A Supported Osteoarthritis Self-Management Program for People with Knee and/or Osteoarthritis. Outcomes and factors associated with response.

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A Supported Osteoarthritis Self-Management Program for people with knee and/or hip osteoarthritis

Outcomes and factors associated with response

Thérése Jönsson

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DOCTORAL DISSERTATION

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Title and subtitle
A Supported Osteoarthritis Self-Management Program for people with knee and/or hip osteoarthritis. Outcomes and factors associated with response.

Abstract:
Introduction:
Patient education, exercise, and weight control is the first-line treatment for people with osteoarthritis (OA). In Sweden, a Supported Osteoarthritis Self-Management Program (SOASP), including patient education and exercise is provided by health professionals at more than 500 primary care units. The result of this intervention is still unclear. The overall aim of this thesis was to increase understanding about the results of the SOASP for people with knee and/or hip OA delivered in a real-world setting
Methods:
The thesis comprises four studies. In Study I, the change in OA symptoms and health behavior after conducted SOASP were evaluated. In Study II, the extent of change in pain intensity after SOASP was compared between patients who received 1) education only, 2) education + home-based exercise, or 3) education + supervised exercise. In Study III, individual- and disease-related factors at the baseline, associated with reaching a minimal clinical difference in pain were identified. In Study IV, changes in physical activity levels 3 and 12 months after the SOASP were evaluated objectively using accelerometers.
Results:
In Study I, patients with knee and/or hip OA experienced lower pain intensity, higher health-related quality of life, and greater self-efficacy. Fewer patients reported daily pain, took OA medication, reported willingness to undergo surgery, reported fear of movement, and self-reported a higher level of physical activity. In Study II, patients receiving home-based exercise or supervised exercise experienced greater pain reduction compared with patients who received only education. In Study III, the strongest factors associated with reaching the minimal clinical difference of pain, were less frequent pain, unilateral OA, being unwilling to undergo surgery and a lower body mass index. In study IV, the number of minutes spent in sedentary behavior or physical activity did not differ significantly at the 3-month follow-up. At the 12-month follow-up, minutes in moderate to vigorous physical activity did decrease compared with the baseline for patients with knee and/or hip OA.
Conclusion:
The results from these studies extend previous evidence showing that exercise and patients education reduce knee and/or hip symptoms in people with OA also when provided in real-world settings. People participating in SOASP reported reductions in OA symptoms, reduced their willingness to undergo surgery, took less OA medication and sick leave. Despite the reduced symptoms, the patients did not decrease their average sedentary time or increase their level of physical activity. Participating in a home-based or supervised exercise program produced similar reductions in pain intensity and was more effective than education only, suggesting that a structured self-management program, as the SOASP, play an important role in OA care.

Key words Ostearthrithis, knee, hip, education, excerise, self-management

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MADE IN SWEDEN

To my family

”If you want to go fast go alone
If you want to go far go together“

African Proverb

Table of Contents

Abstract

Introduction: Osteoarthritis (OA) is the most common joint disease and affects more than 300 million people worldwide. Exercise combined with patient education is the first-line treatment, and its use is based on results of more than 67 randomized clinical trials (RCTs) that included people with knee and/or hip OA. In Sweden, a Supported Osteoarthritis Self-Management Program (SOASP), including patient education and exercise is provided by health professionals at more than 500 primary care units. Despite promising results from RCTs, there are few reports of the results of patient education and exercise as a part of a self-management program implemented in real-world settings. The overall aim of this thesis was to increase understanding about the results of the SOASP for people with knee and/or hip OA delivered in real-world settings.

Methods: Studies I-III were observational registry-based studies of data from the Swedish National Quality registry; Better Management of Patients with OsteoArthritis (BOA). Study IV was an intervention study with a reference group. This thesis includes data for more than 40 000 patients with knee and/or hip OA who had participated in SOASP and completed evaluations at the baseline and 3 and/or 12 months after treatment. In Study I, the change in OA symptoms and health behavior after conducted SOASP were evaluated. In Study II, the extent of change in pain intensity after SOASP was compared between patients who received 1) education only, 2) education + home-based exercise, or 3) education + supervised exercise. In Study III, individual- and disease-related factors at the baseline, associated with reaching a minimal clinical difference in pain were identified. In Study IV, changes in physical activity levels 3 and 12 months after the SOASP were evaluated objectively using accelerometers.

Results: The results of the four studies are summarized as follows.
Study I. Three months following the self-management program, patients with knee and/or hip OA experienced lower pain intensity, higher health-related quality of life, and greater self-efficacy. Fewer patients reported daily pain,

took OA medication, reported willingness to undergo surgery, reported fear of movement, and self-reported a higher level of physical activity.
Study II. Patients receiving home-based exercise or supervised exercise experienced greater pain reduction compared with patients who received only education. Pain reduction after treatment was more prominent in patients with knee OA than in those with hip OA.
Study III. The strongest factors associated with reaching the minimal clinical difference of pain, were less frequent pain, unilateral OA, being unwilling to undergo surgery and lower body mass index (BMI). Study IV. After the 3-month self-management program, the number of minutes spent in sedentary behavior or physical activity did not differ significantly at the 3-month follow-up, at the 12-month follow-up, minutes in moderate to vigorous physical activity did decrease compared with the baseline for patients with knee and/or hip OA.

Conclusion: These studies extend results from previous RCTs showing that patient education and exercise can reduce knee and/or hip OA symptoms also when provided in real-world settings. Patients participating in SOASP reported reductions in OA symptoms, reduced their willingness to undergo surgery and took less OA medication and sick leave. Despite the reduced symptoms, the patients did not decrease their average sedentary time or increase their level of physical activity. Participating in a home-based or supervised exercise program produced similar reductions in pain intensity and was more effective than education only, suggesting that structured self-management programs, as the SOASP, play an important role in OA care.

Svensk sammanfattning

Artros är den vanligaste ledsjukdomen och drabbar omkring 25% av världens befolkning över 45 år. Sjukdomen beräknas att öka framöver, dels då befolkning blir äldre, dels på grund av en förändrad livsstil med både mer tid i stillasittande och fler personer som är överviktiga (1).

Enligt nationella och internationella behandlingsriktlinjer är grundbehandlingen för artros, träning, information och vid behov viktreduktion. Vid otillräcklig effekt av grundbehandlingen kan denna kompletteras med läkemedel, passiva behandlingar, hjälpmedel och operation. Trots att dessa behandlingsriktlinjer funnits sedan ett 10-tal år tillbaka, så är det endast cirka 50% av dem som söker vård för artros som erbjuds detta.

Mot denna bakrund, startade år 2008 ett implementeringsprojekt i Sverige som heter Bättre Omhändertagande av Patienter med artros (BOA). Projektets huvudsyfte var ursprungligen; 1) att utbilda fysioterapeuter och arbetsterapeuter i att behandla artrospatienter enligt rådande evidens, 2) att behandla patienter enligt rådande evidens genom artrosskola och 3) att utvärdera behandlingen med artrosskola via ett register, BOA-registret.

BOA artrosskola bygger på rådande evidens som visar att träning och information leder till symtomlindring hos patienter med knä- och/eller höftledsartros. Det är däremot fortfarande oklart vilka resultat dessa behandlingar leder till när de ingår i en artrosskola och används i den dagliga kliniska verksamheten runt om i Sverige. Det övergripande syftet med denna avhandling var att få en fördjupad kunskap om resultatet av behandling med artrosskola, som bedrivs på fler än 500 primärvårdsenheter runt om i Sverige.

Delarbete I var en registerstudie där 44 634 patienter med knä- och/eller höftledsartros som deltagit i artrosskola var inkluderade. Förändring av patient-rapporterat utfall från före baslinjen till 3- och 12-månader efter behandlingen undersöktes. Resultaten vid 3-månaders uppföljningen visade att patienterna upplevde en minskad smärtintensitet, en ökad hälsorelaterade

livskvalitet och en ökad tilltro till sin egen förmåga. Färre patienter angav att de upplevde daglig smärta, tog ledrelaterade läkemedel, var rörelserädda, önskade operation (av dem som önskade operation före start i artrosskola) och var fysiskt inaktiva. Efter 12-månader, upplevde patienterna fortfarande en minskad smärta och en ökad hälsorelaterad livskvalitet. Dessutom angav färre patienter att de upplevde daglig smärta, var rörelserädsla, önskade operation (endast de med höftledsartros) och var i mindre utsträckning sjukskrivna.

Delarbete II var en registerstudie där 38 030 patienter med knä- och/eller höftledsartros som deltagit i artrosskola var inkluderade. I denna studie undersöktes om resultatet gällande smärtlindring var baserat på vilken del av artroskolan som patienterna deltagit i; 1) endast teori, 2) teori + hemträning eller 3) teori + handledd träning. I denna studie undersöktes även om resultatet skiljde sig mellan patienter med knä- respektive höftledsartros. Resultatet visade att patienter som deltagit i hemträning eller handledd träning upplevde större smärtreduktion än de som endast deltagit i teoridelen. Patienter med knäledsartros svarade bättre på behandlingen än patienter med höftledsartros.

Delarbete III var en registerstudie där 26 638 patienter med knä- och/eller höftledsartros som deltagit i artrosskola var inkluderade. I denna studie undersöktes vilka faktorer före start i artrosskolan som var associerade med en kliniskt meningsfull smärtreduktion. Resultatet visade att patienter som inte upplevde daglig smärta, inte hade önskemål om operation, hade unilateral artros och ett lägre BMI, hade högre odds att uppnå en kliniskt meningsfull smärtreduktion.

Delarbete IV var en klinisk studie med en kontrollgrupp, där 250 patienter med knä- och/eller höftledsartros var inkluderade. Behandlingsgruppen deltog i artrosskola och kontrollgruppen erbjöds ingen behandling. I denna studie mättes fysisk aktivitet med en accelerometer innan samt 3- och 12-månader efter start i artrosskolan. Resultatet visade att varken tid i stillasittande eller fysisk aktivitet på måttlig nivå förändrades vid 3 månaders uppföljningen. Efter 12 månader minskade antal minuter av fysisk aktivitet på måttlig nivå.

Denna avhandling har fördjupat kunskapen om resultet av artrosskola bedriven i den daglig kliniska verksamheten. Hur deltagande i olika delar av artrosskolan påverkar resultatet och vilka faktorer som är associerade med smärtreduktion efter behandling med artrosskola.

Thesis at a glance

Aim	Main results	Conclusion
Study I To evaluate whether the Supported Osteoarthritis Self-Management Program (SOASP) would lead to the following changes: 1) decreased pain, 2) improved health-related quality of life, 3) increased self-efficacy, 4) reduced number of patients taking OA medication, 5) decreased fear-avoidance behavior, 6) increased level of physical activity, 7) decreased willingness to undergo surgery, 8) reduced sick leave	At the 3-month follow-up, patients with knee and hip OA reported lower pain intensity and increased health-related quality of life and self-efficacy. Fewer patients reported frequent pain, took OA medication, were willing to undergo surgery, reported fear–avoidance behavior, and were physically inactive.	The SOASP led to experienced a reduction in symptoms, willingness to undergo surgery, use of OA medication, and sick leave. These results suggest that offering this intervention as the first-line treatment for people with OA in real-world settings can reduce the burden of this disease.
Study II To compare the effectiveness of pain reduction after participating in different parts of the SOASP: 1) education only, 2) education + home exercise or 3) education + supervised exercise.	At the 3- and 12-month follow-up, patients who participated in the home-based or supervised exercise program reported greater pain reduction compared with those who participated only in the theory part. Patients with knee OA showed larger improvements than did those with hip OA.	Patients with OA who participated in supervised or unsupervised exercise experienced greater pain reduction than patients who received education alone, with those who had knee OA experiencing a greater benefit. Patients who are not willing or cannot undergo supervised exercise may experience similar benefits from home-based exercise.
Study III To identify individual and disease-related factors at the baseline that are associated with the response to the SOASP.	In patients with knee and hip OA at both the 3- and 12-month follow-up, younger participants, and those with a lower BMI, unilateral OA, less pain frequency, and unwillingness to undergo surgery were more likely to respond to the SOASP.	The results of this study generally agree with those of previous studies showing that a positive response to a self-management program is related to lower BMI, unilateral OA, less frequent pain, and being unwilling to undergo surgery. These findings suggest that to improve the outcomes of first-line OA treatment in the general OA population, greater emphasis should be allocated to those who show less improvement.
Study IV To evaluate whether physical activity level and sedentary time change after treatment within the SOASP.	At the 3-month follow-up, the mean change in the number of minutes spent in sedentary or physical activity did not differ between the intervention and reference groups.	Participation in the SOASP did not decrease the average amount of sedentary time or increase the physical activity level.

Abbreviations

ACR	American Collage of Rheumatology
ANOVA	Analysis of Variance
ASES	Arthritis Self Efficacy Score
BMI	Body Mass Index (kg/m²)
BOA	Better Management of Patients with Osteoarthritis
CI	Confidence Interval
ES	Effect Size
EULAR	European League Against Rheumatism
EQ-5D	EuroQoL Five Dimensions
HRQoL	Health-Related Quality of Life
ICF	International Classification of Functioning, Disability, and Health
ICHOM	International Consortium for Health Outcomes Measurement
IQR	Inter Quartile Range
MET	Metabolic Equivalent
MVPA	Moderate to Vigorous Physical Activity
NRS	Numeric Rating Scale
OA	Osteoarthritis
OARSI	Osteoarthritis Research Society International
OR	Odds Ratio
OT	Occupational Therapist
PT	Physical Therapist
PROM	Patient-Reported Outcome Measure
SD	Standard Deviation
SOASP	Supported Osteoarthritis Self-Management Program
VAS	Visual Analogue Scale
WHO	World Health Organization

Definitions

Exercise	“subset of physical activity that is planned, structured, and repetitive and has a final or an intermediate objective of improving or maintaining physical fitness” (2).
Minimal clinical important difference	“the smallest difference in score in the domain of interest which patients perceive as beneficial and which would mandate, in the absence of troublesome side effects and excessive cost, a change in the patient's management“ (3).
Pain	“an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (4).
Patient education	“helping patients acquire or maintain the competencies they need to manage as well as possible their lives with a chronic disease. It is an integral and continuing part of patient care. It comprises organized activities, including psychosocial support, designed to make patients aware of and informed about their disease and health care, hospital organization and procedures, and behavior related to health and disease, so that they (and their families) understand their disease and their treatment, collaborate with each other and take responsibility for their own care as a means of maintaining or improving their quality of life” (5).

Physical activity	"any bodily movement produced by skeletal muscles that result in energy expenditure, and exercise are defined as a subset of physical activity that is planned, structured, and repetitive and has a final or an intermediate objective of improving or maintaining physical fitness" (2).
Self-efficacy	"belief in one´s capability to organize and execute the courses of action required to produce given attainments" (6).
Self-management education	"Interactive educational interventions specifically designed to enhance patient self-management. Self-management education is patient-driven and focuses on building generalizable skills such as goal setting, decision making, problem-solving, and self-monitoring" (7).

List of papers

This thesis is based on the following papers, referred to in the text by roman numerals.

I. Jönsson T, Eek F, Dell`lsola A, Dahlberg LE, Hansson EE. The better management of patients with osteoarthritis program; outcomes after education and exercise delivered nationwide in Sweden. PloS one. 2019;14(9):e0222657.

II. Dell`lsola A, Jönsson T, Ranstam J, Dahlberg LE, Hansson EE. Education, home exercise and supervised exercise for people with hip and knee osteoarthritis as a part of a nationwide implementation programme; data from the BOA registry. Arthritis Care Res (Hoboken). 2019 Jul 19. doi: 10.1002/acr.24033.

III. Jönsson T, Eek F, Hansson EE, Dahlberg LE, Dell`lsola A. Factors associated with response to a self-management program with education and exercise for individuals with knee and hip osteoarthritis: data from the BOA registry. Manus

IV. Jönsson T, Hansson EE, Thorstensson CA, Eek F, Bergman P, Dahlberg LE. The effect of education and supervised exercise on physical activity, pain, quality of life and self-efficacy – an intervention study with a reference group. BMC Musculoskelet Disord. 2018 Jun 21;19(1):198. doi: 10.1186/s12891-018-2098-3.

Introduction

Osteoarthritis (OA) is the most common joint disease and affects more than 300 million people worldwide; it is the fastest-growing cause of disability in the world (1, 8). OA affects cartilage, bone, synovium, and other intra- and periarticular tissues (9) and occurs most often in the knee, hip, and hand, but can affect all joints (1, 10). This thesis focuses on people with knee and/or hip OA. People with OA experience impairments such as pain, joint stiffness, and pain-related psychological distress (11), which can limit physical activity level and restrict participation in activities of daily living. The International Classification of Functioning, Disability, and Health (ICF) is a classification of health and health-related domains and describes changes in body function and structures that affect what people with a health condition can do in a standard environment, as well as in their usual environment. These domains are classified into the following categories: 1) impairments caused by body function and body structure, 2) activity limitations (problems in the execution of a task), 3) participation restrictions (problems in taking part in situations of life) and 4) personal and environmental factors (12). The possible impairments in people with knee and/or hip OA are described In Fig. 1.

OA is a chronic disease with no cure, and the treatment options aim to alleviate symptoms, increase function and participation. Exercise combined with patient education is considered to be the first-line treatment (13-15) based on the results of more than 67 randomized clinical studies (RCTs) that included people with knee and/or hip OA (16). Only 50% of patients with OA are offered health care in line with the guidelines (17, 18). In Sweden, self-management programs include patient education and exercise programs for people with knee and/or hip OA and are provided by health professionals in the primary care settings. Despite the promising results of RCTs, there is a gap in applying the evidence to clinical practice, and the effects of these self-management programs when implemented in real-world settings are not well documented.

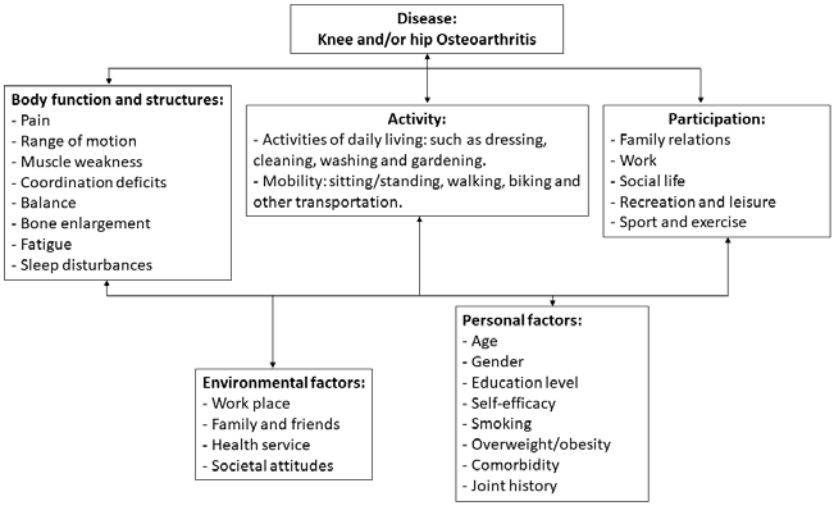

Fig. 1. The International Classification of Functioning, Disability, and Health model (ICF) for people with knee and/or hip OA.

Osteoarthritis

Definition

OA is a joint disease that affects cartilage, bone, synovium and all other intra and periarticular tissues (9). OA can affect all joints, but the knee, hip, and hand are most commonly affected (1, 10). The Osteoarthritis Research Society International (OARSI), defines OA as a: “disorder involving movable joints characterized by cell stress and extracellular matrix degradation initiated by micro- and macro-injury that activates maladaptive repair responses including pro-inflammatory pathways of innate immunity. The disease manifests first as a molecular derangement (abnormal joint tissue metabolism) followed by anatomic, and/or physiologic derangements (characterized by cartilage degradation, bone remodeling, osteophyte formation, joint inflammation and loss of normal joint function), that can culminate in illness” (19).

Risk factors for OA

The prevalence of OA increases with age because of cumulative exposure to different risk factors over many years as well as biological age-related changes in joint structures (20). For knee OA, the most common risk factors are female sex, obesity, knee malalignment, and a previous knee injury (21-23). For hip OA, hip deformities are a common risk factor and other risk factors such as female sex and obesity are less important (24). Genetics is also a risk factor for OA, and its contribution has been estimated at 40% to 80%, with a stronger genetic contribution to hand and hip OA than knee OA (25). Heavy work activities are risk factors for both knee and hip OA. Employment in the farming or construction industry is especially associated with hip OA (26), and work that involves frequent kneeling and heavy lifting are associated with knee OA (27). High-impact sports as football, handball, hockey, wrestling, and weightlifting also pose a higher risk for both knee and hip OA (28, 29).

Symptoms and disabilities

Common symptoms for both knee and hip OA are pain, morning stiffness (lasting less than 30 minutes, a longer duration increases the likelihood of rheumatoid disease), reduced range of motion, crepitus, joint instability, swelling, muscle weakness, fatigue, and pain-related psychological distress (11).

People with OA experience pain as the most disabling symptom and OA-related pain is a major driver of clinical decision-making and health service use (30). The pain usually develops over months to years. The pain in knee OA is often intermittent and is related mainly to weight-bearing. Intermittent pain may be predictable in the beginning, but pain is categorized as unacceptable when it becomes more severe, more frequent, or unpredictable (31). People with hip OA often describe an achy groin pain, which is first intermittent, becomes worse at the end of the day, and is related to activity. Pain during rest and at night may occur at all disease stages but becomes more severe as the disease progresses (32).

Walking impairment and decreased physical activity level are more common in people with OA than in healthy people (33), and decreased physical activity level is associated with comorbidities.

Around 25% of people with OA at the age of 65 years and older, will have one or more comorbidity (34). People with OA have an increased risk of cardiovascular disease compared with people without OA (35, 36) and a slightly increased risk of cardiovascular death (36, 37). Previous studies have shown an association between OA and atherosclerosis-related disease (38) and that people with OA have a slightly increased risk of stroke compared with people without OA (39). The presence of at least one comorbidity is associated with symptoms such as pain and performance-based impaired physical functioning (34).

Diagnosis of OA

According to national and international guidelines, OA requires a clinical diagnosis. Radiographic evidence is not needed for the diagnosis but can be considered if the symptoms are atypical or if another diagnosis is suspected (40). There is a discrepancy between radiographic OA and symptomatic OA, and a weak correlation between symptoms and the radiographic grade of OA (41). It may take many years from the onset of OA until OA can be shown radiographically (41).

Different clinical criteria are used to diagnose knee and hip OA. The most common are published by the European League Against Rheumatism (EULAR) (only for knee OA) (42), the American College of Rheumatology (ACR) (43, 44), and the National Institute for Health and Care Excellence (NICE) (45). According to the National Board of Health and Welfare in Sweden, the clinical diagnosis should be a combined assessment of the patient's history, three common symptoms for OA, and three typical clinical findings for OA (46). An overview of the different criteria for knee and hip OA is provided in Table 1.

Table 1. Criteria for the clinical diagnosis of knee OA (42, 44, 45) and hip OA (43, 47).

Knee OA				Hip OA		
	NICE	EULAR	ACR		NICE	ACR
Age	≥ 45 ●	≥ 40 ●	≥ 50 ▲	Age	≥ 45 ●	≥ 50 ▲
Symptoms						
Activity/Usage-related joint pain	●	●	●	Activity/Usage-related joint pain	●	●
No EMS or EMS ≤ 30 minutes	●	●	▲	No EMS or EMS ≤ 30 minutes	●	
Functional limitation		●		No EMS or EMS ≤ 60 minutes		▲
				Functional limitation		▲
Clinical signs						
Crepitus		▲	▲	Hip internal rotation ≤15 °		▲
Restricted Range of Motion		▲		Pain present on internal rotation of the hip		▲
Bone enlargement		▲	▲			
Bone margin tenderness			▲			
No palpable warmth			▲			
Minimum criteria						
Minimum criteria: all ● plus		≥ 1 ▲	≥ 3 ▲	Minimum criteria: all ● plus		≥ 1 ▲
NICE= National Institute for Health and Care Excellence, EULAR= European League Against Rheumatism, ACR= American College of Rheumatology, EMS=Early morning stiffness						

Incidence and prevalence of OA

The incidence and prevalence of OA vary between studies and differ according to the definition of OA used (radiographic or symptomatic), as well as the age categories, birth country, and sex distribution of the study population (48). The prevalence is higher for radiographic OA than for symptomatic OA in people with knee OA (48). In this thesis, OA is defined according to the symptoms through clinical diagnosis.

A previous study, that estimated the incidence of clinically diagnosed knee and/or hip OA among people aged 40 years and older, reported an overall incidence of 6.5/1000 person-years for knee OA and 2.1/1000 person-years for hip OA (10). When classified according to sex, the incidence of knee OA was 8.3/1000 person-years in women and 4.6/1000 person-years in men. In the same study, the incidence rates of hip OA were 2.4/1000 and 1.7/1000 person-years for women and men, respectively (10). In women with knee and hip OA, the incidence increased progressively with age and the steepest slope was observed in the age range 50-70 years. In men, the incidence of knee and hip OA increased continuously with age and peaked only in the oldest age group (>85 years) (10).

The prevalence of symptomatic OA in people aged 45 years or older is 6.7% to 15. 9 % in those with knee OA and 1.6% to 9.2 % in those with hip OA (10). A Swedish cohort study reported prevalence rates of 13.8% for knee OA (diagnosed by a medical doctor) and 5.8% for hip OA in a population aged 45 or older (1).

Physical activity

The World Health Organization (WHO) has provided internationally accepted recommendations for physical activity. Adults are recommended to perform at least 150 minutes of moderate-intensity physical activity or 75 minutes of vigorous-intensity physical activity throughout the week (49). The metabolic equivalent (MET) is commonly used to express the intensity of physical activity. A MET is the ratio of a person's working metabolic rate. One MET is defined as the energy cost of sitting still and is equivalent to a caloric consumption of 1 kcal/kg/hour. Compared with sitting still, a person´s caloric consumption is 3-6 times higher when performing a moderate activity (3-6 METs) and more >6 times higher when performing a vigorous activity level (>6 METs) (49).

In 2016, one quarter of the world's adult population did not meet the WHO recommendations for physical activity (50). Data from Sweden has shown that only 50% of the population in Sweden achieved the recommendation (when measured objectively with an accelerometer) (51). Physical activity is vital for preventing non-communicable diseases, such as cardiovascular disease, hypertension, diabetes, and cancer (52, 53). Physical activity has a positive effect on mental health, delays the onset of dementia, and can help in the maintenance of healthy body weight (52).

People with OA are less likely to perform a sufficient physical activity level compared with healthy people without OA (33, 54). Physical inactivity is associated with poorer general health in people with knee and/or hip OA and with the development of comorbidities such as obesity, diabetes, and heart disease (55). Consistent with the effects of exercise, increased physical activity is associated with better physical function and decreased pain in people with knee and/or hip OA (56).

Treatments for OA

According to national and international guidelines, first-line treatments for people with knee and/or hip OA should include patient education, exercise and if needed, weight control (for those with a body mass index (BMI) of 25kg/m2 or higher) (Fig. 2) (13-15, 57). If patient education and exercise are unsuccessful for decreasing pain and improving function, the physical therapist (PT) may offer complementary treatment such as aids, passive treatments, and pharmacological pain relief (13-15). People who still experience unacceptable joint pain and reduced quality of life because of end-stage OA after first-line treatment and additional treatments should be referred to a surgeon for consideration of surgery involving total joint replacement (13, 14).

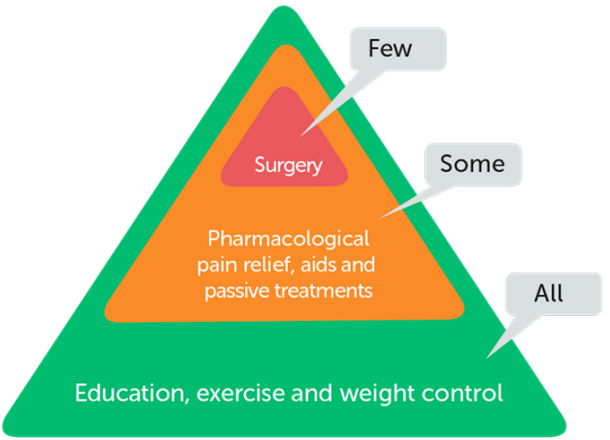

Fig. 2. Osteoarthritis treatment pyramid; reproduced with permission from Joint Academy.

First-line treatment

Patient education

The WHO recommends patient education as a part of the treatment for all chronic diseases including OA. The WHO defines patient education as: “helping patients acquire or maintain the competencies they need to manage as well as possible their lives with a chronic disease. It is an integral and continuing part of patient care. It comprises organized activities, including

psychosocial support, designed to make patients aware of and informed about their disease and health care, hospital organization and procedures, and behavior related to health and disease, so that they (and their families) understand their disease and their treatment, collaborate with each other and take responsibility for their own care as a means of maintaining or improving their quality of life" (5).

For people with knee and/or hip OA, a Delphi survey suggested that educational component should include information about the disease, its causes and diagnosis criteria, and management of the disease (58). Providing information in combination with other treatments helps people to adhere to the treatment because they obtain a better understanding of their condition (59, 60).

Exercise

Exercise is the core treatment for people with knee and/or hip OA, both because of the positive effects on OA (61-63) and because exercise and physical activity help prevent many chronic conditions (64) and improve symptoms of several chronic conditions (65). The guidelines from OARSI, EULAR, and ACR include strong recommendations for exercise, for people with knee and/or hip OA (13-15). More than 54 RCTs have evaluated the effects of exercise in people with knee OA (61), and more than 10 RCTs have evaluated the effects of exercise in people with hip OA (62). The message from those studies is clear: pain and physical function are improved following performed exercise in people with knee and/or hip OA (61, 62).

The mechanisms responsible for the effects of exercise on pain and physical function in people with knee and/or hip OA are insufficiently understood (66). Increased upper-leg strength, improved knee extension, and improved proprioception have been identified as possible mediators and a positive association has been reported between exercise and improvement in OA-symptoms in people with knee OA (67). Another potential mechanism is the reduction in symptoms secondary to the physiological responses to exercise training (66). In people with hip OA, lower limb strength is associated with better self-reported physical function (68).

Exercise should be individualized, structured land-based exercise and can include strengthening, cardiorespiratory training, balance training, neuromuscular exercise, or mind-body exercise such as Tai Chi or yoga (13, 69). The effects are similar in people with knee and/ hip OA who perform

aerobic, resistance, or performance-based exercise (70). Water-based exercise may be an alternative for people unable to perform land-based exercise because of their inability to tolerate load-bearing exercise or comorbidities such as severe obesity (71). Supervised exercise has been shown to produce better results for people with knee and/or hip OA than home-based exercise (72-74). The optimal dosage of exercise for people with knee and/or hip OA is unclear, but it is more effective to perform supervised exercise >12 times compared with <12 times (70). Interventions that follow the recommendations of the American College of Sports Medicine for strength training (75) produce greater decreases in pain compared with exercise interventions that do not follow these recommendations (76).

Long-term adherence to exercise is poor among many people with knee and/or hip OA, which limits the ability for these people to obtain sustained symptom relief (77). Booster sessions may be one way to help people with OA to continue their exercise program (78). A recent study has suggested that the use of messages sent by the short message service (SMSs) may be useful as booster sessions, but the effect of this approach is still unknown (79, 80).

Weight control

Overweight and obesity are very common in people with knee and/or hip OA (81). Weight-loss interventions may help in the treatment of these conditions but only for people with knee OA (82). A meta-analysis of weight loss concluded that physical function improves with a decrease in weight of about 5%, but the effects of weight loss on pain were less consistent (83). The combination of dietary weight management and exercise has better effects on pain and function than either diet or exercise alone (84). A reduction of about 5 kg reduced the risk of new symptomatic knee OA by 50% and was associated with a reduced risk of development of radiographic knee OA (85).

Additional treatments

Pharmacological pain relief

Pain is the most disabling symptom in people with knee and/or hip OA (30). Because the pain can be disabling, first-line treatments may be combined with pharmacological pain relief. According to previously updated recommendations, topical Non-steroidal Anti-Inflammatory Drugs (NSAIDs) are preferred over oral pharmacological pain relievers because they have

fewer side effects. Paracetamol is not recommended now because of its poor clinical effects (13).

Passive treatments and aids

Passive treatments and aids should always be offered in combination with patient education, exercise, and, if needed weight control. Passive treatments include joint mobilization and manipulation, which have shown moderate benefit for people with knee OA (86) and may be considered in the treatment of hip OA (87).

Acupuncture is commonly used in primary care as a complement to painkillers. In people with knee and/or hip OA, there is insufficient evidence to conclude whether acupuncture is an effective treatment for OA. One review concluded that there is little or no effect for people with hip OA (88) whereas another review noted a small effect of acupuncture on knee symptoms (89).

There is no evidence of the effectiveness of other passive treatments such as massage, neuromuscular electrical stimulation, transcutaneous electrical nerve stimulation, ultrasound, and laser. These treatments should not be offered to people with knee and/or hip OA (13, 14).

Braces, insoles, and shoes may be recommended to people with knee OA, although their effects have been insufficiently investigated to make specific recommendations (13).

Activity limitation caused by OA is common in people with knee and/or hip OA. To manage the activities of daily life without help, aids may be needed. According to the EULAR treatment recommendations (14), the frequent use and high satisfaction rates of assistive technology indicate that walking aids, assistive technology, and adaptations are useful for people with knee and/or hip OA (90, 91). No RCTs have reported on the effects of assistive technology except for the use of a cane in people with knee OA (92). However, the EULAR group agreed that walking aids, assistive technology, and adaptations at home and/or at work should be considered as a part of the treatment for all people with knee and/or hip OA (14).

Surgery

People who still have unacceptable joint pain after first-line and additional treatments because of end-stage OA can experience greatly reduced quality of life. These people should be referred to a surgeon for consideration of

surgery. The most common form of surgery for people with knee and/or hip OA is a total joint replacement, which is a clinically relevant and cost-effective treatment for end-stage OA (93).

The Better Management of Patients with Osteoarthritis

There is a discrepancy between the treatment recommended by guidelines and what people with knee and/or hip OA receive (94). In Sweden, unpublished studies from different geographic regions have shown that >50 % of people with knee and/or hip OA are referred to surgery without receiving first-line treatment. This is consistent with published international studies showing that only about 50% of people with knee and/or hip OA receive treatment according to the guidelines (17, 18, 95). To reduce the discrepancy between guidelines and practice, a Swedish national program, "The Better Management of Patients with Osteoarthritis" (BOA), was initiated in 2008 (96).

The BOA program had three arms:

1) Education of PTs and occupational therapists (OTs) to deliver health care according to guidelines.
2) Education of patients through a Supported Osteoarthritis Self-Management Program (SOASP).
3) Collection of patient-reported and PT-reported outcomes before and after treatment by the National Quality Register, the BOA registry.

The founder of the BOA program hypothesized:

a) That a "ready-to-use" program based on existing evidence would be feasible in clinical practice and could be extended through education.
b) That the potential for adapting the intervention to local PT practices or patient preferences was crucial for acceptability.
c) That patients with good experiences of exercise as treatment could be used as "role models", and that transforming information into knowledge was important for adherence.

1. Education of physiotherapists and occupational therapists

Between 2008 and 2016, around 3000 PTs and OTs interested in the BOA program participated in a 1- or 2-day course showing them how to diagnose OA and deliver OA care according to clinical guidelines. They also received access to digital material, including PowerPoint presentations, to support them in the delivery of the SOASP and to maximize the adherence to the program.

2. The Supported Osteoarthritis Self-Management Program.

The content of the SOASP was based on existing evidence at the time, national and international treatment guidelines, and patients' views, thoughts, and tolerance of treatment and exercise for OA (96). The SOASP combined information delivered by health-care professionals with individually adapted exercise (Fig. 3).

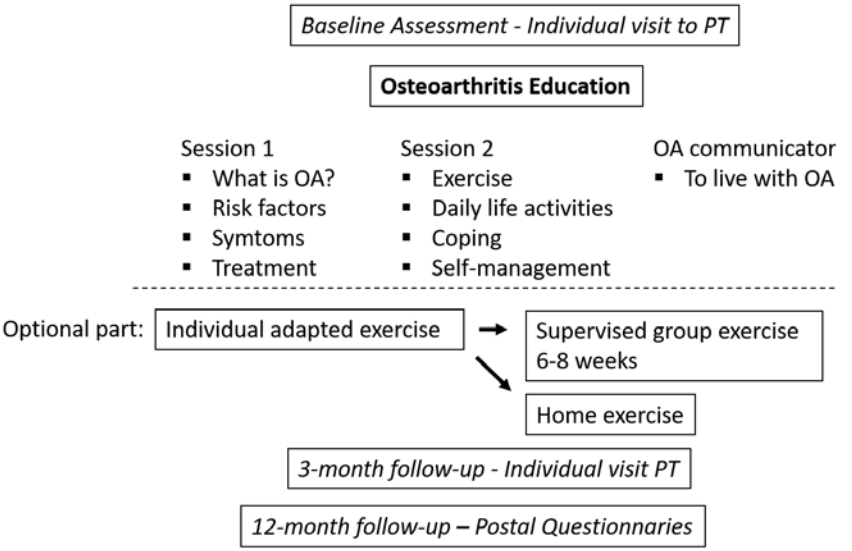

Fig. 3. Concept of the Supported Osteoarthritis Self-Management Program (97).

The SOASP included a minimal intervention of two theoretical group sessions with 7-12 participants in each group, led by a PT. The minimal intervention could not be modified, but PTs could choose to adjust the content or sessions above and beyond the minimal intervention, to suit their clinical routines. For example, they could add a session about weight loss and diet, pharmacological and surgical treatment, or hand function and activities to reduce symptoms caused by hand OA. These extra sessions could be provided by dieticians, physicians, or OTs.

The SOASP is based on the transtheoretical model of behavioral change (98), and the self-determination theory (99). The first session provided information about the pathology and etiology of OA, and treatments according to guidelines. The second session focused on the role of exercise in OA and the need for exercise, barriers to exercise, how exercise can be incorporated into daily life, and self-management strategies to reduce pain and other symptoms. The third session was not mandatory but was offered by an OA communicator who was a person with OA who had been trained to talk about his/her experiences living with OA, and with first-line interventions (96). The theory part aimed to explain the mechanisms underlying the benefits of exercises and to increase patients' motivation to exercise and be physically active.

After the theory component, patients could choose to participate in an optional exercise part. The exercise part included a face-to-face session with a PT to go through an individually adapted exercise program. After that, the patients could choose to perform the exercises on their own or during PT-supervised exercise classes held twice a week for 6-8 weeks (96). The individually adapted exercise program was based on each patient's specific needs and goals. Strength training exercises were individualized based on the following biomechanical principles: to ensure proximal strength, align the hip–knee–ankle, and achieve good neuromuscular control. The intensity and progression of exercises were based on each patient's function and capacity, and the ability to maintain alignment and control (Fig. 4).

Exercise may be painful in patients with OA, and a model of "acceptable pain" was used to facilitate the patients' ability to exercise (100). This model allows the patients to experience pain during exercise if it is perceived as "acceptable" or does not exceed 5 on a 0–10 scale, and if the pain normalizes within 24 hours (100).

Fig. 4. Examples of exercises used in the SOASP. Photo: Thérése Jönsson

The intervention was followed up at 3 and 12 months after the start. The 3-month follow-up focused continuously incorporating exercise and physical activity into daily life (96). The 12-month follow-up included a questionnaire sent to the patients by mail.

The SOASP was developed and trialed at Spenshult Hospital for Rheumatic Diseases, Spenshult, Sweden, in 2006 (96). Various self-management programs for patients with knee and/or hip OA are used nationally and internationally (101). A role model for the self-management program is Kate Lorig from Stanford University School of Medicine who started in the late 1970s with an Arthritis Self-Management Program based on the self-efficacy theory (102-104). The definition of self-management education has been described as “Interactive educational interventions specifically designed to enhance patient self-management. Self-management education is patient-driven and focuses on building generalizable skills such as goal setting, decision making, problem-solving, and self-monitoring”(7).

In Sweden Maria Klässbo, started self-management programs for patients with hip OA in the late 1980th (105). In the southern part of Sweden, a self-management program for patients with knee, hip and/or hand OA has been used since the late 1990th (106). These programs included only the theory part and did not include exercise. Previous studies have shown that adding an exercise part to the self-management program will increase the effect

concerning pain reduction and self-efficacy (107, 108), physical function (109) and may postpone surgery with total joint replacement (110).

It has been shown that patients with knee OA who participate in self-management programs experience positive effects on outcomes such as pain (111, 112), health-related quality of life (HRQoL) (106, 111), self-efficacy (113), and function (107, 111, 113) and that these effects may postpone the need for total joint replacement (114, 115). In patients with hip OA, self-management programs have been shown to have positive effects on outcomes such as pain (105, 116), HRQoL (105), and function (116), and that these effects may postpone the need for total joint replacement (110).

3. The BOA registry

The BOA registry started in 2008 and became a National Quality Registry in 2010. Between 2008 and 2016, the registry aimed to evaluate the results from the SOASP in patients with knee, hip and/or hand OA.

The treated PT was told to send data to the BOA registry only for patients with specific inclusion and exclusion criteria. The inclusion criteria were joint problems in the hip, knee, or hand that required visits to a health-care professional and receipt of clinical diagnosis of OA. The exclusion criteria were confirmed or suspected cancer, rheumatoid arthritis, hip fracture sequelae, chronic pain or fibromyalgia, total joint replacement within the past 12 months, other surgery of the knee or hip joint within the past 3 months, or inability to read or understand Swedish. These criteria were used between 2008 and 2016.

The register contains patient-reported data about their symptoms, HRQoL and psychological factors (Table 2) and PT-reported data about previous health care, diagnosis, and compliance with the intervention (Table 3).

The level of coverage was defined as the number of units offering the SOASP, which also registered in the BOA registry. The level of completeness was defined as the number of patients who participated in a SOASP and had been reported to the registry. The coverage level was calculated at the end of 2016 as 86% and the level of completeness as 72% (117). The response rates for each reported question were 97% at the baseline and 3 months, and 84% at 1 year and the dropout rate in the registry was about 31% (117).

After the start of the BOA in Sweden, similar implementation programs have been started in Denmark through Godt Liv med Artrose I Danmark (GLA:D®) (118), and in Norway through Aktiv med Artrose (Aktiv A) (119). A web-based self-management program based on the SOASP, called Joint Academy has been evaluated in Sweden (120).

Table 2. Patient-reported outcomes in the BOA registry.

Variable	**Baseline**	**3-month follow-up**	**12-month follow-up**
Age	x	x	x
Gender	x	x	x
Born in Sweden	x		
Swedish citizen	x		
Educational level	x		
Current employment	x		
Sick leave	x		x
Smoking	x		
Weight (kg)	x		x
Height (cm)	x		x
Body mass index (kg.m2)	x		x
Comorbidity	x	x	x
Most affected joint: knee/hip/hand/shoulder	x	x	x
During the last week to what degree have ailments originating from your arm, shoulder or hand impaired your work or other daily activities?	x	x	x
Mean pain intensity during the last week in the most affected joint	x	x	x
Fear of movement	x	x	x
Willingness to undergo surgery of knee/hip	x	x	x
EuroQol-five dimisions	x	x	x
EuroQol Visual analogue scale	x	x	x
Self-reported physical activities	x	x	x
Arthritis Self-Efficacy Scale (subscales: pain and other symptoms)	x	x	x
Satisfaction with the BOA program		x	x
Frequency of using what was learned in the BOA program		x	x

Table 3. Physiotherapist-reported outcomes in the BOA registry

Variable	Baseline	3-month follow-up
Most affected knee/hip/hand joint	x	x
Other affected knee and/or hip joints	x	x
Prior surgery of most affected joint	x	
Prior surgery to the contralateral side of most affected joint	x	
X-ray of most affected joint	x	x
MRI of most affected joint	x	x
On the waiting list for surgery	x	x
Prior explanation of knee/hip problems	x	
Prior treatment of knee/hip problems	x	
Prior information about weight reduction	x	
Use of OA medication and type	x	x
Using walking aids	x	
Treatment other than the BOA program during follow-up		x
Participation in theory sessions and number of supervised exercise sessions in the BOA program		x

MRI=Magnetic resonance imaging

Clinical assessment and outcome measures

It is important to evaluate the results of different treatments, and this may be done in different ways. For people with knee and/or hip OA, it is recommended to combine patient-reported outcome measures (PROMs) and performance-based outcome measures (121). The International Consortium for Health Outcomes Measurement (ICHOM) has defined a standard set of outcome measures for monitoring the care of people with clinically diagnosed knee or hip OA (122). The ICHOM suggest that pain, HRQoL, and work status are the core outcomes in combination with the satisfaction of the result of the treatment, for assessing the results of treatment. The OARSI also recommends that PROMs should be combined with a set of performance-based tests of physical function that include tests of typical activities relevant to people with knee and/or hip OA (123).

Baseline characteristics

Different baseline characteristics may affect the outcomes of treatment in people with knee and/or hip OA. Baseline characteristics should be included and, in some cases, adjusted for (122). Recommended baseline characteristics are:

- Age
- Sex
- Education
- Living Status
- BMI
- Physical activity
- Smoking status
- Comorbid conditions
- Joint history (trauma, malalignment, other joint disorder)
- Joint specific surgical history (joint replacement, osteotomy, arthroscopic)

Disease-specific outcome measures

Different instruments for evaluating knee and/or hip symptoms are used to assess outcomes in people with OA. The Western Ontario and McMaster Universities Arthritis Index (WOMAC) assesses pain, disability and joint stiffness in people with knee and/or hip OA (124). The Knee Injury and Osteoarthritis Outcome Score (KOOS) and the Hip Disability and Osteoarthritis Score (HOOS) have been developed from the WOMAC (125, 126). Pain is recommended to be measured by using either a visual analog scale (VAS) or numeric rating scale (NRS), these instruments provide congruent results (127). It is recommended that pain should be measured for all affected joints (e.g. hip, knee, spine) (122).

Generic health-related quality of life

The two main alternatives to measure HRQoL are the Short Form health surveys (SF-36) and the EuroQol health outcome measure (EQ-5D). The EuroQol-5 domain (EQ-5D) is a generic measure of health status developed by the EuroQoL group (128). It includes questions that assess five health outcome domains, which can be summarized into a single score and a VAS that assesses the current overall health state. Although there are alternative

versions, the original EQ-5D with three levels of response options is the most commonly used and best validated instrument for people with OA (129).

Performance-based outcome measures

The performance-based outcome measures recommended by OARSI are the 30 s chair stand test, 40 m fast-paced walk test, stair-climb test, timed up-and-go test, and 6-min walk test (121).

Physical activity

Physical activity can be measured in different ways, using self-reported questionnaires or diaries, direct observation and/or devices such as accelerometers, pedometers, heart rate monitors, or sensors contained in armbands (130). Physical activity is a multidimensional construct and no measure can assess all facets of physical activity (130). The measurement should be selected with a clear concept of the type of data and, in many cases, combining different assessment methods is recommended (131). The self-reported questionnaires are the most commonly used method to measure physical activity (132). In people with knee and/or hip OA, a review that evaluated self-reported physical activity scores in people with OA concluded, "Although many instruments were identified as being potentially suitable for use in people with OA, none demonstrated adequate measurement properties across all domains of reliability, validity, and responsiveness" (133). The National Board of Health and Welfare in Sweden recommends the inclusion of two questions to measure self-reported physical activity, "How much time do you spend, during an ordinary week, on physical activity, e.g. walking, cycling or gardening?" and "How much time do you spend, during an ordinary week, on physical exercise that makes you breathless, such as running, aerobics, or ball sports?" Each question has several possible answers in terms of the minutes spent in physical activity: "no time", "less than 30 min", "30–60 min", "60–90 min", "90–150 min", "150–300 min" and "more than 300 min". Possible answers for physical exercise include: "no time", "less than 30 min", "30–60 min", "60–90 min", "90–120 min" and "more than 120 min. These questions were developed by the National Board of Health and Welfare in Sweden for population-based studies on physical activity and have been validated against accelerometry-based data (134).

An accelerometer is a movement sensor capable of measuring sedentary behavior and light or moderate-to-vigorous physical activity (MVPA). Accelerometers are reliable tools for measuring the acceleration of movement with the ability to estimate the frequency, intensity, and duration of daily physical activity (135-137). Accelerometers remain the most commonly used device to measure physical activity in research settings. Accelerometers have been used as objective measures of physical activity in people with OA (138, 139).

Interpretability of outcome measures

Outcome measures are important in health care, especially because they allow for the quantitative evaluation of the results of interventions. The use of different methods and outcome measure(s). The reason for the quality of different measurements, such as their validity, reliability, and responsiveness to change, may be hard to find (140). Results can be presented as a change between time points and/or absolute mean scores, which can be difficult to interpret clinically. For example, it is not always clear to what extent a change after treatment indicates the success or failure of that treatment. There are different ways to interpret the results of different outcomes.

Effect size

Effect size (ES) is a way of quantifying the size of the difference between two groups or the difference between pre- and post-treatment values (141). ES is calculated as the mean change score for a group divided by the pooled standard deviation (SD) (x–x/pooled SD) in this group (142). ES is frequently used as a measure of the magnitude of the change and responsiveness. Cohen suggested that ES can be categorized as small (0.20 to < 0.50), medium (0.50 to < 0.80), and large (≥ 0.80) (142).

Minimal clinically important difference

The minimal clinically important difference (MCID) is the smallest change in a treatment outcome that a patient would identify as important, and is defined as “the smallest difference in score in the domain of interest which patients perceive as beneficial and which would mandate, in the absence of troublesome side effects and excessive cost, a change in the patient’s management” (3).

There are several techniques to calculate MCID, for example, anchor-based methods and the Delphi method. The anchor-based method compares changes in scores with an "anchor" as a reference. An anchor establishes if the patient is better after treatment compared to baseline according to the patient’s own experience. One anchor method is to ask the patient after treatment: ‘‘Do you feel that the treatment improved your symptoms?’’, answers could vary from a simple yes/no, to ranked options, e.g., "much better", "slightly better", "about the same", "somewhat worse" and "much worse" (143). The differences between those average scale score for who answered "better" and those who answered "about the same" create the benchmark for the anchor method (143). The Delphi method relies on a panel of experts who reach consensus regarding the MCID (144). At present, there is no consensus about how to identify an MCID (145).

Rationale

Patient education combined with exercise is considered first-line treatment based on results of >67 RCTs that included people with knee and/or hip OA (13-16). Worldwide, only 50% of patients with OA are offered health care as recommended by international guidelines (17, 18). In Sweden, a Supported Osteoarthritis Self-Management Program (SOASP), including patient education and exercise is provided by health professionals at more than 500 primary care units. Despite the promising results of RCTs, there is a gap in applying the evidence to clinical practice, and the results of this self-management program, when implemented in real-world settings are not well documented. With this background, a general aim and specific aims of the thesis were developed as described in the following section.

Aims

Overall aim

The overall aim of this thesis was to increase understanding about the results of the SOASP for people with knee and/or hip OA delivered in a real-world setting.

Specific aims

I. To evaluate whether the SOASP would lead to the following changes: 1) decreased pain, 2) improved HRQoL, 3) increased self-efficacy, 4) reduced number of patients taking OA medication, 5) decreased fear of movement, 6) increased level of physical activity, 7) decreased willingness to undergo of surgery and 8) reduced sick leave.

II. To compare the effectiveness of pain reduction after participating in different parts of the SOASP: 1) education only, 2) education + home-based exercise, and 3) education + supervised exercise.

III. To identify individual and disease-related factors at the baseline that are associated with response to the SOASP.

IV. To evaluate whether physical activity level and sedentary time change after treatment within the SOASP.

Methods

Study design

Intervention

All patients included in this thesis have participated in the SOASP (Fig 3.).

Setting and recruitment

The participants were recruited from two different populations. In Studies I-III, data were obtained from the BOA registry between 2008 and 2016. In study IV, patients were recruited through the orthopedic clinic at Sahlgrenska University Hospital in Gothenburg and Skåne University Hospital in Malmö between 2009 and 2014. All patients in Study IV were referred by an orthopedic doctor and all had undergone x-ray before inclusion into the SOASP. Study IV was registered at ClinicalTrials.gov (NCT02022566). An overview of the study design, participants, settings, and inclusion and exclusion criteria in Studies I-IV, and the criteria for data selection in Studies I-III are described in Table 4.

Table 4. Overview of the study design, participants, settings, inclusion and exclusion criteria and data selection in Studies I-IV.

	Study I	Study II	Study III	Study IV
Design	Observational registry-based study	Observational registry-based study	Observational registry-based study	Intervention study with a reference group
Participants	Total n=44 634 Knee OA (n=30 686) Hip OA (n=13 948)	Total n=38 030 Knee OA (n=26 049) Hip OA (n=11 981)	Total n=26 731 Knee OA (n=18 964) Hip OA (n=7767)	Total, n=264 Knee OA (n=152) Hip OA (n=43)
Settings	BOA registry Data from 2008 to 2016	BOA registry Data from 2008 to 2016	BOA registry Data from 2008 to 2016	Sahlgrenska University Hospital Skånes University Hospital, 2009 to 2014
Inclusion criteria	-Symptoms in the knee and/or hip that resulted in contact with the health-care system -Clinical diagnosis of OA	-Symptoms in the knee and/or hip that resulted in contact with the health-care system -Clinical diagnosis of OA	-Symptoms in the knee and/or hip that resulted in contact with the health-care system -Clinical diagnosis of OA	-Symptoms in the knee and/or hip that resulted in contact with the health-care system -Clinical diagnosis of OA -Age between 18-75 years
Exclusion criteria	-Reason other than OA for joint problems (e.g., sequelae of hip fracture, chronic widespread pain; inflammatory joint disease, or cancer) -Total joint replacement within the past 12 months -Other surgery in the knee or hip joint within the past 3 months -Inability to read or understand Swedish	-Reason other than OA for joint problems (e.g., sequelae of hip fracture, chronic widespread pain; inflammatory joint disease, or cancer) -Total joint replacement within the past 12 months -Other surgery in the knee or hip joint within the past 3 months -Inability to read or understand Swedish	-Reason other than OA for joint problems (e.g., sequelae of hip fracture, chronic widespread pain; inflammatory joint disease, or cancer) -Total joint replacement within the past 12 months -Other surgery in the knee or hip joint within the past 3 months -Inability to read or understand Swedish	-Reason other than OA for joint problems (e.g., sequelae of hip fracture, chronic widespread pain; inflammatory joint disease, or cancer) -Total joint replacement within the past 12 months -Other surgery in the knee or hip joint within the past 3 months -Inability to read or understand Swedish
Criteria for data selection	-Index joint (knee/hip) defined by the PT -Participation in the theory part -Data at the 3- or 12-month follow-up -≤ 150 days between the baseline and 3-month follow-up -≤ 450 days between the baseline and 12-month follow	-Index joint (knee/hip) self-reported by the patient -Participation in the theory part -Data at the 3- or 12-month follow-up -≤ 150 days between the baseline and 3-month follow-up -≤ 450 days between the baseline and 12-month follow	-Index joint (knee/hip) defined by the PT -Participation in the theory part -Data at the 3- or 12-month follow-up -≤ 150 days between the baseline and 3-month follow-up -≤ 450 days between the baseline and 12-month follow-up	N/A

Flowchart for Studies I-IV

The flowcharts from Studies I-IV are shown in Figs 5-9.

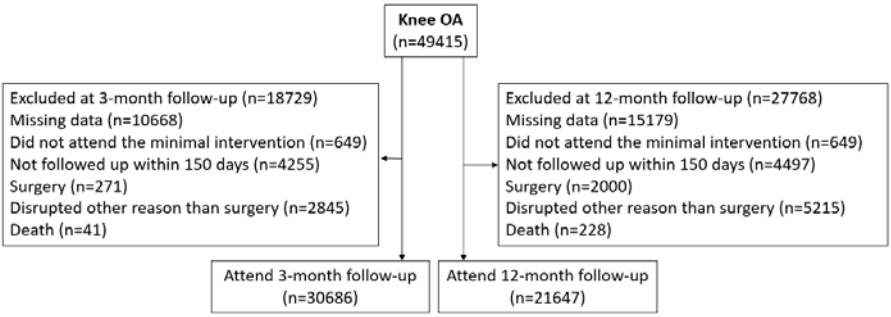

Fig. 5, Flowcharts for patients with knee OA in Study I.

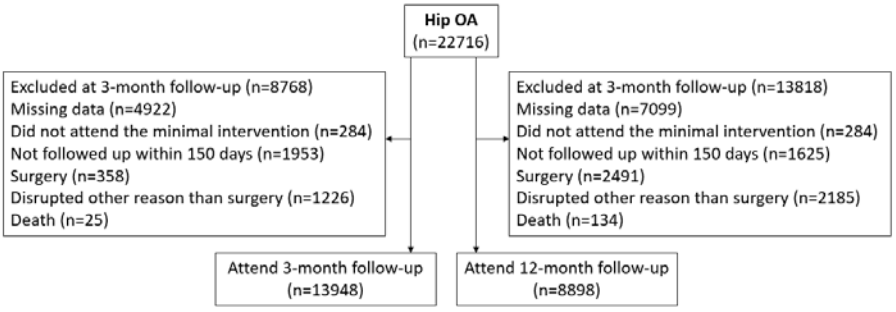

Fig. 6, Flowcharts for patients with hip OA in Study I.

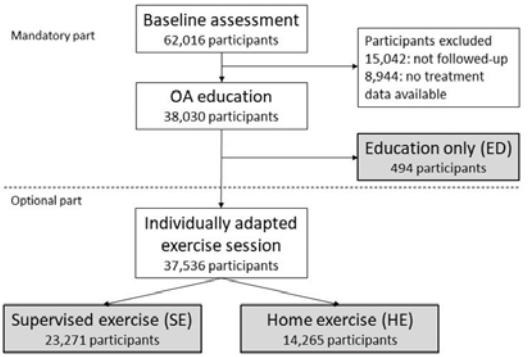

Fig. 7, Flowchart for Study II.

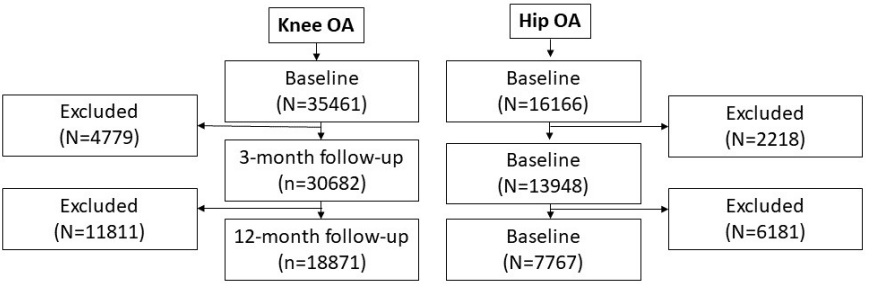

Fig. 8, Flowchart for Study III.

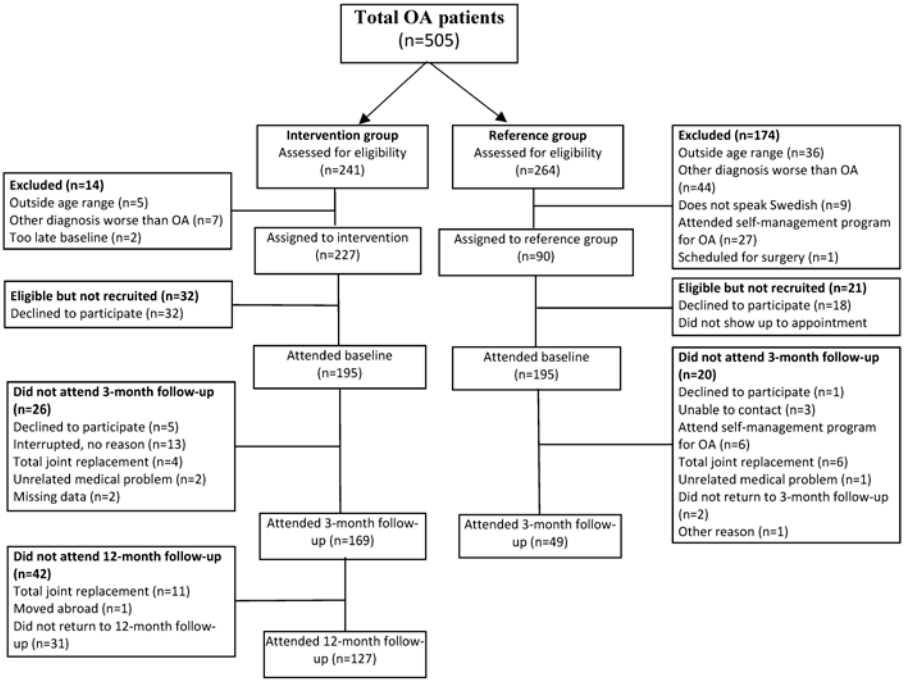

Fig. 9, Flowchart for Study IV.

Assessments and outcome measures

All baseline characteristics (Table 2), patient-reported outcomes (Table 2), and PT-reported outcomes (Table 3) in Studies I-IV were obtained from the questionnaires included in the BOA registry.

The patient-reported outcomes were assessed at the baseline and the 3-month follow-up during a visit with the PT. The treating PT entered the data into the registry. At the 12-month follow-up, the questionnaire was sent by mail through the BOA registry to patients with a prepaid envelope for them to return the completed questionnaire.

Outcome measures

All outcome measures used in Studies I-IV are described in Table 5.

Table 5. Overview of outcome measures used in Study I-IV.

Outcome measures	Study I	Study II	Study III	Study IV
Accelerometer GTM1				X
ASES/other symptoms	X			X
ASES/pain	X			X
Charnley Score	X	X	X	X
EQ-5D-3L				X
EQ-5D-5L	X			
EQ-5D- VAS			X	
Fear of movement	X			
Intake of OA medication	X			
Numeric rating scale (NRS)	X	X	X	
Pain frequency	X		X	
Self-reported physical activity	X			
Sick leave	X			
Visual analogue scales (VAS)				X
Willingness to undergo surgery	X		X	

ASES=Arthritis Self-efficacy Score, EQ-5D=Euro-Qol five Dimension, Charnley Score categorizes patients into one of three groups: A—one joint with OA (unilateral knee or hip); B—bilateral OA (both knees or both hips); C—OA in multiple joint sites (hip and knee), or presence of any other disease that affects walking ability.

Comorbidity

In Studies I-IV, comorbidity was assessed using the Charnley score, which categorizes people into one of three groups: A, one joint with OA (unilateral knee or hip); B, bilateral OA (both knees or both hips); C, OA in multiple

joint sites (hip and knee), or the presence of any other disease that affects walking ability (146). This score is used to evaluate comorbidity in patients with total hip replacement (146).

Pain intensity

In Studies I-III, the NRS was used to measure the mean pain intensity during the last week in the most affected joint (knee or hip). The NRS is graded from 0 to 10, where 0 represents “no pain” and 10 represents “worst pain possible” (147, 148). The NRS is considered to be a valid way to measure pain intensity (147).

In Study IV, the VAS was used to measure the mean pain intensity during the last month in the most affected joint (knee or hip). The VAS is graded from 0 to 100, where 0 represents “no pain” and 100 represents “worst pain possible.” The VAS is well established in clinical practice and research for measuring pain intensity in populations with OA and is considered to be a valid way to measure pain intensity (147, 149).

In the BOA registry, pain rated on the VAS was used to measure pain intensity between 2008 and 2016 and was then replaced with the NRS for pain. All data in the BOA registry have been transferred from the VAS to NRS pain.

Pain frequency

Pain frequency was assessed with one question from the KOOS score: “How often do you have pain in your knee/hip”. There were five possible answers: never, every month, every week, every day, or all the time. The KOOS score has been shown to have sufficient reliability, validity, and responsiveness to surgery and physical therapy after reconstruction of the anterior cruciate ligament (125).

In Study I, this question was dichotomized into, frequent pain (every day, or all the time) and rare pain (never, every month, or every week) to obtain an overview of the number of patients whose pain frequency changed from daily to weekly or less often.

In Study III, the answers to this question were classified into four groups (all the time, every day, every week, and every month or never), because of the

low numbers in the categories never and every month, which were merged into one group.

OA medication

In Study I, intake of OA medication was evaluated by the PT, who asked the patients whether they had taken any OA medication, including painkillers, during the past 3 months because of their knee/hip pain. The possible answers were “yes” or “no”.

Physical activity

In Study I, physical activity was self-reported using one out of two questions recommended by the National Board of Health and Welfare in Sweden. “How much time do you spend, during an ordinary week, on physical activity, e.g. walking, cycling or gardening?”. The possible answers for minutes spent in physical activity were “no time”, “less than 30 min”, “30–60 min”, “60–90 min”, “90–150 min”, “150–300 min” and “more than 300 min”.

In Study IV, physical activity and sedentary time were measured using a GT1M actigraphy accelerometer (ActiGraph, Pensacola, FL), a small uniaxial accelerometer that measures vertical acceleration and deceleration (137). The validity and reliability of ActiGraph accelerometers have been established in different populations, including people with OA (135, 136, 150, 151).

Participants also maintained a daily activity log to record the time spent in aquatic and cycling activities, which may not be fully captured by an accelerometer. Oral and written instructions were given to the participants to wear the accelerometer on a belt at the natural waistline, on the right hip, and aligned with the right axilla, and to wear it continuously (except for aquatic activities) from morning until bedtime for seven consecutive days (Fig. 10).

The accelerometer was set to collect data using a 10 s epoch (time frame). After data collection, data were treated according to the following procedures, which are similar to a previous accelerometer study of a Swedish population (51). For a day to be considered valid, the wear time had to exceed 600 min/day after periods of >20 min of consecutive epochs with 0 counts had been removed. Only patients with 4 days of valid monitoring were included in the subsequent analysis.

To calculate the duration of physical activity at different intensities, the commonly used cut-point of <100 counts/min (152) was used for sedentary behavior. The cut-points developed by Freedson et al. (153) were used for physical activity: 100–1951 counts/min for light physical activity, 1952–5723 counts/min for moderate physical activity, and 5724 counts/min for vigorous physical activity. The sum of all epochs with 1952 counts/min was defined as moderate to vigorous physical activity (MVPA).

Fig. 10. An accelerometer on a belt on the right hip.

Health-related quality of life

The EuroQol (EQ-5D) is a generic measure of HRQoL. Using this instrument, patients classify their health status into five dimensions (5D): mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (154). In EQ-5D-3L each dimension has three levels of answer: no problems, moderate problems and severe problems (154). The EQ-5D-3L has been validated in a population with chronic pain (129).

The EQ-5D-5L was developed from the EQ-5D-3L. The EQ-5D-5L has five instead of three levels for each dimension: no problems, minimal problems, some problems, many problems, and extreme problems (155). Results from the initial testing of EQ-5D-5L showed greater reliability, sensitivity, and feasibility compared with the EQ-5D-3L (156-158).

The results of both the EQ-5D-3L and EQ-5D-5L may be presented as a health profile or as a global health index. In the BOA registry, the UK tariff is used and the global health index is given a value between -0.594 and 1.0

where 1 corresponds to full health, and lower EQ-5D values reflect poorer HRQoL (154). All data in the BOA registry have been replaced with EQ-5D-5L values. This has been done using the UK cross-walk index (159).

In Study I, the EQ-5D-5L global health index was used. In Study III the global health profile, EQ-5D-VAS, was used. In Study IV the EQ-5D-3L global health index was used.

Self-efficacy

In Study I, and IV, self-efficacy was assessed using the Arthritis Self-Efficacy Scale (ASES), which is designed to measure confidence in one's own ability to manage chronic arthritis. This instrument comprises 20 statements, that are divided into three subscales: pain, function, and other symptoms. Each item is scored on a 10-point Likert scale from 10 (very uncertain) to 100 (very certain) (160). The subscales for pain and other symptoms are included in the BOA registry. The ASES has been used previously to evaluate self-management programs for patients with arthritis (160, 161). The Swedish version has been shown to be valid (162).

Fear of movement

In Study I, fear of movement was assessed by the question, "Are you afraid your joints will be injured by physical training/activity?" (Yes/No). To my knowledge, this question has not been validated.

Willingness to undergo surgery

In Study I and III, the patients' willingness to undergo surgery was assessed using the question: "Are your knee/hip symptoms so severe that you wish to undergo surgery?" (Yes/No).

In Study I the reduction in willingness to undergo surgery was calculated for patients being willing to undergo surgery at baseline.

Walking difficulties

In Study III, walking difficulties was assessed using the question: “Do you have walking difficulties caused by your OA?” (Yes/No).

Sick leave

In Study I, sick leave was assessed using the question, “What does your work situation look like today? Tick the option that best suits your situation.” There were five possible answers: 1) working or in full-time study; 2) on full-time sick leave; 3) on part-time sick leave (defined as being on sick leave for part of the work time, but not full time); 4) retired; and 5) unemployed. In Study I, the answers to this question were dichotomized into full- or part-time sick leave (Yes/No).

Statistical methods

In Studies I-IV, descriptive statistics are presented as the mean and standard deviation (SD) or median and interquartile range (IQR). The level of significance was set at $p < 0.05$. An overview of the statistical methods is described in Table 6.

Table 6. Overview of the statistical methods used in Study I-IV.

Statistical methods	Study I	Study II	Study III	Study IV
Chi-squared tests				X
Effect Size	X			
GLM ANOVA				X
GLMs repeated measures	X			
Logistic regression			X	
Mann-Whitney U-test				X
McNemar’s test	X			
Mean (SD)	X	X	X	X
Mean (CI)	X	X		
Median (IQR)				X
Mixed effects model		X		
Odds Ratios (CI)			X	
Wilcoxon Signed-Rank test				X
GLM=General linear model, SD=Standard Devition, CI=Confidence interval,IQR=Interquartile Range				

Study I

In Study I, the changes in scale variables (NRS-pain, EQ-5D-3L, ASES-other symptoms, and ASES-pain) between the baseline and 3 months, and between the baseline and 12 months were analyzed using general linear models (GLMs) with repeated measures. The results are presented as means with 95% confidence intervals (CIs). The standardized ESs for scale variables were presented as Cohen's d: (x–x/Saverage). ESs were categorized as small ($d \approx 0.20$ to $d < 0.50$), medium ($d \geq 0.50$ to $d < 0.80$), and large ($d \geq 0.80$) (142). Changes in binary variables (pain frequency, intake of OA medication, willingness to undergo surgery, fear of movement, physical activity, and sick leave) were analyzed using McNemar's test.

Study II

In Study II, a random coefficient model was fitted to the data, which included a random intercept term and a fixed slope term for the participants and fixed intercept and slope terms for follow-up time (baseline, 3 months and 12 months), joint (hip or knee) and treatment (education only, education + home-based exercise, education + supervised exercise). The covariance structure was set to first-order autoregressive. Treatment*time and a joint*time interaction terms were assessed in two separate models to identify possible differences in pain reduction at the follow-ups between participants undergoing the different treatments offered in SOASP and between participants with knee or hip OA. Potential confounders were selected based on theoretically driven direct and shared pathways involving the exposure (treatment) and the outcome (pain) (163). The models included adjustments for differences in age, sex, BMI, affected joint (hip or knee), pain at baseline, Charnley score, and education level.

Follow-up analysis was used to compare the CIs of the estimated means to evaluate the clinical significance of group differences. The results are presented as absolute values and percentages; negative values indicate a reduction in pain intensity on the NRS scale from the baseline to the follow-up. Finally, a sensitivity analysis including only participants who attended ≥ 10 supervised sessions (>80% of the program) was performed to estimate the influence of treatment adherence on the outcome of supervised exercise.

In Study II, a relative reduction of 15% on the NRS scale was used to identify an MCID. This cut-off was previously validated against the patients' global

impression of change categories in a sample of people with OA and other chronic rheumatic conditions, and was found to indicate that the participants felt “slightly better” after the intervention (164). A relative change in the reduction of pain was used because it is a more stable indicator of MCID than the absolute change, which is influenced more by the baseline values (165).

Study III

Logistic regression models were applied to examine the odds of being a responder at the 3- and/or 12-month follow-up according to the individual and disease factors. The results are present as odds ratios (ORs) and 95% CIs from both crude and adjusted models. Covariates were included in the model according to manual stepwise backward deletion. A threshold of $p \leq 0.2$ was used when excluding covariates. All analyses were stratified by the most affected joint (knee/hip).

Responders

A responder was defined as a person who showed a decrease of >15% (“slightly better”) or >33% (“much better”) on the NRS for pain (164). These cutoffs have been previously validated in a sample of people with OA and/or other chronic rheumatic conditions (164). The decrease in NRS-pain was calculated between the baseline and 3-month and between the baseline and 12-month follow-up.

Individual factors

The independent variables included individual factors such as sex and age categorized into three groups: working age (18-64 years), younger retirees (65-74 years), and older retirees (≥75 years). BMI was classified according to the WHO criteria into underweight (<18.5 kg/m^2), normal weight (18.5–24 kg/m^2), overweight (≥25 kg/m^2) and obese (≥30 kg/m^2) (166). Because of low numbers in the underweight category, underweight and normal-weight participants were merged into one category. Educational level was classified into three groups: compulsory school, high school, and university. The Charnley classification is a comorbidity score and categorizes people into one of three groups: A –, one joint with OA (unilateral knee or hip); B – bilateral OA (both knees or both hips); and C – OA in multiple joint sites (hip and knee) or presence of any other disease that affects walking ability (146).

Previous surgery to the most affected joint was recorded by the PT at the baseline.

Disease factors

Pain frequency was assessed by the question: “How often do you have pain in your knee/hip,” with five possible answers: never, every month, every week, every day or all the time. Because of low numbers in the categories never and every month, these two were merged into one category. Walking disability was assessed by the question: “Do you have a walking disability caused of your OA” (Yes/No). Willingness to undergo surgery was assessed by the question: “Are your knee/hip symptoms so severe that you wish to undergo surgery?” (Yes/No).

Covariates

The covariates HRQoL (EQ-5D VAS), NRS-pain at the baseline, and previous surgery to the most affected joint, were included as potential confounders in the analyses. HRQoL was measured using the EuroQol five dimensions VAS (EQ-5D VAS 0–100) (154). The EQ-5D VAS was used to adjust for baseline mental status, as recommended by the ICHOM for people with hip and knee OA (122). The answer to the question about previous surgery was used to adjust for worst symptoms after surgery because previous surgery is associated with worse symptoms over the long term in people with knee OA (167).

Study IV

In the comparison between the intervention group and the reference group, the differences in outcome variables between the baseline and 3-month follow-up were the dependent variables. A histogram of the differences in scores was analyzed visually to determine whether there was a normal distribution and was judged as approximately normal. Hence, a GLM univariate analysis of variance was used to compare the intervention and reference groups. In the various models developed, the dependent variables were the computed difference between the baseline and 3-month follow-up for time (mins) spent in sedentary behavior, low-intensity physical activity, and MVPA, VAS for pain, EQ-5D, ASES for pain, and ASES for other symptoms. The primary outcomes were the changes from the baseline to the 3-month follow-up in sedentary time and in low and MVPA time.

The fixed factors were, group (intervention/reference), sex, education level, affected joint (knee/hip) and Charnley score. The covariates were age and baseline values for the dependent variable in each model. The final selection of covariates to be included in the model was performed using a stepwise backward deletion approach, in which the least significant variable was removed from the model until only covariates with significant ($p<0.2$) effects remained in the model. The changes over time within each group, (baseline to 3-month follow-up, and, for the intervention group, baseline to 12-month follow-up) were analyzed using the Wilcoxon signed-rank test because the data were not normally distributed. The results are presented as median with IQR. A dropout analysis was performed and included the variables sex, age, BMI, Charnley score, affected joint (knee/hip), educational level, minutes in sedentary behavior, minutes in low-intensity physical activity, minutes in MVPA, VAS-pain, EQ-5D, ASES-other or ASES-pain. Chi-squared tests were used for the dropout analyses of sex, Charnley score, affected joint (knee/hip), and educational level. The Mann-Whitney U tests was used for dropout analyses of other variables including age, physical activity, VAS-pain, EQ-5D, and the ASES subscales.

Sample size

In Study IV, the power calculation was based on a previous study that used accelerometry to measure physical activity level in patients with a light to moderate grade of OA (150). To detect a between-group difference of 10 ± 17 min with a 5% probability of making a type I error and 20% probability of making a type II error, 50 participants in each group were needed. To accommodate a potential dropout rate of 20%, we aimed to recruit 120 patients. However, during the study, we observed that the actual dropout rate reached 30%. To compensate for the higher-than-expected dropout rate, we included 195 patients in the intervention group.

Ethics

Ethical approval

Studies I-III was approved by the Regional Ethical Review Board in Gothenburg (1059-16). All patients received oral or written information about their registration in the BOA registry.

Study IV was approved by the Regional Ethical Review Board in Gothenburg (747-08). All patients received oral and written information about the study and provided their written informed consent before inclusion.

Ethical consideration

In studies I-III, which included data from the BOA registry, all data were processed using the encrypted unique personal identification number without access to the patients' personal information (such as name, residential address, or unique personal identification number). All results were presented at the aggregated level which prevented any individual patient from being identified.

In Study IV, the patients who were eligible for inclusion in the study were asked about their willingness to participate and be treated by the PT. This may have meant that some participants may have felt pressured to participate to satisfy their treating PT. To minimize this risk, all patients were informed that participation was entirely voluntarily.

In Study IV, the reference group was on the waiting list to visit an orthopedic doctor because of their knee and hip symptoms. A PT phoned them and asked about their interest in having their physical activity level measured. Those who were interested received one visit to a PT at the orthopedic clinic. They were told that their access to the planned visit would not be influenced by

their decision to participate or not to participate in the study. However, some patients may have felt that not participation would affect their ability to receive an appointment with the doctor at the orthopedic clinic.

Results

The general results of Studies I-IV are presented in this part of the thesis. The full details are available in separate studies at the end of the thesis.

Participants in Studies I-IV

Baseline characteristics of included patients and adherence to different parts of the SOASP in Studies I-IV are described in table 7.

Table 7. Baseline characteristics of included patients in Study I-IV, including adherence to different parts of the SOASP.

	Study I		Study II	Study III		Study IV	
Variable	Knee OA (n=30686)	Hip OA (n=13948)	Knee and hip OA (n=30030)	Knee OA (n=18964)	Hip OA (n=7767)	Intervention group (n=195)	Reference group (n=69)
Women, %	70	69	69	70	70	64	58
Age, mean (± SD) ,years	66 (9)	67 (9)	66 (9)	66 (9)	67 (9)	60 (10)	66 (7)
BMI, mean (± SD)	28 (5)	27 (4)	28 (5)	28 (5)	27 (4)	28 (5)	28 (5)
Charnley Score*							
A, %	38	38	39	39	38	29	35
B, %	23	10	17	24	11	41	33
C, %	39	52	44	37	51	30	32
Education level							
Elementary school, %	34	35	34	34	35	24	35
High school, %	37	36	37	37	35	40	36
University, %	29	29	29	29	30	36	29
Adherence to different parts of the SOASP							
Theory part %	100		100	100		100	
Face-to face exercise %	86		99	87		98	
HE, %	41		38	42		37	
SE, %	59		62	58		63	
1-6 times in SE, %	12		19	16		28	
7-9 times in SE, %	17		12	12		16	
10-12 times in SE, %	30		31	30		19	

BMI=Body Mass Index, HE= Home exercise, SE=Supervised Exercise, *Charnley Score categorizes patients into one of three groups: A—one joint with OA (unilateral knee or hip); B—bilateral OA (both knees or both hips); C—OA in multiple joint sites (hip and knee), or presence of any other disease that affects walking ability

Study I

Between the baseline and the 3-month follow-up, patients with knee and/or hip OA showed significant improvements in scores for NRS-pain, EQ-5D index, ASES-other symptoms, and ASES-pain (Table 8). Standardized ES was 0.25 to 0.57 for patients with knee OA and 0.15 to 0.39 for those with hip OA (Table 8). Significantly fewer patients with knee and hip OA reported daily pain, took OA medication, reported willingness to undergo surgery, reported fear of movement, and were physically inactive (Table 9).

Between the baseline and the 12-month follow-up, patients with knee and/or hip OA exhibited significant improvements in NRS-pain and the EQ-5D index, and significant decreases in ASES-other symptoms and ASES-pain scores. Standardized ES was -0.04 to 0.43 for patients with knee OA and -0.18 to 0.22 for those with hip OA (Table 10). Significantly fewer patients reported daily pain, reported willingness to undergo surgery (only for hip OA), reported fear of movement, and were on sick leave (Table 11).

Table 8. Mean (SD) differences in NRS-pain, EQ-5D index, ASES-pain, and ASES-other symptoms, between baseline and the 3-month follow-up.

Knee OA					
Outcome	n	Baseline mean (SD)	3 months mean (SD)	Mean difference [95% CI]	Cohen´s d
NRS/pain	30,501	5.24 (1.96)	4.07 (2.17)	1.18 [1.15–1.20]	0.57
EQ-5D-index	29,865	0.636 (0.220)	0.702 (0.197)	0.065 [0.063–0.068]	0.31
ASES-O	27,290	68.1 (16.8)	72.2 (17.0)	4.1 [3.9–4.3]	0.24
ASES-P	27,575	64.2 (18.6)	68.9 (19.5)	4.7 [4.5–4.9]	0.25
Hip OA					
NRS/pain	13,864	5.39 (1.93)	4.57 (2.21)	0.82 [0.79 – 0.85]	0.39
EQ-5D-index	13,570	0.611 (0.232)	0.654 (0.225)	0.043 [0.040–0.047]	0.19
ASES-O	12,339	66.0 (17.0)	68.6 (17.8)	2.6 [2.4–2.9]	0.15
ASES-P	12,477	60.5 (18.8)	63.5 (20.6)	3,1 [2.7–3.4]	0.16

CI=Confidence Intervall, SD= Standard Deviation, NRS=Numeric Rating Scale, EQ-5D=Euro-Qol five dimensions, ASES=Arthritis Self-Efficacy Scale. Standardized Effect Size (ESs) were present as Cohen´s d: (x-x/Pooled SD). ES were considered as small (d=0.2), medium (d=0.5), and large (d=0.8).

Table 9. Percentage changes in patients taking OA-medication, pain frequency, exhibiting fear of movement, willingness to undergo surgery, and physical activity between baseline and 3-month follow-up.

	Knee OA				**Hip OA**			
		Baseline	**3-month**			**Baseline**	**3-month**	
Outcome	n	Yes (%)	Yes (%)	P	n	Yes (%)	Yes (%)	P
Intake of OA medication	30,392	75	55	<0.001	13,811	77	62	<0.001
Pain frequency*	30,017	82	60	<0.001	13,720	85	67	<0.001
Fear of movement	30,358	17	4	<0.001	13,794	15	3	<0.001
Willingness to undergo surgery	29,739	23	12	<0.001	13,580	29	19	<0.001
Physical inactivity**	25,419	60	39	<0.001	11,725	59	39	0.041

OA=Osteoarthritis, *Daily pain or all the time, **Physically active < 150 min/week, the significance level was set at P<0.05.

Table 10. Mean (SD) differences in NRS-pain, EQ-5D index, ASES-pain, and ASES-other symptoms, between the baseline and the 12-month follow-up.

Outcome	*n*	Baseline mean (SD)	12 months mean (SD)	Mean difference [95% CI]	Cohen´s d
Knee OA					
NRS/pain	*21,283*	5.15 (1.94)	4.23 (2.32)	0.92 [0.89–0.95]	0.43
EQ-5D-index	*20,571*	0.653 (0.207)	0.692 (0.198)	0.039 [0.036–0.042]	0.19
ASES-O	*15,447*	68.9 (16.3)	68.2 (18.3)	–0.75 [–1 to –0.5]	-0.04
ASES-P	*15,619*	65.1 (18.2)	64.2 (20.6)	–0.9 [–1.2 to –0.62]	-0.04
Hip OA					
NRS/pain	*8,736*	5.16 (1.92)	4.7 (2.3)	0.46 [0.42–0.51]	0.22
EQ-5D-index	*8,448*	0.642 (0.211)	0.650 (0.218)	0.009 [0.004–0.014]	0.04
ASES-O	*6,221*	67.7 (16.4)	64.9 (18.8)	– 2.8 [–3.2 to –2.4]	-0.16
ASES-P	*6,283*	62.3 (18.2)	58.7 (21.2)	–3.6 [–4.1 to –3.1]	-0.18

CI=confidence interval, SD= Standard deviation, NRS=Numeric Rating Scale, EQ-5D=Euro-Qol five dimensions, ASES-O=Arthritis Self-efficacy Scale Other symptoms, ASES-P=Arthritis Self-efficacy Scale Pain. Standardized effect size (ESs) were present as Cohen´s d: (x-x/Pooled SD). ES were considered as small (d=0.2), medium (d=0.5) and large (d=0.8).

Table 11. Percentage changes in patients taking OA-medication, pain frequency, exhibiting fear of movement, willingness to undergo surgery, and physical activity between the baseline and the 12-month follow-up.

	Knee OA				**Hip OA**			
	Baseline		**12-month**		**Baseline**		**12-month**	
Outcome	n	Yes (%)	Yes (%)	P	n	Yes (%)	Yes (%)	P
Pain frequency*	*21,181*	81	56	<0.001	8,703	81	62	<0.001
Fear of movement	21,186	16	4	<0.001	8,713	13	3	<0.001
Willingness to undergo surgery	20,992	19	10	0.962	8,616	20	12	<0.001
Physical inactivity**	17,328	58	39	0.902	7,279	59	39	0.531
Sick leave	7,309	14	5	<0.001	2,646	12	5	0.017

OA=Osteoarthritis, *Daily pain or pain all the time, **Physically inactive < 150 min/week.
The significance level was set at P<0.05.

Study II

Patients with knee and/or hip OA exhibited significant pain reduction at both the 3-and 12-month follow-up (Table 12). However, the reduction was clinically significant only at the 3-month follow-up, –19% [95% CI –21 to –18%] but not at the 12-month follow-up, –14% [95% CI –17 to –12]. Patients who participated in only eduction improved less at both follow-ups when compared to patients who participated in the home-based or supervised exercise. Even though this difference was not clinically significant, only patients participating in the home-based or supervised exercise had a reduction in the pain intensity that approached clinical significance at 12 months (pain reduction for both home-based and supervised exercise – 15 % [95% CI –16 to –14].

Both patients with knee and hip OA showed a statistically significant improvement at the 3-month and 12-month follow-up (Table 12). However, only patients with knee OA reached a clinically significant pain reduction at both follow-ups (at 3-month follow-up, –23% [95% CI –23 to –22], at the 12-month follow-up, –18% [95% CI –18 to –17].

In a secondary analysis stratified by joint, we did not find any statistical and clinically significant difference in pain intensity in patients with hip OA participating in the different treatment options at either follow-up (Table 12). In contrast, patients with knee OA participating in home-based or supervised exercise showed a clinically significant reduction in the pain intensity at the 3-month follow-up, –23% [95% CI –24 to –21], which was maintained at the 12-month follow-up –18% [95% CI –19 to –17].

Table 12. Differences in pain intensity (NRS 0-10), between the baseline and the 3- and 12-month follow-up stratified by affected joint and treatment group.

Pain intensity (NRS 0-10), Knee OA + Hip OA*			
	Baseline mean [95 % CI]	The difference mean [95% CI] 3 months	The difference mean [95% CI] 12 months
All participants	5.39 [5.32 to 5.46]	-1.03 [-1.11 to -0.95]	-0.74 [-0.84 to -0.64]
Only education	5.50 [5.30 to 5.69]	-0.91 [-1.15 to -0.68]	-0.58 [-0.87 to -0.30]
Education + HE	5.32 [5.29 to 5.36]	-1.06 [-1.10 to -1.01]	-0.82 [-0.87 to -0.76]
Education + SE	5.35 [5.32 to 5.38]	-1.12 [-1.15 to -1.08]	-0.82 [-0.86 to -0.77]
Pain intensity (NRS 0-10), Knee OA**			
All participants	5.34 [5.28 to 5.40]	-1.21 [-1.24 to -1.17]	-0.95 [-0.99 to -0.91]
Only education	5.34 [5.11 to 5.58]	-0.95 [-1.25 to -0.66]	-0.62 [-0.98 to -0.26]
Education + HE	5.22 [5.18 to 5.27]	-1.18 [-1.23 to -1.12]	-0.97 [-1.03 to -0.90]
Education + SE	5.27 [5.23 to 5.30]	-1.23 [-1.27 to -1.19]	-0.95 [-1.00 to -0.90]
Pain intensity (NRS 0-10), Hip OA**			
All participants	5.43 [5.37 to 5.50]	-0.85 [-0.89 to -0.80]	-0.50 [-0.56 to -0.44]
Only education	5.63 [5.30 to 5.96]	-0.84 [-1.25 to -0.43]	-0.50 [-1.00 to -0.20]
Education + HE	5.36 [5.29 to 5.42]	-0.82 [-0.90 to -0.74]	-0.48 [-0.57 to -0.38]
Education + SE	5.33 [5.28 to 5.39]	-0.86 [-0.92 to -0.80]	-0.51 [-0.59 to -0.44]

*The analysis is adjusted for baseline pain, Body Mass Index (BMI), age, sex, level of education, comorbidities, affected joint.
**The analysis is adjusted for baseline pain, Body Mass Index (BMI), age, sex, level of education, comorbidities.
NRS=Numeric rating scale for pain, CI=confidence intervals.HE=Home-based exercise, SE=Supervised Exercise

Study III

Similar factors were found to be associated with the odds of responding both as slightly and much better. Therefore is only factors associated with respond with much better presented here, for complete data, see paper III at the end of the thesis.

In patients with knee OA, both the crude and adjusted models showed that higher education, lower BMI and younger age were individual factors associated with responding to the treatment at both follow-ups. The disease factors associated with being a responder in patients with knee OA were less pain frequency, unilateral OA, being unwilling to undergo surgery and not having walking difficulties (only at the 12-month follow-up) at both follow-ups (Table 13).In patients with hip OA, both the crude and adjusted models showed that lower BMI was an individual factor associated with responding to the treatment. The disease factors associated with being a responder in patients with hip OA were less pain frequency, being unwilling to undergo surgery, unilateral OA and not having walking difficulties (Table 14).

Table 13: Individual and disease-related factors associated with a reduction in pain with 33 % at the 3- and 12-month follow-up after treatment with SOASP in patients with knee OA.

Knee OA*						
	Pain reduction with 33 % at the 3-month follow-up			Pain reduction with 33 % at the 12-month follow-up		
Independent factors	n	Crude OR [95% CI]	Adjusted OR [95% CI]	n	Crude OR [95% CI]	Adjusted OR [95% CI]
Pain frequency						
Less than every month	981	**1.42 [1.25-1.62]**	**2.18 [1.8-2.6]**	968	**1.69 [1.48-1.94]**	**2.12 [1.78-2.54]**
Every week	1914	**1.47 [1.32-1.63]**	**1.9 [1.7-2.18]**	1893	**1.64 [1.47-1.83]**	**1.82 [1.58-2.09]**
Every day	9198	**1.37 [1.26-1.48]**	**1.46 [1.33-1.61]**	9127	**1.41 [1.3-1.53]**	**1.42 [1.29-1.58]**
All the time	2523	1	1	2504	1	1
Charnley Score						
A	5934	**1.63 [1.52-1.74]**	**1.62 [1.5-1.76]**	5878	**2.03 [1.9-2.17]**	**1.96 [1.8-2.1]**
B	3069	**1.19 [1.1-1.28]**	**1.14 [1.04-1.26]**	3045	**1.26 [1.16-1.37]**	**1.2 [1.08-1.3]**
C	5613	1	1	5569	1	1
Willingness of surgery						
No	1152	**1.38 [1.3-1.48]**	**1.6 [1.4-1.7]**	12125	**1.64 [1.5-1.77]**	**1.7 [1.54-1.88]**
Yes	2781	1	1	2367	1	1
Education						
Compulsory school	4775	1	1	4721	1	1
High school	5473	**1.08 [1.01-1.16]**	1.05 [0.97-1.15]	5426	**1.19 [1.11-1.28]**	**1.16 [1.07-1.27]**
University	4369	**1.24 [1.15-1.33]**	**1.2 [1.11-1.32]**	4345	**1.5 [1.4-1.62]**	**1.45 [1.33-1.59]**
Body Mass Index						
< 25	3859	**1.29 [1.2-1.4]**	**1.28 [1.17-1.41]**	3822	**1.52 [1.41-1.65]**	**1.38 [1.25-1.52]**
≥ 25-30	6417	**1.18 [1.1-1.26]**	**1.13 [1.04-1.23]**	6361	**1.28 [1.19-1.38]**	**1.23 [1.13-1.34]**
≥ 30	4340	1	1	4309	1	1
Age						
18-64	5471	**1.19 [1.1-1.3]**	**1.18 [1.06-1.3]**	5436	**1.27 [1.17-1.39]**	**1.24 [1.11-1.37]**
65-74	6441	**1.2 [1.1-1.3]**	**1.16 [1.05-1.23]**	6375	**1.28 [1.18-1.39]**	**1.21 [1.09-1.33]**
≥ 75	2704	1	1		1	1
Walking difficulties						
No	3208	1.03 [0.96-1.1]	1.0 [0.92-1.1]	3177	**1.23 [1.14-1.3]**	**1.14 [1.04-1.25]**
Yes	1140	1	1	11315	1	1

*The adjusted analysis is adjusted for sex, age, Body Mass Index (BMI), level of education, comorbidities, pain frequency, walking difficulties, the willingness of surgery, baseline pain, Euro-QoL analog scale (EQ-5D-VAS) and previous surgery to the most affected joint. *Charnley Score categorizes patients into one of three groups: A—one joint with OA (unilateral knee or hip); B—bilateral OA (both knees or both hips); C—OA in multiple joint sites (hip and knee), or presence of any other disease that affects walking ability Bold text is a significant difference ($p<0.05$)

Table 14: Individual and disease-related factors associating with a reduction in pain with 33 % at the 3- and 12-month follow-up after treatment with SOASP in patients with hip OA.

Hip OA*						
Independent factors	Pain reduction with 33 % 3-month follow-up			Pain reduction with 33 % 12-months follow-up		
	n	Crude OR [95% CI]	Adjusted OR [95% CI]	*n*	Crude OR [95% CI]	Adjusted OR [95% CI]
Pain frequency						
Less than every month	343	**1.55 [1.23-1.94]**	**2.39 [1.76-3.1]**	338	**1.53 [1.2-1.96]**	**2.2 [1.63-2.98]**
Every week	828	**1.43 [1.21-1.7]**	**1.72 [1.39-2.13]**	823	**1.71 [1.43-2.05]**	**1.9 [1.51-2.39]**
Every day	3902	**1.29 [1.14-1.47]**	**1.39 [1.19-1.62]**	3873	**1.43 [1.24-1.64]**	**1.46 [1.23-1.73]**
All the time	1037	1	1	1019	1	1
Willingness of surgery						
No	4880	**1.5 [1.34-1.71]**	**1.75 [1.5-2.04]**	4842	**1.69 [1.48-1.93]**	**1.86 [1.57-2.2]**
Yes	1230	1	1	1213	1	1
Body Mass Index						
< 25	2255	**1.19 [1.05-1.36]**	1.11 [0.96-1.29]	2236	**1.65 [1.43-1.9]**	**1.5 [1.28-1.78]**
≥ 25-30	2578	**1.14 [1.01-1.3]**	1.06 [0.92-1.23]	2555	**1.43 [1.24-1.65]**	**1.35 [1.15-1.58]**
≥ 30	1277	1	1	1264	1	1
Charnley score						
A	2244	**1.22 [1.1-1.35]**	**1.23 [1.1-1.39]**	2219	**1.48 [1.33-1.65]**	**1.44 [1.27-1.63]**
B	529	**1.19 [1.03-1.39]**	**1.24 [1.02-1.5]**	527	**1.39 [1.19-1.63]**	**1.29 [1.23-1.32]**
C	3337	1	1	3309	1	1
Walking difficulties						
No	1339	**1.14 [1.02-1.27]**	**1.11 [0.97-1.28]**	1331	**1.38 [1.23-1.55]**	**1.32 [1.15-1.53]**
Yes	4771	1	1	4724	1	1

*The adjusted analysis is adjusted for sex, age, Body Mass Index (BMI), level of education, comorbidities, pain frequency, walking difficulties, the willingness of surgery, baseline pain, Euro-QoL analog scale (EQ-5D-VAS) and previous surgery to the most affected joint. *Charnley Score categorizes patients into one of three groups: A—one joint with OA (unilateral knee or hip); B—bilateral OA (both knees or both hips); C—OA in multiple joint sites (hip and knee), or presence of any other disease that affects walking ability Bold text is a significant difference ($p<0.05$)

Study IV

The change in minutes spent in sedentary behavior and low-intensity physical activity or MVPA from the baseline to the 3-month follow-up did not differ significantly between the intervention group and the reference group (Table 15).

The within-group analysis showed a significant decrease in the number of minutes of low-intensity physical activity in the intervention group from the baseline to the 3-month follow-up. In the reference group, no significant change in activity level or time in sedentary behavior occurred from the baseline to the 3-month follow-up.

Analysis of the changes in the secondary outcomes (VAS-pain, EQ-5D, ASES-other symptoms, and ASES-pain), showed significantly greater changes in patients in the intervention groups than in the reference group for all outcomes. In the reference group, none of these secondary outcomes changed significantly from the baseline to the 3-month follow-up. Within the intervention group at the 12-month follow-up, there was a significant decrease in minutes of MVPA and significant improvements in VAS-pain, EQ-5D, ASES-other and ASES-pain (Table 16).

Table 15. Differences in mean daily minutes of sedentary behavior, low activity, moderate-vigorous activity, VAS/pain, EQ-5D-index, ASES/pain, and ASES/other symptoms for the intervention group compared to the reference group, from the baseline to the 3-month follow-up, mean difference, 95% confidence interval (CI).

	Intervention group (n=169)	**Reference group (n=49)**	
	mean change [95% CI]	mean change [95% CI]	Mean diff [95% CI]
Minutes in sedentary	-2 [-12, 8]	-11 [-30, 8]	-9 [-31, 12]
Minutes in LPA	-8 [-15, -2]	- 11 [-24, 2]	-3 [-17, 12]
Minutes in MVPA	4 [-0.6, 8]	0.2 [-8, 9]	-4 [-14, 6]
VAS pain (0-100)	-9 [-13, -6]	4 [-2, 9]	**13 [7, 19]**
EQ-5D-index	0.03 [-0.004, 0.07]	-0.14 [-0.19, -0.08]	**-0.17 [-0.24, -0.10]**
ASES-O (10-100)	2 [-0.3, 5]	-3 [-7, 1]	**-5 [-10, -0.3]**
ASES-P (10-100)	5 [2, 8]	-2 [-7, 3]	**-7 [-13, -2]**

All measurements are calculated using linear ANOVA and adjusted for sex, index joint (hip/knee), age, education level, Charnley score and baseline value of outcome measures; only potential confounders with significant (p<0.2) effect were kept in each model.LPA=Low intensity physical activity, MVPA= moderate to vigorous physical activity. ASES-O=Arthritis Self-efficacy Score Other symptoms, ASES-P=Arthritis Self-efficacy Scale Pain, The significance level was set at P<0.05. Bold text is a significant difference.

Table 16. Median (IQR) changes in daily minutes of sedentary behavior, low-intensity physical activity, and MVPA from the baseline to the 3- and 12-month follow-up.

	Intervention group Median (IQR)	**P**	**Reference group Median (IQR)**	**P**
Sedentary				
Baseline	562 (523-605) n=141		572 (505-599) n=52	
3 months	556 (507-602) n=129	*0.538*	556 (504-592) n=33	*0.891*
12 months	552 (499-598) n=110	*0.178*		
Low activity				
Baseline	181 (150-214) n=141		169 (130-218) n=52	
3 months	170 (144-205) n=129	*0.023**	169 (118-220) n=33	*0.072*
12 months	178 (140-228) n=110	*0.633*		
MVPA activity				
Baseline	34 (22-52) n=141		20 (11-30) n=52	
3 months	34 (19-52) n=129	*0.998*	21 (10-37) n=33	*0.820*
12 months	32 (18-52) n=110	*0.026**		

MVP=moderate-vigorous physical activity. Wilcoxon Signed-Rank test was used, and *p*-values were calculated from the baseline to the 3-month follow-up and the baseline to 12-month follow-up. The significance level was set at P<0.05.

General discussion

The overall aim of this thesis was to increase understanding of the SOASP results for patients with knee and/or hip OA delivered in a real-world setting. The main results are discussed below.

Our results in comparison with other studies

The overall results from the SOASP, as implemented in real-world settings, are in line with the results of previous studies.

A Cochrane systematic review that evaluated the effect of exercise in patients with knee OA showed significantly reduced pain and increased HRQoL (61). The effect on pain was sustained for 2-6 months, but the effect on HRQoL was not (61). A similar Cochrane systematic review that evaluated the effect of exercise in patients with hip OA showed significantly reduced pain, but no benefit of exercise was demonstrated for HRQoL (62). Pain reduction was more prominent in patients with knee OA than in patients with hip OA (61, 62). Those results are in line with our results; i.e.; we found better results for patients with knee OA than hip OA and better results in pain reduction than in HRQoL.

A program similar to the SOASP has been implemented in Denmark (GLA:D ®) (118). Results from GLA:D ® showed better outcomes for knee OA patients than hip OA patients, pain reduction both in the short and the long term, increased self-reported physical activity in the short term, fewer patients taking OA medication, and fewer patients on sick leave (118), in line with our results. However, patients in the GLA:D ® experienced greater pain reduction, (knee OA, 29% [95% CI: 27% to 30%], hip OA, 23% [95 % CI: 21% to 26%]) (118) compared with the patients in the SOASP (knee OA; 23% [95% CI, 22% to 23%] , hip OA; 16% [95% CI; 15% to 16%]. There may be different reasons for the difference in results between the SOASP and GLA:D ®. The proportion of patients with knee and/or hip OA in the SOASP is similar to the proportion in GLA:D ®; however, GLA:D ® has younger

patients and a higher number of women, which may affect the results. Another reason may be that most of the units in the GLA:D ® are private and patients pay most of the treatment costs themselves (118), which probably attracts more motivated patients, and subsequently leads to better results. However, the biggest difference in the self-management program between the SOASP and the GLA:D ® is that the exercise part is optional in the SOASP, but mandatory in the GLA:D ®. In the GLA:D ®, 84% of the patients attended at least 10 supervised exercise sessions while only 26% of patients in the SOASP did. A systematic review showed that higher adherence to exercise increases the effects on pain intensity (70) and this is a probable reason for the difference between the SOASP and GLA:D ® outcomes.

In Study I, we found a significant increase in HRQoL both for patients with knee OA and hip OA at the 3- and 12-month follow-up. The increases were small and it is hard to know whether this increase is of clinical importance. In a metanalysis, the MCID for HRQoL has been calculated to be between 0.03 and 0.54 in musculoskeletal disorders (168). Both patients with knee OA and hip OA had improved by more than 0.03 at the 3-month follow-up, but only patients with knee OA showed improvement at this level at the 12-month follow-up. In a study of patients with back and neck problems, an EQ-5D value of 0.6 was classified as a sufficient capacity to work (169). If we assume that 0.6 is a cut-off value for a high EQ-5D, both patients with knee OA (mean EQ-5D, 0.636 [± SD=0.220] and hip OA (mean EQ-5D, 0.611 [± SD=0.232]) showed a high level of HRQoL before starting the SOASP and a potential ceiling effect may be the reason for the limited improvement. Through EQ-5D, we measured the overall HRQoL, including different factors that make sense after a self-management program. However, a high number of people with OA have comorbidities that will affect the HRQoL and despite an improvement in OA-related symptoms, the HRQoL may remain unchanged. To better understand the joint-related QoL it would be preferable to use the KOOS-PS (170) and HOOS-PS (123).

Results from the 3-month follow-up were not maintained at the 12-month follow-up

OA is a life-long condition. Thus, the primary aim of the SOASP was to enable the patients to continue to exercise and be physically active by themselves. The overall result for all outcomes in Studies I-IV was better at the 3-month follow-up than the 12-month follow-up. This is in line with a

meta-analysis that evaluated the effect of exercise for patients with knee and/or hip OA, showing the best results directly after treatment and thereafter decreasing (16). However, this result indicates that there is room for improvement, in obtaining sustained results from the SOASP. It has been shown that long-term adherence to exercise is poor among many people with knee and/or hip OA and this may limit sustained symptom relief (77). Strategies are needed to enhance patients' compliance with the intervention and to reinforce behavior changes to maintain the improvements experienced after the intervention over an extended period. Indeed, previous studies have shown that a reduction in the outcome after an intervention can be expected and how the addition of booster sessions might help to maintain the results over time (80). Studies also suggest that SMSs (79) and digital health may help to maintain results over time (171), but evidence for those interventions remains unclear.

However, maintaining behavior changes probably requires more complex strategies than simply adding booster sessions. Two previously published systematic reviews reported several barriers influencing adherence to exercise and physical activity, suggesting a complex interaction between internal and external factors (172, 173). The internal factors that may influence the effect of the intervention include personality, motivation, previous experience from exercise. External factors include family support and engagement by the PT and training partners (173, 174). The treatment PT needs to be aware of those factors and help the patients on an individual level to change their behavior. A systematic review suggests that PTs do not possess the required knowledge of behavioral theories or techniques to apply them effectively in their clinical practice with patients (175). Even if the SOASP is based on the framework of the transtheoretical model of behavioral change (98), this is a small part of the education received by PTs and we do not know whether the different PTs reporting data to the BOA registry were competent in behavior change.

Patients with knee OA achieve better results than patients with hip OA

In Study II, we found that patients with knee OA experienced greater improvements than patients with hip OA, and only patients with knee OA reached the MCID for pain reduction. This is in line with results from

previous studies investigating the effectiveness of exercise, where patients with knee OA had greater improvements than patients with hip OA (61, 62).

The reason for the difference in results between patients with knee and hip OA is still poorly understood. One reason for the difference may be in the disease mechanisms and joint mechanics; i.e., the hip is a ball and socket joint and the knee is a hinge joint, and the hip is a more stable joint but with angular motion in more directions than the knee.

The progress from mild to severe OA (using x-ray evaluation) has been shown to be faster in hip OA. These patients have more severe pain and a more severe radiographic OA when they seek health care than patients with knee OA (176). In Study I, there was not a big difference in pain intensity at baseline between patients with knee OA (mean = 5.24 [± SD = 1.96]) and hip OA (mean = 5.39 [± SD = 1.93]), however, the faster progression of the hip OA to a more severe OA may be one reason for the lack of improvement for these patients.

In Study III, we found that patients with Charnley C (OA in multiple joint sites (hip and knee)), or presence of any other disease that affects walking ability) had a lower odds to reach the MCID in pain. More than half (52%) of the hip population in Study I, reported Charnley C compared with 39 % of the patients with knee OA, which may explain part of the difference.

Further, it needs to be considered that the evidence used to develop guidelines and recommendations for education and exercise for patients with knee and/or hip OA, is mainly based on studies of knee OA. It is possible that patients with hip OA need a different type, intensity, or dose of exercise. A previous systematic review including patients with hip OA showed that interventions that followed the recommendations from the American College of Sports Medicine regarding strength training (75) achieved greater pain reduction than exercise interventions that did not follow these recommendations (76). We had no information about the dose or intensity from the BOA registry, but an increased dose and intensity would probably lead to a better pain reduction result in the patients with hip OA.

Finally, it has been shown that greater strength of the hip extensors, hip flexors, and knee extensors in patients with hip OA is associated with better physical function (68). We did not measure the function and may have underestimated the benefit from the SOASP in patients with hip OA.

No difference between home-based and supervised exercise

We did not find any difference in pain reduction between patients participating in the home-based or supervised exercise in Study II. The effect size for the pain of supervised exercise has been repeatedly shown to be larger than the one for home-based exercise (72-74).

One reason for our results may be the low adherence to exercise in the supervised exercise group, compared with previous RCTs studies (72-74). Only 30 % of the patients participated in the supervised exercise for 10-12 exercise sessions. Another reason that we did not find any difference between the groups may be that the patients in the SOASP could choose to undertake home-based or supervised exercise rather than being assigned to a specific treatment option. It has been shown that patients' preference towards a treatment may enhance their outcomes (177). Around 40% of the patients in the SOASP choose to do home-based exercise, with no information about the dosage or intensity of the exercise done at home. It may also be assumed that patients with exercise experience choose to participate in the home-based exercise and those patients were more likely to continue with exercises, which may have positively affected our results for the home-based group (172). Another reason may be that the patients in the supervised group had a more severe OA, those patients were slightly older and 46 % of the patients reported Charnley C (OA in multiple joint sites (hip and knee)) compared to 41 % in the home-based exercise group.

Despite decreased OA symptoms, the level of physical activity was unchanged

One of the aims of the SOASP was to increase patients' efficacy to self-manage the disease and increase their level of physical activity. Several factors are associated with a lower level of physical activity in people with OA, including comorbidity, high age, high BMI, impaired function, fear of movement, and pain (33, 54, 178, 179). In Study IV, we showed that despite a reduction in pain intensity, the time spent in sedentary and physical activity was unchanged between baseline and the 3-month follow-up. A meta-analysis found similar results for patients with OA who underwent total joint replacement, with unchanged physical activity levels after surgery, despite achieving pain relief (180). This result indicates that it requires more than pain reduction to increase the level of physical activity.

Although it has been shown that patients with OA have a lower level of physical activity than the general population (33), this did not hold in our Study IV population, which had the same level of physical activity as the general population in Sweden (51). However, the study population was younger, had a higher level of education, and a higher proportion of men than the BOA population, all factors that may positively affect the level of physical activity (172). If patients are already physically active at baseline it is harder to increase their physical activity level. In Study IV, the number of daily minutes of MVPA at baseline and follow-up was similar (baseline: median=34 [IQ =22-52]; 3-month follow-up: median=34 [IQR=19-52]; 12-month follow-up: median=32 [IQR=18-52]). This indicates that most people were slaves to their habits and performing the same activity week after week. Changing health behavior and maintaining a healthy lifestyle requires a continuous commitment (98), which takes time and effort (172). Facilitators and barriers for making a behavior change are discussed in the section about sustained results after the SOASP.

In Study I, we measured self-reported physical activity. The proportion of patients who reached the recommendation of physical activity increased at the 3-month follow-up, but the increase was not sustained until the 12-month follow-up. In Study IV, moderate level activity had decreased at the 12-month follow-up, indicating the importance of finding strategies to sustain and/or increase the level of physical activity. It is well known that physical activity has beneficial effects on OA symptoms and several comorbidities, including overweight and obesity (65). A high proportion of the BOA population is overweight or obese, with a mean BMI of 28 [±SD =5]. In the future, we need to work further in this area to help patients with OA lead a healthier life.

Factors associated with response

In Study III, we showed that the strongest factors associated with reaching the MCID in pain were less frequent pain, unilateral OA, being unwilling to undergo surgery and a lower BMI.

Patients should seek help early in their disease course, which appears to be important for pain reduction. It is important that patients change their behavior if they are to get improvement from treatment and to sustain that improvement (172). In Study III, we showed that patients with less pain frequency and unilateral OA were more likely to reach the MCID for pain;

i.e., patients with weekly pain or less were twice as likely to reach the MCID than patients who had pain all the time. Previous studies have shown that only 50% of patients with OA receive treatment according to the guidelines (95). In the BOA registry, only 4% of the patients were seeking health care for their OA for the first time and more than 70% of patients had OA changes defined by X-ray (117). It has been shown that it takes many years before the changes from OA are shown on X-ray (41). Altogether, this indicates that patients with OA in Sweden do not get the SOASP as a first-line treatment, which indicates the importance of continuing to work on the implementation of guidelines for OA in Sweden to help more people with OA to decrease their symptoms.

Unwilling to undergo surgery was another factor associated with increased odds of reaching the MCID for pain. In some regions in Sweden, the SOASP is mandatory before patients can be referred to see a surgeon to discuss surgery. It can be assumed that patients willing to undergo surgery before starting the SOASP may see surgery as the best solution for their problems and may have lower expectations from PT treatment. Shared decision-making has been shown to improve health outcomes, but providing a mandatory treatment before surgery is not considered to constitute shared decision-making with the patients (181). However, patients with OA on the waiting list for surgery have shown good pain reduction results (114, 115), and change from being willing to unwilling to undergo surgery (182, 183) and delaying surgery (110, 115), which indicates that those patients may be helped by the SOASP. Rather than force the patient to participate in the SOASP, the health professional needs to give enough information to the patients to make their own decision that they want to participate in the SOASP by themselves. We also need to work with the information given to the general population about OA, to increase the knowledge about first-line treatment for OA. Another reason for the association between being unwilling to undergo surgery and more likely to respond to the treatment may be that the patients willing to undergo surgery have a more severe OA and it is time for surgery, but our measurements did not capture this statistic. To increase the results for those patients, we need to better understand which factors are associated with the willingness to undergo surgery in the BOA population.

Overweight and obesity are huge problems for patients with OA, and are associated with radiographic worsening of the OA, increased pain and increased risk of comorbidity (184, 185). In the BOA population, around

75% were overweight or obese (117). In Study III, we showed that patients with a lower BMI were more likely to reach the MCID for pain reduction. In the SOASP, there is information about weight control, but to my knowledge, no units with an integrated weight management program are available. Exercise in combination with dietary weight management has shown a better effect on function and pain than either diet or exercise alone in patients with knee OA (92, 93). To increase the results from the SOAPS and help more patients with OA achieve a healthier lifestyle, a dietary weight management program should be added as an optional part of the SOASP.

Strengths

To my knowledge, the BOA registry is the largest registry in the world that evaluates a first-line intervention for patients with knee and/or hip OA in a real-world setting with both short- and long-term follow-ups. This increases the generalizability of the results. Studies I-III were registry-based studies, that used data that had been collected. This form of data collection is cost-effective, maximizes the public value of the already collected data and enables researchers to work with data from large cohorts. The data collection process, which is independent of the study question, and inclusion of the whole population of a geographic helps to minimize the selection bias and can prevent the misclassification of exposure, confounders, and outcomes (186). Study IV was an intervention study with a control group, to evaluate the same interventions through different study designs makes a bigger picture of the results. In this thesis, we have evaluated four out of five domains (impairments caused by body function and body structure, activity limitations, participation restrictions as well as personal factors) according to ICF and physical activity have both been evaluated objectively with an accelerometer and self-reported, which give us a good overview of the results from SOASP.

Limitations

The primary aim of a National Quality Registry is to evaluate health care for continuous learning, improvement, research, and management to create the best possible health and care together with the patients. However, sometimes the origin of questions in the National Quality Registries is not described and therefore unclear.

In the BOA-registry, HRQoL was measured with the EQ-5D-3L between 2008 and 2016 and then replaced with EQ-5D-5L. All data in my thesis were measured with the EQ-5D-3L; however, these data were transformed to EQ-5D-5L since we first obtained access to the data from the BOA registry in 2017. This transformation was done using the UK cross-walk index (159). Since all data in this thesis have been evaluated the same way, and we have evaluated the change in HRQoL, the risks for over/underestimating the results are small.

Fear of movement is evaluated through one question; “Are you afraid your joints will be injured by physical training/activity?” (Yes/No). The evaluation of fear of movement is more complex than this, therefore the results from this question should be used with caution. There are no performance-based tests of physical function in the BOA-registry, which is a limitation and may lead to underestimating the results from the SOASP.

In Study I-III, 38% of the patients at the 3-month follow-up and 58% of patients at the 12-month follow-up had missing data or had not been followed up within our timeframe. A high dropout rate is very common in registry-based studies using real-world data (119). Around 55% of the patients were excluded for missing data. This lack of information means that it is unclear whether the patients dropped out of the SOASP or the PT did not enter the data into the registry. Further, we do not know whether the excluded patients had better or worse results than the included patients. It has been shown that even patients who improve during the intervention may discontinue the treatment thinking that exercising further is not necessary, while others keep exercising because they are afraid of getting worse (187). In Studies I-III, the excluded patients had a higher HRQoL, and more patients reported daily pain, were on sick leave and were willing to undergo surgery. This may have affected our result positively; e.g., in Study III, we showed that both less frequent pain and unwillingness to undergo surgery were associated with reaching the MCID for pain.

Despite most of the questionnaire and measurements used in the BOA registry being validated, most of the data were self-reported; therefore, the results may be affected by patients wanting to "do well" and please health-care providers by reporting exaggerated improvements. A potential "regression to the mean" effect must also be considered in the interpretation, especially given the absence of a control group. In Study IV, however, similar increases in pain, QoL, and self-efficacy were shown for the treatment group, while the control group showed a trend towards worsening OA symptoms during the study period, refuting the possibility of "regression to the mean".

In Study I, we used one of two recommended questions (the question about physical activity) to measure physical activity. Because we were studying the change in physical activity over time, our results would not be affected. However, the total number of patients reaching the level of physical activity was probably higher than reported in Study I.

In Study II, we classified a pain reduction of 15% as an MCID based on a validated cut-off (164). Because the use of different cut-offs may lead to different results, interpretations of the clinical significance of the pain reduction showed in Study II requires caution.

In Study III, two different cut-offs of NRS pain reduction were used to define responders. In recommendations from OARSI, the definition of a responder should include both a decrease in symptoms and an increase in function (188). Unfortunately, there are no data on functions in the BOA registry; therefore function could not be used to define responders.

In Study IV, the patients were not randomized into intervention versus control groups. The two groups were not matched according to sex, age, and joint (knee/hip), but we did observe a difference in baseline values between the two groups. However, we adjusted for these discrepancies using a statistical model (i.e., GLM-ANOVA). The PT was not blinded to the two groups, and the intervention group met a PT 5-18 times, while the control only met a PT once. More frequent PT-led training may improve outcomes (189) and could thus be a reason for the between-group differences seen in our study.

Future perspectives

The studies in this thesis have increased our knowledge about the results of the SOAPS conducted in real-world settings. Nevertheless, to increase our knowledge even further and improve the SOASP results, we must;

- Work at a society level to increase the knowledge about first-line treatment for patients with OA and help these patients to make well-informed decisions about their treatment.
- Continue working with the implementation of the treatment guidelines for OA in Sweden to assist health professionals to help these patients correctly.
- Acknowledge that because OA is a disease with multiple comorbidities and not a single joint disease, treatment goals must focus on overall increased health rather than specific treatments.
- Increase the professionals' understanding of behavioral coaching strategies to help patients with OA.
- Find strategies to increase adherence to exercise and physical activity in patients with OA.
- Better understand which exercise and dosage we should recommend to patients with OA, in particular patients with hip OA.

Conclusions

This thesis has deepened the knowledge about treatment using SOASP for patients with knee and/or hip OA in a real-world setting. In these studies, patients who participated in the SOASP experienced decreased symptoms and increased HRQoL, however, these changes did not seem to change the level of physical activity.

Specific conclusions from the four studies can be summarized as follows:

- Overall the results from the SOASP, when implemented in real-world settings, are in line with the results of previous studies, indicating that patients participating in the SOASP reduced their OA symptoms, reduced their willingness to undergo surgery, and took less OA medication and sick leave (Study I).
- When exercise was added as part of the SOASP, there was a greater reduction in pain regardless of whether the exercise is home-based or supervised (Study II).
- Patients with knee OA seem to benefit more from the SOASP than patients with hip OA (Study II).
- Less frequent pain, unilateral OA, unwillingness to undergo surgery, and a lower BMI were associated with reaching the MCID for pain (Study III).
- Despite the decrease in pain, and increases in HRQoL, and self-efficacy, the SOASP does not seem to reduce the average amount of sedentary time or increase the physical activity (Study IV).
- The burden of disease may be reduced by offering the SOASP as the first-line treatment for patients with OA.

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