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FACTORS ASSOCIATED WITH FUNCTIONAL DECLINE IN HAND AND HIP/KNEE OSTEOARTHRITIS AFTER A YEAR'S TIME: DATA FROM THE EPOSA STUDY

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ABSTRACT

OBJECTIVE: The study investigated factors that together with hand or hip/knee osteoarthritis (OA) could contribute to functional decline over a year's time in elderly individuals.

METHODS: The data of 1,886 individuals between the ages of 65-85 in a prospective, observational population-based study with 12-18 month follow-up in the context of the European Project on OSteoArthritis were analyzed. The outcome measures were self-reported hand and hip/knee functional decline evaluated using a Minimal Clinically Important Difference of 4 on the AUStralian/CANadian hand OA Index and of 2 on the Western Ontario and McMaster Universities hip/knee OA physical function subscales, both normalized to 0-100. Using regression models adjusted for sex, age, country, and education level, the baseline factors considered were: clinical hand or hip/knee OA, pain, analgesic/anti-inflammatory medications, comorbidities, social isolation, income, walking time, grip strength, physical activity time, and medical/social care.

RESULTS: After a year, 453 participants were identified as having "worse" hand functionality and 1,389 as "not worse". Hand OA, anxiety, walking time and grip strength were risk factors for hand functional decline; pain was a confounder of the effect of hand OA.

Analgesic/anti-inflammatory medications mediated the combined effect of hip/knee OA+pain on functional decline in the 554 individuals classified as having "worse" hip/knee functionality and the 1,291 "not worse" persons. Peripheral artery disease, obesity, and cognitive impairment were other baseline risk factors.

CONCLUSION: Study findings showed that together with emotional status, chronic physical and cognitive conditions, OA affects hand and hip/knee functional decline.

Significance and Innovations

- Longitudinal findings confirmed some evidence of previous cross-sectional analyses on the same cohort of older European community dwellers.
- Together with emotional status, chronic physical and cognitive conditions, OA affects hand and hip/knee functional decline.

Functional limitation and pain, which tend to worsen over time, are two important symptoms of hand, hip and knee osteoarthritis (OA). There is nevertheless a paucity of information concerning the longitudinal relationship between these factors in hand, hip/knee OA patients [1], and only a few studies have investigated the risk factors for decline [2-4].

As far as the hand is concerned, functional limitation and pain are markedly associated to impairment in activities of daily living (ADL) and, therefore, to worse quality of life (QoL) [5-9]. Risk factors associated with hand OA include older age, the female sex, and genetics; other possible risk factors are obesity, some specific occupations and sport activities, and ethnicity [10]. A previous study reported that hand OA is associated with both self-reported and performance-based physical function impairment; the association was found to be partially mediated (reduced) by pain. Other risk factors such as depression and osteoporosis have been associated to hand OA [11].

Dekker et al. identified a variety of variables (physical manifestations linked to OA (pain, stiffness, reduced muscle strength, knee joint laxity, proprioceptive inaccuracy, poor standing balance and impaired joint motion range), cognitive and visual impairment, comorbidity and overweight, psychological and social factors (anxiety, depression, fatigue, poor self-efficacy and social support), health behaviors and sociodemographic factors (being older or a female, ethnicity, lower social class and being retired)) that are risk factors for functional decline in hip or knee osteoarthritis [12]. A longitudinal study with a 5-year follow-up conducted on older hip/knee OA patients reported that more avoidance of physical activity, greater pain, multiple comorbidities, longer duration of complaints, lower knee extension, and reduced muscle strength were all predictors of functional decline over time [13].

Since knowing the risk factors for functional decline could contribute to the efforts to design and implement appropriate rehabilitation and life style interventions to reduce their risk, the current work set out to identify the baseline risk factors that, together with clinical hand OA or hip/knee OA, are associated with functional decline in elderly persons over a 12-18 month period.

METHODS

Study design and Participants

The data for our analysis were those collected by the European Project on OSteoArthritis (EPOSA), a population-based study involving cohorts of adults between the ages of 65 and 85 residing in Germany, Italy, the Netherlands, Spain, Sweden, and the UK. Further details regarding

the EPOSA study are described elsewhere [14]. All the participants gave written informed consent, and the study design and protocol were granted approval by the appropriate local ethics committees.

Between November 2010 and November 2011, 2,942 participants underwent a baseline evaluation; 12-18 months later, 2,455 (83%) were available for a follow-up assessment.

As the data regarding the AUSCAN/WOMAC physical function scores of the German cohort (n=336, 14% of 2,455) were incomplete, they were not considered in our analysis. The data of 1,886 participants (89% out of 2,119), i.e., those with complete baseline and follow-up records, were analyzed.

Measures

The study's primary outcome measures were self-reported functional hand and hip/knee decline, as measured respectively by the Australian/Canadian Hand OA Index (AUSCAN) [15] and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) [16, 17] at baseline and 12-18 months later. The AUSCAN is made up of 3 subscales (9 items for physical function, 5 items for pain, and 1 item for stiffness); the WOMAC is also composed of three subscales measuring physical function (17 items), pain (5 items), and stiffness (2 items) in each joint. The items were rated on a five point Likert scale ranging from none to extreme (0=none, 1=mild, 2=moderate, 3=severe, and 4=extreme). The normalized total scores of each scale ranged from 0 to 100, with higher scores indicating worse health status. The decline in the AUSCAN hand and the WOMAC hip/knee physical function scores registered 12-18 months after baseline were assessed using a previously established Minimum Clinically Important Difference (MCID) cut-off value [18]. The cut-offs utilized were derived from the application of anchor- and distribution-based approaches converging to identify 4 points as the MCID for the decline in the AUSCAN hand physical function and 2 points as the MCID for the decline in the WOMAC hip/knee physical function [18]. Using these cut-offs, the participants were classified as having "worse" or "not worse" functionality with respect to their baseline evaluation.

Clinical OA was diagnosed in accordance with the clinical classification criteria developed by the American College of Rheumatology [19] and the recommendations of the European League Against Rheumatism [20]. The clinical diagnosis of hand and hip/knee OA was based on the medical history and physical examination at baseline.

Clinical hand OA was diagnosed [15] in the presence of: hand pain ≥3 and stiffness ≥1, as measured by specific AUSCAN subscales, and at least two of the following: a) hard tissue

enlargement of two or more joints, b) hard tissue enlargement of two or more distal inter-phalangeal joints, c) deformity of at least one hand joint. Swelling of the metacarpophalangeal joints was assessed only in the English and German participants.

Clinical hip/knee OA was diagnosed in the presence of OA in at least one or both joints together with the following: in the case of the hip, hip pain [16, 17], as defined by the WOMAC (the cut-off score that was used was ≥3), and all of the following: a) pain on at least one side associated with restricted hip internal rotation at the physical examination; b) morning stiffness lasting <60 minutes, evaluated using the stiffness section of the WOMAC (a score from mild to extreme). In the case of the knee, pain in the knee [16] as defined by the WOMAC (the cut-off score that was used was ≥3) and at least 2 of the following: a) morning stiffness, as evaluated by the stiffness section of the WOMAC (a score from mild to extreme); b) crepitus on active motion on at least one side; c) bone tenderness on at least one side; d) bone enlargement on at least one side; e) no palpable warmth of synovium in either knees.

The baseline factors included the participant's demographic features, i.e., age, sex, country, and education level (an elementary school education only vs higher levels of education), social isolation, income, walking time, grip strength, physical activity time, medical and social care, the medications the patient was taking, his/her comorbidity data, and the AUSCAN and WOMAC pain scores. Possible responses to a monthly income capable of making ends were: 'only with great difficulty', 'with some difficulty', 'fairly easily' and 'easily'. Social isolation was assessed using the Lubben's Social Network Scale (LSNS-6) [21] and the Maastricht Social Participation Profile (MSPP) [22], and was defined as a LSNS-6 score lower than 12 [21] or less or equal to the median values of the five scores of which the scale is composed [21, 23]. Walking time was based on a timed three-meter walk test and classified according to country-specific quartiles. Grip strength was defined as the maximum value of the mean of two right and left hand measurements carried out by a dynamometer [24]. Physical activity was measured using the LASA Physical Activity Questionnaire (LAPAQ) [25], which assesses the frequency and duration of activities such as: walking, cycling, gardening, household work (light and heavy) and participation in sports over the past two weeks. The total time dedicated to physical activity was calculated in minutes/day. Medical/social care was defined as health care services utilization (hospitalization, primary care use, specialist services use) and home care services (formal and informal). Medical/social care was dichotomized as "yes" or "no" responses.

The medications used over the preceding two weeks (dichotomized as "yes" or "no" responses) referred to analgesic and/or anti-inflammatory drugs. Comorbidity referred to the presence versus the absence of common pathologies such as obesity, which was defined as a body mass index ≥30 kg/m^2 [26]. A score of ≤23 on the Mini-Mental State Examination (MMSE) defined cognitive impairment [27]. A score of ≥8 on the anxiety subscale and a score of ≥8 on the depression subscale of the Hospital Anxiety Depression Scale (HADS) respectively defined those conditions [28]. Chronic conditions such as chronic non-specific respiratory disorders (i.e., asthma, chronic bronchitis or pulmonary emphysema, etc.), cardiovascular diseases (i.e., cardiac valve disease, coronary heart diseases, arrhythmia, pacemaker, cardiac arrest, etc.), peripheral artery disease, diabetes mellitus, ictus, cancer and, finally, osteoporosis lasting at least three months or which caused the individual to seek a physician's attention were registered. All these conditions were self-reported.

Statistical Analysis

The baseline factors, classified considering the MCID score, were analyzed using a set of design weights calculated for sex and five-year age category utilizing the 2010 European Standard Population as its reference [14].

The continuous variables (age, the AUSCAN and WOMAC pain scores, grip strength, physical activity), which were expressed as means, standard deviations, medians and interquartile ranges (IQRs), were compared using the Wilcoxon rank-sum test. The categorical variables (the change in physical function, clinical OA of the hand, clinical OA of the hip/knee, sex, country, educational level, social isolation, income, walking time, medical/social care, medications used, and comorbidities) were expressed using percentages and were compared using the Chi-square test.

Regression models were developed to assess the baseline factors that together with clinical hand OA or with clinical hip/knee OA determined a clinically significant functional decline over a one-year period. The models were adjusted for demographic factors (sex, age, country, education level) following a hierarchical approach to assess the effects of confounding or mediating variables, in particular, of the AUSCAN or WOMAC pain scores, the analgesic/anti-inflammatory medications, and of the comorbidities. The collinearity of these variables was examined. The linearity in the logit model for continuous variables such as age, the AUSCAN and the WOMAC

pain scores was also checked, and the transformations to achieve linearity were applied whenever necessary.

All the interactions among the variables were explored. A SAS macro based on the counterfactual framework was used [29] to test the effect of mediation and to obtain estimates and confidence intervals (CIs) for the direct (through mechanisms excluding the mediator) and indirect (through the mediator mechanism) effects of hand or hip/knee clinical OA decline.

A modified Poisson approach was used to estimate the relative risk (RR) and CIs by using robust error variances instead of a logistic regression with Odds Ratio (OR) that could overestimate the RRs [30], particularly in those cases in which the two binary outcomes of interest were common [31].

Two-sided <.05 p values were considered statistically significant. All the analyses were performed using version 9.4 SAS software (SAS System, SAS Institute Inc., Cary, NC).

RESULTS

Out of the 1,886 participants whose baseline and end-of-study records were complete, 1,842 had complete AUSCAN measurement records and 1,845 had all WOMAC measurement records.

Hand physical function decline

Out of the 1,842 participants with complete AUSCAN records, a MCID score of -2 identified (using a similar methodology as described in Siviero et al. [18]) 432 (23.5%) with clinically significant hand physical function improvement, while a MCID score of 4 identified 453 (24.4%) with clinically significant hand physical function decline 12-18 months after baseline, who were classified as “worse”. The “worse” participants tended: to be older and female, to walk slower and with a poorer grip strength, to dedicate more time to physical activity, to require more medical and social care, to take more analgesic/anti-inflammatory medications, to have more baseline physical function impairment, a higher prevalence of anxiety, depression, osteoporosis, clinical hand OA, and a higher baseline AUSCAN pain score with respect to those belonging to the group without deteriorating function (who were classified as “not worse”, n=1,389) (**Table 1**, weighted data).

The change with respect to the baseline AUSCAN physical function score was significantly different and in opposite directions in the two groups: for the worsening (mean±SD= 14.1±10.1, median (IQR)= 11 (6,18)) and non-worsening (mean±SD= -3.3±7.9, median (IQR)= 0 (-3,0)) (Supplementary material Table S1, weighted data).

Using multivariable regression models (**Table 2**) adjusted for sex, age, country, and education level, we analyzed the baseline factors that together with clinical hand OA determined a clinically significant functional decline 12-18 months after baseline. The AUSCAN pain score was dichotomized at the third quartile (<5 vs ≥5), the physical activity and the grip strength were categorized as variables with four levels using three cut-off points based on the quartiles. The analyses showed that the use of analgesic/anti-inflammatory drugs and comorbidities were not confounders. When baseline pain was included, a 43% difference in the clinical hand OA coefficient was detected, but the coefficient was not significant. Indeed, hand OA did not continue to be highly significant. The interaction of clinical hand OA and the AUSCAN baseline pain score was not statistically significant. Mediation analyses from a counterfactual-based perspective did not confirm that pain was a mediator of the hand OA/hand functionality association, but that it was a confounder.

Hand OA was found to interact with anxiety: the results outlined in **Table 2** show that each of these factors significantly increased the relative risk of worse functionality in the absence of the other factor, with the relative risk of clinical hand OA only slightly less than that of anxiety (1.34 vs 1.39). When the other factor was present, the relative risk of hand OA and of anxiety was no longer significant. The walking time and the grip strength were significantly associated to functional decline.

Hip/knee physical function decline

Out of the 1,845 participants with complete WOMAC records, a MCID score of -2 identified (using a similar methodology as described in Siviero et al. [18]) 406 (22%) with clinically significant hip/knee physical function improvement, while a MCID score of 2 identified 554 (30%) with clinically significant decline ("worse" group) 12-18 months after the baseline assessment. The "worse" participants tended: to be female, older, Italian/ Dutch/ or Spanish, to have a lower income, to walk slower, to have a poorer grip strength, to require more medical/social care services, to have a lower education level, a higher prevalence of diseases (in particular of hip/knee OA), and higher scores on the WOMAC pain scale, and to use more analgesic/anti-inflammatory medication with respect to "no worse" (n=1,291) (**Table 3**, weighted data). There were no differences between the two groups in the prevalence rates of diabetes mellitus, cancer and osteoporosis.

The change with respect to the baseline of the WOMAC physical function score between the two groups was likewise significantly different and in opposite directions: for the worsening, the

mean±SD= 12.9±11 with median (IQR)= 9 (5,17) and for the non-worsening, the mean±SD= -3.4±7.3 with median (IQR)= 0 (-4,0) (Supplementary material Table S2, weighted data).

Age was classified as >73 years (median value) versus others, the WOMAC pain score was dichotomized at the third quartile (<15 vs ≥15), the physical activity and the grip strength were categorized as variables with four levels using three cut-off points based on the quartiles in the multivariable regression models (**Table 4**) evaluating the clinically significant hip/knee functional decline 12-18 months after baseline. When the comorbidities were added, including the baseline pain adjusted the effect of clinical hip/knee OA by approximately 49%, but the baseline pain was not found to be significant and hip/knee OA lost its significance. Since a null frequency resulted when the WOMAC pain x hip/knee OA interaction variable was added, a new variable equal to their combined effect was identified and modelled as the main effect variable: hip/knee OA and WOMAC pain score ≥15 vs other. When the analgesic/anti-inflammatory medication variable was added, there was a 23% change in the coefficient for clinical hip/knee OA and pain. From a counterfactual perspective, mediation analyses confirmed that the analgesic/anti-inflammatory medication variable mediated approximately 27% of the combined effect of OA + pain on physical function decline. In addition to hip/knee OA and a ≥15 pain score [RR 1.27, 95% CI 1.09-1.48] mediated by analgesic/anti-inflammatory medication, other factors (peripheral artery disease, obesity, cognitive impairment) were associated to the functional decline registered at the end of the study.

DISCUSSION

The study aimed to investigate baseline factors such as pain, medication and comorbidity that together with hand or hip/knee OA could contribute to clinically meaningful functional decline over a 12-18 month period in an elderly population.

The MCIDs for decline used in the present work are lower with respect to those in other studies [18]. Differences could be due to diversified time periods, baseline health status, interventions and/or the direction of the change in the MCID considered (improvement or decline).

The analysis of our data uncovered that hand OA, anxiety, walking time and grip strength were indeed risk factors for hand physical function decline over the study period. The association between the hip/knee OA + a ≥15 WOMAC pain score combination and a clinically meaningful physical function decline 12-18 months after baseline was reduced when it was adjusted for analgesic/anti-inflammatory medication, which seemed to partially mediate the association.

Peripheral artery diseases, obesity, cognitive impairment were other baseline risk factors for hip/knee physical function deterioration.

The longitudinal data on the hand outlined here did not confirm the role of pain as a mediator in the OA and physical function decline association that was uncovered during one of our cross-sectional studies [11, 32-35], but showed that it was a confounder. In accordance with our previous results, the current study found associations between the participant's physical function and psychological factors [36-37]. Anxiety, which is an emotional reaction associated to a non-specific stimulus, could lead to preventative behaviors, such as avoidance of potentially painful stimuli or activities [36].

An analysis of our hip/knee physical function decline data showed that some conditions, such as obesity, cognitive impairment, and peripheral artery diseases played a confounding effect on the OA/physical function interaction. In fact, although they were independently associated with functional decline, they did not decrease the strength of the OA association.

Our analysis confirmed the findings of one of our previous works examining the cross-sectional association between clinical OA, comorbidity, and physical function in the same cohort of persons [9]. Individuals with OA generally tend to have a significantly higher cluster of comorbid conditions than those without [39, 40]. Many of these conditions share, in fact, similar pathophysiologic pathways, and some, such as peripheral artery diseases, may affect the physical function, limiting endurance performance [41]. In addition, cognitive impairment affects day-to-day decision-making and motivation and is therefore associated with functional limitation in ADL and IADL, independently of the effect of somatic conditions [42].

Obesity seems to have an important impact on individuals with OA. Some studies have, in fact, demonstrated its effect on pain scores [43] and on OA progression [44]. While some cross-sectional evidence does exist concerning the associations between obesity and QoL, physical function, and exercise, only a few studies have examined the impact over time of obesity on disability [45-48]. According to a recent study analyzing older individuals who were monitored over a 6-year period, obesity led to worse physical function and reduced ability to engage in physical activity as well as disability in individuals with or at risk of OA [49].

As the co-presence of obesity and OA seems to represent a "hazardous duet," identifying strategies that can contribute to weight loss has become an ever more salient objective. Peripheral artery diseases and cognitive impairment appear to be another dangerous pair: the frequent co-occurrence of these conditions in older OA patients underlines the importance of implementing

comprehensive geriatric assessments to identify and better manage synergistic effects that may lead to worse functional status.

The higher risk of functional decline in individuals using analgesic/anti-inflammatory medication at baseline was not surprising, as higher pain levels can, logically speaking, lead to worse functional decline. Although there is still no cure for OA, interventions based on the principle of reducing pain in order to maintain functional ability over short periods of time seem reasonable. A better understanding of the pathological mechanisms underlying OA onset will contribute to formulating better prevention strategies [50].

The study has, of course, some limitations. First, as the samples were drawn from selected areas in each of the participating countries, they may not be representative of the national population. Second, our results can be generalized only to individuals with clinical and *not* radiographic OA, as none of participants underwent radiographic exams. Third, only self-reported physical function scales, not confirmed by any performance tests, were used as the study's outcomes. Although validated, reliable, standardized, and patient-centered, the AUSCAN and WOMAC physical function subscale scores might in any case mirror cultural, educational, psychological, health, cognitive factors, and differences across countries reflecting discrepancies in these underlying variables. An analysis using performance-based tests measuring OA-related physical limitations could provide more reliable results. While the AUSCAN test is rarely adopted in population-based studies, here it was utilized to assess *both* pain and physical function. Nevertheless, while it is true that the AUSCAN was used to evaluate these variables, it was also utilized to diagnose hand OA, although several other factors, for the most part linked to the physical examination, were taken into consideration [8, 9]. Finally, comorbidity was based on self-reported diseases and selected screening tests and not on clinically ascertained diagnoses. The reliability of self-reported diagnoses, also confirmed by the patients' use of medication, is, nevertheless, generally considered high.

The study's greatest strength is its large population of randomly selected community-dwelling older Europeans *some with and some without OA* residing in different countries. The same methodology was used across all of those countries, and the participants were diagnosed with OA in accordance with standardized international guidelines [14]. The use of standardized, validated measures to evaluate self-reported physical function represents another important strength. Finally, the current study adds to the existing body of knowledge given its longitudinal character and its population-based focus.

In conclusion, the study provides additional longitudinal evidence that treating pain can contribute to preventing the functional decline associated to hip/knee OA. The fact that it was also found to be a significant predictor of functional decline indicates that further efforts should be made to learn more about the disease's pathophysiology. Emotional status is another factor that should be taken into consideration at the time the impact of physical disorders on functioning is being evaluated and the treatment for disorders causing chronic pain is being contemplated. As some physical and cognitive disorders and chronic illness have been identified as independent risk factors for hip/knee functional decline, a multifaceted, geriatric approach seems appropriate. Individuals with OA who have any of these conditions are at greater risk of functional decline and may benefit from prevention strategies.

Further research will be able to answer the many questions that still remain concerning the physical, social and psychological factors linked to OA onset and progression and functional decline.

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Table 1. Weighted baseline factors for MCID classifications of hand AUSCAN physical function score 12-18 months after baseline.

Baseline factors		**Total (n = 1,842)**	**Worse (n=453)**	**Not worse (n=1,389)**	***P***
Female sex		52.0	69.3	46.3	***<.001***
Age, years, mean±SD, median (IQR)		73.7±5.0	74.4±5.0	73.5±4.9	***.001***
		73 (70-77)	74 (70-78)	73 (70-77)	
Country	Italy	17.2	20.7	16.0	*.17*
	The Netherlands	22.2	22.4	22.2	
	Spain	21.1	19.8	21.6	
	Sweden	23.3	23.1	23.4	
	UK	16.1	14.0	16.8	
Up to elementary education		40.5	42.6	39.8	*.29*
Social isolation		20.3	20.7	20.2	*.83*
Income	Easily	31.7	29.8	32.3	*.71*
	Fairly easily	49.9	51.1	49.5	
	With some difficulty	15.4	16.4	15.0	
	With great difficulty	3.1	2.7	3.2	
Walking time[a], %	<Q1	28.6	21.7	30.9	***<.001***
	Q1-Q2	26.5	21.3	28.2	
	Q2-Q3	22.7	25.9	21.6	
	> Q3	22.3	31.1	19.3	
Grip strength[b], kg, mean±SD, median (IQR)		27.7±10.0	24.0±7.9	29.0±10.4	***<.001***
		26.0 (20.0-34.5)	23 (19-28)	27.5 (21-37)	
Physical activity time (LAPAQ), min/day, mean±SD,		197.3±132.2	209.4±137.7	193.3±130.1	***.03***
median (IQR)		172.9 (107.1-252.9)	180.4 (115.7-267.1)	167.9 (105.0-248.6)	
Medical/Social care		79.2	83.4	77.8	***0.01***
Obesity		25.3	25.7	25.2	*.85*
Cognitive impairment		7.0	8.6	6.5	*.13*
Anxiety		18.6	24.9	16.6	***<.001***
Depression		10.2	13.8	9.0	***.004***
Chronic lung disease		12.5	12.7	12.4	*.88*
Cardiovascular disease		24.4	25.9	23.9	*.39*
Peripheral arterial disease		9.8	11.7	9.1	*.12*
Diabetes mellitus		11.6	9.2	12.4	*.07*
Stroke		4.9	6.3	4.4	*.10*
Cancer		13.4	14.3	13.1	*.54*
Osteoporosis		16.2	19.7	15.0	***.02***
Analgesic/Anti-inflammatory medication		25.7	30.3	24.1	***.01***
Clinical hand osteoarthritis		16.7	23.3	14.6	***<.001***
AUSCAN pain[b] **subscale score**, mean±SD, median (IQR)		7.6±15.2	10.0±16.6	6.8±14.7	***<.001***
		0 (0-5)	0 (0-15)	0 (0-5)	

All of the data except for the numbers of participants, age, and sex are weighted. Except where indicated otherwise, the values are the percent of participants. AUSCAN: AUStralian CANadian Osteoarthritis Hand Index; MCID:

Minimum Clinically Important Difference; SD, standard deviation; IQR, interquartile range; Q1, Q2, Q3, quartiles; LAPAQ, LASA Physical Activity Questionnaire;

a By country quartiles, class ≤ Q1 indicates best performance, class > Q3 indicates worst performance.

[b] Lower values indicate worse performance.

[b] AUSCAN pain scores for the hand ranging from 0 to 100, with 0 indicating no pain.

Table 2. Baseline factors associated to hand functional decline evaluated 12-18 months after baseline.

Baseline factors		B	Standard Error	*P*	RR	95% CI
Social isolation		0.03	0.10	*0.81*	1.03	(0.84-1.26)
Income	Easily				1.00	
	Fairly easily	-0.07	0.10	0.46	0.93	(0.76-1.13)
	With some difficulty	-0.16	0.14	0.25	0.85	(0.65-1.12)
	With great difficulty	-0.51	0.26	0.05	0.60	(0.36-0.99)
Walking time[a], %	≤Q1				1.00	
	Q1-Q2	0.01	0.13	*0.93*	1.01	(0.79-1.30)
	Q2-Q3	0.25	0.12	***0.04***	**1.28**	**(1.01-1.63)**
	> Q3	0.32	0.13	***0.01***	**1.37**	**(1.07-1.76)**
Grip strength[b], kg	>35				1.00	
	≤20.5	0.56	0.20	***0.006***	**1.74**	**(1.17-2.59)**
	20.5-26.75	0.58	0.19	***0.002***	**1.78**	**(1.23-2.58)**
	26.75-35	0.48	0.17	***0.004***	**1.61**	**(1.17-2.24)**
Physical activity time (LAPAQ), min/day	>252.9				1.00	
	≤105.0	-0.09	0.12	*0.47*	0.92	(0.73-1.16)
	105.0- 171.1	-0.04	0.11	*0.74*	0.96	(0.77-1.20)
	171.1-252.9	-0.15	0.11	*0.18*	0.87	(0.70-1.07)
Medical/Social care		0.15	0.12	*0.21*	1.16	(0.92-1.46)
Obesity		-0.05	0.09	*0.62*	0.95	(0.79-1.15)
Cognitive impairment		0.07	0.14	*0.58*	1.08	(0.83-1.40)
Depression		0.13	0.12	*0.29*	1.14	(0.90-1.44)
Chronic lung disease		-0.004	0.12	*0.98*	1.00	(0.88-1.25)
Cardiovascular disease		0.04	0.09	*0.62*	1.05	(0.88-1.25)
Peripheral arterial disease		0.18	0.12	*0.13*	1.20	(0.95-1.53)
Diabetes mellitus		-0.16	0.14	*0.25*	0.86	(0.65-1.12)
Stroke		0.17	0.16	*0.30*	1.19	(0.86-1.63)
Cancer		0.02	0.11	*0.87*	1.02	(0.82-1.27)
Osteoporosis		-0.08	0.11	*0.45*	0.92	(0.75-1.14)
Analgesic/Anti-inflammatory medication		0.005	0.10	*0.96*	1.01	(0.83-1.21)
AUSCAN pain score[c] **≥5**		0.10	0.11	*0.35*	1.11	(0.89-1.37)
Clinical hand OA						
	No anxiety	0.29	0.14	***.03***	**1.34**	**(1.03-1.75)**
	Anxiety	-0.17	0.18	*.37*	0.85	(0.60-1.20)
Anxiety						
	No clinical hand OA	0.33	0.11	***.004***	**1.39**	**(1.11-1.73)**
	Clinical hand OA	-0.14	0.18	*.44*	0.87	(0.62-1.23)

Model adjusted for age, sex, country, education level. β, regression coefficient RR, relative risk; CI, Confidence Intervals; Q1, Q2, Q3, quartiles; LAPAQ, LASA Physical Activity Questionnaire; AUSCAN: AUStralian CANadian Osteoarthritis Hand Index;

[a] By country quartiles, class ≤ Q1 indicates best performance, class > Q3 indicates worst performance.

[b] Lower values indicate worse performance.

[c] AUSCAN pain scores for the hand ranging from 0 to 100, with 0 indicating no pain.

Table 3. Weighted baseline factors for MCID classifications of hip/knee WOMAC physical function score 12-18 months after baseline.

Baseline factors		**Total (n=1,845)**	**Worse (n=554)**	**Not worse (n=1,291)**	***P***
Female sex		51.3	56.0	49.3	***.008***
Age, years, mean (SD), median (IQR)		73.7 (5.0)	74.5 (5.2)	73.4 (4.8)	***<.001***
		73 (70-77)	74 (70-78)	73 (70-77)	
Country	Italy	17.2	20.9	15.6	***<.001***
	The Netherlands	21.1	25.6	19.1	
	Spain	22.8	23.7	22.4	
	Sweden	23.4	16.6	26.3	
	UK	15.6	13.3	16.6	
Up to elementary education		41.3	49.5	37.8	***<.001***
Social isolation		21.0	23.8	19.8	***.06***
Income	Easily	31.5	27.3	33.3	***.003***
	Fairly easily	49.9	49.4	50.1	
	With some difficulty	15.6	19.3	14.0	
	With great difficulty	3.0	4.1	2.6	
Walking time[a], %	<Q1	28.9	22.8	31.6	***<.001***
	Q1-Q2	26.0	26.2	26.0	
	Q2-Q3	22.9	23.4	22.7	
	> Q3	22.1	27.6	19.8	
Grip strength[b], kg,, mean±SD, median (IQR)		27.8±10.2	26.3±9.6	28.4±10.4	***<.001***
		26.3 (20-35)	24.5 (19.5-32.5)	27 (20.5-36.0)	
Physical activity time (LAPAQ), min/day, mean±SD,		196.7±132.2	199.1±139.1	195.7±129.2	*0.6*
median (IQR)		172.9 (105.7-252.9)	173.6 (105.4-255.0)	172.9 (105.7-252.9)	
Medical/Social care		79.3	84.9	76.8	***<.001***
Obesity		25.0	31.3	22.3	***<.001***
Cognitive impairment		7.0	9.9	5.8	***.002***
Anxiety		18.7	23.1	16.8	***.002***
Depression		10.3	13.1	9.1	***.01***
Chronic lung disease		12.6	15.1	11.6	***.04***
Cardiovascular disease		24.2	29.1	22.1	***.002***
Peripheral arterial disease		9.5	14.5	7.3	***<.001***
Diabetes mellitus		11.8	11.1	12.1	*.55*
Stroke		4.9	6.4	4.2	***.05***
Cancer		13.1	14.6	12.4	*.22*
Osteoporosis		16.1	18.6	15.0	*.06*
Clinical hip/knee osteoarthritis		22.6	32.6	18.3	***<.001***
Analgesic/Anti-inflammatory medication		25.5	35.7	21.1	***<.001***
WOMAC hip/knee pain score[c], mean (SD), median (IQR)		10.0 (14.3)	13.3 (15.1)	8.6 (13.8)	***<.001***
		5 (0-15)	10 (0-20)	0 (0-10)	

All of the data except for the numbers of participants, age, and sex are weighted. Except where indicated otherwise, the values are the percent of participants. WOMAC, Western Ontario and McMaster Universities hip/knee Index;

MCID: Minimum Clinically Important Difference; SD, standard deviation; IQR, interquartile range; Q1, Q2, Q3, quartiles; LAPAQ, LASA Physical Activity Questionnaire;

[a] By country quartiles, class ≤ Q1 indicates best performance, class > Q3 indicates worst performance.

[b] Lower values indicate worse performance.

[c] WOMAC pain score for hip/knee ranging from 0 to 100, with 0 indicating no pain.

Table 4. Baseline factors associated to hip/knee functional decline evaluated 12-18 months after baseline.

Baseline factors		β	Standard Error	*P*	RR	(95% CI)
Social isolation		0.05	0.09	***0.57***	**1.05**	**(0.89-1.25)**
Income	Easily				1.00	
	Fairly easily	0.09	0.09	*0.31*	1.10	(0.92-1.31)
	With some difficulty	0.10	0.12	*0.41*	1.10	(0.87-1.39)
	With great difficulty	0.14	0.20	*0.50*	1.15	(0.77-1.70)
Walking time[a], %	≤Q1				1.00	
	Q1-Q2	0.07	0.10	*0.49*	1.07	(0.87-1.32)
	Q2-Q3	0.06	0.11	*0.57*	1.06	(0.86-1.31)
	> Q3	0.08	0.11	*0.49*	1.08	(0.87-1.34)
Grip strength[b], kg	>35.5				1.00	
	≤20.5	0.32	0.15	*0.03*	1.37	(1.03-1.83)
	20.5-27	0.24	0.13	*0.06*	1.28	(0.99-1.65)
	27-35.5	1.17	0.12	*0.18*	1.17	(0.93-1.47)
Physical activity time (LAPAQ), min/day	>252.1				1.00	
	≤105	-0.07	0.10	*0.53*	0.94	(0.76-1.15)
	105-170.1	0.01	0.10	*0.90*	1.01	(0.83-1.24)
	170.1-252.1	-0.07	0.10	*0.51*	0.94	(0.77-1.14)
Medical/Social care		0.12	0.11	*0.28*	1.12	(0.91-1.39)
Obesity		0.22	0.08	***.005***	**1.24**	**(1.07-1.44)**
Cognitive impairment		0.23	0.11	***.045***	**1.25**	**(1.00-1.56)**
Anxiety		0.13	0.09	*.14*	1.14	(0.96-1.36)
Depression		-0.18	0.11	*.11*	0.83	(0.67-1.04)
Chronic lung diseases		0.08	0.09	*.38*	1.09	(0.90-1.31)
Cardiovascular diseases		0.14	0.08	*.069*	1.15	(0.99-1.34)
Peripheral artery diseases		0.31	0.09	***<.001***	**1.36**	**(1.14-1.62)**
Diabetes mellitus		-0.13	0.11	*.24*	0.88	(0.71-1.09)
Stroke		0.15	0.13	*.23*	1.17	(0.91-1.50)
Cancer		0.09	0.10	*.33*	1.10	(0.91-1.32)
Osteoporosis		-0.01	0.10	*.89*	0.99	(0.82-1.19)
Analgesic/Anti-inflammatory medication		0.39	0.08	***<.001***	**1.48**	**(1.27-1.73)**
Clinical hip/knee osteoarthritis with WOMAC pain score[c] **≥15**		0.24	0.08	***.003***	**1.27**	**(1.09-1.48)**

Model adjusted for age, sex, country, education level. β, regression coefficient; RR, relative risk; CI, Confidence Intervals; Q1, Q2, Q3, quartiles; LAPAQ, LASA Physical Activity Questionnaire; WOMAC, Western Ontario and McMaster Universities Osteoarthritis hip/knee Index.

[a] By country quartiles, class ≤ Q1 indicates best performance, class > Q3 indicates worst performance.

[b] Lower values indicate worse performance.

[c] WOMAC pain score for hip/knee ranges from 0 to 100, with 0 indicating no pain.