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COMPARISON OF CLINICAL BURDEN BETWEEN PATIENTS WITH EROSIVE HAND OSTEOARTHRITIS AND INFLAMMATORY ARTHRITIS IN SYMPTOMATIC COMMUNITY-DWELLING ADULTS: THE KEELE CLINICAL ASSESSMENT STUDIES

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# ABSTRACT

## Objectives

To investigate in the general population the clinical impact of erosive osteoarthritis (EOA) in interphalangeal joints (IPJs) compared to symptomatic radiographic hand OA (RHOA) and inflammatory arthritis.

## Methods

Standardised assessments with hand radiographs were performed in participants of two population-based cohorts in North Staffordshire with hand symptoms lasting  $\geq 1$  day in past month. EOA was defined as the presence of an eroded or remodeled phase in  $\geq 1$  IPJ using the Verbruggen-Veys method. RHOA was defined as the presence of  $\geq 1$  IPJ/1st carpometacarpal joint with Kellgren-Lawrence score of  $\geq 2$ . Diagnoses of inflammatory arthritis were based on medical records. Hand pain/disability were assessed with AUSCAN. Linear regression analyses were used to compare clinical determinants between groups and calculate mean differences with 95% confidence intervals (95%CI), adjusted for age and sex.

## Results

Of 1076 participants with hand symptoms (60% women, mean age 64.8 years (SD 8.3)); 80 persons (7.4%) had EOA. The population prevalence of EOA in  $\geq$ 1 IPJ was 2.4% (95%CI 1.8, 3.0). Persons with EOA reported more pain and disability than persons with symptomatic RHOA (adjusted mean difference 1.3 (95%CI 0.3, 2.3) and 2.3 (95%CI 0.4, 4.2), respectively). Individuals with inflammatory arthritis (n=44) reported more pain and disability than those with EOA (adjusted mean difference 1.7 (95%CI 0.05, 3.4) and 6.3 (95%CI 2.8, 9.9), respectively).

## Conclusion

While EOA has a greater impact than symptomatic RHOA in the general population, it is not as severe in terms of hand pain and disability as those with inflammatory rheumatic arthritis.

## INTRODUCTION

Erosive hand osteoarthritis (erosive OA) is thought to be a subset of hand osteoarthritis (OA)<sup>1</sup> and was first described by Peter *et al.* in 1966<sup>2</sup>. The clinical features in erosive OA can appear as pain, swelling, redness, warmth and limited function of the interphalangeal joint (IPJ), which can be absent in non-erosive OA<sup>3</sup>. However, it is only recently that research of the occurrence of erosive OA in large-scale epidemiological studies has become possible with the development and validation of standardized methods for scoring cardinal features of IPJs, central erosions and collapse of the subchondral bone plate on radiographs<sup>4-6</sup>.

The Rotterdam cohort was one of the first studies to provide a population prevalence of erosive OA in the IPJs of 2.8% in adults aged  $\geq$ 55 years in the general population, equivalent to 1 in 10 people with symptomatic hand OA<sup>7</sup>. Shortly after this, the Framingham study showed age-standardised prevalence estimates for erosive OA of in 9.9% in women and 3.3% in men<sup>8</sup>. These, and other previous studies in clinical populations, have consistently found more severe symptoms and functional limitations among those with erosive OA than those with non-erosive OA<sup>7-10</sup>, raising the concern that erosive OA may carry the same burden as seen in inflammatory arthritis. This concern was mainly raised by studies performed in rheumatology practices in secondary and tertiary care comparing patients with hand OA with patients with rheumatoid arthritis<sup>11,12</sup>. In rheumatology practices, the proportion of patients with erosive OA is relatively high. In these studies the clinical burden was similar between patients with hand OA and rheumatoid arthritis. However, a study comparing patients groups referred to a rheumatology outpatient clinic may lead to selection bias, since the high clinical burden in itself can be a reason for referral.

The aims of this study were to confirm the prevalence of erosive OA in a general population sample in the United Kingdom, to explore the impact of erosive OA on clinical outcomes further and to investigate the clinical impact of erosive OA in comparison to inflammatory arthritis arising from a population-based cohort with hand symptoms in the United Kingdom.

## **METHODS**

#### Population and study design

Data were collected from the Clinical Assessment Study of the Hand (CAS-HA) and Knee (CAS-K); both prospective, population-based, observational cohort studies in North Staffordshire, UK. Study protocols of these studies are described elsewhere in detail<sup>13,14</sup>. In short, all adults aged  $\geq$  50 years registered with two general practices were invited to participate in a two-stage postal survey. If they indicated that they had experienced hand pain or hand problems within  $\leq$  12 months on the first postal questionnaire, they were invited to the research clinic. Those who attended the research clinic were included in the CAS-HA study (n=623)<sup>13</sup>. CAS-K participants (n=819) were recruited from a further three different general practices using recruitment methods identical to CAS-HA, except that participants were invited for a clinical assessment in

the CAS-K study if they reported knee pain (rather than hand pain or hand problems) within last year<sup>14</sup>. Ethical approval was obtained from the North Staffordshire Local Research Ethics Committee and all participants gave written consent. Only CAS-HA or CAS-K participants who indicated that they experienced hand symptoms (pain, aching, stiffness)  $\geq$  1 day during last month are included in this paper. This criterion was selected in order enable comparison of prevalences with the Rotterdam Study<sup>7</sup>, where patients with hand pain during last month were selected (instead of using the selection of pain during last year).

#### OA definitions

Radiographic hand OA was defined as KL-grade  $\geq 2$  in at least one IPJ or 1<sup>st</sup>CMCJ. Symptomatic radiographic hand OA was defined as having hand symptoms (pain, aching or stiffness  $\geq$  1 day during last month) and radiographic OA. Erosive OA is defined as having  $\geq$  1 E- or R-phase according to Verbruggen-Veys in the DIPJ, PIPJ or 1<sup>st</sup>IPJ.

#### Radiographic assessment and scoring

Plain radiographs were completed of each hand in posteroanterior (PA) view<sup>13</sup>. Distal, proximal and thumb interphalangeal joint (DIP, PIP and 1<sup>st</sup>IPJ) and 1<sup>st</sup>CMCJ were scored by two trained assessors (MM scored n=521, JH scored n=555), blinded for clinical data. Joints were scored for presence and severity of OA with the Kellgren-Lawrence (KL) grade (range 0-4)<sup>15</sup>. Both observers re-scored fifty pairs to calculate inter- and intra-observer reliability. Inter-observer reliability for the presence of hand OA was moderate (kappa= 0.5, percentage agreement (PA) 90%). The intra-observer reliability for presence of hand OA was excellent (kappa=0.92 and 0.85, PA 98% and 98% for reader 1 and 2, respectively).

Erosions were scored by the Verbruggen-Veys scoring method<sup>5</sup> and defined as having eroded (E-phase) or remodeled, irregular, sclerotic subchondral plates (R-phase) in DIPJs, PIPJs and 1<sup>st</sup>IPJs. The Verbruggen-Veys scoring does not include 1<sup>st</sup> IPJs; however the same rules for DIPJs and PIPJs were applied to this joint, again permitting direct comparison with the Rotterdam study<sup>7</sup>. Erosions were scored by a single reader (WK), blinded for clinical data. The intra-observer reliability for erosions as a dichotomous variable in the Verbruggen-Veys scoring method was excellent (kappa= 0.94)<sup>16</sup>.

## Sample selection for scoring erosive disease in hand radiographs

The majority of hand radiographs were scored for erosions; exceptions were those radiographs that had no or very few osteoarthritic features. The assumption was that erosions are not present in subjects with (almost) normal radiographs. To determine the selection for scoring erosions, KL-scores in the DIPJs, PIPJs, 1<sup>st</sup> IPJs and 1<sup>st</sup>CMCJs were summed to form an overall score (KLsum) for every participant. The population was divided in subgroups by the summation scores (range 0-72). All radiographs in subgroups with KLsum  $\geq$ 3 were scored. Random samples of at least 10% of subgroups with KLsum <3 were screened for erosions.

## Diagnosis of systemic inflammatory arthritis

Three sources of information were used to identify potential cases of diagnosed systemic inflammatory arthritis – specifically rheumatoid arthritis (RA), seronegative RA, psoriatic arthritis, and scleroderma: retrospective local Rheumatology hospital medical records, retrospective general practitioner medical records, and the consultant radiologist's clinical reports on participants' study radiographs. All searches were conducted by a researcher abstracting information using a standard form and blinded to the study clinical assessments and, in the cases of the medical record reviews, the study radiographs. The abstracted information on potential cases was reviewed by members of the research team, including a consultant rheumatologist, to determine which diagnosis was made. These persons were used in the analyses of the comparison of clinical burden between erosive OA and inflammatory arthritis and were therefore excluded in the group used for erosive OA analyses only.

#### **Clinical outcomes**

General characteristics of age and gender were recorded in postal surveys and height and weight were measured at the research clinics held at a local Rheumatology outpatients department.

#### Hand pain and stiffness

The pain and stiffness subscale of the Australian/Canadian Hand Osteoarthritis Index (AUSCAN, range 0-20 and 0-4, respectively) were completed by all participants<sup>17</sup>. Self-reported pain was also assessed with the pain subscale of the Arthritis Impact Measurement Scales health status questionnaire (AIMS-2, range 0-10)<sup>18</sup>. Higher scores indicate more pain or stiffness. The presence of pain in the finger IPJs and the thumb was determined from hand drawings; participants shaded areas where they had experienced pain lasting  $\geq$ 1 day during past month.

#### Hand function and performance

Self-reported hand function was assessed with the function subscales of the AUSCAN (range 0-36) and AIMS-2 hand and finger function subscale (range 0-10). Higher scores represent more limitation in hand function. The maximum gross and pinch grip strength was assessed with the JAMAR dynomometer (Sammons Preston, Chicago, IL) and B&L pinch gauge (B&L Engineering, Tustin, CA), respectively. In addition, the Grip Ability Test (GAT) was performed in the CAS-HA participants<sup>13</sup>. The GAT consisted of 3 tasks (putting a flexigrip stocking over the non-dominant hand, putting a paperclip on an envelope, pouring water from a jug into a cup) which participants had to perform within 2-3 minutes<sup>19,20</sup>. Scores are based on the time to complete the 3 tasks; higher scores correspond to poorer hand function. GAT scores of <20 seconds are considered normal<sup>19</sup>.

#### General health perceptions

General health perceptions were measured by the Short-Form 12 (SF-12), a widely used generic health status questionnaire yielding summary component scores for

physical health (PCS, 0-100) and mental health (MCS, 0-100), where lower scores represent poorer perceived health and a population average is  $50^{21}$ .

#### Aesthetics and impact of hand problems

Appearance of the hand was measured with the aesthetics subscale score of the Michigan Hand Outcomes Questionnaire (MHQ, range 0-100), which is composed by four questions for both hands <sup>22</sup>. The impact of hand symptoms was measured with the impact subscale of the AIMS-2 (range 0-10). Higher scores represent more satisfaction with aesthetics of the hand and a higher impact.

#### Statistical analysis

Prevalence of erosive OA in the population with hand symptoms and symptomatic radiographic hand OA population was calculated by dividing the number of persons with erosive OA by the sample size. Associated 95% confidence intervals (95%CI) were calculated based on a binomial distribution. The true population prevalence of symptomatic erosive OA was calculated using a combined approach of multiple imputation and weighted logistic regression, calculated for CAS-HA participants only<sup>23</sup>. Multiple imputation was used to estimate erosive OA prevalence in participants unable to attend the clinical assessment; weighted logistic regression was used to obtain prevalence rates adjusted for participants' likelihood to return the initial survey questionnaire.

Linear regression analyses were used to investigate differences in clinical characteristics between participants with and without erosive OA and also those with erosive OA in comparison to those with inflammatory arthritis. The beta-estimate is presented as the mean difference (with 95%CI), adjusted for age and gender. Data of participants with inflammatory arthritis were only used for the comparison of the clinical burden outcomes between participants with erosive OA and those with inflammatory arthritis of the hand and for estimates of overall population prevalence.

Data were analyzed using SPSS, version 17 (SPSS Inc, Chicago, Illinois) and STATA version 11.0 (Stata Corporation, College Station, TX, USA).

## RESULTS

## Clinical characteristics and demographics

The cohorts yielded a combined sample of 1442 potentially eligible participants. Participants with incomplete radiographs (n=47), without hand symptoms  $\geq$ 1 day during last month (n=275) and those with inflammatory arthritis (n=44) were excluded (table 1), leaving a total of 1076 eligible participants (60% women, mean age 64.8 years (SD 8.3)). The 44 persons with inflammatory arthritis were used in the analysis of clinical burden between erosive OA and inflammatory arthritis. Symptomatic radiographic hand OA was present in 74% of participants (table 2).

#### Occurrence of erosive OA

Among the 80 persons with  $\geq$ 1 erosive/remodeled joint in their DIPJ, PIPJ or 1<sup>st</sup> IPJ, a total of 216 erosive/remodeled joints were found (median 2, range 1-11), most





Table 2: Baseline characteristics of 1076 persons in the population with hand symptoms lasting  $\geq$  1 day during last month.

Female, no. (%)	650 (60)
Age (years), mean (SD)	64.8 (8.3)
BMI (kg/m²), mean (SD)	29.1 (5.1)
Pain in at least one IPJ, no. (%)	527 (49)
Pain in left or right thumb, no. (%)	605 (56)
Symptomatic radiographic hand OA*, no (%)	798 (74)
Erosive persons** with IPJ-erosions, no. (%)	80 (7.4)

SD = standard deviation, BMI = Body Mass Index, OA= osteoarthritis, \* = presence of Kellgren and Lawrence grade  $\ge 2$  in at least one DIPJ, PIPJ or 1<sup>st</sup> IPJ, \*\* = at least having one eroded (E-phase) or remodelled joint (R-phase), according to the Verbruggen-Veys scoring method.

commonly in the 2<sup>nd</sup> DIPJs in both hands (34 joints in DIP2 left, 39 joints in DIP2 right). The 2<sup>nd</sup> PIPJs (1 joint in PIP2 left/right) were least commonly involved. Of the 216 joints, 34 joints (16%) were in the E-phase; the remainder was classed as R-phase. Twenty-three persons presented  $\geq$ 1 E-phase in their hands and 57 persons presented only R-phases. Within the 23 persons 76 erosive/remodelled joints were present, whereas 140 erosive/remodelled joints were present in the 57 persons with only R-phases.

The true population prevalence estimate of erosive OA in the general population of adults  $\geq$ 50 years was 2.4% (95%Cl 1.8, 3.0). This represented 7.4% (95%Cl 5.9, 9.2)

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of the sub-population with hand symptoms in this age range and 10.0% (95%Cl 7.9, 12.1) of those with symptomatic radiographic hand OA. The prevalence of erosive OA in IPJs in the sub-population with hand pain in the IPJs was 15.2% (95%Cl 12.1, 18.2) and in the subgroup with symptomatic radiographic IPJ OA population 23.3% (95%Cl 18.8, 27.7). The prevalence of erosive OA was examined by gender and it was found that estimates for women were at least double of those for men (table 3).

Table 3: Prevalence of erosive OA in the total population aged 50 years and over in those with hand symptoms and symptomatic radiographic hand OA, stratified for sex.

Prevalence erosive OA	All	Males	Females
Total population aged $\geq$ 50 yrs Sub-population with hand pain (n=1076) Sub-population with hand pain in IPJs	2.4 (1.8, 3.0) 7.4 (5.9, 9.2) 15.2 (12.1, 18.2)	0.9 (0.3, 1.4) 3.1 (1.6, 5.2) 7.3 (4.0, 12.2)	3.7 (2.7, 4.7) 10.3 (8.0, 12.6) 19.2 (15.1, 23.3)
Sub-population with symptomatic	10.0 (7.9, 12.1)	4.5 (2.4, 7.6)	13.2 (10.2, 16.1)
Sub-population with symptomatic radiographic hand OA in IPJs as well (n=344)	23.3 (18.8, 27.7)	13.8 (7.6, 22.5)	26.8 (21.3, 32.3)

Numbers are percentages (range 0-100%) with 95% confidence intervals in brackets, Sub-population with hand pain= having pain of the hands  $\geq$  1day during last month, Sub-population with symptomatic radiographic hand OA = meeting the criteria for hand symptoms and at least one joint in distal, proximal or 1<sup>st</sup> interphalangeal joints (=DIP, PIP, 1<sup>st</sup> IP) or 1<sup>st</sup> carpometacarpal joint (CMCJ) with Kellgren-Lawrence grade  $\geq$ 2, IPJs = including DIP, PIP or 1<sup>st</sup> IPJ.

# Clinical burden of erosive OA in relation to symptomatic radiographic hand OA

Persons with erosive OA reported significantly more pain, stiffness and functional limitations than persons with symptomatic non-erosive radiographic hand OA on both AUSCAN and AIMS-2 questionnaires (table 4). The power grip and pulp pinch strength tended to be lower in persons with erosive OA than those with symptomatic radiographic hand OA, after adjustment for age and sex but not significantly different. In the performance of the GAT, no significant differences in time taken to complete the tasks were found between persons with erosive OA and persons with symptomatic radiographic hand OA.

No statistically significant differences were seen in the AIMS-2 Impact subscale and PCS between persons with erosive OA and those with symptomatic radiographic hand OA. Persons with erosive OA scored significantly better on the MCS, but worse on the MHQ Aesthetics subscale than persons with symptomatic radiographic hand OA (table 4). The results mentioned above did not change when the analyses were also adjusted for BMI.

### Clinical burden in different stages of erosive OA

Within erosive OA, those with only R-phases reported less stiffness and better hand and finger function as assessed by AIMS-2 than persons with at least one E-phase on the radiographs; also self-reported hand function scores assessed by AUSCAN were lower,

Outcome	Persons with symptomatic	Persons with	Adjusted mean
	radiographic hand OA	erosiveOA	difference*
	(n=718), mean (SD)	(n=80), mean (SD)	(95%Cl)
Female, no. (%)	442 (62%)	67 (84%)	22.2% (13.4, 31.0)
Age (years)	66.1 (8.1)	69.2 (7.8)	3.1 (1.3, 5.0)
BMI (kg/m²)	29.3 (5.1)	28.7 (5.1)	-0.6 (-1.7, 0.6)
AUSCAN pain	6.6 (4.2)	8.0 (4.2)	1.3 (0.3, 2.3)
AUSCAN stiffness	1.1 (0.9)	1.5 (1.0)	0.3 (0.1, 0.6)
AUSCAN function	10.4 (8.1)	13.8 (8.0)	2.3 (0.4, 4.2)
AIMS-2 Pain subscale	3.8 (2.3)	4.7 (2.6)	0.8 (0.3, 1.4)
AIMS-2 Hand/finger function	2.2 (2.1)	3.1 (2.4)	0.8 (0.2, 1.3)
AIMS-2 Impact subscale	2.2 (2.1)	2.6 (2.2)	0.5 (-0.05, 1.0)
Power grip (lbs)	50.7 (25.6)	37.4 (18.9)	-3.0 (-7.1, 1.1)
Pulp pinch (lbs)	10.3 (4.1)	8.4 (2.7)	-0.3 (-1.0, 0.4)
GAT: Grip ability test	31.8 (12.9)	32.3 (9.8)	-0.7 (-4.7, 3.4)
SF-12 PCS	37.6 (11.8)	37.0 (11.3)	0.5 (-2.4, 3.4)
SF-12 MCS	50.4 (10.8)	53.0 (9.3)	2.9 (0.2, 5.5)
MHQ aesthetics subscale	72.2 (20.5)	52.2 (23.7)	-17.6 (-22.8, -12.5)

Table 4: Demographic characteristics and clinical outcomes in the symptomatic radiographic hand OA subpopulation (n=798), with mean differences in outcomes between persons with and without erosive OA.

Values are means (SD) unless stated otherwise, erosive OA = Erosive hand osteoarthritis in one or more IPJ (including DIPJ, PIPJ or 1 <sup>st</sup> IPJ), BMI= Body Mass Index, AUSCAN= Australian/Canadian Hand Osteoarthritis Index, AIMS-2= Arthritis Impact Measurement Scales health status, \*= adjusted for age and sex (exception: crude mean differences for age and sex), 1 lb= 0.453 kg, SF-12= Short-Form 12, PCS= physical component summary score, MCS= Mental component summary score, questionnaire, MHQ: Michigan Hand Outcomes Questionnaire.

however this difference was not statistically significant. There was no difference between E- or R-phases in pain, AIMS-2 impact subscale, MCS and MHQ Aesthetic subscale. Furthermore, those with only R-phases had a better perception of their perceived physical health than those with  $\geq$ 1 E-phase on their radiographs (adjusted mean difference 5.8 (95%CI 0.2, 11.5), table 5). When adjusted for also BMI, the results did not change.

## Clinical burden of erosive OA in relation to inflammatory arthritis

A total of 44 cases of pre-existing systemic inflammatory arthritis were identified (39 rheumatoid arthritis, 4 psoriatic arthritis, 1 scleroderma), with a mean age (SD) of 66.2 (9.3) years and mean BMI (SD) of 28.4 (5.2) kg/m<sup>2</sup>. 61% were women, which is significantly lower than in the erosive OA patient group (mean difference (95%CI) -24.7% (-41.3 to -0.8). In 36 patients, this diagnosis had been made by a rheumatologist. The remaining 8 relied on a combination of GP diagnosis and consultant radiologist report on the study radiographs.

Compared to cases with diagnosed inflammatory arthritis, persons with erosive OA had less hand pain, stiffness and functional limitation on both AUSCAN and AIMS-2

Table 5: Demographic characteristics and outcome measures of general health and diseasespecific questionnaires and performance tests in erosive persons (n=80), stratified for presence of erosive (E-) or remodeled (R-) phase with mean differences of outcomes between E-phase and R-phase persons.

Outcome	Erosive, ≥1 E-phase	Erosive, R-phase only	Adjusted mean
	(n=23, 76 affected	(n=57, 140 affected	difference*
	joints)	joints)	(95%Cl)
AUSCAN pain	8.7 (4.6)	7.7 (4.0)	-1.0 (-3.0, 1.0)
AUSCAN stiffness	2.0 (0.9)	1.3 (1.0)	-0.7 (-1.2, -0.2)
AUSCAN function	15.5 (7.9)	13.1 (8.1)	-2.4 (-6.4, 1.5)
AIMS-2 Pain subscale	5.3 (2.8)	4.4 (2.5)	-0.8 (-2.1, 0.5)
AIMS-2 Hand/finger function	3.9 (2.7)	2.8 (2.2)	-1.1 (-2.2, -0.1)
AIMS-2 Impact subscale	2.5 (2.3)	2.6 (2.2)	0.1 (-1.0, 1.3)
SF-12 PCS	33.2 (11.1)	38.7 (11.1)	5.8 (0.2, 11.5)
SF-12 MCS	53.1 (9.5)	52.9 (9.3)	-0.3 (-5.1, 4.6)
MHQ aesthetics subscale	48.1 (23.7)	54.3 (23.7)	5.4 (-6.6, 17.3)

Values are means (SD) unless stated otherwise, SD= Standard deviation, E-phase= eroded joint according to the Verbruggen-Veys scoring method, R-phase= remodelled joint according to the Verbruggen-Veys scoring method, AUSCAN= Australian/Canadian Hand Osteoarthritis Index. AIMS-2= Arthritis Impact Measurement Scales health status questionnaire, \*= adjusted for age and sex,

SF-12= Short-Form 12, PCS= Physical component summary score, MCS= Mental component summary score, MHQ= Michigan Hand Outcomes Questionnaire.

subscales. Persons with erosive OA had also better perceptions of both their physical and mental health than persons with inflammatory arthritis. No difference was seen in the MHQ aesthetics subscale score between persons with erosive OA and those with inflammatory arthritis (table 6). The results did not change when also adjusted for BMI.

## DISCUSSION

This study makes several contributions to current knowledge on the occurrence and impact of erosive OA. Firstly, we have confirmed with a high degree of consistency, previous estimates of the prevalence of erosive OA in the general population. Secondly, we showed that in a population-based study symptomatic subjects with erosive OA report more pain, functional disability and aesthetic damage as assessed with hand OA specific questionnaires than symptomatic subjects with non-erosive radiographic signs. In this population-based study, erosive OA does have not appear to impact as strongly on pain and function as prevalent inflammatory arthritis identified from the same population.

The additional value of the present study concerns the detailed assessments of the hand (e.g. clinical examination, AUSCAN, AIMS-2 and SF-12) in contrast to the Rotterdam and Framingham studies. The use of hand OA specific questionnaires in this study makes it possible to quantify pain, functional limitation and health status in erosive OA in a general population sample with hand symptoms in more detail than previous studies have allowed. In both Rotterdam and Framingham Studies, a question of having hand pain or symptoms on most days of their joints<sup>8</sup>, or during last month was asked<sup>7</sup>,

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Outcome	Persons with erosive OA (n=80), mean (SD)	Persons with inflammatory arthritis (n=44)*, mean (SD)	Mean difference** (95%Cl)
Female, no. (%)	67 (84%)	26 (61%)	-24.7% (-41.3, -0.8)
Age (years)	69.2 (7.8)	66.2 (9.3)	-3.0 (-6.1, 1.6)
BMI (kg/m²)	28.7 (5.1)	28.4 (5.2)	-0.3 (-2.3, 1.6)
AUSCAN pain	8.0 (4.2)	10.2 (4.1)	1.7 (0.05, 3.4)
AUSCAN stiffness	1.5 (1.0)	2.0 (0.8)	0.4 (0.02, 0.8)
AUSCAN function	13.8 (8.0)	20.3 (9.4)	6.3 (2.8, 9.9)
AIMS-2 Pain subscale	4.7 (2.6)	6.1 (1.9)	1.2 (0.2, 2.2)
AIMS-2 Hand/finger function	3.1 (2.4)	4.8 (2.9)	1.6 (0.5, 2.6)
AIMS-2 Impact subscale	2.6 (2.2)	4.5 (2.9)	1.7 (0.8, 2.8)
SF-12 PCS	37.0 (11.3)	28.4 (9.5)	-8.4 (-12.9, -3.9)
SF-12 MCS	53.0 (9.3)	46.0 (11.3)	-7.3 (-11.5, -3.0)
MHQ aesthetics subscale	52.2 (23.7)	52.7 (27.5)	-1.3 (-11.6, 9.0)

Table 6: Clinical outcomes for participants with erosive OA and those with inflammatory arthritis (n=80 and n=44).

Values are means (SD) unless stated otherwise, erosive OA= erosive hand osteoarthritis in one or more IPJ (including DIPJ, PIPJ or 1 \* IPJ), \*= One person of the inflammatory arthritis category was missing, SD = Standard deviation, \*\*= adjusted for age and sex (crude mean differences for age and sex), AUSCAN= Australian/Canadian Hand Osteoarthritis Index, AIMS-2= Arthritis Impact Measurement Scales health status questionnaire, SF-12= Short-Form 12, PCS= Physical component summary score, MCS= Mental component summary score, MHQ= Michigan Hand Outcomes Questionnaire.

where the Rotterdam Study in addition used the hand-specific questions of the Health Assessment Questionnaire (HAQ)<sup>24,25</sup> to describe the increased disability in persons with erosive OA compared to the general population<sup>7</sup>. However, the HAQ includes more domains of functionality and these hand-specific questions were not validated in patients with hand OA<sup>24,25</sup>. In the present study, the quantification of pain and function could be made since both AUSCAN and AIMS-2 were used, showing the same direction of the outcomes. Another advantage of the present study is the additional information obtained from the clinical examination and the SF-12, which extends the knowledge regarding the impact of EOA in people with symptomatic hand OA.

The prevalence estimates in the present study are very similar to those found in the Rotterdam Study. In the Rotterdam Study, 2.8% of adults aged 55 years and over in the general population were estimated to have symptomatic erosive OA (equivalent to 6.9% in those with hand symptoms and 10.2% in the subgroup with symptomatic radiographic hand OA<sup>7</sup>). In the present study in adults aged 50 years and over the estimates are 2.4%, 7.4%, and 10.0% respectively. Recently, Haugen et al. reported apparently higher prevalence estimates of erosive OA (9.9% for women and 3.3% for men aged 40-84 years) using data from the Framingham Study<sup>8</sup>. These estimates were based on erosions defined by the OARSI atlas while the Rotterdam and Keele studies used the Verbruggen-Veys scoring method. More importantly, the Framingham estimates were of erosive OA irrespective of symptoms. Persons with erosive OA experience not only more pain, but also more functional limitation and impact than those with symptomatic radiographic hand OA, measured with AUSCAN and AIMS-2 questionnaires. Scores of the AUSCAN subscales in the present study were slightly lower than reported for persons with erosive OA in secondary care<sup>9</sup>. Regardless of the study population, all these studies confirm that persons with erosive OA have a higher clinical burden than persons with symptomatic radiographic hand OA. Persons with erosive OA did not report poorer overall perceived physical health than persons with hand OA, as reflected by the PCS. This finding is in line with Bijsterbosch *et al.*, who reported no difference in health-related quality of life in persons with erosive OA compared to persons with non-erosive OA<sup>9</sup>.

The clinical burden of erosive OA is lower than prevalent inflammatory arthritis in this population-based study. Individuals with inflammatory arthritis experienced a higher clinical burden than persons with erosive OA in terms of pain, functional limitation and physical health status. Recently, Wittoek et al. showed that patients with erosive OA visiting a rheumatology clinic have more funtional impairment and pain, compared to patients with controlled inflammatory arthritis<sup>26</sup>. An explanation for this contrary finding could be selection bias due to the different setting of the investigation (general population versus secondary care). Furthermore, the patients with inflammatory arthritis in the present study could have a higher disease activity (however not measured since this was not the aim of the present study) than the patients in the Belgian study. During the development of the SACRAH questionnaire, which is a score for assessment and quantification of chronic rheumatic affections of the hand, the scores concerning function, pain and stiffness were not significantly different between 69 OA and 103 RA patients<sup>11</sup>. The finding of a lower perceived physical health status in persons with inflammatory arthritis is in line with a population-based study in Spain reporting mean PCS scores from the SF-12 in persons with rheumatoid arthritis of 29.1 compared to 35.5 in persons with hand OA, after adjustment for age and sex<sup>27</sup>. The study of Slatkwosky et al., showed that patients with RA and hand OA score worse on the SF-36 compared to the general population but RA patients score worse than OA patients (SF-36 scores of 59.1 for hand OA patients, 48.4 for RA patients and 81.6 for controls, respectively)<sup>12</sup>. However, in all three above mentioned studies, the comparison with erosive OA directly was not investigated. The novelty of the present study is that health-related quality of life, pain and function scales of the AUSCAN and AIMS-2 in persons with erosive OA were directly compared to persons with inflammatory arthritis from the same source population.

Several limitations in the present study deserve mention. Although both cohorts (CAS-HA and CAS-K) gathered comparable data, they were assembled in subtly different ways – one based on knee symptoms, the other on the basis of hand symptoms in the past 12 months. Biased estimates from the knee cohort would be a concern although the difference in frequency of erosive OA between the two cohorts was not large (8.1% in CAS-HA vs. 6.8% in CAS-K) which justifies their combination. The identification of cases of inflammatory arthritis was based predominantly on a pre-existing recorded diagnosis by rheumatologist. In the absence of a thorough diagnostic screen for all inflammatory arthritis in the research clinics (which was

beyond the scope of the present study) there could be the potential for some cases of inflammatory arthritis to have been missed due to incomplete records or early arthritis not yet diagnosed. Also no specific information about swollen tender joints (such as disease activity scores like DAS-28) was available.

Furthermore, the number of persons with erosive OA, differentiation between Eand R-phases and persons with inflammatory arthritis were small and results may not be significant due to these small numbers. However, no earlier studies did investigate these groups in detail with specific outcomes. These results needed to be confirmed in future studies.

In conclusion, erosive OA in the general population is an infrequent hand OA subset that occurs mostly in the DIPJs, with a predominance in females, and has consistent and substantial impact on pain and self-reported function, although appearing not as great as in persons with prevalent inflammatory arthritis.

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# **REFERENCE LIST**

- Zhang W, Doherty M, Leeb BF, Alekseeva L, Arden NK, Bijlsma JW et al. EULAR evidence-based recommendations for the diagnosis of hand osteoarthritis: report of a task force of ESCISIT. Ann Rheum Dis 2009; 68:8-17.
- Peter JB, Pearson CM, Marmor L. Erosive osteoarthritis of the hands. Arthritis Rheum 1966; 9:365-88.
- Punzi L, Frigato M, Frallonardo P, Ramonda R. Inflammatory osteoarthritis of the hand. Best Pract Res Clin Rheumatol 2010; 24:301-12.
- Altman RD, Gold GE. Atlas of individual radiographic features in osteoarthritis, revised. Osteoarthritis Cartilage 2007; 15 Suppl A:A1-56.
- 5. Verbruggen G, Veys EM. Numerical scoring systems for the anatomic evolution of osteoarthritis of the finger joints. Arthritis Rheum 1996; 39:308-20.
- 6. Punzi L, Ramonda R, Sfriso P. Erosive osteoarthritis. Best Pract Res Clin Rheumatol 2004; 18:739-58.
- Kwok WY, Kloppenburg M, Rosendaal FR, van Meurs JB, Hofman A, Bierma-Zeinstra SM. Erosive hand osteoarthritis: its prevalence and clinical impact in the general population and symptomatic hand osteoarthritis. Ann Rheum Dis 2011; 70:1238-42.
- Haugen IK, Englund M, Aliabadi P, Niu J, Clancy M, Kvien TK et al. Prevalence, incidence and progression of hand osteoarthritis in the general population: the Framingham Osteoarthritis Study. Ann Rheum Dis 2011; 70:1581-6.
- Bijsterbosch J, Watt I, Meulenbelt I, Rosendaal FR, Huizinga TW, Kloppenburg M. Clinical burden of erosive hand osteoarthritis and its relationship to nodes. Ann Rheum Dis 2010; 69:1784-8.
- Pattrick M, Aldridge S, Hamilton E, Manhire A, Doherty M. A controlled study of hand function in nodal and erosive osteoarthritis. Ann Rheum Dis 1989; 48:978-82.
- 11. Leeb BF, Sautner J, Andel I, Rintelen B. SACRAH: a score for assessment and quantification of chronic rheumatic affections of the hands. Rheumatology (Oxford) 2003; 42:1173-8.
- 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.

- Myers H, Nicholls E, Handy J, Peat G, Thomas E, Duncan R et al. The Clinical Assessment Study of the Hand (CAS-HA): a prospective study of musculoskeletal hand problems in the general population. BMC Musculoskelet Disord 2007; 8:85.
- Peat G, Thomas E, Handy J, Wood L, Dziedzic K, Myers H et al. The Knee Clinical Assessment Study--CAS(K). A prospective study of knee pain and knee osteoarthritis in the general population. BMC Musculoskelet Disord 2004; 5:4.
- Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis 1957; 16:494-502.
- 16. 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.
- Bellamy N, Campbell J, Haraoui B, Gerecz-Simon E, Buchbinder R, Hobby K et al. Clinimetric properties of the AUSCAN Osteoarthritis Hand Index: an evaluation of reliability, validity and responsiveness. Osteoarthritis Cartilage 2002; 10:863-9.
- Meenan RF, Mason JH, Anderson JJ, Guccione AA, Kazis LE. AIMS2. The content and properties of a revised and expanded Arthritis Impact Measurement Scales Health Status Questionnaire. Arthritis Rheum 1992; 35:1-10.
- Dellhag B, Bjelle A. A Grip Ability Test for use in rheumatology practice. J Rheumatol 1995; 22:1559-65.
- 20. Poole JL. Measures of Adult Hand Function. Arthritis Rheum 2003; 49:S59-S66.
- 21. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996; 34:220-33.
- Chung KC, Pillsbury MS, Walters MR, Hayward RA. Reliability and validity testing of the Michigan Hand Outcomes Questionnaire. J Hand Surg Am 1998; 23:575-87.
- 23. StataCorp 2009. Multiple Imputatation Reference Manual. 2009.
- 24. Bruce B, Fries JF. The Stanford Health Assessment Questionnaire: dimensions and practical applications. Health Qual Life Outcomes 2003; 1:20.

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- Fries JF, Spitz PW, Young DY. The dimensions of health outcomes: the health assessment questionnaire, disability and pain scales. J Rheumatol 1982; 9:789-93.
- 26. Wittoek R, Cruyssen BV, Verbruggen G. Predictors of functional impairment and pain in erosive osteoarthritis of the interphalangeal joints: comparison with

controlled inflammatory arthritis. Arthritis Rheum 2012; 64:1430-6.

27. Carmona L, Ballina J, Gabriel R, Laffon A. The burden of musculoskeletal diseases in the general population of Spain: results from a national survey. Ann Rheum Dis 2001; 60:1040-5.