

## EXTENDED REPORT

## Prevalence and pattern of radiographic hand osteoarthritis and association with pain and disability (the Rotterdam study)

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Ann Rheum Dis 2005;64:682–687. doi: 10.1136/ard.2004.023564

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Accepted  
1 September 2004  
Published Online First  
16 September 2004

**Objective:** To investigate the prevalence and pattern of radiographic osteoarthritis (ROA) of the hand joints and its association with self reported hand pain and disability.

**Methods:** Baseline data on a population based study (age  $\geq 55$  years) were used (n = 3906). Hand ROA was defined as the presence of Kellgren–Lawrence grade  $\geq 2$  radiological changes in two of three groups of hand joints in each hand. The presence of hand pain during the previous month was defined as hand pain. The health assessment questionnaire was used to measure hand disability.

**Results:** 67% of the women and 54.8% of the men had ROA in at least one hand joint. DIP joints were affected in 47.3% of participants, thumb base in 35.8%, PIP joints in 18.2%, and MCP joints in 8.2% (right or left hand). ROA of other joint groups (right hand) co-occurred in 56% of DIP involvement, 88% of PIP involvement, 86% of MCP involvement, and 65% of thumb base involvement. Hand pain showed an odds ratio of 1.9 (1.5 to 2.4) with the ROA of the hand (right). Hand disability showed an odds ratio of 1.5 (1.1 to 2.1) with ROA of the hand (right or left).

**Conclusions:** Hand ROA is common in the elderly, especially in women. Co-occurrence of ROA in different joint groups of the hand is more common than single joint disease. There is a modest to weak association between ROA of the hand and hand pain/disability, varying with the site of involvement.

Osteoarthritis is the most common form of arthritis among the elderly and one of the leading musculoskeletal causes of disability in Western countries.<sup>1,2</sup> The hand is often involved in patients suffering from osteoarthritis. The estimated prevalence of osteoarthritis in the hand varies depending on the definition. Although point prevalence of radiographic osteoarthritis (ROA) is reported to be as high as 29–76% in population based studies, the prevalence of symptomatic hand osteoarthritis is much lower, with a point prevalence of between 4% and 6.2%.<sup>3–5</sup> The pattern of hand joint involvement found among affected individuals remains contentious. In addition, despite advances in our understanding of the disease, a discrepancy remains between structural markers of pathology and the clinical syndrome of osteoarthritis typified by joint pain and disability.<sup>6–8</sup> Zhang *et al* reported that symptomatic hand osteoarthritis limited several daily functional activities in the Framingham study.<sup>9</sup> Jones *et al* reported a modest association between the presence of ROA and hand pain or disability in a population with diagnosis of hand osteoarthritis.<sup>10</sup>

However, whether the association between ROA and hand pain or disability differentiates between different hand joint groups has not been evaluated. Our aim in this study was to explore the prevalence and pattern of ROA in the hand joints, and to investigate the association between ROA of different joints in the hand and self reported hand pain and/or disability in an open population.

## METHODS

## Study population

For this study we used cross sectional baseline data from the Rotterdam study, a population based cohort. The medical ethics committee of the Erasmus Medical Centre approved the study, and written informed consent was obtained from all participants.

The baseline measurements were conducted between 1990 and 1993. The complete study design has been described previously.<sup>11</sup> All inhabitants of a suburb of Rotterdam aged 55 years and older were invited to participate. In all, 7983 participants were examined (a response rate of 78%). At baseline, trained interviewers undertook an extensive home interview on demographic characteristics, medical history, risks factors for chronic diseases, and therapeutic drug use. Radiographs were taken at the research centre at baseline. For feasibility reasons we scored hand radiographs for ROA on only 3906 of the participants, including all those who were available for follow up six years later (n = 3585).

## Radiographic scoring

Two trained assessors (S Dahaghin and U Cimen), who were blinded to the clinical and demographic data, scored standard anteroposterior radiographs of both hands in 2002. Radiographs were scored for six individual radiographic features of osteoarthritis in the five distal interphalangeal (DIP) joints, four proximal interphalangeal (PIP) joints, five metacarpophalangeal (MCP) joints, the first carpometacarpal joint (CMC1), and the trapezioscapoid joint (TS). Osteophytes were differentiated into three grades (small, moderate, large), while joint space narrowing, sclerosis, cysts, lateral deformity, and cortical collapse were scored as either present or absent. Lateral deformity was defined as malalignment of at least 15° (modified Kallman score).<sup>12</sup> Each joint was graded for overall ROA using a modified Kellgren–Lawrence (K-L) grade scaled from 0 to 4 (appendix 1).<sup>13</sup> ROA for each joint was defined as a K-L grade of  $\geq 2$ . DIP, PIP,

**Abbreviations:** CMC1/TS, first carpometacarpal and trapezioscapoid joint; DIP, distal interphalangeal joint; K-L, Kellgren–Lawrence radiological grade; MCP, metacarpophalangeal joint; PIP, proximal interphalangeal joint; ROA, radiographic osteoarthritis

**Table 1** Baseline characteristics of the study population (n = 3906)

Characteristic		Right/left	Right	Left
Female (%)	58.3			
Age (years) (mean (SD))	66.6 (7.3)			
+Hand disability (%)	5.8			
++Overall disability index (%)	20.2			
*ROA of DIP joints (%)	47.3	38.6	34.8	
*ROA of PIP joints (%)	18.2	13.4	11.6	
*ROA of MCP joints (%)	8.2	6.1	4.4	
*ROA of CMC1/TS (%)	35.8	25.8	30.2	
†Hand ROA (%)	28.3	21.5	20.6	
Hand pain (%)	16.8	14.2	13.5	

+Hand disability: mean score of 0.5 or more of various components composed of eight questions related to hand function on the Stanford health assessment questionnaire (HAQ).  
 ++Overall disability index: mean score of 0.5 or more on HAQ index (scored 0 to 3).  
 \*ROA: presence of K-L  $\geq 2$  in at least one joint of the group.  
 †Hand ROA: presence of K-L  $\geq 2$  in two of three groups (DIP, PIP, CMC1/TS).  
 CMC1/TS, first carpometacarpal plus trapezioscapoid (base of thumb); DIP, distal interphalangeal; K-L, Kellgren–Lawrence radiological grade; MCP, metacarpophalangeal; PIP, proximal interphalangeal; ROA, radiographic osteoarthritis.

MCP, and CMC1/TS joint groups were defined as positive if at least one joint of the group had a K-L grade of  $\geq 2$ . Hand ROA was defined as the presence of a K-L grade of  $\geq 2$  in two of three groups of hand joints (DIP, PIP, and CMC1/TS) of each hand. The same definition was used for the cut off point K-L  $\geq 3$  or K-L = 4.

To investigate the reliability of the scoring, the two assessors both scored a random subset of 205 radiographs independently. The interobserver reliability for K-L  $\geq 2$  as a dichotomous variable expressed by the  $\kappa$  statistic was as follows: DIP joints, 0.60; PIP joints, 0.61; MCP joints, 0.63; and CMC1/TS (base of thumb), 0.74.

**Hand pain**

The following questions were asked during the home interview:

- Did you have pain on the right (left) hand during the last month?
- How long have you had the pain?

The answer to the second question ranged from less than one month to more than five years.

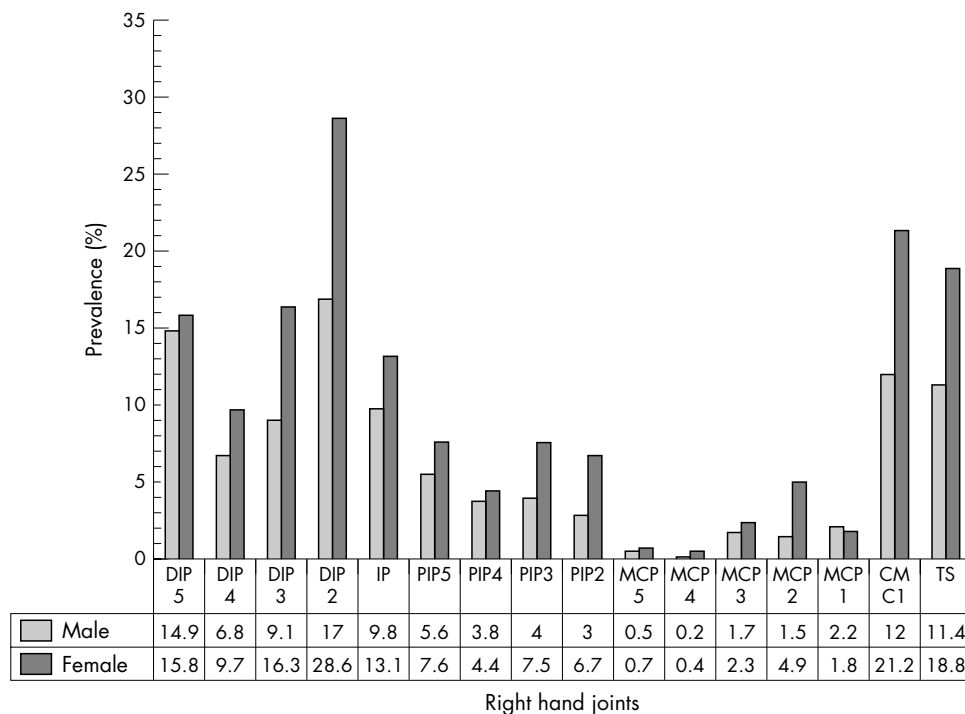
**Hand disability**

Stanford health assessment questionnaire (HAQ) was used to assess disability. Eight questions on the HAQ concerning hand function were used to assess hand disability (appendix 2). Each question scored from “no difficulty” (0) to “unable to do” (3). Of the components with more than one question related to the hand function, the highest score was considered (as in the original HAQ).<sup>14 15</sup> Dependence on equipment or physical assistance was ignored; this represents residual disability after compensatory efforts. The scores were averaged into an overall hand disability score on a scale from 0 (no hand disability) to 3 (hand severely disabled). A mean score of  $\geq 0.5$  was considered to mean a moderate to severe hand disability.

**Data analysis**

Point prevalence of ROA was calculated for each joint, for the joint groups, and for the whole hand. A rectangle diagram (Venn diagram with four variables) was used to show the distribution of ROA in the four hand joint groups.

Univariate and multivariate logistic regression analysis was used to evaluate the strength of the association of ROA in the different hand joint groups in each hand and also to examine associations between ROA and hand pain and/or disability. The associations are presented as odds ratios (OR) with 95% confidence intervals (CI) and were adjusted for age and sex. All analyses were carried out at the level of the person. The association between ROA and hand pain was evaluated for each hand separately, while the association with hand



**Figure 1** Point prevalence of radiographic osteoarthritis (Kellgren–Lawrence radiological grade  $\geq 2$ ) in the hand joints of men and women (n = 3906).

disability was evaluated for the presence of ROA in either the right or the left hand as well as for ROA of the dominant hand. The association with hand pain and/or disability was also examined in relation to the number of joints with ROA (as a continuous variable) and for the more severe forms of ROA ( $K-L \geq 3$  or  $K-L = 4$ ).

The SPSS (version 10) program was used for all analyses. The Span program was used to generate rectangle diagrams.<sup>16</sup>

## RESULTS

In all, we evaluated 3906 participants (53.8% female, 46.2% male), of mean age 66.6 years (table 1).

### Prevalence and pattern of ROA

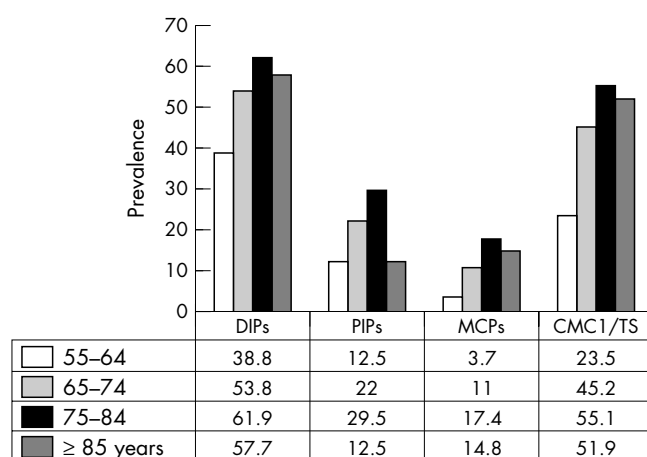
In all, 61.7% of our study population had  $K-L \geq 2$  in at least one of the joints of the hand (67% of the women and 54.8% of the men). DIP joints had the highest frequency (47.3%), followed by CMC1/TS joints (35.8%), PIP joints (18.2%), and MCP joints (8.2%) of the right or left hand.

ROA in the separate DIP joints (right hand) occurred in 6.8–17% of men and in 9.7–28.6% of women. The ranges were 3.0% to 5.6% and 4.4% to 7.6% in the PIP joints, 0.2% to 2.2% and 0.4% to 4.9% in the MCP joints, and 11.4% to 21.2% in the CMC1/TS joints for men and women, respectively (fig 1).

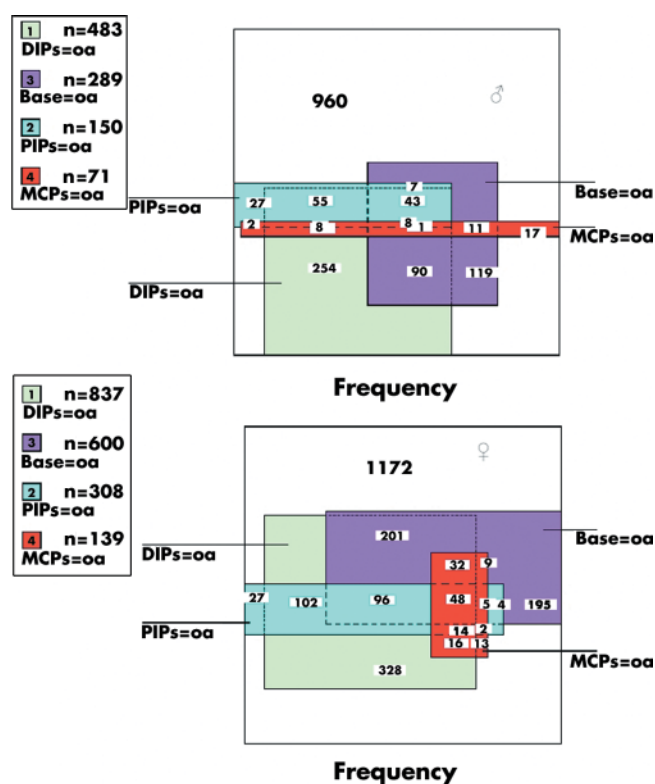
Except for DIP 2 (right = 23.5%, left = 16.8%), CMC1 (right = 17.2%, left = 21.3%), and TS (right = 15.6%, left = 17.6%), the other hand joints showed almost the same frequency in the right and left hands.

Hand ROA was present in 21.5% of right hands and 20.6% of left hands. The prevalence of ROA increased with age up to 84 years, but decreased in the group aged 85 years and older (fig 2).

Use of a rectangle diagram showed that ROA in one joint group more often co-occurred with ROA in other joint groups in women than in men: DIP joints, 61% (women) v 47% (men); PIP joints, 91% v 82%; MCP joints, 91% v 77%; CMC1/TS joints, 68% v 59% (all in the right hand, fig 3). Evaluating the strength of the relations, the PIP joints and the MCP joints had the highest odds ratios with ROA of the other joint groups of the right hand (OR = 9.1 (95% CI, 6.8 to 12.4) and OR = 5.4 (3.6 to 8.0), respectively). CMC1/TS joints showed the lowest association with other joint groups of the right hand (OR = 3.1 (2.6 to 3.6)) (table 2). The left hand showed similar results.



**Figure 2** Age specific point prevalence (%) of osteoarthritis in hand joint groups (right/left).



**Figure 3** Rectangle diagram of radiographic osteoarthritis in the hand joint groups ( $n = 3906$ ). The coloured rectangles represent osteoarthritis (oa) of Kellgren–Lawrence radiological grade  $\geq 2$  in at least one joint of the group (DIP, PIP, MCP, base) in the right hand for men (top panel) and women (bottom panel). Base, first carpometacarpal and trapezioscapoid joint (thumb base); DIP, distal interphalangeal joint; MCP, metacarpophalangeal joint; PIP, proximal interphalangeal joint.

### ROA and hand pain

Prevalence of hand pain (right) was 14.2%; 97% of the participants suffered from this for longer than one month. Table 3 shows the association between hand pain and ROA in the joint groups of the right hand, the strongest being with the CMC1/TS. Right hand pain showed an association with ROA of the related hand (OR = 1.9 (95% CI, 1.5 to 2.4)). With the cut off point at  $K-L \geq 3$  the association was nearly the same (OR = 1.8 (1.3 to 2.5)), but when the cut off point was increased to  $K-L = 4$ , there was a stronger association with pain in the right hand (OR = 3.6 (2.2 to 5.8)). Increasing the number of joints with ROA produced a greater association with pain (OR = 1.1 (1.1 to 1.2), right hand). Generalised hand osteoarthritis (ROA of all four joint groups of the right hand) showed an increased association with hand pain (OR = 2.7 (1.4 to 5.2)). The associations of hand pain and ROA in the left hand were similar but are not presented here.

### ROA and hand disability

The prevalence of hand disability was 5.8%. The presence of hand ROA (right/left) showed an association with hand disability (OR = 1.5 (1.1 to 2.1)). Specification to the dominant hand gave nearly the same results. Table 4 shows the association between hand disability and ROA (right/left) differentiated for hand joint group; the association was only significant for the MCP joints (OR = 2.0 (1.3 to 3.0)). The association of ROA of the base of the thumb became significant when the analysis was specified to the dominant hand. However, MCP joints of the dominant hand showed odds ratios similar to the base of the thumb for hand disability.

**Table 2** Pattern of radiographic osteoarthritis of the hand joint groups of the right hand (n = 3906)

	Right hand			
	PIP	MCP	CMC1/TS	Any other joint group
DIP	9.1 (7.1 to 11.7)	3.9 (2.9 to 5.5)	2.9 (2.5 to 3.4)	4.4 (3.7 to 5.0)
PIP		4.7 (3.5 to 6.4)	2.8 (2.3 to 3.5)	9.1 (6.8 to 12.4)
MCP			3.8 (2.9 to 5.2)	5.4 (3.6 to 8.0)
CMC1/TS				3.1 (2.6 to 3.6)

Values are odds ratios and 95% confidence intervals adjusted for age and sex.

CMC1/TS, first carpometacarpal and trapezioscapoid joint (base of thumb); DIP, distal interphalangeal joint; MCP, metacarpophalangeal joint; PIP, proximal interphalangeal joint.

Using the cut off points K-L  $\geq 3$  and K-L = 4 (right/left) showed nearly the same association with hand disability (OR = 1.6 (1.1 to 2.5) and OR = 1.6 (0.9 to 2.9), respectively). An increase in the number of hand joints with ROA showed a borderline significant association with hand disability. This association increased to a significant level when the number of joints with ROA in only the dominant hand was analysed in relation to hand disability (OR = 1.1 (1.0 to 1.2)). Generalised hand osteoarthritis (ROA in all four hand joint groups) also showed a stronger association with hand disability (OR = 2.7 (1.3 to 6.0)).

## DISCUSSION

The results of our study confirm that hand ROA is a common disease in the elderly, especially in women. It is more likely to occur in several different hand joint groups simultaneously than in single joints, the latter being more prevalent in women than in men. More than 80% of ROA affecting the PIP and MCP joints co-occurred with the other hand joint groups. We confirmed a modest association between ROA and hand pain, the strongest relation being with involvement of the base of the thumb. Hand disability showed a rather weak association with ROA, the strongest relation being with the MCP joints and the base of the thumb.

As the hand joints are small and the features of osteoarthritis often difficult to define, interpreting the radiographs of these joints is challenging. However, our interobserver reliability was good and similar to the results of other studies.<sup>9-17</sup> The predominance given to osteophytes in the original Kellgren–Lawrence grading scheme has been discussed previously.<sup>18</sup> In the present study we used the modified definition which defines grade 3 ROA as a diminution in joint space regardless of whether or not there are osteophytes. This eliminates the predominance given to the osteophyte and thus probably provides more valid results. The definition of hand osteoarthritis (ROA in two of three hand joint groups) which we used, reported by Hirsch *et al*,<sup>17</sup>

does not include the MCP joints. To evaluate whether including the MCP joints in the definition would change the association with hand pain or disability we also tested an alternative definition of hand ROA that included the MCP joints (ROA in two of four hand joint groups in each hand). With this alternative definition the results were the same.

In our study, over 55% of the participants had ROA in at least one hand joint. This means that cartilage degeneration or subchondral bone reaction is present in at least one joint of the hand in more than half the open population aged 55 years and over. This high frequency of ROA, increasing with age and more frequent in the women, confirms previous findings.<sup>4-12, 19</sup> Van Saase<sup>4</sup> reported a slight decrease in the prevalence of ROA in very old people, which was confirmed in our study in people aged 85 years and over. However, only 47 participants of our study population (1.2%) reached this age, which may have produced an unstable estimate in this group. Considering that osteoarthritis is a chronic disease, another possible explanation is the selection of healthy survivors or a lower response rate of disabled persons.

The order of involvement of the hand joint groups in our study was also comparable with other findings. DIP joints and the base of the thumb were involved most often, followed by the PIP joints. This was also reported by Kellgren *et al* and Egger *et al*.<sup>20-21</sup> The MCP joints had the lowest frequency in our population, in accordance with findings of Chaisson *et al* but in contrast to van Saase *et al*, who reported a higher prevalence of ROA in MCP than in PIP joints.<sup>4</sup> Chaisson *et al* also reported this inconsistency.<sup>22</sup>

For the first time, we have visualised the pattern of ROA of the hand joint groups occurring solely or co-occurring with other joint groups in a rectangle diagram. This shows that the PIP and MCP joints are more affected concurrently with the other joint groups and are rarely affected alone. This finding was confirmed by logistic regression analysis. The base of the thumb had the lowest odds ratio with the other joint groups. This supports the view that systemic factors play a more

**Table 3** Association of hand pain with radiographic osteoarthritis in the hand joint groups (right hand)

Joint group	Univariate	Multivariate
*DIP	1.5 (1.2 to 1.8)	1.1 (0.9 to 1.4)
*PIP	1.8 (1.4 to 2.3)	1.4 (1.1 to 1.9)
*MCP	1.6 (1.1 to 2.3)	1.2 (0.8 to 1.7)
*CMC1/TS	2.0 (1.6 to 2.4)	1.7 (1.4 to 2.2)

Values are odds ratios (95% confidence intervals) adjusted for age and sex.

\*Presence of Kellgren–Lawrence radiological grade  $\geq 2$  in at least one joint of the group.

CMC1/TS, first carpometacarpal and trapezioscapoid joint (base of thumb); DIP, distal interphalangeal joint; MCP, metacarpophalangeal joint; PIP, proximal interphalangeal joint.

**Table 4** Association of hand disability with radiographic osteoarthritis in the hand joint groups

Joint group	Univariate	Multivariate
*DIP	1.3 (0.9 to 1.8)	1.2 (0.8 to 1.7)
*PIP	1.1 (0.8 to 1.7)	0.9 (0.6 to 1.4)
*MCP	2.0 (1.3 to 3.0)	1.8 (1.2 to 2.9)
*CMC1/TS	1.3 (1.0 to 1.9)	1.2 (0.8 to 1.7)

Values are odds ratios (95% confidence intervals) adjusted for age and sex.

Presence of Kellgren–Lawrence radiological grade  $\geq 2$  in at least one joint of the group in the right/left hand.

CMC1/TS, first carpometacarpal and trapezioscapoid joint (base of thumb); DIP, distal interphalangeal joint; MCP, metacarpophalangeal joint; PIP, proximal interphalangeal joint.

important role than physical factors in ROA of the PIP and MCP joints, but local mechanical factors may play a greater role in ROA of the base of the thumb.

With regard to the association between a structural marker of osteoarthritis and its clinical impact, the presence of hand ROA shows a modest to weak association with clinical symptoms such as hand pain and/or disability, as reported previously.<sup>9–10</sup> Surprisingly, our analysis in an open population gave a similar association of ROA with hand pain or disability to that reported by Jones *et al*,<sup>10</sup> who analysed a group of subjects with a diagnosis of hand osteoarthritis. In addition, we found a dose–response relation with hand pain, which increased with the number of joints affected by ROA, with generalised hand ROA (with all four hand joint groups involved), and with the severe form of ROA (Kellgren–Lawrence grade 4). However, only generalised hand ROA, and not the severity of Kellgren–Lawrence grade, showed a significant increase in the association with hand disability.

We examined the relation between hand pain and ROA of the different hand joint groups and showed that ROA of the base of the thumb had the strongest association with hand pain. This supports the hypothesis that ROA of the base of the thumb has a greater impact on pain than the other hand joint groups. ROA of the base of the thumb (right or left side) was less associated with hand disability than ROA of the MCP joints. However, ROA of the base of the thumb on the dominant hand had a significant association with hand disability, similar to that of the MCP group in the dominant hand. We initially thought that the relation with MCP joint disease might reflect the presence of another inflammatory disorder such as rheumatoid arthritis. However, ROA of the MCP joints was concurrent in more than 80% of cases with ROA of the other hand joint groups, while it is rare in rheumatoid arthritis. Thus the result suggests that ROA at the MCP joints is more disabling than at other sites, or indicates again that a more generalised form of hand ROA is more disabling.

This study has several potential limitations. First, it was primarily designed as a study of determinants and prognosis of chronic diseases in elderly people and not specifically for hand disease. Thus we did not have data on the exact location of hand pain or a pain severity measure. Second, there was some selection bias in our study population compared with the total population of the Rotterdam study. We scored radiographs of 3906 participants including all those available for follow up six years later. Our study population was younger, had a smaller proportion of women, and was less disabled than the total population at baseline. To examine whether the results of our study can be generalised to the overall Rotterdam population, we estimated the point prevalence of hand ROA in the whole of the Rotterdam study. Adjusted for the different age groups this resulted in an almost 3% higher estimate. The estimate was almost 2% higher when adjusted for the severity of general disability. Thus the point prevalence of ROA shown in our study is probably somewhat of an underestimate. However, the prevalence of hand pain was the same for both populations. The association with hand pain and/or disability might also be underestimated in our population.

## Conclusions

We present extensive data on the prevalence of ROA of hand joint groups in a large open population of elderly people of both sexes which will add to the existing knowledge of this disorder. Our study also showed that the PIP and MCP joint groups were often affected concurrently with the other joint groups and rarely alone. Of the separate hand joint groups, ROA of the thumb base was the main determinant of hand pain, followed by the PIP joints. Although the DIP joints were

the most affected joints in the hand, ROA in this joint group seems clinically unimportant. ROA of the MCP joints and the base of the thumb were both associated with hand disability.

## ACKNOWLEDGEMENTS

We thank Mrs R Bernsen for statistical analysis and Mr U Cimen for scoring the radiographs, and F van Rooij, E van der Heijden, R Vermeeren, and L Verwey for collecting the data. We also thank the general practitioners, pharmacists, and the many field workers at the research centre in Ommoord, and of course all the participants.

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## APPENDIX 1

### DEFINITION OF THE KELLGREN–LAWRENCE RADIOGRAPHIC GRADES

Grade 0, none: no features of osteoarthritis

Grade 1, doubtful: minute osteophyte, doubtful significance

Grade 2, minimal: definite osteophyte, unimpaired joint space

Grade 3, moderate: diminution of joint space

Grade 4, severe: joint space impaired with sclerosis of subchondral bone

## APPENDIX 2

### QUESTIONS ON THE HEALTH ASSESSMENT QUESTIONNAIRE (HAQ) USED FOR THE HAND DISABILITY INDEX

Are you able to?

- Dress yourself, including handling of closures?
- Comb your hair or do your own make-up?
- Turn taps on and off?
- Cut your meat, and lift a full cup or glass to your mouth?
- Open a new milk carton?
- Open car doors?
- Hold a pen or a pencil?
- Open jars which have been opened previously?

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## MATTERS ARISING

### Are autoantibodies against a 25-mer synthetic peptide of M3 muscarinic acetylcholine receptor a new diagnostic marker for Sjögren's syndrome?

We read with great interest the article by Naito and colleagues,<sup>1</sup> who recently proposed the autoantibodies against M3 muscarinic acetylcholine receptor (anti-M3R) as a new diagnostic marker for patients with Sjögren's syndrome (SS).

We have been studying anti-M3R recently<sup>2</sup> and reviewed some theoretical aspects.<sup>3</sup> The results of our work with the same 25-mer synthetic peptide (K-R-T-V-P-P-G-E-C-F-I-Q-F-L-S-E-P-T-I-T-F-G-T-A-I) as used by Naito *et al* showed a similar prevalence of anti-M3 in patients with SS (table 1). Nevertheless, we did not draw the same conclusions and could not agree with the statement that antibodies against the 25-mer synthetic peptide might be a new diagnostic marker for SS.

We believe that the authors should mention a misleading fact in the article by Bacman *et al*,<sup>4</sup> which was discussed by Cavill *et al* and Dawson *et al*<sup>5,6</sup>—namely, the sequence of 25-mer synthetic peptide used by Bacman *et al* was in fact the amino acid sequence from the second extracellular loop of M4 muscarinic acetylcholine receptor. Neither of the two groups were able to detect the activity of anti-M3R with conventional immunological approaches. Furthermore, Gao *et al* constructed a CHO cell line expressing the human M3R gene and found positive anti-M3R antibodies in 9/11 patients with SS and in none of 11 healthy controls.<sup>7</sup>

The enzyme linked immunosorbent assay (ELISA) used by Naito *et al* was somewhat similar to our procedure. In our ELISA, Costar medium binding microtitre plates were coated with the same 25-mer peptide in absolute ethanol (10 mg/l), and incubated at 4°C for at least 3 hours. Serum samples were first diluted 1:100 in 1% bovine serum albumin (BSA)/phosphate buffered saline (PBS) (Naito *et al* 1:50 in 5% BSA/PBS) and incubated for 1 hour at room temperature (Naito *et al* for 2 hours at 37°C). Optical density values of anti-M3R were not normally distributed in any of our tested groups. Therefore, the cut off value was estimated at the 95th centile of 349 controls. Neither sensitivity nor specificity of the ELISA

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for SS was improved by binding the synthetic peptide to BSA by a cross linker (N-( $\gamma$ -maleimidobutyryloxy)succinimide ester; Pierce).

In conclusion, it seems that the 25-mer synthetic peptide used in routine immunological techniques<sup>2,3,6</sup> does not disclose clinically relevant antibodies, suggesting that a short linear peptide does not depict an adequate epitope for the binding of anti-M3R. Data presented by Gao *et al*, applying native M3R protein, seem far more promising, but they should be verified on a larger group of patients and controls.

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## Author's reply

Dr Tanja Kveder *et al* point out two messages about our paper.<sup>1</sup> Firstly, that our previous results<sup>1</sup> are supported by their further experiments using the same 25-mer synthetic peptides. Secondly, they suggest that our statement that antibodies (Abs) to the 25-mer synthetic peptide might be a new diagnostic marker for SS is open to criticism.

We agree with Dr Kveder's comments, in part, because we did not elucidate the function of the anti-25-mer synthetic peptide Abs using M3R transfected cells<sup>2</sup> or HSG cell lines. However, Abs against the second extracellular portion of M3R are detected in a subgroup of patients with SS and the presence of this Ab is significantly associated with anti-SSB Ab.<sup>1</sup> Therefore, we consider that anti-25-mer synthetic peptide Abs might be a new diagnostic marker in a subgroup of patients with SS. Of course, further experiments on the functional analysis using anti-25-mer synthetic peptide Abs and anti-M3R protein Abs would be helpful to clarify the better diagnostic marker in patients with SS.

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## Short course prednisolone for adhesive capsulitis

Adhesive capsulitis is a condition whose pathogenesis remains unclear and for which there is no consensus about the best medical treatment.

Writing recently in the *Annals*, Buchbinder and her colleagues examined 50 participants (24 receiving active treatment, 26 placebo) from community based rheumatology practices.<sup>1</sup> The trial concluded that a "3 week course of 30 mg prednisolone daily is of

**Table 1** Anti-M3R antibodies in patients with Sjögren's syndrome (SS), systemic lupus erythematosus (SLE), and healthy controls (C)

Abs (mOD)	C (n=349)	SS† (n=107)	SLE (n=101)	pSS* (n=75)
Average	117	179	116	159
Standard deviation	122	266	120	220
Median	88	92	89	81
Maximum	1216	1755	872	1162
Minimum	2	7	2	7
95th Centile	285	635	355	572
Number of positive sera	17	16	6	11
Percent of positive sera	4.8	15.0	5.9	14.7

\*pSS, primary SS; †SS, primary + secondary SS.

significant short term benefit in adhesive capsulitis, but benefits are not maintained beyond 6 weeks".

Although the authors were careful with their inclusion criteria, they failed to set a cut off point from the time of onset of pain and stiffness of the shoulder. Their subjects had a mean (SD) duration of symptoms of 25.3 (13.2) weeks. This indicates that some of the participants in this study had had a frozen shoulder for 38.6 weeks or approximately 9 months. The treatment period was limited to 3 weeks, regardless of the duration of symptoms. There were no other interventions.

Other reported studies have also included patients with long established adhesive capsulitis.<sup>2,3</sup> The latter with a mean duration at presentation of 5.5 months before oral corticosteroids were used in a trial.

This study makes an important contribution to the subject, but the authors make the point that future research should evaluate different combinations of treatment and their optimal duration.

Based on my experience, I support this recommendation. I have reported the treatment of 30 patients with idiopathic frozen shoulder (IFS). The mean duration of symptoms before referral was 9 weeks. The treatment was with 1–3 intra-articular injections of betamethasone (Celestone Chronodose) followed by oral prednisone 15–20 mg daily, initially for 2 weeks. A home exercise programme was advised. All 30 patients regained full range of movement of the affected shoulder with freedom from pain and without relapse.<sup>4</sup>

Future trials should incorporate a treatment group that includes a combination of oral and intra-articular corticosteroids. Double blind trials are problematic given the generally poor outcome for untreated IFS.<sup>5</sup> Patients with frozen shoulder with an onset greater than 16 weeks should be excluded from further trials.

IFS is a debilitating condition that is currently perceived as having a poor prognosis. Although it is not life threatening, it has a major impact on quality of life. It is therefore important that rheumatologists establish best practice for the management of this condition and educate other medical practitioners of the value of early, active treatment in achieving good outcomes.

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## Author's reply

I thank Dr Douglas for his interest and observations about our trial. He has

documented his positive anecdotal experience in treating 30 patients with adhesive capsulitis with a combination of intra-articular and oral corticosteroids in a brief letter to the editor.<sup>1</sup> Unfortunately, this has not been published as a full report so no details are provided. It is not clear whether this was an open prospective trial or a retrospective chart review, and, if the latter, whether all patients with adhesive capsulitis were included in the review. Similarly, no numerical data are provided and the time interval between the 1–2 intra-articular steroid injections and the start of oral prednisone was not reported. None the less, his claim that all patients fully recovered, on average 4.5 weeks from initiation of treatment (although no measure of variance is provided) is noteworthy, lends broad support to the conclusions of our trial,<sup>2</sup> and, we agree, may warrant a formal trial.

We disagree that double blind trials pose a problem trial in studying adhesive capsulitis, as this is the best method for minimising bias in assessment of treatment outcome. Placebo controlled trials are appropriate when there are no known effective treatments, and controlled trials are essential for self limiting conditions such as adhesive capsulitis. While we agree that adhesive capsulitis is a painful, disabling condition, most studies have in fact established that it has a good prognosis, with resolution of symptoms in 2–3 years, on average, in the majority of patients.<sup>2</sup>

We also disagree with the suggestion that potential trial participants should be excluded if symptoms have been present for longer than 16 weeks. Although we agree that corticosteroids may be more effective in the earlier phase of adhesive capsulitis, and therefore attempting to limit participation in trials of corticosteroids to those with recent onset of symptoms may appear to have merit, early recruitment has proved universally difficult for trialists in this field.<sup>2</sup> Furthermore, our positive trial, which included participants with an average of 21–25 weeks of symptoms, provides clear evidence that this constraint is not necessary.

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## CORRECTION

doi: 10.1136/ard.2004.023564corr1

**Prevalence and pattern of radiographic hand osteoarthritis and association with pain and disability (the Rotterdam study)** (Dahaghin S, Bierma-Zeinstra S M A, Ginai A Z, Pols H A P, Hazes J M W, Koes B W. *Ann Rheum Dis* 2005;**64**:682–7.)

Figure 3 in this article should have been published in colour but mistakenly appeared

in black and white. The correct figure has now been inserted in the Online version and subscribers to the journal can see the amended article at <http://ard.bmjournals.com/cgi/content/full/64/5/682>

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