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## Physical activity and Mobile Health among people with hip and knee osteoarthritis

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# Physical activity and Mobile Health among people with hip and knee osteoarthritis

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# Physical activity and Mobile Health among people with hip and knee osteoarthritis

Elin Östlind



**LUND**  
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<b>Abstract</b>		
<p><b>Introduction</b> Hip and knee osteoarthritis (OA) is a highly prevalent condition with a substantial impact on work ability and health. Physical activity (PA) is a part of the core treatment in OA, but many individuals are insufficiently active. Mobile Health (mHealth) and wearable activity trackers (WATs) have been shown to increase PA but knowledge on their effect on work ability and other health outcomes in OA is lacking. The overall aim of this thesis was to obtain knowledge of the impact of mHealth and PA on work ability, health, and molecular biomarkers and to explore experiences of mHealth in individuals of working age with hip and knee OA.</p> <p><b>Methods</b> Individuals of working age with hip and knee OA (n =160) were included in a cluster-randomised controlled trial (C-RCT). All individuals participated in a Supported Osteoarthritis Self-management Program (SOASP) and were randomised to either a control or intervention group. The intervention was an add-on to the SOASP and consisted of self-monitoring PA with a WAT for 12 weeks. Participants in the control group only took part in the SOASP. Online questionnaires about work ability, PA, work productivity and joint function were filled out at baseline and after three, six and twelve months. WAT-data for the intervention group was retrieved and molecular biomarkers were collected at baseline and after three months in a subsample from both groups (n =91). Three focus group discussions were conducted with a subsample of individuals (n =18) from the intervention group.</p> <p><b>Results</b> Participants in the intervention group had high levels of objectively measured PA and adherence to WAT use although there was a slight decrease over the 12 week study period. No differences were found between the groups in the C-RCT regarding change over time in work ability, PA, or work productivity. No or only weak associations were found between PA, joint function, and molecular biomarkers. In focus group discussions, WATs were experienced as facilitating PA but opinions also emerged noting that WATs could be discouraging. mHealth was seen as an appreciated part of OA care and several important features were highlighted.</p> <p><b>Conclusion</b> The participants included in this project already had good work ability, were highly physically active, and probably had a greater interest in mHealth than the general OA population. This might have reduced the possibility of seeing an effect in the intervention. However, high adherence to the WATs and the participants' experiences noting that WATs facilitated and aided in optimizing PA levels indicate that they could be beneficial for this population. Participants' experiences and perceptions of mHealth in OA care could be useful when designing future hybrid OA care. Lastly, although no or only weak associations between PA, joint function and molecular biomarkers were found, there were study limitations that could have affected the results and we therefore suggest that additional research might be needed.</p>		
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Elin Östlind



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*To my family.*

*Some journeys take us far from home. Some  
adventures lead us to our destiny.*

*C.S Lewis, The Lion, the Witch and the Wardrobe*



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## Abstract

**Introduction** Hip and knee osteoarthritis (OA) is a highly prevalent condition with a substantial impact on work ability and health. Physical activity (PA) is a part of the core treatment in OA, but many individuals are insufficiently active. Mobile Health (mHealth) and wearable activity trackers (WATs) have been shown to increase PA but knowledge on their effect on work ability and other health outcomes in OA is lacking. The overall aim of this thesis was to obtain knowledge of the impact of mHealth and PA on work ability, health, and molecular biomarkers and to explore experiences of mHealth in individuals of working age with hip and knee OA.

**Methods** Individuals of working age with hip and knee OA (n =160) were included in a cluster-randomised controlled trial (C-RCT). All individuals participated in a Supported Osteoarthritis Self-management Program (SOASP) and were randomised to either a control or intervention group. The intervention was an add-on to the SOASP and consisted of self-monitoring PA with a WAT for 12 weeks. Participants in the control group only took part in the SOASP. Online questionnaires about work ability, PA, work productivity and joint function were filled out at baseline and after three, six and twelve months. WAT-data for the intervention group was retrieved and molecular biomarkers were collected at baseline and after three months in a subsample from both groups (n =91). Three focus group discussions were conducted with a subsample of individuals (n =18) from the intervention group.

**Results** Participants in the intervention group had high levels of objectively measured PA and adherence to WAT use although there was a slight decrease over the 12 week study period. No differences were found between the groups in the C-RCT regarding change over time in work ability, PA, or work productivity. No or only weak associations were found between PA, joint function, and molecular biomarkers. In focus group discussions, WATs were experienced as facilitating PA but opinions also emerged noting that WATs could be discouraging. mHealth was seen as an appreciated part of OA care and several important features were highlighted.

**Conclusion** The participants included in this project already had good work ability, were highly physically active, and probably had a greater interest in mHealth than the general OA population. This might have reduced the possibility of seeing an effect in the intervention. However, high adherence to the WATs and the participants' experiences noting that WATs facilitated and aided in optimizing PA levels indicate that they could be beneficial for this population. Participants' experiences and perceptions of mHealth in OA care could be useful when designing future hybrid OA care. Lastly, although no or only weak associations between PA, joint function and molecular biomarkers were found, there were study limitations

that could have affected the results and we therefore suggest that additional research might be needed.

## Svensk sammanfattning

Artros är en vanligt förekommande ledsjukdom och drabbar ofta höft- och knälederna. Förekomsten av artros ökar med stigande ålder och är vanligare hos kvinnor. Vid artros påverkas ledbrosket, intilliggande ben samt ligament och muskulatur. Den som drabbats upplever ofta smärta och stelhet, framför allt vid belastning. Artros i höft och knä kan innebära svårigheter att utföra vissa rörelser eller aktiviteter som att ta på strumpor, gå i trappor eller att utöva sporter och fritidsintressen. Artros kan också påverka arbetsförmågan hos de som drabbas.

Grundbehandlingen vid artros i höft och knä är information, fysisk aktivitet och (vid behov) vikttnedgång. I Sverige bör man bli erbjuden denna behandling i form av artrosskola som vanligen ges inom primärvården. Fysisk aktivitet är inte bara viktigt som en del av grundbehandlingen vid artros, det är även effektivt som en hälsofrämjande och sjukdomsförebyggande insats. Enligt internationella rekommendationer bör alla vuxna vara fysiskt aktiva 150–300 minuter i veckan på måttlig intensitetsnivå och/eller minst 75–150 minuter på hög intensitetsnivå. Trots betydelsen av fysisk aktivitet vid artros har dock stora forskningsstudier visat att många människor med höft- och knäartros inte är tillräckligt fysiskt aktiva. Tidigare forskning har också visat att individer med artros har sämre arbetsförmåga än de som inte har artros.

På senare tid har användningen av digitala hjälpmedel och mobil hälsa blivit allt vanligare som hälsofrämjande stöd. Aktivitetsmätare (som oftast bärs på handleden) kan ge information om till exempel antalet steg eller minuter i fysisk aktivitet på måttlig/hög nivå. I forskningsstudier har man visat att aktivitetsmätarna kan användas för att främja fysisk aktivitet hos användarna. Såvitt vi vet har man dock inte tittat på hur mätarna kan påverka arbetsförmåga hos arbetsföra individer med höft- och knäartros.

Det övergripande syftet med denna avhandling var att öka kunskapen om mobil hälsa och fysisk aktivitet och deras inverkan på arbetsförmåga, hälsa och molekylära biomarkörer hos individer i arbetsför ålder med höft- och knäartros. Mer specifikt ville vi i vår huvudstudie undersöka effekten av att använda en aktivitetsmätare (Fitbit Flex 2) i tolv veckor i kombination med att delta i artrosskola (interventionsgrupp) jämfört med att bara delta i artrosskola (kontrollgrupp).

Avhandlingen utgörs av fyra delstudier som är baserade på samma studiepopulation. Vi rekryterade 160 individer med höft- och knäartros som arbetade minst 50 procent. De lottades till antingen intervention- eller kontrollgrupp. Alla deltagare

fick besvara frågeformulär om bland annat arbetsförmåga, fysisk aktivitet och ledfunktion. Formulären fylldes i vid projektstart samt vid uppföljning efter tre, sex och tolv månader. Information om dagligt stegantal och minuter i fysisk aktivitet hämtades också in från aktivitetsmätarna. Tre fokusgruppsdiskussioner genomfördes också med 18 individer som deltagit i interventionsgruppen. Diskussionerna handlade om deltagarnas erfarenheter av att använda aktivitetsmätarna och deras upplevelser av mobil hälsa och digitalt stöd vid artrosbehandling. Vi undersökte även sambandet mellan fysisk aktivitet, ledfunktion och molekylära biomarkörer (brosk och inflammation) och därför fick 91 deltagare även lämna blodprover vid två tillfällen. Data från de olika studierna i projektet analyserades och sammanställdes med statistiska eller kvalitativa metoder.

Resultatet visade att användning av aktivitetsmätare i kombination med artrosskola inte hade större effekt på arbetsförmåga och fysisk aktivitet, jämfört med enbart artrosskola. Det fanns ingen signifikant skillnad mellan grupperna avseende förändring i arbetsförmåga och fysisk aktivitet från projektstart till uppföljningarna. Vad gäller arbetsproduktivitet fanns det en skillnad till fördel för interventionsgruppen men bara för en av instrumentets fyra delskalor och bara till första uppföljningen. Resultatet av data som inhämtades från aktivitetsmätarna visade att deltagarna i genomsnitt gick drygt 10 000 steg per dag och att majoriteten var fysiskt aktiva på minst måttlig nivå mer än 150 minuter per vecka. Aktivitetsmätarna bars i genomsnitt 88 procent av de tolv veckorna. Vid fokusgruppsdiskussionerna framkom att aktivitetsmätarna uppskattades och att de upplevdes kunna främja och optimera deltagarnas fysiska aktivitet. Deltagarna tyckte dock också att det kunde upplevas som stressande eller nedslående om man inte kunde nå sitt stegmål på grund av smärta. De var generellt sett positiva till mobil hälsa och digitalt stöd vid artros men tyckte att det helst skulle ges i kombination med traditionell vård. Slutligen fann vi inga eller svaga samband mellan fysisk aktivitet, ledfunktion och molekylära biomarkörer hos våra deltagare.

Att användningen av aktivitetsmätare inte hade någon effekt på arbetsförmåga eller fysisk aktivitet skulle kunna bero på att deltagarna i detta projekt redan hade god arbetsförmåga och en hög nivå av fysisk aktivitet. Det fanns alltså inte mycket utrymme till förbättring. Den höga följsamheten till att bära aktivitetsmätaren samt deltagarnas erfarenheter ger dock en indikation på att de kan vara till hjälp både för att uppmuntra till att röra på sig och för att hitta rätt mängd fysisk aktivitet då många med artros upplever mer smärta vid överbelastning. Resultatet från avhandlingen kan vara till hjälp för både patienter, vårdgivare och forskare vid utformning av den framtida artrosvården som förmodligen kommer att bli en hybrid av traditionell och digital vård.

# Thesis at a glance

	Paper I	Paper II	Paper III	Paper IV
<b>Aim</b>	Describe PA patterns and adherence to using a WAT, Fitbit Flex 2, among individuals of working age with hip and knee OA, during a 12-week period. A secondary aim was to explore the correlation between self-reported function and PA.	Examine the effects of adding self-monitoring PA with a WAT to the SOASP on work ability and the secondary objectives PA and work productivity among individuals of working age with hip and knee OA compared to the SOASP only.	Explore the experience of using a WAT to monitor PA and the general perceptions of digital support in individuals of working age with hip and knee OA.	Explore the associations between PA or self-reported joint function and molecular biomarkers of cartilage and inflammation in individuals of working age with hip and knee OA.
<b>Methods</b>	Individuals with hip and knee OA of working age who participated in the intervention group of the C-RCT with at least 50% WAT-data were included (n =75). WAT data was analysed with linear mixed models.	Individuals with hip and knee OA of working age were included in C-RCT. Questionnaires were filled out at baseline and three follow-ups. Those with data from baseline and at least one follow-up were included in the analyses (n =124). Data was analysed with linear mixed models and ANCOVA.	Individuals with hip and knee OA of working age who participated in the intervention group of the C-RCT were included (n =18). Three focus group discussions were conducted. Qualitative content analysis was applied to the data.	Individuals with hip and knee OA who participated in the C-RCT were included (n =91). Serum samples were collected at baseline and three month follow-up. Questionnaire data on joint function, PA and WAT data were used in the analyses. Data was analysed with Spearman's rank correlation.
<b>Main results</b>	On average, participants walked 10,593 steps/day, spent 48.1 minutes in MVPA/day and used the WAT for 88.4% of the 12-week period. Daily steps, minutes in MVPA and adherence to WAT-use decreased significantly over the 12 weeks.	No statistically significant difference between groups in pattern of change in work ability or PA, from baseline to follow-ups was found. Neither group had a statistically significant change in work ability between baseline and follow-ups.	The analysis resulted in two main categories: <i>WATs may aid in optimization of PA, but is not a panacea and Digital support is an appreciated part of OA care</i> with three sub-categories respectively.	The correlation between change in self-reported PA and change in COMP was weak (rs = -0.256, p =0.040). No other associations were found.
<b>Conclusions</b>	A majority of participants reached the recommended level of MVPA per week and adherence to Fitbit use was high. However, both PA and adherence decreased slightly over time. Understanding PA patterns and the use of a WAT to promote PA could be beneficial in tailoring interventions for individuals with hip and/or knee OA.	The SOASP and self-monitoring PA with a WAT did not have any effect on the work ability. Participants at baseline already had good work ability and were physically active, which could have reduced possibility for improvements. Future interventions should target a population with lower work ability and PA levels.	WATs may facilitate physical activity but also aid individuals with OA to find the optimal level of PA to avoid increased pain. Digital support in OA care was appreciated, particularly as a part of traditional care including physical visits. Digital support should be easy, comprehensive, early, and continuous.	In general, no, or only weak associations were found between PA/joint function and molecular biomarkers. Future research is recommended to include participants with lower PA-level, have a longer follow-up and use a design that allows for comparisons.

## Abbreviations

ANCOVA	Analysis of co-variance
ARGS	Neoepitope of aggrecan
BCT	Behaviour change technique
BMI	Body mass index
BOA	Better Management for Patients with OA
C2C	Collagen type II cleavage
CI	Confidence interval
COMP	Cartilage oligomeric matrix protein
C-RCT	Cluster-randomised controlled trial
CRP	C-reactive protein
eHealth	Electronic Health
ELISA	Enzyme-linked immunosorbent assay
GBD	Global Burden of Disease
GLA:D	The Good Life with Osteoarthritis
HOOS	Hip Osteoarthritis and disability Outcome Score
ICF	International classification of functioning, disability and health
KOOS	Knee Osteoarthritis and injury Outcome Score
IPAQ–SF	International physical activity questionnaire–short form
LPA	Light physical activity
M	Median
MET	Metabolic equivalent of tasks
mHealth	Mobile Health
MVPA	Moderate to vigorous physical activity
NSAID	Non-steroidal anti-inflammatory drugs
OA	Osteoarthritis
OARSI	Osteoarthritis Research Society International
PA	Physical activity



PT	Physiotherapist/physiotherapy
SD	Standard deviation
SOASP	Supported osteoarthritis self-management program
VO <sub>2</sub>	Oxygen uptake
WAI	Work ability index
WAT	Wearable activity tracker
WHO	World health organization
WPAI:OA	Work productivity and activity scale: osteoarthritis

## List of papers

This thesis is based on the following papers. In the text, the papers will be referred to by the Roman numerals I–IV.

- I. Östlind E, Sant'Anna A, Eek F, Stigmar K, Ekvall Hansson E. Physical activity patterns, adherence to using a wearable activity tracker during a 12-week period and correlation between self-reported function and physical activity in working age individuals with hip and/or knee osteoarthritis. *BMC Musculoskelet Disord.* 2021 May 15;22(1):450. <https://doi.org/10.1186/s12891-021-04338-x>
- II. Östlind E, Eek F, Stigmar K, Sant'Anna A, Hansson EE. Promoting work ability with a wearable activity tracker in working age individuals with hip and/or knee osteoarthritis: a randomized controlled trial. *BMC Musculoskelet Disord.* 2022 Feb 3;23(1):112. <https://doi.org/10.1186/s12891-022-05041-1>
- III. Östlind E, Ekvall Hansson E, Eek F, Stigmar K. Perceptions and experiences of digital support and activity monitoring in working individuals with hip and/or knee osteoarthritis – a focus group study. *In manuscript, submitted.*
- IV. Östlind E, Eek F, Stigmar K, Sant'Anna A, Ekvall Hansson E, Struglics A. Associations between physical activity, self-reported joint function, and molecular biomarkers in working age individuals with hip and/or knee osteoarthritis. *Clin Med Insights Arthritis Musculoskelet Disord.* 2022 Mar 23;15:11795441221081063. <https://doi.org/10.1177/11795441221081063>

# Descriptions of contributions

## I.

Study design	Elin Östlind, Anita Sant'Anna, Frida Eek, Kjerstin Stigmar, Eva Ekvall Hansson
Data collection	Elin Östlind, Anita Sant'Anna
Data analyses	Elin Östlind, Anita Sant'Anna, Frida Eek
Manuscript writing	Elin Östlind, Anita Sant'Anna, Frida Eek, Kjerstin Stigmar, Eva Ekvall Hansson

## II.

Study design	Elin Östlind, Frida Eek, Kjerstin Stigmar, Anita Sant'Anna, Eva Ekvall Hansson
Data collection	Elin Östlind, Anita Sant'Anna
Data analyses	Elin Östlind, Anita Sant'Anna, Frida Eek
Manuscript writing	Elin Östlind, Frida Eek, Kjerstin Stigmar, Anita Sant'Anna, Eva Ekvall Hansson

## III.

Study design	Elin Östlind, Kjerstin Stigmar, Frida Eek, Eva Ekvall Hansson
Data collection	Elin Östlind, Kjerstin Stigmar, Eva Ekvall Hansson
Data analyses	Elin Östlind, Kjerstin Stigmar
Manuscript writing	Elin Östlind, Kjerstin Stigmar, Frida Eek, Eva Ekvall Hansson

## IV.

Study design	Elin Östlind, Frida Eek, Kjerstin Stigmar, Anita Sant'Anna, Eva Ekvall Hansson, André Struglics
Data collection	Elin Östlind, Anita Sant'Anna, André Struglics
Data analyses	Elin Östlind, Frida Eek, André Struglics
Manuscript writing	Elin Östlind, Frida Eek, Kjerstin Stigmar, Anita Sant'Anna, Eva Ekvall Hansson, André Struglics

# Preface

Since I graduated as a physiotherapist in 2008 from Lund University, I have mainly worked in primary health care. After a couple of years as a clinician, my need for further knowledge led me to pursue a master's degree and a speciality. My master's thesis was conducted within a research project called WorkUp with my current co-supervisor Kjerstin Stigmar as my main supervisor. It was then my interest in research really awakened. A year after finishing my master's degree, I was accepted as a PhD student.

## Context of this thesis

This PhD-project was carried out in a project called Active@Work. The project was initiated several years before I became involved, and the project plan was developed by researchers from Lund University and Halmstad University. It received funding from the Swedish Research Council in 2016. The aim of the project was to explore whether mobile technology, including a personalized decision support system, could have any effect on physical activity level, health, work ability, health related quality of life, work productivity or sick leave among working individuals with hip and/or knee osteoarthritis. The specific research questions in Active@Work were:

- Can an intervention, comprised of mobile technology have any effect on physical activity level, self-rated health, work ability, quality of life or work productivity among individuals with OA?
- Is there any difference in effect between using mobile technology and activity monitoring alone or when continuous feedback concerning physical activity is added?

However, Active@Work was not granted the amount of funding they applied for. That and various other reasons resulted in an inability to develop the personalized decision support system in the original project plan, and the project was thus gradually redesigned into the content of this thesis. I would think that this process is by no means unique in research and for me personally, it has been a great learning experience. I believe that the results of this project can provide new knowledge in the research field despite the change of course.

# Introduction

This thesis mainly concerns hip and knee osteoarthritis (OA), physical activity (PA) and Mobile Health (mHealth) which are explored from different points of view. In the introduction, I will describe OA and its impact on health and work. I will also highlight molecular biomarkers and their potential utility in OA treatment and research. The other central concepts in this study, PA, and the use of mHealth (especially wearable activity trackers (WATs)) to promote PA will also be described.

## Hip and knee osteoarthritis

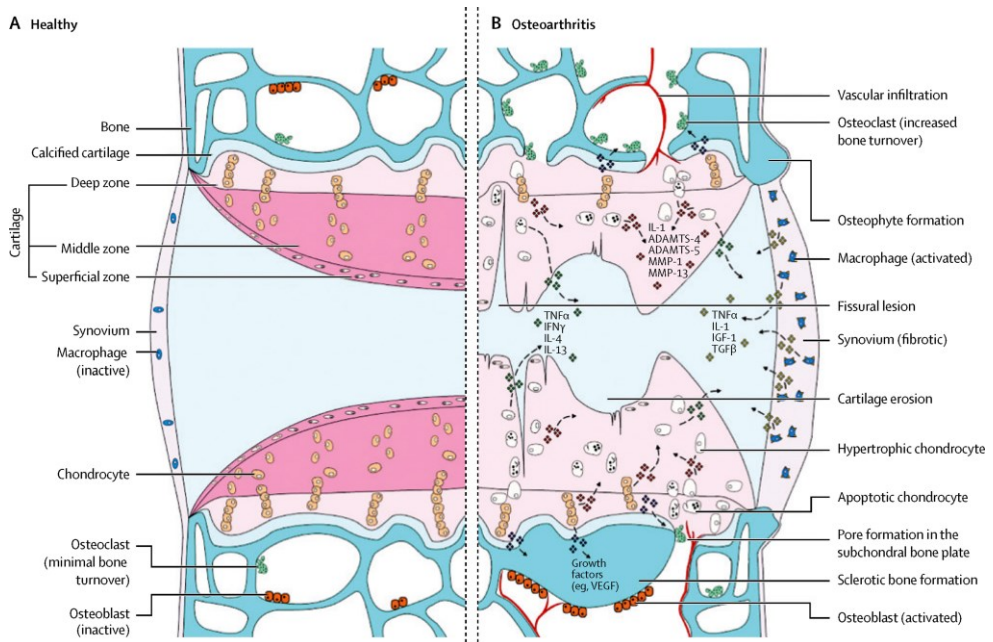
### **Pathogenesis**

OA has a relatively long medical history and was described and classified by physicians in the 19<sup>th</sup> century (1). Earlier, it had been seen as a wear-and-tear disease mostly affecting articular cartilage, but is now seen as an organ disease affecting the synovial joints as well as the surrounding tissues (1,2). The cause of OA seems to be multifactorial and there are still gaps in knowledge about its aetiology (2).

In the healthy synovial joint, there is a balance, a homeostasis, between breakdown and repair of the joint tissues, but in OA, this homeostasis has been disrupted (3). The bones in the synovial joints are covered with articular cartilage, which is a smooth, viscoelastic, and avascular tissue (i.e., in healthy cartilage) that distributes the mechanical load of the joint. Since healthy cartilage is avascular, nutrition is provided through diffusion from the synovial fluid in the joint cavity (4). This diffusion is supported by movement and loading/unloading of the joint (4).

The cartilage is organized in layers and divided into four zones; superficial, middle, deep, and the zone of calcified cartilage, illustrated in Figure 1 (4,5). It consists of the extracellular matrix (mainly water, hyaluronic acid and proteins such as collagens and proteoglycans) and chondrocytes (cartilage specific cells) (5–8). To maintain the mechanical functions of the cartilage, it is important to maintain the water in the extracellular matrix (4). In OA, there is an increase in the metabolism with loss of extracellular matrix and chondrocytes leading to a destruction of the

cartilage (7,9). Since healthy cartilage is avascular, it has a poor regenerative capacity, and this destruction cannot be reversed (9).



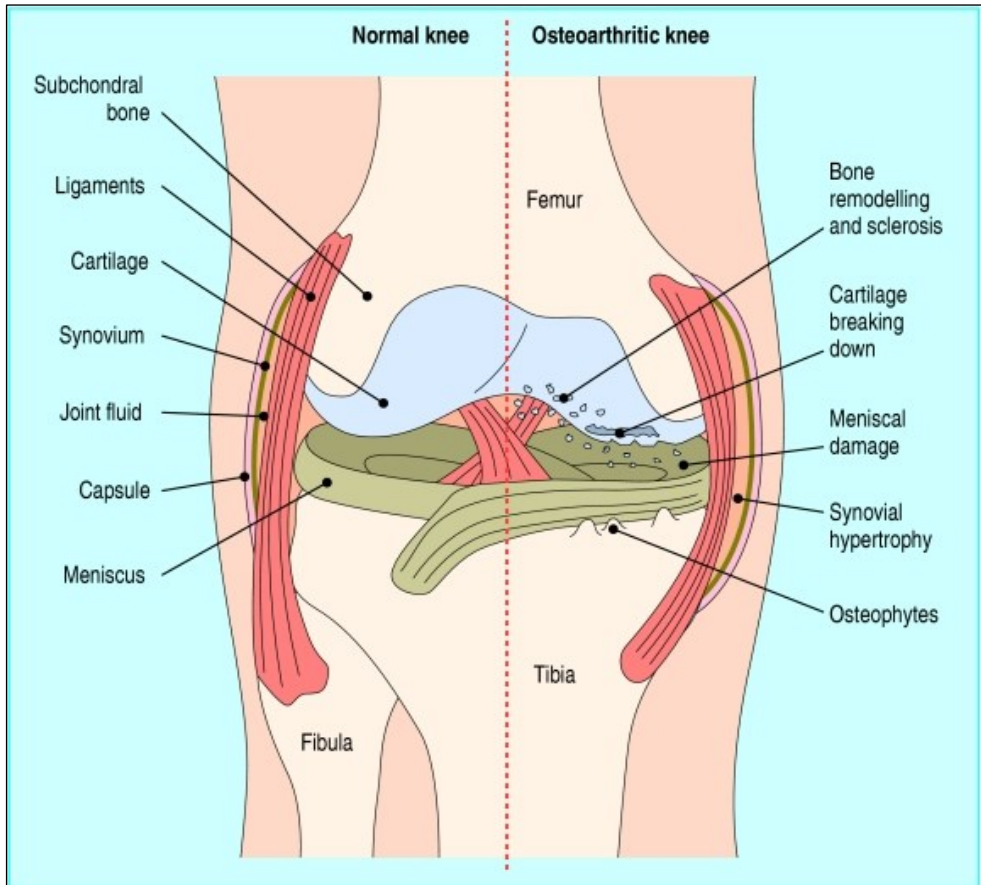
**Figure 1. Signalling pathways and structural changes in the development of osteoarthritis.**

(Reproduced from Osteoarthritis, Glyn-Jones S et al, The Lancet 386, 376–387, 2015, with permission from Elsevier Ltd)

OA does not only affect the cartilage but also the synovia, soft tissues (ligaments and menisci), and subchondral bone (Figure 2). Synovial hypertrophy and inflammation in the synovial membrane (synovitis) as well as increased vascularity and inflammatory cell infiltration are common in OA (8,10). Clinically, synovitis and the related effusion could be contributing factors to the experience of pain in individuals with OA (11).

The joint capsule, ligaments, and the meniscus (knees) are also affected in OA, although they have not received as much attention as cartilage and bone. Degenerative changes with increased fibrosis and a loss of flexibility can be seen in these soft tissues in individuals with OA (12). There is a strong relationship between degenerated menisci and knee OA and the direction of the relationship seems to go in both directions; a meniscus tear might facilitate the development of OA and a healthy meniscus could degenerate due to OA (13). Changes that develop in the subchondral bone in response to disrupted homeostasis are remodelling of the bone, and the formation of osteophytes and bone cavities (cysts) (2). These changes,

together with joint space narrowing, are a part of the diagnostic criteria in the radiological assessment of hip and knee OA (14).



**Figure 2. Features of pathogenesis consistent with osteoarthritis in the knee.**

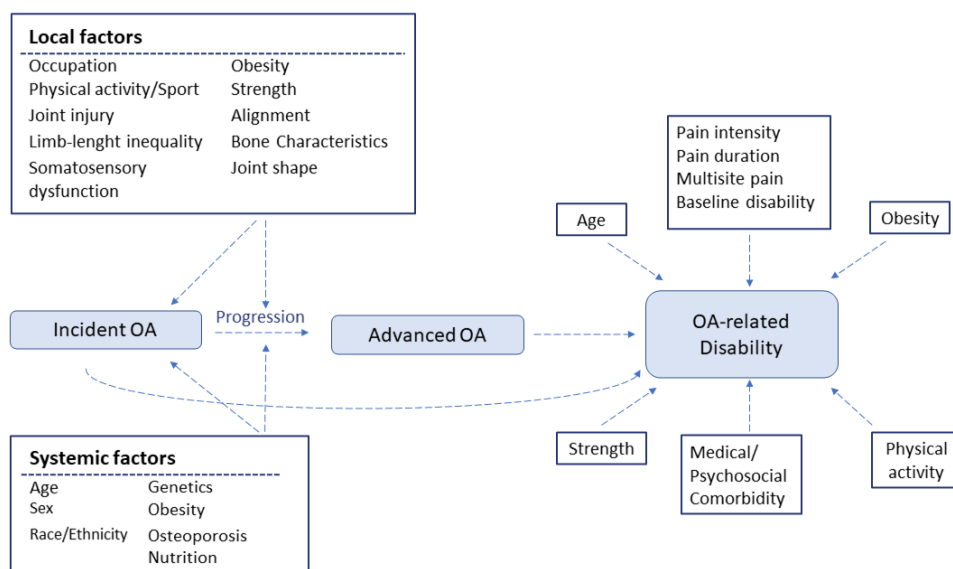
(Reproduced from Osteoarthritis, David J Hunter and David T Felson, BMJ 333, 639–642, 2006, with permission from BMJ Publishing Group Ltd.)

What causes and drives the progression of OA is not fully understood, but recent research suggests that metabolic syndrome and inflammation (both local and systemic) might be important factors (15,16). In a joint affected by OA, there is an increase in proinflammatory cytokines, which is believed to relate to the structural changes in OA (17). Compared to rheumatoid arthritis, which is characterized by high-grade inflammation, the inflammation in OA is low-grade and chronic in character (18).



### Risk factors

There are several risk factors associated with OA incidence and the progression of the disease, as illustrated in Figure 3. Some of the risk factors are local and joint-specific, while others are systemic (19). One of the most important local risk factors is injury to the joint (commonly the knee). A recent systematic review and meta-analysis reported that the odds of developing OA after a previous knee injury are four to six times higher compared to a non-injured knee (20). An injury to the anterior cruciate ligament in the knee leads to altered homeostasis and a low-grade inflammation which is still present five years following the injury according to an exploratory study (21). PA/sport has also been suggested as a local risk factor, but it is the consequence of the sport (i.e., injury), rather than recreational PA itself that increases the risk of OA (19,22–24). Other possible local risk factors for OA are certain occupations involving heavy manual work (25,26), muscle strength and other biomechanical factors (19).



**Figure 3. Risk factors for osteoarthritis and related disability.**

(Reproduced from Epidemiology of Osteoarthritis and Associated Comorbidities, David J. Hunter, David C. Morgenroth, Pradeep Suri, PM&R, 4: S10-S19, 2012, with permission from Elsevier Ltd.) (19)

Obesity is both a local risk factor due to a higher biomechanical load as well as a systemic factor driving the low-grade inflammation associated with OA (15,16). A systematic review and meta-analysis reported an almost three-fold risk of knee OA for obese/overweight individuals, compared to normal weight individuals (27). Other important individual systemic risk factors associated with OA are age and sex.

OA prevalence increases with higher age. The incidence of knee OA peaks at 70–79 years and the incidence of hip OA peaks at 60–64 years according to data from the Global Burden of Disease (GBD) studies (28–30). However, hip and knee OA also affects younger individuals, which could impact work participation (31). Female sex has consistently been reported as a risk factor for hip and knee OA, although the risk is more attenuated for knee than hip OA (32). The reason for this is not yet understood, although previous research has found that oestrogen has some effect on knee OA (33).

### *Molecular biomarkers*

The diagnosis of OA is based on clinical and radiological findings, but the structural changes and increased metabolism of the cartilage can also be detected by molecular biomarkers in synovial fluid, blood (serum/plasma) and urine (34,35). A working group of The National Institute of Health has defined a biomarker as “a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacological responses to therapeutic intervention” (36). Molecular biomarkers have gained increased attention as a method to detect OA early and to monitor its progress (35,37,38). The destruction of the extracellular matrix in cartilage causes a loss of matrix fragments to synovial fluid, blood, and urine. Compared to healthy controls, individuals with OA have higher circulating levels of cartilage biomarkers (34). Systematic molecular biomarkers (blood and urine) do not provide information about a specific joint but can be used to detect a total disease burden (35,39).

There is no single molecular biomarker that can be used as a measure for OA but rather a combination of biomarkers (35). The molecular biomarkers ARGS-aggrecan (i.e., aggrecan neoepitope of Alanine (A) - Arginine (R) - Glycine (G) – Serine (S)), generated by aggrecanase proteases, and type II collagen (i.e., collagen-II neoepitope C2C) generated by collagenase proteases, are both related to cartilage metabolism and are included on a list of the best candidates for evaluating OA (34). In previous studies with knee-injured individuals or individuals with OA, ARGS-aggrecan and C2C were increased in synovial fluid and serum samples (21,40–42). The cartilage oligomeric matrix protein (COMP) is a joint structure protein also used as a molecular biomarker in OA. Previous research has shown an association between PA and COMP (43,44). Molecular biomarkers for inflammation, such as C-reactive protein (CRP), have also been suggested as markers of OA diagnosis and progression (45).

## Prevalence and burden of disease

The hips and knees are two of the most common sites affected by OA. Knee OA is more common than hip OA. The prevalence of OA increases with age and this increase accelerates between 50 and 75 years, especially in women (16). The reported prevalence of hip and knee OA varies, depending on the definitions used in studies (radiographic, clinical, or symptomatic) (46).

### *Hip OA*

The age-standardized incidence of hip OA has increased from 17.02 per 100,000 individuals in 1990 to 18.70 per 100,000 individuals in 2019 according to the GBD study in 2019 (30). Population-based studies in the US have reported a prevalence of *symptomatic* hip OA in middle-aged and older adults of 4.2 % (age-standardized) and 9.7% (47,48). This is in line with results from a Spanish study of individuals  $\geq 40$  years of age, reporting a prevalence of 5.1% based on *radiographic* and *clinical* criteria (49). In Sweden, a large population-based study of individuals  $\geq 45$  years of age reported the proportion of individuals with physician-diagnosed hip OA at 5.8% (50). The authors of that study also estimated that the prevalence of doctor-diagnosed hip OA would increase to 6.9% by 2032 (50).

### *Knee OA*

From a global perspective, the prevalence of knee OA was estimated to be 3.8% in the 2010 GBD study (29). In a more recent systematic review and meta-analysis, the global prevalence in individuals  $\geq 40$  years was estimated to be 22.9% (51). In US individuals  $\geq 50$  years of age, a population-based study reported a prevalence of *symptomatic* knee OA of 17% (52), which is in line with the results from a recent systematic review and meta-analysis, reporting a prevalence of symptomatic knee OA of 14.6% in a Chinese cohort (53). In Sweden, the prevalence of knee OA diagnosed by a physician was 13.8% in a large population of individuals  $\geq 45$  years of age. By the year 2032, that prevalence is estimated to increase to 15.7% (50).

### *Burden of disease*

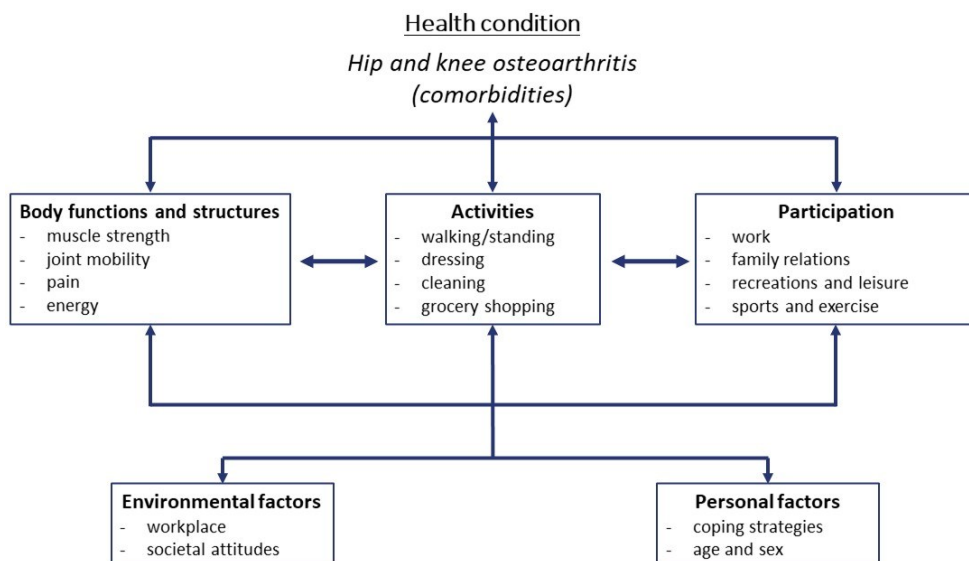
According to the 2010 GBD study, hip and knee OA was ranked 11<sup>th</sup> out of 291 total conditions as the top contributors of years lived with disability (29). Another more recent study on GBD data showed that the overall burden of hip OA, measured via disability-adjusted life-years increased from 11.54 disability-adjusted life-years per 100,000 individuals in 1990 to 12.57 per 100,000 individuals in 2019 (30). OA-related disability also leads to high costs for both the individual and society due to reduced capacity and performance at work (54–56). An US study estimated that the direct all-cause health care costs and indirect costs (lost wages) were \$1778 and \$189, respectively, for individuals with OA compared to those without OA (57). In Sweden, a study showed that individuals with knee OA had an almost two-fold risk of sick leave compared to those without knee OA (58).

## **Impact on health and work ability**

OA in the hip and knee can have an impact on an individual's function and ability to perform activities and participate in work or other recreations. This impact on different domains can be described using the International Classification of Functioning, Disability and Health (ICF) model developed by the World Health Organization (WHO) (59). The ICF model illustrates how the different domains interact with each other. In Figure 4, the ICF-model is illustrated with examples from the ICF core set for OA (60). The interactions can go in both directions. In the following paragraphs, the general impact that OA can have on different domains in the ICF is presented. The contextual factors that represent the complete background of an individual's life are also presented, as they could influence and interact with other domains (59).

### *Body functions and structure*

In OA, there are several local structural alterations in the affected joint(s) and the surrounding tissues as described in the previous paragraphs on the pathogenesis. Individuals with OA also experience impacts on body functions with joint pain as the most predominant symptom (61). In a previous study, two types of pain associated with hip and knee OA were described. One type was described as a more constant, dull, aching, throbbing pain and the other type was characterized as a shorter, more intense, unpredictable, and emotionally exhausting pain. Pain that was unpredictable and had a higher intensity had the greatest impact on activities and quality of life (62). Other clinical symptoms that are often present in hip and knee OA are reduced joint mobility, reduced muscle strength, joint swelling, and fatigue (31,32).



**Figure 4. The International Classification of Functioning, Disability and Health (ICF) model with examples from the core set for OA.**

### *Activities*

The alterations in body functions and structure associated with OA can also impact an individual's ability to perform different activities such as walking, stair climbing, carrying, self-care, and housekeeping (63,64). Already in early knee OA, pain and low vitality is associated with avoidance of activities (65). Also work-specific tasks, sport-specific tasks, and other activities of daily living can be affected by impairments to body function and structure (3,26,31). Individuals with hip OA experience somewhat other difficulties than those with knee OA.

Secondary analyses from two studies with 42 focus groups comprised of individuals with hip and knee OA showed that those with hip OA often mentioned groin and sidedness (ex. problems with lying one's side) while individuals with knee OA were more concerned about stairs, weight, and stiffness (66). However, a recent longitudinal study from Denmark with more than 30,000 participants showed similar results for individuals with hip OA as for individuals with knee OA on walking speed, pain intensity and quality of life (67). In a US population, individuals in OA had higher pain interference with activities and more functional limitations than individuals without OA (57).

### *Participation*

Due to reduced function or reduced capacity to perform different activities, participation in work, sport or other leisure activities may also be affected (60). As

mentioned previously, studies have shown a lower work ability in individuals with OA than those without, but this is also dependent on the demands of the work and possibilities for adaptations at the workplace (25,68). In a Swedish cohort of individuals with hip and knee OA, female-dominated occupations such as health care, cleaning, and childcare were associated with an increased risk of sick leave or disability pension (25). However, being at work with reduced capacity (presenteeism) seems to be more common than being absent from work (absenteeism) due to OA (54,69,70). OA can also lead to difficulties for individuals in engaging with leisure or sport activities due to limitations in function and activities, pain, and fatigue (71,72).

### *Contextual factors (Environmental and personal)*

Contextual factors are also important to take into consideration when describing OA's impact on health and work ability. As described in the previous paragraph, certain occupations and work tasks might increase the risk of OA (25,26,73). Also, since work ability is related to occupational demands, individuals with OA might experience more difficulties in a physically demanding occupation (25,74). An individual's ability to participate in different activities can also be affected by environmental factors, social support, and access to health care (75,76). Age and sex are important personal factors that increases the incidence and progression of OA (19,32). An individual's motivation and coping strategies are also relevant personal factors that might impact on activities and participation (77).

## **Comorbidities**

The presence of additional diseases i.e., comorbidities, is common in individuals with OA. Stroke, peptic ulcers, and metabolic syndrome are the most common comorbidities according to a recent systematic review and meta-analysis (78). Other diseases, such as cardiovascular disease and depression, have also been reported in previous research as more prevalent in individuals with OA compared to those without OA (54,79–81). In a large Swedish cohort (70,000 with OA and 216,000 without OA), a larger proportion of those with OA had comorbidities (85%) compared to those without OA (78%) (82). That result was most evident in younger individuals and individuals with OA in the knee (82). The aetiology of the relationship between OA and certain comorbidities is still largely unknown and difficult to explore since several diseases share common risk factors (78). The presence of comorbidities has been shown to be associated with worsening of pain and physical functioning in individuals with hip and/or knee OA (83).

The association between OA and mortality has been explored in several systematic reviews and meta-analyses, with conflicting results (84–86). In the most recent meta-analysis, Leyland et al. (86) reported a higher risk of premature mortality in individuals with painful knee OA but not for individuals with OA without pain.

## Treatment

Despite the voluminous research conducted during the last century, there is still no treatment that can cure OA or halt its progression (87,88). Consequently, treatment is mainly focused on alleviating symptoms and reducing the impact of the disease (87). Since OA is a chronic disease marked by slow progression, self-management is an important approach in managing the condition. In self-management, the individual is responsible for his/her own health and interventions are developed to improve health status (89).

A large number of national and international clinical practice guidelines on OA have been published during the last decade according to a recent systematic review that compiled and assessed the guidelines (90). All guidelines on hip and knee OA included in that systematic review consistently recommended that *patient education/information, exercise, and weight management* (for those who are overweight) should be offered as core treatment in hip and knee OA (90). In the guidelines from the OA Research Society International (OARSI), core treatments were also recommended in conjunction with additional treatments (91). These guidelines have been implemented in treatment programmes in several countries and are often illustrated as a treatment pyramid (Figure 5) (92,93).

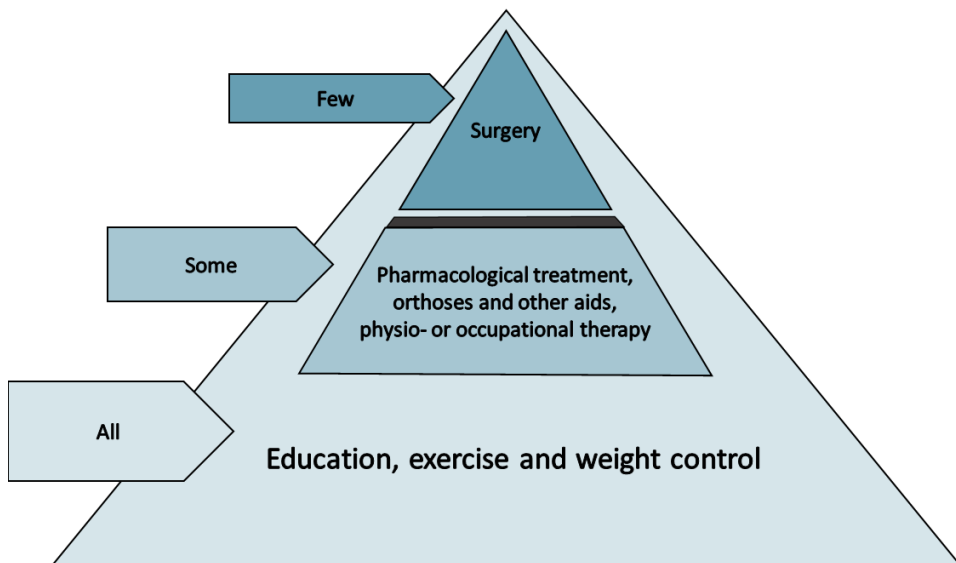


Figure 5. Core treatment of osteoarthritis in hip and knee. (92,93)



### *The Supported Osteoarthritis Self-management Programme*

In Sweden, the core treatment for OA is offered in the form of Supported Osteoarthritis Self-management Programme (SOASP) (92). SOASP was developed in 2008 and aims to support individuals with OA in coping with their disease, improving health-related quality of life, increasing PA, reducing health care consumption, and reducing sick leave (92,94). Patients seeking health care for hip or knee OA should be referred to SOASP as the first-line treatment. Patients are often offered an individual visit with a PT before participating in the SOASP. The SOASP constitutes of two group lectures (often held by a PT), a session with an OA communicator and individual- or group-led exercise (Figure 6). A national quality registry, “Better Management for Patients with OA” (BOA), previously provided educational material and trained PTs and occupational therapists in offering SOASP. As of 2019, BOA is no longer responsible for the SOASP, and education is offered by other organisations such as the Swedish Rheumatism Association (95).

Similar versions of SOASP have been spread to other countries, “The Good Life with Osteoarthritis” (GLA:D) is the Danish version, which in turn has spread to a number of countries (93). A digital version of SOASP has also been developed in Sweden; the “Joint Academy” (96).

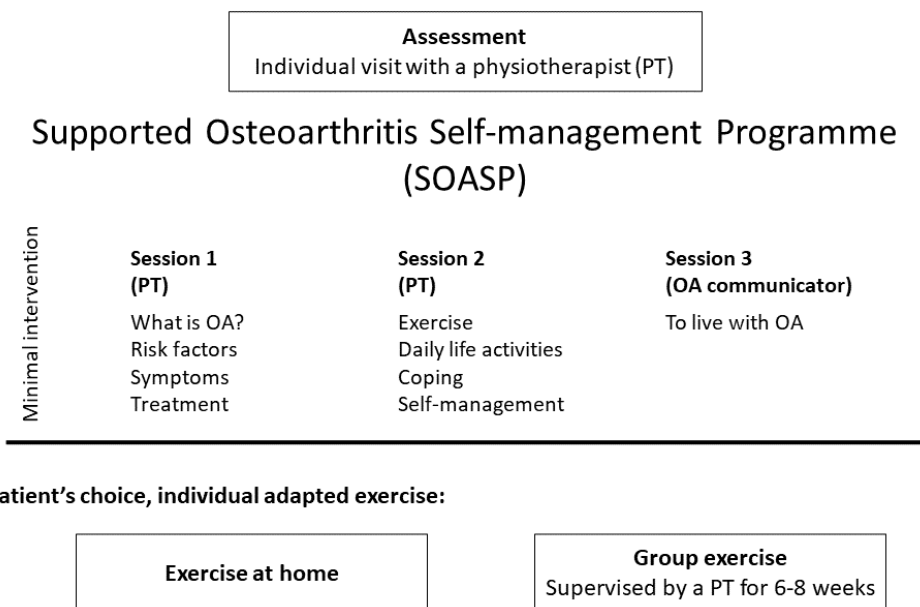


Figure 6. The Supported Osteoarthritis Self-management Programme (SOASP).

### *Additional treatments and surgery*

In some cases, additional treatments or surgery are needed to complement the core treatment in hip and knee OA. The OARSI clinical guidelines from 2019 strongly recommend topical non-steroidal anti-inflammatory drugs (NSAIDs) for knee OA (91) in addition to core treatments. Non-selective oral NSAIDs could be recommended in both hip and knee OA for patients without comorbidities, preferably with the addition of proton pump inhibitor or selective COX-2 inhibitors. Aquatic exercise, gait aids and cognitive behavioural therapy in combination with exercise were also recommended as additional treatments. The recommendations were, in general, stronger for knee OA than for hip OA.

Acupuncture has also been suggested as an additional treatment for knee OA. A recent systematic review and meta-analysis showed beneficial effect on reducing pain and improving function (97). For hip OA, acupuncture seems to have little or no effect on improving pain and function (98).

If the core treatment in combination with additional treatments are insufficient to relieve pain and improve function, surgery might be an option. Total joint replacement is effective in reducing pain and improving physical functioning (99,100).

## Physical activity

### **Definitions and concepts**

PA includes all movements made during different activities in leisure, work, and transportation. It is defined as “any bodily movement produced by skeletal muscles that results in energy expenditure”. *Exercise* is a sub-category of PA and is defined as an activity that “is planned, structured, repetitive, and purposive in the sense that improvement or maintenance of one or more components of physical fitness is an objective” (101). Engaging in sports and other leisure activities are consequently often regarded as exercise.

PA is carried out at different intensity levels that can be defined and measured as *absolute* or *relative* intensity (102). *Absolute intensity* is a general measure of the energy expenditure needed to perform any form of PA. It can be measured in terms of, for example, kilojoules, kilocalories, oxygen consumption (VO<sub>2</sub>) or Metabolic Equivalent of Tasks (METs) (103). One MET is the rate of energy expenditure for an individual at rest and it is calculated based on an average oxygen uptake of 3.5 millilitres/kilogram per minute. METs increase with higher intensity. Examples of METs in different activities are presented in Table 1. *Relative intensity* is related to an individual’s physical capacity. This can be measured in different ways, for

example, percent of maximum heartrate, percent of VO<sub>2</sub>max or percent of heart rate reserve. Relative intensity can also be self-rated using different scales such as the Borg's rating of perceived exertion scale (102).

**Table 1. Examples of Metabolic Equivalent of Tasks (METs) in different activities.**

Intensity	METs	Activities
Sedentary	<1.5	Lying down, sleeping, sitting.
Light	1.6–2.9	Slow walk, cooking, easy cleaning.
Moderate	3.0–5.9	Brisk walking, vacuuming, weightlifting (squats), bicycling 15 km/h.
Vigorous	>6.0	Running >6.4 km/h, skiing cross country, playing squash.

METs are often categorized into different intensity levels where intensities >3.0 METs are considered moderate to vigorous (MV) (104). PA, especially MVPA, has received much attention in medical research as a method to promote health and prevent disease in the last 70 years (105,106). MVPA of ≥30 minutes per day most days a week has been recommended in the US since 1995 (104).

### **Physiological effects of physical activity**

There are several physiological responses to PA that drive its positive health effects. During muscle contractions, myokines (proteins) are produced which influence metabolism in other organs (107,108). The insulin sensitivity increases while glucose levels, blood pressure and inflammation are reduced (107,109,110). The anti-inflammatory effect of PA is important in reducing the risk of several common diseases that are driven by a low-grade inflammation (111).

The physiological response to MVPA can be measured after a single session of exercise (acute response) or after longer periods of regular exercise (chronic response) (112,113). The acute biological response following MVPA depends on several factors such as the intensity and duration of the activity and the physical fitness of the individual (112,113). Individuals that have a higher fitness level can exercise at a higher intensity level and for a longer time, which increases the acute effects of the exercise session. According to the WHO, physical activity has a positive effect on all-cause mortality; cardiovascular disease mortality; the incidence of hypertension, type 2 diabetes, site-specific cancers, and mental health issues (reduced symptoms of anxiety and depression); an on cognitive health and sleep. Adiposity and lipid profiles may also be improved by exercise (114,115).

# Physical activity in hip and knee osteoarthritis

## Benefits and recommendations

In several aspects, PA is vital for individuals with hip and knee OA. Since synovial joint cartilage is avascular, its nutrient supply and metabolism relies on diffusion and the mechanical load/unload cycle in the joint (4). Consequently, cartilage requires loading to remain healthy (116). Immobilisation of a joint leads to atrophy of the cartilage (117,118) which might lead to a more rapid progress of OA (119). Voinier et al. (120) reported that both joint underloading and overloading might be associated with worsening damage to knee cartilage and suggests that a (theoretical) U-shaped relationship between PA and cartilage damage may exist.

PA is recommended in clinical guidelines as a part of non-surgical core treatment of hip and knee OA (90,91,121) Previous research has shown that any type of exercise programme can improve pain, physical function and quality of life in individuals with knee OA (122,123). The type of PA (land- or water-based) does not seem to matter (123). In Sweden, a combination of aerobic PA, strength training and functional exercises are recommended for individuals with hip and knee OA (124).

However, recent research comparing PA with other non-surgical treatments or placebo in the knee has shown similar beneficial effects for different treatments including placebo with saline injections on OA-related pain (125,126). A systematic review ranked PA as the superior treatment for knee OA, followed by nonsteroidal anti-inflammatory drugs and opioids but the differences in effect were small (126). Notwithstanding these recent findings, PA is also important in improving other health outcomes and in reducing the risk of diseases (114). The general international recommendation from WHO of 150–300 minutes of MPA or 75–100 min of VPA, or a combination of these per week also applies for individuals with OA. According to a longitudinal observational study, meeting the PA guidelines might also have a protective effect for radiographic OA progression in individuals with knee OA (127,128).

Global PA recommendations has also been translated into the number of required steps per day, where 7,000 steps to correspond to 150 min in MVPA per week (129). White et al.(130) also showed that walking <6,000 steps per day seemed to be a preliminary estimate to prevent functional decline in individuals with knee OA. A recent dose-response meta-analysis investigating the association between daily steps and all-cause mortality showed a non-linear association where >7,500 steps only rendered marginal health effects (131). Another study has shown linear associations between steps and cardiovascular disease markers up to 10,000 steps in a middle-aged population (132).

## **Physical activity levels in individuals with osteoarthritis**

Despite the beneficial effect of PA, previous research have shown that most individuals with hip and knee OA do not meet the recommended guidelines of at least 150 minutes of MPA or 75 minutes of VPA per week (133–136). A systematic review and meta-analysis reported that 58% of individuals with hip OA and 41% of individuals with knee OA engaged in PA >150 minutes/week although the quality of the evidence was low (133). Chang et al.(135) found that only 22% of the women and 44% of the men in a US cohort of 1,922 individuals who either had or were at risk of knee OA met the PA guidelines. A European study including individuals with knee OA from six countries showed that individuals with OA had lower PA levels and were less likely to reach recommended PA guidelines compared to individuals without OA. However, in Sweden, the study showed that the participants with OA from Sweden were equally as active as those without OA (136). Data from the Swedish BOA registry in 2019 showed that 38% of participants in SOASP (n =15,718) self-reported PA <150 min of MVPA/week (94).

## **Behavioural strategies to promote physical activity**

During the last decades, a large number of studies on methods and intervention to promote and increase PA in populations with musculoskeletal pain has been published (137,138). According to two systematic reviews, most interventions lead to little or no difference in PA levels compared to no or minimal intervention (137,138). Interventions containing only information and exercise classes might not be effective in changing individuals' PA behaviour (137). Adding behavioural strategies to PA interventions using behaviour change techniques (BCTs) might increase the effect of and adherence to the intervention (139–143). A BCT is defined as an “observable and replicable component designed to change behaviour” and can be used alone or in combination with several BCTs (144). Michie et al. (144,145) constructed a hierarchically-structured taxonomy of 93 BCTs clustered in 16 different areas. Examples of a few BCTs, their definition and practical implication are shown in Table 2 (146).

**Table 2. Examples of Behaviour Change Techniques Taxonomy v 1: 93 hierarcically clustered techniques.**

Number	Label	Definition	Examples
<b>1.</b>	<b>Goals and planning</b>		
1.1	Goal setting	Set or agree on a goal defined in terms of the behaviour to be achieved.	A walking goal of 6000 steps/day.
<b>2.</b>	<b>Feedback and monitoring</b>		
2.2	Feedback on behaviour	Monitor and provide informative or evaluative feedback on performance of the behaviour.	Inform the person of how many steps they walked each day (as recorded on a pedometer).
2.3	Self-monitoring of behaviour	Establish a method for the person to monitor and record their behaviour(s) as part of a behaviour change strategy.	Use a pedometer and a form for recording daily total number of steps.
<b>7.</b>	<b>Associations</b>		
7.1	Prompts/cues	Introduce or define environmental or social stimulus with the purpose of prompting or cueing the behaviour. The prompt or cue would normally occur at the time or place of performance	Put a sticker on the bathroom mirror to remind people to brush their teeth. Receive reminders to move from an app.

A review study conducting a meta-regression found that interventions using the BCT ‘self-monitoring’ in combination with other self-regulatory techniques (‘intention formation’, ‘goal setting’, ‘feedback on performance’ and ‘review of behaviour goal’) are the most effective BCTs in promoting PA and healthy eating (145). Regarding increased adherence to PA in an OA population, ‘behavioural contract’, ‘non-specific reward’, ‘patient-led goal setting’, ‘self-monitoring’ and ‘social support’ were the most effective BCTs (142).

## Mobile Health and activity monitoring

In recent decades, BCTs have been utilized in technology-based behavioural change interventions and the number of studies published annually has increased from 2 in 2001 to 95 in 2018 (147). Some of these technology-based interventions utilize Mobile Health (mHealth) which is a part of electronic Health (eHealth). mHealth has been defined as “*a medical and public health practice supported by mobile devices such as mobile phones, patient monitoring devices, personal digital assistants and other wireless devices.*” (146, p. 6). Some of these wireless devices can be used to measure and monitor PA (149).

## Wearable activity trackers

Wearable activity trackers (WATs) are wireless devices often worn on the wrist as a watch (Figure 7). They are produced by several commercial manufactures, such as Nike, Fitbit, and Garmin, and common functions include step counting, distance, heart rate, stairs climbed, minutes in different activity levels, sleep tracking, etc. (150). The feature of the WAT depends on the kind of device. One simple WAT is the pedometer, a spring-levered step counter which has been used for a long time to measure steps and distance (151).

Today, most WATs are accelerometer-based which enables a more comprehensive measurement of PA (152). The accelerometer-based WAT use a piezoelectric triaxial accelerometer which can detect acceleration in three different dimensions (149). The output from an accelerometer consists of *counts* in the three different dimensions. A higher number of *counts* means a higher level of acceleration/intensity of the measured activity (152). In commercial accelerometers, the counts are already transformed and presented to the user as steps, distance, and active minutes (149). These outputs are based on pattern recognition and algorithms that are unknown to the users (151).



Figure 7. Examples of wearable activity trackers (Picture by Eliza Lake from Pixabay.com)

A commercial wrist-worn WAT is often connected to the manufacturer's app on the user's smartphone, tablet, or computer (150). In the app, the user can change the settings, enter a step or activity goal, and monitor their PA, heartrate, and other

features. Some WATs have a display and others do not. The features of various WATs and their associated apps can differ significantly depending on the manufacturer and WAT model. In general, WATs utilize several BCTs that can be effective in promoting PA such as ‘self-monitoring’, ‘goal setting’, ‘feedback on performance’ and ‘facilitating social comparison’ (153,154).

#### *Effects of monitoring physical activity*

The use of and research on WATs have both increased rapidly during the last decade (155). WATs are popular in interventions to increase/support PA and other health outcomes in different populations in most studies published after 2015 (156). A recent systematic review and meta-analysis included 48 published articles and showed that interventions using WATs significantly increased the number of daily steps and weekly MVPA, but that the effect was dependent on the user and type of intervention (156). The results from another systematic review and meta-analysis that only included interventions that had used a Fitbit device showed an increase in steps and time in MVPA (157). That result is in line with the results from other reviews on WATs in different populations (158–162). In the review by Oliveira et al. (158) mobility was also reported to improve in interventions using WATs.

The effect of WAT-use on PA in populations with OA have also been explored previously. A systematic review and meta-analysis on WATs to support PA in individuals with musculoskeletal and rheumatic diseases also showed that WAT use increased steps per day and time spent in MVPA (163). In addition, a high short-term adherence to WAT use was reported in the review. Research on WAT use and the potential effect on work ability and work productivity in a working population with hip and knee OA is, to our knowledge, lacking.



# Rationale

When the initial plan for this project was designed, mHealth and activity monitoring with WATs had started to be used more frequently in interventions aimed at improving health outcomes in different populations. Since then, there has been a considerable increase in the use of mHealth in intervention and research projects (147).

Previous research has shown that the prevalence of hip and knee OA is increasing worldwide and that individuals with OA have more comorbidities and worse work ability than the healthy population (30,58,78). PA has been and still is recommended as a vital part of the core treatment of OA (90,91,121). In addition, the general recommendation from WHO regarding PA also applies to individuals with hip and knee OA (114). However, this population, in general, does not seem to reach the recommended levels of PA (135).

In the early phases of planning this project, technical solutions to monitor and support PA had begun to emerge as a promising method (164). However, knowledge about the effect of activity monitoring with more advanced WATs in OA population was lacking. Only a few studies using simple pedometers in interventions had been published (163). In addition, information about OA individuals' experiences of and adherence to using a WAT was lacking.

The rationale and design for the fourth study of this thesis were developed in collaboration with Assoc Prof André Struglics, a molecular biomarker researcher within the OA field at Lund University. Molecular biomarkers have shown potential to be used in evaluating the progress of the disease and the effect of PA in individuals with hip and knee OA, but the relationship between PA and biomarkers in this population merits further exploration (165).

# Aims

## The overall aim

The overall aim of this thesis was to obtain knowledge of the impact of mHealth and PA on work ability, health, and molecular biomarkers and to explore experiences of mHealth in individuals of working age with hip and knee OA.

## Specific aims of the four studies

- I. To describe PA patterns and adherence to using a WAT, (Fitbit Flex 2) among individuals of working age with hip and knee OA during a 12-week period. A secondary aim was to explore the correlation between baseline self-reported function and subsequent PA.
- II. To examine the effects of adding self-monitoring PA with a WAT to SOASP on work ability and the secondary objectives of PA and work productivity among individuals of working age with hip and knee OA compared to SOASP only.
- III. To explore the experience of using a WAT to monitor PA and the general perceptions of digital support in individuals of working age with hip and knee OA.
- IV. To explore the associations between PA or self-reported joint function and molecular biomarkers of cartilage and inflammation in individuals of working age with hip and knee OA.

# Methods

## Setting

The main setting for this project is a cluster-randomised controlled trial (C-RT) conducted in southern Sweden, which recruited participants living in the counties Skåne and Halland. The recruitment of participants was initiated in autumn 2017. Participants were initially recruited through health care centres or physiotherapy (PT) clinics that offered SOASP. SOASP has been described more extensively in the introduction of this thesis but, in essence, it is the recommended core treatment for OA (hip, knee, and hand) in Sweden and consists of lectures about OA, exercise, and self-management. These lectures are often succeeded by PT-led group training or home-based exercises.

## Study design and timeline

All participants in this project took part in the C-RCT and were recruited continuously from October 2017 to May 2019. Figure 8 illustrates a timeline of the project. Three of the studies in the project are of quantitative design (I, II, IV) and one is qualitative (III).

Study I is an exploratory longitudinal study analysing 12 weeks of WAT data from participants in the intervention group of the C-RCT. Data for this study was collected from October 2017 to August 2019.

In Study II, the C-RCT, the addition of 12 weeks of PA self-monitoring with a WAT to SOASP was compared with participating in SOASP alone. Data was collected at baseline and at three follow-ups from November 2017 to May 2020.

Study III has a qualitative design and explores participants' experiences and perceptions of WAT use and digital support. The data was collected in three focus group discussions taking place in November to December 2019. Participants in this study had taken part in the C-RCT intervention.

Study IV encompasses an exploratory longitudinal design including participants from the C-RCT's intervention and control groups. In this study, data was collected from October 2018 to August 2019.

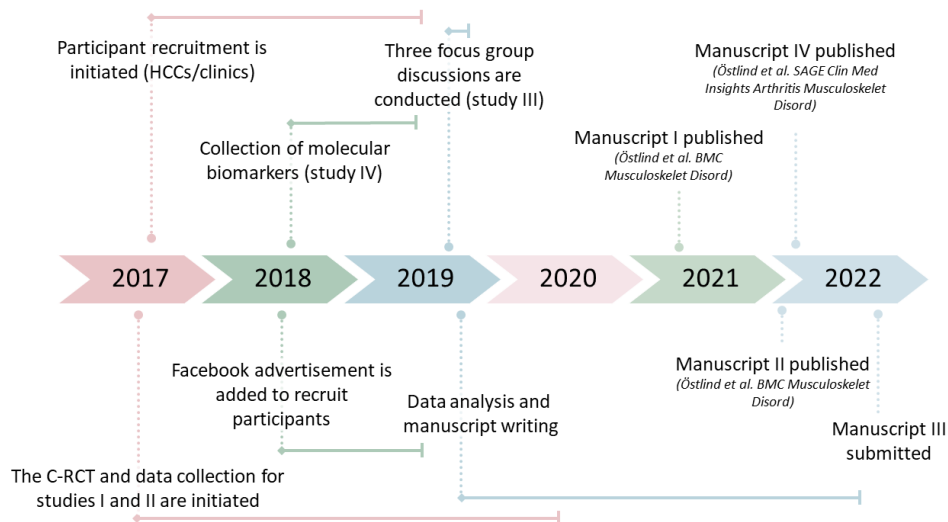


Figure 8. Timeline of the project process.

## Participants and recruitment

Eligible for participation in this project were individuals of working age with hip and knee OA living in Skåne or Halland. The inclusion criteria for the C-RCT were working  $\geq 50\%$  (20 hours/week), aged between 18 and 67 years, who were able to understand Swedish in speech and writing, and who were able to participate in PA. Furthermore, having access to a smartphone, tablet or computer and being able to wear a WAT for 12 weeks was necessary. Before the recruitment of participants was initiated, a project website was created. The website contained information about the project and was designed to enable participant self-registration and informed consent via an electronic identification service (166).

Since SOASP is a part of the core treatment for hip and knee OA in Sweden, we decided to recruit individuals that participated in the SOASPs in southern Sweden. We used the 2015 annual report from the BOA registry to inform us about centres/clinics in Skåne and Halland with the highest number of registered individuals that had participated in the SOASP in 2015 (167). In the next step, we contacted PTs at centres/clinics with  $>30$  registered participants in 2015, who were then informed about the project and asked if they could assist in recruiting individuals. The PTs that agreed to aid in the recruitment process were asked to inform EÖ about upcoming SOASPs by e-mailing dates.

EÖ or the PT responsible for the SOASP then informed participants about the project. The information was delivered orally and took place at one of the lectures in the SOASP. Written information about the project and how to register was handed out to individuals that met inclusion criteria. In the information letter, there was a code with the name of the centre together with a number; e.g., “Carecentre2”. Those interested in participating in the project were asked to self-register and enter that code so that they could be recognised in the project’s server. Additional centres/clinics were added during the recruitment period, resulting in a total of 32 centres/clinics in Skåne and Halland, of which 18 contributed participants. The recruitment process is presented in Figure 9.

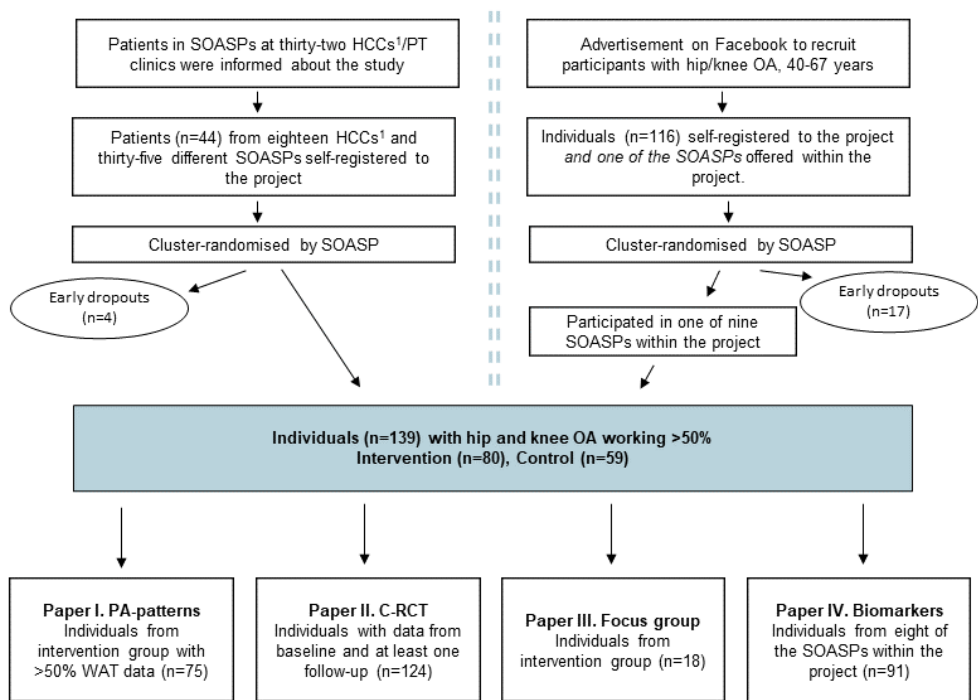


Figure 9. Flowchart of the recruitment process.

The recruitment rate from health care centres was low, and <30 individuals were enrolled after six months of multicentre recruitment. We decided to use an advertisement on Facebook and to post information on Lund University’s webpage. The advertisement reached individuals between 40–67 years living within a specified geographical area in Skåne. There were two reasons for the limitations in the advertisement: first, the number of individuals reached by the advertisement needed to be narrowed down and few individuals below 40 years of age have OA.

Secondly, potential participants needed to be able to travel to the health care centre where the SOASPs within the project were held. This method of recruitment was more effective compared to the original method. Since the previously recruited individuals had participated in the SOASP at health care centres or PT clinics, individuals enrolled through the Facebook advertisement were also offered SOASP held within the project. These SOASPs consisted of three lectures; EÖ held two and a third lecture was held by an OA communicator. Nine SOASPs were given within the project.

After early dropouts (n =21) left due to various personal reasons, 139 participants were included in the project (Table 3).

**Table 3. Participant characteristics at baseline.**

	n	Intervention (n =80)	Control (n =59)	Total (n =139)
<b>Age (years), mean (SD)</b>	138	56.6 (0.6)	55.3 (0.8)	56.1 (5.7)
<b>Sex, female, % (n)</b>	139	86.3 (69)	72.9 (43)	80.6 (112)
<b>Married or living with partner, % (n)</b>	138	75.9 (60)	71.2 (42)	73.9 (102)
<b>Education (postsecondary), % (n)</b>	138	67.1 (53)	55.9 (33)	62.3 (86)
<b>Most affected joint, % (n)</b>	139			
Hip		22.5 (18)	27.1 (16)	24.0 (34)
Knee		77.5 (62)	72.9 (43)	76.0 (105)
<b>Physically demanding work, % (n)</b>	138			
No		68.4 (54)	72.9 (43)	70.3 (97)
Yes, several times a week		10.1 (8)	15.3 (9)	12.3 (17)
Yes, daily		19.0 (15)	11.9 (7)	15.9 (22)
<b>Regular use of a WAT during the last three months before this project, % (n)</b>	133	42.7 (32)	34.5 (20)	39.1 (52)
<b>Present physical activity compared to before OA, % (n)</b>	137			
More physically active		10.3 (8)	15.3 (9)	12.4 (17)
Less physically active		56.4 (44)	50.8 (30)	54.0 (74)
Equally physically active		33.3 (26)	33.9 (20)	33.6 (46)
<b>WAI, categorical, % (n)</b>	130			
Poor (7–27 points)		3.9 (3)	1.9 (1)	3.1 (4)
Moderate (28–36)		18.4 (14)	25.9 (14)	24.6 (28)
Good (37–43)		43.4 (33)	25.9 (14)	36.2 (47)
Excellent (44–49)		34.2 (26)	46.3 (25)	39.2 (51)
<b>IPAQ, categorical, % (n)</b>	124			
Low		20.0 (14)	13 (7)	16.9 (21)
Moderate		35.7 (25)	42.6 (23)	38.7 (48)
High		44.3 (31)	44.4 (24)	44.4 (55)

\*Proportions are presented as valid percent, not including missing values.

SD: standard deviation; WAT: wearable activity tracker; OA: osteoarthritis; WAI: Work Ability Index

IPAQ: International Physical Activity Questionnaire

### *Participants and recruitment in studies III and IV*

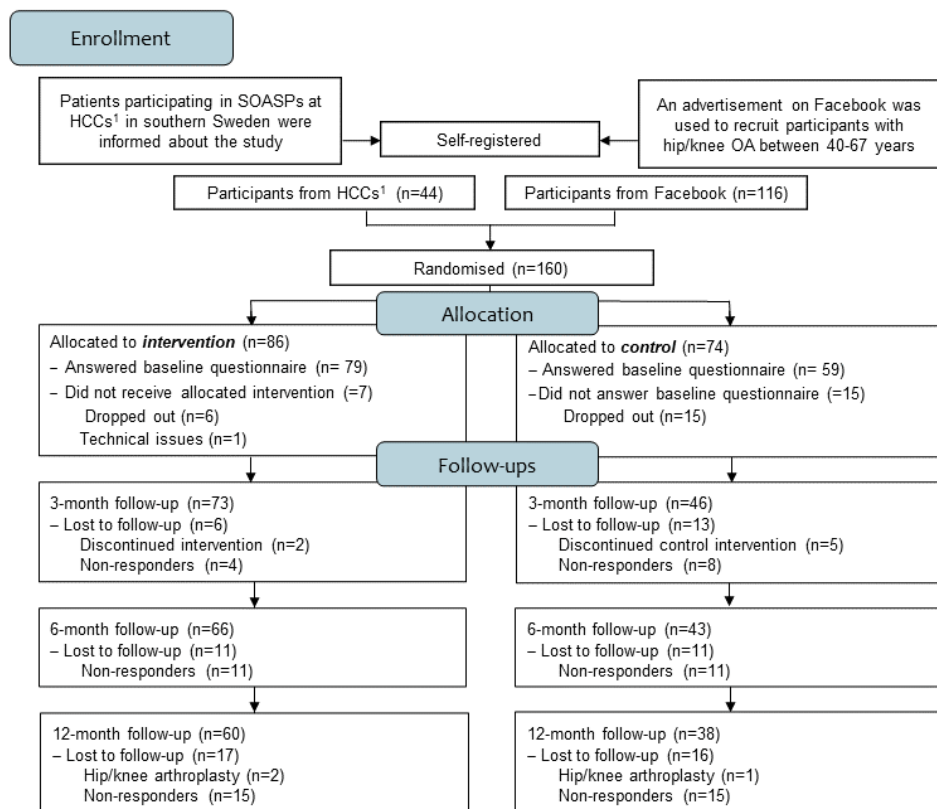
A combination of purposive and convenience sampling methods were used to recruit participants to the focus group study (III) (168). Participants from the intervention group in the C-RCT that took part of the intervention in 2019 were approached by e-mail in autumn 2019 (n =57) and asked to share their experiences using WATs and their perceptions of digital support in OA care. Twenty individuals agreed to participate in the three focus group discussions. Two individuals dropped out due to unforeseen reasons and consequently, eighteen individuals eventually participated in the discussions.

Participants in Study IV were all recruited via the Facebook advertisement and participated in both groups of the C-RCT. Nine SOASPs were given within the project and participants from the eight first SOASPs were included in Study IV (n =91). Fifty-six participants were randomised to the intervention group of the C-RCT and 35 to the control group.

### **Randomisation**

A randomisation 1:1 plan was generated from randomization.com. Block randomisation was used since the final number of randomisations needed was unknown. Seven blocks and 128 sealed envelopes (64 control and 64 intervention) were generated in total. EÖ handled the randomisation plan and EEH handled the sealed envelopes.

Each SOASP (from centres or within the project) was seen as a cluster and randomised as such. When EÖ received/decided the start date for upcoming SOASPs, a sealed envelope was used to randomise the SOASP to control or intervention. Hence, the SOASPs were consecutively randomised in date order. A total of 125 sealed envelopes were used; 63 SOASPs were randomised to intervention and 62 were randomised to control. The randomisation took place before participants were informed and recruited. The participants were informed about group allocation after they had self-registered to the project. Neither participants nor authors were blinded after the allocation to control or intervention. Figure 10 illustrates the progress through the phases of the C-RCT; enrolment, randomisation, and data collection, according to CONSORT guidelines (169).



<sup>1</sup> Health care centers

Figure 10. Flow of participants and progress of the cluster-randomised controlled trial.

## Intervention

The C-RCT intervention (Study II) entailed self-monitoring PA with a WAT (a Fitbit Flex 2) for 12 consecutive weeks in addition to participating in the SOASP. The Fitbit Flex 2 is a wrist-worn commercial WAT that tracks and measures steps, distance, active minutes, energy expenditure and sleep. The device was connected to the Fitbit app, where participants created an account and entered personal information such as age, sex, weight and height. At the time of data collection in this project, the Fitbit app had default activity goals which could be manually altered. The default step goal was 10,000 steps per day but we decided to change this to 7,000 daily steps. This was changed due to the results from previous research showing that 7,000-8,000 steps might be equivalent to 150 minutes in MVPA per



week (129). It was also changed to make the step goal more more achievable for participants.

The Fitbits, together with instructions on installment and usage were given consecutively to the individuals in the intervention group at the time of their participation in the SOASP. In a few cases, the Fitbits, together with information, were sent by mail. A personal account was created for each participant and a step goal of 7,000 steps was entered. The participants gave informed consent (electronic identification) to transfer data from the Fitbit to the projects' servers.

Participants were asked to monitor their activity by using the app on a daily basis. An example of a Fitbit app interface is illustrated in Figure 11. They were also asked to wear the Fitbit from morning to bedtime and to remember to charge the device when needed (approximately two times a week).



Figure 11. Example of the Fitbit app interface. (Picture from Fitbit.com).

## Data collection and outcomes

We collected data using several different methods. Activity data was collected from the Fitbits used by the participants in the intervention group. Self-reported data on work ability, PA, work productivity, and joint function were collected via questionnaires at baseline and follow-up at 3, 6 and 12 months. Focus group discussions were conducted to collect data on participants' experiences and perceptions of WAT use and digital support. Lastly, molecular biomarkers in patient serum were collected from blood samples taken at baseline and follow-up at three months.

### Study I

The outcomes in Study I were WAT-measured activity data, adherence to the WAT, and self-reported joint function. We obtained the activity information from the Fitbit's Web API, which allows third parties to access activity information from Fitbit devices (170). The information requested from the Fitbit's Web API were the number of steps and number of minutes in light, moderate, and vigorous activity for every minute of the previous day. Fitbit uses a proprietary algorithm to define the intensity of PA according to METs. MVPA or "active minutes" were achieved if an activity lasted more than 10 minutes and exceeded 3 METs (171). The validity and reliability of the Fitbit Flex and Fitbit Flex 2 has shown that the WATs overestimate the number of steps and time in MVPA compared to the actigraph commonly used in research (172–174). Adherence to Fitbit use was also collected where all days with >1,500 steps were seen as valid days and days with <1,500 steps were seen as missing.

Self-reported joint function was measured using the Hip Osteoarthritis and disability Outcome Score (HOOS) (175) for the participants with hip OA or Knee Osteoarthritis and injury Outcome Score (KOOS) (176) for those with knee OA. The HOOS/KOOS were provided in the questionnaire with the other self-reported outcomes in this project at baseline and at follow-up after 3, 6 and 12 months. HOOS/KOOS consists of several subscales: *Pain*, *Symptoms*, *Activities of Daily Living (ADL)*, *Sport and Recreating function (sport/rec)* and *hip/knee-related Quality of Life (QoL)* (175,176). Each subscale is separately calculated, with 0 indicating extreme symptoms and 100 indicating no symptoms (177). HOOS/KOOS have shown adequate psychometric qualities for individuals with OA (178,179). Only baseline HOOS/KOOS was used in Study I.

## Study II

Online questionnaires created in Sunet Survey were sent to participants' e-mails at baseline, and at follow-up after 3, 6 and 12 months. The questionnaires comprised self-reported instrument and questions about participant characteristics, their work, and PA.

The primary outcome variable of work ability was measured with the Work Ability Index (WAI), which contains questions about health, work demands, and sick leave (180). Higher WAI score indicate higher work ability and it can also be categorized into four different categories; poor, moderate, good, and excellent (181). It has shown acceptable predictive validity and test-retest reliability (182,183).

The two secondary outcome variables of PA and work productivity were measured with the International Physical Activity Questionnaire - Short Form (IPAQ-SF) (184) and Work Productivity and Activity Impairment Scale: Osteoarthritis (WPAI:OA) (185). IPAQ-SF is comprised of nine questions about time spent in moderate and high intensity, walking, and time spent sedentary in the last 7 days. The results were calculated according to the IPAQ-SF scoring protocol (186) and the outcome are MET-minutes/week and PA category score (low, moderate, or high). Only MET minutes were used in the analyses. WPAI:OA entails questions about OA-related work productivity, absence from work, and impairment during activities. Results were calculated and generated four types of scores: 1. *Absenteeism* (work time missed), 2. *Presenteeism* (impairment at work/ reduced on-the-job effectiveness), 3. *Work productivity loss* (overall work impairment/ absenteeism plus presenteeism), 4. *Activity impairment* (187).

Self-reported instruments on joint function and health-related quality of life were also filled out as a part of the questionnaires but not used in Study II.

## Study III

Three focus group discussions with EÖ serving as a moderator and KS or EEH as assistants were conducted. A questioning route (188) was used with questions about experiences of using a WAT and general perceptions of digital support and mHealth in OA care. The questioning route consisted of (mainly open-ended) opening question, introductory questions, key questions and ending questions. Participants were encouraged to discuss among themselves and not with the moderator. The discussions were audio-recorded and transcribed verbatim. At the end of each discussion, the assistant verbally summarized the content of the discussion and allowed the participants to comment or add information.

## Study IV

Baseline serum samples were collected in conjunction with one of the lectures in the SOASPs offered within the project and a follow-up sample was collected after three months. They were collected at the health care centre where the lectures took place and analysed at the Biomedical Centre (BMC) at Lund University, Sweden.

Molecular biomarkers of cartilage (ARGS-aggrecan, C2C and COMP) and inflammation (CRP) were analysed. ARGS-aggrecan was quantified using electrochemiluminescence on Meso Scale Discovery platform (189), and COMP and C2C were quantified using enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's instructions. Serum CRP were quantified using Cobas platform's accredited method.

Self-reported data on joint function (HOOS or KOOS) collected in the online questionnaires at baseline and at follow-up after three months were used in Study IV. A more detailed description of this data collection is provided in Study I. WAT data from participants in the intervention group and self-reported data from the IPAQ-SF were also outcomes in Study IV. This data was also used in Study I and Study II and data collection is therefore described previously.

## Analyses

In this thesis, several different types of data have been collected and different types of analyses have been utilized. Three of the papers used quantitative research methods and one paper used qualitative methods. All statistical analyses were conducted using SPSS versions 25–27 (IBM Corp., Armonk, NY). The statistical significance level, alpha, was set to 0.05 in Studies I, II and IV. Descriptive statistics were presented as mean and standard deviation (SD), median and interquartile range (IQR), or proportions (%).

## Studies I and II

### *Sample size*

A sample size calculation was made for Study II with a power of 80% and a two-tailed significance level of 0.05. The calculation was based on the primary outcome variable of 'work ability' measured via WAI. Effect sizes (between-group differences) were based on SD reported in previous studies (74,190) with the assumption of 0.45 SD as the minimal clinically-important difference (191). The sample size calculation showed that approximately 80 individuals per group were needed. Studies I and IV were of an exploratory design and therefore no sample size calculations were made.

In Studies I and II, data was measured several times for each individual and linear mixed models (192) were used as the primary statistical method to analyse the data. In Study I, the number of steps and minutes in light PA (LPA) and MVPA per day during the 12-week intervention were analysed to explore the PA-pattern over time. The WAT-use calculated as percent of valid days per week was also analysed to explore adherence to the Fitbit. The linear trend shown as the (unstandardized)  $\beta$ -coefficient represents the average change per week during the 12-week period. The association between PA-data from WATs and self-reported data from HOOS/KOOS were also assessed using Spearman's rank correlation.

In Study II, data from WAI, IPAQ-SF and WPAI:OA were analysed. Data from IPAQ-SF and WPAI:OA were non-normally distributed and therefore log-transformed before the analyses. A linear mixed model was conducted with a first-order autoregressive covariance structure to examine the effect of the intervention on the outcomes from baseline to the follow-up questionnaires at 3, 6 and 12 months. Group and time were added as fixed factors and the interaction group\*time was added to assess the difference in pattern of change between the two groups. The differences between baseline and each follow-up for the three outcomes were also calculated and Analysis of Covariance (ANCOVA), with adjustments for the baseline value, was used to analyse the difference between baseline and each follow-up for WAI, IPAQ-SF and WPAI:OA (193). Mean adjusted differences and confidence intervals (CI) were calculated.

### **Study III**

Qualitative content analysis using an inductive approach was applied to the data from the focus group discussions in Study III (194). All three transcribed focus group discussions were seen as a single unit of analysis, and they were read through several times by two of the authors (EÖ and KS). The software program NVivo (realised 2020) was used in the organization and coding process. Similar codes were grouped in sub-categories and similar sub-categories were grouped into main categories. Significant quotes were chosen to represent the different sub-categories.

### **Study IV**

The differences between the baseline values and the 3-month follow-up values for molecular biomarkers, self-reported PA (IPAQ-SF), and self-reported function (HOOS/KOOS) were calculated. The variables were, in general, non-normally distributed and the Spearman's rank correlation was therefore used to evaluate the association between the variables. Fifty-three participants also had WAT-data and the association between the mean number of steps per day and the molecular biomarkers at three-month follow-up were also evaluated using Spearman's rank correlation.

## Ethical considerations

The studies included in this thesis are all conducted as clinical research and several ethical considerations have been made in different phases of the project. All participants were included in the C-RCT, in Study II. The participants in the intervention group were not exposed to anything that was directly harmful, but WAT use may have some negative effects. To not be able to reach one's activity goal due to pain or other reasons might lead to feelings of discouragement for the user (195). Also, a rapid increase in the number of steps per day could lead to an increase in perceived pain. However, individuals that self-registered to the project received information that they should seek care at their health care centre if they experienced additional pain during their participation in this project. They could also always contact EÖ.

Another ethical consideration was that the participants had to create a Fitbit account and that the US-based company Fitbit gained access to their personal information and activity information. This was not optimal, but participants were aware of this and gave their consent using electronic ID. Moreover, nowadays it is probably more the rule than the exception that people share information with a plethora of different companies.

Participation in this project was voluntarily, participants self-registered and there was no patient–clinician contact between EÖ and the individuals that chose to register. In general, we believe that the benefits outweighed the small risks of harm in this project. Most participants were offered to take part in SOASP and those in the intervention group were provided with a WAT for three months. All participants received the core treatment in OA.

## Ethical approval

The methods used in the studies in this thesis were performed in accordance with the WMA declaration of Helsinki (196). All participants received written information about the study and provided their informed consent with an electronic identification service before registering. There are ethical approvals for all four studies included in this thesis. Studies I and II were approved in 2017 by the Regional Ethical Review Board in Lund, Sweden (2017/596). In 2018, we also applied to recruit participants using a Facebook advertisement, to add additional questions to the intervention group, and to measure molecular biomarkers (Study IV). This was approved by the Regional Ethical Review Board in Lund, Sweden (2018/593 and 2019/00594). In 2019, we sought and received ethical approval for Study III from the Swedish Ethical Review Authority (2019-03691).

# Results

## Studies I and II: Physical activity levels and the effects of using an activity tracker

### *Study I*

Participants in the intervention group of the C-RCT walked on average of 10,593 steps per day (SD 3,431) during the 12 weeks. The mean number of daily steps decreased slightly (but statistically significantly) during the 12 weeks, by 117 steps per week ( $\beta$ -coefficient  $-117$  [95% CI  $-166$  to  $-68$ ]  $p = < 0.001$ ). The highest number of daily steps was observed in week 2, at 11,162 (SD 3,830) steps and the lowest in week 11, at 9,589 (SD 3,169) steps (Figure 12).

The participants spent on average 48.1 (SD 35.5) minutes in MVPA per day during the intervention. Time spent in MVPA decreased gradually and statistically significantly over time (Figure 13). The decrease in daily MVPA was small, at 0.6 minutes/day per week ( $\beta$ -coefficient  $-0.6$ , [95% CI  $-1.01$  to  $-0.16$ ],  $p = 0.008$ ).

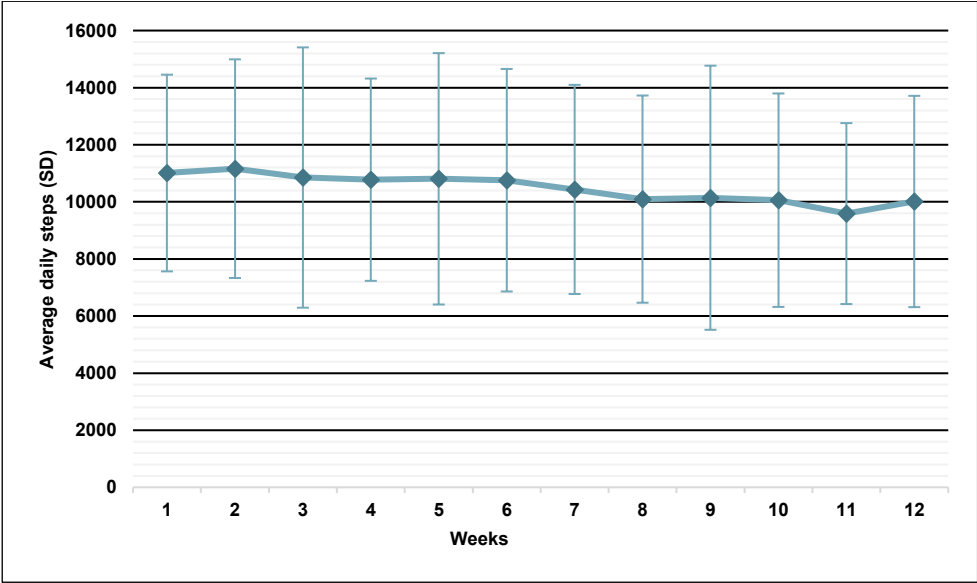


Figure 12. Mean (SD) daily steps for each week during the 12 week intervention (n =75).

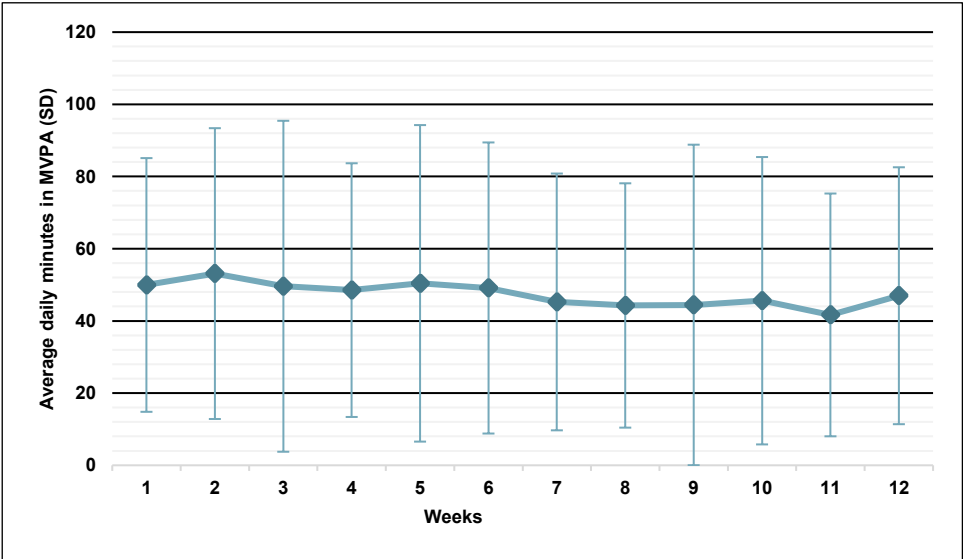


Figure 13. Mean (SD) daily minutes in moderate-to-vigorous physical activity (MVPA) for each week during the 12 week intervention (n =75).



A similar pattern was seen regarding adherence to WAT use (Figure 14). The WAT was used, on average, 88.4 % (SD 11.6) of the intervention period with the highest mean adherence in week 2 (94.7%) and the lowest in week 12 (80.5%). The adherence gradually but slightly decreased over the 12 weeks ( $\beta$ -coefficient  $-1.3$ , [95% CI  $-1.8$  to  $-0.8$ ],  $p = <0.001$ ).

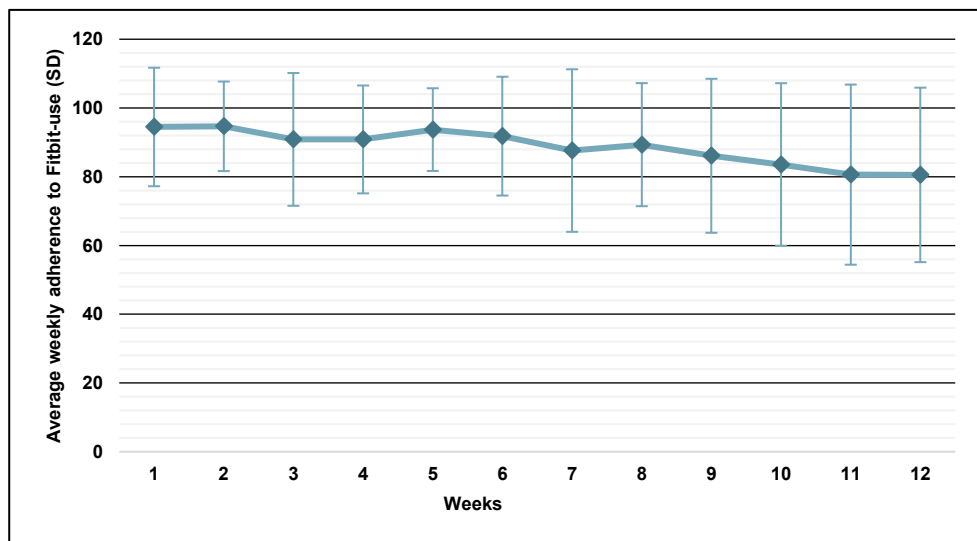


Figure 14. Mean weekly adherence to WAT-use for each week during the 12 week intervention (n =75).

There were no statistically significant correlations between HOOS/KOOS subscales at baseline and PA (mean number of steps/day and minutes in LPA and MVPA/day) during the 12-week intervention.

### Study II

A majority of the participants had good or excellent work ability at baseline, as measured via WAI, and were moderately or highly physically active according to IPAQ-SF (Table 3, baseline characteristics). The linear mixed model showed no statistically significant interaction between *group\*time* for the primary outcome of work ability ( $p = 0.948$ ). There was also no significant interaction for the secondary outcome variables of PA and three out of the four scores in WPAI:OA measuring work productivity. There was, however, a statistically significant effect for *group\*time* for the WPAI:OA score *presenteeism*.

The results from the ANCOVA with adjustments for baseline values showed no statistically significant between-group differences regarding change in work ability or PA for any of the periods (baseline to 3, 6 or 12 month). There was a statistically significant difference between the groups regarding change from baseline to 3

months for WPAI:OA *presenteeism* and *work productivity loss* but not regarding change from baseline to the 6 or 12 month follow-ups. For the other two WPAI:OA scores, *absenteeism* and *activity impairment*, there were no statistically significant differences in changes. The results from the ANCOVA are presented in Tables 4 and 5.

**Table 4. Work ability and physical activity at all measurements. Changes within and differences between the groups from baseline to follow-ups.**

OUTCOME	INTERVENTION		CONTROL		BETWEEN GROUP DIFFERENCES	
	Mean (SD)	Adj.* change from baseline; mean [95% CI]	Mean (SD)	Adj.* change from baseline; mean [95% CI]	Adj.* difference; mean [95% CI]	p
<b>WAI</b>						
Baseline	40.1 (6.3)	n/a	41.6 (6.8)	n/a	n/a	n/a
3-month	39.4 (7.3)	-0.6 [-1.9, 0.6]	41.0 (6.9)	-0.8 [-2.4, 0.8]	0.2 [-1.8, 2.1]	0.877
6-month	39.1 (7.4)	-1.0 [-2.1, 0.2]	41.2 (6.2)	-1.4 [-2.8, 0.0]	0.4 [-1.4, 2.2]	0.650
12-month	40.1 (6.4)	-0.6 [-1.7, 0.6]	40.2 (7.3)	-1.0 [-2.5, 0.4]	0.5 [-1.4, 2.3]	0.618
<b>MET-minutes/week</b>						
Baseline	3167 (2410)	n/a	2654 (1817)	n/a	n/a	n/a
3-month	3471 (2395)	<b>647 [146, 1148]</b>	2864 (1908)	-95 [-698, 509]	741 [-44, 1526]	0.064
6-month	3319 (2527)	365 [-191, 921]	2918 (1809)	139 [-530, 808]	226 [-653, 1104]	0.611
12-month	2774 (2114)	-3 [-511, 505]	2636 (1714)	-136 [-763, 491]	133 [-679, 945]	0.745

Analysis of Covariance (ANCOVA) were performed to analyse the difference between the groups regarding change.

SD: standard deviation; CI: confidence interval; WAI: Work Ability Index; MET: Metabolic Equivalent of Task (from IPAQ-SF: International Physical Activity Questionnaire-short form

\*Adjusted for baseline values.

**Table 5. Work productivity at all measurements. Changes within and differences between the groups from baseline to follow-ups.**

OUTCOME	INTERVENTION		CONTROL		BETWEEN GROUP DIFFERENCES	
	Mean (SD)	Adj.* change from baseline; mean [95% CI]	Mean (SD)	Adj.* change from baseline; mean [95% CI]	Adj.* difference; mean [95% CI]	p
<b>Absenteeism</b>						
Baseline	2.4 (14.1)	n/a	0.0 (0.0)	n/a	n/a	n/a
3-month	1.2 (6.9)	-0.6 [-2.3, 1.0]	0.3 (2.2)	-1.1 [-2.9, 0.7]	0.5 [-2.0, 2.9]	0.711
6-month	3.1 (12.1)	1.1 [-1.8, 4.0]	0.7 (2.9)	-0.9 [-4.4, 2.7]	2.0 [-2.6, 6.6]	0.390
12-month	3.8 (13.7)	2.1 [-1.5, 5.6]	1.7 (8.7)	0.2 [-4.3, 4.6]	1.9 [-3.8, 7.6]	0.508
<b>Presenteeism</b>						
Baseline	19.7 (25.7)	n/a	18.7 (24.9)	n/a	n/a	n/a
3-month	11.8 (20.2)	-8.1 [-13.1, -3.1]	19.8 (28.6)	3.1 [-3.1, 9.4]	-11.3 [-19.3, -3.2]	<b>0.006</b>
6-month	16.5 (24.6)	-2.8 [-8.8, 3.2]	13.9 (22.9)	-3.2 [-10.1, 3.7]	0.4 [-8.7, 9.5]	0.934
12-month	14.2 (20.8)	-0.5 [-5.8, 4.9]	18.9 (25.4)	4.2 [-2.3, 10.7]	-4.6 [-13.1, 3.8]	0.277
<b>Work productivity loss</b>						
Baseline	18.6 (24.9)	n/a	18.0 (24.7)	n/a	n/a	n/a
3-month	15.0 (22.5)	-6.1 [-12.1, -0.2]	18.9 (26.5)	3.2 [-3.5, 9.9]	-9.3 [-18.3, -0.4]	<b>0.042</b>
6-month	19.5 (26.9)	0.4 [-5.8, 6.7]	12.6 (19.9)	0.1 [-7.6, 7.8]	0.3 [-9.7, 10.3]	0.947
12-month	16.3 (24.8)	2.1 [-2.9, 7.2]	18.8 (23.6)	5.0 [-1.3, 11.3]	-2.9 [-10.9, 5.2]	0.481
<b>Activity impairment</b>						
Baseline	30.9 (24.7)	n/a	28.8 (23.4)	n/a	n/a	n/a
3-month	26.6 (27.0)	-4.4 [-9.5, 0.7]	26.1 (25.9)	-3.7 [-10.0, 2.7]	-0.7 [-8.8, 7.5]	0.868
6-month	35.6 (31.4)	5.9 [-0.7, 12.4]	25.1 (25.4)	-3.0 [-10.8, 4.8]	8.8 [-1.4, 19.0]	0.089
12-month	29.0 (29.4)	0.7 [-4.9, 6.3]	22.9 (21.0)	-3.3 [-10.3, 3.8]	4.0 [-5.0, 13.0]	0.382

Analysis of Covariance (ANCOVA) were performed to analyze the difference between the groups regarding change.

SD: standard deviation; CI: confidence interval; WPAI/OA: Work Productivity and Activity Impairment scale: Osteoarthritis

\*Adjusted for baseline values.

## Study III: Experiences and perceptions of Mobile Health and activity tracker use

In the analysis process, two main categories were identified; *WATs may aid in optimization of PA, but is not a panacea* and *Digital support is an appreciated part of OA care*. The main categories and their sub-categories are presented in Figure 15.

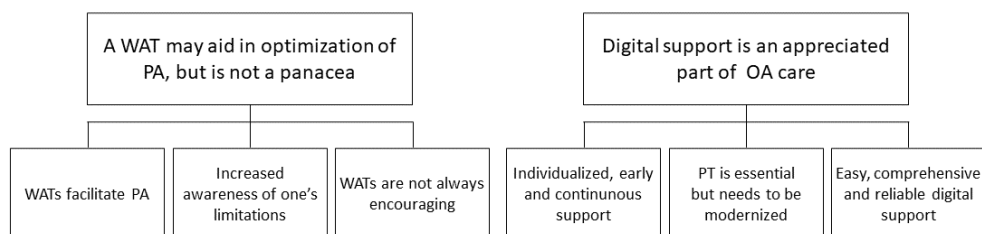


Figure 15. Main categories and sub-categories.

### *WATs may aid in optimization of PA, but is not a panacea*

Contrasting experiences of WAT use during the interventions emerged in the focus group discussions. The sub-category *WATs facilitate PA* entails participants' experiences of being encouraged by the WAT and that the WAT facilitated PA, especially walking. Reaching the step goal was important and could encourage them to take an extra walk in the evening if they were some steps short of reaching it. The different feedback and prompts to move could be a useful reminder if they had been sedentary for some time. The content in the second sub-category, *Increased awareness of one's limitations* is characterised by expressions suggesting that participants became more aware of the relationships between PA and perceived pain. An individualized optimal number of steps could be identified. When staying within that limit, they experienced fewer pain flares and better continuity regarding exercise.

The third sub-category, *WATs are not always encouraging*, covers experiences of more negative aspects of WAT use that also emerged in the discussions. If pain limited their ability to walk at all and they were far from reaching their step goal, they were discouraged by the WAT instead of being encouraged. Other negative aspects were that the prompts might be disturbing if they were unable to move (sitting in a car for example) and that there was a risk of never feeling satisfied with the amount of PA achieved.

### *Digital support is an appreciated part of OA care*

In general, the participants appreciated digital support in OA care but stated that, it should be offered as a part of traditional care including physical visits. The need for OA care to be delivered early in disease progression and for it to be individualized was highlighted and characterised in the sub-category *Individualized, early and continuous support*. They experienced that the SOASP was designed for older individuals and should be modified to also suit younger, working individuals with OA. The need for continuous care in OA was also expressed, and it was suggested that a combination between digital support and physical visits might be suitable.

The sub-category *PT is essential but needs to be modernized* describes participants' experiences of PTs having a central role in OA care. The participants expressed that they would gladly share activity information from WATs with the PT if it would improve their care. Exercise drawings were also discussed, participants preferred them in video instead of stick figures drawn on a paper.

Several desired features of digital support emerged in the discussions and these experiences and perceptions were gathered in sub-category *Easy, comprehensive, and reliable support*. It should be easy to use so that even those not interested in or having knowledge of technology can use the WAT or digital support. They also wanted WATs to be able to measure activity, sleep, to support weight loss, and to provide feedback and information. If the digital support or WAT measured activity, it should be reliable. They experienced that the WAT they used in the intervention, the Fitbit, did not measure all PA (cycling for instance), and that was experienced as frustrating.

## Study IV: Associations of physical activity and molecular biomarkers

Descriptive results of the outcomes are presented in Table 6.

**Table 6. Outcomes at baseline and follow-up and change between baseline and 3-month follow-up.**

	BASELINE	FOLLOW-UP	CHANGE
	Median (IQR)	Median (IQR)	Median (IQR)
<b>Molecular biomarkers</b>			
CRP (µg/ml)	1.30 (0.56–2.95)	1.35 (0.62–3.04)	–0.02 (–0.50–0.50)
ARGS (pmol/ml)	0.15 (0.12–0.17)	0.15 (0.12–0.17)	0.01 (–0.02–0.02)
COMP (ng/ml) <sup>a</sup>	800 (544–1051)	798 (576–1095)	11 (–109–134)
C2C (ng/ml)	194 (153–239)	214 (164–254)	2 (–20–36)
<b>HOOS/KOOS</b>			
Pain	61.1 (41.7–75.0)	66.7 (47.5–80.6)	5.55 (–2.8–15.0)
Symptoms	54.3 (35.7–67.9)	53.6 (42.9–71.4)	7.1 (–4.6–14.3)
ADL	72.1 (52.6–86.8)	76.7 (61.8–86.8)	1.5 (–6.8–8.8)
Sport/Recreation	30.0 (10.0–50.0)	30.0 (10.0–55.0)	0.0 (–11.9–10.0)
QoL	43.8 (29.7–56.3)	43.8 (31.3–61.5)	0.0 (–6.3–12.5)
<b>IPAQ-SF</b>			
MET-minutes/week	2337 (1395–4626)	2876 (1538–4334)	588 (–817–1677)

Abbreviations: ADL, activities of daily living; ARGs, neoepitope of aggrecan; C2C, collagen type II cleavage; COMP, cartilage oligomeric matrix protein; CRP, C-reactive protein; HOOS, Hip disability and Osteoarthritis Outcome Score; IPAQ-SF, International Physical Activity Questionnaire–Short Form; IQR, interquartile range (Q1–Q3); KOOS, Knee injury and Osteoarthritis Outcome Score; MET, metabolic equivalent of tasks; QoL, hip/knee-related quality of life.

<sup>a</sup>n = 85 for COMP follow-up due to one value below the lower limit of detection.

A weak negative correlation ( $r_s = -0.256$ ,  $p = 0.040$ ) was found between change in self-reported PA and change in COMP, but not for the other molecular biomarkers and self-reported PA (Table 7). There were also no significant correlations between change in self-reported joint function and change in molecular biomarkers (Table 7), or objectively measured steps per day and molecular biomarkers (Table 8).

**Table 7. Correlation (Spearman's Rho,  $r_s$ ) between change in self-reported joint function/PA and change in molecular biomarkers.**

	<b>CRP</b> $r_s$	<i>P</i>	<b>ARGS</b> $r_s$	<i>P</i>	<b>COMP</b> $r_s$	<i>P</i>	<b>C2C</b> $r_s$	<i>P</i>
<b>KOOS/HOOS (n = 83)</b>								
Pain	0.016	0.886	0.096	0.389	-0.037	0.744	-0.095	0.391
Symptoms	-0.050	0.654	0.026	0.812	0.111	0.318	0.141	0.201
ADL	0.104	0.347	0.051	0.648	0.071	0.521	0.112	0.310
Sport/Rec	0.057	0.618	-0.003	0.978	-0.006	0.955	-0.105	0.356
QoL	0.206	0.060	0.171	0.120	0.032	0.777	-0.100	0.366
<b>IPAQ-SF (n = 65)</b>								
MET-minutes/week	0.107	0.390	-0.083	0.508	-0.256	0.040	-0.089	0.475

**PA** physical activity; **CRP** C-reactive protein; **ARGS** neoepitope of aggrecan; **COMP** cartilage oligomeric matrix protein; **C2C** collagen type II cleavage; **KOOS** knee injury and osteoarthritis outcome score; **HOOS** hip disability and osteoarthritis outcome score; **ADL** Activities of daily living; **QoL** knee/hip-related quality of life; **IPAQ-SF** international physical activity questionnaire – short form; **MET** metabolic equivalent of tasks

**Table 8. Correlation (Spearman's Rho,  $r_s$ ) between the average number of steps per day for 12 weeks and molecular biomarkers at three month follow-up (n = 51).**

	<b>CRP</b> $r_s$	<i>P</i>	<b>ARGS</b> $r_s$	<i>P</i>	<b>COMP</b> $r_s$	<i>P</i>	<b>C2C</b> $r_s$	<i>P</i>
<b>Steps/day</b>	0.034	0.811	-0.163	0.254	0.024	0.865	0.113	0.430

**CRP** C-reactive protein; **ARGS** neoepitope of aggrecan; **COMP** cartilage oligomeric matrix protein; **C2C** collagen type II cleavage

# Discussion

## Main findings

The outcomes in this thesis represents several different domains in the ICF—from body function on a molecular level (biomarkers) to activities and participation (PA and work ability). The intervention in the C-RCT showed no statistically significant effect on work ability, PA, or work productivity compared to the SOASP alone. A majority of the individuals in the intervention group were physically active >150 minutes per week and had high adherence to using the WAT, although PA levels and adherence decreased slightly during the 12-week intervention. Experiences and perceptions that WATs facilitated PA and that digital support in OA care was appreciated were highlighted during the focus group discussions. No or only weak statistically significant correlations were found between PA, joint function, and molecular biomarkers.

### **Physical activity and work ability in hip and knee osteoarthritis**

The hypothesis in Study II that self-monitoring PA in addition to participating in the SOASP would improve/increase work ability, PA, and work productivity compared to the SOASP alone was not supported. Previous research on WAT use in interventions has mainly focused on the effect on PA level and, to our knowledge, no study has examined the effect on work ability or work productivity. Several meta-analyses have shown that interventions with WATs are effective in increasing PA in different populations, which contrasts with the results of Study II (158–160,162). We believe that one important explanation for this is that the participants in our project already were highly physically active at baseline. The PA level in this study is in line with data from the BOA registry in 2019 showing higher PA levels in Swedish than in US populations (94,133,135).

The data from the WATs also showed a high level of objectively measured PA in the intervention group, although there was a slight decrease during the 12 weeks. Having a step goal of 7,000 steps might also have limited the increase in PA in the intervention group compared to the control group. A recent study, albeit in healthy young women, showed that participants were adherent to the given step goal. Those who had been given a higher step goal in that study took significantly more steps than those who had been given a lower step goal (197). We can only speculate



whether the participants in the intervention group might have had even higher levels of PA with a higher step goal.

Previous research has shown that pain and functional limitations might be barriers to engaging in PA (71,198), but in this project, the participants had better self-reported function compared to other individuals with OA. This could be a contributing factor explaining the high PA levels at baseline (179).

Some previous studies have focused on the importance of increasing PA and on finding the minimal level of PA to gain health benefits (199) but there are also published studies suggesting a potential U-shaped dose response relationship between PA and OA progression (200). Doré et al. (200) showed that too much weightbearing PA might be detrimental in knee OA, particularly if structural changes already exist. This U-shaped relationship has also been suggested in animal studies, where a high daily dose of PA had a negative impact on the cartilage matrix composition while a moderate dose of PA had a positive impact (201). In this project, the participants in the focus group discussions described that self-monitoring PA with a WAT had helped them realize how many steps per day were optimal in relation to their perceived pain and wellbeing. This corresponds with results from other qualitative studies where individuals with OA expressed that self-monitoring PA could be helpful in finding the optimal amount of PA (195).

The primary outcome in the C-RCT was self-reported work ability measured with WAI. To our knowledge, there are no causal pathways between WAT-use and work ability/work productivity, but PA can improve pain, function and quality of life (123) which might in turn affect health and potentially work ability in individuals with OA. However, work ability and work productivity are dependent on the interaction between several factors: for example, work assignments, health, and individual characteristics (202). Given the characteristics of OA and the functional limitations it might lead to, having a physically demanding job might affect work ability to a higher extent than a less demanding type of work (25,60,74). Furthermore, being able to reduce or adjust work assignments when ill (high adjustment latitude), might enable the employee to remain at work (203). In this project, less than one third of participants had physically demanding work tasks and their work ability might have been lower if they had more physically demanding work (58,204,205). We did not study work adjustments within this project.

The participants' work ability was on average categorised as *good* according to WAI, which might also have limited the possibility for improvements. Their work ability might also have been affected by other factors which are unknown to us, such as other diseases, or work-related or personal factors. Several different domains of work productivity were measured with WPAI:OA in the C-RCT and presenteeism/impairment at work were more common than absenteeism. This result is in line with previous research showing that individuals with OA may experience some difficulties at work but are not absent (54,69,206). In the C-RCT, a statistically

significant difference between the groups in change from baseline to 3 month follow-up were present for WPAI:OA *presenteeism* and *impairment at work* in favour of the intervention group. This could indicate an effect of the intervention, but the results were not consistent throughout the remaining follow-ups. For *presenteeism*, there was a significant interaction (group\*time) effect, but not for *impairment at work*.

There was a statistically significant *within-group* increase in PA (baseline to 3 month follow-up) for the intervention group, but no statistically differences *between-group differences* in PA change. There were no significant *within-group* changes for the other periods (baseline to 6 and 12 month follow-up). Hence, the within-group result should be interpreted with caution.

## **Mobile Health and activity monitoring**

Although the intervention did not have superior effect on work ability, PA and work productivity compared to control, the results from Studies I and III highlight the potential value of WAT use for individuals with OA. In Study I, data from the WATs used in the intervention group were analysed and the results indicated a high PA level and high adherence to using the device throughout the 12-week intervention. Even though adherence was high in Study I, previous research has reported slightly higher adherence to WAT use in other interventions (163). One explanation for this might be that the participants in previous studies had follow-ups which was not the case in our intervention (207,208).

Although the adherence and PA were high throughout the intervention, there was a slight but statistically significant decrease over time. This is also reported in previous research, especially in studies with longer interventions and those without follow-ups or booster sessions (209,210). Having a positive attitude towards technology seems to be an important factor in remaining adherent to WAT use over time (209,211). This was echoed by the participants in the focus group discussions in Study III. They expressed that an interest in technology facilitated WAT use in the beginning and that technical malfunction, battery charging issues, etc. made them lose interest. Similar results were reported in a US study where former WAT users expressed reasons to stop using the WAT: they became bored using it, the device broke, and it was uncomfortable to wear (211).

The high adherence of WAT-use in this project could indicate that the Fitbits were well accepted by the participants, a conception which also emerged in the discussions. They experienced that the WAT facilitated PA and that they became aware of a connection between pain flares, health, and the number of steps they took. These results are in line with previous qualitative research, and with interventional studies examining the effect of WAT use (156,195,211). Finding the optimal level of PA was highlighted in all three focus groups, and this might be

particularly important for individuals with OA. Pain might be a limiting factor to participating in PA and other activities, but at the same time, PA and other weight-bearing activities might induce pain which could render a catch-22 situation (71).

Finding a PA level that does not increase pain might facilitate continuous PA and improve health in the long run. Other types of activities than walking; cycling or water-based exercise, for example, might be better accepted for some individuals with hip and knee OA (212,213). However, some WATs (including the Fitbit used in this project) do not measure all PA as well as they measure ambulatory activities (214). This limitation also emerged in the focus group discussions where the participants expressed that they felt frustrated when not receiving credit from the WAT for cycling 20 minutes. WAT use can also be discouraging for those who are unable to walk due to pain. That this could have a negative impact, has also been reported previously (195,215).

mHealth is an important domain in this thesis, especially regarding the use of WATs, but also to gain increased knowledge of individuals' perceptions of mHealth and digital support in OA care. mHealth seemed to be appreciated in general, but was preferred as part of traditional, in-person health care. One hybrid solution could be to share activity data with treating health care professionals. In a previous qualitative study on OA management, patients expressed that sharing their PA data would increase health care professionals' knowledge about their patients and might improve treatment (216). This result was echoed in our discussions. If the PA data from WATs were handled in a secure way and only by treating PT, they were positive towards the idea of sharing data.

Other opinions about mHealth and digital support in OA care were that OA care should be individualized, early, continuous, and comprehensive. To reduce the risk of, for example, avoidance of activities and comorbidities, offering early and continuous care might be beneficial (65). A recent narrative review on predictors and measures of adherence to the core treatment in OA recommended long term monitoring and a patient-centred approach taking the individual's goals, abilities, and barriers into consideration (217). Booster sessions and the use of BCTs to increase adherence were also recommended in the review.

The BCTs incorporated in the Fitbit were appreciated by the participants in Study III. They talked about the importance of the step goal, the positive feedback when they reached their goal and that the prompts reminded them to move when sedentary. These BCTs have also shown to be some of the most effective BCTs in increasing PA in recent systematic reviews (138,142).

## Physical activity and molecular biomarkers

In Study IV, the associations between PA, joint function, and molecular biomarkers were explored and, with the exceptions of a weak correlation between change in self-reported PA and change in COMP, no statistically significant associations were found and all correlation coefficients were weak or close to zero. Molecular biomarkers in OA are a relatively new research area that might be clinically useful in diagnosing and monitoring the effect of treatments on the disease (38). However, few studies have reported any clear associations between PA and molecular biomarkers in OA populations (23).

A systematic review and meta-analysis showed that the inflammatory marker CRP decreased after exercise, which contrasts with the results of this project (218). However, the greatest improvements in CRP levels in that review were had by individuals who also reduced their BMI/body fat. The participants included in Study IV were on average only slightly overweight and probably had no major changes in weight from baseline to follow-up. Another possible explanatory factor was the low mean CRP-level at baseline with little change to follow-up. Taken together, these factors might explain the non-associations between CRP and PA/function.

The cartilage biomarkers ARGS-aggrecan and C2C had differences close to zero between the baseline and follow-up measurements, while self-reported PA increased slightly. The results are in line with those from a previous study which showed that ARGS-aggrecan might not be sensitive to PA (219).

The third cartilage biomarker included in study IV was COMP. Change in COMP did have a weak but statistically significant negative correlation with change in self-reported PA, indicating that an increase in PA was associated with a decrease in COMP. A similar result was seen in a pilot-RCT where individuals with OA participating in a 10-week intervention with strengthening exercises had significantly reduced COMP-levels compared to controls at follow-up (220).

## Methodological considerations

Participants in all four studies were recruited for the C-RCT (Study II) but the combination of different methodological approaches yielded a broader perspective on the studied phenomena (221). The use of a RCT-design in Study II provides a higher level of evidence compared to most other study designs (222) and was added to the clinical trials registry (No: NCT03354091) before recruitment was initiated. The cluster-randomisation design in Study II was chosen to limit the interference between the intervention and control group (223). To improve transparency and the structure when reporting the C-RCT, CONSORT was followed (169).

Participants in the same SOASP met each other several times and each SOASP was therefore cluster-randomised to avoid having participants from both control and intervention groups in the same SOASP. However, it did also contribute to the somewhat unequal group size due to the difference in number of participants in each randomised SOASP. Most SOASPs at health care centres only had one or two participants while the SOASPs offered within the project had up to fifteen participants. Due to the high number of health care centres, PTs, and SOASPs in this project, we were unable to retrieve reliable information on the number of eligible individuals that received information about the project.

There were also other limitations of the design of the C-RCT which may have reduced the internal and external validity of the results in this thesis. The recruitment of participants in this project was not optimal. The initial recruitment plan had to be reinforced by an advertisement on Facebook. The positive aspects of doing this was that the inclusion rate increased considerably, but a self-selection bias was probably also introduced which might have had an effect on the results in this project (224). First, the advertisement reached only those who used Facebook. Second, only those interested in the information about the project followed the link and e-mailed EÖ to receive additional information.

Taken together, we believe that the individuals who eventually self-registered to the project already had an interest in PA and WATs. This was partly confirmed later in the project when we found that 40% of participants already owned and used a WAT. The participants also had good work ability and were already highly physically active at baseline, factors which could be due to the recruitment method. Consequently, the high baseline values limit the possibility for improvements, and we therefore believe that selection bias might have affected the results of this project. It might not be reasonable to think that the primary outcome of work ability could improve when the baseline values already showed that a majority of the participants already had good or excellent work ability.

Furthermore, the content in the intervention and control was not identical for all individuals. Those recruited from different health care centres had already participated in SOASP. Consequently, SOASP had to be offered within the project to participants recruited via Facebook advertisements. Due to differences in the health care centres, SOASP delivery, different PTs, and other unforeseen aspects, treatment was not identical which might have affected the studies' internal validity (225).

SOASPs offered within this project were held by EÖ and hence, there was some patient/clinician contacts for many of the participants. This might have influenced participants' responses to the questionnaires and the opinions they expressed in the focus group discussions. However, the questionnaires or focus group discussions did not entail questions regarding EÖ's role in the project. Another limitation of the C-RCT was that there was no blinding. Due to the nature of the intervention, it was

not possible to blind the participants to what group they were in. The data was, however, collected objectively through online questionnaires.

The different studies covered several components of the ICF from function/structure on a molecular level to participation in work and PA. The outcome measures we used have, in general, high psychometric properties although the IPAQ primarily is recommended for large population-studies and not RCTs (186). Furthermore, the WAT used in this project, the Fitbit Flex 2, has limitations in measuring PA in a free-living setting (172–174). However, we believe that the device had sufficient properties to justify its use in this project; to self-monitoring PA and measuring PA patterns. PA was also measured objectively during a longer period and the PROMs had several follow-ups, which probably strengthens the studies' internal validity (225). In the qualitative study, measures to achieve trustworthiness were considered throughout the study period and the COREQ checklist was used when reporting results (226). The results from the focus group study may also have been affected by the recruitment of participants that are already positive towards WAT use and are physically active.

In this thesis, there were several collaborations with researchers from different areas which we consider a strength. Study IV was also conducted within a new and promising area in need of more research. However, a limitation of that study was that additional variables that could have affected the molecular biomarkers were not collected. BMI was collected for some of the participants subsequently but information regarding (among others) smoking, intake of non-steroidal anti-inflammatory drugs and recent exercise were lacking. Since these variables are unknown, they cannot be controlled for. However, possible confounders probably have less effect on the associations between *changes* in the outcomes than on cross-sectional associations.

# Conclusion

Self-monitoring PA with a WAT did not have any significant effect on work ability, PA, or work productivity. However, the WATs seemed to be well-accepted by the participants, as illustrated by their high adherence to using WATs throughout the intervention. The slight decrease in both adherence and PA might, however, suggest the need for follow-ups or booster sessions. The participants already at baseline had good work ability, were highly physically active and many already used a WAT. This might have limited the possibilities for improvement and of detecting any effect of the intervention.

Participants expressed that WATs facilitated PA and helped them see a connection between PA level, pain, and health, although negative opinions also emerged. WATs and digital support in OA care was perceived as helpful when used in a hybrid form with traditional in-person care. Individualized, comprehensive, and reliable were some of the wanted features of digital support in OA care.

Molecular biomarkers could potentially be clinically useful in diagnosing and monitoring treatment effects in OA care, but we cannot make any recommendations based on the findings in this thesis. The limitations in data collection might have affected the results and additional research in this area might be warranted.

# Clinical implications

The future of OA care will most likely be a hybrid between traditional in-person care and digital care. Since OA is a chronic, often slow-progressing disease, digital support with self-management could be an essential part of the treatment. This might offer more continuous care, which could have positive long-term effects on health and work ability. The SOASP might also need to be adjusted to the requirements of younger, working individuals.

Although self-monitoring PA with a WAT did not have any effects on the outcomes in the C-RCT, high adherence throughout the intervention in combination with the participants' positive experiences implies that WATs may be appreciated as a facilitator of PA in some cases and as an aid in optimizing PA in other cases. In primary care, patients with OA often meet with a PT and are offered advice about PA and exercise. We suggest that WATs might be used as an aid to facilitate or optimize PA for these patients. One future possibility is that health care centres or other clinics lease or lend WATs to patients during a period. Patients should also be offered individualized, comprehensive care with achievable activity goals and follow-up visits with the PT.

The participants had, on average, good work ability and low absence from work but higher levels of self-reported impairment at work, or *presenteeism*, due to their OA. Impairment at work might have consequences both for the individual, the employer and society at large. The results of this thesis supports the idea that PTs and other health care professionals treating individuals with hip and knee OA talk about the patient's work and possible difficulties. Patients might need work accommodation or other work assignments to reduce their impairment at work.



# Future perspectives

Based on the results from this thesis, we have identified several areas in which future research are needed. We have also identified several limitations in the C-RCT and suggest that similar research studies are conducted in different settings.

- We suggest that the intervention in this study could be repeated with some alterations: target individuals (could be different populations) in primary care identified as having low PA. The individuals meet with a PT, set activity goals, borrow a WAT for 3 months and have a follow-up visit. PA before and after WAT use could be measured with an actigraph, possibly in combination with an exercise diary.
- Work presenteeism seems to be common for individuals with OA—do some individuals with OA need more adjustments or work relocation? We suggest that factors related to sick leave in hip and knee OA are explored, especially occupational factors.
- Explore already existing WATs. Could digital support in OA care be combined with a WAT? What might be supported by the primary health care system?
- The use of molecular biomarkers in hip and knee OA care needs to be further explored. Based on the findings in this study, we suggest that future research focuses on the association between the cartilage biomarker COMP and PA, preferably with a RCT design.
- Future research should explore the effect of finding the optimal individual PA level for individuals with hip and knee OA. Work ability, work productivity and health-related quality of life, pain and function might be important outcomes.

# Acknowledgements

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## Physical activity and Mobile Health among people with hip and knee osteoarthritis

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Osteoarthritis is an increasingly common joint disorder that affects individuals as well as the society at large. Physical activity is recommended as the core treatment in hip and knee osteoarthritis and is also important to prevent several common diseases. The usage of Mobile Health to promote physical activity and other health outcomes are novel and promising. This thesis increased the knowledge of the impact of Mobile Health and physical activity on work ability, health, and molecular biomarkers. It also explores experiences of Mobile Health in individuals of working age with hip and knee osteoarthritis.



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