Odd Magne Hals

Objective measurement of physical activity to evaluate treatment effect in knee osteoarthritis: a pilot study

Master's thesis in Human Movement Science

Supervisor: Paul Jarle Mork

Co-supervisor: Håvard Østerås

Trondheim, November 2017

Norwegian University of Science and Technology

Faculty of Medicine and Health Sciences

Department of Neuroscience

NTNU
Norwegian University of Science and Technology

Abstract

Background and aim: Knee osteoarthritis (OA) is a chronic disease characterized by pain and loss of function. People with knee OA are less active than their peers, although regular physical activity (PA) is associated with improved physical function for those with knee OA. Physical therapy has proven beneficial for pain and function for those with knee OA. Several studies have shown that Medical Exercise Therapy (MExT) has positive effects for various knee conditions. Current outcome measures for people with knee OA include tests for physical function and questionnaires. These outcome measures have limitations in terms of transferability to daily functioning. Accelerometry have proven to be a preferred method for objective measurements of habitual PA, and have the potential to measure daily functioning. The aim of this study was to investigate whether objective measurements of PA can be used to evaluate treatment effect of MExT in patients with knee OA.

Methods: Six patients between 60 and 77 years (mean age 67.5 years) diagnosed with knee OA volunteered to participate in the study. The intervention consisted of twelve weeks of MExT, three sessions per week. Pre- and post-intervention, habitual PA was recorded by two AX3 three-axis accelerometers over a seven-day period. In addition, the Knee Injury and Osteoarthritis Outcome Score (KOOS) and the Tampa Scale for Kinesiophobia (TSK) questionnaires were completed pre- and post-intervention.

Results: There were no significant changes in PA or the TSK questionnaire pre- to post-intervention. The KOOS subscale Activity of Daily Living showed an increase pre- to post-test (p 0.006). Delta values of objectively measured PA was converging with delta values of the KOOS ADL subscale.

Conclusion: This pilot study indicates that objective measurements of PA can be used to evaluate treatment effect of MExT in patients with knee OA. There were no missing data from the accelerometer recordings, and participant’s compliance to the exercise regimen and accelerometer recordings were high. There was no change in PA or the TSK questionnaire pre- to post-test. The KOOS ADL subscale showed an improvement from pre- to post-test, and converging delta values with objectively measured PA, thus indicating a potential association. Further studies should investigate whether there is an association between changes in objective measured PA level and the KOOS questionnaire.

Sammendrag

Bakgrunn og mål: Kneleddsartrose (KA) er en kronisk sykdom karakterisert av smerte og funksjonstap. Personer med KA er mindre aktive enn den generelle befolkningen, til tross for at jevnlig fysisk aktivitet (FA) er assosiert med forbedret funksjon for de med KA. Fysioterapi har positive effekte på smerte og funksjon for personer med KA. Flere studier har vist at Medisinsk Treningsterapi (MTT) har positiv effekt ved ulike kneplager. Vanlige utfallsmål for personer med KA er tester for fysisk funksjon og spørreskjema. Disse utfallsmålene har begrenset overførbarhet til funksjon i dagliglivet. Bruk av akselerometer har vist seg som en foretrukken metode for objektive målinger av sedvanlig FA, og har potensial til å måle dagliglivets funksjon. Målet til dette studiet var å undersøke om objektive målinger av FA kan brukes til å vurdere behandlingseffekt av MTT for pasienter med KA.

Metode: Seks pasienter mellom 60 og 77 år (gjennomsnittsalder 67.5 år) som var diagnostisert med KA sa seg villige til å delta i denne studien. Intervensjonen bestod av tolv uker med MTT med tre behandlinger per uke. Før og etter intervensjonen ble sedvanlig FA målt ved bruk av to AX3 tre-aksede akselerometer over en sju dager lang periode. I tillegg ble spørreskjemaene «Knee Injury and Osteoarthritis Outcome Score» (KOOS) og «Tampa Scale for Kinesiophobia» (TSK) fylt ut før og etter intervensjonen.

Resultat: Det var ingen signifikante endringer i FA eller i TSK spørreskjemaet fra før til etter intervensjonen. KOOS underkategori «Activity of Daily Living» (ADL) viste en økning fra pre- til post-test (p 0.006). Deltaverdier av objektive målinger av FA var sammenfallende med deltaverdier av underkategorien ADL av KOOS.

Konklusjon: Denne pilotstudien indikerer at objektive målinger av FA kan brukes til å vurdere behandlingseffekt av MTT for pasienter med KA. Det var ingen manglende data fra akselerometermålingene, og deltakerne hadde høy etterlevelse av treningsregimet og akselerometermålingene. Det var ingen endring i FA eller TSK spørreskjema fra før til etter intervensjonen. KOOS underkategori ADL viste en forbedring fra pre- til post-test, og hadde sammenfallende deltaverdier med objektive målinger av FA, noe som kan indikere en potensiell assosiasjon. Framtidige studier bør undersøke om det er en assosiasjon mellom endringer i objektive målinger av FA og KOOS spørreskjema.

Acknowledgement

Several people have contributed in the conduction of this thesis. I would like to thank my supervisor, Paul Jarle Mork for his good advices and help in the writing process. My co-supervisor Håvard Østerås for coordinating the data collection and as a general motivator. Fredrik Paulsberg, Lasse Haugerud and Anders T. Bakken at Rosenborgklinikken for their work with recruitment of participants and the data collection. I would also thank Atle Kongsvold for all the help with data analysis. Lastly, thank you to my wife for supporting me and for keeping up with me through these years.

Table of Contents

Introduction

Knee osteoarthritis (OA) is a chronic disease, and a major cause of disability worldwide (McAlindon et al., 2014). Knee OA is characterized by joint pain, stiffness and loss of function (Fransen et al., 2015; Lee et al., 2015), and is one of the most common forms of arthritis (Lee et al., 2015). Nearly 40% of adults above 60 years have signs of knee OA as detected by radiography (Lee et al., 2015; Lo et al., 2015). Knee OA is strongly associated with increased risk of disability, hospitalization and premature mortality, as well as being a main driver of health care costs (Lee et al., 2015; Song et al., 2017).

Age and obesity are strong risk factors for knee OA (Fransen et al., 2015), thus, the obesity epidemic along with a growing elderly population will likely increase the prevalence of knee OA in the coming years (Lo et al., 2015; Sun et al., 2014). The severity of knee OA is usually measured by standard radiography using the Kellgren- Lawrence (KL) grading, which range from 0-4, and the higher grade, the more severe condition (Emrani et al., 2008). There is no known cure for knee OA, and it has been considered that its progression cannot be stopped until the joint is replaced with a prosthesis (Fransen et al., 2015; Gay et al., 2016). For people with severe knee OA, total knee arthroplasty is associated with self-reported decreased pain, improved function and quality of life (Kahn & Schwarzkopf, 2016). The Norwegian Arthroplasty Register reports an 9% increase in the number of total knee arthroplasty from 2014 to 2016, and based on historical data the trend shows an exponential growth (Havelin L I, 2016). This increase is somewhat of a paradox, as knee pain is poorly correlated to findings by radiographic imaging, and knee OA is considered a predisposing factor for knee pain, rather than the cause (Lo et al., 2015). Land based exercises, general physical activity (PA) and weight loss are among the preferred non-surgical managements of knee OA (McAlindon et al., 2014), and have the potential to be a cost-effective option to surgery (Skou & Roos, 2017).

PA have general health benefits such as preventing cardiovascular disease, diabetes, obesity and premature mortality (Lee et al., 2015). WHO recommends at least 150 minutes per week of moderate-intensity aerobic PA. These recommendations are for the general population, and targeted towards cardiorespiratory health, metabolic health, bone health, breast and colon cancer and depression ("WHO Guidelines Approved by the Guidelines Review Committee," 2010). PA can be quantified into PA levels, for example described as sedentary time, or time with moderate to vigorous activity (Liu et al., 2016). Others use

WHOs four components: Frequency, Intensity, Time and Type (FITT) to describe PA levels (Verlaan et al., 2015)

Several studies have shown that people with knee OA are less active than the healthy population (Gay et al., 2016; Liu et al., 2016; Voelker, 2011). In 2002, the US National Health Interview Survey found that 37% of people with knee and/or hip OA are inactive (Gay et al., 2016). Maintaining physical function is a key factor for independent community participation for people with knee OA (Lee et al., 2015). This is reflected in the Osteoarthritis Research Society International (OARSI) guidelines for the non-surgical management of knee OA, as land-based exercise is among the core treatments for all individuals with knee OA (McAlindon et al., 2014). Although exercise has proven to be effective as a treatment for knee OA, a Cochrane review from 2015 suggests that high-intensity exercise may be more harmful than low-intensity (Regnaux et al., 2015). Several studies show that over time regular PA, not exercise, is associated with improved physical function for individuals with knee OA (Gay et al., 2016; Liu et al., 2016; Sun et al., 2014). In the Multicenter Osteoarthritis study (White et al., 2014), more walking was associated with a lower risk of incident function limitation in persons with or at higher risk for knee OA.

Physical therapy is one of the preferred conservative treatments of knee OA, and can provide improvements of pain, stiffness and function (Deyle et al., 2005; Rogind et al., 1998). Physical therapists can provide patient education, exercises for strength, balance and coordination, as well as home exercise programs. In a RCT from 2015, Skou et al. found that a non-surgical treatment, including physical therapy, for people with knee OA is more efficacious at 12 months follow up than information alone. Medical Exercise Therapy (MExT) is an exercise regimen based on global, semi-global and local exercises for musculoskeletal pain and loss of function (Loras et al., 2015). Global exercises involves dynamic use of the whole body, such as stationary bicycling, while semi-global exercises requires the work of an entire limb. Work focusing on a specific joint, local exercises, together with semi-global exercises aims at improving coordination, range of motion and normalize movement patterns (Loras et al., 2015). The idea is that combining these forms of exercises will reduce pain during the session. Global exercises with an intensity of >70% of VO_2 max have the potential to provide endogenous analgesia by stimulating supraspinal nociceptive inhibitory mechanisms (Naugle et al., 2012). By performing global exercises with moderate- to vigorous intensity, this effect can result in generalized pain reduction when performing the local/semi-global exercises. The ultimate goal for dosage for these exercises is three sets of 30 repetitions. To achieve this goal, the patient is involved in deciding load, range of motion and number of repetitions. This can allow the patient to exercise without pain, and avoid negative emotions and conquer fear-avoidance beliefs (Loras et al., 2015). Several studies have shown positive long term effects of pain and function by utilizing MExT for various knee conditions (Osteras et al., 2013; Osteras et al., 2012; Osteras et al., 2014). In theory, pain reduction and improvements in function, should provide higher PA levels. However, whether individuals with knee pain who comply with a MExT regimen will have their PA level increased is still unclear.

Traditionally, PA and PA levels have been assessed with self-report questionnaires (Verlaan et al., 2015). Most questionnaires have limited validity and are prone to bias and misclassification (Kahn & Schwarzkopf, 2016; Lee et al., 2015; Verlaan et al., 2015). To avoid these limitations and properly assess the association between PA and health outcomes, accelerometers have proven to be a preferred method. In addition to being an objective measure, they are relatively inexpensive, small, and have the potential to quantify activity. Depending on placement and data models used for analysis, the use of accelerometers also have the possibility to discriminate between different activities, i.e. weight bearing and sitting (Verlaan et al., 2015).

The Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire is a widely used outcome measure for knee OA (Roos & Lohmander, 2003), and is recommended by the OARSI (Fitzgerald et al., 2015). However, PA is not implemented in KOOS, and the questionnaire is most responsive to the quality of life and pain subscales. Tampa Scale for Kinesiophobia (TSK) is also used as outcome measure, as fear of movement is associated with greater psychological disability and slower gait speed for individuals with knee OA (Shelby et al., 2012). The association between TSK and PA level has not yet been investigated.

There is consensus that pain and physical function are the most important variables to measure in knee OA (Fransen et al., 2015; Skou & Roos, 2017; Wang et al., 2012). Traditionally, physical function has been assessed by standardized test such as the 30 Second Chair Stand Test and 40 m self-paced test, whereas pain level is obtained with Visual Analog Scale (McAlindon et al., 2015). In a systematic review from 2012, Dobson et al. found no consensus on how to assess performance-based physical function in knee OA. It has been suggested that pain in the context of PA levels discriminated symptoms better than pain measurements alone (Lo et al., 2015). Thus, objectively measured PA may be the ultimate goal for symptom assessment in knee OA.

The aim of this study was to investigate whether objective measurements of PA can be used to evaluate treatment effect of MExT in patients with knee OA. People with knee OA are less active than their peers, presumably due to their symptoms of stiffness, pain and loss of function. The hypothesis is that MExT can improve these symptoms, and increase PA levels for these individuals accordingly.

Methods

Participants

Six patients aged 60 to 77 years diagnosed with knee OA volunteered to participate in the study. All patients were recruited from the public physical therapy service in Trondheim, Norway. They were all diagnosed with knee OA by their primary doctor or orthopedist, and referred to physical therapy for treatment. After they were screened for inclusion, patients were informed about the study and written consent was obtained. The enrollment of participants started November 2016, and ended March 2017. Table 1 shows characteristics of the participants in detail.

The inclusion criteria for this study were loss of function and pain lasting longer than 3 months, X-ray verified KL grade I-III and age between 45-85 years. Patients who had received physical therapy treatment during the last 3 months were excluded from participation. Knee injury, inflammatory arthritis, hip symptoms greater than knee symptoms, planned knee surgery six months ahead, and heart and/or lung problems limiting the intervention were all exclusion criteria.

This study was approved by the Regional Committees for Medical and Health Research Ethics (2016/872/REK), and registered in ClinicalTrials.gov (NCT02905747) prior to enrollment.

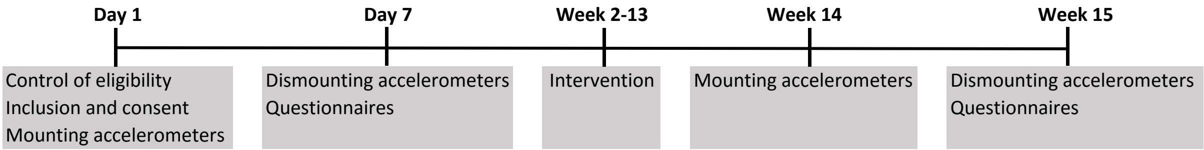
Table 1. Characteristics of the study sample.

	Mean±SD (range)
Age (years)	67.5±6.2 (60-77)
Weight (kg)	79.8±12.3 (66-100)
Height (cm)	173.8±9.2 (168-191)
Body mass index (kg/m^2)	26.5±3.4 (22.7-32.2)

Design

This study is a pilot intervention study. The intervention consisted of MExT supervised by a physical therapist, and took place over 12 weeks. Pre- and post-intervention, habitual PA was recorded over a seven-day period. Likewise, questionnaire data was collected pre- and post-intervention. An overview of the study timeline is presented in figure 1.

Figure 1. Study timeline



Test procedures

After signing the informed consent, all eligible patients wore two accelerometers for seven consecutive days. On day seven the accelerometers were dismounted, and descriptive data such as height, weight and body mass index, was collected using a questionnaire. The KOOS and TSK questionnaires were used to obtain information about status of knee OA and kinesiophobia. After the intervention, patients again filled in the KOOS and TSK questionnaires, and wore accelerometers for seven consecutive days. Following is a more detailed description of physical activity recordings and questionnaires.

Objective measurements of physical activity

PA was measured by AX3 three-axis accelerometers (Axivity Ltd., UK). Participants wore two accelerometers 24h a day, for seven consecutive days. The placement of the accelerometers shown in figure 2. Accelerometers were configured using the AX3 OMGUI Configuration and Analysis Tool (version 1.0.0.30), with a sample frequency of 100Hz and dynamic range of ±8 g. For synchronization of the accelerometers in the time domain, participants were instructed to perform heel-drops, creating reference points for the data analysis. Three heel-drops were conducted in the beginning and at the end of the recordings.

Figure 2. Placement of the accelerometers

Knee Injury and Osteoarthritis Outcome Score

For assessment of symptoms and function, participants were asked to complete the KOOS questionnaire (Norwegian version LK1.0) pre- and post-intervention. KOOS addresses five domains of patient’s daily living: pain, function in daily living (ADL), Function in sport and recreation (Sport/Rec), and knee-related quality of life (QOL). The score ranges from 0 to 100, and higher scores indicate less symptoms and better function. The minimal clinically important change for knee OA has been set to a cutoff value of an increase/decrease of 10 points (Roos & Lohmander, 2003). KOOS is widely used in research and monitoring of individuals, and is validated for several different populations, among knee OA (Roos et al., 1998)

Tampa Scale for Kinesiophobia

The TSK is a 17-item self-report checklist developed as a measure of fear of movement or re-injury. Participants in this pilot study completed the Norwegian version of the TSK (Haugen et al., 2008) pre- and post-intervention. TSK is based on the model of fear avoidance, fear of work related activities, fear of movement and fear of re-injury, and was originally developed for individuals with low back pain and fibromyalgia (Vlaeyen et al., 1995). The questionnaire has recently been validated for patients with Knee OA (Shelby et al., 2012). A total score ranges between 17 and 68, and the cutoff score is 37. Scores above 37 indicate a high degree of kinesiophobia, and scores below 37 are considered low.

Intervention

All patients performed twelve weeks of MExT. They were instructed to follow an 80-90 minute exercise regimen three times a week supervised by a physical therapist. The regimen consisted of global aerobic exercises using a stationary ergometer bicycle, and semi-global and local exercises. Cycling was performed in three bouts for at least 10 minutes with an intensity equivalent of Borg Scale of Perceived Exertion >12. The rationale for performing global exercises was to stimulate pain-modulating mechanisms, such as the gate control in the dorsal horn of the spinal cord, as well as release of endogenous neuropeptides by the central nervous system (Loras et al., 2015). Before and after the second bout of cycling, they performed eight knee exercises with a high number of repetitions (3x30) and relatively low workload. Symptoms and clinical findings were the basis for individual starting level, range of motion and weight resistance. A full description of the exercise protocol can be found in table 2. During each session, the physical therapist recorded the score on Borg Scale, number of repetitions and load for all exercises in a log. To avoid adverse effects, such as increased pain and inflammation, participants were encouraged to avoid exceeding their pain threshold.

Table 2. Exercise protocol

	Exercise	Dosage
1	Stationary bicycling	10 - 20 minutes
2	Squat	3 × 30 repetitions
3	Loaded knee flexion, open chain	3 × 30 repetitions
4	Deloaded* step up	3 × 30 repetitions
5	Stationary bicycling	10 minutes
6	Deloaded* knee extention	3 × 30 repetitions
7	Deloaded* knee flexion, open chain	3 × 30 repetitions
8	Deloaded* step down	3 × 30 repetitions
9	Loaded knee flexion, open chain	3 × 30 repetitions
10	Loaded knee extention, open chain	3 × 30 repetitions
11	Stationary bicycling	10 minutes

*Exercises in closed kinetic chain with less than body weight.

Data analysis

Raw data was extracted from the accelerometers using the AX3 OMGUI Configuration and Analysis Tool. Using a Human Activity Recognition (HAR) system developed by Hessen and Tessem (2015), raw data was processed and categorized into minutes spent in six categories. These categories were cycling, running, walking, and standing, sitting and lying. The HAR system was developed by using two AX3 three-axis accelerometer as in the present study. They used chest mounted video cameras and accelerometers to record two PA protocols in, one consisting of rapid movements for 10 min, and another with tasks such as running around a track, sitting in three different chairs and finding a bench to lay down on. To discriminate these recordings into categories, they developed an algorithm by using a combination of deep learning and dynamic classification, two machine learning methods. By using their HAR system, they were able to classify accelerometer recorded PA with an accuracy of 97.9% for adults.

In the present study, the HAR system was used to categorize PA, as it covers frequency, time and type of the WHO FITT components. For people with knee OA, time spent in moderate-intensity PA with weight bearing of the knee is of special interest. In the present study, PA categories walking and cycling were chosen as the most relevant to evaluate treatment effect in patients with knee OA.

Statistical analysis

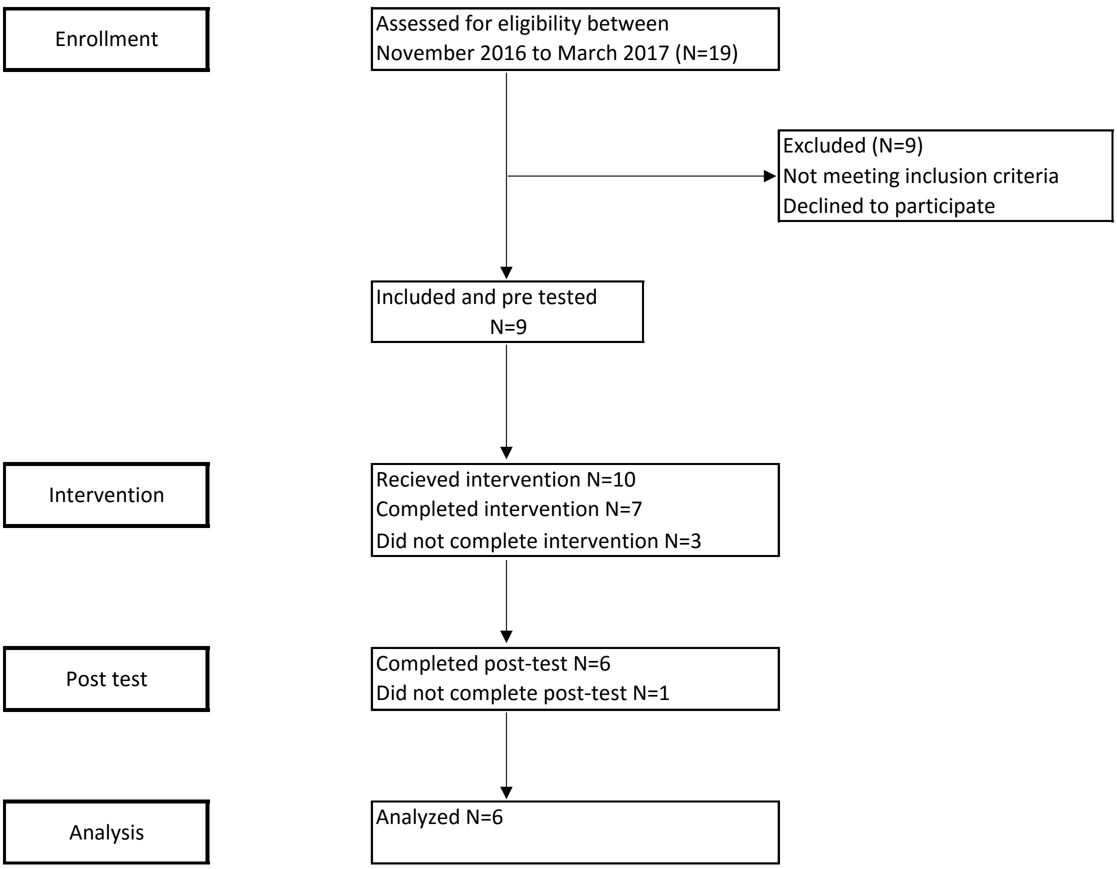
Statistical analysis was performed in IBMs SPSS for Windows 10 (version 23). Within-subject differences were tested by Paired Samples T-test. This parametric test was chosen based on expected normal distribution of data. The level of significance was set at <0.05 and all tests were two-tailed. Results are presented in mean±SD (range). A scatter plot with delta values from the KOOS ADL subscale and PA category total time walking and cycling was created to visualize the converging values of the KOOS ADL subscale versus change in PA. Figures and tables were created using Microsoft Excel for Windows 10 (version 16.0.4549.1000).

Results

Recruitment

Procedures for recruitment of participants are shown in figure 3. A total of 19 participants were found eligible for the study during the enrollment from November 2016 until March 2017. Nine participants were excluded for not meeting inclusion criteria (n=7) or declining participation (n=2). After inclusion, 10 participants were pre tested with questionnaires and activity recordings. Three participants did not complete the intervention of various reasons, such as other health problems and acute surgery, leaving a total of 6 subjects for this study.

Figure 3. Flowchart of participants throughout the study



Compliance

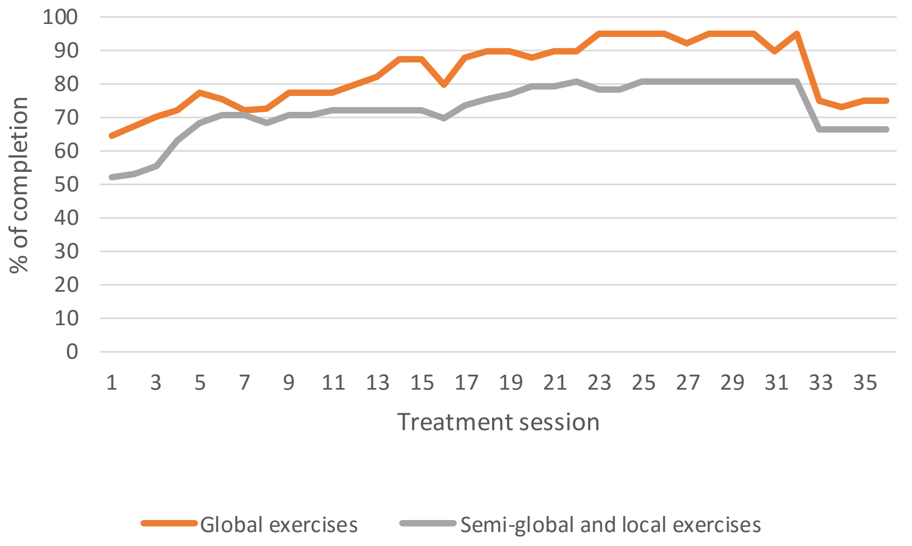
Maximum number of treatment sessions was 35, and the percentage of total participation for each participant is shown in table 3. For each session, the ultimate goal for total number of repetitions of the semi-global and local exercises was 720. For global exercises, the goal was

40 min of stationary cycling. Percentages of these goals were calculated for each treatment, and the mean percentage for all subjects is presented in figure 4.

Table 3. Percentage of total participation

Subject	% of total participation
S01	85 %
S02	100 %
S03	100 %
S04	100 %
S05	92 %
S06	88 %

Figure 4. Compliance to the exercise regimen in %



Activity recordings

Measurements were obtained from November 2016 to July 2017. Figure 5 shows a typical week of activity recording for one participant. Activity is measured in minutes in each category for every day the recording lasted. As shown in table 4, there were no significant differences in activity level for any of the activity categories pre- to post-test. Total time walking and cycling had the greatest improvements (13.5%, p=0.088), followed by total time in activity weekdays (7.9%, p=0.249) and total time in activity (4.7%, p=0.917). A decrease (1.2%, p=0.917) was found in total activity weekend. Changes in activity pre- to post-test are shown in figure 6.

Figure 5. Bar chart of a typical activity recording (minutes spent in PA categories per day)

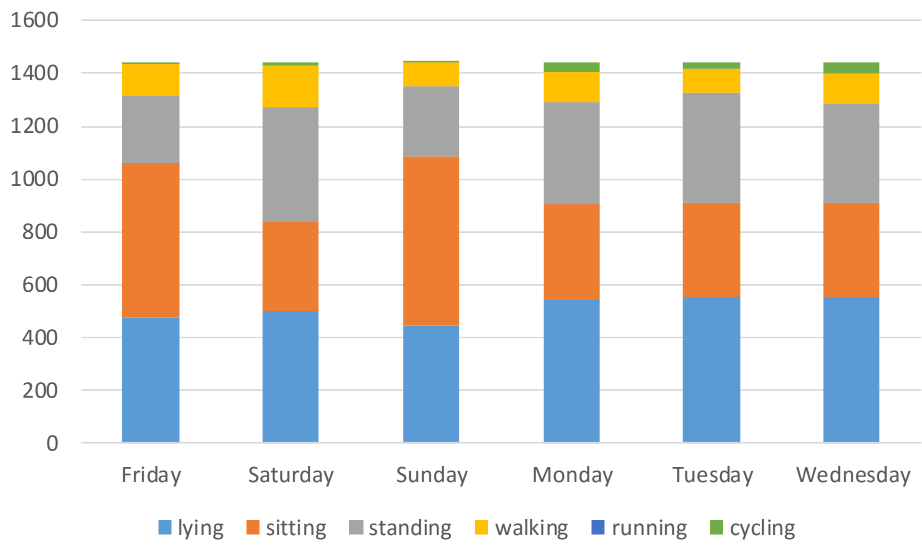


Figure 6. Change in PA pre- to post-test in % for individual participants. Positive values indicate an increase in activity pre- to post test.

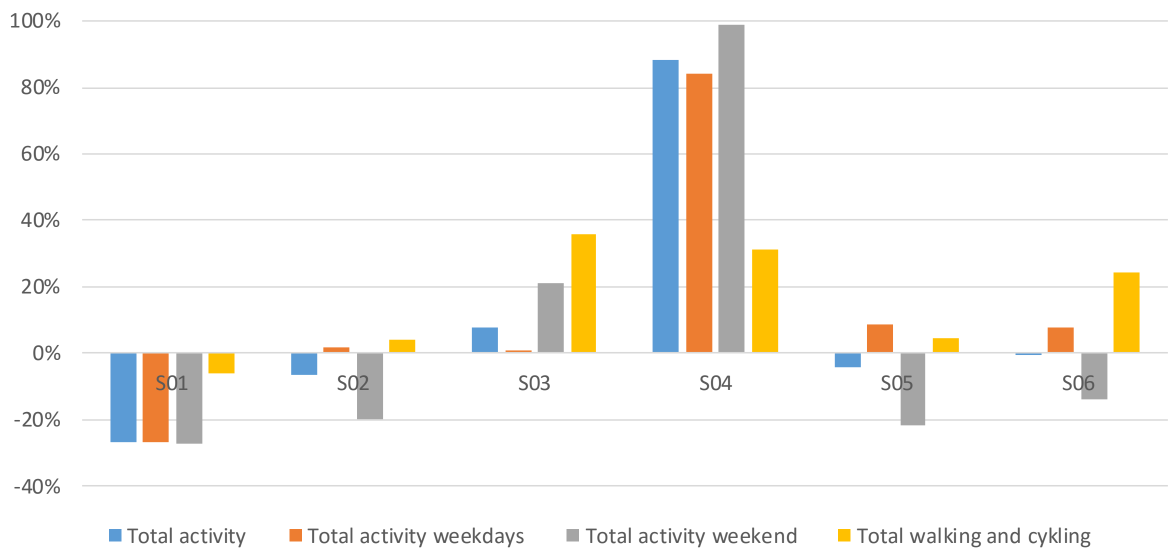


Table 4. Results of activity recordings in minutes (Paired samples T-test)

Outcome variable	N	Pre-test mean±SD (range)	Post-test mean±SD (range)	p value
Total time in activity	6	2233.9±411.8 (1551.8-2659.7)	2339.5±452.9 (1912.3-2923.6)	0.723
Total time in activity weekend	6	783.4±169.3 (448.1-907.2)	774.2±189.9 (570.8-1097.3)	0.936
Total time in activity weekdays	6	1450.5±297.5 (1103.7-1836.1)	1565.3±290.7 (1275.3-2032.6)	0.567
Total time walking and cycling	6	688.9±164.4 (463.2-953.9)	782.2±152.3 (575.2-991.8)	0.088

Tampa scale of kinesiophobia

As shown in table 5, there were no significant (p=0.952) differences from pre- post-test.

Table 5. TSK results

Outcome variable	N	Pre-test mean±SD (range)	Post-test mean±SD (range)	p value
TSK	6	30.9±7.1 (23-42)	30.5± (24-38)	0.952

Knee injury and Osteoarthritis Outcome Score

Results from KOOS subscales are presented in table 6. The score on KOOS ADL improved significantly (p=0.006) from pre- to post-test. Categories KOOS pain, KOOS sport/rec and KOOS symptom (p 0.099, p 0.137 and p 0.623 respectively) provided no significant improvements.

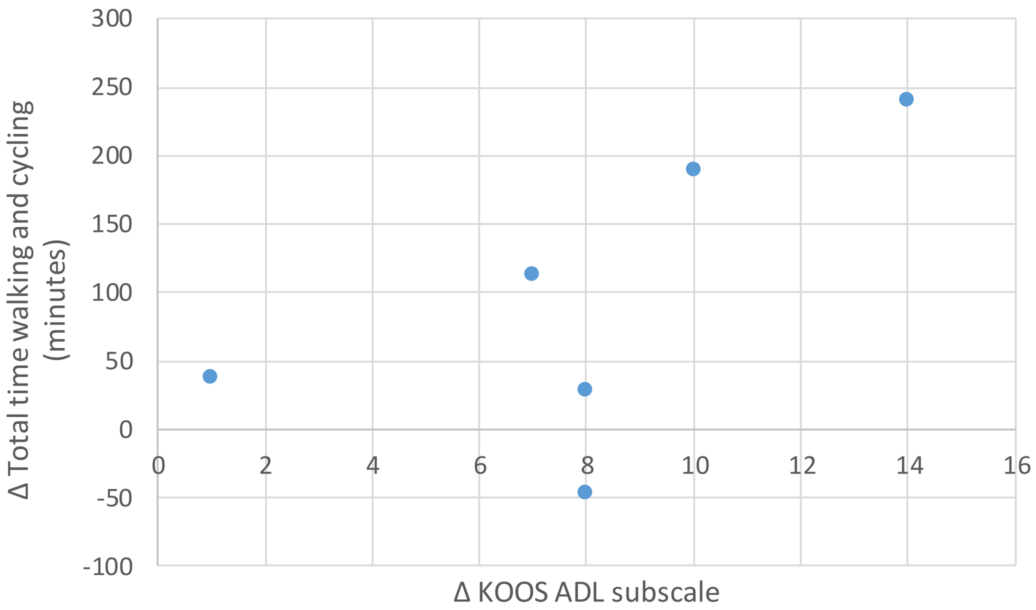
Table 6. KOOS results

Outcome variable	N	Pre-test mean±SD (range)	Post-test mean±SD (range)	p value
KOOS pain	6	64.8±13.4 (47-78)	70.5±17.5 (44-92)	0.099
KOOS ADL	6	71.8±10.3 (59-88)	79.8±12.6 (60-96)	0.006
KOOS Sport/Rec	6	26.6±23.8 (0-65)	37.5±21.6 (25-80)	0.137
KOOS Symptom	6	71.8±10.8 (64-93	74.8±17.6 (46-96)	0.623
KOOS QOL	6	42.0±19.7 (19-63)	39.5±22.8 (19-81)	0.701

Relationship between KOOS and PA

A scatter plot was created to visualize the converging changes in the KOOS ADL subscale and PA category total time walking and cycling. This convergence of delta values is shown in figure 7, indicating that an increase in time spent walking and cycling is associated with an improvement in the KOOS ADL subscale.

Figure 7. Delta values KOOS ADL subscale and PA category total time walking and cycling.



Discussion

The main objective of this pilot study was to investigate whether objective measurement of PA can be used to evaluate treatment effect in knee OA. After the 12- week intervention with MExT, there was no increase in PA. The results from the TSK questionnaire showed minimal changes, and provided no significant results. Participants had no improvements in the KOOS subscales pain, sport/rec and symptom. The ADL subscale provided statistically significant improvements. Delta values in the PA category total time walking and cycling showed converging values with delta values of the KOOS ADL subscale. This finding may indicate an association between changes in these variables.

The present study investigated objective measurements of PA as a possible outcome measure to evaluate treatment effect in knee OA. To the author's knowledge, this method has previously not been used in clinical trials. Physical function has traditionally been assessed by using standardized test, such as the 30 second chair stand test and 40 m self-paced test. Pain level is usually obtained with Visual Analog Scale (Skou et al., 2012).

A longitudinal study by Verlaan et al. (2015) demonstrated that accelerometry is a feasible method to measure habitual PA in people with knee OA. In addition, they were able to discriminate PA between all WHO FITT components. In another longitudinal study from 2015, White et al. found that during a two-year period, walking ≥6000 steps per day was associated with less functional limitation in people with, or at risk of knee OA. Participants in this study were ≥ 50 years of age, female, had previous knee injury/surgery, as well as being overweight. They used an accelerometer to measure number of steps per minute for seven days at baseline, and measured objectively measured and self-reported functional limitations in the two year follow up. The association was examined by establishing risk ratios for developing loss of function. However, they did not use objective measurements of PA in the follow up, and the authors acknowledge that the threshold should ideally be tested in clinical trials to determine its effectiveness in reducing function.

In a cross-sectional study from 2015, Lee and colleges and found a positive association between being less sedentary and better physical function in people with knee OA. They identified sedentary behavior by calculating accelerometer counts in vertical acceleration per minute. Physical function was assessed by walk pace and the 30 second Chair Stand Test, and the cross-sectional association was examined by multiple linear regression.

All of these findings indicate that objectively measured PA can be used to evaluate physical function in people with knee OA. As in the present study, Lee et al. (2015) and White et al. (2015) focused on weight bearing PA, i.e. walking. However, these two studies were not able to discriminate PA into categories, such as standing and cycling, both activities involving weight bearing of the knee joint.

The present study indicates that changes in time spent walking and cycling converges with changes in the KOOS ADL subscale, indicating a potential association. This finding highlights the importance of gaining further insight into habitual PA and its association with pain and function in knee OA, as well as transferability to daily functioning. There are no findings in the present study that indicates that MExT has any effect on PA level. With the lack of clinical trials using objective measurements of PA, exercise treatments effect on PA levels for people with knee OA remain unclear.

Future research and practical implications

The KOOS questionnaire has predetermined cut-off point for minimal clinically important change validated for knee OA. Although the present study found changes in KOOS ADL subscale, it did not exceeded this threshold. The study by White et al. (2015) is, to the author`s knowledge, the only study to investigate a clinically important change in objectively measured PA in knee OA. The converging changes in objectively measured PA and KOOS ADL subscale indicate a potential association, and further studies should investigate the relationship between objectively measured PA and current outcome measures, such as KOOS. An association between PA and KOOS could provide an opportunity for establishing cut-off points for clinically important change in PA level, in the same way as in KOOS. Such cut-off points could have the potential to complement questionnaires and test for physical function as outcome measures in research and clinical settings, as well as translate into guidelines for PA. Objectively measured PA may also represent an outcome measure that has transferability to daily functioning.

One of the challenges when analyzing data from objectively measured PA is to calculate the independent effect of categories. In a 24-hour recording, time spent in all categories constitutes a day, and therefore, categories are codependent. Associations between time spent in one or several categories and health outcomes should consider this codependence. In a cross-sectional study from 2015, Chastin el al. used a compositional analysis paradigm, which accounts for this intrinsic codependence. They found that time spent in sleep, sedentary behavior and physical activity together constitute a composite whole in its association with obesity and cardio-metabolic health markers. This approach have the potential to provide a true association between one or several PA categories and its effect on pain and function in knee OA. This codependence has not been taken into account in the present study, and should be implemented in further research.

Another factor that could affect the results of objective measurements of habitual PA is seasonal changes. In the northern hemisphere, winter is many places associated with cold weather and snow, and can have a profound impact on habitual PA. The present study collected PA measurements from November to July, and the change of seasons from pre- to post-test may affect the results. A solution to this problem is to increase the number of participants and perform measurements through all seasons.

Pilot testing

According to Arain et al. (2010), a pilot study is a miniature version of a main study to test that components can work together, whereas feasibility studies are pieces of research used to estimate important parameters for the main study. The present study is designed as a pilot study, as all components in the research process is important to investigate whether objective measurements of PA can be used to evaluate treatment effect.

Only 6 of 19 eligible participants completed this study. One of the main reason for this was not meeting inclusion criteria (n=7). The relative stringent inclusion criteria for this study was to ensure a homogenous study population, thus reducing confounders and increase the likelihood of finding a true association between MExT and PA levels. However, the negative impact of these criteria is excluding patients with knee OA that visit clinicians in a real life setting. Broader inclusion criteria would affect the internal validity, but generalize application of positive results.

Throughout the study, the compliance to the exercise regimen, accelerometer recordings and questionnaires were high. The layout of this study requires both time and motivation from the participant, but there was no adverse events and a low number of dropouts. During the study, data from every accelerometer recording was extracted and analyzed with no error. These findings suggest that the exercise treatment and seven-day accelerometer recordings can be used in people with knee OA. A follow up of the participants would provide insight into the adherence to any changes in PA level.

Strengths and limitations

To the author`s knowledge, this is the first study to evaluate treatment effect in knee OA using objectively measured PA. The exercise regimen was extensive with high compliance, and has previously proven beneficial for various knee conditions. Compliance was recorded by physical therapists after each session, and is dependable. Another strength is utilizing two accelerometers, allowing further insight into categories of PA. This allowed for discrimination of time spent in weight bearing activities, an important insight in knee OA

There are several limitations to this study. First, the low number of participants. This reduces the statistical power and can lead to a potential overestimation of treatment effect. Second, for some participants the pre-test was during the winter, and post-test in the spring or summer. This could affect the changes in PA level before and after the intervention. Third, there were no tests for physical function to compare with objective measurements of PA. As there are indications that habitual PA is associated with physical function, tests such as the 30 second chair stand test and 40 m self-paced test could give further insight into whether these tests are associated with PA level. Fourth, the MExT regimen does not follow the OARSI guidelines for non-surgical management of knee OA (McAlindon et al., 2014), and using these guidelines could affect the outcome of this study.

Conclusion

This pilot study indicates that objective measurements of PA can be used to evaluate treatment effect of MExT in patients with knee OA. There were no missing data from the accelerometer recordings, and compliance to the exercise regimen and accelerometer recordings were high. There was no change in PA or the KOOS and TSK questionnaires pre- to post intervention, but the KOOS ADL subscale showed converging delta-values with objectively measured PA, thus indicating a potential association. Further studies should investigate whether there is an association between changes in objectively measured PA level and the KOOS questionnaire.

References

Arain M., Campbell M. J., Cooper, C. L., & Lancaster, G. A. (2010). What is a pilot or feasibility study? A review of current practice and editorial policy. *BMC Medical Research Methodology, 10,* 67-67. doi:10.1186/1471-2288-10-67

Chastin, S. F. M., Palarea-Albaladejo, J., Dontje, M. L., & Skelton, D. A. (2015). Combined Effects of Time Spent in Physical Activity, Sedentary Behaviors and Sleep on Obesity and Cardio-Metabolic Health Markers: A Novel Compositional Data Analysis Approach. *PLOS ONE, 10(10),* e0139984. doi:10.1371/journal.pone.0139984

Deyle, G. D., Allison, S. C., Matekel, R. L., Ryder, M. G., Stang, J. M., Gohdes, D. D., Garber, M. B. (2005). Physical therapy treatment effectiveness for osteoarthritis of the knee: a randomized comparison of supervised clinical exercise and manual therapy procedures versus a home exercise program. *Phys Ther, 85(12),* 1301-1317.

Dobson, F., Hinman, R. S., Hall, M., Terwee, C. B., Roos, E. M., & Bennell, K. L. (2012). Measurement properties of performance-based measures to assess physical function in hip and knee osteoarthritis: a systematic review. *Osteoarthritis Cartilage, 20(12),* 1548-1562. doi:10.1016/j.joca.2012.08.015

Emrani, P. S., Katz, J. N., Kessler, C. L., Reichmann, W. M., Wright, E. A., McAlindon, T. E., & Losina, E. (2008). Joint space narrowing and Kellgren-Lawrence progression in knee osteoarthritis: an analytic literature synthesis. *Osteoarthritis Cartilage, 16(8),* 873-882. doi:10.1016/j.joca.2007.12.004

Fitzgerald, G. K., Hinman, R. S., Zeni, J., Risberg, M. A., Snyder-Mackler, L., & Bennell, K. L. (2015). OARSI Clinical Trials Recommendations: Design and conduct of clinical trials of rehabilitation interventions for osteoarthritis. *Osteoarthritis Cartilage, 23(5),* 803-814. doi:https://doi.org/10.1016/j.joca.2015.03.013

Fransen, M., McConnell, S., Harmer, A. R., Van der Esch, M., Simic, M., & Bennell, K. L. (2015). Exercise for osteoarthritis of the knee. *Cochrane Database of Systematic Reviews(1).* doi:10.1002/14651858.CD004376.pub3

Gay, C., Chabaud, A., Guilley, E., & Coudeyre, E. (2016). Educating patients about the benefits of physical activity and exercise for their hip and knee osteoarthritis. Systematic literature review. *Ann Phys Rehabil Med, 59(3),* 174-183. doi:10.1016/j.rehab.2016.02.005

Haugen, A. J., Grovle, L., Keller, A., & Grotle, M. (2008). Cross-cultural adaptation and validation of the Norwegian version of the Tampa scale for kinesiophobia. *Spine, 33(17),* E595-601. doi:10.1097/BRS.0b013e31817c6c4b

Havelin L I, F. O., Engesaeter L. B., Fenstad A. M., Johannessen C. B., Dybvik E., Fjeldsgaard K., Gundersen T. (2016). *The Norwegian Arthroplast Register. Annual report 2016.*

Kahn, T. L., & Schwarzkopf, R. (2016). Do Total Knee Arthroplasty Patients Have a Higher Activity Level Compared to Patients With Osteoarthritis? *Geriatr Orthop Surg Rehabil, 7(3),* 142-147. doi:10.1177/2151458516654518

Lee, J., Chang, R. W., Ehrlich-Jones, L., Kwoh, C. K., Nevitt, M., Semanik, P. A., Dunlop, D. D. (2015). Sedentary behavior and physical function: objective evidence from the Osteoarthritis Initiative. *Arthritis Care Res (Hoboken), 67(3),* 366-373. doi:10.1002/acr.22432

Liu, S. H., Driban, J. B., Eaton, C. B., McAlindon, T. E., Harrold, L. R., & Lapane, K. L. (2016). Objectively Measured Physical Activity and Symptoms Change in Knee Osteoarthritis. *Am J Med, 129(5),* 497-505.e491. doi:10.1016/j.amjmed.2015.12.029

Lo, G. H., McAlindon, T. E., Hawker, G. A., Driban, J. B., Price, L. L., Song, J., Dunlop, D. D. (2015). Symptom assessment in knee osteoarthritis needs to account for physical activity level. *Arthritis Rheumatol, 67(11),* 2897-2904. doi:10.1002/art.39271

McAlindon, T. E., Bannuru, R. R., Sullivan, M. C., Arden, N. K., Berenbaum, F., Bierma-Zeinstra, S. M., Underwood, M. (2014). OARSI guidelines for the non-surgical management of knee osteoarthritis. *Osteoarthritis Cartilage, 22(3),* 363-388. doi:10.1016/j.joca.2014.01.003

Naugle, K. M., Fillingim, R. B., & Riley, J. L. (2012). A meta-analytic review of the hypoalgesic effects of exercise. *The journal of pain : official journal of the American Pain Society, 13(12),* 1139-1150. doi:10.1016/j.jpain.2012.09.006

Osteras, B., Osteras, H., & Torstensen, T. A. (2013). Long-term effects of medical exercise therapy in patients with patellofemoral pain syndrome: results from a single-blinded randomized controlled trial with 12 months follow-up. *Physiotherapy, 99(4),* 311-316. doi:10.1016/j.physio.2013.04.001

Osteras, H., Osteras, B., & Torstensen, T. A. (2012). Medical Exercise Therapy is Effective After Arthroscopic Surgery of Degenerative Meniscus of the Knee: A Randomized Controlled Trial. *J Clin Med Res, 4(6),* 378-384. doi:10.4021/jocmr1100w

Osteras, H., Osteras, B., & Torstensen, T. A. (2014). Is postoperative exercise therapy necessary in patients with degenerative meniscus? A randomized controlled trial with one year follow-up. *Knee Surg Sports Traumatol Arthrosc, 22(1),* 200-206. doi:10.1007/s00167-012-2354-2

Regnaux, J.-P., Lefevre-Colau, M.-M., Trinquart, L., Nguyen, C., Boutron, I., Brosseau, L., & Ravaud, P. (2015). High-intensity versus low-intensity physical activity or exercise in people with hip or knee osteoarthritis. *Cochrane Database of Systematic Reviews(10).* doi:10.1002/14651858.CD010203.pub2

Rogind, H., Bibow-Nielsen, B., Jensen, B., Moller, H. C., Frimodt-Moller, H., & Bliddal, H. (1998). The effects of a physical training program on patients with osteoarthritis of the knees. *Arch Phys Med Rehabil, 79(11),* 1421-1427.

Roos, E. M., & Lohmander, L. S. (2003). The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health and Quality of Life Outcomes, 1*, 64-64. doi:10.1186/1477-7525-1-64

Roos, E. M., Roos, H. P., Lohmander, L. S., Ekdahl, C., & Beynnon, B. D. (1998). Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. *J Orthop Sports Phys Ther, 28.* doi:10.2519/jospt.1998.28.2.88

Shelby, R. A., Somers, T. J., Keefe, F. J., DeVellis, B. M., Patterson, C., Renner, J. B., & Jordan, J. M. (2012). Brief Fear of Movement Scale for Osteoarthritis. *Arthritis care & research, 64(6),* 862-871. doi:10.1002/acr.21626

Skou, S. T., Odgaard, A., Rasmussen, J. O., & Roos, E. M. (2012). Group education and exercise is feasible in knee and hip osteoarthritis. *Dan Med J, 59.*

Skou, S. T., Rasmussen, S., Laursen, M. B., Rathleff, M. S., Arendt-Nielsen, L., & Simonsen, O. (2015). The efficacy of 12 weeks non-surgical treatment for patients not eligible for total knee replacement: a randomized controlled trial with 1-year follow-up. *Osteoarthritis Cartilage, 23.* doi:10.1016/j.joca.2015.04.021

Skou, S. T., & Roos, E. M. (2017). Good Life with osteoArthritis in Denmark (GLA:D™): evidence-based education and supervised neuromuscular exercise delivered by certified physiotherapists nationwide. *BMC Musculoskeletal Disorders, 18(1),* 72. doi:10.1186/s12891-017-1439-y

Song, J., Gilbert, A. L., Chang, R. W., Pellegrini, C. A., Ehrlich-Jones, L. S., Lee, J., . . . Dunlop, D. D. (2017). Do Inactive Older Adults Who Increase Physical Activity Experience Less Disability: Evidence From the Osteoarthritis Initiative. *J Clin Rheumatol, 23(1),* 26-32. doi:10.1097/rhu.0000000000000473

Sun, K., Song, J., Lee, J., Chang, R. W., Eaton, C. B., Ehrlich-Jones, L., . . . Dunlop, D. D. (2014). Relationship of meeting physical activity guidelines with health-related utility. *Arthritis Care Res (Hoboken), 66(7),* 1041-1047. doi:10.1002/acr.22262

Tessem AJ, Hessen H-O. (2015). Human Activity Recogniton with two Body-Worn Accelerometer Sensors Norway. *Norwegian University of Science and Technology 1-53.*

Verlaan, L., Bolink, S. A., Van Laarhoven, S. N., Lipperts, M., Heyligers, I. C., Grimm, B., & Senden, R. (2015). Accelerometer-based Physical Activity Monitoring in Patients with Knee Osteoarthritis: Objective and Ambulatory Assessment of Actual Physical Activity During Daily Life Circumstances. *Open Biomed Eng J, 9*, 157-163. doi:10.2174/1874120701509010157

Vlaeyen, J. W. S., Kole-Snijders, A. M. J., Rotteveel, A. M., Ruesink, R., & Heuts, P. H. T. G. (1995). The role of fear of movement/(re)injury in pain disability. *Journal of Occupational Rehabilitation, 5(4),* 235-252. doi:10.1007/BF02109988

Voelker, R. (2011). Few adults with knee osteoarthritis meet national guidelines for physical activity. *JAMA, 306(13),* 1428-1430. doi:10.1001/jama.2011.1388

White, D. K., Tudor-Locke, C., Zhang, Y., Fielding, R., LaValley, M., Felson, D. T., Neogi, T. (2014). Daily walking and the risk of incident functional limitation in knee osteoarthritis: an observational study. *Arthritis Care Res (Hoboken), 66(9),* 1328-1336. doi:10.1002/acr.22362

WHO Guidelines Approved by the Guidelines Review Committee. (2010*). In Global Recommendations on Physical Activity for Health. Geneva: World Health Organization*

Copyright (c) World Health Organization 2010.