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# The association of clinical and structural knee osteoarthritis with physical activity in the middle-aged population: the NEO study

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SUMMARY

*Objective:* To investigate if knee osteoarthritis (OA) is associated with lower physical activity in the general middle-aged Dutch population, and if physical activity is associated with patient-reported outcomes in knee OA.

*Design:* Clinical knee OA was defined in the Netherlands Epidemiology of Obesity population using the ACR criteria, and structural knee OA on MRI. We assessed knee pain and function with the Knee Injury and Osteoarthritis Score (KOOS), health-related quality of life (HRQoL) with the Short Form-36, and physical activity (in Metabolic Equivalent of Task (MET) hours) with the Short Questionnaire to Assess Health-enhancing physical activity. We analysed the associations of knee OA with physical activity, and of physical activity with knee pain, function, and HRQoL in knee OA with linear regression adjusted for potential confounders.

*Results:* Clinical knee OA was present in 14% of 6,212 participants, (mean age 56 years, mean BMI 27 kg/m$^2$, 55% women, 24% having any comorbidity) and structural knee OA in 12%. Clinical knee OA was associated with 9.60 (95% CI 3.70; 15.50) MET hours per week more physical activity, vs no clinical knee OA. Structural knee OA was associated with 3.97 (−7.82; 15.76) MET hours per week more physical activity, vs no structural knee OA. In clinical knee OA, physical activity was not associated with knee pain, function or HRQoL.

*Conclusions:* Knee OA was not associated with lower physical activity, and in knee OA physical activity was not associated with patient-reported outcomes. Future research should indicate the optimal treatment advice regarding physical activity for individual knee OA patients.



## 1. Introduction

Rheumatic musculoskeletal disorders (RMDs) are among the leading causes of disability in the middle-aged population. One of the most common RMDs is osteoarthritis (OA), which affected approximately 300 million people globally in 2017, and its prevalence is expected to keep rising[1].

Currently, no disease-modifying treatment is available for OA, which often leads to chronic use of analgesics to suppress symptoms, until eventually joint replacement surgery is performed in end-stage disease[2]. As pain, reduced quality of life and functional complaints are among the most prevalent knee OA symptoms and can impede physical activity[1], insight in lifestyle factors that reduce pain, increase functional performance and perhaps even slow down progression is highly warranted.

Physical activity is such a modifiable lifestyle factor that has shown to be associated with better disease outcomes. In elderly individuals with knee OA, lack of physical activity has been shown to be associated with depressive symptoms, poorer functional

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performance, cardiovascular events, and increased mortality[3–6]. This underscores the vital need for estimates of the level of physical activity in individuals with knee OA, and of its impact on quality of life and patient-reported outcomes.

Previous studies have reported low adherence to physical activity guidelines in individuals with knee OA[7–9], which might be caused by pain and psychological distress caused by OA[8]. Furthermore, physical activity has shown to be an effective intervention for weight loss, which in turn diminishes the risk and complaints of knee OA[9]. However, some studies found no clear difference in physical activity between individuals with and without knee OA[10–13]. Most available studies concerning physical activity in individuals with knee OA studied relatively old populations in countries where a sedentary lifestyle is common[14]. Large-scale measurement of physical activity across general worldwide populations revealed differences in physical activity between countries[15,16]. This might be caused by cultural and lifestyle differences. For example, in some countries such as the Netherlands, Denmark and Germany, walking and cycling are regularly used as ways of transportation, instead of transport by car[17].

Furthermore, data on individuals having early stages of knee OA were not found, while lifestyle interventions in knee OA preferably take place in an early disease stage[18]. The median age of knee OA diagnosis was 55 years of age in the general population of the United States of America[19]. Because of this, information on physical activity status in the middle-aged OA population is warranted. This is vital in order to assess the potential of physical activity as a target for intervention in early stages of knee OA.

Therefore, we investigated if knee OA is associated with lower physical activity compared with no knee OA in the general middle-aged Dutch population. Furthermore, as lack of physical activity has shown to be associated with wide-ranging adverse health outcomes[3–6], we investigated the association of physical activity with patient-reported outcomes such as knee pain, function and health-related quality of life (HRQoL) in individuals with knee OA.

## 2. Materials and methods

### 2.1. Study population

The Netherlands Epidemiology of Obesity (NEO) study is a population-based, prospective cohort study, with an oversampling of overweight or obese individuals. Detailed study design and data collection have been described elsewhere[20]. In short, men and women between 45 and 65 years with a self-reported body mass index (BMI) $\geq$ 27 kg/m$^2$ living in the greater area of Leiden (the Netherlands) were eligible to participate. In addition, all inhabitants aged between 45 and 65 years from one municipality (Leiderdorp) were invited to participate irrespective of their BMI, allowing for a reference BMI distribution comparable to the general Dutch population[21]. The collection of data started in September 2008 and was completed at the end of September 2012. In total, 6,671 participants were included in the NEO study. The Medical Ethical Committee of the Leiden University Medical Center (LUMC) approved the design of the study. All participants gave their written informed consent.

### 2.2. Questionnaires

Participants completed a general questionnaire to report demographic, lifestyle and clinical information, including a medical history on inflammatory rheumatic diseases, fibromyalgia and general comorbid diseases. We investigated the following general comorbid diseases: cardiovascular disease, chronic pulmonary disease, liver disease, diabetes, kidney disease and cancer.

Physical activity was measured with the validated Short Questionnaire to Assess Health-enhancing physical activity (SQUASH)[22], which includes questions on activities regarding a normal week in recent months. The SQUASH consists of three main queries: days per week, average time per day, and intensity. Items were converted to age-specific metabolic equivalent tasks (METs), derived from Ainsworths's compendium of physical activity[23], in hours per week based on reported frequency and duration of the activities[24]. SQUASH items were combined to calculate a total physical activity level in Metabolic Equivalent of Task (MET) hours per week. In addition, we combined the SQUASH items sports, walking, gardening, cycling and household activities in order to assess the category of "leisure time" physical activity in concordance with the SQUASH guideline.

Knee specific symptoms were measured with the Knee Injury and Osteoarthritis Outcome Score (KOOS)[25,26]. The Knee Injury and Osteoarthritis Score (KOOS) consists of five subscales: pain, symptoms, function in activities of daily living (ADL), sport and recreation function and knee-related quality of life. All patients scored the KOOS for their right knee considering the previous week. Items were scored from 0 (no problems) to 4 (extreme problems) on a 5-point Likert scale. Subscale scores were calculated according to the KOOS user's guide[27] as the sum of the items included, and subsequently transformed to a 0–100 scale, with zero representing extreme knee problems and 100 representing no knee problems. A KOOS subscale score was considered valid when at least 50% of the items were completed. If more than 50% of data from a subscale was missing, the participant was excluded from analyses of that subscale[27]. In the current analyses we included the KOOS subscales pain and ADL function.

HRQoL was measured with the Short Form (SF)-36[28]. The physical health summary component score (PCS) and mental health summary component score (MCS) were calculated. Age- and sex-specific Dutch population-based norm scores[29] were used to derive norm-based scores with a mean of 50 and a standard deviation (SD) of 10. Higher SF-36 scores represent better quality of life.

### 2.3. Accelerometer

Physical activity was measured for the duration of four consecutive days by an accelerometer in a random subset ($n = 955$) of the study population. An accelerometer was combined with two ECG electrodes (ActiHeart, CamNtech Ltd, UK), which was placed on the chest of the participants at the level of the third intercostal space. This combined heart rate monitor and accelerometer simultaneously measures heart rate and uniaxial (vertical when standing up) acceleration of the torso. Using a branched equation algorithm the acceleration and heart rate information was translated into calibrated estimates of physical activity energy expenditure[30,31]. Participants with a valid wear time <24 h were excluded from the analyses. To allow comparison with the SQUASH, we converted the data from the accelerometer (kJ/kg/day) to MET hours per week by dividing by 4.2 and subsequently multiplying by 7[27].

### 2.4. Clinical assessment

BMI was calculated from measured body weight and height (kg/m$^2$). In addition, extensive physical examination of the knees was performed by trained research nurses, with a standardized scoring form. The presence of bony swellings, palpable pain and warmth, crepitus and movement restriction were assessed.

### 2.5. Clinical and structural knee OA definitions

We used self-reported knee pain on most days of the last week, in combination with the physical assessment of the knee, to define a clinical knee OA phenotype according to the American College of Rheumatology (ACR) clinical classification criteria[32].

Structural knee OA in the right knee was defined on magnetic resonance imaging (MRI), in a random sample of 1,285 participants without contra-indications (most notably metallic devices, claustrophobia or a body circumference of more than 1.70 m). Imaging was performed on a MR system operating at a 1.5T field strength (Philips, Medical Systems, Best, the Netherlands), using a dedicated knee coil and a standardized scanning protocol as described earlier[33]. All MRI images were analysed using the validated semi-quantitative knee OA scoring system (KOSS)[34] as described previously[33]. Structural knee OA was defined according to the modified criteria by Hunter *et al.*,[35] when a definite osteophyte and full thickness cartilage loss was present, or one of these features with at least two of the following: subchondral bone marrow lesions, cyst, meniscal subluxation, maceration or degenerative tear, or partial thickness cartilage loss.

### 2.6. Statistical analyses

For individuals from the city of Leiden and its surroundings ($n$ = 4,541), oversampling was done of individuals with BMI $\geq$ 27 kg/m$^2$. In order to correctly represent associations in the general Dutch population, individuals from the general population from Leiderdorp without any oversampling were included ($n$ = 1,671), as the BMI distribution of this municipality is representative for the general Dutch population[21]. Due to weighting of the BMI of our study to the general Leiderdorp population, our results will apply to a Dutch population-based study without oversampling of participants with BMI $\geq$27 kg/m$^2$ [36].

We performed a cross-sectional analysis of baseline measurements. We excluded participants who reported to have inflammatory rheumatic disease or fibromyalgia, participants with missing physical examination of the knees, or missing physical activity data. Population characteristics were summarized as mean (SD), median (25th, 75th percentiles) or as percentages.

Linear regression analyses were performed to investigate the association of clinical and structural knee OA (independent variables) with physical activity (dependent variable, MET hours per week), compared with respectively no clinical and no structural knee OA. Additionally, in order to assess the effect of the individual potential confounding factors on the association, we added these factors to the model in a stepwise manner. In the subgroup of participants with clinical knee OA, linear regression analyses were performed for each patient-reported outcome measure to investigate the association between physical activity (independent variable) and knee specific outcomes measured by the KOOS, and the PCS and MCS of the SF-36 (dependent variables). In order to account for possible biases commonly observed in self-reported physical activity measures (for example social desirability bias)[37], we performed a sensitivity analysis to assess the association between clinical knee OA and physical activity measured by an accelerometer. All analyses were adjusted for age, sex, BMI, education, ethnicity and comorbidities, as these factors were assessed as likely associated with both knee OA and physical activity based on previous literature[38,39]. Stata V14.1 (StataCorp LP, TX, USA) was used for all analyses.

## 3. Results

### 3.1. Study population

The NEO study population consisted of 6,671 participants. After exclusion of participants with concomitant other rheumatic diseases ($n$ = 323), with missing physical examination ($n$ = 14), or missing SQUASH data ($n$ = 120) the study population for the current analyses consisted of 6,212 participants (Fig. 1). The percentage missing of all included variables can be found in Supplementary Table S1. Demographic characteristics of the population stratified by clinical knee OA classification status are shown in Table I.

Clinical knee OA was present in 14% of participants. Compared with participants without clinical knee OA, those with clinical knee OA were slightly older (mean (SD) 57.5 (5.0) vs 55.4 (6.1) years), were more often female (67% vs 54%), had a somewhat higher BMI (27.6 (5.1) vs 26.1 (4.3) kg/m$^2$), and were less often highly educated (38% vs 48%). Participants having clinical knee OA also had a worse KOOS pain (median (IQR) 83 (64; 94) vs 100 (97; 100)) and ADL function (88 (70; 97) vs 100 (99; 100)), as well as physical HRQoL (mean (SD) 47.7 (9.5) vs 54.8 (7.8)) compared with participants without clinical knee OA (Table I). The random subsample having knee MRI ($n$ = 1.205) was comparable to the total study population in terms of age, sex, BMI and patient-reported outcome measures. Structural knee OA was present in 12% of participants who underwent MRI of the knee. Of the participants having structural knee OA, 15% was also classified with clinical knee OA.

### 3.2. Association of knee OA with self-reported physical activity

Clinical knee OA was positively associated with physical activity, having a crude effect of on average 4.77 (−1.22; 10.76) more MET hours. However, structural knee OA was negatively associated with physical activity, having a crude effect of −2.95 (−15.15; 9.24) MET hours compared with no structural knee OA.

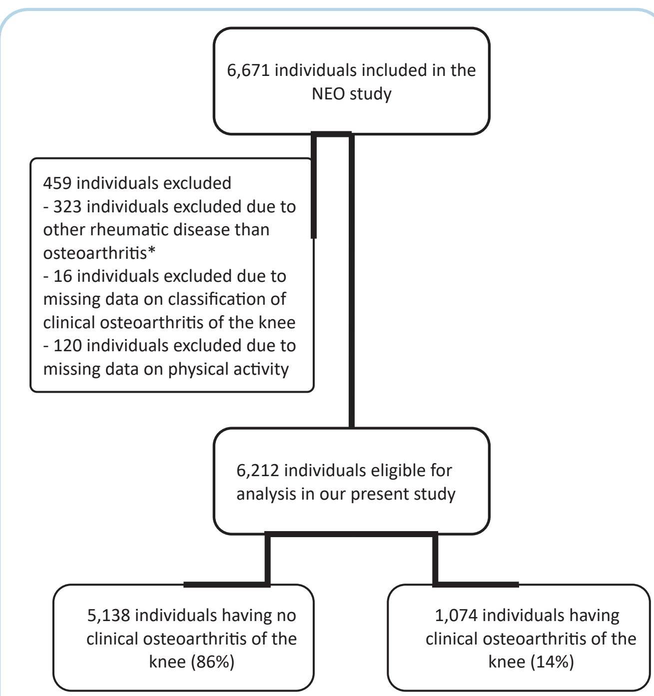


**Fig. 1** Flowchart of the individuals included in the present study. *Rheumatic diseases excluded were: rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, psoriatic arthritis and fibromyalgia.

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**Table I** Characteristics of the weighted NEO study population

| | All $n = 6{,}212$ | No clinical knee OA 86% ($n = 5.138$) | Clinical knee OA 14% ($n = 1.074$) |
|---|---|---|---|
| **General patient characteristics** | | | |
| Age (year) | 55.7 (6.0) | 55.4 (6.1) | 57.5 (5.0) |
| Sex (% women) | 55 | 54 | 67 |
| BMI (kg/m$^2$) | 26.3 (4.4) | 26.1 (4.3) | 27.6 (5.1) |
| Education (% high) | 46 | 48 | 38 |
| Ethnicity (% white) | 95 | 95 | 94 |
| Comorbidities (% present) | 24 | 23 | 32 |
| **Patient reported outcomes** | | | |
| KOOS pain* | 100 (94; 100) | 100 (97; 100) | 83 (64; 94) |
| KOOS ADL function* | 100 (96; 100) | 100 (99; 100) | 88 (70; 97) |
| SF-36 physical component scale | 53.8 (8.4) | 54.8 (7.8) | 47.7 (9.5) |
| SF-36 mental component scale | 51.2 (8.9) | 51.1 (8.8) | 51.6 (9.6) |
| **Physical activity** | | | |
| Total* (MET hours per week) | 118.8 (76.8; 155.0) | 118.4 (76.6; 154.4) | 123.5 (77.8; 157.2) |
| Leisure time* (MET hours per week) | 30.0 (15.8; 49.5) | 29.0 (15.5; 49.0) | 33.2 (18.5; 50.8) |

Results are based on analyses weighted towards the BMI distribution of the general population. KOOS scale range 0–100, higher scores are better. SF-36 norm based scores with mean of 50, SD of 0, higher scores are better. Numbers represent mean (SD) unless otherwise specified.
Abbreviations: ADL = activities of daily living, BMI = body mass index, KOOS = Knee Injury and Osteoarthritis Outcome Score, $n$ = number, OA = osteoarthritis, SF = short form, MET = metabolic equivalent of task.
* Median (25th, 75th percentiles).

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Adjusted for age, sex, BMI, education, ethnicity and comorbidities, there was a positive association between physical activity and clinical knee OA (Table II). In comparison with participants without clinical knee OA, those with clinical knee OA had on average 9.60 (95% CI 3.70; 15.50) MET hours per week more total physical activity. There was a weak positive association between physical activity and structural knee OA, as participants with structural knee OA had on average 3.97 (−7.82; 15.76) MET hours per week more total physical activity than participants without structural knee OA. The stepwise addition of individual potential confounders to the regression model is shown in Supplementary Figs. S1 and S2. The association of knee OA with leisure time physical activity was less evident. However, the association suggested that participants with knee OA were more physically active than participants without knee OA during leisure time (Table II).

### 3.3. *Association of self-reported physical activity with patient reported outcomes*

In the subpopulation of individuals with knee OA, physical activity was not associated with knee pain, function or HRQoL (Table III).

### 3.4. *Sensitivity analysis*

To account for possible information bias commonly associated with self-reported physical activity measures, we additionally investigated the association between clinical knee OA and physical activity measured by an accelerometer. Of the 955 participants having an accelerometer, 831 were eligible for inclusion in our sensitivity analysis (Fig. 2). In this analysis, we observed 2.78 (−5.73; 11.29) MET hours per week more physical activity in participants with clinical knee OA, than in individuals without clinical knee OA. Correlation between physical activity measured by the SQUASH questionnaire, and physical activity measured by an accelerometer was low ($r = 0.239$).

## 4. Discussion

We aimed to assess the potential of physical activity as a target for lifestyle intervention in middle-aged individuals. Therefore, this study investigated if knee OA was associated with lower physical activity compared with no knee OA in a large middle-aged Dutch population, and investigated the association of physical activity with patient reported outcomes in individuals with clinical knee OA.

We did not find an association of knee OA with lower physical activity compared with no knee OA, as we observed that clinical knee OA was associated with somewhat higher physical activity compared with no clinical knee OA. Also, structural knee OA was not associated with lower physical activity, compared with no structural knee OA.

Our study did not show less physical activity in individuals with knee OA compared with those without knee OA, which was in line with most comparable studies. One of these studies investigated a group of 4,125 participants aged above 50 years from the Netherlands[10], using the SQUASH questionnaire. No major differences were found in the amount of physical activity between individuals having knee OA and individuals not having knee OA, being respectively 15.3, 12.3, 18.1 and 17.8 h per week for individuals in primary care, secondary care, post total-joint arthroplasty care, and the general population.

A second study investigated 2,551 individuals aged 65–85 from Sweden, the United Kingdom, Germany, Italy, Spain and the Netherlands[11]. The study recorded physical activity using an accelerometer (Activity Monitor) as well as the self-reported Longitudinal Aging Study Amsterdam (LASA) physical activity questionnaire. In individuals having knee OA, on average 18.6 min per day less physical activity was found compared with individuals having no knee OA. This finding is in contrast with our study. However, in the Swedish and Dutch subpopulations no lower physical activity was found in individuals having knee OA compared with individuals having no knee OA. This lack of difference is in line with our findings in our Dutch population.

**Table II** Association of clinical and structural knee OA with physical activity

| | Clinical knee OA ($n$ = 1.074 (14%)) Beta (95% CI)* | | Structural knee OA ($n$ = 163 (12%)) Beta (95% CI)* | |
|---|---|---|---|---|
| | Crude | Adjusted† | Crude | Adjusted† |
| Total | 4.77 (−1.22; 10.76) | 9.60 (3.70; 15.50) | −2.95 (−15.15; 9.24) | 3.97 (−7.82; 15.76) |
| Leisure time | 3.38 (−0.12; 6.88) | 2.55 (−1.21; 6.32) | 3.65 (−2.96; 10.25) | 3.45 (−3.09; 9.98) |

Results are based on analyses weighted towards the BMI distribution of the general population.
Abbreviations: CI = confidence interval, MET = metabolic equivalent of task, OA = osteoarthritis.
* The beta can be interpreted as the mean difference in MET hours physical activity between individuals with, and without knee OA.
† Analyses were adjusted for age, sex, BMI, education, ethnicity and comorbidities.

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A study from the United States of America compared individuals 491 individuals aged 50–79 with symptomatic knee OA with 449 individuals without symptomatic knee OA using an accelerometer[12]. Levels of physical activity were found to be similarly low in both groups. Time of moderate to vigorous physical activity was found to be comparable between individuals with symptomatic knee OA and the general population without symptomatic knee OA.

Another study from the United States of America compared the physical activity status of 486 individuals having symptomatic knee OA with a control group of 1,455 individuals having no symptomatic knee OA[13]. Physical activity was measured using an accelerometer. The odds of walking at least 10 min per day were found to be similar for individuals with symptomatic knee OA relative to the general population.

We found 9.60 (3.70; 15.50) more MET hours per week of physical activity in individuals with clinical knee OA, compared with individuals with no clinical knee OA. This is approximately equivalent to walking 30 min per day for most days of the week, or performing 1 h per week of vigorous sports[20]. The finding contrasts with previous studies, which might be due to several reasons. First of all, these previous study populations consisted of mostly elderly individuals[10–13], as opposed to our middle-aged study population. Since ageing has been associated with decreased physical activity[40], it is likely that our relatively young study population is more active in general than these older study populations. This is underscored by a relatively strong positive effect of adjustment for age in our study on the association between knee OA and physical activity (Supplementary Fig. S1.1, S1.2). Related to this, it is also likely that our study population consisted of individuals with knee OA in an early disease stage, as knee OA is a progressive disease[41]. Probably, middle-aged individuals are not restricted in their activities, or even well-motivated to address their complaints by a targeted increase in physical activity or by physical therapy. Indeed, the encouragement to be physically active is usually part of the treatment of early-stage knee OA in the Netherlands[42].

Another factor that might explain this contrast we found, is a difference in the method of physical activity measurement. For example, one study used a different physical activity questionnaire than our study (LASA)[11]. Also, three out of four studies solely investigated physical activity measured by an accelerometer, and used a different accelerometer than our study[10,12,13].

Our usage of an accelerometer in our sensitivity analysis solves the problem of social desirability bias. This analysis showed an association in line with the aforementioned association between structural knee OA and self-reported physical activity. The association found by sensitivity analysis is also in line with the association between clinical knee OA and physical activity mentioned previously, although somewhat weaker. Therefore, all adjusted

**Table III** Association of physical activity with disease burden in participants with clinical knee OA

| | Physical activity | |
|---|---|---|
| | Total Beta (95% CI)* | Leisure Beta (95% CI)* |
| KOOS pain | −0.0041 (−0.026; 0.018) | −0.0073 (−0.048; 0.034) |
| KOOS ADL function | −0.0073 (−0.029; 0.014) | −0.0059 (−0.043; 0.031) |
| SF-36 PCS | −0.0012 (−0.017; 0.014) | 0.010 (−0.018; 0.038) |
| SF-36 MCS | −0.0032 (−0.015; 0.0088) | −0.015 (−0.042; 0.012) |

Results are based on analyses weighted towards the BMI distribution of the general population.
Abbreviations: ADL = activities of daily living, CI = confidence interval, KOOS = Knee Injury and Osteoarthritis Outcome Score, MCS = mental component score, MET = metabolic equivalent of task, $n$ = number, OA = osteoarthritis, PCS = physical component scale, SF = short form.
* The beta can be interpreted as the mean difference in outcome score per MET hour of physical activity. Analyses were adjusted for age, sex, BMI, education, ethnicity and comorbidities. KOOS scale range 0–100, higher scores are better. SF-36 norm based scores with mean of 50, SD of 0, higher scores are better.

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analyses of knee OA suggest a positive association of knee OA with physical activity.

As a second aim, this study aimed to investigate the association of physical activity with patient reported outcomes in individuals with clinical knee OA. We did not observe any association between physical activity and knee pain, knee function or HRQoL in these individuals. Our lack of association between physical activity and knee pain is in line with a recent cross-sectional Korean study including 9,196 participants with structural knee OA[43]. This study did not find an association between physical activity levels and knee pain status.

The lack of association between physical activity and physical functioning we found contrasts with a systematic review comprising eight cross-sectional studies[44]. The review investigated factors associated with a low level of physical activity in patients with OA of the hip or knee. Studies of relatively young as well as relatively old individuals were included. The review concluded that lower physical function is associated with lower physical activity for individuals having knee OA. However, limited evidence was found for this conclusion.

One Turkish study cross-sectionally investigated the association between physical activity and HRQoL in 55 individuals over 65 years of age having structural knee OA[45]. Mean physical functioning score of the SF-36 scale was found to be higher in the physically active group than in the physically inactive group (42.0 vs 33.7), which is in contrast with the lack of association we found. The mental component score however was comparable between physically active and physically inactive individuals (48.6 vs 47.7), which is in line with our results. The difference in physical component score between this study and our study could be due to the older age or smaller sample size in the Turkish study, or due to cultural differences[15].

Our study has several strengths. One of the key strengths of our study is the large study population. Other strengths are the facts that we included both clinical and structural knee OA in our analyses, and performed a sensitivity analysis. In addition, we investigated patient-reported outcome measures. Moreover, the middle-aged population we investigated likely gives a reflection of an early disease stage in which interventions should be started when indicated.

Notably, there are also some limitations to our study. We used a cross-sectional design, which hinders causal inference and leaves the potential of reverse causation. Currently, 10-year follow-up measurements are being performed in the NEO study population, which will give us more insight in the causality of our findings. Another limitation of our study is the subjective nature of the physical activity data we used. Self-reported physical activity is likely to be less accurate than objectively measured activity as it is for example prone to forms of response bias, such as social desirability bias[37]. This might cause overestimation of the physical activity reported. The possibility of this bias is supported by our sensitivity analysis, which showed that the association of knee OA and physical activity was somewhat weaker using objectively measured physical activity instead of self-reported physical activity, although it points in the same positive direction. It is further supported by the weak but positive correlation between self-reported physical activity and physical activity measured by an accelerometer. Another limitation of our study is that MRI of the knee was solely performed in the right knee due to logistical reasons. This means that patients having solely structural left knee OA were missed, leading to underestimation of the presence of structural knee OA in our cohort. However, previous literature has shown that structural knee OA is mostly bilateral, and that the right and left knee have a comparable disease course[46,47].

In conclusion, knee OA was not associated with lower physical activity in this middle-aged Dutch population. Future research should indicate what the optimal treatment advice is regarding physical activity for individual knee OA patients, and we should not discourage individuals with knee OA to be physically active.

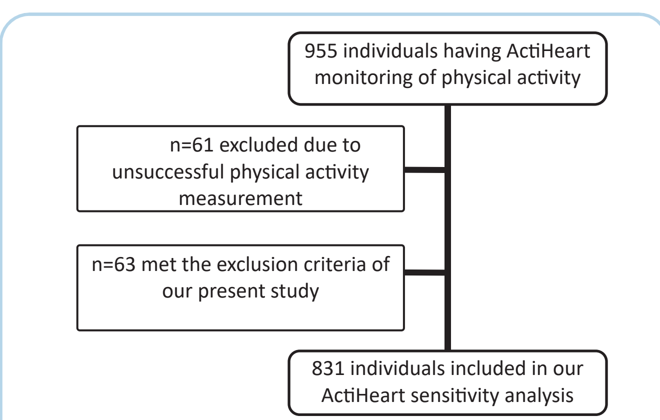


**Fig. 2** Flowchart of the individuals included in our ActiHeart sensitivity analysis.

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## Author contribution

SEST and ML contributed to the design of the study, data analysis and interpretation and drafting of the article. JvV, RdM, LS, MR and FRR contributed to study design, data acquisition, data interpretation and critically revising of the article. DS and MKL contributed to design of the study, interpretation of the data and critically revising the article. ML was the principle investigator. All authors give final approval of the submitted article.

## Conflict of interest

All other authors have declared no conflicts of interest.

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## Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.joca.2021.07.008.

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