

**ASSOCIATION BETWEEN OSTEOARTHRITIS AND SOCIAL ISOLATION: DATA
FROM THE EPOSA STUDY**

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IMPACT STATEMENT

We certify that this work is novel.

The potential impact of this research on clinical care or health policy includes the following:

- The study is the first to assess the association between OA and social isolation using prospective data.
- OA is associated with incident social isolation, adjusting for cognitive impairment, depression, and worse walking time.

75 – The findings suggest that interventions addressing this topic could/should be developed.

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ABSTRACT

OBJECTIVE: To determine whether there is an association between osteoarthritis (OA) and incident social isolation using data from the European Project on Osteoarthritis (EPOSA) study.

DESIGN: Prospective, observational study with 12-18 months of follow-up.

SETTING: Community-dwelling.

PARTICIPANTS: Older people living in six European countries.

MEASUREMENTS: Social isolation was assessed using Lubben's Social Network Scale and the Maastricht Social Participation Profile. Clinical OA of the hip, knee and hand was assessed according to ACR criteria. Demographic characteristics including, age, sex, multi-joint pain and medical comorbidities were assessed.

RESULTS: Out of the 1,967 individuals with complete baseline and follow-up data, 382 (19%) were socially isolated and 1,585 were non-socially isolated at baseline; of these, 222 (13.9%) experienced social isolation during follow-up. Using logistic regression analyses, after adjustment for age, sex and country, four factors were significantly associated with incident social isolation: clinical OA, cognitive impairment, depression, and worse walking time. Compared to those without OA at any site or with only hand OA, clinical OA of the hip and/or knee, combined or not with hand OA, led to a 1.47 times increased risk of social isolation (95% confidence intervals: 1.03-2.09).

CONCLUSION: Clinical OA, present in one or two sites of the hip and knee, or in two or three sites of the hip, knee and hand increased the risk of social isolation, adjusting for cognitive impairment and depression, and worse walking times. Clinicians should be aware that individuals with OA may be at greater risk of social isolation.

Key words: osteoarthritis; social isolation; EPOSA; epidemiology.

INTRODUCTION

Social isolation has been defined as the consequence of a small social network with few social contacts.¹ It has been reported to be associated with poor physical and mental health. (2-4) Previous literature has suggested there is an association between musculoskeletal pain and social isolation.¹ This has been attributed to comorbid disease²⁻⁶ and physical impairment.⁷ The signs and symptoms commonly associated with osteoarthritis (OA), most notably joint pain and reduced function, may increase the risk of social isolation.^{8,9} People with OA often present with health risk factors that may increase their probability of social isolation. These include anxiety and depression, kinesiphobia, physical inactivity, reduced self-efficacy, which, depending on their severity, may reduce functional independence.^{1, 10, 11} However, there has been limited research on the relationship between OA and social isolation.¹ Given that the high prevalence of OA^{12, 13} in older people, affecting about 30% of persons over 65 and especially affecting lower limbs, is associated with poor quality of life and disability, a better understanding of social isolation in this specific population has become urgent. If studies show that age is associated with OA, preventative health and social interventions may be able to reduce the impact of social isolation and to improve quality of life.^{8,9} Given these considerations and basing its analysis on data from the European Project on OsteoArthritis (EPOSA) study, a large European cohort study with 12 to 18 months follow-up, the current study aimed to determine whether there is an association between OA and incident social isolation and to identify OA's unique contribution in the presence of other predictors for social isolation.

METHODS

Population and Data Collection

Participants were identified from the EPOSA cohort. This is a population-based study of 2,942 adults between the ages of 65 to 85 years old, who are resident in six European countries (Germany, Italy, the Netherlands, Spain, Sweden, and the UK). More details about the EPOSA cohort are described elsewhere.¹²

After obtaining written informed consent, all participants underwent a baseline assessment including a clinical examination and interview on health status performed at home or in a health care centre between November 2010, and November 2011. A follow-up interview was performed 12 to 18 months later.

The local research ethics committees approved the study (Germany: Universitat Ulm Ethikkommission [312/08]. Italy: Comitato Etico Provinciale Treviso [XLIV-RSA/AULSS7]. The Netherlands: Medisch Ethische Toetsingscommissie Vrije Universiteit Amsterdam [2002/141]. Spain: Comité Ético de Investigación Clínica del Hospital Universitario La Paz Madrid [PI-1080]. Sweden: Till forskningsetikskommittén vid Karolinska Institutet Stockholm [00-132]. UK: Hertfordshire Research Ethics Committee [10/H0311/59]).

Outcome

The current study's primary outcome was the social isolation of the participants at baseline and 12 to 18 months later. Social isolation was assessed using two instruments (**Supplementary Table S1**): Lubben's Social Network Scale (LSNS-6)¹⁴ and the Maastricht Social Participation Profile (MSPP).¹⁵

The LSNS-6 tool measures the number and frequency of social contacts with friends (three items) and family members (three items); each question is scored from zero ('not at all') to five ('nine times or more a month'); the total score ranges from zero (indicating high isolation/few

social resources) to 30 (indicating low isolation/many social resources); as proposed by Lubben a cut-off point of less than 12 indicates social isolation.¹⁴

The MSPP measures the participant's actual social participation over the preceding four weeks.

¹⁵ It is composed of three indexes: consumptive participation (CP) which refers to organised activities (six items), formal social participation (FSP) which refers, for example, to volunteer activities (three items) and informal social participation (ISP) which refers to contacts with family members, friends and acquaintances. The responses are classified using a Likert-type scale from 0 ('not at all') to 3 ('more than twice a week'). Two types of scores are foreseen for each index: diversity (the number of items on which a respondent scored at least one) and frequency (mean score of the items). There is also a total diversity score that refers to the number of indices with a score of at least one.¹⁵ Higher scores indicate more diverse or more frequent social participation.

Since the EPOSA study needed to harmonize data from 6 countries, it used 2 of the 3 MSPP subscales, the CP and FSP. As the third subscale (ISP) of the MSPP is similar to the Lubben scale, we used the latter, together with its cut-off value (12). The total diversity score of our analysis¹⁵ was calculated considering the CP and the FSP of the MSPP and the LSNS-6. A participant's diversified social participation index was calculated considering the median value of each of the following: total diversity, CP diversity, CP frequency, FSP diversity and FSP frequency. Since the MSPP does not define cut-off points, we used medians in our analysis as they are considered the most appropriate statistical method for evaluating continuous variable scores.

Social Isolation was defined as LSNS-6 < 12¹⁵ or \leq the median values of all five scores.

Clinical diagnosis of OA

The study's primary aim was to estimate the effect of the clinical diagnosis of OA on the outcome variable (**Supplementary Table S1**).

In accordance with the clinical criteria of the American College of Rheumatology (ACR)¹⁶ and European League Against Rheumatism,¹⁷ the clinical diagnosis of OA was determined at baseline on the basis of the participant's medical history and a physical examination. Clinical hand OA was diagnosed using specific sections of the AUSCAN.¹⁸ Clinical hip/knee OA, defined as the presence of OA in at least one or both of these joints, was diagnosed using specific WOMAC sections examining pain and stiffness.^{8,9} Pain in the hip/knee on at least one side was also evaluated during the physical examination.¹⁸

As far as clinical OA was concerned, the participants were classified as: (1) no OA, (2) only hand OA, (3) hip and/or knee OA, (4) hip and/or knee OA combined with hand OA.

Baseline characteristics

The baseline characteristics (**Supplementary Table S1**) considered included: age, sex, country of residence, education level, marital status, income, comorbidity, medications being taken, joint replacements, clinical examination, health, and lifestyle characteristics.

Education level was categorized as up to elementary education versus higher levels of education. Marital status was categorized as being single or never married, divorced, widowed, living apart versus married or cohabitating, or a registered partnership. A monthly income capable of making ends meet was classified as 'only with great difficulty', 'with some difficulty', 'fairly easily' and 'easily'. Comorbidity in our analysis referred to: obesity¹⁹, cognitive impairment²⁰, anxiety and depression²¹, self-reported presence of chronic conditions such as non-specific lung disease (i.e. asthma, chronic bronchitis or pulmonary emphysema, etc.), cardiovascular disease (i.e. cardiac valve disease, coronary heart diseases, arrhythmia, pacemaker, cardiac arrest, etc.), peripheral artery disease, diabetes mellitus, stroke, cancer and osteoporosis, lasting at least three months or which caused the individual to seek a physician's attention (each dichotomized as present versus absent).

Medication used over the past two weeks referred to analgesic and/or anti-inflammatory drugs, the variable was dichotomized as medication use versus non-use. The presence of previous joint replacements was assessed by asking participants if they had ever had joint replacement surgery. If the response was affirmative, the participant was questioned about the location and time of and the reason for the joint replacement. Self-rated health assessment²² classified as 'fair', 'bad', 'very bad', 'good' and 'very good'. Health-related quality of life was assessed using the EuroQoL (EQ-5D, EQ VAS).²³

The clinical examination assessed grip strength and walking-test time. The mean of two right and left hand measurements by a dynamometer of the maximum *grip strength* was calculated.²⁴ The *walking-test time* was determined during a timed three-meter walk test. The participants' times were classified according to country-specific quartiles in order to take account the specific methodology used in each country.

Physical activity was measured using the validated LASA Physical Activity Questionnaire (LAPAQ)²⁴ which assesses the frequency and duration of activities such as: walking, cycling, gardening, light and heavy household work, and participation in sports over the past two weeks. The total time dedicated to physical activity was calculated in minutes/day and the total amount of energy was expressed as kcal/day.

Health characteristics considered physical function, pain, and stiffness in hand, hip and/or knee. These were assessed using subscales of the AUSCAN¹⁸ and of WOMAC.^{8,9} Hip/knee pain and stiffness were defined as the maximum value reported across two joints.

All the AUSCAN and WOMAC subscales (responses ranging from 0=none to 4=extreme) were normalized to a 0 to 100 range: higher scores indicated worse health status.^{8,9}

Statistical Analysis

Only participants with complete data on all the variables were included in the analyses. As the age and sex distribution varied in the cohorts from the different countries participating in the

EPOSA study, they calculated a weighting variable for each individual within each country. The weights, which were based on sex and five-year age categories according to the 2010 Standard European Population, were applied only in the descriptive and not in the analytic statistics.¹² Categorical variables were reported as proportions, and continuous variables as means and standard deviations, or medians with interquartile ranges (IQRs). Significant differences between the groups of participants were evaluated using Wilcoxon rank-sum test, or χ^2 testing.

The predictors of social isolation were assessed using logistic regression models adjusted for sex, age, and country. Each independent variable was tested using a significance level $P \leq 0.20$ as the screening criterion.²⁵ The appropriate categories for the categorical variables and the linearity in the logit for continuous variables were then examined, and the scale for the continuous variables in the logit was checked.

A multivariable model containing all the variables identified for inclusion was fitted using a stepwise selection procedure (P to enter $=0.15$ and P to remain $=0.10$) to select them. Those excluded were controlled for confounding effects. The collinearity of the predictor variables was assessed with the variance inflation factor, using a cut-off of 2 to exclude a variable. All the interactions between the variables in the final model were checked; interaction terms with $P \leq 0.10$ were retained in the final model. Odds ratios (ORs) were presented with their 95% confidence intervals (CIs).

Statistical analyses were performed with SAS software (SAS Institute Inc, Cary, NC), version 9.4. All the tests were two-sided, and $P < 0.05$ was considered statistically significant.

RESULTS

Out of the 2,942 individuals originally enrolled in the EPOSA, 1,967 (67%) presented complete baseline and follow-up data on all the variables used in the analyses.

With respect to the participants with complete follow-up data (n=1,967), those whose data were incomplete (n=488) were significantly older, more likely to be female, single/divorced/widowed or living apart, and predominantly Dutch (**Supplementary Table S2**).

The median age of the 1,967 participants was 73 years (IQR: 70 to 77 years); 50% were women, and almost 30% had a diagnosis of OA (**Table 1**). At baseline, 382 (19%) of the participants were categorized as socially isolated and 1,585 as non-socially isolated. The non-socially isolated individuals differed from the socially isolated participants in many important ways (data not shown), including being younger, being residents in all countries except Spain, being more educated and with higher income. The non-socially isolated people also presented a significantly lower prevalence of cognitive impairment, anxiety, depression, chronic lung disease, and stroke. They were less likely to use analgesic/anti-inflammatory medications. They reported a lower rate of clinical OA, but only when all the sites (hand, hip and/or knee) were considered; they had a better health status, and were more likely to partake in physical activity. They were quicker on the walking test, were stronger, and had less physical function impairment and a lower perception of pain.

According to logistic regression analyses, when clinical OA was adjusted for age, sex and country, it was associated with social isolation only when it was present in all three sites. But this association was not confirmed in the multivariable model in which low education, low income, depression, joint replacement (protective) and a pattern of fair/bad/very bad self-rated health and anxiety were found to be associated with social isolation (data not shown).

Baseline demographic and clinical characteristics of incident cases of social isolation

Out of the 1,585 non-socially isolated individuals at baseline, 222 (13%) incident cases of social isolation were found 12 to 18 months after baseline (**Table 1**). The participants who had become socially isolated were less educated and predominantly Spanish, Dutch and Italian. They reported that their income easily or fairly easily covered their needs. They presented higher percentages of cognitive impairment, depression, and clinical OA of the hip and/or knee and of the hand and hip and/or knee. They presented worse self-rated health status (self-rated health and EQ VAS), and lower levels of physical activity. They had slower walking times, higher levels of physical functioning impairments, worst stiffness in the hip/knee and hand, and a higher perception of pain in the hip/knee.

Predictors of incident social isolation

According to logistic regression analyses, adjusted for age, sex and country, clinical OA was associated with incident social isolation. As only the hip and/or knee level was significantly associated to social isolation (data not shown), at the next step “no OA” or “only hand OA” was compared to “hip and/or knee OA” and “hand OA and hip and/or knee OA”. The other 11 univariable predictors of social isolation that were identified were: income, cognitive impairment, depression, cancer, self-rated health, EQ-5D, EQ VAS, walking time, physical function, pain (dichotomized in correspondence with the third quartile as <15 vs ≥ 15) and stiffness of the WOMAC hip/knee (**Table 2**).

Four variables proved significant in the multivariable analysis (**Table 2**): clinical OA, cognitive impairment, depression, and walking time. The distribution of these variables at baseline among those who will develop social isolation versus those who will remain socially active is presented in **Figure 1**. When we controlled for confounding factors, no mediators were found. The resulting model uncovered only one significant interaction: depression and sex.

The estimate of the odds ratio for clinical OA of the hip and/or knee combined or not with hand OA was 1.47 (95% CI: 1.03 to 2.09) times greater than the odds for someone with similar

characteristics (with respect to the other covariates in the model) without OA or with only hand clinical OA. The estimate of the odds ratio for cognitive impairment was 1.90 (95% CI: 1.09-3.29). Walking time was associated to social isolation with odds at each level greater than 1 (Q1-Q2: OR 2.11, 95% CI: 1.36-3.28; Q2-Q3: OR 2.12, 95% CI: 1.35-3.33; >Q3: OR 2.06, 95% CI: 1.28-3.33). The odds of incident social isolation for a person with worse walking times was 2 times greater than the odds for a person whose walking time was better (\leq Q1). There was an interaction between depression and sex: each increased the odds of social isolation in the presence of the other. Females who were depressed were found to be almost three times more likely to become socially isolated 12 to 18 months after baseline with respect to their female counterparts without depression (OR 2.78, 95% CI: 1.50-5.15).

DISCUSSION

This study shows that OA increases the risk of incident social isolation onset. People with hip and/or knee OA combined or not with hand OA at baseline are at increased risk of social isolation in a community cohort. The presence of cognitive impairment and worse walking times in both genders and depression in the females also increased the risk of becoming socially isolated during the follow-up period.

While it is absolutely known that a complex of deficits, including mobility limitations predict isolation, we focused on OA, because in our opinion it is interesting that OA remains an independent predictor in the multivariate analyses, even after adjusting for functional limitations and pain. Moreover, as we have previously reported²⁶ OA has an independent effect also on self-reported physical function impairment, even after adjusting for pain, which can probably be explained by the “expected pain” that OA may cause during physical activity. Probably the fear of pain is more important than pain itself as far as OA patients are concerned. This would explain why OA independently predicts isolation.

A large meta-analysis examining 148 studies assessing the association of social isolation and mortality reported that individuals who had more supportive social relationships had a lower mortality risk.²⁷ Similarly, socially isolated older adults tend to have an increased risk of experiencing a decline in mobility.²⁸ Finally, social isolation is associated with an increased risk of cardiovascular disease²⁹ and dementia.³⁰ Since social isolation is a potentially reversible condition, increasing research efforts are attempting to identify as early as possible socially isolated older people.

This study was the first analysis to assess an association between OA and social isolation based on prospective data. Several explanations for the association could be proposed. First, people with OA are more disabled and show poorer physical performance, which are both independent risk factors for social isolation.³¹ Moreover, worse walking times in the patients studied were

found to be a significant predictor of social isolation. Second, OA has also been associated with depression.³¹ In the current study, depression was in fact another significant predictor of social isolation.³²

The findings suggest that people with OA are at increased risk of social isolation. Given the important negative health outcomes associated with social isolation, interventions should be developed and tested to address this unmet healthcare need. These should include forms of physical activity, social engagement and community participation as well as some type of psychological assistance.³³ According to a systematic review on interventions to reduce social isolation, educational and social activities targeting specific groups can lower social isolation in older people.³⁴ Referring older adults with OA to social activity/senior centres in their area offering these types of activities may be useful especially when these interventions are specifically designed for older people with OA presenting physical impairments limiting social participation.

The study presents some limitations. First, the presence of comorbidity was evaluated on the basis of self-reported information and was not ascertained clinically. Self-reported information regarding comorbidities has nevertheless a good accuracy compared to gold standard methods of diagnosis.³⁵ Second, although a 12 to 18 month follow-up time may be considered insufficient to determine incident cases of social isolation, a large number of participants did indeed become socially isolated during that time period. Third, variables linked to life events such as the death of a family member or friend or being admitted to hospital, which may be important predictors of isolation, were not considered by the designers of the EPOSA study. Finally, the high number of participants whose data was incomplete might have caused a selection bias. Nevertheless, the high number of participants living in six different European nations who were studied can be considered the study's strength. Moreover, standardized international guidelines were used for the clinical diagnosis of OA in all participants.¹²

359 **CONCLUSION**

360 In conclusion, data from the EPOSA study suggest that OA is associated with incident social
361 isolation, adjusting for cognitive impairment, depression, and worse walking times. Future
362 research is warranted.

363

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484 **LEGENDS**

485

486 **Figure 1** Proportion of isolated and not isolated participants at follow-up by baseline factors.

487 Weighted data.

488 Walking time is classified by country quartiles, reference class \leq Q1 indicates best performance.

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490 **Supplementary Material . Table S1.** Construction of variables.

491 **Supplementary Material . Table S2.** Characteristics of excluded participants at Baseline and 12-18

492 months later

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Table 1. Baseline characteristics for social isolation at 12-18 months Follow-up

Baseline Characteristics		Total (n=1,967)	12-18 months Follow-up (n=1,585)		P-value
			Isolated (n=222)	Not isolated (n=1,363)	
Age, mean±SD, median (IQR), years		73.7±5.3 73 (70-77)	74.0±5.0 73.5 (70-78)	73.3±4.8 73 (70-76)	0.058
Female sex, %		49.6	49.7	54.1	0.234
Country, %	Germany	13.3	9.8	15.2	<.001
	Italy	15.5	20.3	15.3	
	The Netherlands	17.5	20.5	17.6	
	Spain	19.7	25.9	14.8	
	Sweden	20.4	14.9	22.2	
	UK	13.6	8.7	14.9	
Up to elementary education, %		41.7	47.0	36.8	0.005
Marital status (single/divorced/widowed/living apart), %		32.4	32.6	31.7	0.804
Income, %	With great difficulty	2.7	2.4	2.5	0.001
	With some difficulty	13.9	18.5	10.9	
	Fairly easily	50.4	53.7	50.3	
	Easily	33.1	25.4	36.4	
Obesity (BMI ≥30 kg/m ²), %		24.7	26.1	23.8	0.479
Cognitive impairment (MMSE ≤23), %		6.1	9.7	4.2	0.001
Anxiety (HADS ≥8), %		17.8	19.1	16.1	0.292
Depression (HADS ≥8), %		9.6	12.0	6.0	0.001
Chronic lung disease, %		12.5	11.4	11.5	0.97
Cardiovascular disease, %		23.6	22.1	23.1	0.744
Peripheral artery disease, %		9.8	10.0	9.3	0.728
Diabetes mellitus, %		11.6	12.7	10.9	0.453
Stroke, %		4.5	5.8	3.7	0.143
Cancer, %		13.9	10.6	14.9	0.101
Osteoporosis, %		14.7	16.4	14.4	0.448
Analgesic/Anti-inflammatory medication, %		24.8	27.6	22.8	0.128
Clinical osteoarthritis, %	No	70.5	63.9	72.2	0.007
	Hand	8.4	6.9	8.8	
	Hip and/or knee	13.6	20.3	12.5	
	Hand and (hip and/or knee)	7.6	9.0	6.5	
Joint replacements, %		10.9	12.8	11.0	0.452
Self-rated health (fair/bed/very bed), %		33.5	41.0	28.9	<.001
EQ-5D [#] (time trade-off), mean±SD,		0.8±0.2	0.82±0.20	0.84±0.18	0.12
median (IQR)		0.8(0.7-1.0)	0.8(0.7-1.0)	0.85(0.73-1.0)	
EQ VAS [§] (health state today), mean±SD		75.9±17.7	73.6±18.5	77.1±17.3	0.006
median (IQR)		80(70-90)	75 (65-90)	80(70-90)	
median (IQR), sec		2.9(2.3-3.6)	3.0(2.5-3.7)	2.7(2.2-3.5)	0.054
Grip strength [†] , mean±SD,		28.0±10.1	26.5±9.4	28.5±10.3	
median (IQR), kg		26.5(20-35)	25.5(20.0-32.5)	27.0(20.5-36.5)	<.001
Walking time [‡] , %	≤ Q1	27.4	15.5	31.3	
	Q1-Q2	26.2	30.5	25.6	
	Q2-Q3	23.6	27.3	22.8	
	> Q3	22.8	26.8	20.3	
Total physical activity time (LAPAQ), mean±SD		201.8±130.8	201.1±137.9	207.3±126.8	0.11
median (IQR), min/day		180.0(110.7-262.5)	169.3(105.1-258.9)	184.3(120.0-267.9)	0.01
Total physical activity amount (LAPAQ), mean±SD		870.8±644.4	824.0±635.2	907.3±635.4	
median (IQR), kcal/day		717.2(451.8-1101.1)	6501.4(440.0-1026.1)	754.5(489.6-1148.9)	0.001
WOMAC* hip/knee physical function score, mean±SD		7.4±12.4	9.3±13.6	6.6±11.9	
median (IQR)		1(0-10)	3 (0-13)	0(0-8)	0.006
WOMAC* hip/knee pain score, mean±SD		9.6±14.1	10.8±13.4	8.8±13.7	
median (IQR)		0(0-15)	5 (0-20)	0(0-10)	0.04
WOMAC* hip/knee stiffness score, mean±SD		11.9±18.1	14.3±19.0	11.9±17.5	
median (IQR)		0(0-25)	0(0-25)	0(0-25)	0.025
AUSCAN* hand physical function score, mean±SD		7.7±13.9	8.8±14.5	7.2±13.5	
median (IQR)		0(0-8)	0(0-11)	0(0-8)	0.76
AUSCAN* hand pain score, mean±SD,		7.2±14.9	6.8±14.2	6.9±14.6	
median (IQR)		0(0-5)	0(0-5)	0(0-5)	0.453
AUSCAN* hand stiffness score, mean±SD,		9.4±17.9	10.8±18.3	9.4±18.0	
median (IQR)		0(0-0)	0(0-25)	0(0-25)	

Weighted data except numbers of participants, age, and sex. BMI, body mass index; MMSE, Mini-Mental State Examination score; HADS, Hospital Anxiety and Depression Scales; Q1, Q2, Q3, quartiles; EQ-5D, Health status using five dimensions; EQ VAS, Health status using the visual analogue scale; LAPAQ, LASA Physical Activity Questionnaire; WOMAC, Western

498 Ontario and McMaster Universities Osteoarthritis Index; AUSCAN, AUStralian CANadian Osteoarthritis Hand Index; SD,
499 standard deviation; IQR, interquartile range.
500 #Possible scores range from -0.594 to 1, lower values indicating worse health status. §Possible scores range from 0 to 100, with
501 0 indicating worse health status.† Lower values indicate worse performance. ‡By country quartiles, class \leq Q1 indicates best
502 performance, class $>$ Q3 indicates worst performance. *Possible scores range from 0 to 100, with 100 indicating worse status.
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Table 2. Univariable and Multivariable models for social isolation 12-18 months after baseline.

		Univariable adjusted model					Multivariable adjusted model				
		β	SE	P-value	OR	95% CI	β	SE	P-value	OR	95% CI
Clinical osteoarthritis				0.004					0.032		
	no/only hand				1.00					1.00	
	(hip and/or knee); hand and (hip and/or knee)	0.487	0.169		1.63	1.17-2.27	0.384	0.179	0.032	1.47	1.03-2.09
Income				0.160							
	With great difficulty				1.00						
	With some difficulty	0.6541	0.5138	0.203	1.92	0.70-5.27					
	Fairly easily	0.3325	0.4938	0.501	1.39	0.53-3.67					
	Easily	0.1102	0.5106	0.829	1.12	0.41-3.04					
Cognitive impairment (MMSE \leq23)		0.673	0.275	0.015	1.96	1.14-3.36	0.640	0.282	0.022	1.90	1.09-3.29
Depression [§] (HADS \geq8)		0.592	0.242	0.014	1.81	1.13-2.90	-0.434	0.435			
	Male sex								0.332	0.66	0.28-1.54
	Female sex								0.001	2.78	1.50-5.15
Cancer		-0.390	0.235	0.097	0.68	0.43-1.07					
Self-rated health (fair/bad/very bad)		0.298	0.164	0.068	1.35	0.98-1.86					
EQ-5D[#] (time trade-off)		-0.639	0.373	0.087	0.53	0.25-1.10					
EQ VAS[§] (health state today)		-0.007	0.004	0.076	0.99	0.99-1.00					
Walking time[‡]				0.0008					0.003		
	\leq Q1				1.00					1.00	
	Q1-Q2	0.742	0.224	0.001	2.10	1.36-3.26	0.748	0.225	<0.001	2.11	1.36-3.28
	Q2-Q3	0.807	0.229	<0.001	2.24	1.43-3.51	0.750	0.231	0.001	2.12	1.35-3.33
	> Q3	0.870	0.238	<0.001	2.39	1.50-3.81	0.724	0.244	0.003	2.06	1.28-3.33
WOMAC[*] hip/knee physical function score		0.010	0.005	0.069	1.01	1.00-1.02					
WOMAC[*] hip/knee pain score (\geq15)		0.436	0.160	0.006	1.55	1.13-2.12					
WOMAC[*] hip/knee stiffness score		0.006	0.004	0.139	1.01	1.00-1.01					

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Models adjusted for age, sex and country.

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BMI, body mass index; MMSE, Mini-Mental State Examination score; HADS: Hospital Anxiety and Depression Scales; OA: osteoarthritis; Q1, Q2, Q3; quartiles; EQ-5D: Health status using five dimensions; EQ VAS: Health status using the visual analogue scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; β , regression coefficient; SE, standard error; OR, odds ratio; CI, confidence intervals.

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[#] Possible scores range from -0.594 to 1, lower values indicating worse health status.

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[§] Possible scores range from 0 to 100, with 0 indicating worse health status.

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[‡] By country quartiles, reference class \leq Q1 indicates best performance, class > Q3 indicates worst performance.

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^{*} Possible scores range from 0 to 100, with 100 indicating worse health status.

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Table S1. Construction of variables.

OUTCOME: Social isolation		TIME: BASELINE and FOLLOW-UP 12-18 months
<ul style="list-style-type: none">• Six-item Lubben’s Social Network Scale (LSNS). Total score ranges from 0 (high isolation) to 30 (low isolation)• Maastricht Social Participation Profile (MSPP) measures actual social participation with three indices: consumptive participation (CP), formal participation (FSP), informal participation (ISP). For each index, were calculated: diversity (number of items scored at least one); frequency (mean scores of the items). In addition, a total diversity score is calculated as number of indices with a score of at least one. EPOSA used only CP and FSP, ISP ≈ LSNS-6		Total diversity participation score (number of indices with a score of at least one between CP diversity, FSP diversity) <u>OR</u> LSNS-6 ≥12 => Social isolation: LSNS-6 <12 <u>OR</u> [(≤ median value of Total diversity) <u>AND</u> (≤ median value of CP diversity) <u>AND</u> (≤ median value of FSP diversity) <u>AND</u> (≤ median value of CP frequency) <u>AND</u> (≤ median value of FSP frequency)]
MAIN VARIABLE: Osteoarthritis (OA)		TIME: BASELINE
OA classification		1) no OA, 2) only hand OA, 3) hip and/or knee OA, 4) hip and/or knee OA combined with hand OA.
OA clinical diagnosis		self-reported WOMAC and AUSCAN subscales (5-point Likert scale: 0=none, 1=mild, 2=moderate, 3=severe, 4=extreme) and physical examination
<ul style="list-style-type: none">• Knee OA clinical diagnosis		score ≥3 in WOMAC pain subscale <u>AND</u> at least 2 of: <ul style="list-style-type: none">• score ≥1 in WOMAC stiffness subscale• crepitus with active motion on at least one side;• bone tenderness on at least one side;• bone enlargement on at least one side;• no palpable warmth of synovium in either knees.
<ul style="list-style-type: none">• Hip OA clinical diagnosis		score ≥3 in WOMAC pain subscale <u>AND</u> score ≥1 in WOMAC stiffness subscale <u>AND</u> pain on at least one side associated with restricted hip internal rotation at the physical examination
<ul style="list-style-type: none">• Hand OA clinical diagnosis		score ≥3 in AUSCAN pain subscale <u>AND</u> score ≥1 in AUSCAN stiffness subscale <u>AND</u> at least 2 of: <ul style="list-style-type: none">• hard tissue enlargement of two or more joints,• hard tissue enlargement of two or more distal inter-phalangeal joints, deformity of at least one hand joint.
VARIABLES		TIME: BASELINE
Age (years), sex, country of residence		
Education		up to elementary vs higher levels
Marital status		single/divorced/widowed/living apart vs other
Income: ability to makes end meet		great difficulty, some difficulty, fairly, easily fairly
COMORBIDITY		
Obesity		Body Mass Index score ≥30 kg/m2
Cognitive function: Mini-Mental State Examination (MMSE)		Cognitive impairment: MMSE score ≤23
Anxiety: Hospital Anxiety Depression Scales (HADS)		Anxiety subscale: score≥8

Depression: Hospital Anxiety Depression Scales (HADS)	Depression subscale: score \geq 8
Chronic diseases: chronic lung disease, cardiovascular disease, peripheral artery disease, diabetes mellitus, stroke, cancer, osteoporosis	Each disease lasting at least three months or which caused the individual to seek a physician's attention: yes vs no
MEDICATION used over the past two weeks: Analgesic/Anti-inflammatory medication	medication use vs non-use
PREVIOUS JOINT REPLACEMENTS	yes vs no
HEALTH AND LIFESTYLE CHARACTERISTICS	
Self-rated health	fair/bad/very bad vs good/very good
EQ-5D: EuroQol 5 questions on mobility, self-care, usual activities, pain/discomfort, anxiety/depression	Scores range from -0.594 to 1, lower values indicating worse health status
EQ VAS: EuroQol visual analogue scale about health state	Scores range from 0 to 100, with 0 indicating worse health status
<ul style="list-style-type: none"> • Pain hand: Australian/Canadian OA Hand Index (AUSCAN) pain subscale • Pain hip/knee: Western Ontario and McMaster Universities OA Index (WOMAC) pain subscale 	Scores range from 0 to 100, with 100 indicating worse status
<ul style="list-style-type: none"> • Stiffness hip/knee: WOMAC subscale • Stiffness hand: AUSCAN subscale 	
<ul style="list-style-type: none"> • Physical function hip/knee: WOMAC subscale • Physical function hand: AUSCAN subscale 	
Physical Activity: LASA Physical Activity Questionnaire (LPAQ)	
	<ul style="list-style-type: none"> • Total time: minutes/day • Total amount: kcal/day
Grip strength: strain-gauged dynamometer	Total score kg: sum of the maximum values of the right and the left hand, divided by two
Walking time-test 3 meter	classified according the country-specific quartiles (the fourth was the worst)

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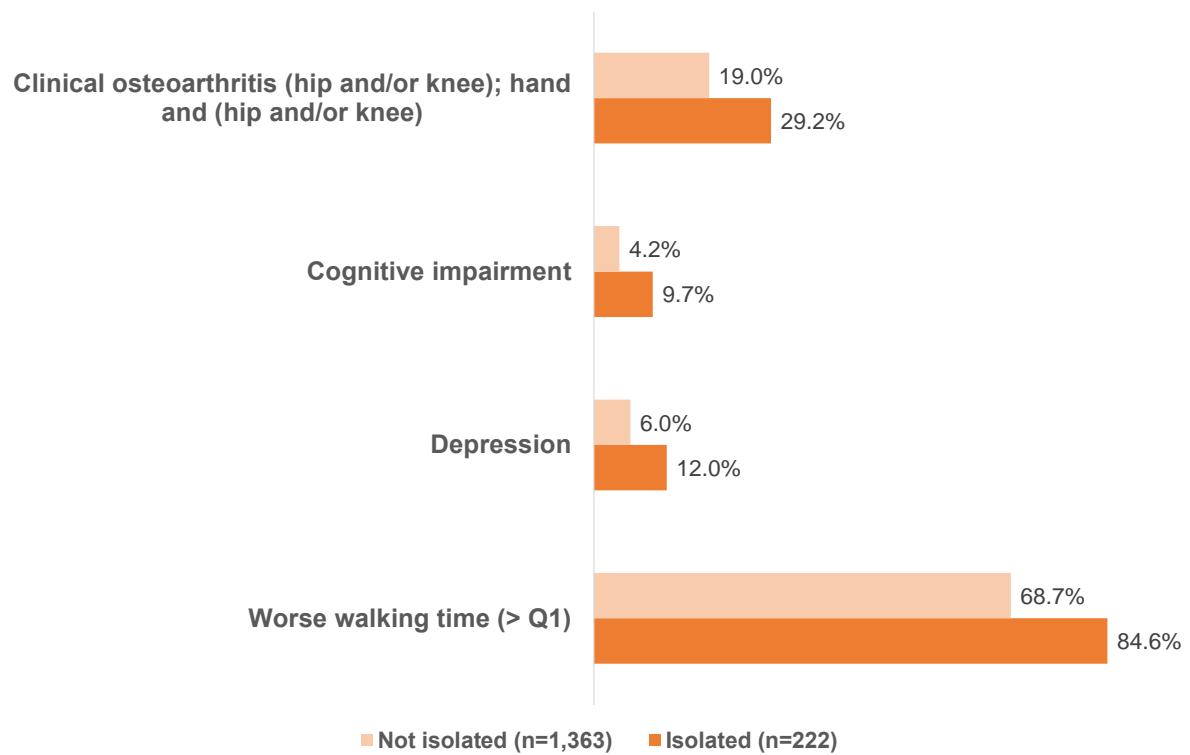
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Table S2. Characteristics of excluded participants at Baseline and 12-18 months later

	Baseline			P-value	12-18 months Follow-up		P-value
	Total (n=2,942)	Drop (n=487)	Continue (n=2,455)		No Complete (n=488)	Complete (n=1,967)	
Age, mean±SD, median (IQR), years	74.2±5.1 74 (70-78)	75.4±5.6 75 (71-80)	74.0±5.0 74 (70-78)	<.001	75.1±5.2 75 (71-79)	73.7±4.9 73 (70-77)	<.001
Female sex, %	51.9	57.5	50.8	0.007	55.5	49.6	0.018
Country, %				<.001			<.001
Germany	13.1	13.3	13.1		12.3	13.3	
Italy	16.4	31.5	13.3		15.5		
The Netherlands	20.2	19.5	20.4		31.6	17.5	
Spain	18.7	17.1	19.0		16.3	19.7	
Sweden	19.2	12.9	20.4		20.6	20.4	
UK	12.4	5.6	13.9		14.8	13.6	
Up to elementary education, %	45.0	59.3	49.1	<.001	43.5	41.7	0.491
Marital status (single/divorced/widowed/living apart), %	35.0	37.4	34.5	0.212	42.5	32.4	<.001
Income, %				<.001			0.259
With great difficulty	3.6	6.8	3.0		4.2	2.6	
With some difficulty	15.7	23.4	14.1		15.1	13.9	
Fairly easily	49.6	47.8	50.0		48.3	50.4	
Easily	31.1	22.0	32.9		32.4	33.1	

519 Weighted data except numbers of participants, age, and sex.

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