

Health-related Quality of Life in Patients with Hand Osteoarthritis from the General Population and the Outpatient Clinic

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ABSTRACT. Objective. To investigate the association of hand osteoarthritis (OA) and concurrent hand and knee OA with health-related quality of life (HRQOL) in the general population, and in patients consulting a rheumatology outpatient clinic.

Methods. In the population-based Netherlands Epidemiology of Obesity (NEO) study, participants were recruited from the greater area of Leiden, the Netherlands. In the Hand OSTeoArthritis in Secondary care (HOSTAS) study, patients with a rheumatologist's diagnosis of hand OA were recruited from a Leiden-based hospital. In both cohorts, hand and knee OA were defined by the American College of Rheumatology clinical criteria. In NEO, self-reported hospital-based specialist consultation for OA was recorded. Physical and mental HRQOL was assessed with normalized Medical Outcomes Study Short Form-36 scores. Associations were analyzed using linear regression, adjusted for age, sex, education, ethnicity, and body mass index.

Results. Hand OA alone and concurrent hand and knee OA was present in 8% and 4% of 6334 NEO participants, and in 57% and 32% of 538 HOSTAS patients. In NEO, hand OA alone, and concurrent hand and knee OA, were associated with lower physical component summary (PCS) scores [mean difference -2.4 (95% CI -3.6, -1.3) and -7.7 (95% CI -9.3, -6.2), respectively] compared with no OA. Consulting a specialist was associated with worse PCS scores. In the HOSTAS cohort, mean PCS scores were lower than norm values (-3.5 and -7.9 for hand OA and combined OA, respectively). Mental HRQOL was not clinically relevantly associated in either cohort.

Conclusion. Hand OA was associated with reduced physical, but not mental, HRQOL in the general population and hospital patients. Physical HRQOL was further reduced in hospital care, and with concurrent knee OA. (First Release June 15 2020; J Rheumatol 2020;47:1409-15; doi:10.3899/jrheum.190781)

Key Indexing Terms:

OSTEOARTHRITIS HAND QUALITY OF LIFE EPIDEMIOLOGY

The hand is one of the most frequently affected joint sites by osteoarthritis (OA), next to OA of the knee^{1,2}. In addition, hand and knee OA frequently co-occur³. Hand OA may affect the health-related quality of life (HRQOL), which may vary

between patient populations. The effect of OA on HRQOL is often studied in patients recruited from secondary or tertiary care. However, these patients may represent a distinct patient group that might differ from the general population. Differences between these populations might be present in symptom severity, disabilities, or the co-occurrence of OA in other joints such as the knee. Studies that have investigated the effect of hand OA on physical HRQOL in the general population have shown no or very limited effect^{3,4}, which is in contrast to findings in patients recruited from the rheumatology clinic^{5,6,7}. A similar difference may be present for the effect of hand OA on mental HRQOL³⁻⁹. While some studies have shown a high prevalence of mental disorders in hand OA patients^{6,9}, a previous systematic review did not support that depression and anxiety occurred more often in patients with OA than in individuals without OA¹⁰. This lends further support to the hypothesis that HRQOL might be affected differently in individuals with hand OA from the general population compared to patients from rheumatology clinics. However, owing to a variety of OA definitions and

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phenotypes used by previous studies, a valid comparison of available findings is hindered, and a direct comparison of the effect of OA on HRQOL in the general population and in patients referred to secondary care is currently lacking.

In the current study, we had the unique opportunity to investigate individuals with hand OA from the general population and a rheumatology outpatient clinic in the same region. We investigated the effect of hand OA on physical and mental HRQOL in the general population, and subsequently compared the effect of hand OA between patients who have and who have not been referred to a medical specialist. Further, we investigated the added effect of concurrent knee OA on HRQOL.

MATERIALS AND METHODS

NEO study population. The Netherlands Epidemiology of Obesity (NEO) study is a population-based cohort study, with an oversampling of individuals with overweight or obesity. Detailed description of study design has been described elsewhere¹¹. In short, men and women between 45 and 65 years with a self-reported body mass index (BMI) ≥ 27 kg/m² living in the greater area of Leiden (the Netherlands) were eligible to participate. In addition, all inhabitants aged between 45 and 65 years from 1 municipality (Leiderdorp) were invited to participate irrespective of their BMI, allowing for a reference BMI distribution comparable to the general Dutch population¹². In total, 6671 participants were included. We excluded participants with inflammatory rheumatic disease ($n = 157$) or fibromyalgia ($n = 178$), or with missing physical examination ($n = 14$). The Medical Ethical Committee of the Leiden University Medical Center (LUMC) approved the design of the study (NL21981.058.08). All participants gave their written informed consent.

NEO clinical assessment. Measurement of height (cm) and weight (kg) allowed for calculation of BMI (kg/m²). In addition, trained research nurses examined the hands and knees, using a standardized scoring form. Of both hands, bony and soft swellings and deformities of distal interphalangeal, proximal interphalangeal, metacarpophalangeal, carpometacarpal, and wrist joints were assessed. Regarding the knees, presence of bony swellings, palpable pain and warmth, crepitus, and movement restriction were assessed. Hand and knee OA were defined according to the American College of Rheumatology (ACR) clinical classification criteria^{13,14} and in patients with a prosthesis or arthrodesis.

NEO questionnaires. Questionnaires included demographic information, as well as presence of rheumatic diseases other than OA, and whether patients consulted a hospital-based medical specialist for OA (specification of OA type was not available). Education was reported in categories according to the Dutch education system and grouped into high (including higher vocational school, university, and post-graduate education) versus low education (reference). The Australian/Canadian Hand OA Index (AUSCAN)¹⁵ was used to determine self-reported hand pain and function. Higher scores indicate greater disease burden. Further, the Medical Outcomes Study Short Form-36 (SF-36) was used to assess HRQOL^{16,17}. We calculated separate subscale and summary component scores: physical health (PCS) and mental health (MCS), and standardized scores on a scale of 0 to 100. Age- and sex-specific Dutch population-based norm scores¹⁸ were used to derive norm-based scores with a mean of 50 and an SD of 10. Higher SF-36 scores represent better QOL.

HOSTAS study population. The Hand OSTeoArthritis in Secondary care (HOSTAS) study included consecutive patients from the LUMC rheumatology outpatient clinic between June 2009 and October 2015, based on the rheumatologist's diagnosis of primary hand OA. The LUMC serves both as a secondary and tertiary referral center for rheumatic diseases. Exclusion criteria included presence of other rheumatic diseases or secondary OA

[including inflammatory joint diseases such as rheumatoid arthritis (RA), psoriatic arthritis, spondyloarthritis, and current sarcoidosis; bone diseases such as osteitis deformans and osteochondritis; intraarticular fractures; metabolic diseases associated with joint diseases such as hemochromatosis, Wilson's disease, and ochronosis; endocrine diseases such as acromegaly, major congenital or developmental diseases, bone dysplasias; and major local factors such as hypermobility and severe gout]. The study was approved by the LUMC medical ethical committee (NL26201.058.08) and written informed consent was obtained from all participants.

HOSTAS clinical assessment. Physical examination was performed by trained research nurses. BMI was calculated using measured weight and height (kg/m²). Physical examination of hands and knee was performed similarly as described in the NEO study; the ACR clinical classification criteria for hand and knee OA were applied to define clinical OA phenotypes^{13,14}. Also, joints with a prosthesis were regarded as having endstage OA.

HOSTAS questionnaires. Demographic data were collected using standardized questionnaires. Education level was grouped into high versus low education, similar to the NEO study methods. The AUSCAN was used to determine hand OA specific disease burden. HRQOL was measured with the Dutch Research and Development translation (version 1) of the SF-36¹⁷. Similar to the NEO study, we used the scoring algorithm and age- and sex-specific Dutch population-based norm scores from the Dutch SF-36 translation to apply norm-based scoring¹⁸ for the summary component scores and subscales with a mean of 50 and SD of 10.

Statistical analyses. In the NEO study there is an oversampling of individuals with BMI ≥ 27 kg/m². Adjustments were made for the oversampling by weighing all individuals toward the BMI distribution of participants from the Leiderdorp municipality ($n = 1671$)¹⁹, with a BMI distribution similar to the general Dutch population¹². All results presented are based on weighted analyses, using probability weights. Consequently, results from the NEO study apply to a population-based study without oversampling. Multivariable linear regression analysis, adjusting for age, sex, education, ethnicity, and BMI, was used to study cross-sectional associations of hand and concurrent hand and knee OA with HRQOL in both study populations. We verified absence of multicollinearity, normality, and homoskedasticity, using a correlation matrix, quantile-quantile plots, and residual versus fitted plots, respectively. Data are presented as regression coefficients with 95% CI. The mean differences in SF-36 scores were compared with the minimal clinically important difference (MCID) of 2 points to evaluate clinical relevance²⁰. All analyses were performed using STATA version 14.1 (StataCorp LP).

RESULTS

Study populations. The NEO study population consisted of 6671 participants. After exclusion of participants with missing physical examination or presence of concomitant other rheumatic diseases, the study population consisted of 6334 participants, with 55% women and a mean age of 56 years. Eight percent fulfilled only the ACR criteria for hand OA and an additional 4% of participants for both hand and knee OA (Table 1). Compared with participants without hand and knee OA, participants with OA were more frequently women, older, and less educated. The HOSTAS cohort consisted of 538 patients with hand OA, with 86% women and a mean age of 61 years. All patients from the HOSTAS cohort were diagnosed with hand OA by the rheumatologist. In 57% of patients, only the ACR criteria for hand OA was fulfilled and 171 (32%) were classified with hand and knee OA. In 11% of patients, assessment of the ACR clinical criteria was not possible or they did not fulfill the criteria; therefore, these patients were not included in the current analyses.

Table 1. Demographics and hand OA-specific disease burden.

Variables	NEO, n = 6334			HOSTAS, n = 538*	
	No Hand/knee OA, 78%	Hand OA, 8%	Hand/knee OA, 4%	Hand OA, 57%	Hand/knee OA, 32%
Demographics					
Age	55 (6)	58 (5)	58 (5)	61 (9)	62 (8)
Sex, % women	52	74	86	86	87
Height, cm	174 (10)	169 (9)	169 (7)	168 (8)	167 (9)
Weight, kg	79 (16)	77 (16)	78 (15)	75 (15)	76 (14)
BMI, kg/m ²	26 (4)	27 (5)	27 (5)	27 (5)	27 (5)
Education level, % high	48	40	36	36	31
Ethnicity, % white	95	94	92	98	96
AUSCAN, median (IQR)					
Total	0 (0–2)	7 (3–15)	13 (8–23)	20 (12–25)	20 (15–27)
Pain	0 (0–0)	3 (0–6)	6 (3–9)	9 (6–12)	10 (7–12)
Function	0 (0–2)	3 (1–10)	7 (3–14)	8 (4–12)	9 (6–12)

Results from the NEO study are based on weighted analyses of the study population. Values indicate mean (SD) unless otherwise specified. Higher AUSCAN scores reflect higher hand OA specific-burden. * 11% did not fulfill ACR criteria or were missing data. OA: osteoarthritis; NEO: Netherlands Epidemiology of Obesity study; HOSTAS: Hand OSTeoArthritis in Secondary care study; BMI: body mass index; AUSCAN: Australian/Canadian Hand Osteoarthritis Index; IQR: interquartile range.

The association of hand OA with HRQOL in the general population. The mean SF-36 scores in the NEO study are shown in Figure 1. Table 2 shows the mean differences

in participants with hand OA compared with participants without hand and knee OA. In participants with only hand OA the PCS was 2.4 points (95% CI -3.6, -1.3) lower than

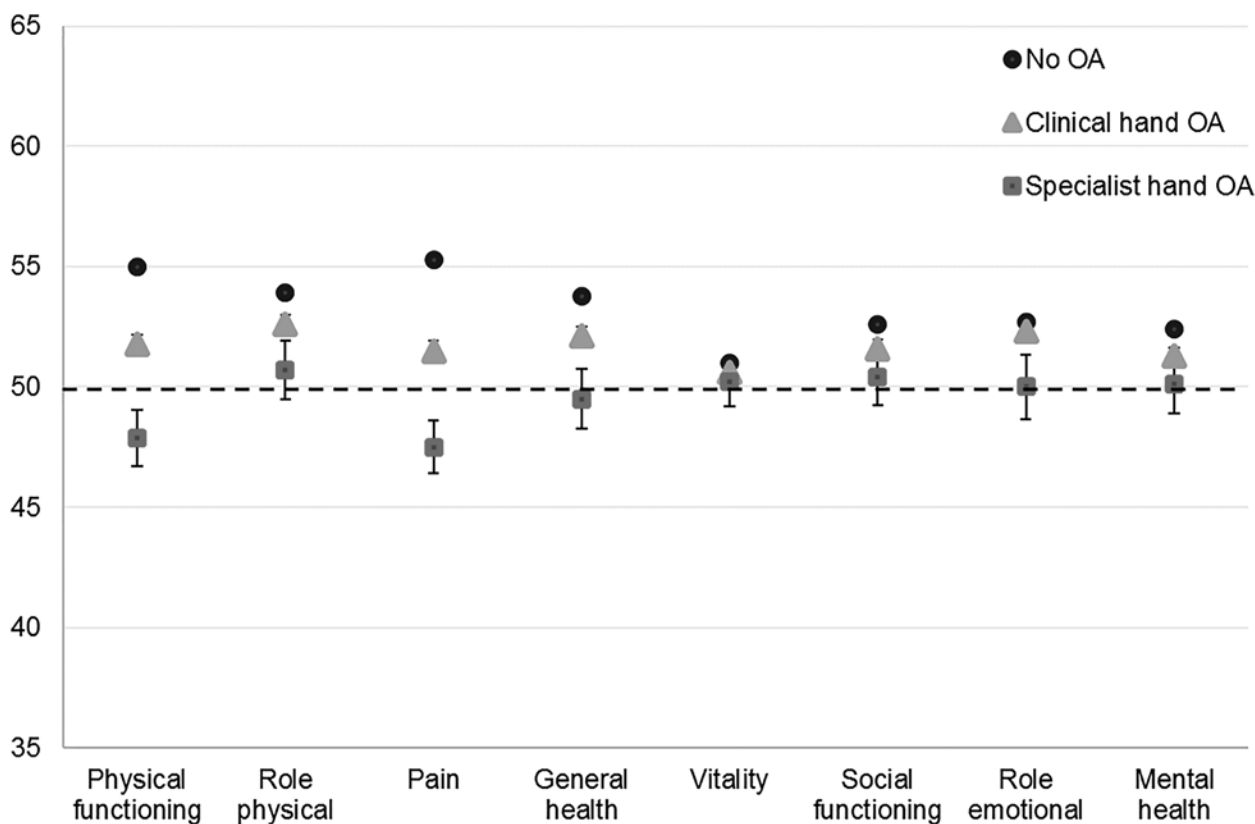


Figure 1. Health-related quality of life in individuals classified with hand OA in the general population. Results from the NEO study are based on weighted analyses of the study population. The datapoints reflect mean scores of the SF-36 scales, stratified by hand OA group. SF-36 scores of 50 are the norm; higher/lower values indicate better/worse quality of life. The “No hand/knee OA” group are participants not fulfilling either the ACR criteria for hand or knee OA. The “clinical hand OA” group fulfilled only the ACR criteria for hand OA, and the “specialist hand OA group” comprises participants fulfilling the ACR criteria for hand OA, as well as reporting to have visited a hospital-based medical specialist for OA. Error bars represent SEM. OA: osteoarthritis; NEO: Netherlands Epidemiology of Obesity study; SF-36: Medical Outcomes Study Short Form-36; ACR: American College of Rheumatology; SEM: standard error of the mean.

Table 2. Health-related quality of life (HRQOL) in the general population.

	No Hand/knee OA, 78%	Hand OA, 8%	NEO, n = 6334 Mean Difference (95% CI)	Hand/knee OA, 4%	Mean Difference (95% CI)
Physical component score	55.1 (7.6)	52.0 (8.7)	-2.4 (-3.6, -1.3)	45.9 (9.7)	-7.7 (-9.3, -6.2)
General health	53.8 (8.1)	52.1 (8.6)	-1.5 (-2.6, -0.3)	49.4 (9.6)	-3.4 (-4.9, -1.8)
Bodily pain	55.3 (8.4)	51.5 (8.9)	-3.4 (-4.6, -2.2)	46.3 (7.6)	-8.1 (-9.4, -6.8)
Vitality	51.0 (8.8)	50.6 (8.6)	-0.6 (-1.6, 0.5)	47.4 (9.3)	-3.2 (-4.8, -1.7)
Physical functioning	55.0 (7.0)	51.8 (8.0)	-2.1 (-3.0, -1.1)	45.3 (9.7)	-7.8 (-9.4, -6.2)
Role functioning, physical	53.9 (7.6)	52.6 (8.8)	-0.9 (-2.0, 0.2)	48.9 (10.5)	-4.1 (-5.8, -2.3)
Mental component score	51.1 (8.8)	51.3 (8.9)	0.2 (-1.0, 1.3)	51.7 (9.4)	0.9 (-0.5, 2.3)
Mental health	52.4 (7.8)	51.3 (7.8)	-0.8 (-1.7, 0.2)	49.9 (8.6)	-1.7 (-3.1, -0.3)
Social functioning	52.6 (8.0)	51.6 (8.4)	-0.6 (-1.7, 0.4)	49.7 (9.2)	-1.9 (-3.4, -0.5)
Role functioning, emotional	52.7 (8.0)	52.3 (8.6)	-0.2 (-1.3, 0.8)	51.8 (8.9)	-0.5 (-1.7, 0.8)

Results are based on weighted analyses of the study population. Higher SF-36 scores represent a better HRQOL. Values indicate mean (SD). Results are adjusted for age, sex, BMI, education, and ethnicity. NEO: Netherlands Epidemiology of Obesity study; OA: osteoarthritis; SF-36: Medical Outcomes Study Short Form-36; BMI: body mass index.

in participants without OA. The subscales bodily pain and physical functioning showed greatest differences of -3.4 (95% CI -4.6, -2.2) and -2.1 (95% CI -3.0, -1.1), respectively, while vitality was the least different in participants with hand OA compared to participants without hand OA. Mental HRQOL was not reduced in participants with hand OA compared with participants without OA. Relative to participants without OA, the PCS was -7.7 (95% CI -9.3, -6.2), and all physical subscales were reduced below the clinically relevant threshold in participants with concurrent hand and knee OA. The subscales mental health and social functioning were lower with mean differences of -1.7 (-3.1, -0.3) and -1.9 (-3.4, -0.5), respectively. However, these differences were smaller than the MCID of 2 points.

Comparison with hand OA patients referred to secondary care. Of all participants classified with hand OA in the general population, 14% reported to have visited a medical specialist for OA. The participants with hand OA who had not been referred to secondary care reported a median (IQR) AUSCAN total score of 7 (3-13), compared to 14 (4-27) in participants who visited a specialist. Comparison of the HRQOL in participants with hand OA who had been referred to the medical specialist with participants with hand OA who had not reported consulting secondary care for OA showed a lower physical HRQOL with a mean difference in the PCS of -3.9 (95% CI -6.7, -1.2). The subscales bodily pain and physical functioning showed the greatest mean differences of -4.9 (95% CI -7.6, -2.1) and -4.3 (95% CI -7.0, -1.7), respectively. In the group classified with concurrent hand and knee OA, 38% reported to have visited a specialist for OA. In these participants, the greatest difference with participants who had not consulted secondary care was seen in the subscale physical functioning. Mental HRQOL did not differ between participants with hand OA who had and who had not been referred to the medical specialist (Table 3).

In the HOSTAS study, no reference group without OA was available. Comparison of the HRQOL in patients with

only hand OA from the rheumatology outpatient clinic to the reference group without hand or knee OA in the NEO study showed a mean difference in the PCS of -7.8 (95% CI -8.8, -6.8). Similar to the comparisons within the NEO study population, the subscales bodily pain and physical functioning were associated with the largest mean differences (data not shown). The MCS did not differ between patients with hand OA from the HOSTAS study and the NEO study reference group. However, because the mean scores of the reference group in the NEO study were higher than the normative values, we deemed this was an unsuitable reference group for the HOSTAS cohort. Therefore, Table 4 shows the mean SF-36 scores of the HOSTAS patients compared with the normative value of 50. In patients with only hand OA, the PCS (-3.5), bodily pain (-4.9), vitality (-2.5), and physical role functioning (-2.2) scales were clinically relevantly lower, but mental HRQOL was not associated with hand OA alone. In patients with concurrent hand and knee OA, all physical HRQOL scales were clinically relevantly lower, as well as the mental HRQOL scale social functioning, with a difference of -2.9.

The added burden of concurrent knee OA. Concurrent hand and knee OA was associated with a lower physical HRQOL compared to only hand OA, with mean differences (95% CI) in the PCS of -5.3 (-7.2, -3.4) in the NEO cohort and -3.9 (-5.4, -2.4) in the HOSTAS cohort. Table 5 shows that the observed mean differences were above the MCID in both populations, indicating a clinically relevant lower HRQOL in patients with concurrent hand and knee OA compared to patients with only hand OA. Physical functioning showed the greatest mean differences in patients with additional knee OA, with mean differences of -5.7 (95% CI -7.5, -3.9) in the NEO cohort and -4.7 (95% CI -6.4, -3.0) in the HOSTAS cohort. No differences in mental HRQOL were observed in participants of the NEO study classified with concurrent hand and knee OA compared to participants with only hand OA. In the HOSTAS study, social functioning

Table 3. Health-related quality of life (HRQOL) in participants who had and who had not been referred to the medical specialist.

	NEO, n = 6334					
	Hand OA Spec-, 6.6%	Hand OA Spec+, 1.0%	Mean Difference (95% CI)	Hand/knee OA Spec-, 2.5%	Hand/knee OA Spec+, 1.5%	Mean Difference (95% CI)
Physical component score	52.6 (8.4)	48.5 (9.4)	-3.9 (-6.7, -1.2)	48.5 (9.4)	41.7 (8.8)	-5.9 (-8.5, -3.4)
General health	52.5 (8.3)	49.5 (10.0)	-2.6 (-6.2, 0.9)	50.7 (9.7)	47.2 (8.9)	-2.2 (-4.8, 0.5)
Bodily pain	52.2 (8.8)	47.5 (8.9)	-4.9 (-7.6, -2.1)	47.4 (8.1)	44.4 (6.3)	-2.6 (-4.6, -0.5)
Vitality	50.7 (8.7)	50.2 (8.1)	-0.6 (-3.2, 1.9)	47.8 (9.3)	46.8 (9.5)	-0.4 (-3.6, 2.7)
Physical functioning	52.5 (7.6)	47.9 (9.5)	-4.3 (-7.0, -1.7)	48.2 (9.1)	40.7 (9.1)	-7.1 (-9.8, -4.4)
Role functioning, physical	52.9 (8.6)	50.7 (9.9)	-2.1 (-5.0, 0.8)	50.8 (9.8)	45.8 (11.0)	-4.3 (-7.7, -0.8)
Mental component score	51.3 (8.5)	50.9 (11.3)	-0.6 (-5.0, 3.8)	50.9 (9.9)	53.0 (8.6)	2.0 (-0.7, 4.8)
Mental health	51.5 (7.4)	50.1 (9.8)	-1.5 (-5.2, 2.1)	50.0 (9.2)	49.6 (7.5)	-0.3 (-2.8, 2.2)
Social functioning	51.8 (8.2)	50.4 (9.6)	-1.4 (-4.8, 2.0)	50.2 (9.4)	48.9 (8.9)	-0.8 (-3.5, 1.9)
Role functioning, emotional	52.6 (8.2)	50.0 (10.8)	-2.5 (-6.3, 1.3)	51.5 (9.2)	52.2 (8.5)	0.6 (-1.9, 3.1)

Results are based on weighted analyses of the study population. Higher SF-36 scores represent a better HRQOL. Values indicate mean (SD). Results are adjusted for age, sex, BMI, education, and ethnicity. NEO: Netherlands Epidemiology of Obesity study; OA: osteoarthritis; spec-: not referred to specialist; spec+: referred to specialist; SF-36: Medical Outcomes Study Short Form-36; BMI: body mass index.

Table 4. Health-related quality of life (HRQOL) of patients with hand OA in the rheumatology clinic.

	HOSTAS, n = 538*			
	Hand OA 57%	Δ	Hand/knee OA 32%	Δ
Physical component score	46.5 (8.1)	-3.5	42.1 (7.7)	-7.9
General health	49.2 (6.3)	-0.8	46.5 (6.6)	-3.5
Bodily pain	45.1 (7.7)	-4.9	42.6 (6.7)	-7.4
Vitality	47.5 (8.8)	-2.5	46.0 (8.4)	-4.0
Physical functioning	48.8 (9.2)	-1.2	43.3 (9.3)	-6.7
Role functioning, physical	47.8 (10.2)	-2.2	44.5 (10.4)	-5.5
Mental component score	51.7 (8.8)	1.7	51.2 (8.8)	1.2
Mental health	51.0 (8.3)	1.0	49.4 (8.3)	-0.6
Social functioning	50.1 (9.1)	0.1	47.1 (9.5)	-2.9
Role functioning, emotional	51.1 (9.5)	1.1	49.6 (10.3)	-0.4

Higher SF-36 scores represent a better HRQOL. Results are adjusted for age, sex, BMI, education, and ethnicity. In HOSTAS, the delta (Δ) between population scores and norm scores were calculated. * 11% did not fulfill ACR criteria or were missing data. HOSTAS: Hand OSTeoArthritis in Secondary care study; OA: osteoarthritis; SF-36: Medical Outcomes Study Short Form-36; BMI: body mass index; ACR: American College of Rheumatology.

Table 5. The effect of concurrent knee OA on HRQOL compared to hand OA alone.

	NEO	HOSTAS
	Mean Difference (95% CI)	Mean Difference (95% CI)
Physical component score	-5.3 (-7.2, -3.4)	-3.9 (-5.4, -2.4)
General health	-1.9 (-3.8, -0.0)	-2.6 (-3.8, -1.3)
Bodily pain	-4.7 (-6.4, -3.1)	-2.2 (-3.6, -0.9)
Vitality	-2.7 (-4.4, -0.9)	-1.5 (-3.2, 0.1)
Physical functioning	-5.7 (-7.5, -3.9)	-4.7 (-6.4, -3.0)
Role functioning, physical	-3.2 (-5.2, -1.2)	-3.1 (-5.1, -1.1)
Mental component score	0.7 (-1.0, 2.5)	-0.7 (-2.4, 1.0)
Mental health	-0.9 (-2.5, 0.7)	-1.5 (-3.1, 0.1)
Social functioning	-1.3 (-3.0, 0.4)	-3.0 (-4.8, -1.2)
Role functioning, emotional	-0.2 (-1.8, 1.3)	-1.3 (-3.2, 0.6)

OA: osteoarthritis; HRQOL: health-related quality of life; NEO: Netherlands Epidemiology of Obesity study; HOSTAS: Hand OSTeoArthritis in Secondary care study.

was significantly and clinically relevantly lower in the presence of concurrent hand and knee OA compared to hand OA alone with a mean difference of -3.0 (95% CI -4.8, -1.2).

DISCUSSION

In the current study, we investigated the association of hand OA with HRQOL in the general population and in patients with hand OA referred to the medical specialist. Further, we investigated the association of concurrent knee OA with HRQOL, and compared this between the general population and patients from the rheumatology outpatient clinic. In participants with hand OA in the general population, physical HRQOL was modestly but clinically relevantly lower than in participants without OA. Moreover, physical HRQOL was lower in patients with hand OA who had consulted a medical specialist. Mental HRQOL was not associated with hand OA alone, neither in the general population nor in patients in secondary care. In both patient

groups we observed a lower physical HRQOL in patients with concurrent hand and knee OA, compared with patients with hand OA alone. Further, concurrent hand and knee OA was weakly associated with mental HRQOL; however, in addition to the effect on social functioning in the HOSTAS cohort, the effect on mental HRQOL was below the MCID threshold in both populations.

Our findings disprove the misconception that hand OA in the general population has no relevant effect on HRQOL. Although hand OA was not significantly associated with a reduced physical HRQOL in a Spanish population-based cohort³, they used the less extensive SF-12, which might explain the discordance with our findings. In line with our results, hand OA patients in the population-based MUST cohort experienced a reduction in general health⁴. However, in our cohort, bodily pain and physical functioning was more strongly associated with hand OA. In the current study, we did not observe an association of hand OA with mental HRQOL. This is supported by other population-based studies^{3,4}. Moreover, a systematic review also did not support that depression and anxiety occurred more often in OA patients compared to individuals without OA¹⁰.

Further, we investigated whether HRQOL was associated with hand OA in secondary care patients. We showed that within the population-based NEO study, participants with hand OA who consulted a hospital-based specialist had a lower physical HRQOL than participants classified with hand OA who had not been referred to the medical specialist. In addition, we found that patients with hand OA in the HOSTAS study also experienced a lower physical HRQOL. Previous research in another cohort from our outpatient clinic supports our findings⁵, as well as results from a Norwegian study that showed that hand OA patients from the rheumatology department had a lower physical HRQOL compared to healthy controls. In contrast to our findings, they also observed worse mental health in hand OA patients recruited from their specialized clinic⁶. We did not see an association with lower mental HRQOL in patients referred to the medical specialist in a population-based cohort, nor in patients recruited from the rheumatology outpatient clinic. A number of other studies are in line with our findings, showing no association of hand OA with mental HRQOL in patients from outpatient clinics^{5,7}.

The additional presence of knee OA was associated with an even lower physical HRQOL in hand OA patients from the general population, as well as in patients from the outpatient clinic. This is supported by previous studies, which all concluded that polyarticular OA has a greater influence on physical HRQOL compared to patients with only hand OA^{3,4,6,7}. Further, we observed that the additional presence of knee OA was also associated with a lower score on the social functioning subscale in patients from the rheumatology clinic.

Comparison of HRQOL with other study cohorts should be made with caution because of differences in patient

selection, OA definitions, and reference groups. In addition, some studies lacked the use of norm-based scoring, further hampering the comparison. These obstacles highlight the importance of research that compares the general population with patients from specialized care. To our knowledge we are the first to make a comparison between patients from the general population and patients referred to secondary care. Because these cohorts were selected from the same area in the Netherlands, the NEO study population is likely a proper representative for the population of which the patients from our outpatient clinic are sampled. Further, both our cohorts are of substantial size, resulting in well-powered analyses and thus allowing robust conclusions.

However, our study also has some limitations. The reported HRQOL of the NEO study participants without OA was higher than the normative value of 50. This may indicate a healthy candidate bias, which is commonly seen in population-based studies. In addition, we cannot exclude that some NEO study participants who reported to have consulted a hospital-based specialist for OA may have also been included in the HOSTAS study. Unfortunately, we were not able to assess whether, or to what extent, this may have happened. For this reason we focused on within-cohort differences, and in addition compared the mean scores from the HOSTAS cohort to the normative values. Therefore, we deem it unlikely this will have affected our conclusions. Further, in the NEO study no distinction could be made in the type of OA that was the indication for specialist consultation, which may have led to misclassification. Also, the intra- and interobserver agreement for the scoring of OA signs on physical examination of the hands and knees was not assessed. However, because these scores were obtained by trained research nurses in a standardized way, we do not expect that this will have affected our results. Lastly, the cross-sectional study design does not allow exploration of how the effect of OA on HRQOL develops over time and hinders causal interpretations. Future research is needed to investigate the association between OA progression and the effect this may have on HRQOL.

Hand OA is associated with a clinically relevant lower physical, but not mental, HRQOL in both the general population and in patients referred to secondary care. In patients in secondary care, HRQOL was lower compared to patients with hand OA from the general population. In addition, co-occurrence of knee OA was associated with an even lower physical HRQOL than hand OA alone. The burden of hand and knee OA on the QOL in the general population as well as in hospital care should be carefully considered in the management of patient care.

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REFERENCES

1. Oliveria SA, Felson DT, Reed JI, Cirillo PA, Walker AM. Incidence of symptomatic hand, hip, and knee osteoarthritis among patients in a health maintenance organization. *Arthritis Rheum* 1995; 38:1134-41.
2. van Saase JL, van Romunde LK, Cats A, Vandenbroucke JP, Valkenburg HA. Epidemiology of osteoarthritis: Zoetermeer survey. Comparison of radiological osteoarthritis in a Dutch population with that in 10 other populations. *Ann Rheum Dis* 1989;48:271-80.
3. Carmona L, Ballina J, Gabriel R, Laffon A; EPISER Study Group. The burden of musculoskeletal diseases in the general population of Spain: results from a national survey. *Ann Rheum Dis* 2001;60:1040-5.
4. Lombnaes GØ, Magnusson K, Østerås N, Nordsletten L, Risberg MA, Hagen KB. Distribution of osteoarthritis in a Norwegian population-based cohort: associations to risk factor profiles and health-related quality of life. *Rheumatol Int* 2017;37:1541-50.
5. Kwok WY, Vliet Vlieland TP, Rosendaal FR, Huizinga TW, Kloppenburg M. Limitations in daily activities are the major determinant of reduced health-related quality of life in patients with hand osteoarthritis. *Ann Rheum Dis* 2011;70:334-6.
6. Slatkowsky-Christensen B, Mowinckel P, Loge JH, Kvien TK. Health-related quality of life in women with symptomatic hand osteoarthritis: a comparison with rheumatoid arthritis patients, healthy controls, and normative data. *Arthritis Rheum* 2007;57:1404-9.
7. Moe RH, Grotle M, Kjekken I, Hagen KB, Kvien TK, Uhlig T. Disease impact of hand OA compared with hip, knee and generalized disease in specialist rheumatology health care. *Rheumatology* 2013;52:189-96.
8. Cuperus N, Vliet Vlieland TPM, Mahler EAM, Kersten CC, Hoozeboom TJ, van den Ende CH. The clinical burden of generalized osteoarthritis represented by self-reported health-related quality of life and activity limitations: a cross-sectional study. *Rheumatol Int* 2015;35:871-7.
9. Axford J, Butt A, Heron C, Hammond J, Morgan J, Alavi A, et al. Prevalence of anxiety and depression in osteoarthritis: use of the Hospital Anxiety and Depression Scale as a screening tool. *Clin Rheumatol* 2010;29:1277-83.
10. Stubbs B, Aluko Y, Myint PK, Smith TO. Prevalence of depressive symptoms and anxiety in osteoarthritis: a systematic review and meta-analysis. *Age Ageing* 2016;45:228-35.
11. de Mutser R, den Heijer M, Rabelink TJ, Smit JW, Romijn JA, Jukema JW, et al. The Netherlands Epidemiology of Obesity (NEO) study: study design and data collection. *Eur J Epidemiol* 2013;28:513-23.
12. Ministry of Health, Welfare and Sport. How many people are overweight? [Internet. Accessed May 5, 2020.] Available from: www.rivm.nl/nldemaat
13. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis Rheum* 1986;29:1039-49.
14. Altman R, Alarcón G, Appelrouth D, Bloch D, Borenstein D, Brandt K, et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand. *Arthritis Rheum* 1990;33:1601-10.
15. Bellamy N, Campbell J, Haraoui B, Buchbinder R, Hobby K, Roth JH, et al. Dimensionality and clinical importance of pain and disability in hand osteoarthritis: Development of the Australian/Canadian (AUSCAN) Osteoarthritis Hand Index. *Osteoarthritis Cartilage* 2002;10:855-62.
16. Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30:473-83.
17. Van Der Zee K, Sanderman R. Measuring general health with the RAND-36, a manual. 2nd ed. [Manual in Dutch] Groningen: University of Groningen, Northern Center for Health Issues; 2012.
18. Aaronson NK, Muller M, Cohen PD, Essink-Bot ML, Fekkes M, Sanderman R, et al. Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations. *J Clin Epidemiol* 1998; 51:1055-68.
19. Lumley T. Analysis of complex survey samples. [Internet. Accessed May 5, 2020.] Available from: <http://www.jstatsoft.org/v09/i08/paper>
20. Angst F, Aeschlimann A, Stucki G. Smallest detectable and minimal clinically important differences of rehabilitation intervention with their implications for required sample sizes using WOMAC and SF-36 quality of life measurement instruments in patients with osteoarthritis of the lower extremities. *Arthritis Rheum* 2001;45:384-91.