the Hungarian version of the Musculoskeletal Health Questionnaire (MSK-HQ) that was developed by our research group following the protocol of and in collaboration with Oxford University Innovation. Other standard measurement tools were used to examine general health (MEHM), HRQoL (EQ-5D-5L), physical functioning (HAQ-DI) and well-being (ICECAP-A/-O, WHO-5, Happiness VAS). All standard instruments are introduced in chapter 1.2.3.

3.1.3 Statistics

The validation of the Hungarian version of the MSK-HQ was performed in accordance with the COnsensus-based Standards for the selection of health status Measurement INstruments (COSMIN) guideline. (180)

The characteristics of the study sample were examined with descriptive statistical methods. Differences in the MSK-HQ score by socio-demographic subgroups and self-reported general health state, mobility problems, MSK status, healthcare utilization and informal care status were analyzed with the Mann-Whitney U and Kruskal-Wallis tests.

The convergent validity was assessed by calculating Spearman's Rho ($r_s > 0.5$ strong, $0.5 \geq r_s \geq 0.3$ medium, $r_s < 0.3$ weak) between the MSK-HQ and other standard measures. (181) The internal consistency was measured with the Cronbach's Alpha (0.7-0.8 acceptable, 0.8-0.9 good, >0.9 excellent). (182) Test-retest reliability was examined with the intraclass correlation coefficient (ICC), ranging from 0 to 1 (level of agreement: <0.5 poor, 0.50-0.749 moderate, 0.75 – 0.90 good, >0.90 excellent). (183)

The association of the MSK-HQ total score with the EQ-5D-5L index (HRQoL), the HAQ-DI score (functional ability) and socio-demographic characteristics were examined in a multiple regression analysis. Three models were developed, and the independent variable was the MSK-HQ score in all models. Socio-demographic characteristics were included as background variables in all models. In addition, the EQ-5D-5L and the HAQ-DI were included as predictors in the first and second models, respectively, and together in the third model to assess how they influence each other's effect on the MSK-HQ score.

The significance level was $p>0.05$ in all statistical tests. 'Do not know' and 'Do not want to answer' responses were treated as missing values and omitted from the respective analysis.

3.2 Living with implantable medical devices: focus on musculoskeletal patients (Study 2a)

3.2.1 Data collection and survey design

This study is based on the first research module of a larger cross-sectional online survey that was conducted among the Hungarian general population aged 40 and older. (168) Selection of participants was done by quota sampling to ensure representativeness in terms of sex, age, education and type of settlement. Ethical approval was obtained from the Hungarian Medical Research Council (no. IV/5651-1/2021/EKU). All participants completed the whole survey. Apart from the research module-specific elements, socio-demographic characteristics (sex, age, education, type of settlement, employment status, marital status, number of household members, and household income) were recorded. In addition, the HRQoL and eHealth literacy of all participants were surveyed using standard outcome measurements described in Chapter 1.2.3. Specific to the first module, the following data were recorded:

1. The epidemiological characteristics of IMDs were investigated by presenting respondents with the following pre-defined set of 15 different IMDs, including implants with MSK relevance: bone fixation (screws or plates), hip replacement, knee replacement, spinal implant, intraocular lens, dental implant, dental bone graft (for dental implants), pacemaker, artificial heart valve, coronary stent, abdominal mesh, breast implant, glucose sensor, intrauterine device (only for females), other type (free-text response to indicate any type of IMD not listed above). If the respondent reported ever having had an IMD, the year of implantation and whether he/she was still living with it were recorded.
2. Participants who reported living with an IMD were asked if they had received written ’instructions for use’ for their IMD. The four possible response options were: yes, and read it; yes, but did not read it; did not receive; do not remember.
3. The knowledge of IMDs was explored among participants living with an IMD in four domains: familiarity with general instructions for use (‘How familiar are you with the instructions and lifestyle advice for the daily use of the implanted device?’), familiarity with safety requirements (‘How familiar are you with the specific safety requirements for the implanted device you are using?’), ability to recognize need for medical control (‘How confident are you that you will be able to recognise in time if there is a problem with the implanted device that needs

medical control?'), and the ability to recognize the need for information security or privacy control ('How confident are you that you will be able to recognise in time if there is a problem with the implanted device that requires information security or privacy control?' – only for participants who were living with an electronic IMD). The self-perceived level of knowledge in each domain could be indicated on a visual analogue scale (VAS) ranging from 0 (worst possible knowledge – 'not at all') to 10 (best possible knowledge – 'completely').

4. Those living with an IMD were asked about the impact of the device on their life ('How do you think your IMD affected your life overall? Including the circumstances of the implantation and the IMDs' impact on your quality of life and daily activities.'). Responses could be given on a 5-level scale: 1 – very negative, 2 – rather negative, 3 – neither negative nor positive, 4 – rather positive, 5 – very positive.

3.2.2 Standard measurement tools

In the study, participants' HRQoL, eHealth literacy and self-perceived involvement in shared decision making were assessed using the EQ-5D-5L, the eHEALS and the SDM-Q-9 instruments introduced in Chapter 1.2.3.

3.2.3 Statistical methods

The characteristics of the study sample (socio-demographics, health status, eHealth literacy) and the frequency of IMDs were analyzed with descriptive methods.

The mean age at implantation and the time of living with the device were calculated for each IMD type, and differences were compared with analysis of variance (ANOVA).

In the subsample of respondents living with an IMD, the means of each knowledge domain were calculated and analysed by socio-demographic subgroups, received instructions for use and IMD's impact on life using the Kruskall-Wallis test. Also, in the subsample living with an IMD, the correlation of knowledge with the standard outcome measures (EQ-5D-5L index, EQ VAS, eHEALS, SDM-Q-9) was examined with Spearman's Rho ($r_s > 0.5$ strong, $0.5 \geq r_s \geq 0.3$ medium, $r_s < 0.3$ weak). (181)

The consistency of the four knowledge scales was examined with Cronbach's Alpha (0.7-0.8 acceptable, 0.8-0.9 good, >0.9 excellent). (182) A combined knowledge score was calculated by averaging the scores on the four knowledge scales to represent respondents'

general knowledge. This combined score was used to analyze knowledge differences by IMD type and sex.

IMD's overall impact on life by IMD type was assessed with descriptive statistics. Also, factors associated with the impact of IMDs on participants' lives were explored by multiple linear regression in the subsample of respondents living with an IMD. All in all, seven regression models were developed. In all models, the dependent variable was IMD's overall impact on life. In order to test the effect of background characteristics, the following independent variables were added to models 1-3 and included in all subsequent models: IMD types (Model 1), socio-demographics and EQ-5D-5L index score (Model 2), combined knowledge score (Model 3). The eHEALS score, the received instructions for use and the SDM-Q-9 score were added in a mutually exclusive manner to models 4 - 7 to test how they individually affected IMD's impact on life when controlling for background characteristics. The final model (Model 7) included all of the above variables together.

'I do not know' and 'I do not wish to answer' responses were treated as missing values and were excluded from the respective analysis. The significance level was $p<0.05$ for all statistical tests.

3.3 Social preferences and attitudes towards the use of artificial intelligence-based technologies in hip replacement surgery (Study 2b)

3.3.1 Data collection and survey design

This study focused on the second research module of the larger cross-sectional online survey described in Chapter 3.2.1. (177)

In brief, respondents aged 40 and over were selected by quota sampling, and, in addition to their socio-demographic characteristics, their general health, HRQoL and eHealth literacy were assessed using standard measures.

Specific to the second module, social preferences and attitudes towards robot-assisted hip replacement surgery were assessed. Participants were placed in a hypothetical decision making situation. At first, they were asked to imagine that they have a hip joint disease, due to which their physician recommended to have hip replacement surgery. Basic information on the prosthesis and the surgery were briefly introduced. Then, participants were asked to choose which method they would prefer to perform the surgery: when the surgeon does the operation independently (conventional surgery) or when the surgeon uses robotic assistance to do the operation (robot-assisted surgery). It was explained that

the robot is able to do some phases of the operation completely independently, but the surgeon is present and can take over in case of emergency. Also, the two methods are equally safe and effective. The decision making situation was followed by a willingness-to-pay (WTP) task, in which participants were informed that they had been assigned to the surgery with the method contrary to their choice but that they could be reassigned to the preferred method for a fee. They were then asked to indicate in the following nine categories how much they would be willing to pay in return: 0 EUR; 0-28 EUR; 28-84 EUR; 84-140 EUR; 140-280 EUR; 280-560 EUR; 560-1120 EUR; 1120-2240 EUR; 2240< EUR (in the highest category the respondent had to indicate the exact amount).

3.3.2 Standard measurement tools

Participants' HRQoL and eHealth literacy were assessed with the EQ-5D-5L and eHEALS scales that were introduced in Chapter 1.2.3.

3.3.3 Statistical methods

Sample characteristics and participants' preferences (choice of methods and WTP) were analyzed with descriptive statistical methods. For the purpose of the analysis, participants' WTP was converted and handled as a continuous variable by taking the middle value of the categories. Participants' preferences and WTP were analyzed by socio-demographic subgroups, eHealth literacy (eHEALS) and HRQoL (EQ-5D-5L) using the Chi-squared, Kruskal-Wallis and the two-sample t-test. The effect size was measured with Cohen's D (small = 0.2; medium = 0.5; large = 0.8). (184)

Correlations were examined by calculating Pearson's correlation coefficient ($r > 0.5$ strong, $0.5 \geq r \geq 0.3$ moderate, $r < 0.3$ weak). (181) The association of WTP with the choice of surgery and background characteristics (socio-demographics, implant status, eHEALS, EQ-5D-5L, level of difficulty in answering questions about the task) was further explored in a multiple regression analysis.

'Do not know' and 'Do not want to answer' responses were treated as missing values and excluded from the analysis. The significance level was accepted as $p<0.05$ for all tests.

4 RESULTS

The results underlying the thesis are presented in the following chapters according to the three studies.

4.1 Development and validation of the Hungarian version of the MSK-HQ and assessment of the musculoskeletal health of the population (Study 1)

4.1.1 Development and validation

We successfully developed the Hungarian language version of the MSK-HQ, which was accepted by the owner (Oxford University Innovation). (54, 185) Its validity was evaluated in a study involving N=2004 respondents (Study 1). (53) Their mean age was 48.3 (SD=16.6) years and 53.1% were female. Respondents' socio-demographic characteristics are presented in Table 1.

Table 1: Sample characteristics

[a] There were 55 and 4 participants in age groups 75–84 and 85–94, respectively.
[b] Conversion: 1 EUR = 348.35 HUF (the exchange rate in May 2020)
** For variables with missing values, the basis of comparison (100%) is the total sample size minus the number of missing data*
GALI - Global Activity Limitations. Differences were tested using the Kruskal–Wallis and Mann–Whitney U test. Source: Hölgyesi et al, 2022. (53) (CC BY 4.0). The table is presented in its original form.

Variables	N	%	MSK-HQ score Mean (SD)
Total	2004	100.0*	44.13 (9.94)
Gender			p= .001
Men	940	46.9	44.85 (9.81)
Women	1064	53.1	43.50 (10.01)
Age[a]			p= .000
18-24	192	9.6	47.28 (7.71)
25-34	306	15.3	46.26 (8.29)
35-44	387	19.3	45.90 (8.95)
45-54	332	16.6	43.77 (10.54)
55-64	328	16.4	40.54 (10.87)
65-74	400	20.0	42.97 (10.42)
75+	59	2.9	41.17 (10.15)
Education			p= .000
Primary	608	30.3	42.12 (11.13)
Secondary	968	48.3	44.68 (9.34)
Tertiary	428	21.4	45.77 (8.97)
Settlement type			p= .000
Capital	358	17.9	45.89 (8.88)
Town	1053	52.6	44.26 (9.98)
Village	593	29.6	42.86 (10.29)
Married/having a partner			p= .857
Yes	1300	64.9	44.18 (9.74)
No	704	35.1	44.04 (10.30)

Variables	N	%	MSK-HQ score Mean (SD)
Living with someone in the household			p= .224
Yes	1686	84.1	44.24 (9.93)
No	318	15.9	43.59 (10.00)
Paid work			p= .000
Yes	1158	57.8	45.14 (9.21)
No	846	42.2	42.76 (10.71)
Household income category (not reported N=304)[b]			p= .000
0-718 EUR	752	44.2	41.78 (10.95)
718-1435 EUR	763	44.9	44.76 (9.23)
Above 1435 EUR	185	10.9	48.25 (7.27)

In the total sample, the mean MSK-HQ score was 44.1 (SD=9.9). Known-groups validity analysis indicated that MSK-HQ differed significantly by respondents' general health status and MSK health problems. (53) The MSK-HQ total score was lower for those having poorer self-perceived health, reporting the presence of a longstanding illness, or limitations in their daily activities for at least the past six months. It was also lower for respondents with more severe mobility problems, difficulties with walking 500 meters on ground level or walking up or down 12 steps. Those who reported having a specific MSK problem were in poorer MSK health; the MSK-HQ total score was lowest when the respondent had a diagnosed problem and was taking medication for it. In this subgroup, the MSK-HQ score differed significantly (ANOVA $F_{(4,392)}=24.56$, $p<0.001$) by the number of MSK problems: respondents with more concurrent problems had worse MSK health. In addition, lower MSK-HQ scores were recorded if a hospital admission in the past year or a visit to a specialist or general practitioner in the past three months was required because of an MSK problem. (164, 165) The results of the analysis of MSK-HQ scores by general and MSK health problems are shown in Table 2.

Table 2: MSK-HQ scores by general and MSK health problems

[a] Questions of the Minimum European Health Module (MEHM)
[b] Questions of the European Health Interview Survey (EHIS
** For variables with missing values, the basis of comparison (100%) is the total sample size minus the number of missing data*
Differences were tested using the Kruskal–Wallis test. Source: Hölgyesi et al, 2022. (53) (CC BY 4.0). The table is presented in its original form.

Variables	N	%	Mean (SD)
Total sample	2004	100*	44.13 (9.94)
Self-perceived health[a]			p= .000
Very good	207	10.3	51.25 (6.25)
Good	809	40.4	48.63 (6.20)
Fair	784	39.1	41.65 (8.54)
Bad	186	9.3	29.38 (9.59)
Very bad	18	0.9	20.89 (12.51)
Long standing illness[a] (not reported N= 90)*			p= .000
No	899	47.0	48.55 (7.10)
Yes	1015	53.0	40.26 (10.63)
GALI[a] (not reported N= 32)			p= .000
Severely limited	106	5.4	26.75 (11.37)
Limited, but not severely	590	29.9	38.34 (9.17)
Not limited	1276	64.7	48.26 (6.79)
EQ-5D-5L: Mobility			p= .000
No	1254	62.6	49.06 (6.14)
Slight problems	414	20.7	41.11 (6.61)
Moderate problems	250	12.5	31.23 (8.12)
Severe problems	77	3.8	25.19 (7.89)
Unable to walk	9	0.4	17.89 (14.82)
Difficulty in walking 500 meters on level ground without the use of any aid[b] (not reported N= 18)			p= .000
No difficulty	1527	76.9	47.49 (7.18)
Any difficulty	459	23.1	33.05 (9.78)
Difficulty in walking up or down 12 steps[b] (not reported N= 13)			p= .000
No difficulty	1406	70.6	48.21 (6.58)
Any difficulty	585	29.4	34.46 (8.37)
Low back pain or chronic problem[b] (not reported N=146)			p= .000
No	1108	59.6	48.25 (7.72)
Yes, but not diagnosed	444	23.9	41.73 (8.51)
Diagnosed	98	5.3	39.10 (9.95)
Diagnosed and taking medicine	208	11.2	32.51 (10.56)
Back pain or chronic problem[b] (not reported N= 110)			p= .000
No	1342	70.9	47.14 (8.24)
Yes, but not diagnosed	277	14.6	41.43 (8.61)
Diagnosed	103	5.4	38.87 (9.62)
Diagnosed and taking medicine	172	9.1	30.48 (10.20)

Variables	N	%	Mean (SD)
Neck pain or chronic problem[b] (not reported N=106)			p= .000
No	1389	73.2	46.85 (8.44)
Yes, but not diagnosed	310	16.3	41.14 (8.91)
Diagnosed	78	4.1	36.15 (10.81)
Diagnosed and taking medicine	121	6.4	30.00 (9.87)
Osteoarthritis of the knee[b] (not reported N=101)			p= .000
No	1468	77.1	46.49 (8.67)
Yes, but not diagnosed	164	8.6	40.68 (9.13)
Diagnosed	114	6.0	39.77 (9.53)
Diagnosed and taking medicine	157	8.3	32.11 (10.36)
Osteoarthritis of the hip[b] (not reported N=98)			p= .000
No	1602	84.1	46.20 (8.58)
Yes, but not diagnosed	81	4.2	38.95 (11.17)
Diagnosed	93	4.9	36.85 (10.48)
Diagnosed and taking medicine	130	6.8	30.97 (10.00)
Hospital admission in the last year due to MSK health problems (not reported N= 39)			p= .000
Yes	235	12.0	36.06 (11.48)
No	1730	88.0	45.35 (9.12)
Seen by a specialist in the last three months due to MSK health problems (not reported N= 42)			p= .000
Yes	322	16.4	36.63 (11.33)
No	1640	83.6	45.79 (8.84)
Seen by family doctor in the last three months due to MSK health problems (not reported N= 34)			p= .000
Yes	231	11.7	34.87 (10.65)
No	1739	88.3	45.53 (9.02)

When testing the convergent validity of MSK-HQ with standard outcome measures, strong correlations were seen with the EQ-5D-5L index, the EQ VAS and the HAQ-DI. With the well-being measures (ICECAP-A/O and WHO-5) and the Happiness VAS, the correlations were moderate and weak, respectively. (53) Results are shown in Table 3.

Table 3: Spearman's correlations of MSK-HQ scores with the EQ-5D-5L index, EQ VAS, HAQ-DI, WHO-5, Happiness VAS, ICECAP-A (age group 18-64) and ICECAP-O (age group 65+) scores

All correlations are significant at the 0.05 level. Source: Hölgyesi et al, 2022. (53) (CC BY 4.0). The table is presented in its original form.

	MSK-HQ	EQ-5D-5L index score	EQ VAS	HAQ-DI	ICECAP-A	ICECAP-O	WHO-5 score	Happiness VAS
MSK-HQ	1.000	.788	.644	-.698	.471	.460	.443	.317
EQ-5D-5L index score	-	1.000	.661	-.702	.566	.474	.485	.388
EQ VAS	-	-	1.000	-.550	.517	.501	.517	.450
HAQ-DI	-	-	-	1.000	-.379	-.427	-.324	-.241
ICECAP-A	-	-	-	-	1.000	-	.628	.606
ICECAP-O	-	-	-	-	-	1.000	.606	.579
WHO-5 score	-	-	-	-	-	-	1.000	.621
Happiness VAS	-	-	-	-	-	-	-	1.000

In the item-level comparison, the MSK-HQ items showed strong and moderate correlations with the EQ-5D-5L and HAQ-DI items ($p < 0.05$ in all cases). An exception was the 12th item of the MSK-HQ, which exhibited weak correlations with all items of the two standard measures. For detailed results, see the article published by Hölgyesi et al. (53)

With a Cronbach's alpha of 0.924, the internal consistency of the MSK-HQ was considered good. (53) The MSK-HQ scores of the 50 respondents were found to be highly consistent between the first and second completion, as the intraclass correlation coefficient (ICC) indicated excellent test-retest reliability (ICC=0.936; 95% CI 0.884 – 0.964).

4.1.2 Population normative data and differences by socio-demographic characteristics

In the total sample, the MSK-HQ score decreased by age, indicating worse MSK health in older individuals. (53) Results are shown in Figure 3.

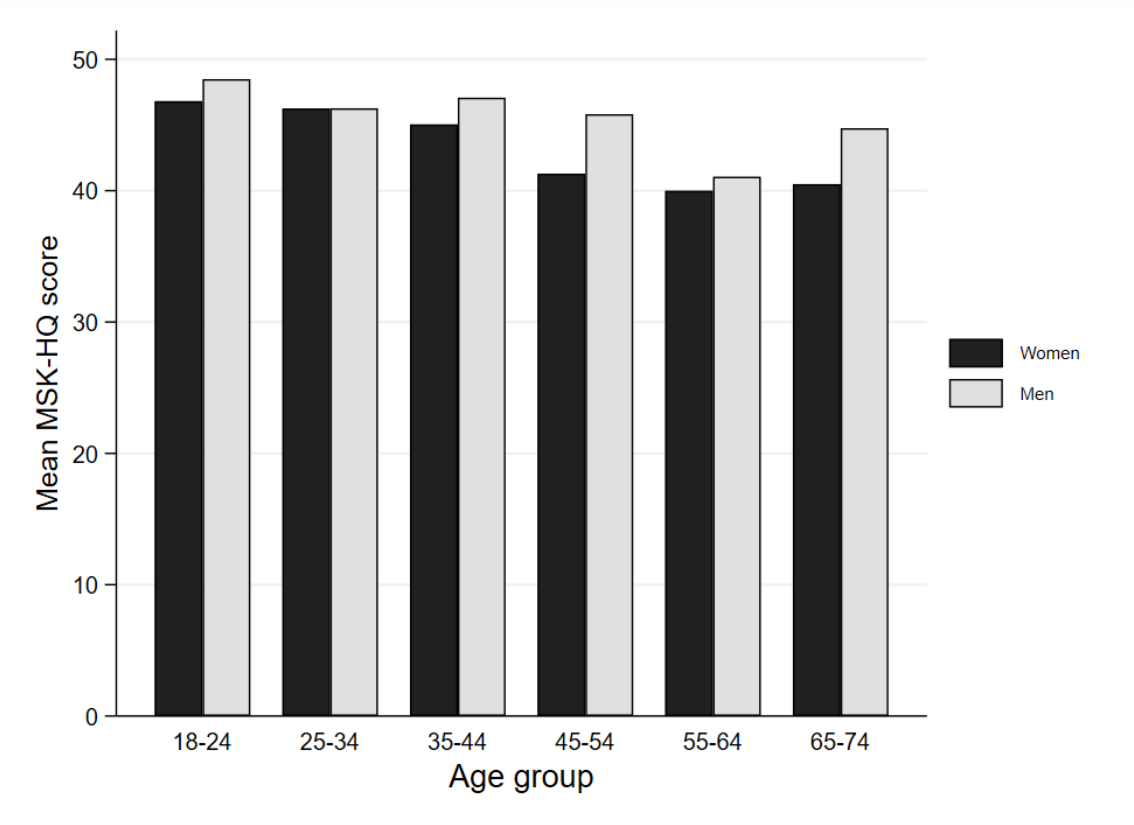

Figure 3: Mean MSK-HQ scores by age groups and gender.
The number of respondents was N=192 in age group 18-24, N=306 in age group 25-34, N=387 in age group 35-44, N=332 in age group 45-54, N=328 in age group 55-64 and N=400 in age group 65-74. Source: The figure was created based on data published in Hölgyesi et al., 2022 (53) with the permission of the authors under the Creative Commons 4.0 license (CC BY 4.0).

Also, respondents with higher education and those who were living in a town or the capital tended to have higher MSK-HQ scores. Furthermore, having a higher income and a paid job were also associated with higher scores. Mean MSK-HQ scores by socio-demographic characteristics, work status and income are shown in Table 1.

The relationship between socio-demographic characteristics and MSK health was investigated in a regression analysis. It was revealed that being a woman, older age, lower educational level (primary compared to tertiary), and being in a relationship were associated with lower MSK-HQ scores. Conversely, living in the capital, as opposed to residing in a village, and having an income above 1435 EUR, compared to the lowest income category (0 – 718 EUR), were associated with higher MSK-HQ scores, indicating

better MSK health in these subgroups. These associations were significant in all three models, with the exception of age and marital status in Model 2. The results of the regression analysis are presented in the article published by Hölgyesi et al. (53)

4.1.3 Informal caregivers: MSK health and HRQoL

Respondents providing informal care for more than two weeks made up 11.9% (N=238) of the total sample; their mean age was 50.8 (SD=15.2) years and 63.9% of them were women. There were N=23 (1.1%) respondents in the total sample who were both informal caregivers and care recipients at the same time. (53, 166, 167)

Informal caregivers had significantly ($t_{(2002)}$=4.21, p<0.001) lower MSK-HQ scores (41.6, SD=10.7) than those who did not participate in such a service (44.5, SD=9.8). Similarly, HRQoL (EQ-5D-5L index) and functional status (HAQ-DI score) were also significantly worse in this subgroup ($t_{(2002)}$=-3.63, p<0.001 and $t_{(2002)}$=-5.22, p<0.001, respectively). (166, 167) Results are shown in Table 4.

Table 4: General health, mobility problems, HRQoL and functional status by informal caregiving situation

Percentages may not add up to 100% due to rounding. Source: The table was created based on data published in Hölgyesi et al., 2022. (166) with the permission of the authors under the Creative Commons 4.0 license (CC BY 4.0).

	Total sample	**Informal caregiver**	**Not informal caregiver**
N	**2004**	**238**	**1766**
MEHM questions			
Self-perceived health: bad / very bad	10.2%	12.6%	9.9%
Long standing illness: yes	50.6%	65.5%	48.6%
Global Activity Limitation Indicator: severely limited / limited but not severely	34.7%	47.1%	33.1%
EQ-5D-5L Mobility domain			
No problems	62.6%	47.5%	64.6%
Slight problems	20.7%	28.2%	19.7%
Moderate problems	12.5%	21.0%	11.3%
Severe problems	3.8%	2.9%	4.0%
Unable to	0.5%	0.4%	0.5%
EQ-5D-5L index score; mean (SD)	0.87 (0.20)	0.83 (0.20)	0.88 (0.19)
HAQ-DI score; mean (SD)	0.28 (0.47)	0.42 (0.52)	0.26 (0.46)

4.2 Living with implantable medical devices: focus on musculoskeletal patients (Study 2a)

In the following chapters, I present the descriptive epidemiological results, specifically focusing on IMDs with MSK relevance. Accordingly, figures show data for persons living with MSK implants. Results of the subgroup analyses, correlation analysis and regression were performed for all respondents living with any type of IMD (as described in Chapter 3.2.1), and results are presented accordingly.

4.2.1 Epidemiology of IMDs

All in all, 1400 respondents completed the survey. Their mean age was 58.3 (SD=11.1) years, and 53.7% were women. Detailed socio-demographic characteristics of the sample have been published by Hölgyesi et al. (168) In the total sample, 41.7% had had at least one IMD in their life, with 9.3%, 2.3% and 0.4% who had had two, three or more, respectively. The most common of all IMDs studied was bone fixation, with 12.3% of respondents having at least once, while hip, knee and spinal implants accounted for 2.4%, 1.4% and 1.4%, respectively. Respondents' average age at the first implantation was 45.2 (SD=16.2) years, which differed by IMD type ($p<0.001$). In the case of bone fixation, the average age at surgery was 40.5 (SD=16.4) years. Still, for other MSK implants, the intervention was generally performed at an older age, ranging from 53.4 (SD=14.1) years for spinal implant to 58.3 (SD=10.8) years for hip replacement. At the time of the survey, N=433 (30.9% of the total sample) lived with at least one IMD, out of which 21.0%, 4.2% and 0.2% were wearing two, three, or more devices, respectively. Of those living with an IMD, 17.8% reported having bone fixation. The occurrence of hip, knee and spinal implants was lower in this subsample (7.4%, 4.4% and 4.2%, respectively). The average duration of living with the device was 11.5 (SD=10.5) years for bone fixation, 8.4 (SD=7.7) years for hip replacement, 7.2 (SD=6.0) years for knee replacement and 10.1 (SD=7.9) years for spinal implant. (168-170) The epidemiological characteristics of the persons living with IMDs are presented in Table 5.

Table 5: Epidemiological characteristics of participants with IMDs

Source: Hölgyesi et al, 2023. (168) (CC BY 4.0) The order of the devices has been modified, and device categories have been added compared to the original version.

Category	Device	Participants who have ever had IMD N=583		Age at implantation (ever had)		Subsample currently living with IMD N=433		Duration of IMD in the subsample living with IMD	
		N	*% of the total sample*	*Mean (years)*	*SD*	*N*	*% of subsample*	*Mean (years)*	*SD*
Trauma	Bone fixation	172	12.3	40.5	16.4	77	17.8	11.5	10.5
Joints	Hip replacement	33	2.4	58.3	10.8	32	7.4	8.4	7.7
	Knee replacement	19	1.4	55.3	10.3	19	4.4	7.2	6
	Spinal implant	19	1.4	53.4	14.1	18	4.2	10.1	7.9
Dentistry	Tooth implant	141	10.1	51.5	13.4	134	30.9	8.4	7.9
	Bone graft for dental implant	35	2.5	51.5	12.3	32	7.4	7.2	6.2
Cardiovascular system	Coronary stent	27	1.9	59.4	10.5	26	6.0	7.6	5.6
	Pacemaker	15	1.1	53.9	17.9	15	3.5	8.8	7
	Artificial heart valve	6	0.4	48.2	20.4	6	1.4	14.3	11.3
Contraception	Intrauterin device	131	9.4	32.9	8	18	4.2	9.2	10.4
Eye	Intraocular lens	119	8.5	61.3	12.7	116	26.8	6.8	7.1
Abdomen	Abdominal surgical mesh	38	2.7	55.4	11.9	37	8.5	8.4	6
Breast	Breast implant	13	0.9	42.5	8.7	13	3.0	12.6	10.3
Implantable biosensors	Glucose sensor	4	0.3	31.8	24.3	1	0.2	13	-
Other		29	2.1	49.2	14.8	19	4.4	11.1	8.6

The analysis of the lifetime prevalence of IMDs by gender and age groups showed a positive age-related tendency. In men, bone fixation was more common in younger age groups, but in women, it was more evenly distributed. The prevalence of orthopaedic implants increased with age for both genders. The results of the analysis are shown in Hölgyesi et al. 2022. (168)

4.2.2 The overall impact of IMDs on patients' HRQoL

More than two-thirds (69.7%) of participants living with an IMD reported that their device positively impacted their lives. Almost a fifth (19.4%) indicated a neutral impact, while only a tenth (10.9%) said they experienced negative effects. For bone fixation, neutral life impact was reported to be relatively high (47%). Other IMDs with MSK relevance were generally more positively rated. The share of respondents whose implant had a positive life impact was the highest for hip replacement (78%). For knee replacement and spinal implant, a lower proportion of positive effects were observed (58% and 55%, respectively). (168, 170, 172) Results for IMDs with MSK relevance are shown in Figure 4.

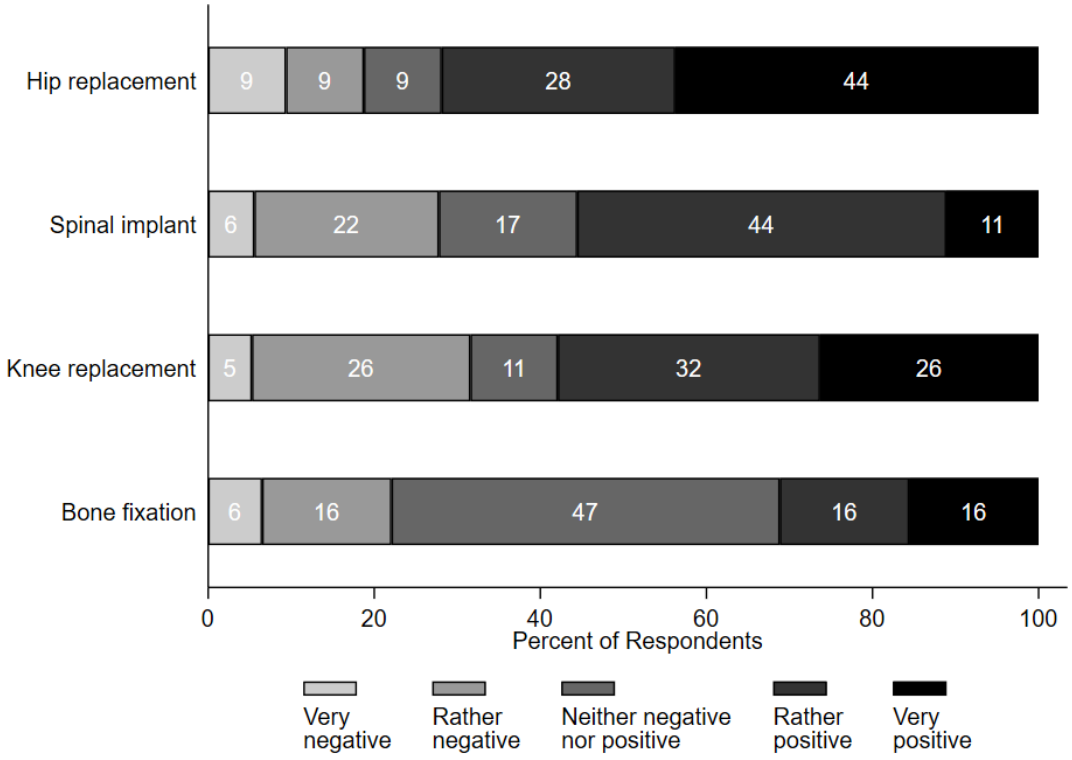

Figure 4: Respondents' views about IMD's overall impact on their life
Source: Hölgyesi et al, 2023. (168) (CC BY 4.0) The figure has been modified to show only IMDs with MSK relevance.

4.2.3 Patients' knowledge of IMDs, eHealth literacy and involvement in shared decision making

In the total sample (N=1400), the mean EQ-5D-5L index and EQ VAS score were 0.83 (SD=0.26), and 75.1 (SD=19.9), while the mean eHEALS score was 28.1 (SD=5.8). Shared decision making was only assessed in the subgroup living with an IMD (N=433), the mean SDM-Q-9 was 32.0 (SD=11.8). In the subsample wearing an IMD, respondents' IMD-related knowledge was fairly similar in the four domains, ranging from 5.5 (SD=3.8) points for safety requirements to 6.5 (SD=3.3) points for instructions and lifestyle advice for the daily use as measured on the VAS scales (range: 0-10). (168, 169, 171)

Of those living with an IMD (N=433), 33.5% reported that they had previously received and read written instructions for use, and only 3.0% reported that they had received but not read it. Those who did not remember receiving written instructions accounted for 17.3% of the sample, while the vast majority, 46.2%, reported receiving no instructions at all. The proportion of respondents who received instructions and read them was 16% for knee replacement, closely followed by bone fixation with 19%. In the case of spinal implant and hip replacement, 33.0% and 47% reported having received and read the instructions, respectively. The results of the detailed analysis of the received instructions for use by IMD type were published by Hölgyesi et al. (168)

When respondent's IMD-specific knowledge was analysed along background variables in the subsample living with an IMD (N=433), no significant differences were observed by socio-demographic characteristics and income (except for recognising the need for medical control, which differed by income quintiles). However, respondents who received instructions for use or reported a positive life impact of their IMD had a higher level of self-reported knowledge ($p<0.001$ for both) in all but one domain (ability to recognise the need for information security or privacy control did not differ by any subgroups). (168, 170) The results of the subgroup comparison are published in Hölgyesi et al. 2022. (168) Respondents' knowledge by IMD type and gender showed numerical, but statistically not significant, differences. (168, 172) Results for IMDs with MSK relevance are presented in Figure 5.

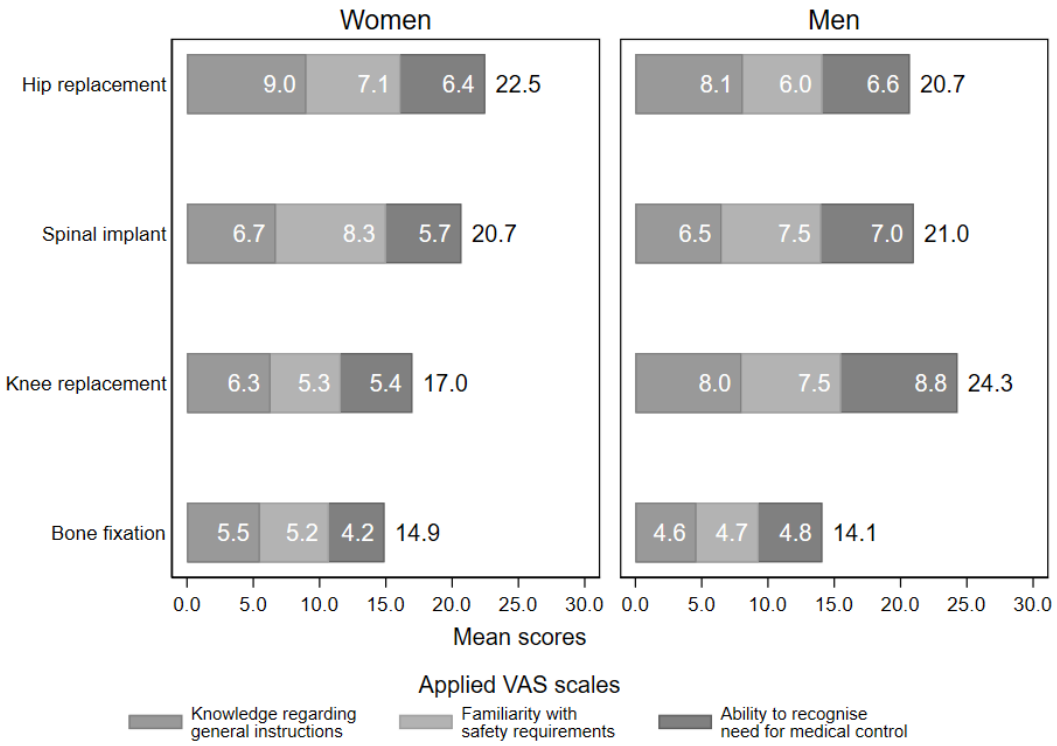

Figure 5: Patients' knowledge regarding living with IMDs with MSK relevance as measured on visual analogue scales (0 –'not at all'; 10 –'completely').
Numbers outside of columns represent the sum of the corresponding VAS scales. Results for 'Ability to recognise need for information security or privacy control' are not shown as it was reported only by patients wearing electronic devices. Number of women and men was N=15 and N=17 for hip replacement, N=12 and N=6 for spinal implant, N=13 and N=6 for knee replacement, N=34 and N=43 for bone fixation. Source: Hölgyesi et al, 2023. (168) (CC BY 4.0) The figure has been modified to show only IMDs with MSK relevance.

The associations of respondents' knowledge, standard measures of HRQoL, current health state and eHealth literacy were analysed in the subsample living with an IMD (N=433). The knowledge scales were weakly correlated with the EQ-5D-5L index and the EQ VAS. Concerning respondents' eHealth literacy, the eHEALS weakly correlated with all the knowledge VAS scales, the EQ-5D-5L and the EQ VAS. In terms of participation in the decision making about IMD surgery, the SDM-Q-9 also weakly correlated with the EQ-5D-5L and the EQ VAS, although its correlation with the knowledge scales was moderate. The fourth knowledge domain (ability to recognise the need for information security or privacy control did not differ by any subgroups) was an exception in the correlation analysis, as it did not show a significant correlation with any of the other measures. The eHEALS and the SDM-Q-9 correlated weakly. The detailed results of the correlation analysis are published in Hölgyesi et al. 2022. (168, 169, 171)

The regression analysis revealed that in the subsample living with an IMD (N=433), tertiary education and EQ-5D-5L index score were positively associated with IMD's impact on the respondent's life ($p<0.05$ in Models 2-7). Respondent's knowledge of IMDs also showed a significant positive association ($p<0.05$, Models 3-5). However, it lost significance in Models 6 and 7, when SDM-Q-9 was also included, while the latter was positively associated with IMD's impact on life in both models ($p<0.05$). Among trauma and orthopaedic implants, only bone fixation showed a negative association, which was consistently significant in all models. The detailed results of the regression analysis are published in Hölgyesi et al. 2022. (168)

4.3 Social preferences and attitudes towards the use of artificial intelligence-based technologies in hip replacement surgery (Study 2b)

4.3.1 Stated preferences for robot-assisted hip replacement surgery

All in all, 1400 respondents were involved in the study with a mean age of 58.3 (SD=11.1) years. In the hypothetical decision-making situation, more respondents chose the robot-assisted surgery over the conventional surgery (N=762, 54.4% vs. N=638, 45.6%). The analysis by socio-demographic subgroups revealed significant differences by sex, education and settlement type. A higher proportion of those who opted for conventional surgery were women, had lower education and lived in a village compared to those choosing robot-assisted surgery. Also, respondents opting for conventional surgery were more likely to be in lower income categories. The mean eHEALS score differed between the two subgroups, although the effect size was small as measured with Cohen's D (D=-0.159, 95% CI -0.264 - -0.053). The mean EQ-5D-5L index and EQ VAS scores did not differ significantly, indicating comparable general health states in the two subgroups. (175, 176) Respondents' characteristics in the total sample and by the preferred method of surgery are shown in Table 6.

Table 6: Sample characteristics

Statistical tests were used to investigate whether subgroups opting for either conventional or robot-assisted surgery differed in terms of demographic characteristics. [a]Chi-square test; [b]Mann-Whitney U test; [c]two sample t-test; [d] 'Do not know' and 'Do not want to answer' responses were treated as missing values and excluded from the analysis.

Source: Hölgyesi et al, 2024. (177) (CC BY 4.0) *Compared to the original table, only data for the hip replacement surgery task is shown.*

	Total sample	**Preferred method of surgery**	
		Conventional	**Robot-assisted**
Variables	**N (%)**	**N (%)**	
Total	1400 (*100*)	638 (*100*)	762 (*100*)
Sex		**p=0.001[a]**	
Men	648 (*46.3*)	263 (*41.2*)	385 (*50.5*)
Women	752 (*53.7*)	375 (*58.8*)	377 (*49.5*)
Age group, years		p=0.101[b]	
40-44	190 (*13.6*)	99 (*15.5*)	91 (*11.9*)
45-49	188 (*13.4*)	88 (*13.8*)	100 (*13.2*)
50-54	163 (*11.6*)	74 (*11.6*)	89 (*11.7*)
55-59	198 (*14.1*)	95 (*14.9*)	103 (*13.5*)
60-64	227 (*16.2*)	87 (*13.6*)	140 (*18.4*)
65-69	182 (*13.0*)	83 (*13.0*)	99 (*13.0*)
70-74	127 (*9.1*)	52 (*8.2*)	75 (*9.8*)
75+	125 (*8.9*)	60 (*9.4*)	65 (*8.5*)

	Total sample	Preferred method of surgery	
		Conventional	Robot-assisted
Education		**p<0.001[b]**	
Primary	410 (*29.3*)	228 (*35.7*)	182 (*23.9*)
Secondary	533 (*38.1*)	244 (*38.2*)	289 (*37.9*)
Tertiary	457 (*32.6*)	166 (*26.0*)	291 (*38.2*)
Health education		p=0.213[a]	
Yes	103 (*7.4*)	53 (*8.3*)	50 (*6.6*)
No	1297 (*92.6*)	585 (*91.8*)	712 (*93.4*)
Settlement type		**p=0.020[b]**	
Capital	315 (*22.5*)	131 (*20.5*)	184 (*24.1*)
Town	749 (*53.5*)	337 (*52.8*)	412 (*54.1*)
Village	336 (*24.0*)	170 (*26.7*)	166 (*21.8*)
Married/having a partner		p=0.928[a]	
Yes	854 (*61.0*)	390 (*61.1*)	464 (*60.9*)
No	546 (*39.0*)	248 (*38.9*)	298 (*39.1*)
Living with someone in the household		p=0.540[a]	
Yes	1064 (*76.0*)	480 (*75.2*)	584 (*76.6*)
No	336 (*24.0*)	158 (*24.8*)	178 (*23.4*)
Paid work (missing=30)		p=0.451[a]	
Yes	1287 (*91.9*)	581 (*91.1*)	706 (*92.7*)
No	83 (*5.9*)	41 (*6.4*)	42 (*5.5*)
Household income category[d] (missing=217)		**p=0.001[b]**	
1st quintile	261 (*18.6*)	144 (*22.6*)	117 (*15.4*)
2nd quintile	224 (*16.0*)	107 (*16.8*)	117 (*15.4*)
3rd quintile	237 (*16.9*)	102 (*16.0*)	135 (*17.7*)
4th quintile	201 (*14.4*)	84 (*13.2*)	117 (*15.4*)
5th quintile	260 (*18.6*)	98 (*15.4*)	162 (*21.4*)
Any implant ever		p=0.237[a]	
Yes	584 (*41.7*)	277 (*43.4*)	307 (*40.3*)
No	816 (*58.3*)	361 (*56.6*)	455 (*59.7*)
eHEALS score; mean (SD)		**p=0.003[c]**	
	28.1 (*5.8*)	27.6 (*6.0*)	28.5 (*5.5*)
EQ-5D-5L index score; mean (SD)		p=0.070[c]	
	0.83 (0.26)	0.82 (0.28))	0.84 (0.25)
EQ VAS; mean (SD)		p=0.060[c]	
	75.1 (19.9)	74.0 (20.5)	76.0 (19.3)

4.3.2 Strength of preferences towards conventional and robot-assisted hip replacement surgery

In the willingness to pay task, nearly one-third of respondents were not willing to offer any amount of money in exchange to make the hip replacement surgery with their originally chosen method. (175, 176) The distribution of willingness to pay in the sample is shown in Figure 6.

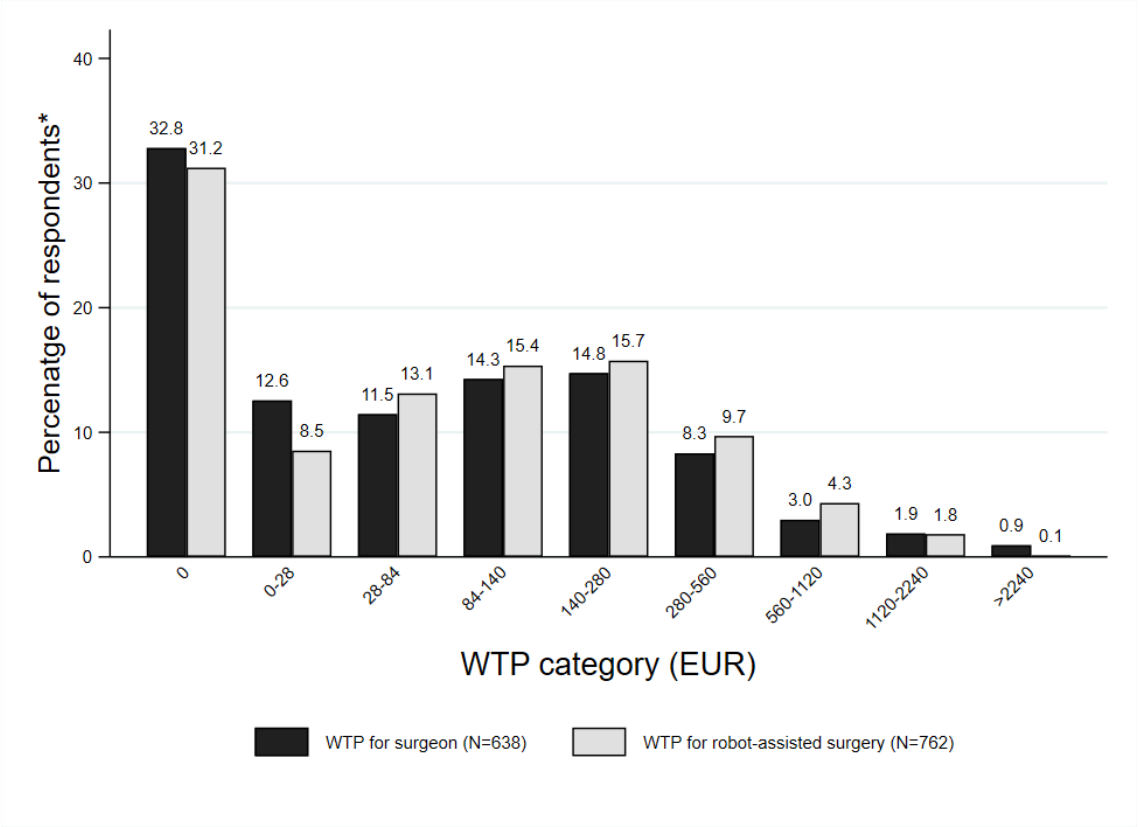

Figure 6: Distribution of willingness to pay by the chosen method of hip replacement surgery.

** Proportions are expressed as the percentage of respondents who reported any difficulty in the respective subgroup. Percentages may not add up to 100% due to rounding. Source: The figure was created based on data published in Hölgyesi et al., 2024. (177) (CC BY 4.0)*

The average amounts offered (including respondents with zero WTP) were 178.5 (SD=429.5) EUR for the conventional and 170.4 (SD=300.0) EUR for the robot-assisted surgery, but the difference was not significant (p=0.153). The analysis by sociodemographic characteristics revealed differences by education and income quintiles, with higher WTP for respondents having higher education and higher income in both subgroups. (175, 176) The detailed results are shown in Table 7.

Table 7: Subgroup analysis of willingness to pay

Differences in WTP were tested with Kruskal-Wallis tests.[a] 'Do not know' and 'Do not want to answer' responses were treated as missing values and excluded from the analysis. Source: Hölgyesi et al, 2024. (177) (CC BY 4.0) *Compared to the original table, only data for the hip replacement surgery task is shown.*

	Preferred method of surgery	
Variables	**Conventional (N=638)**	**Robot-assisted (N=762)**
	EUR; mean (SD)	
Total	p=0.153	
	178.5 (429.5)	170.4 (300.0)
Sex	p=0.311	p=0.485
Men	168.4 (405.7)	167.8 (268.9)
Women	185.6 (445.9)	173.0 (329.0)
Age group, years	**p=0.001**	p=0.085
40-44	115.3 (228.7)	184.1 (293.6)
45-49	168.3 (395.8)	143.5 (247.4)
50-54	103.4 (228.1)	114.6 (214.4)
55-59	145.9 (372.9)	145.7 (282.5)
60-64	189.4 (334.7)	177.4 (306.0)
65-69	156.5 (275.6)	160.2 (244.7)
70-74	317.8 (759.9)	219.3 (374.1)
75+	338.2 (753.5)	251.5 (436.5)
Education	**p=0.013**	**p=0.026**
Primary	124.2 (290.1)	146.3 (288.0)
Secondary	181.4 (478.3)	144.2 (232.5)
Tertiary	249.3 (500.9)	211.4 (357.7)
Health education	p=0.531	p=0.300
Yes	272.3 (653.4)	210.9 (330.3)
No	170.0 (402.9)	167.5 (297.8)
Settlement type	p=0.832	**p=0.028**
Capital	198.5 (406.9)	204.1 (310.9)
Town	193.9 (500.4)	178.2 (327.7)
Village	132.7 (260.1)	113.4 (188.9)
Household income category[a] (missing=217)	**p<0.001**	**p<0.001**
1st quintile	117.2 (288.2)	83.8 (195.9)
2nd quintile	79.5 (118.9)	121.5 (219.3)
3rd quintile	249.8 (640.8)	176.7 (313.5)
4th quintile	217.3 (330.9)	174.4 (252.8)
5th quintile	311.4 (666.8)	239.2 (381.0)
Any implant ever	p=0.058	p=0.058
Yes	200.3 (455.3)	188.4 (311.3)
No	161.8 (408.6)	158.2 (291.9)

In the total sample, respondents' WTP was significantly correlated with age (r=0.107, p<0.001 and net income per capita (r=0.162, p<0.001), but not with the eHEALS score (r=0.019, p=0.481), nor with the EQ-5D-5L index (r=0.018, p=0.496) and the EQ VAS score (r=0.046, p=0.084). (175, 176)

In the multiple linear regression, respondents' choice of method was significantly associated with willingness to pay, being lower for those opting for the robot-assisted surgery. Age and income also showed a positive association. Contrary to the results of the subgroup analysis, education failed to show a significant effect. Furthermore, neither the eHEALS score nor the EQ-5D-5L index score were associated with respondents' willingness to pay. The results of the regression analysis are shown in more detail in the manuscript by Hölgyesi et al., published in 2024. (177)

5 DISCUSSION

In my thesis, I focused on five new perspectives of HRQoL assessment in patients with MSK disorders: new HRQoL assessment tools, new needs in epidemiology, new areas of HRQoL assessment, new aspects of patient involvement, and new innovative digital health technologies. Based on these perspectives, a total of eight research objectives were formulated, which were investigated in three population surveys.

In the first study, the development and validation of the Hungarian version of the MSK-HQ was carried out, and the association of MSK health with statistical health data and standard tools such as well-being measures was investigated. Also, the study was the first to establish population normative data with the MSK-HQ, and it made it possible to assess the MSK health of the Hungarian population, including informal caregivers.

The second study successfully assessed the prevalence of implanted medical devices (IMDs) with MSK-relevance in the Hungarian population over 40 years of age and their overall impact on the patients' lives. In addition, patients' awareness of their IMD, eHealth literacy and involvement in the decision making about the implantation was investigated, and it was also assessed how these factors are associated with the impact of IMDs on patients' lives.

The third study assessed public attitudes and preferences towards advanced digital health technologies. It provided data on the preference for robot-assisted hip replacement surgery. Also, it assessed the strength of public preferences using the willingness-to-pay method.

The following chapters discuss the results in detail according to the three studies.

5.1 Development and validation of the Hungarian version of the MSK-HQ and assessment of the musculoskeletal health of the population

Our results have proved the validity of the Hungarian language version of the MSK-HQ. (53) It had excellent internal consistency, comparable to that reported in previous studies. (52, 96, 186-188) It also showed excellent test-retest reliability, with an ICC of 0.936, which was slightly higher than that observed by other authors. (52, 96, 186-190) However, this difference can be explained by the short time interval between test and retest measures used in our study.

The MSK-HQ performed well when analysing known groups' validity as it could make a distinction between subgroups hypothesised to differ in their level of MSK health. (53, 164, 165) Respondents who reported walking difficulties or specific MSK problems in the European Health Interview Survey (EHIS) questions had significantly lower MSK-HQ scores than those who did not have such problems. (115) The lowest scores (and consequently the worst MSK health) were found for back pain, neck pain and hip osteoarthritis. In addition, the results confirm that MSK problems are also associated with poorer general health, as the MSK-HQ score was significantly lower if the respondent had poorer self-perceived health, reported the presence of a longstanding illness, or limitations in the daily activities according to the Minimum European Health Module (MEHM) questions. (49) It should be emphasised that in previous studies, the MSK-HQ has only been applied to well-defined patient groups and has not yet been used in a population study. The relationship confirmed between MSK-HQ and routinely collected MSK health statistics can be used as a good proxy to estimate MSK-HQ scores from a time series of EHIS data.

The MSK-HQ also showed a good convergent validity that has been examined against several widely used standard measurement tools. (53) Similarly to previous studies, we also observed that the EQ-5D-5L, EQ VAS and HAQ DI strongly correlated with the MSK-HQ, indicating that general HRQoL and physical functioning are associated with MSK health. (52, 96, 188, 191, 192) To broaden the scope of our study, we also examined the correlation of MSK-HQ with widely accepted and used well-being measures, as these have been less frequently applied in MSK studies, and therefore the relationship between MSK health and well-being has remained underexplored. (122, 123) The MSK-HQ showed moderate correlation with the ICECAP-A/O, the WHO-5 and the Happiness VAS, suggesting a weaker association of MSK health with well-being compared to what has been seen with HRQoL and physical functioning. This observation can be explained by the fact that well-being does not only include aspects related to health, and therefore, these measures allow for a broader assessment of a person's condition. (193, 194) Our results also show that in addition to MSK health, it is recommended to assess well-being as a complementary measure.

This study was the first to provide population normative data with the MSK-HQ and to examine its association with socio-demographic characteristics on the general population

level. (52, 96, 187-191, 195) The MSK-HQ score, and therefore MSK health, decreases with age, and women generally have lower MSK health than men. (53) However, a slight increase was observed among respondents aged 65 and over. This may be due to the fact that the online sample was guaranteed to be representative up to 65, so it is assumed that above this age, respondents in better health than the population average were involved. Previous studies on well-defined patient groups have not provided information on MSK health by socio-demographic characteristics, and population-level data with the MSK-HQ are not yet available for international comparisons. (52, 94, 96, 187-189, 191, 192, 195, 196) However, similar observations have been made previously with other standard instruments. The level of functional disability as measured with the HAQ-DI increases with age, and women have slightly worse functional status. (197) In addition, with the Musculoskeletal Function Assessment (MFA), it has been observed in a population sample that older people and women generally have poorer MSK health. (198, 199) One of the strengths of our study is that we conducted a multiple regression analysis to better understand the relationship between socio-demographic characteristics and MSK health. The results not only confirmed the role of age and gender but also drew attention to the importance of education, residence and income. Furthermore, general HRQoL (EQ-5D-5L index) and physical functioning (HAQ-DI score) were also associated with the MSK-HQ score and, consequently, with MSK health. Our results contribute to the existing body of knowledge, as no such comprehensive multivariate analysis has been performed with the MSK-HQ in a population sample. Nonetheless, our observations align with a previous study in patients presenting to primary care due to MSK pain, which also demonstrated the predictive ability of several sociodemographic factors, physical activity and HRQoL (EQ-5D index) for the MSK-HQ score. (200)

The proportion of informal caregivers in the total sample was remarkable (11.9%), with every tenth of them being an informal care recipient at the same time. (166, 167) Previous estimates of the proportion of informal caregivers in the Hungarian population show considerable variation. According to the European Social Survey, 8.2% of people aged 18 and over were informal caregivers in 2014. (201) In contrast, Baji et al. found a rate of 14.9% in a representative population sample, but other authors have reported an even higher prevalence (25.5%). (202, 203) Differences may be partly explained by the different sampling methods and definitions of informal caregiving used in the studies. In

addition, alongside positive experiences, negative effects of caregiving on mental and physical health, and high levels of physical strain and musculoskeletal discomfort have also been described. (107, 108, 204, 205) A possible explanation for this phenomenon is that informal caregiving can be a mentally and physically demanding task that can lead to significant fatigue and MSK discomfort and is often associated with poor health behaviours. (107, 108) Accordingly, we also observed that informal caregivers in our study had worse general health status (indicated on the MEHM questions) and poorer physical functionality. Moreover, as one of the strengths of our study, we comprehensively assessed MSK health using the MSK-HQ and found that informal caregivers generally have worse MSK status than those who are not caregivers. Therefore, our results provide new evidence and highlight that the proportion of MSK patients providing informal care in the Hungarian population is remarkable. In my opinion, this social subgroup deserves more attention, and further studies are recommended to gain a better insight into their health problems and to identify unmet needs, as targeted interventions can only be tailored to well-defined patient groups.

5.2 Living with implantable medical devices: focus on musculoskeletal patients

We found that nearly one in three people in the Hungarian population aged over 40 years live with at least one IMD. (168, 169, 171) Bone fixation accounted for a significant proportion of all IMD types studied, but the prevalence of other IMDs with MSK relevance, such as hip, knee and spinal implants, is also notable. (168, 170, 172) The likelihood of having an IMD increased with age. Accordingly, hip, knee and spinal implants were more common in older people, but bone fixation was typically inserted at a younger age. One of the strengths of our study is that we measured the prevalence and baseline characteristics of patients with IMDs, including those who have implants for MSK problems, in a large population-based study. Therefore, these results significantly contribute to the literature, as the current knowledge of IMDs is primarily available from single-centre studies and device-specific and national registries, and data from high-quality, large-scale epidemiological studies are still needed. (111-113) Our study fills this gap and provides new information for both the clinical and public health sectors. A possible direction for future research could be to expand the survey to include more types of IMDs and a wider age range.

As it has been pointed out in several studies, HRQoL data for people living with IMDs are often incomplete and of low quality. (128, 129) Our study significantly contributes to this field, as we determined the overall life impact of several IMDs, including those with MSK relevance. (168, 169, 171, 206) The results show that the majority of patients with bone fixation experienced a neutral impact on their lives, although, in reality, this is certainly not the case, as it is the plating that heals the bone fracture. In contrast, they generally rated orthopaedic implants more positively, with hip replacement rated the highest, followed by knee replacement and spinal implant. (168, 170, 172) Although the study did not examine the reasons for these differences in HRQoL, several factors could be considered based on observations described in the literature. Previous studies have reported that patient satisfaction with IMDs is associated with a number of factors, such as subjective expectations regarding implantation, surgical factors, postoperative complications, postoperative rehabilitation and implant survivorship. (207-210) However, further studies are needed to determine exactly what factors and to what extent they play a role in shaping subjective outcomes associated with IMDs, including MSK implants.

Our study adds to the body of knowledge on patient awareness, as although patient attitudes towards IMDs have been investigated, IMD-related knowledge has remained largely unexplored so far, especially in the field of MSK implants. (211, 212) The results suggest that respondents generally have a moderate knowledge of their IMDs, as fairly similar scores were observed for all four knowledge VAS scales in the subgroup living with an IMD. (168, 169, 171) We found no differences either by socio-demographic subgroups or by IMD type. However, higher knowledge was observed in respondents who received written instructions for use and read it, indicating that patient information and education are important factors in improving knowledge of IMDs. We find it important to point out that nearly half of the sample indicated not receiving instructions for use. It has been described in the literature that patients undergoing knee or hip replacement surgery often do not receive the adequate information they expected. (211) Our results are in line with these findings, as in the case of knee replacement, only 16% reported receiving instructions for use. However, for hip replacement, a roughly 3-fold increase was observed, indicating that these patients were generally better informed in our study. (168, 170, 172)

Respondents' average level of eHealth literacy and involvement in shared decision making were comparable to that observed in samples of the Hungarian general population. (60, 62) The correlations between the knowledge VAS scales and the eHEALS were only weak, indicating that higher eHealth literacy does not necessarily translate into better knowledge of IMDs. In contrast, shared decision making (as measured with the SDM-Q-9) was moderately correlated with all the knowledge scales. These results show the avenue for public health interventions, i.e. improving eHealth literacy may not result in better health knowledge, but the focus should be on educating the health staff about shared decision making, as greater involvement in the decision about IMD implantation can be an important factor in improving patients' awareness. (168, 171)

It has previously been found that higher device-specific knowledge is associated with improved functional outcomes in patients undergoing knee and hip arthroplasty. (213, 214) These results suggest that patient education may play a key role in improving health outcomes. In our study, we also found that respondents' knowledge differed by the IMD's overall impact on their life, being higher among those indicating positive life impact. (168-170, 172) However, the multiple regression analysis showed that knowledge, eHealth literacy and instructions for use received are not related to the impact of IMD on life, while SDM-Q-9 is significantly associated. (168) These results suggest that shared decision-making is more important in improving IMDs' subjective life impact and that effective communication is essential for knowledge transfer. Furthermore, our findings also highlight that passive communication, such as providing only paper-based or electronic information, is not sufficient to provide patients with adequate health information and to achieve desired health outcomes. However, the active involvement of clinicians in patient education, appropriate and effective communication, and the involvement of patients in therapeutic decisions are essential. Given the high prevalence and the expected increase in more advanced IMDs, the importance of these aspects is likely to increase in the future.

5.3 Social preferences and attitudes towards the use of artificial intelligence-based technologies in hip replacement surgery

In terms of preferences for robot-assisted hip replacement surgery, our study showed slightly different results from what has been found in previous studies. Abdelaal et al.

have described that patients awaiting total knee arthroplasty mainly preferred conventional surgery, with more than 40% of them opting for robot-assisted surgery. (215) Similarly, in the study by Muaddi et al., only one-third of patients favoured the robot-assisted surgery over the conventional method. (216) In contrast, our results suggest a higher acceptance of robot-assisted surgery as more respondents in our study preferred this advanced method of hip replacement. (175, 176) The acceptability of robot-assisted surgery in different countries may depend on several factors, such as differences in economic and cultural environments, as well as differences in healthcare systems, and, therefore, it would deserve further investigation in future studies.

Respondents opting for the robot-assisted surgery had generally higher levels of education and eHealth literacy (eHEALS score), suggesting that knowledge and awareness seem to influence acceptance of advanced digital health technologies. (175, 176) The role of other socio-demographic variables also emerges, such as income, which was higher among those who chose robot-assisted surgery. We also assessed current health status, but no difference between the two subgroups was found. In addition, respondents were asked whether they have had any implants in their lives, as current preferences may be influenced by past health experiences. However, this could only be tested to a limited extent in our study because, on the one hand, we had a population sample, and it is, therefore, likely that only a small proportion of participants had experience with the health condition presented in the hypothetical decision task. On the other hand, the population is less likely to have real experience with robot-assisted surgery, as it is not yet widely available in clinical practice. Accordingly, in our study, there were only 33 participants who had a hip replacement. In my view, future studies could further elucidate how previous experiences affect preferences for digital health technologies.

When analysing respondents' WTP, we found that a third of them offered no money in exchange for their chosen method. (175, 176) Very low or zero WTP may indicate that these respondents are less attached to their choice and, therefore, have weaker preferences for advanced health technologies. However, in a previous study by Abdelaal et al., patients awaiting total knee replacement had even weaker preferences, with less than a tenth of them willing to pay for robot-assisted knee replacement. (215) In light of this, the number of respondents with zero WTP in our study can be considered quite low. It

must be emphasised that affordability (i.e. the individual's financial status) can be a potential source of bias in a WTP task, but I believe that its impact was negligible in this study as respondents were able to offer even very small amounts. (217) Nevertheless, it would be worthwhile in future studies to assess preferences using other elicitation methods and to investigate real decision situations.

Overall, the amount of money offered was very similar in the subgroups choosing the conventional or the robot-assisted surgery, indicating no difference in the strength of preferences. (175, 176) Analysis by socio-demographic characteristics showed that respondents with higher education or income had higher WTP. The correlation analysis further reinforced the positive association between WTP and income, although it was only weak. It should be noted that these results are consistent with previous studies that have found that education level and income affect WTP, presumably because higher income may lead to more spending. (217)

The multiple regression showed different results from the descriptive analysis, as it revealed a significant association between WTP and the choice of surgery, indicating that respondents who chose the robot-assisted surgery had lower WTP. (175, 176) Among the socio-demographic characteristics, only age and income were positively related to WTP. However, other factors described in the literature as common determinants of WTP, such as gender, marital status and education, were not significantly associated. (218) In addition, the results suggest that respondents' eHealth literacy plays less of a role in shaping the preferences for advanced digital health technologies, as the eHEALS score failed to show an association with WTP in the correlation and the regression analysis.

Given the limitations of the WTP method, we suggest refining our results using other preference elicitation methods and, maybe more importantly, in real-world decision making situations. Nonetheless, the openness of the population towards robot-assisted surgery revealed by our research is encouraging and stimulating to robot-oriented developments.

6 CONCLUSIONS

The thesis was organized around five new perspectives of HRQoL assessment in patients with MSK disorders that were investigated in three population studies.

The first study has successfully demonstrated the validity of the Hungarian version of the MSK-HQ, making available a new disease group-specific combined measure in Hungary. The Hungarian MSK-HQ enables general practitioners, MSK and other specialists to assess and monitor the MSK health of patients in general and with diverse MSK diagnoses. The MSK-HQ could also be useful for the public health sector and health policymakers as it allows for the comprehensive assessment of the MSK field, thus providing the opportunity to assess and compare the burden of different MSK diseases and to help plan health interventions targeting MSK patients. In terms of new needs in epidemiology, the study adds significant knowledge to the literature as it was the first to obtain population normative data for the MSK-HQ, which could serve as a reference point in future studies to determine the health status of MSK patients and would open up the possibility for international comparisons. In addition, the results of this study raise awareness of MSK patients providing informal care and provide essential baseline data for health policymakers to develop targeted social interventions and health strategies to support them. Regarding new areas of HRQoL assessment, the study gives an insight into the relationship of MSK health with statistical data collected by the Eurostat and widely used well-being measures; therefore, it could support clinicians and decision-makers to make better use of already available health data.

The second study assessed the prevalence of IMDs in the Hungarian population aged 40 and over, including implants with MSK relevance, providing essential epidemiological data for clinicians and the public health sector. In terms of new areas of HRQoL assessment, the study examined patients' experiences of IMDs and, therefore, provides essential data on their expected real-life effectiveness, which can be used to prepare health coverage decisions. In addition, the study gives an insight into new aspects of patient involvement by examining patients' knowledge, eHealth literacy and involvement in medical decision making. Our findings help clinicians to identify which patient groups have low levels of knowledge and, therefore, need appropriate education and draw attention to the expected subjective health outcomes of IMDs. However, one of the key messages of the research is that good doctor-patient communication and greater patient

involvement in healthcare decisions (shared decision making) are essential factors not only in improving knowledge but also in reaching better health outcomes. The SDM-Q-9 is an available measure in Hungary, and it would be advisable to use it more in clinical practice, especially in the field of IMDs. Finally, the results of this study could be beneficial for developers in the design and development phase to identify which devices are more challenging to use and are associated with poorer patient experience and, therefore, need further improvement.

The third study demonstrated an openness in the Hungarian society to new innovative digital health technologies, with high public acceptance of robot-assisted hip replacement surgery, which, however, is not yet broadly reflected in the strength of preferences. Furthermore, the results show no association between public attitudes towards innovative digital health technologies and eHealth literacy as measured by the rather internet-focused eHEALS tool. The results presented in the Thesis suggest that a new measurement tool for assessing eHealth literacy from a new perspective may be needed in the future. These findings may be of great interest to both clinicians making therapeutic decisions and professionals involved in the planning of healthcare, as patient preferences could fundamentally influence therapeutic decisions in the future and would also have an impact on the adherence to, satisfaction with, and implementation of new technologies. In addition, HTA organizations involved in preparing health coverage decisions also benefit from this study, as the results allow patient preferences to be considered alongside health-related factors when determining the benefits associated with new innovative digital health technologies.

7 SUMMARY

The thesis focuses on five new perspectives of health-related quality of life (HRQoL) measurement in patients with musculoskeletal (MSK) disorders. The research questions were addressed in three large cross-sectional population-based studies.

In response to the demand for new HRQoL measurement tools, in the first study, the Hungarian version of the Musculoskeletal Health Questionnaire (MSK-HQ) was successfully developed and validated, making this combined measure available in Hungary. The study provides new epidemiological data on the MSK health and functional status of the Hungarian population, including the subgroup of MSK patients providing informal care. Another locally and internationally significant result is that the study is the first to report population normative data with the MSK-HQ. In addition, the results provide essential information on the relationship between MSK health and the statistical health data routinely collected by Eurostat and other standard tools, including well-being measures, thus creating the opportunity for clinicians and policymakers to make better use of already available health information, even at the international level.

The second study highlighted that nearly one in three people in the Hungarian population lives with an implantable medical device (IMD), and the proportion of MSK implants is remarkable, thus providing essential epidemiological data for the public health sector. In addition, the study provides information on the impact of IMDs on patients' HRQoL, an area of HRQoL measurement currently under intense international research. However, one of the main messages for all healthcare professionals and policymakers worldwide is that effective doctor-patient communication and patients' involvement in therapeutic decisions are key factors in improving subjective health outcomes, as shared decision making was found to be an important factor in shaping the IMDs' impact on HRQoL.

The third study provided new data on public attitudes and preferences towards advanced digital health technologies. The results show openness in society as the general acceptance of robot-assisted surgery was high. However, the study found no significant difference in the strength of preferences between conventional and robot-assisted methods, which shows the population's uncertainty towards advanced technologies. With the increasing adoption of innovative digital technologies, the results of this study can be used not only locally but also internationally in healthcare planning.

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