



# EULAR evidence-based recommendations for the diagnosis of hand osteoarthritis: report of a task force of ESCISIT

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## ABSTRACT

**Objectives:** To develop evidence-based recommendations for the diagnosis of hand osteoarthritis (OA).

**Methods:** The multidisciplinary guideline development group, representing 15 European countries, generated 10 key propositions regarding diagnosis using a Delphi consensus approach. For each recommendation, research evidence was searched for systematically. Whenever possible, the sensitivity, specificity and likelihood ratio (LR) were calculated; relative risk and odds ratios were estimated for risk factors for hand OA. Quality of evidence was categorised using the European League Against Rheumatism (EULAR) hierarchy, and strength of recommendation was assessed by the EULAR visual analogue scale.

**Results:** Diagnostic topics included clinical manifestations, radiographic features, subgroups, differential diagnosis, laboratory tests, risk factors and comorbidities. The sensitivity, specificity and LR varied between tests depending upon the cut-off level, gold standard and controls. Overall, no single test could be used to define hand OA on its own (LR <10) but a composite of the tests greatly increased the chance of the diagnosis. The probability of a subject having hand OA was 20% when Heberden nodes alone were present, but this increased to 88% when in addition the subject was over 40 years old, had a family history of nodes and had joint space narrowing in any finger joint.

**Conclusion:** Ten key recommendations for diagnosis of hand OA were developed using research evidence and expert consensus. Diagnosis of hand OA should be based on assessment of a composite of features.

Hand osteoarthritis (OA) is highly prevalent.<sup>1,2</sup> It occurs commonly, though not exclusively, in the context of generalised OA,<sup>3-5</sup> and can result in considerable disability.<sup>6,7</sup> Although a number of criteria have been used to define hand OA (HOA),<sup>8-11</sup> diagnosis presents certain difficulties due to the large number of joints involved, the broad spectrum of disease severity and possible subsets (table 1).

After developing evidence-based recommendations for management of knee OA,<sup>12,13</sup> hip OA<sup>14</sup> and HOA,<sup>15</sup> the EULAR OA Task Force agreed that issues relating to diagnosis of HOA merit their own consideration. Therefore the following recommendations were developed using an evidence-based format involving a systematic review of research evidence and expert consensus.<sup>16</sup>

## METHODS

A multidisciplinary guideline development group, comprising 21 OA experts from 15 European countries, was commissioned by the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Each participant contributed independently up to 10 propositions related to key clinical aspects in diagnosis of HOA. Consensus was reached using the Delphi technique.<sup>15,17</sup> A systematic search of the literature published between January 1945 and January 2006 was undertaken; the search for HOA<sup>15</sup> was combined with searches for each diagnostic issue<sup>17</sup> (see extended version of this article online at <http://ard.bmj.com> for full search details). The best available evidence was used to support the recommendations according to the EULAR hierarchy for diagnostic tests (table 2).<sup>17</sup> Statistical pooling was undertaken as appropriate if there was no systematic review.<sup>18</sup>

## Outcome measures

As there is no agreed gold standard for diagnosis of HOA, established methods such as radiographic changes and expert diagnosis were used as the diagnostic reference to determine the validity of a test. Validity was evaluated by sensitivity, specificity and likelihood ratio (LR) (LR = sensitivity/(1-specificity)).<sup>17</sup> LRs above 10 or below 0.1 are considered strong evidence to respectively rule in or rule out a diagnosis in most circumstances.<sup>19</sup> For continuous data, we used receiver operating curve (ROC).<sup>20</sup> ROC = 1 means 100% sensitive and specific. Test reliability was assessed using kappa statistics (dichotomous data) and intra-class correlation analysis (continuous data). Relative risk (RR) and odds ratio (OR) were calculated for risk factors and comorbidities associated with HOA.<sup>15,21</sup> For economic evaluations, the incremental cost-effective ratio (ICER) was presented.<sup>17</sup> Strength of recommendation (SOR) was graded using the EULAR 0–100 mm visual analogue scale (VAS).<sup>14</sup>

## Future research agenda

After the propositions for diagnosis had been searched, reviewed and discussed, each participant proposed independently 10 propositions for future research. Consensus was obtained using the Delphi technique.

**Table 1** Glossary

| Term                        | Definition   |
|-----------------------------|--|
| Heberden and Bouchard nodes | Clinically defined posterolateral firm/hard swellings. Heberden: distal IPJ; Bouchard: proximal IPJ.<br>Nodes can occur with or without radiological and/or clinical abnormalities characteristics of HOA. |
| Nodal OA                    | Heberden and/or Bouchard nodes plus underlying IPJ OA, defined clinically and/or radiologically.   |
| Non-nodal OA                | IPJ OA, defined clinical and/or radiographically, without nodes  |
| Erosive OA                  | Subset of HOA defined radiographically by subchondral erosion, cortical destruction and subsequent reparative change, which may include bony ankylosis.  |
| Generalised OA              | HOA plus OA at other sites.  |
| Thumb base OA               | First CMCJ with or without STJ OA  |
| Gold standard               | The diagnostic reference used for a particular study   |

CMCJ, carpometacarpal joint; HOA, hand OA; IPJ, interphalangeal joint; OA, osteoarthritis; STJ, scapho-trapezoid joint.

**RESULTS**

**General literature**

The literature search yielded 6101 hits. After deleting duplications, 2525 hits remained. Of them, only 108 studies met the inclusion criteria. Whist over half of them (52%) were studies for risk factors or comorbidities, others were studies for clinical features (22%), radiographs (9%), clinical and radiographic features (6%), other imaging (8%) (eg, ultrasound, MRI, scintigraphy) and laboratory markers (3%) (eg, erythrocyte sedimentation rate (ESR) and rheumatoid factor (RF)) (fig 1). Radiographs were the main “gold” standard used in these studies (39%). Other “gold” standards included clinical (21%), clinical and radiographic (23%) and indeterminate (17%). The majority of studies were cross-sectional (63%), followed by case control (23%), cohort (11%) and systematic review (3%).

**EULAR recommendations**

Of 184 propositions suggested for diagnosis, 10 were agreed after 3 anonymous Delphi rounds (table 3).

**Proposition 1**

Risk factors for HOA include female sex, increasing age over 40, menopausal status, family history, obesity, higher bone density, greater forearm muscle strength, joint laxity, prior hand injury and occupation or recreation-related usage.

**Strength of recommendation (95% CI): 69 (54 to 84)**

The gender difference for HOA has been systematically reviewed, examining 2 incidence and 14 prevalence studies. Women have a slightly greater prevalent risk of HOA than men, with relative risks of 1.54 (95% CI 0.83 to 2.86) for incidence and 1.23 (95% CI 1.11 to 1.34) for prevalence respectively.<sup>22</sup> When female gender is used as a diagnostic criterion to differentiate HOA from other types of hand arthritis the LR is not statistically significant (LR = 0.94, 95% CI 0.80 to 1.13).<sup>8</sup>

**Table 2** EULAR evidence hierarchy for diagnosis based on study design<sup>17</sup>

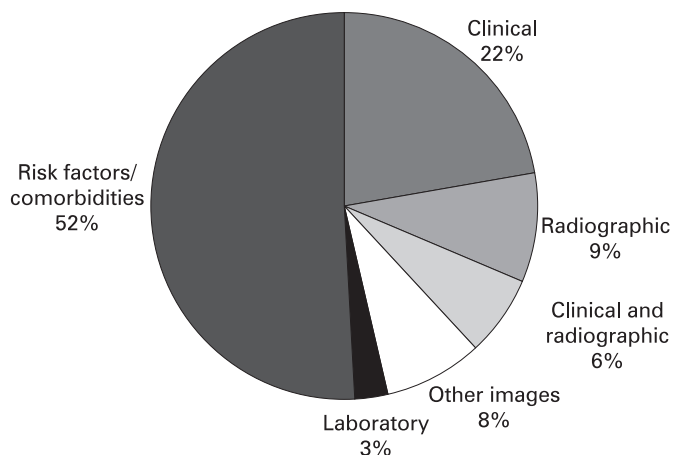
| Hierarchy level | Description                                      |
|-----------------|--|
| Ia              | Meta-analysis of cohort studies                  |
| Ib              | Meta-analysis of case control studies            |
| IIa             | Cohort studies                                   |
| IIb             | Case control/cross sectional comparative studies |
| III             | Non-comparative descriptive studies              |
| IV              | Expert opinion                                   |

It is rare for HOA to develop before the age of 40, but after this age the incidence increases dramatically, especially in women (fig 2).<sup>23</sup> Age has been confirmed in many studies as one of the major risk factors for HOA<sup>23-28</sup> and when a cut-off of 40 years is used it has an LR of 3.73 (95% CI 2.69 to 5.18) (fig 3)<sup>8</sup>

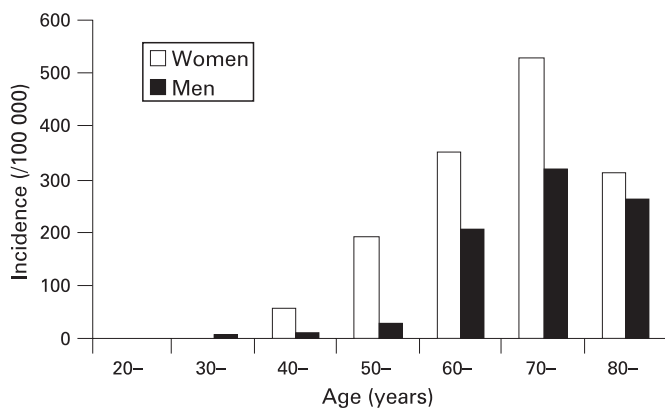
Certain occupations such as cotton picking<sup>29</sup> increase the risk of HOA. This was confirmed by a systematic review of 11 case control and cross-sectional studies. The risk was dose-dependent, mainly targeting distal interphalangeal (DIP) joints and metacarpophalangeal (MCP) joints but showing differential joint distribution within the hand depending on the repetitive tasks involved.<sup>30</sup>

Sex hormones may influence the development of HOA in women. It was signalled by the gender difference dependent on age, ie, women have lower incidence of HOA before the age of 40 but higher incidence after this age than men.<sup>28-31</sup> The reduction in oestrogen due to the menopause is therefore suggested. However, this is not supported by the evidence observed from the hormone replacement therapy (HRT) studies, where the use of HRT was not associated with the reduced risk of HOA.<sup>32-35</sup> As these studies were observational studies, they may be confounded by other factors such as the increased bone density (a potential risk factor for HOA) due to HRT.<sup>36-40</sup> Randomised controlled trials in this regard are still required.

Other well established risk factors for HOA include positive family history,<sup>8 41-44</sup> obesity,<sup>8 26 40 45-49</sup> and joint injury.<sup>40</sup> High forearm extensor muscle strength has also been suggested as a risk factor, presumably by increasing damaging mechanical forces in the hand<sup>50</sup> (table 4).



**Figure 1** Diagnostic tests or elements examined in hand osteoarthritis.



**Figure 2** Incidence of hand osteoarthritis by age and sex 1991–1992.

In summary, major risk factors for HOA include age over 40 years (evidence level IIa), female gender (evidence level Ib), positive family history (evidence level Ib), occupational usage (evidence level Ib), obesity (evidence level IIa) and finger joint injury (evidence level IIb). However, the diagnostic usefulness of these risk factors, singly or in combination, requires further study.

**Proposition 2**

Typical symptoms of HOA are pain on usage and only mild morning or inactivity stiffness affecting just one or a few joints at any one time; symptoms are often intermittent and target characteristic sites (DIPJs, PIPJs, thumb base, index and MCPJs).

With such typical features, a confident clinical diagnosis can be made in adults aged over 40.

**Strength of recommendation (95% CI): 85 (77 to 92)**

Pain on usage has limited value for the diagnosis of HOA. Whilst this feature has excellent reliability (kappa 0.85 to 1.00) and specificity (0.94 to 0.99), the sensitivity is extremely low (0.01 to 0.10) and the LR ranges from 0.50 to 5.50.<sup>11</sup> However, limited duration of localised morning or inactivity stiffness is more specific to HOA than inflammatory arthritis.<sup>51</sup> By contrast, the presence of uncharacterised hand pain (unspecified in terms of location, relationship to usage or rest) is not specific to HOA.<sup>7</sup> Pain in HOA is variable in severity and often varies with time<sup>6</sup>

HOA mainly targets DIP, PIP and thumb base joints.<sup>8 24 25 27 28 52 53</sup> The prevalence of symptomatic HOA is highest with DIP, followed by thumb base, PIP and MCP joints.<sup>27 28 52 54</sup> The distribution of HOA clusters by row and by ray.<sup>52 55</sup> The presence of OA at one finger joint is associated with OA at other finger joints in the same row (OR 6.4, 95% CI 4.3 to 9.4 in men and 5.2, 95% CI 4.5 to 6.0 in women), and the same ray (OR = 5.3, 95% CI 2.9 to 10.0 in men and 3.3, 95% CI 2.6 to 4.2 in women) of the same hand.<sup>52</sup> HOA also shows symmetry between hands,<sup>52 55–57</sup> more so for radiographic joint space narrowing (JSN) than for osteophyte.<sup>57</sup> The presence of OA at a particular finger joint strongly associates with OA in the same joint of the opposite hand (OR = 14.0, 95% CI 7.1 to 27.8 in men and 29.8, 95% CI 19.2 to 46.3 in women).<sup>52</sup>

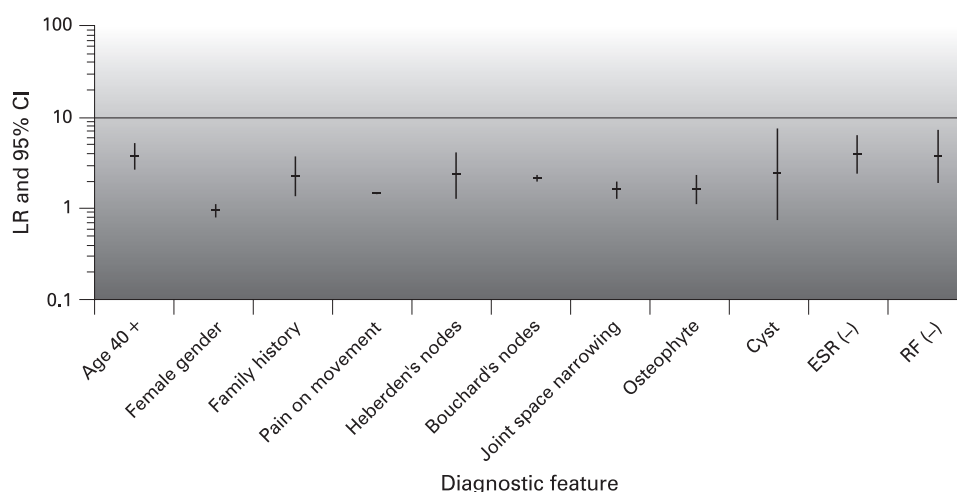
In summary, pain on usage is not a specific clinical marker for HOA (evidence level IIb). However, HOA strongly targets DIP, PIP and thumb base joints and the shorter duration of morning

**Table 3** Propositions and strength of recommendation (SOR) – order according to topic (risk factors, clinical, subsets, differential diagnosis, images and laboratory tests)

| No. | Proposition  | LoE     | SOR (95% CI)  |
|-----|--|---------|---------------|
| 1   | Risk factors for HOA include female sex, increasing age over 40, menopausal status, family history, obesity, higher bone density, greater forearm muscle strength, joint laxity, prior hand injury and occupation or recreation-related usage.   | Ib–IIb  | 69 (54 to 84) |
| 2   | Typical symptoms of HOA are pain on usage and only mild morning or inactivity stiffness affecting just one or a few joints at any one time; symptoms are often intermittent and target characteristic sites (DIPJs, PIPJs, thumb base, index and middle MCPJs). With such typical features, a confident clinical diagnosis can be made in adults aged over 40.   | IIb     | 85 (77 to 92) |
| 3   | Clinical hallmarks of HOA are Heberden and Bouchard nodes and/or bony enlargement with or without deformity (eg, lateral deviation of IPJs, subluxation and adduction of thumb base) affecting characteristic target joints (DIPJs, PIPJs, thumb base and index and middle MCPJs).   | Ib–IV   | 80 (69 to 90) |
| 4   | Functional impairment in hand OA may be as severe as in rheumatoid arthritis. Function should be carefully assessed and monitored using validated outcome measures.  | IIb     | 57 (42 to 73) |
| 5   | Patients with polyarticular HOA are at increased risk of knee OA, hip OA and OA at other common target sites (generalised OA) and should be assessed and examined accordingly.   | IIa–IIb | 77 (62 to 92) |
| 6   | Recognised subsets with different risk factors, associations and outcomes (requiring different assessment and management) include IPJ OA (with or without nodes), thumb base OA and erosive OA. Each may be symptomatic or asymptomatic.   | IIa–IIb | 68 (56 to 79) |
| 7   | Erosive hand OA targets IPJs and shows radiographic subchondral erosion, which may progress to marked bone and cartilage attrition, instability and bony ankylosis. Typically it has an abrupt onset, marked pain and functional impairment, inflammatory symptoms and signs (stiffness, soft tissue swelling, erythaema, paraesthesiae), mildly elevated CRP levels, and a worse outcome than non-erosive IPJ OA. | IIa–IIb | 87 (81 to 93) |
| 8   | The differential diagnosis for HOA is wide. The commonest conditions to consider are psoriatic arthritis (which may target DIPJs or affect just one ray), rheumatoid arthritis (mainly targeting MCPJs, PIPJs, wrists), gout (which may superimpose on pre-existing HOA), and haemochromatosis (mainly targeting MCPJs, wrists).   | Ib–IIb  | 81 (73 to 89) |
| 9   | Plain radiographs provide the gold standard for morphological assessment of HOA. A posteroanterior radiograph of both hands on a single film/field of view is adequate for diagnosis. Classical features are joint space narrowing, osteophyte, subchondral bone sclerosis and subchondral cyst, and subchondral erosion occurs in erosive hand OA. Further imaging modalities are seldom indicated for diagnosis. | Ib–IIb  | 87 (81 to 93) |
| 10  | Blood tests are not required for diagnosis of HOA but may be required to exclude coexistent disease. In a patient with HOA who has marked inflammatory symptoms and/or signs, especially involving atypical sites, blood tests should be undertaken to screen for additional inflammatory arthritides.   | Ib–IIb  | 78 (63 to 92) |

CRP, C-reactive protein; DIPJ, distal IPJ; IPJ, interphalangeal joint; HOA, hand osteoarthritis; LoE, level of evidence (see table 2 for further details), presented in range upon components assessed; MCPJ, metacarpophalangeal joints; PIPJ, proximal IPJ; SOR, strength of recommendation on visual analogue scale (0–100 mm, 0 = not recommended at all, 100 = fully recommended).

**Figure 3** Likelihood ratio (LR) and 95% CI of different diagnostic makers or features (useful ruled in cut-off level LR = 10).



or inactivity stiffness plus clustering pattern and symmetric distribution may be useful to distinguish HOA from other forms of hand arthritis (evidence level IIb).

**Proposition 3**

Clinical hallmarks of HOA are Heberden and Bouchard nodes and/or bony enlargement with or without deformity (eg, lateral deviation of IPJs, subluxation and adduction of thumb base) affecting characteristic target joints (DIPJs, PIPJs, thumb base and index and middle MCPJs).

**Strength of recommendation (95% CI): 80 (69 to 90)**

Heberden nodes (HN) and Bouchard nodes (BN) associate with underlying structural changes of HOA, especially osteophyte (OR = 5.15, 95% CI 4.37 to 6.08).<sup>58-60</sup> However, their sensitivity and specificity for HOA vary widely from 0.3 to 0.9 depending on the cut-off grade, gold standard and control subjects. This in part may reflect the common time lag between development of nodes and appearance of structural x ray change. Subsequently HN or BN have limited value as a single diagnostic marker with an LR ranging from 0.50 to 5.50 and a median of 1.46 (fig 3). However, nodes become more useful when taken in combination with other HOA features (fig 4). For example, the probability of a subject with HOA is 20% when HN alone are considered, but this increases to 88% when the subject is over 40 years old, has a family history of HN and has joint space narrowing in any finger joint.

In brief, HN and BN are important clinical markers for diagnosis of HOA, especially when used in combination with other features of HOA (evidence level Ib). Research evidence for the diagnostic values of other clinically-derived features and their distribution is lacking (evidence level IV).

**Proposition 4**

Functional impairment in hand OA may be as severe as in rheumatoid arthritis. Function should be carefully assessed and monitored using validated outcome measures.

**Strength of recommendation (95% CI): 57 (42 to 73)**

A number of studies have examined the functional impact of HOA.<sup>6, 28, 61-66</sup> Pain<sup>64</sup> and radiographic changes<sup>65</sup> associate with impaired hand function in the setting of HOA. Functional impairment due to HOA may be similar in severity to that resulting from rheumatoid arthritis<sup>67</sup> (evidence level IIb). Indeed, for many patients with HOA functional difficulty is their main presenting complaint. However, in one study the eventual functional outcome of fully established HOA (symptom onset ≥10 years before) was found to be relatively optimistic for nodal OA but not for erosive OA.<sup>66</sup>

A number of validated instruments are available to assess hand function. These include the Health Assessment Questionnaire (HAQ),<sup>68</sup> the Arthritis Hand Function Test (AHFT),<sup>69</sup> the Arthritis Impact Measurement Scale 2 (AIMS2),<sup>70</sup> the Cochin scale,<sup>71</sup> the Score for Assessment and

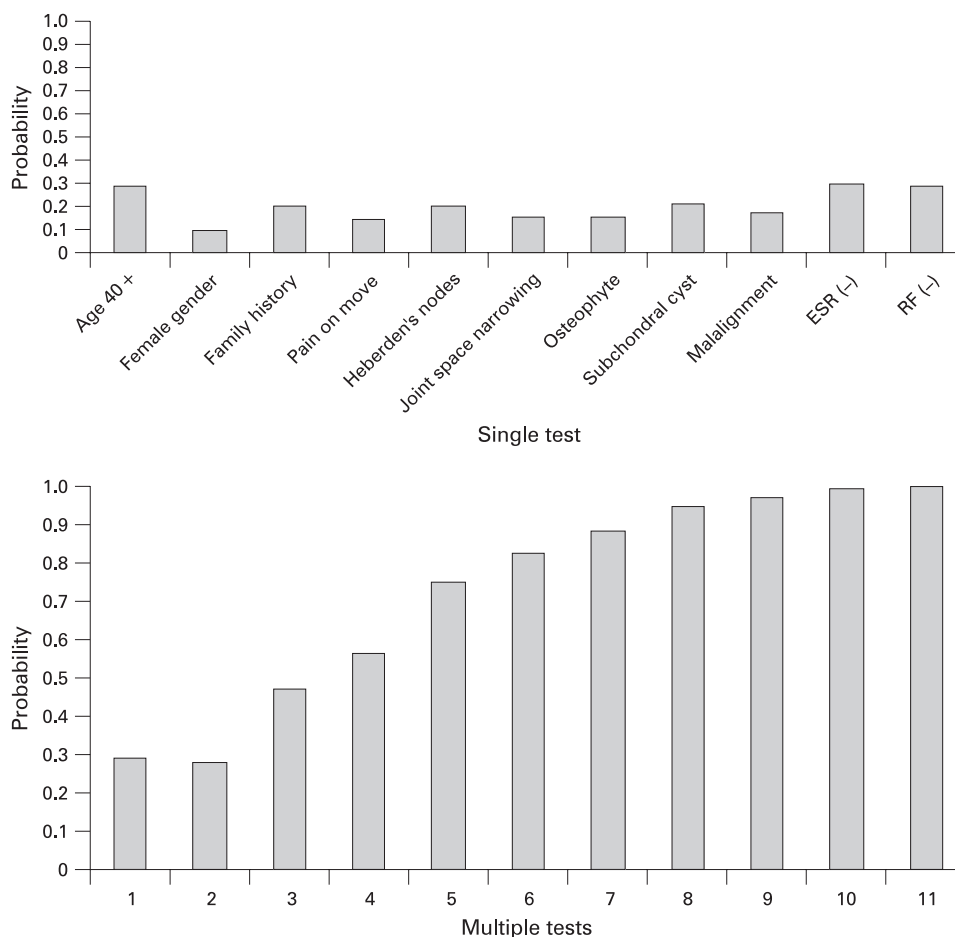
**Table 4** Risk factors and hand osteoarthritis (OA)

| Risk factor                             | LoE* | Sample size          | RR/OR (95% CI)   | Reference   |
|---|------|----------------------|--|---|
| Female gender                           | Ib   | 14 studies           | 1.23 (1.11 to 1.34)                                      | Rovetta <i>et al</i> <sup>22</sup>  |
| Age, >40                                | IIb  | 194                  | 3.68 (2.66 to 5.09)                                      | Altman <i>et al</i> <sup>8</sup>  |
| Family history, 1st degree etc          | Ib   | 3 studies (n = 4183) | 2.57 (1.86 to 3.55)                                      | Altman <i>et al</i> , <sup>8</sup> Marcelli <i>et al</i> , <sup>41</sup> Schneider <i>et al</i> <sup>42</sup> |
| <b>Obesity:</b>                         |      |                      |  |   |
| Relative weight index, per 20% increase | IIa  | 1276                 | 1.69 (1.27 to 2.18)                                      | Spector and MacGregor <sup>46</sup>   |
| BMI, >29 vs ≤24                         | IIb  | 78                   | 8.3 (1.2 to 56.5)  | Carman <i>et al</i> <sup>49</sup>   |
| BMI, kg/m <sup>2</sup>                  | IIb  | 82 pairs             | 1.30 (1.06 to 1.59)                                      | Zhang and Doherty <sup>47</sup>   |
| BMI, kg/m <sup>2</sup>                  | IIb  | 573 women            | 1.03 (0.96 to 1.11)                                      | Hochberg <i>et al</i> <sup>40</sup>   |
| BMD, dg/cm <sup>2</sup>                 | IIb  | 573 women            | 1.11 (0.61 to 2.02) kl ≥ 2<br>1.61 (1.27 to 2.07) kl = 4 | Hochberg <i>et al</i> <sup>40</sup>   |
| Grip strength, third tertile            | IIa  | 756                  | 2.8 (1.2 to 6.7)   | Cicutinni <i>et al</i> <sup>60</sup>  |
| History of hand injury                  | IIb  | 573 women            | 3.64 (1.34 to 9.88)                                      | Hochberg <i>et al</i> <sup>40</sup>   |

\*See table 2 for further description.

BMD, bone mineral density; BMI, body mass index; LoE, level of evidence; OR, odds ratio; RR, relative risk.

**Figure 4** Diagnostic ladder of hand osteoarthritis (OA) (source population prevalence 10%).



quantification of Chronic Rheumatic Affections of the Hands (SACRAH),<sup>67-72</sup> the Functional Index for Osteoarthritis of the Hand (FIHOA)<sup>61</sup> and the Australian/Canadian Osteoarthritis Hand Index (AUSCAN).<sup>73</sup> A systematic review of these instruments has been undertaken.<sup>74</sup> There is no universal instrument and the selection from these options is guided mainly by the clinical question (evidence level Ib).

**Proposition 5**

Patients with polyarticular HOA are at increased risk of knee OA, hip OA and OA at other common target sites (generalised OA) and should be assessed and examined accordingly.

**Strength of recommendation (95% CI): 77 (62 to 92)**

HOA may not only affect multiple joints within the hand, it also can occur as a component of “generalised” OA. Patients with HOA have increased risk of knee OA (OR = 3.0, 95% CI 1.2 to 7.5)<sup>75</sup> and hip OA (OR = 3.25, 95% CI 2.19 to 4.84)<sup>76</sup> (evidence level IIb). A recent population-based cohort study that followed 1235 subjects without hip and knee OA at baseline for over 6 years showed that the risk of developing knee OA or hip OA was two times greater (OR = 2.1, 95% CI 1.3 to 3.1) in those with HOA than in those without HOA at baseline<sup>5</sup> (evidence level IIa).

OA of recognised target joints (DIP, PIP, carpometacarpal (CMC), knee, hip) correlates with each other which often appear in a cluster of three or more involved groups.<sup>25</sup> The strongest associations occur for DIP and PIP, followed by PIP and CMC, CMC and knee, PIP and knee, knee and hip and DIP

and knee (table 5). These data support the concept of “generalised OA” in which some individuals are at increased risk of multiple joint involvement by OA. Classification criteria for generalised versus focal OA have been proposed.<sup>4</sup> There is clear justification to include assessment of other target joints for OA for the purpose of diagnosis and treatment planning of HOA.

**Proposition 6**

Recognised subsets with different risk factors, associations and outcomes (requiring different assessment and management) include IPJ OA (with or without nodes), thumb base OA and erosive OA. Each may be symptomatic or asymptomatic.

**Strength of recommendation (95% CI): 68 (56 to 79)**

A number of studies have identified differences between erosive and non-erosive OA (see proposition 7) (evidence level IIa–IIb).

**Table 5** Association of osteoarthritis between joints<sup>25</sup>

| Index joints | Other joints | OR (95% CI)         |
|--------------|--------------|---------------------|
| DIP          | PIP          | 31.7 (13.8 to 72.5) |
| PIP          | CMC          | 4.8 (2.7 to 8.4)    |
| CMC          | Knee         | 2.4 (1.5 to 4.4)    |
| PIP          | Knee         | 2.4 (1.3 to 4.4)    |
| Knee         | Hip          | 2.1 (1.2 to 3.4)    |
| DIP          | Knee         | 1.8 (1.1 to 3.1)    |

CMC, carpometacarpal; DIP, distal interphalangeal; PIP, proximal interphalangeal; OR, odds ratio.

Although HOA clusters by joints, population-based cross-sectional studies have confirmed that isolated thumb base OA is a common occurrence.<sup>77</sup> Apart from the location, thumb base OA may associate with different risk factors from IPJ OA, although both may share a similar genetic risk.<sup>41</sup> For example, hypermobility has been reported as a risk factor for thumb base OA<sup>78</sup> but a negative risk (“protective”) factor for IPJ OA.<sup>78–79</sup> Studies on functional impairment have not confirmed any clear difference between thumb base OA and IPJ OA<sup>80</sup> (evidence level IIb), however the long-term functional outcome for erosive OA appears worse than for nodal OA.<sup>66</sup> Further research is required to define how clearly such subsets are delineated.

### Proposition 7

Erosive hand OA targets IPJs and shows radiographic subchondral erosion, which may progress to marked bone and cartilage attrition, instability and bony ankylosis. Typically it has an abrupt onset, marked pain and functional impairment, inflammatory symptoms and signs (stiffness, soft tissue swelling, erythema, paraesthesiae), mildly elevated C-reactive protein (CRP) levels and a worse outcome than non-erosive IPJ OA.

#### Strength of recommendation (95% CI): 87 (81 to 93)

An age and gender matched case control study has compared radiographic features of erosive OA (n = 33) and nodal OA (n = 33) using summated scores for individual OA features (JSN, osteophyte, subchondral sclerosis, subchondral cysts) at different joint sites. Erosive OA had significantly higher scores than nodal OA at DIP, PIP and thumb IP joints, but not at MCP and CMC joints, supporting the selective targeting of IP joints by erosive OA.<sup>81</sup> This observation is supported by two cohort studies.<sup>82–83</sup> In two case control studies subchondral erosion, bony collapse and ankylosis of IP joints appeared specific to erosive OA.<sup>81–84</sup> In one case control study comparing hand function in patients with erosive (n = 10), nodal OA (n = 57) and normal subjects (n = 52), hand function was worse in the patients with erosive OA.<sup>66</sup>

One case control study has examined differences in capillaroscopic abnormalities between erosive OA and nodal OA. Although some statistically significant differences were found for frequency of microhaemorrhages, tortuous capillary loops and shortened loops, they did not prove very discriminatory with LR of 2.19 (95% CI 0.62 to 7.78), 1.21 (1.85 to 1.74) and 3.29 (1.34 to 8.07) respectively.<sup>85</sup>

Serum CRP levels have been measured in a case control study examining 67 patients with erosive OA and 31 patients with non-erosive OA. CRP levels were higher in the erosive OA group and the correlations between CRP level, radiographic severity scores and number of joints involved supported CRP as an indicator of disease activity.<sup>86</sup> No differences in serum levels of type II cartilage biomarkers (Col2-3/4C, C2C and CS846 epitope) were demonstrated between 30 patients with erosive OA and 29 patients with non-erosive OA.<sup>87</sup>

Ultrasound has been investigated as a means to differentiate erosive OA, non-erosive OA and normal joints. One case control study (n = 60) including 20 subjects per group found ultrasound to differentiate erosive OA from normal (ROC 0.75; ROC 1 means 100% sensitive and specific) and non-erosive OA from normal (ROC 0.73), but not erosive OA from non-erosive OA (ROC: not reported).<sup>88</sup>

In summary, erosive OA appears to be a specific subgroup of HOA with worse clinical and structural outcomes. It targets mainly the IP joints with structural changes that are often severe (subchondral erosion, ankylosis) and inflammation (elevated CRP) (evidence level IIa–IIb).

### Proposition 8

The differential diagnosis for HOA is wide. The commonest conditions to consider are psoriatic arthritis (which may target DIPJs or affect just one ray), rheumatoid arthritis (mainly targeting MCPJs, PIPJs, wrists), gout (which may superimpose on pre-existing HOA) and haemochromatosis (mainly targeting MCPJs, wrists).

#### Strength of recommendation (95% CI): 81 (73 to 89)

The differential diagnosis between HOA and other arthropathy may be based on clinical manifestations (eg, age, gender, onset and progression of symptoms, degree of stiffness, joints involved (fig 5), presence of HN/BN, examination findings of synovitis and/or damage), radiographic changes (fig 6) and laboratory tests. However, as for diagnosis, a single criterion on its own has limited sensitivity and specificity (figs 3 and 4). For example, although DIP joints are mainly targeted by OA they can also be involved in rheumatoid arthritis (RA),<sup>9</sup> inflammatory symptoms and signs and elevation of CRP may occur with erosive OA and RA, radiographic changes of HOA and calcium pyrophosphate dehydrate deposition disease (CPPD) associated arthritis are extremely similar,<sup>89</sup> and HOA may coexist with CPPD,<sup>90–91</sup> gout or RA.

A composite of multiple features is more useful, such as age, female gender, joint distribution, bone swelling (not soft tissue) and radiographic changes. Laboratory tests, although non-specific, may assist in this, for example strongly positive RF is supportive of RA and elevated urate may support gout. Some individual features do have high specificity (eg non-proliferative marginal erosion for RA, urate crystals for gout).

In brief, differential diagnosis of HOA and other types of hand arthritis depends largely on the use of a composite of features (evidence level Ib). Certain features for individual diseases may be useful for specific cases (evidence level IIb).

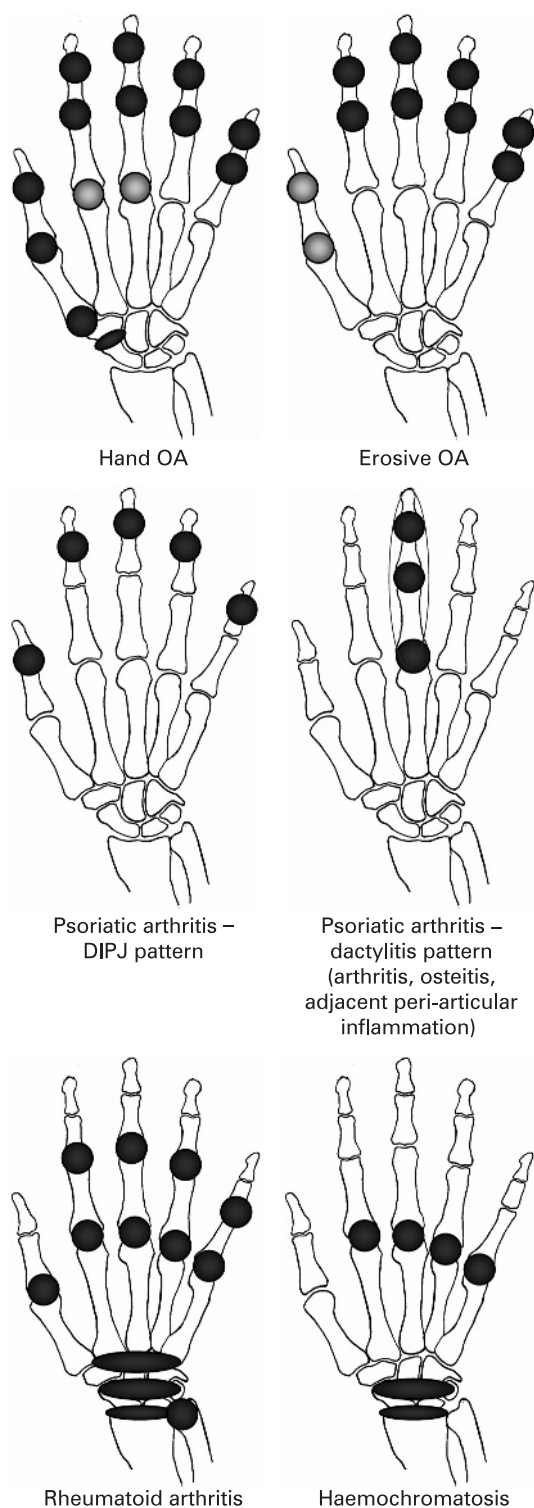
### Proposition 9

Plain radiographs provide the gold standard for morphological assessment of HOA. A posteroanterior radiograph of both hands on a single film/field of view is adequate for diagnosis. Classical features are joint space narrowing, osteophyte, subchondral bone sclerosis and subchondral cyst; subchondral erosion occurs in erosive hand OA. Further imaging modalities are seldom indicated for diagnosis.

#### Strength of recommendation (95% CI): 87 (81 to 93)

Structural changes on plain radiographs have been used by the majority of studies as the “gold standard” for the assessment of a diagnostic test.<sup>92–95</sup> The validity of radiographic change itself has been examined in two case control studies in which the clinical diagnosis was used as the “gold standard”.<sup>8–9</sup> Classical radiographic features such as JSN and osteophyte are sensitive (sensitivity 0.75–1.0) but not specific (specificity 0.18–0.71), resulting in small LR (pooled LR 1.60, 95% CI 1.29 to 1.99 for JSN and 1.61, 95% CI 1.12 to 2.33 for osteophyte) (fig 3). Thus, a single feature (eg, JSN or osteophyte) is less valuable for the diagnosis than a composite of two or more features (fig 4).

The intra-reader reliability (kappa) of radiographic features for HOA ranges from 0.38 to 1.0 (kappa 0.56–1.00 for PIP joints, 0.38–0.87 for DIP joints and 0.58–0.69 for CMC-1 joints) and the inter-reader reliability (kappa) ranges from 0.52–0.92.<sup>96</sup> The latter may be improved by reader’s experience (0.92–1.00).<sup>97–98</sup> Reliability also varies according to the scale used, eg, the Verbruggen and Kellgren and Lawrence scale may have better reproducibility than global and Kallman scales.<sup>98</sup>



**Figure 5** Target sites of involvement with hand osteoarthritis (HOA), erosive OA, psoriatic arthritis, rheumatoid arthritis and haemochromatosis.

Other images such as scintigraphy and MRI have been investigated, especially for the early diagnosis of HOA.<sup>92 94 99</sup> However, their values have yet to be confirmed.

In summary, the plain radiograph is the validated principle imaging technique to examine morphological changes of HOA (evidence level IIb). Diagnosis based on a single radiographic feature (eg, JSN or osteophyte) has limited value, whereas presence of multiple features, especially a composite of clinical

and radiographic changes, dramatically improves diagnostic certainty (evidence level Ib). Other imaging techniques are relatively understudied and their clinical applications have yet to be determined.

**Proposition 10**

Blood tests are not required for diagnosis of HOA but may be required to exclude coexistent disease. In a patient with HOA who has marked inflammatory symptoms and/or signs, especially involving atypical sites, blood tests should be undertaken to screen for additional inflammatory arthritides.

**Strength of recommendation (95% CI): 78 (63 to 92)**

Unlike RA or other forms of inflammatory arthritis, inflammatory markers are not usually elevated in HOA. It is well documented that ESR, RF (evidence level Ib) and CRP (evidence level IIb) are usually normal/negative or only mildly elevated/positive in non-erosive OA (fig 3).<sup>8 9 51 85 86</sup> Therefore more pronounced abnormalities should lead to a search for an alternative explanation. However, as discussed, a single blood test may be unable to differentiate between erosive OA and RA, or confirm the presence of coexisting inflammatory arthropathy. It is necessary to consider other clinical and investigational features that are more characteristic and/or specific for each condition (eg, proliferative or non-proliferative marginal erosions in psoriatic and rheumatoid arthritis respectively, elevated serum uric acid and urate crystal identification on aspiration of a joint or tophus in gout).

**Future research agenda**

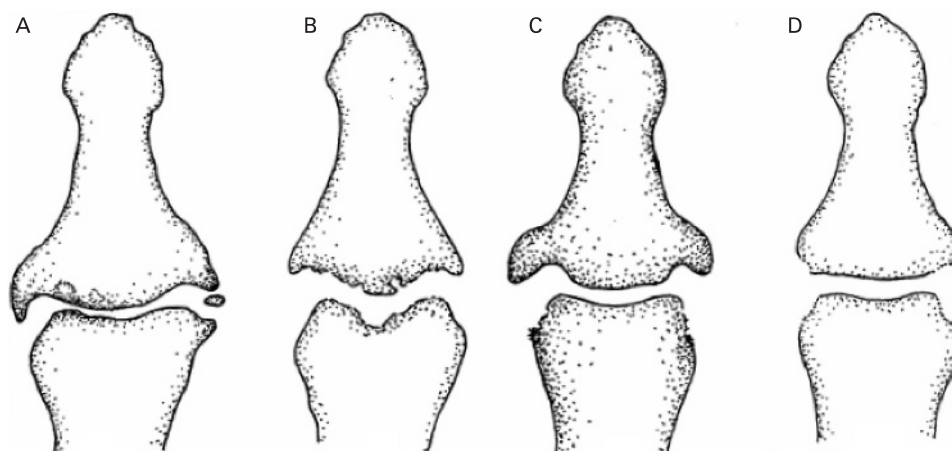
After three Delphi rounds, nine propositions were developed (table 6).

**DISCUSSION**

To our knowledge these are the first evidence-based recommendation for diagnosis of HOA. To date, the main reference cited for diagnosis of HOA has been the American College of Rheumatology (ACR) criteria for classification of HOA.<sup>8</sup> However, the current recommendations differ from the ACR criteria in several important ways. Firstly, the primary purpose of these recommendations is to provide guidance to assist clinicians to diagnose HOA, not to classify HOA for research or clinical trial purposes. The emphasis is on possible subsets and the differential diagnosis to be considered rather than on algorithms for classification of a single entity. Secondly, these are evidence-based recommendations in which research evidence has been summarised systematically from multiple studies undertaken in different countries. Therefore they have more generalisability than recommendations based on a single study population. Thirdly, clinical expertise from many countries across Europe has been incorporated within the recommendations, and importantly, the expertise has been synthesised systematically using a Delphi exercise. Therefore, the recommendations have less parochial and personal bias.<sup>100</sup> Finally, the strength of recommendation and confidence interval has been provided for each proposition, based on research evidence and clinical expertise. This importantly reflects the magnitude of support for each statement and the confidence (variability of opinion) from the Task Force.<sup>100</sup> This information helps clinicians to gauge which statements have good general agreement and which are more open to personal interpretation.

The topics of the 10 generated propositions are wide ranging and include risk factors for HOA, clinical manifestations, subsets, differential diagnosis, imaging and laboratory tests.

**Figure 6** Contrasting radiographic features at interphalangeal joints (IPJs) of (A) osteoarthritis (OA): focal narrowing, marginal osteophyte, sclerosis, osteochondral bodies; (B) erosive OA: subchondral erosion; (C) psoriasis: proliferative marginal erosion, retained or increased bone density; and (D) rheumatoid arthritis: non-proliferative marginal erosion, osteopenia.



The sensitivity and specificity for each recommended marker or test has been examined and the value of each has been presented as a likelihood ratio to allow estimation of the likelihood of HOA given a positive test result. A diagnostic ladder has also been provided to show the probability of diagnosis of HOA when multiple features are considered. Clinicians may estimate the probability of HOA for any composite of the features that a patient may present on the knowledge of the likelihood ratio for each feature (fig 3). The Baye formula or Fagan nomogram may be used to estimate the probability.<sup>17</sup> Overall we found that the diagnosis of HOA cannot be determined with confidence using a single feature and that a composite of several features is required to diagnose HOA.

There are limitations to these recommendations. Firstly, although the evidence-based method is an accepted strategy to increase the power and generalisability of research evidence, it is still open to bias since the pooled studies may carry different confounding factors. Secondly, we only focused on key issues relating to diagnosis of HOA and did not attempt a comprehensive review. Thirdly, generation of the recommendations was driven from a clinical perspective and the relevant research was examined later. Therefore we may have omitted important emerging research information. Such bias, however, should have been minimised by the general literature search and discussion undertaken prior to the Delphi exercise. Finally, the Delphi consensus approach has its own limitations. Although it is systematic it has restricted flexibility and as a result some propositions may overlap or appear repetitive or illogical. Therefore we

discussed the final list of the Delphi results at our last meeting to agree on necessary changes to improve clarity. During this, however, we did not delete or introduce content but did alter some phrasing and ordering of content.

In conclusion, 10 key recommendations for diagnosis of HOA have been generated and the level of research evidence and strength of recommendation have been provided for each. We hope these recommendations will stimulate debate and increase interest in HOA and thereby lead to improved diagnosis and assessment of people with this prevalent condition.

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**Table 6** Future research agenda for diagnosis of hand osteoarthritis (HOA)

| No. | Proposition   |
|-----|---|
| 1   | The relative utility of imaging techniques (plain x rays, MRI, ultrasonography, scintigraphy) in early diagnosis and evaluation of progression of the HOA subsets needs to be determined.   |
| 2   | Risk factors for development and long-term clinical outcome of the different subsets of HOA need to be determined.  |
| 3   | Potential biomarkers of bone, cartilage, synovium and inflammation should be examined in HOA subsets for utility in terms of early diagnosis, assessment of disease activity and prediction of outcome.                               |
| 4   | Diagnostic and classification criteria to better define HOA and its subsets need to be developed and validated.   |
| 5   | Further studies are required to confirm the associations between HOA and systemic risk factors such as menopausal state, bone density, obesity and metabolic syndrome, and to explain the mechanisms that underlie such associations. |
| 6   | The genetic factors that predispose to the different phenotypes of HOA need to be identified.   |
| 7   | The population incidence and prevalence of HOA and its subtypes (symptomatic and asymptomatic), standardised by age and gender, need to be confirmed.   |
| 8   | Studies should be undertaken to determine whether erosive HOA is a discrete subset with specific risk factors and pathogenesis, or a subgroup of HOA with a worse outcome.  |
| 9   | The association between the different HOA phenotypes and large joint OA (ie generalised OA) needs further examination.  |



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REFERENCES

1. **Cushnaghan J**, Dieppe P. Study of 500 patients with limb joint osteoarthritis. 1. Analysis by age, sex, and distribution of symptomatic joint sites. *Ann Rheum Dis* 1991;**50**:8–13.
2. **Mannoni A**, Briganti MP, Di Bari M, Ferrucci L, Costanzo S, Serni U, *et al*. Epidemiological profile of symptomatic osteoarthritis in older adults: a population based study in Dicomano, Italy. *Ann Rheum Dis* 2003;**62**:576–8.
3. **Fickert S**, Puhl W, Gunther KP. Epidemiology of generalised osteoarthritis. *Aktuelle Rheumatologie* 2003;**28**:302–7.
4. **Dougados M**, Nakache JP, Gueguen A. Criteria for generalized and focal osteoarthritis. *Revue du Rhumatisme* 1996;**63**:569–75.
5. **Dahaghin S**, Bierma-Zeinstra SMA, Reijnen M, Pols HAP, Hazes JMW, Koes BW. Does hand osteoarthritis predict future hip or knee osteoarthritis? *Arthritis Rheum* 2005;**52**:3520–7.
6. **Zhang Y**, Niu J, Kelly-Hayes M, Chaisson CE, Aliabadi P, Felson DT. Prevalence of symptomatic hand osteoarthritis and its impact on functional status among the elderly: the Framingham study. *Am J Epidemiol* 2002;**156**:S225.
7. **Dahaghin S**, Bierma-Zeinstra SMA, Reijnen M, Pols HAP, Hazes JMW, Koes BW. Prevalence and determinants of one month hand pain and hand related disability in the elderly (Rotterdam study). *Ann Rheum Dis* 2005;**64**:99–104.
8. **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.
9. **Campion G**, Dieppe P, Watt I. Heberden's nodes in osteoarthritis and rheumatoid arthritis. *BMJ* 1983;**287**:1512.
10. **Hart D**, Spector T, Egger P, Coggon D, Cooper C. Defining osteoarthritis of the hand for epidemiological studies: the Chingford study. *Ann Rheum Dis* 1994;**53**:220–3.
11. **Hart DJ**, Spector TD, Brown P, Wilson P, Doyle DV, Silman AJ. Clinical signs of early osteoarthritis: reproducibility and relation to x ray changes in 541 women in the general population. *Ann Rheum Dis* 1991;**50**:467–70.
12. **Jordan KM**, Arden NK, Doherty M, Bannwarth B, Bijlsma JW, Dieppe P, *et al*. EULAR recommendations 2003: an evidence based approach to the management of knee osteoarthritis: report of a task force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). *Ann Rheum Dis* 2003;**62**:1145–55.
13. **Pendleton A**, Arden N, Dougados M, Doherty M, Bannwarth B, Bijlsma JW, *et al*. EULAR recommendations for the management of knee osteoarthritis: report of a task force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). *Ann Rheum Dis* 2000;**59**:936–44.
14. **Zhang W**, Doherty M, Arden N, Bannwarth B, Bijlsma J, Gunther KP, *et al*. EULAR evidence based recommendations for the management of hip osteoarthritis: report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). *Ann Rheum Dis* 2005;**64**:669–81.
15. **Zhang W**, Doherty M, Leeb BF, Alekseeva L, Arden NK, Bijlsma JW, *et al*. EULAR evidence based recommendations for the management of hand osteoarthritis: report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). *Ann Rheum Dis* 2007;**66**:377–88.
16. **Dougados M**, Betteridge N, Burmester GR, Euller-Ziegler L, Guillemin F, Hirvonen J, *et al*. EULAR standardised operating procedures for the elaboration, evaluation, dissemination, and implementation of recommendations endorsed by the EULAR standing committees. *Ann Rheum Dis* 2004;**63**:1172–6.
17. **Zhang W**, Doherty M, Pascual E, Bardin T, Barskova V, Conaghan P, *et al*. EULAR evidence based recommendations for gout. Part I: Diagnosis. Report of a task force of the standing committee for international clinical studies including therapeutics (ESCISIT). *Ann Rheum Dis* 2006;**65**:1301–11.
18. **Whitehead A**, Whitehead J. A general parametric approach to the meta-analysis of randomized clinical trials. *Statistics Med* 1991;**10**:1665–77.
19. **Deeks JJ**, Altman DG. Diagnostic tests 4: likelihood ratios. *BMJ* 2004;**329**:168–9.
20. **Altman DG**, Bland JM. Statistics notes: diagnostic tests 3: receiver operating characteristic plots. *BMJ* 1994;**309**:188.
21. **Kleinbaum DG**, Kuppler LL, Morgenstern H. *Epidemiologic research – principles and quantitative methods*. Chichester, UK: John Wiley & Sons, Inc, 1982.
22. **Srikanth VK**, Fryer JL, Zhai G, Winzenberg TM, Hosmer D, Jones G. A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. *Osteoarthritis Cartilage* 2005;**13**:769–81.
23. **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.
24. **Butler WJ**, Hawthorne VM, Mikkelsen WM, Carman WJ, Bouthillier DL, Lamphiear DE, *et al*. Prevalence of radiologically defined osteoarthritis in the finger and wrist joints of adult residents of Tecumseh, Michigan, 1962–65. *J Clin Epidemiol* 1988;**41**:467–73.

25. **Cooper C**, Egger P, Coggon D, Hart DJ, Masud T, Cicuttini F, *et al*. Generalized osteoarthritis in women: pattern of joint involvement and approaches to definition for epidemiological studies. *J Rheumatol* 1996;**23**:1938–42.
26. **Haara MM**, Heliovaara M, Kroger H, Arokoski JPA, Manninen P, Karkkainen A, *et al*. Osteoarthritis in the carpometacarpal joint of the thumb: Prevalence and associations with disability and mortality. *J Bone Joint Surg* 2004;**86**:1452–7.
27. **Wilder FV**, Barrett JP, Farina EJ. Joint-specific prevalence of osteoarthritis of the hand. *Osteoarthritis Cartilage* 2006;**14**:953–7.
28. **Dahaghin S**, Bierma-Zeinstra SMA, Ginai AZ, Pols HAP, Hazes JMW, Koes BW. Prevalence and pattern of radiographic hand osteoarthritis and association with pain and disability (the Rotterdam study). *Ann Rheum Dis* 2005;**64**:682–7.
29. **Lawrence JS**. Rheumatism in cotton operatives. *Br J Industry Med* 1961;**18**:270–6.
30. **Jensen V**, Boggild H, Johansen JP. Occupational use of precision grip and forceful gripping, and arthritis of finger joints: a literature review. *Occup Med* 1999;**49**:383–8.
31. **Lawrence JS**, Bremner JM, Bier F. Osteo-arthritis. Prevalence in the population and relationship between symptoms and x ray changes. *Ann Rheum Dis* 1966;**25**:1–24.
32. **Erb A**, Brenner H, Gunther KP, Sturmer T. Hormone replacement therapy and patterns of osteoarthritis: baseline data from the Ulm Osteoarthritis Study. *Ann Rheum Dis* 2000;**59**:105–9.
33. **Spector TD**, Nandra D, Hart DJ, Doyle DV. Is hormone replacement therapy protective for hand and knee osteoarthritis in women?: the Chingford study. *Ann Rheum Dis* 1997;**56**:432–4.
34. **Cooley HM**, Stankovich J, Jones G. The association between hormonal and reproductive factors and hand osteoarthritis. *Maturitas* 2003;**45**:257–65.
35. **Maheu E**, Dreiser R-L, Guillou GB, Dewailly J. Hand osteoarthritis patients characteristics according to the existence of a hormone replacement therapy. *Osteoarthritis Cartilage* 2000;**8**:S33–7.
36. **Haara MM**, Arokoski JPA, Kroger H, Karkkainen A, Manninen P, Knekt P, *et al*. Association of radiological hand osteoarthritis with bone mineral mass: a population study. *Rheumatology* 2005;**44**:1549–54.
37. **Hochberg MC**, Lethbridge-Cejku M, Scott WW Jr, Plato CC, Tobin JD. Appendicular bone mass and osteoarthritis of the hands in women: data from the Baltimore longitudinal study of aging. *J Rheumatol* 1994;**21**:1532–6.
38. **Marcelli C**, Favier F, Kotzki PO, Ferrazzi V, Picot MC, Simon L. The relationship between osteoarthritis of the hands, bone mineral density, and osteoporotic fractures in elderly women. *Osteoporosis Int* 1995;**5**:382–8.
39. **Schneider DL**, Barrett-Connor E, Morton DJ, Weisman M. Bone mineral density and clinical hand osteoarthritis in elderly men and women: the Rancho Bernardo study. *J Rheumatol* 2002;**29**:1467–72.
40. **Sowers M**, Hochberg M, Crabbe JP, Muhich A, Crutchfield M, Updike S. Association of bone mineral density and sex hormone levels with osteoarthritis and the hand and knee in premenopausal women. *Am J Epidemiol* 1996;**143**:38–47.
41. **Jonsson H**, Manolescu I, Stefansson SE, Ingvarsson T, Jonsson HH, Manolescu A, *et al*. The inheritance of hand osteoarthritis in Iceland. *Arthritis Rheum* 2003;**48**:391–5.
42. **Riyazi N**, Meulenbelt I, Kroon HM, Rouday KH, Helliö LG, Rosendaal FR, *et al*. Evidence for familial aggregation of hand, hip, and spine but not knee osteoarthritis in siblings with multiple joint involvement: The GARP study. *Ann Rheum Dis* 2005;**64**:438–43.
43. **Spector TD**, MacGregor AJ. Risk factors for osteoarthritis: genetics. *Osteoarthritis Cartilage* 2004;**12**(Suppl):44.
44. **Zhang W**, Doherty M. How important are genetic factors in osteoarthritis? Contributions from family studies. *J Rheumatol* 2005;**32**:1139–42.
45. **Bagge E**, Bjelle A, Eden S, Svanborg A. Factors associated with radiographic osteoarthritis: results from the population study 70-year-old people in Goteborg. *J Rheumatol* 1991;**18**:1218–22.
46. **Carman WJ**, Sowers M, Hawthorne VM, Weissfeld LA. Obesity as a risk factor for osteoarthritis of the hand and wrist: a prospective study. *Am J Epidemiol* 1994;**139**:119–29.
47. **Cicuttini FM**, Baker JR, Spector TD. The association of obesity with osteoarthritis of the hand and knee in women: a twin study. *J Rheumatol* 1996;**23**:1221–6.
48. **Haara MM**, Manninen P, Kroger H, Arokoski JP, Karkkainen A, Knekt P, *et al*. Osteoarthritis of finger joints in Finns aged 30 or over: prevalence, determinants, and association with mortality. *Ann Rheum Dis* 2003;**62**:151–8.
49. **Oliveria SA**, Felson DT, Cirillo PA, Reed JI, Walker AM. Body weight, body mass index, and incident symptomatic osteoarthritis of the hand, hip, and knee. *Epidemiology* 1999;**10**:161–6.
50. **Chaisson CE**, Zhang Y, Sharma L, Kannel W, Felson DT. Grip strength and the risk of developing radiographic hand osteoarthritis: results from the Framingham study. *Arthritis Rheum* 1999;**42**:33–8.
51. **Huskisson EC**, Dieppe PA, Tucker AK, Cannell LB. Another look at osteoarthritis. *Ann Rheum Dis* 1979;**38**:423–8.
52. **Niu J**, Zhang Y, La Valley M, Chaisson CE, Aliabadi P, Felson DT. Symmetry and clustering of symptomatic hand osteoarthritis in elderly men and women: the Framingham study. *Rheumatology* 2003;**42**:343–8.
53. **Plato CC**, Norris AH. Osteoarthritis of the hand: age-specific joint-digit prevalence rates. *Am J Epidemiol* 1979;**109**:169–80.
54. **Chaisson CE**, Zhang Y, McAlindon TE, Hannan MT, Aliabadi P, Naimark A, *et al*. Radiographic hand osteoarthritis: Incidence, patterns, and influence of pre-existing disease in a population based sample. *J Rheumatol* 1997;**24**:1337–43.
55. **Poole J**, Sayer AA, Hardy R, Wadsworth M, Kuh D, Cooper C. Patterns of interphalangeal hand joint involvement of osteoarthritis among men and women: a British cohort study. *Arthritis Rheum* 2003;**48**:3371–6.

56. **Egger P**, Cooper C, Hart DJ, Doyle DV, Coggon D, Spector TD. Patterns of joint involvement in osteoarthritis of the hand: the Chingford study. *J Rheumatol* 1995;**22**:1509–13.
57. **Neame R**, Zhang W, Deighton C, Doherty M, Doherty S, Lanyon P, et al. Distribution of radiographic osteoarthritis between the right and left hands, hips, and knees. *Arthritis Rheum* 2004;**50**:1487–94.
58. **Caspi D**, Flusser G, Farber I, Ribak J, Leibovitz A, Habet B, et al. Clinical, radiologic, demographic, and occupational aspects of hand osteoarthritis in the elderly. *Semin Arthritis Rheum* 2001;**30**:321–31.
59. **Cicutini FM**, Baker J, Hart DJ, Spector TD. Relation between Heberden's nodes and distal interphalangeal joint osteophytes and their role as markers of generalised disease. *Ann Rheum Dis* 1998;**57**:246–8.
60. **Thaper A**, Zhang W, Wright G, Doherty M. Relationship between Heberden's nodes and underlying radiographic changes of osteoarthritis. *Ann Rheum Dis* 2005;**64**:1214–6.
61. **Dreiser R-L**, Maheu E, Guillou GB, Caspard H, Grouin J-M. Validation of an algofunctional index for osteoarthritis of the hand. *Revue du Rhumatisme* 1995;**62**:43S–53S.
62. **Kjeken I**, Dagfinrud H, Slatkowsky-Christensen B, Mowinckel P, Uhlig T, Kvien TK, et al. Activity limitations and participation restrictions in women with hand osteoarthritis: patients' descriptions and associations between dimensions of functioning. *Ann Rheum Dis* 2005;**64**:1633–8.
63. **Ricci JA**, Stewart WF, Chee E, Leotta C, Foley K, Hochberg MC. Pain exacerbation as a major source of lost productive time in US workers with arthritis. *Arthritis Rheum* 2005;**53**:673–81.
64. **Jones G**, Cooley HM, Bellamy N. A cross-sectional study of the association between Heberden's nodes, radiographic osteoarthritis of the hands, grip strength, disability and pain. *Osteoarthritis Cartilage* 2001;**9**:606–11.
65. **Bagis S**, Sahin G, Yapici Y, Cimen OB, Erdogan C. The effect of hand osteoarthritis on grip and pinch strength and hand function in postmenopausal women. *Clin Rheumatol* 2003;**22**:420–4.
66. **Patrick 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.
67. **Leeb BF**, Sautner J, Andel I, Rintelen B. SACRAH: a score for assessment and quantification of chronic rheumatic affections of the hands. *Rheumatology* 2003;**42**:1173–8.
68. **Ziebland S**, Fitzpatrick R, Jenkinson C, Mowat A, Mowat A. Comparison of two approaches to measuring change in health status in rheumatoid arthritis: the Health Assessment Questionnaire (HAQ) and modified HAQ. *Ann Rheum Dis* 1992;**51**:1202–5.
69. **Backman C**, Mackie H. Arthritis hand function test: inter-rater reliability among self-trained raters. *Arthritis Care Res* 1995;**8**:10–5.
70. **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.
71. **Duruoz MT**, Poiraudou S, Fermanian J, Menkes CJ, Amor B, Dougados M, et al. Development and validation of a rheumatoid hand functional disability scale that assesses functional handicap. *J Rheumatol* 1996;**23**:1167–72.
72. **Sautner J**, Andel I, Rintelen B, Leeb BF. Development of the M-SACRAH, a modified, shortened version of SACRAH (Score for the Assessment and Quantification of Chronic Rheumatoid Affections of the Hands). *Rheumatology* 2004;**43**:1409–13.
73. **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.
74. **Dziedzic KS**, Thomas E, Hay EM. A systematic search and critical review of measures of disability for use in a population survey of hand osteoarthritis (OA). *Osteoarthritis Cartilage* 2005;**13**:1–12.
75. **Englund M**, Paradowski PT, Lohmander LS. Association of radiographic hand osteoarthritis with radiographic knee osteoarthritis after meniscectomy. *Arthritis Rheum* 2004;**50**:469–75.
76. **Hochberg MC**, Lane NE, Pressman AR, Genant HK, Scott JC, Nevitt M. The association of radiographic changes of osteoarthritis of the hand and hip in elderly women. *J Rheumatol* 1995;**22**:2291–4.
77. **Mannoni A**, Briganti MP, Di Bari M, Ferrucci L, Serni U, Masotti G, et al. Prevalence of symptomatic hand osteoarthritis in community-dwelling older persons: The ICARE Dicomano study. *Osteoarthritis Cartilage* 2000;**8**:S11–S13.
78. **Jonsson H**, Valtysdottir ST, Kjartansson O, Brekkan A. Hypermobility associated with osteoarthritis of the thumb base: A clinical and radiological subset of hand osteoarthritis. *Ann Rheum Dis* 1996;**55**:540–3.
79. **Kraus VB**, Li YJ, Martin ER, Jordan JM, Renner JB, Doherty M, et al. Articular hypermobility is a protective factor for hand osteoarthritis. *Arthritis Rheumatism* 2004;**50**:2178–83.
80. **Spacek E**, Poiraudou S, Fayad F, Lefevre-Colau MM, Beaudreuil J, Rannou F, et al. Disability induced by hand osteoarthritis: are patients with more symptoms at digits 2–5 interphalangeal joints different from those with more symptoms at the base of the thumb? *Osteoarthritis Cartilage* 2004;**12**:366–73.
81. **Smith D**, Braunstein EM, Brandt KD, Katz BP. A radiographic comparison of erosive osteoarthritis and idiopathic nodal osteoarthritis. *J Rheumatol* 1992;**19**:896–904.
82. **Verbruggen G**, Goemaere S, Veys EM. Systems to assess the progression of finger joint osteoarthritis and the effects of disease modifying osteoarthritis drugs. *Clin Rheumatol* 2002;**21**:231–43.
83. **Verbruggen G**, Veys EM. Erosive and non-erosive hand osteoarthritis. Use and limitations of two scoring systems. *Osteoarthritis Cartilage* 2000;**8**:S45–S54.
84. **Cobby M**, Cushnaghan J, Creamer P, Dieppe P, Watt I. Erosive osteoarthritis: is it a separate disease entity? *Clin Radiol* 1990;**42**:258–63.
85. **Fioravanti A**, Tofi C, Cerase A, Priolo F, Marcolongo R. Capillaroscopic findings in erosive and nodal osteoarthritis of the hands. *Clin Rheumatol* 2001;**20**:174–6.
86. **Punzi L**, Ramonda R, Oliviero F, Sfriso P, Mussap M, Plebani M, et al. Value of C reactive protein in the assessment of erosive osteoarthritis of the hand. *Ann Rheum Dis* 2005;**64**:955–7.
87. **Silvestri T**, Pulsatelli L, Dolzani P, Punzi L, Meliconi R. Analysis of cartilage biomarkers in erosive and non-erosive osteoarthritis of the hands. *Osteoarthritis Cartilage* 2004;**12**:843–5.
88. **Rovetta G**, Battista S, Brignone A, Monteforte P. Quantitative ultrasound of the proximal phalanges: reproducibility in erosive and nodal osteoarthritis of the hands. *Int J Tissue React* 1999;**21**:121–7.
89. **Riestra JL**, Sanchez A, Rodrigues-Valverde V. Roentgenographic features of the arthropathy associated with CPPD crystal deposition disease. A comparative study with primary osteoarthritis. *J Rheumatol* 1985;**12**:1154–8.
90. **Fam AG**, Stein J, Rubenstein J. Gouty arthritis in nodal osteoarthritis. *J Rheumatol* 1996;**23**:684–9.
91. **Gerster JC**, Rappoport G, Ginalski JM. Prevalence of periarticular calcifications in pyrophosphate arthropathy and their relation to nodal osteoarthritis. *Ann Rheum Dis* 1984;**43**:255–7.
92. **Erturk H**, Bal S, Aydin M, Ugur O, Celiker R. The predictive value of bone scintigraphy in osteoarthritis relationship with age and severity of the disease. *J Rheumatol Med Rehab* 2002;**13**:25–9.
93. **Falsetti P**, Frediani B, Fioravanti A, Acciai C, Baldi F, Filippou G, et al. Sonographic study of calcaneal entheses in erosive osteoarthritis, nodal osteoarthritis, rheumatoid arthritis and psoriatic arthritis. *Scand J Rheumatol* 2003;**32**:229–34.
94. **Tan AL**, Grainger AJ, Tanner SF, Shelley DM, Pease C, Emery P, et al. High-resolution magnetic resonance imaging for the assessment of hand osteoarthritis. *Arthritis Rheum* 2005;**52**:2355–65.
95. **Tan AL**, Grainger AJ, Tanner SF, Emery P, McGonagle D. A high-resolution magnetic resonance imaging study of distal interphalangeal joint arthropathy in psoriatic arthritis and osteoarthritis: are they the same? *Arthritis Rheum* 2006;**54**:1328–33.
96. **Kessler S**, Dieppe P, Fuchs J, Sturmer T, Gunther KP. Assessing the prevalence of hand osteoarthritis in epidemiological studies. The reliability of a radiological hand scale. *Ann Rheum Dis* 2000;**59**:289–92.
97. **Bellamy N**, Klestov A, Muirden K, Kuhnert P, Do KA, O'Gorman L, et al. Perceptual variation in categorizing individuals according to American College of Rheumatology classification criteria for hand, knee, and hip osteoarthritis (OA): observations based on an Australian twin registry study of OA. *J Rheumatol* 1999;**26**:2654–8.
98. **Maheu E**, Cadet C, Gueneugues S, Ravaud P, Dougados M. Reproducibility and sensitivity to change of four scoring methods for the radiological assessment of osteoarthritis of the hand. *Ann Rheum Dis* 2007;**66**:464–9.
99. **McCarthy C**, Cushnaghan J, Dieppe P. The predictive role of scintigraphy in radiographic osteoarthritis of the hand. *Osteoarthritis Cartilage* 1994;**2**:25–8.
100. **Zhang W**, Doherty M. EULAR recommendations for knee and hip osteoarthritis: a critique of the methodology. *Br J Sports Med* 2006;**40**:664–9.

**EULAR EVIDENCE BASED RECOMMENDATIONS FOR THE DIAGNOSIS OF  
HAND OSTEOARTHRITIS - REPORT OF A TASK FORCE OF THE EULAR  
STANDING COMMITTEE FOR INTERNATIONAL CLINICAL STUDIES  
INCLUDING THERAPEUTICS (ESCISIT)**

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## **ABSTRACT**

**Objectives:** To develop evidence based recommendations for the diagnosis of hand osteoarthritis (OA).

**Methods:** The multidisciplinary guideline development group comprised 16 rheumatologists, one physiatrist, one orthopaedic surgeon, one allied health professional, one radiologist and one evidence based medicine expert representing 15 different European countries. Ten key propositions regarding diagnosis were generated using a Delphi consensus approach. Research evidence was searched systematically for each recommendation. Whenever possible, the sensitivity, specificity and likelihood ratio (LR) were calculated. Relative risk and odds ratios were estimated for risk factors associated with hand OA. The quality of evidence was categorised according to the EULAR evidence hierarchy for diagnosis. The strength of recommendation was assessed using the EULAR visual analogue scale.

**Results:** Diagnostic topics included clinical manifestations (pain on usage, short duration of morning stiffness, target joints and pattern of distribution, Heberden's and Bouchard's nodes etc), radiographic features (joint space narrowing, osteophytes, subchondral sclerosis and cysts etc), subgroups (interphalangeal joint with/without nodes, thumb-base, erosive OA), differential diagnosis (RA, psoriatic arthritis, gout and haemochromatosis), laboratory tests (ESR, CRP and RF) and risk factors and co-morbidities (age, gender, BMI, other joint infections etc). The sensitivity, specificity and LR varied from test to test depending upon the cut-off level, gold standard and control subjects. Overall, there was no single

test which could be used to define hand OA on its own (LR <10). However, a composite of the tests greatly increased the chance of the diagnosis. The probability of a subject with hand OA was only 20% when Heberden's nodes alone were present, however the probability increased up to 88% when in addition the subject was over 40 years old, had a family history of the nodes and also had joint space narrowing on any finger joint. The strength of recommendation varied according to available research evidence and expert consensus.

**Conclusion:** Ten key recommendations for the diagnosis of hand OA were developed using a combination of research-based evidence and expert consensus. Clinical diagnosis of hand OA should be based on the assessment of a composite of the features.

## INTRODUCTION

Hand osteoarthritis (OA) is a highly prevalent condition<sup>1;2</sup>. It occurs commonly, though not exclusively, in the context of generalised OA<sup>3-5</sup>, and can result in considerable disability<sup>6;7</sup>. Although a number of criteria have been used to define hand OA (HOA) clinically, radiographically or epidemiologically<sup>8-11</sup>, diagnosis and classification of HOA presents certain difficulties due to a number of issues. For example, the large number of joints that may be affected, presenting a large array of potential patterns of involvement; the nature of Heberden's and Bouchard's nodes and their relationship to underlying interphalangeal joint (IPJ) OA; the poor correlation at one joint between symptoms and structural changes of OA; apparent differentiation between thumb-base and IPJ OA in terms of risk factors and outcome; and lack of agreement concerning the nature and specificity of "erosive OA" as a discrete subset of HOA.

The EULAR OA Task Force has developed evidence-based recommendations for management of knee OA<sup>12;13</sup>, hip OA<sup>14</sup> and more recently HOA<sup>15</sup>. At their last meeting in Zurich in March 2006 the Task Force agreed that issues relating to the diagnosis of HOA merit their own, separate consideration from those of management. Development of recommendations for the diagnosis of HOA should prove very useful, as have recent recommendations for the diagnosis of gout<sup>16</sup>. As before, it was agreed that recommendations should be developed using an evidence based format that involves both a systematic review of research evidence and expert consensus<sup>17</sup>.

## **METHODS**

### **Participants**

A multidisciplinary guideline development group was commissioned by the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Twenty-one experts in the field of OA consisting of rheumatologists (16), physiatrist (1), orthopaedic surgeon (1), allied health professional (1), radiologist (1) and evidence-based medicine expert (1) representing 15 European countries agreed to take part in the study. The objectives were [1] to agree key propositions related to the diagnosis of HOA; [2] to identify and critically appraise research evidence for the diagnostic tests, risk factors and co-morbidities associated with HOA; and [3] to generate recommendations based on a combination of the best available evidence and expert opinion.

### **Experts' consensus**

Each participant was asked to contribute independently up to 10 propositions related to key clinical aspects in the diagnosis of HOA. Consensus regarding the propositions was reached using the Delphi technique. The initial propositions were collated into a single list by a co-chair (MD) who was not involved in the generation of propositions. Where necessary, the propositions were edited for English grammar and phrasing and similar, substantially overlapping propositions were combined. The edited list was then returned to the experts and they were asked to select the 10 most important from the list. Propositions were accepted if over 50% of the participants accepted them in any round, whereas propositions

receiving less than 15% votes were removed. Propositions receiving 15% to 50% votes entered the next Delphi round. The Delphi exercise was terminated when no further propositions had between 15% and 50% of votes. There was no limit to the number of final propositions selected.

### **Systematic literature search**

A systematic search of the literature published between January 1945 and January 2006 was undertaken using MEDLINE (1966- ), EMBASE (1980- ), CINAHL (1980- ), AMED (1985- ) Science Citation Index through Web of Science (WOS) (1945- ) and Cochrane Library databases (1996- ). The search included both a general search and a proposition-specific search. The general search strategy consisted of three basic components: [1] HOA in whatever possible terms in the databases (Appendix 1); [2] types of research in the forms of systematic review/meta-analysis, cohort study, case-control study, cross-sectional study, economic evaluation (Appendix 2); and [3] diagnostic test/accuracy (Appendix 3). The first component search was combined with the second and third separately to retrieve potential studies in the literature for the diagnosis of hand OA. Summary results of the search were reported to the committee prior to the Delphi exercise.

After the Delphi exercise, the proposition-specific search was undertaken to identify evidence for each specific proposition. The search strategy included the terms for HOA and any possible terms for the specific component of each proposition. For example, “Heberden’s nodes” and “Bouchard’s nodes” were searched specifically for the proposition regarding these two clinical markers.



The results of the general search and the proposition-specific search were then combined and duplications removed. Medical subject heading search (MeSH), together with key word search was used whenever possible. All MeSH search terms were exploded. The reference lists within review or systematic reviews were examined and any additional studies meeting the inclusion criteria were included.

The search in the Cochrane Library included MeSH search of the Cochrane review, Abstracts of Quality Assessed Systematic Reviews, The Cochrane Controlled Trial Register, NHS Economic Evaluation Databases, Health Technology Assessment Database and NHS Economic Evaluation Bibliography Details Only.

### **Inclusion/exclusion criteria**

Only studies concerning diagnosis of HOA were included. Studies for OA at several sites were included if data were presented separately for HOA. The main focus of interest was on tests (markers and features) for the purpose of HOA diagnosis. Studies in any form of design were included. Case reports, editorial or reviews were excluded, as were studies on healthy subjects or animals.

### **Level of evidence**

Evidence was categorised according to the EULAR evidence hierarchy for diagnostic tests<sup>16</sup> (Table 2). Questions were answered using the best available evidence. For example, if a question could be answered by level Ia evidence (e.g., systematic review of cohort studies) then studies with a weaker design (e.g., cohort study - level IIa) were not reviewed. Results of the latest systematic

review were used if there was more than one systematic review for the same question. Results of different studies from same level of evidence were presented and statistical pooling was undertaken as appropriate<sup>18</sup>.

## **Outcome measures**

### **1. Gold standard**

Gold standard is the diagnostic reference used to determine the validity (sensitivity and specificity) of a specific diagnostic test in a particular study. As there is no agreed gold standard for the diagnosis of HOA, established methods such as radiographic changes and expert diagnosis were used as a “diagnostic reference” or “gold standard” for HOA.

### **2. Validity**

Diagnostic tests were assessed for validity and reliability. Validity was evaluated by sensitivity and specificity. Sensitivity is the proportion of true positives that are correctly identified by the test, whereas specificity is the proportion of true negatives that are correctly identified by the test<sup>19</sup>. The ideal test would have a value of 1 for both sensitivity and specificity, i.e., 100% sensitive and specific. However, in real life this is rarely possible and as sensitivity increases specificity often decreases. For example, increasing the diagnostic cut-off of joint space narrowing (JSN) grade would reduce the sensitivity but increase the specificity of the test in the detection of HOA. We therefore calculated the likelihood ratio (LR) ( $LR = \text{sensitivity} / (1 - \text{specificity})$ ) to produce an overall trade-off index for both variables<sup>20</sup>. LR summarises how many times more (or less) likely patients with HOA are to be test positive than patients without the disease. A LR greater than

1 indicates that the test result is associated with the presence of HOA, whereas a LR less than 1 indicates that the test result is associated with absence of HOA. LRs above 10 or below 0.1 are considered to be strong evidence to respectively rule in or rule out a diagnosis in most circumstances<sup>20</sup>. In addition, LR allows users to predict the probability of having HOA for a patient, based on the risk of the source population. For continuous data, we used receiver operating curve (ROC) – the analysis for the area under the curve (AUC) between sensitivity (y axis) and 1-specificity (x axis) to determine the overall performance of a particular diagnostic test, given different cut-off indices to the test<sup>21</sup>. ROC =1 means 100% sensitive and specific. For example, ultrasound velocity (m/sec) was compared between HOA and normal control. Different cut-offs of this measure were given. Sensitivity and specificity were calculated for each cut-off point and a curve was drawn upon the derived sensitivities and specificities of all points. This brought about an ROC of 0.73 (ie. 73% of the maximum AUC), suggesting a good overall performance of this technique in the differentiation between HOA and normal joints<sup>22</sup>.

## **2. Reliability**

The reliability of a test was assessed using the kappa statistics (dichotomous data) and intra-class correlation analysis (continuous data) if repeat measures were available.

## **3. Relative risk and odds ratio**

For risk factors and co-morbidities associated with the diagnosis of HOA, the relative risk (RR) and odds ratio (OR) were calculated. The RR was estimated

from cohort studies (for incident risk) or cross sectional studies (for prevalent risk), whereas the OR was calculated from case control studies<sup>23</sup>. Both present how many times more likely (or less likely) subjects who are exposed to the risk factor are to have HOA than those who are not exposed to the same risk factor. RR/OR = 1 indicates no relationship, whereas RR/OR >1 or <1 indicates positive or negative relationships between the risk factor and the disease.

#### **4. Incremental cost-effectiveness ratio (ICER)**

For economic evaluations, the ICER was calculated for the different costs between two diagnostic tests, divided by the different diagnostic values (sensitivity, specificity, or LR) between the two tests. In addition, the study design, comparator, perspective, time horizon, discounting, total costs and effectiveness were critically appraised.

#### **Strength of recommendation**

Following the literature search on each proposition and the initial drafting of the manuscript the Task Force met to discuss each proposition. At this stage, the wording (but not the content) of propositions could be adjusted to better clarify specific statements and to reduce any ambiguity if the majority of the Task Force agreed. The propositions were then ratified and a final adjusted manuscript was approved by all Task Force members.

The strength of recommendation (SOR) was graded using the EULAR visual analogue scale (VAS)<sup>14</sup>. Each participant was asked to score their SOR for each proposition using a 0-100 mm VAS. Participants were asked to determine their scores by taking into account both the research evidence

(sensitivity, specificity, LR and cost-effectiveness, if available) and their clinical expertise (i.e. their clinical experience and opinion regarding logistics of the diagnosis). The mean VAS and 95% CI were calculated.

### **Future research agenda**

After the initial 10 propositions for diagnosis had been searched, reviewed and discussed by the Task Force each participant was asked to propose 10 topics for the future research agenda based on current available evidence and clinical experience in the diagnosis of HOA. Similar, substantially overlapping propositions were combined and then a Delphi approach was used to reach a consensus on the 10 most important topics. The same criteria as those used to select diagnostic propositions were employed (i.e., accepted: more than 50% votes; removed: less than 15% votes; next round: 15% - 50% votes).

## **RESULTS**

### **General literature search**

The literature search yielded 6101 hits, including MEDLINE 2451, EMBASE 1860, CINAHL 243, AMED 55, WOS 757, and Cochrane 735. After deleting duplications, 2,525 hits remained. Of them, only 108 studies met the inclusion criteria. Whist over half of them (52%) were studies for risk factors or co-morbidities, others were studies for clinical features (22%), radiographs (9%), clinical & radiographic features (6%), other imaging (8%) (eg, ultrasound, MRI, scintigraphy) and laboratory markers (3%) (eg, ESR and RF) (Figure 1). Radiographs were the main “gold” standard used in these studies (39%). Other

“gold” standards included clinical (21%), clinical and radiographic (23%) and indeterminate (17%) (Figure 2). The majority of studies were cross-sectional (68/108), followed by case control (25/108), cohort (12/108) and systematic review (3/108) (Figure 3).

### **Expert’s opinion approach**

The experts were informed of the results of the general literature search and then the Delphi exercise was undertaken by email. The first round produced 184 propositions for diagnosis. After 3 anonymous Delphi rounds, 10 final propositions were agreed (Table 3).

### **Assessment of propositions**

The proposition-specific search was then undertaken and the results were merged with the results from the general search to form the basis of evidence for the evaluation of each proposition or tests within each proposition. The following propositions are grouped by topic (risk factors, clinical manifestation, subsets, differential diagnosis, imaging and laboratory investigation) with no weighting according to order.

**1. *Risk factors for HOA include female sex, increasing age over 40, menopausal status, family history, obesity, higher bone density, greater forearm muscle strength, joint laxity, prior hand injury and occupation or recreation-related usage.***

***Strength of recommendation (95%CI): 69 (54, 84)***

The gender difference for HOA has been systematically reviewed, examining 2 incidence and 14 prevalence studies. Women have a slightly greater prevalent

risk of HOA than men, with relative risks of 1.54 (95%CI 0.83, 2.86) for incidence and 1.23 (95%CI 1.11, 1.34) for prevalence respectively<sup>24</sup>. When female gender is used as a diagnostic criterion to differentiate HOA from other types of hand arthritis the LR is not statistically significant (LR=0.94, 95%CI 0.80, 1.13)<sup>8</sup>.

It is rare for HOA to develop before the age of 40, but after this age the incidence increases dramatically, especially in women (Figure 6)<sup>25</sup>. Age has been confirmed in many studies as one of the major risk factors for HOA<sup>25-30</sup> and when a cut-off of 40 years is used as one of the diagnostic features for HOA it has an LR of 3.73 (95%CI 2.69, 5.18) (Figure 4)<sup>8</sup>

Certain occupations such as cotton picking<sup>31</sup> increase the risk of HOA. A systematic review of 11 case control and cross-sectional studies has confirmed the importance of occupational hand usage. The risk of HOA was higher with occupations requiring repetitive precision grip and forceful gripping, such as cotton pickers, cooks, dentists, spinners and dockers. The risk was dose-dependent, mainly targeting DIP and MCP joints but showing differential joint distribution within the hand depending on the repetitive tasks involved<sup>32</sup>.

Sex hormones may influence the development of HOA in women. Before the age of 40 the prevalence and incidence of HOA are lower in women than men, but after this age both become higher in women<sup>25;33</sup>. Because of the high incidence of Heberden's nodes (a marker for risk of generalised OA) after this age, the term "menopausal arthritis" is sometimes used<sup>34</sup>. The reduction in estrogen due to the menopause may be associated with HOA. However, this is not supported by the evidence observed from the hormone replacement therapy

(HRT) studies, where the use of HRT was not associated with the reduced risk of HOA<sup>35-38</sup>. As these studies were observational studies, they may be confounded by the increased bone density (a potential risk factor for HOA) due to HRT<sup>39-43</sup>. Therefore further well controlled prospective studies are required to establish whether oestrogen directly influences the risk of HOA.

Other well established risk factors for HOA include positive family history<sup>8;44-47</sup>, obesity<sup>8;28;43;48-52</sup>, and joint injury<sup>43</sup>. High forearm extensor muscle strength has also been suggested as a risk factor, presumably by increasing damaging mechanical forces in the hand<sup>53</sup> (Table 6).

In summary, major risk factors for HOA include age over 40 years (evidence IIa), female gender (Ib), positive family history (Ib), occupational usage (Ib), obesity (IIa) and finger joint injury (IIb). However, the diagnostic usefulness of these risk factors, singly or in combination, requires further study.

**2. *Typical symptoms of HOA are pain on usage and only mild morning or inactivity stiffness affecting just one or a few joints at any one time; symptoms are often intermittent and target characteristic sites (DIPJs, PIPJs, thumb-base, index and middle MCPJs). With such typical features, a confident clinical diagnosis can be made in adults aged over 40.***

***Strength of recommendation (95%CI): 85 (77, 92)***

Pain on usage has limited value for the diagnosis of HOA. Whilst this feature has excellent reliability (kappa 0.85 to 1.00) and specificity (0.94 to 0.99), the sensitivity is extremely low (0.01 to 0.10) and the LR ranges from 0.50 to 5.50 (Table 4)<sup>11</sup>. However, limited duration of localised morning or inactivity stiffness



is more specific to HOA than inflammatory arthritis (eg, on average, 22 minutes for hand OA versus 58 minutes for RA) <sup>54</sup>. By contrast, the presence of uncharacterised hand pain (unspecified in terms of location, relationship to usage or rest) is not specific to HOA <sup>7</sup>. Pain in HOA is variable in severity and often varies with time <sup>6</sup>.

HOA mainly targets DIP, PIP and thumb base joints <sup>8;26;27;29;30;55;56</sup>. The prevalence of symptomatic HOA (symptoms plus radiographic Kellgren and Lawrence grade  $\geq 2$ ) is highest with DIP, followed by thumb base, PIP and MCP joints <sup>29;30;55;57</sup>. The distribution of HOA clusters by row and by ray <sup>55;58</sup>. The presence of OA at one finger joint is associated with OA at other finger joints in the same row (OR 6.4, 95%CI 4.3, 9.4 in men and 5.2, 95%CI 4.5, 6.0 in women), and the same ray (OR=5.3, 95%CI 2.9, 10.0 in men and 3.3, 95% CI 2.6, 4.2 in women) of the same hand <sup>55</sup>. HOA also shows symmetry between hands <sup>55;58-60</sup>, more so for radiographic joint space narrowing (JSN) than for osteophyte <sup>60</sup>. The presence of OA at a particular finger joint strongly associates with OA in the same joint of the opposite hand (OR=14.0, 95%CI 7.1, 27.8 in men and 29.8, 95%CI 19.2, 46.3 in women) <sup>55</sup>.

In summary, pain on usage is not a specific clinical marker for HOA (evidence IIb). However, HOA strongly targets DIP, PIP and thumb base joints and the shorter duration of morning or inactivity stiffness plus clustering pattern and symmetric distribution may be useful to distinguish HOA from other forms of hand arthritis (evidence IIb).

**3. Clinical hallmarks of HOA are Heberden's and Bouchard's nodes, and/or bony enlargement with or without deformity (e.g. lateral deviation of IPJs, subluxation and adduction of thumb-base) affecting characteristic target joints (DIPJs, PIPJs, thumb-base, and index and middle MCPJs).**

**Strength of recommendation (95%CI): 80 (69, 90)**

Heberden's nodes (HN) and Bouchard's nodes (BN) associate with underlying structural changes of HOA, especially osteophyte (OR=5.15, 95%CI 4.37, 6.08)<sup>61-63</sup>. However, their sensitivity and specificity for HOA vary widely from 0.3 to 0.9 depending on the cut-off grade, gold standard and control subjects used. This in part may reflect the common time lag between development of nodes and appearance of structural x-ray change. Subsequently HN or BN have limited value as a single diagnostic marker with an LR ranging from 0.50 to 5.50 and a median of 1.46 (Table 4; Figure 4). However, nodes become more useful when taken in combination with other HOA features (Figure 5). For example, the probability of a subject with HOA is 20% when HN alone are considered, but this increases to 88% when the subject is over 40 years old, has a family history of HN and has joint space narrowing in any finger joint.

HN and BN may be useful for population screening for HOA. A self-reported instrument for HN and BN has been developed and validated in a random sample of 478 subjects aged 40-79 years<sup>64</sup>. Of 300 respondents, 139 were examined by a trained metrologist (the "gold standard"). Sensitivity of self-reported nodes was 0.71 (95%CI 0.60, 0.83), specificity was 0.96 (0.92, 1.00) and LR was 19.76 (6.43, 60.76)<sup>64</sup>.

In brief, HN and BN are important clinical markers for diagnosis of HOA, especially when used in combination with other features of HOA (evidence Ib). Research evidence for the diagnostic values of other clinically-derived features and their distribution is lacking (evidence IV).

**4. *Functional impairment in hand OA may be as severe as in rheumatoid arthritis. Function should be carefully assessed and monitored using validated outcome measures.***

***Strength of recommendation (95%CI): 57 (42, 73)***

A number of studies have examined the functional impact of HOA<sup>6;30;65-70</sup>. Both pain<sup>68</sup> and radiographic changes<sup>69</sup> associate with impaired hand function in the setting of HOA. Functional impairment due to HOA may be similar in severity to that resulting from rheumatoid arthritis<sup>71</sup> (evidence IIb). Indeed, for many patients with HOA functional difficulty is their main presenting complaint. However, in one study the eventual functional outcome of fully established HOA (symptom onset  $\geq$  10 years before) was found to be relatively optimistic for nodal OA but not for erosive OA<sup>70</sup>.

A number of validated instruments are available to assess hand function. These include the Health Assessment Questionnaire (HAQ)<sup>72</sup>; the Arthritis Hand Function Test (AHFT)<sup>73</sup>; the Arthritis Impact Measurement Scale 2 (AIMS2)<sup>74</sup>; and the Cochin<sup>75</sup> and Score for Assessment and quantification of Chronic Rheumatic Affections of the Hands (SACRAH)<sup>71;76</sup>, the Functional Index for Osteoarthritis of the Hand (FIHOA)<sup>65</sup> and the Australian/Canadian Osteoarthritis Hand Index (AUSCAN)<sup>77</sup>. A systematic review of these instruments has been

undertaken <sup>78</sup>. There is no universal instrument and the selection from these options is guided mainly by the clinical question (evidence Ib).

**5. Patients with polyarticular HOA are at increased risk of knee OA, hip OA and OA at other common target sites (generalised OA) and should be assessed and examined accordingly.**

**Strength of recommendation (95%CI): 77 (62, 92)**

HOA may not only affect multiple joints within the hand, it also can occur as a component of “generalised” OA. Patients with HOA have increased risk of both knee OA (OR=3.0, 95%CI 1.2, 7.5) <sup>79</sup> and hip OA (OR=3.25, 95%CI 2.19, 4.84) <sup>80</sup> (evidence IIb). A recent population-based cohort study that followed 1235 subjects without hip and knee OA at baseline for over 6 years showed that the risk of developing knee OA or hip OA was 2 times greater (OR=2.1, 95%CI 1.3, 3.1) in those with HOA than in those without HOA at baseline <sup>5</sup> (evidence IIa).

OA of recognised target joints (DIP, PIP, CMC, knee, hip) correlates with each other which often appear in a cluster of 3 or more involved groups <sup>27</sup>. The strongest associations occur for DIP and PIP, followed by PIP and CMC, CMC and knee, PIP and knee, knee and hip and DIP and knee (Table 5). These data support the concept of “generalised OA” in which some individuals are at increased risk of multiple joint involvement by OA. Classification criteria for generalised versus focal OA have been proposed <sup>4</sup>. There is clear justification to include assessment of other target joints for OA for the purpose of diagnosis and treatment planning of HOA.

**6. Recognised subsets with different risk factors, associations and outcomes (requiring different assessment and management) include IPJ OA (with or without nodes), thumb-base OA, and erosive OA. Each may be symptomatic or asymptomatic.**

**Strength of recommendation (95%CI): 68 (56, 79)**

A number of studies have identified differences between erosive and non-erosive OA (see next proposition for further details) (evidence IIa - IIb). Although HOA clusters by joints, population-based cross-sectional studies have confirmed that isolated thumb base OA is a common occurrence<sup>81</sup>. Apart from the location, thumb base OA may associate with different risk factors from IPJ OA, although both may share a similar genetic risk<sup>44</sup>. For example, hypermobility has been reported as a risk factor for thumb-base OA<sup>82</sup> but a negative risk (“protective”) factor for IPJ OA<sup>82;83</sup>. Studies on functional impairment have not confirmed any clear difference between thumb base OA and IPJ OA<sup>84</sup> (evidence IIb), however the long-term functional outcome for erosive OA appears worse than for nodal OA<sup>70</sup>. Further research is required to define how clearly such subsets are delineated.

**7. Erosive hand OA targets IPJs and shows radiographic subchondral erosion which may progress to marked bone and cartilage attrition, instability and bony ankylosis. Typically it has an abrupt onset; marked pain and functional impairment; inflammatory symptoms and signs (stiffness, soft tissue swelling, erythema, paraesthesiae); mildly elevated CRP; and a worse outcome than non-erosive IPJ OA.**

***Strength of recommendation (95%CI): 87 (81, 93)***

An age and gender matched case control study has compared radiographic features of erosive OA (n=33) and nodal OA (n=33) using summated scores for individual OA features (JSN, osteophyte, subchondral sclerosis, subchondral cysts) at different joint sites. Erosive OA had significantly higher scores than nodal OA at DIP, PIP and thumb IP joints, but not at MCP and CMC joints, supporting the selective targeting of IP joints by erosive OA<sup>85</sup>. This observation is supported by two cohort studies which further suggest that this pattern is associated with a worse radiographic outcome<sup>86;87</sup>. In two case control studies subchondral erosion, bony collapse and ankylosis of IP joints appeared specific to erosive OA<sup>85;88</sup>. In one case control study comparing observed hand function in patients with established nodal HOA (n = 57), patients with established erosive OA (n = 10) and normal non-OA subjects (n = 52), hand function was worse in the erosive OA patients<sup>70</sup>.

One case control study has examined differences in capillaroscopic abnormalities between erosive OA and nodal OA. Although some statistically significant differences were found for frequency of microhaemorrhages, tortuous capillary loops and shortened loops, they did not prove very discriminatory with LR of 2.19 (95%CI 0.62, 7.78), 1.21 (1.85, 1.74) and 3.29 (1.34, 8.07) respectively<sup>89</sup>.

Serum CRP levels have been measured in a case control study examining 67 patients with erosive OA and 31 patients with non-erosive OA. CRP levels were higher in the erosive OA group and the observed correlations between CRP

level, radiographic severity scores and number of joints involved supported CRP as an indicator of disease activity<sup>90</sup>. No differences in serum levels of type II cartilage biomarkers (Col2-3/4C, C2C, and CS846 epitope) were demonstrated between 30 erosive OA patients and 29 patients with non-erosive HOA<sup>91</sup>.

Ultrasound has been investigated as a means to differentiate erosive OA, non-erosive HOA and normal joints. One case control study (n=60) including 20 subjects per group found ultrasound to differentiate erosive OA from normal (ROC 0.75 - ROC 1 means 100% sensitive and specific) and non-erosive HOA from normal (ROC 0.73), but not erosive OA from non-erosive HOA (ROC: not reported)<sup>22</sup>.

In summary, erosive OA appears to be a specific subgroup of HOA with worse clinical and structural outcomes. It targets mainly the IP joints with structural changes which are often severe (subchondral erosion, ankylosis) and inflammation (elevated CRP) (evidence IIa - IIb).

**8. The differential diagnosis for HOA is wide. The commonest conditions to consider are psoriatic arthritis (which may target DIPJs or affect just one ray); rheumatoid arthritis (mainly targeting MCPJs, PIPJs , wrists); gout (which may superimpose on pre-existing HOA) and haemochromatosis (mainly targeting MCPJs, wrists).**

***Strength of recommendation (95%CI): 81 (73, 89)***

The differential diagnosis between hand OA and other arthropathy may be based on clinical manifestations (eg, age, gender, onset and progression of symptoms, degree of stiffness, joints involved (Figure 7), presence of HN/BN, examination

findings of synovitis and/or damage), radiographic changes (Figure 8) and laboratory tests. However, as for diagnosis, a single criterion on its own has limited sensitivity and specificity (Figure 5). For example, although DIP joints are mainly targeted by OA they can also be involved in rheumatoid arthritis (RA)<sup>9</sup>; inflammatory symptoms and signs and elevation of CRP may occur with both erosive OA and RA; radiographic changes of HOA and calcium pyrophosphate dehydrate deposition disease (CPPD) associated arthritis are extremely similar<sup>92</sup> and HOA may coexist with CPPD<sup>93;94</sup>, gout or RA.

A composite of multiple features is more useful, such as age, female gender, joint distribution, bone swelling (not soft tissue) and radiographic changes. Laboratory tests, although non-specific, may assist in this, for example strongly positive RF is supportive of RA (Table 4) and elevated urate may support gout. However, some individual features do have high specificity (eg non-proliferative marginal erosion for RA, urate crystals for gout).

In brief, differential diagnosis of HOA and other types of hand arthritis depends largely on the use of a composite of features (evidence Ib). Certain features for individual diseases may be useful for specific cases (IIb).

**9. Plain radiographs provide the gold standard for morphological assessment of HOA. A postero-anterior radiograph of both hands on a single film/field of view is adequate for diagnosis. Classical features are joint space narrowing, osteophyte, subchondral bone sclerosis and subchondral cyst; subchondral erosion occurs in erosive hand OA. Further imaging modalities are seldom indicated for diagnosis.**



***Strength of recommendation (95%CI): 87 (81, 93)***

Structural changes on plain radiographs have been used by the majority of studies as the “gold” standard for the assessment of a diagnostic test<sup>95-98</sup>(Figure 2). The validity of radiographic change itself has been examined in two case control studies in which the clinical diagnosis was used as the “gold standard”<sup>8;9</sup>. Classical radiographic features such as JSN and osteophyte are sensitive (sensitivity 0.75-1.0) but not specific (specificity 0.18-0.71), resulting in small LRs (pooled LR1.60, 95%CI 1.29, 1.99 for JSN and 1.61, 95%CI 1.12, 2.33 for osteophyte) (Table 4 and Figure 4). Thus, a single feature (eg, JSN or osteophyte) is less valuable for the diagnosis than a composite of 2 or more features (Figure 5).

Clearly the reliability of any test is an important consideration and several studies have examined specifically the reproducibility of radiographic OA scores<sup>99-101</sup>. The intra-reader reliability (kappa) of radiographic features for HOA ranges from 0.38 to 1.0 (kappa 0.56-1.00 for PIP joints, 0.38-0.87 for DIP joints and 0.58-0.69 for CMC-1 joints) and the inter-reader reliability (kappa) ranges from 0.52 to 0.92<sup>100</sup>. The latter may be improved by reader’s experience (0.92-1.00)<sup>99;101</sup>. Reliability also varies according to the scale used, eg, the Verbruggen and Kellgren and Lawrence scale may have better reproducibility than global and Kallman scales<sup>101</sup>.

The value of MRI in early diagnosis has been examined in a case control setting where chronic OA (symptoms >12 months, n=14), early OA (symptoms ≤12 months, n=16), “latent” OA (asymptomatic, no history of pain and swelling in

a patient with HOA, n=14) and normal controls (n=18) were compared<sup>97</sup>.

Abnormalities in soft tissues and bones were observed in all the HOA categories compared to controls, with periarticular changes being particularly striking in the least affected and latent joints. The suggestion from this study that MRI may help identify early HOA when radiographs are normal requires confirmation.

Scintigraphy has been examined as a means of early diagnosis of HOA in a prospective cohort study in which 30 subjects with normal radiographs but abnormal scintigraphy at baseline were followed for one year. According to the clinical and/or radiographic criteria of HOA the sensitivity of scintigraphy was 98.2%, specificity was 57.1%, and the LR was 2.29<sup>95</sup>. In addition scintigraphy has been used to predict the progression of HOA in a 5-year cohort study, in which moderate sensitivity (0.53, 95%CI 0.42, 0.63) and good specificity (0.93, 95%CI 0.92, 0.94) were observed (Table 4)<sup>102</sup>.

In summary, the plain radiograph is the validated principle imaging technique to examine morphological changes of HOA (evidence IIb). Diagnosis based on a single radiographic feature (eg, JSN or osteophyte) has limited value, whereas presence of multiple features, especially a composite of clinical and radiographic changes, dramatically improves diagnostic certainty (evidence Ib). Other imaging techniques are relatively understudied and their clinical applications have yet to be determined.

**10. Blood tests are not required for diagnosis of HOA but may be required to exclude co-existent disease. In a patient with HOA who has marked inflammatory symptoms and/or signs, especially involving atypical**

***sites, blood tests should be undertaken to screen for additional inflammatory arthritides.***

***Strength of recommendation (95%CI): 78 (63, 92)***

Unlike RA or other forms of inflammatory arthritis, inflammatory markers are not usually elevated in HOA. It is well documented that ESR, RF (evidence Ib) and CRP (evidence IIb) are usually normal/negative or only mildly elevated/positive in non-erosive OA (Table 4)<sup>8;9;54;89;103</sup>. Therefore more pronounced abnormalities should lead to a search for an alternative explanation. However, as discussed, a single blood test may be unable to differentiate between erosive OA and RA, or confirm the presence of coexisting inflammatory arthropathy. It is necessary to consider other clinical and investigational features which are more characteristic and/or specific for each condition (eg, proliferative or non-proliferative marginal erosions in psoriatic and rheumatoid arthritis respectively, elevated serum uric acid and urate crystal identification on aspiration of a joint or tophus in gout).

### **Future research agenda**

After 3 Delphi rounds 9 propositions for future research were developed (Table 7).

## **DISCUSSION**

To our knowledge these are the first evidence based recommendation for the diagnosis of HOA and the second EULAR recommendations to address diagnostic issues in musculoskeletal disorders<sup>16</sup>. Until now the main reference cited for diagnosis of HOA has been the ACR criteria for classification of HOA<sup>8</sup>.

However, the current recommendations differ from the ACR criteria in several important ways. Firstly, the primary purpose of these recommendations is to provide guidance to assist clinicians to diagnose HOA, not to classify the disease for research or clinical trial purposes. The emphasis is on possible subsets and the differential diagnosis to be considered rather than on algorithms for classification of a single entity. Secondly, these are evidence-based recommendations in which research evidence has been summarised systematically from multiple studies undertaken in different countries. Therefore they have more generalisability than recommendations based on a single study population. Thirdly, clinical expertise from many countries across Europe has been incorporated within the recommendations, and importantly, the expertise has been synthesised systematically using a Delphi exercise. Therefore, the recommendations have less parochial and personal bias<sup>104</sup>. Finally, the strength of recommendation and confidence interval has been provided for each proposition, based both on the research evidence and clinical expertise. This is an important marker that reflects the magnitude of support for each statement and the confidence (variability of opinion) from the Task Force<sup>104</sup>. This information should help clinicians to gauge which statements have good general agreement and which are more open to personal interpretation.

Ten key recommendations have been generated. The topics are wide ranging and include risk factors for HOA, clinical manifestations, subsets, differential diagnosis, imaging and laboratory tests. The sensitivity and specificity for each recommended marker or test has been examined and the value of each

has been presented as a likelihood ratio to allow estimation of the likelihood of HOA given a positive test result. A diagnostic ladder has also been provided to show the probability of diagnosis of HOA when multiple features are considered. Clinicians may estimate the probability of HOA for any composite of the features that a patient may present in their daily practice based on the knowledge of the likelihood ratio for each feature (Table 3). Baye's formula or Fagan's nomogram may be used to estimate the probability<sup>16</sup>. Using such data it would be possible to develop a computer based risk prediction model for clinical use in which the proposed diagnostic features are listed and the probability of HOA calculated according to the features entered. Overall we found that the diagnosis of HOA cannot be determined with confidence using a single feature, even Heberden's nodes - the feature generally considered as the hallmark of HOA. A composite of several features is required to diagnose HOA.

There are several limitations to these recommendations. Firstly, although the evidence-based method is a widely accepted strategy to increase the power and generalisability of research evidence, it is still open to bias since the pooled studies may carry different confounding factors. Ideally evidence-based recommendations should reflect, and largely be derived, from the population in which they will be applied. Secondly, we only focused on key issues relating to diagnosis of HOA and did not attempt a comprehensive review of all reported aspects. Thirdly, generation of the recommendations was driven from a clinical perspective and the relevant research was examined later. Therefore we may have omitted important emerging information in the research literature that could

have potential diagnostic value. Such bias, however, should have been minimised by the general literature search and discussion undertaken prior to the Delphi exercise. Finally, the Delphi consensus approach has its own limitations. Although it is systematic it has restricted flexibility and as a result some propositions may overlap or appear repetitive or illogical. Therefore we discussed the final list of the Delphi results at our last face to face meeting to agree on necessary changes to improve clarity. During this, however, we did not delete or introduce content but did alter some phrasing and ordering of content.

In conclusion, ten key recommendations have been generated by the EULAR OA Task Force for diagnosis of HOA. The level of research evidence and strength of recommendation have been provided for each proposition. We hope that these recommendations will stimulate debate and increase interest in HOA and thereby lead to improved diagnosis and assessment of people with this highly prevalent condition.

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**Table 1. Glossary**

| <b>Term</b>               | <b>Definition</b>  |
|---------------------------|--|
| Heberden & Bouchard nodes | Clinically defined postero-lateral firm/hard swellings.<br>Heberden's – distal IPJ; Bouchard's – proximal IPJ.<br>Nodes can occur with or without radiological and/or clinical abnormalities characteristics of HOA. |
| Nodal OA                  | Heberden and/or Bouchard's nodes plus underlying IPJ OA, defined clinically and/or radiologically.   |
| Non-nodal OA              | IPJ OA, defined clinical and/or radiographically, without nodes  |
| Erosive OA                | Subset of HOA defined radiographically by subchondral erosion, cortical destruction and subsequent reparative change which may include bony ankylosis.   |
| Generalised OA            | HOA plus OA at other sites.  |
| Thumb base OA             | First CMCJ with or without STJOA   |
| Gold standard             | The diagnostic reference used for a particular study   |

OA= osteoarthritis; IPJ = interphalangeal joint; CMCJ = carpometacarpal joint; STJ = scapho-trapezioid joint



**Table 2. EULAR evidence hierarchy for diagnosis based on study design<sup>16</sup>**

- Ia – meta-analysis of cohort studies
- Ib – meta-analysis of case control studies
- IIa – cohort studies
- IIb – case control/cross sectional comparative studies
- III – non-comparative descriptive studies
- IV – expert opinion

**Table 3. Propositions and strength of recommendation (SOR) – order according to topic (risk factors, clinical, subsets, differential diagnosis, images and laboratory tests)**

| No. | Proposition  | LoE       | SOR (95%CI)    |
|-----|--|-----------|----------------|
| 1   | Risk factors for HOA include female sex, increasing age over 40, menopausal status, family history, obesity, higher bone density, greater forearm muscle strength, joint laxity, prior hand injury and occupation or recreation-related usage.   | lb - llb  | 69<br>(54, 84) |
| 2   | Typical symptoms of HOA are pain on usage and only mild morning or inactivity stiffness affecting just one or a few joints at any one time; symptoms are often intermittent and target characteristic sites (DIPJs, PIPJs, thumb-base, index and middle MCPJs). With such typical features, a confident clinical diagnosis can be made in adults aged over 40.   | llb       | 85<br>(77, 92) |
| 3   | Clinical hallmarks of HOA are Heberden's and Bouchard's nodes, and/or bony enlargement with or without deformity (e.g. lateral deviation of IPJs, subluxation and adduction of thumb-base) affecting characteristic target joints (DIPJs, PIPJs, thumb-base, and index and middle MCPJs).  | lb - IV   | 80<br>(69, 90) |
| 4   | Functional impairment in hand OA may be as severe as in rheumatoid arthritis. Function should be carefully assessed and monitored using validated outcome measures.  | llb       | 57<br>(42, 73) |
| 5   | Patients with polyarticular HOA are at increased risk of knee OA, hip OA and OA at other common target sites (generalised OA) and should be assessed and examined accordingly.   | lla - llb | 77<br>(62, 92) |
| 6   | Recognised subsets with different risk factors, associations and outcomes (requiring different assessment and management) include IPJ OA (with or without nodes), thumb-base OA, and erosive OA. Each may be symptomatic or asymptomatic.  | lla - llb | 68<br>(56, 79) |
| 7   | Erosive hand OA targets IPJs and shows radiographic subchondral erosion which may progress to marked bone and cartilage attrition, instability and bony ankylosis. Typically it has an abrupt onset; marked pain and functional impairment; inflammatory symptoms and signs (stiffness, soft tissue swelling, erythema, paraesthesiae); mildly elevated CRP; and a worse outcome than non-erosive IPJ OA.                | lla - llb | 87<br>(81, 93) |
| 8   | The differential diagnosis for HOA is wide. The commonest conditions to consider are psoriatic arthritis (which may target DIPJs or affect just one ray); rheumatoid arthritis (mainly targeting MCPJs, PIPJs, wrists); gout (which may superimpose on pre-existing HOA) and haemochromatosis (mainly targeting MCPJs, wrists).  | lb - llb  | 81<br>(73, 89) |
| 9   | Plain radiographs provide the gold standard for morphological assessment of HOA. A postero-anterior radiograph of both hands on a single film/field of view is adequate for diagnosis. Classical features are joint space narrowing, osteophyte, subchondral bone sclerosis and subchondral cyst; subchondral erosion occurs in erosive hand OA. Further imaging modalities are seldom indicated for diagnosis [figure]. | lb - llb  | 87<br>(81, 93) |
| 10  | Blood tests are not required for diagnosis of HOA but may be required to exclude co-existent disease. In a patient with HOA who has marked inflammatory symptoms and/or signs, especially involving atypical sites, blood tests should be undertaken to screen for additional inflammatory arthritides.  | lb - llb  | 78<br>(63, 92) |

LoE: level of evidence (see Table 2 for further details), presented in range upon components assessed; SOR: strength of recommendation on visual analogue scale (0-100 mm, 0=not recommended at all, 100 = fully recommended); CI: confidence interval.

**Table 4 Tests and markers used in the diagnosis of hand osteoarthritis**

| Diagnostic test      | Study design          | N    | Gold standard   | Sensitivity (95%CI) | Specificity (95%CI) | LR (95%CI)               | Reliability (Kappa/ICC) | Ref           |
|----------------------|-----------------------|------|-----------------|---------------------|---------------------|--------------------------|-------------------------|---------------|
| <b>General</b>       |                       |      |                 |                     |                     |                          |                         |               |
| Age >40 yrs          | Case control (RA etc) | 194  | Clinical        | 1.00                | 0.73 (0.64, 0.82)   | 3.73 (2.69, 5.18)        | -                       | <sup>8</sup>  |
| Female sex           | Case control (RA etc) | 199  | Clinical        | 0.71 (0.62, 0.79)   | 0.25 (0.17, 0.34)   | 0.94 (0.80, 1.13)        | -                       | <sup>8</sup>  |
| Family history of HN | Case control (RA etc) | 197  | Clinical        | 0.39 (0.29, 0.48)   | 0.83 (0.75, 0.90)   | 2.26 (1.37, 3.72)        | -                       | <sup>8</sup>  |
| <b>Clinical</b>      |                       |      |                 |                     |                     |                          |                         |               |
| Pain on usage        | Cross-sectional       | 541  | DIP, k/l≥2      | 0.01                | 0.99                | 1.00                     | 0.85                    | <sup>11</sup> |
|                      |                       |      | k/l≥2 + symptom | 0.03                | 0.94                | 0.50                     | <sup>11</sup>           |               |
|                      |                       |      | PIP, k/l≥2      | 0.05                | 0.99                | 5.00                     | 1.00                    | <sup>11</sup> |
|                      |                       |      | k/l≥2 + symptom | 0.10                | 0.95                | 2.00                     | <sup>11</sup>           |               |
|                      |                       |      | CMC, k/l≥2      | 0.22                | 0.96                | 5.50                     | 1.00                    | <sup>11</sup> |
|                      |                       |      | k/l≥2 + symptom | 0.57                | 0.61                | 1.46                     |                         |               |
| <b>Median</b>        |                       |      |                 |                     |                     | <b>1.46</b>              |                         |               |
| HN (+/-)             | Case control (RA etc) | 199  | Clinical        | 0.91 (0.85, 0.97)   | 0.67 (0.57, 0.76)   | 2.73 (2.05, 3.63)        | -                       | <sup>8</sup>  |
| HN (≥1)              | Case control joints   | 6590 | OST ≥1          | 0.41 (0.38, 0.44)   | 0.92 (0.91, 0.93)   | 5.13 (4.57, 5.76)        | 0.78                    | <sup>62</sup> |
| HN (≥1)              | Case control joints   | 3730 | OST ≥1          | 0.83 (0.82, 0.85)   | 0.51 (0.48, 0.55)   | 1.72 (1.61, 1.83)        | 0.6-0.8                 | <sup>63</sup> |
|                      |                       |      | JSN ≥1          | 0.78 (0.76, 0.79)   | 0.34 (0.32, 0.37)   | 1.18 (1.13, 1.24)        | 0.6-0.8                 | <sup>63</sup> |
| HN (+/-)             | Cross-sectional       | 541  | k/l≥2           | 0.49                | 0.90                | 4.90                     | 0.68                    | <sup>11</sup> |
|                      |                       |      | k/l≥2 + symptom | 0.82                | 0.49                | 1.61                     |                         |               |
| <b>Pooled</b>        |                       |      |                 |                     |                     | <b>2.30 (1.30, 4.07)</b> |                         |               |
| BN (+/-)             | Case control          | 199  | Clinical        | 0.81 (0.73, 0.88)   | 0.65 (0.55, 0.74)   | 2.29 (1.73, 3.04)        | -                       | <sup>8</sup>  |
| BN (+/-)             | Case control joints   | 3730 | OST ≥1          | 0.44 (0.40, 0.46)   | 0.80 (0.78, 0.81)   | 2.13 (1.92, 2.35)        | 0.5-0.7                 | <sup>63</sup> |
| BN (+/-)             | Cross-sectional       | 541  | k/l≥2           | 0.40                | 0.87                | 3.08                     | 0.75                    | <sup>11</sup> |
|                      |                       |      | k/l≥2 + symptom | 0.75                | 0.49                | 1.47                     |                         |               |
|                      |                       |      | JSN ≥           | 0.37 (0.33, 0.40)   | 0.74 (0.73, 0.76)   | 1.42 (1.28, 1.59)        | 0.5-0.7                 | <sup>63</sup> |
| <b>Pooled</b>        |                       |      |                 |                     |                     | <b>2.15 (1.95, 2.36)</b> |                         |               |
| <b>Radiographic</b>  |                       |      |                 |                     |                     |                          |                         |               |
| JSN                  | Case control          | 82   | Clinical        | 0.83 (0.71, 0.94)   | 0.62 (0.47, 0.77)   | 2.17 (1.44, 3.27)        | -                       | <sup>9</sup>  |
|                      | Case control (RA)     | 140  | Clinical        | 0.83 (0.71, 0.94)   | 0.40 (0.30, 0.50)   | 1.38 (1.11, 1.70)        | -                       | <sup>9</sup>  |
| JSN                  | Case control (RA etc) | 199  | Clinical        | 0.75 (0.67, 0.83)   | 0.54 (0.44, 0.63)   | 1.61 (1.27, 2.05)        | -                       | <sup>8</sup>  |
| <b>Pooled</b>        |                       |      |                 |                     |                     | <b>1.60 (1.29, 1.99)</b> |                         |               |
| OST                  | Case control          | 82   | Clinical        | 1.00                | 0.26 (0.13, 0.39)   | 1.35 (1.13, 1.62)        | -                       | <sup>9</sup>  |
|                      | Case control (RA)     | 140  | Clinical        | 1.00                | 0.18 (0.10, 0.26)   | 1.22 (1.11, 1.34)        | -                       | <sup>9</sup>  |
| OST                  | Case control (RA etc) | 199  | Clinical        | 0.83 (0.76, 0.90)   | 0.71 (0.62, 0.80)   | 2.83 (2.06, 3.90)        | -                       | <sup>8</sup>  |
| <b>Pooled</b>        |                       |      |                 |                     |                     | <b>1.61 (1.12, 2.33)</b> |                         |               |

|                           |                       |             |                                   |                   |                   |                          |      |     |
|---------------------------|-----------------------|-------------|-----------------------------------|-------------------|-------------------|--------------------------|------|-----|
| Cysts                     | Case control          | 82          | Clinical                          | 0.85 (0.74, 0.96) | 0.81 (0.69, 0.92) | 4.46 (2.36, 8.43)        |      | 9   |
|                           | Case control (RA)     | 140         | Clinical                          | 0.85 (0.74, 0.96) | 0.39 (0.29, 0.49) | 1.39 (1.14, 1.71)        | -    | 9   |
| <b>Pooled</b>             |                       |             |                                   |                   |                   | <b>2.39 (0.76, 7.47)</b> |      |     |
| Erosions                  | Case control (RA etc) | 199         | Clinical                          | 0.43 (0.33, 0.53) | 0.58 (0.48, 0.67) | 1.01 (0.73, 1.40)        | -    | 8   |
| Malalignment              | Case control (RA etc) | 199         | Clinical                          | 0.51 (0.41, 0.61) | 0.74 (0.65, 0.82) | 1.94 (1.32, 2.84)        | -    | 8   |
| <b>Other images</b>       |                       |             |                                   |                   |                   |                          |      |     |
| Scintigraph               | Cohort, 1 year        | 30          | Clin/radiographic                 | 0.98              | 0.57              | 2.29                     |      | 95  |
| Scintigraph (progression) | Cohort, 5 yr          | 2278 joints | Increase in OST, JSN or sclerosis | 0.53 (0.42, 0.63) | 0.93 (0.92, 0.94) | 7.38 (5.75, 9.47)        | 0.84 | 102 |
| <b>Laboratory</b>         |                       |             |                                   |                   |                   |                          |      |     |
| ESR < 20 mm/hr            | Case control (RA etc) | 155         | Clinical                          | 0.61 (0.49, 0.72) | 0.80 (0.71, 0.88) | 3.00 (1.90, 4.73)        | -    | 8   |
| ESR (-)                   | Case control          | 200         | Clinical & x-ray                  | 0.94 (0.89, 0.99) | 0.81 (0.73, 0.89) | 4.94 (3.29, 7.44)        | -    | 54  |
| <b>Pooled</b>             |                       |             |                                   |                   |                   | <b>3.89 (2.39, 6.34)</b> |      |     |
| RF < 1:80                 | Case control (RA etc) | 103         | Clinical                          | 0.86 (0.77, 0.96) | 0.68 (0.56, 0.79) | 2.67 (1.83, 3.90)        | -    | 8   |
| RF (-)                    | Case control (RA)     | 140         | Clinical                          | 1.00              | 0.81 (0.73, 0.89) | 5.26 (3.51, 7.89)        | -    | 9   |
| <b>Pooled</b>             |                       |             |                                   |                   |                   | <b>3.73 (1.92, 7.25)</b> |      |     |

N = subjects or joints as specified; CI = confidence interval; LR = likelihood ratio; ICC = intra-class correlation; RA = rheumatoid arthritis; DIP = distal interphalangeal joint; PIP = proximal interphalangeal joint; CMC = carpometacarpal joint; k/l = Kellgren and Lawrence; HN = Heberden's nodes; BN = Bouchard's nodes; OST = osteophytes; JSN = joint space narrowing; ESR = erythrocyte sedimentation rate; RF = Rheumatoid factor

Table 5. Association of osteoarthritis between joints<sup>27</sup>

| Index joints | Other joints | OR (95%CI)        |
|--------------|--------------|-------------------|
| DIP          | PIP          | 31.7 (13.8, 72.5) |
| PIP          | CMC          | 4.8 (2.7, 8.4)    |
| CMC          | Knee         | 2.4 (1.5, 4.4)    |
| PIP          | Knee         | 2.4 (1.3, 4.4)    |
| Knee         | Hip          | 2.1 (1.2, 3.4)    |
| DIP          | Knee         | 1.8 (1.1, 3.1)    |

OR = odds ratio; CI = confidence interval; DIP = distal interphalangeal; PIP = proximal interphalangeal; CMC = carpometacarpal.

Table 6. Risk factors and hand OA

| Risk factor                                | Evidence <sup>#</sup> | Sample size        | RR/OR (95%CI)          | References |
|--|-----------------------|--------------------|------------------------|------------|
| Female gender                              | Ib                    | 14 studies         | 1.23 (1.11, 1.34)      | 24         |
| Age, >40                                   | IIb                   | 194                | 3.68 (2.66, 5.09)      | 8          |
| Family history, 1 <sup>st</sup> degree etc | Ib                    | 3 studies (n=4183) | 2.57 (1.86, 3.55)      | 8;44;45    |
| Obesity                                    |                       |                    |                        |            |
| Relative weight index, per 20%↑            | IIa                   | 1276               | 1.69 (1.27, 2.18)      | 49         |
| BMI, >29 vs. ≤24                           | IIb                   | 78                 | 8.3 (1.2, 56.5)        | 52         |
| BMI, kg/m <sup>2</sup>                     | IIb                   | 82 pairs           | 1.30 (1.06, 1.59)      | 50         |
| BMI, kg/m <sup>2</sup>                     | IIb                   | 573 women          | 1.03 (0.96, 1.11)      | 43         |
| BMD, dg/cm <sup>2</sup>                    | IIb                   | 573 women          | 1.11 (0.61, 2.02) kl≥2 | 43         |
|  |                       |                    | 1.61 (1.27, 2.07) kl=4 |            |
| Grip strength, 3 <sup>rd</sup> tertile     | IIa                   | 756                | 2.8 (1.2, 6.7)         | 53         |
| History of hand injury                     | IIb                   | 573 women          | 3.64 (1.34, 9.88)      | 43         |

# please see table 2 for further description

RR = relative risk; OR = odds ratio; CI = confidence interval; BMI = body mass index

Table 7. Future research agenda for diagnosis of hand OA

| No. | Proposition   |
|-----|---|
| 1   | The relative utility of imaging techniques (plain x-rays, MRI, ultrasonography, scintigraphy) in both early diagnosis and evaluation of progression of the HOA sub-sets needs to be determined.                                       |
| 2   | Risk factors both for development and long term clinical outcome of the different sub-sets of HOA need to be determined.  |
| 3   | Potential biomarkers of bone, cartilage, synovium and inflammation should be examined in HOA subsets for utility in terms of early diagnosis, assessment of disease activity and prediction of outcome.                               |
| 4   | Diagnostic and classification criteria to better define HOA and its sub-sets need to be developed and validated.  |
| 5   | Further studies are required to confirm the associations between HOA and systemic risk factors such as menopausal state, bone density, obesity and metabolic syndrome, and to explain the mechanisms that underlie such associations. |
| 6   | The genetic factors that predispose to the different phenotypes of HOA need to be identified.   |
| 7   | The population incidence and prevalence of HOA and its sub-types (both symptomatic and asymptomatic), standardised by age and gender, need to be confirmed.   |
| 8   | Studies should be undertaken to determine whether erosive HOA is a discrete subset with specific risk factors and pathogenesis, or a subgroup of HOA with a worse outcome.  |
| 9   | The association between the different HOA phenotypes and large joint OA (ie generalised OA) needs further examination.  |

## Reference List

- (1) Cushnaghan J, Dieppe P. Study of 500 Patients with Limb Joint Osteoarthritis .1. Analysis by Age, Sex, and Distribution of Symptomatic Joint Sites. *Ann Rheum Dis* 1991; 50(1):8-13.
- (2) Mannoni A, Briganti MP, Di Bari M, Ferrucci L, Costanzo S, Serni U et al. Epidemiological profile of symptomatic osteoarthritis in older adults: a population based study in Dicomano, Italy. *Ann Rheum Dis* 2003; 62(6):576-578.
- (3) Fickert S, Puhl W, Gunther KP. Epidemiology of Generalised Osteoarthritis. *Aktuelle Rheumatologie* 2003; 28(6):302-307.
- (4) Dougados M, Nakache JP, Gueguen A. Criteria for generalized and focal osteoarthritis. *Revue du Rhumatisme (English Edition)* 1996; 63:569-575.
- (5) Dahaghin S, Bierma-Zeinstra SMA, Reijman M, Pols HAP, Hazes JMW, Koes BW. Does hand osteoarthritis predict future hip or knee osteoarthritis? *Arthritis & Rheumatism* 2005; 52(11):3520-3527.
- (6) Zhang Y, Niu J, Kelly-Hayes M, Chaisson CE, Aliabadi P, Felson DT. Prevalence of symptomatic hand osteoarthritis and its impact on functional status among the elderly: The Framingham Study. *Am J Epidemiol* 2002; 156(11):S225.
- (7) Dahaghin S, Bierma-Zeinstra SMA, Reijman M, Pols HAP, Hazes JMW, Koes BW. Prevalence and determinants of one month hand pain and hand related disability in the elderly (Rotterdam study). *Ann-Rheum-Dis* 2005; 64(1):99-104.
- (8) Altman R, Alarcon 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 & Rheumatism* 1990; 33(11):1601-1610.
- (9) Campion G, Dieppe P, Watt I. Heberden's nodes in osteoarthritis and rheumatoid arthritis. *British Medical Journal* 1983; 287(6404):1512.
- (10) Hart D, Spector T, Egger P, Coggon D, Cooper C. Defining osteoarthritis of the hand for epidemiological studies: The Chingford Study. *Ann-Rheum-Dis* 1994; 53(4):220-223.
- (11) Hart DJ, Spector TD, Brown P, Wilson P, Doyle DV, Silman AJ. Clinical signs of early osteoarthritis: reproducibility and relation to x ray changes in 541 women in the general population. *Ann-Rheum-Dis* 1991; 50(7):467-470.
- (12) Jordan KM, Arden NK, Doherty M, Bannwarth B, Bijlsma JW, Dieppe P et al. EULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis: Report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). *Annals of the Rheumatic Diseases* 2003; 62(12):1145-1155.
- (13) Pendleton A, Arden N, Dougados M, Doherty M, Bannwarth B, Bijlsma JW et al. EULAR recommendations for the management of knee osteoarthritis: report of a task force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). *Annals of the Rheumatic Diseases* 2000; 59(12):936-944.
- (14) Zhang W, Doherty M, Arden N, Bannwarth B, Bijlsma J, Gunther KP et al. EULAR evidence based recommendations for the management of hip osteoarthritis: report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). *Ann Rheum Dis* 2005; 64(5):669-681.



- (15) Zhang W, Doherty M, Leeb BF, Alekseeva L, Arden NK, Bijlsma JW et al. EULAR evidence based recommendations for the management of hand osteoarthritis: Report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). *Ann Rheum Dis* 2007; 66(3):377-388.
- (16) Zhang W, Doherty M, Pascual E, Bardin T, Barskova V, Conaghan P et al. EULAR evidence based recommendations for gout. Part I: Diagnosis. Report of a task force of the standing committee for international clinical studies including therapeutics (ESCISIT). *Ann Rheum Dis* 2006; 65(10):1301-1311.
- (17) Dougados M, Betteridge N, Burmester GR, Euller-Ziegler L, Guillemin F, Hirvonen J et al. EULAR standardised operating procedures for the elaboration, evaluation, dissemination, and implementation of recommendations endorsed by the EULAR standing committees. *Ann Rheum Dis* 2004; 63(9):1172-1176.
- (18) Whitehead A, Whitehead J. A general parametric approach to the meta-analysis of randomized clinical trials. *Statistics in Medicine* 1991; 10(11):1665-1677.
- (19) Altman DG, Bland JM. *Statistics Notes: Diagnostic tests 1: sensitivity and specificity.* *BMJ* 1994; 308(6943):1552.
- (20) Deeks JJ, Altman DG. *Diagnostic tests 4: likelihood ratios.* *BMJ* 2004; 329(7458):168-169.
- (21) Altman DG, Bland JM. *Statistics Notes: Diagnostic tests 3: receiver operating characteristic plots.* *BMJ* 1994; 309(6948):188.
- (22) Rovetta G, Battista S, Brignone A, Monteforte P. Quantitative ultrasound of the proximal phalanges: reproducibility in erosive and nodal osteoarthritis of the hands. *International Journal of Tissue Reactions* 1999; 21(4):121-127.
- (23) Kleinbaum DG, Kuppler LL, Morgenstern H. *Epidemiologic Research - Principles and Quantitative Methods.* John Wiley & Sons, INC.; 1982.
- (24) Srikanth VK, Fryer JL, Zhai G, Winzenberg TM, Hosmer D, Jones G. A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. *Osteoarthritis & Cartilage* 2005; 13(9):769-781.
- (25) 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 & Rheumatism* 1995; 38(8):1134-1141.
- (26) Butler WJ, Hawthorne VM, Mikkelsen WM, Carman WJ, Bouthillier DL, Lamphiear DE et al. Prevalence of radiologically defined osteoarthritis in the finger and wrist joints of adult residents of Tecumseh, Michigan, 1962-65. *Journal of Clinical Epidemiology* 1988; 41(5):467-473.
- (27) Cooper C, Egger P, Coggon D, Hart DJ, Masud T, Cicuttini F et al. Generalized osteoarthritis in women: pattern of joint involvement and approaches to definition for epidemiological studies. *J Rheumatol* 1996; 23(11):1938-1942.
- (28) Haara MM, Heliövaara M, Kroger H, Arokoski JPA, Manninen P, Karkkainen A et al. Osteoarthritis in the carpometacarpal joint of the thumb: Prevalence and associations with disability and mortality. *Journal of Bone & Joint Surgery - American Volume* 2004; 86(7):1452-1457.

- (29) Wilder FV, Barrett JP, Farina EJ. Joint-specific prevalence of osteoarthritis of the hand. *Osteoarthritis & Cartilage* 2006; 14(9):953-957.
- (30) Dahaghin S, Bierma-Zeinstra SMA, Ginai AZ, Pols HAP, Hazes JMW, Koes BW. Prevalence and pattern of radiographic hand osteoarthritis and association with pain and disability (the Rotterdam study). *Ann-Rheum-Dis* 2005; 64(5):682-687.
- (31) Lawrence JS. Rheumatism in cotton operatives. *British Journal of Industry Medicine* 1961; 18:270-276.
- (32) Jensen V, Boggild H, Johansen JP. Occupational use of precision grip and forceful gripping, and arthrosis of finger joints: a literature review. *Occupational Medicine (Oxford)* 1999; 49(6):383-388.
- (33) Lawrence JS, Bremner JM, Bier F. Osteo-arthritis. Prevalence in the population and relationship between symptoms and x-ray changes. *Ann Rheum Dis* 1966; 25(1):1-24.
- (34) Spector TD, Campion GD. Generalised osteoarthritis: a hormonally mediated disease. *Ann-Rheum-Dis* 1989; 48(6):523-527.
- (35) Erb A, Brenner H, Gunther KP, Sturmer T. Hormone replacement therapy and patterns of osteoarthritis: baseline data from the Ulm Osteoarthritis Study. *Ann-Rheum-Dis* 2000; 59(2):105-109.
- (36) Spector TD, Nandra D, Hart DJ, Doyle DV. Is hormone replacement therapy protective for hand and knee osteoarthritis in women?: The Chingford Study. *Ann-Rheum-Dis* 1997; 56(7):432-434.
- (37) Cooley HM, Stankovich J, Jones G. The association between hormonal and reproductive factors and hand osteoarthritis. *Maturitas* 2003; 45(4):257-265.
- (38) Maheu E, Dreiser R-L, Guillou GB, Dewailly J. Hand osteoarthritis patients characteristics according to the existence of a hormone replacement therapy. *Osteoarthritis & Cartilage* 2000; 8(SUPPL. A):S33-S37.
- (39) Haara MM, Arokoski JPA, Kroger H, Karkkainen A, Manninen P, Knekt P et al. Association of radiological hand osteoarthritis with bone mineral mass: A population study. *Rheumatology* 2005; 44(12):1549-1554.
- (40) Hochberg MC, Lethbridge-Cejku M, Scott Jr WW, Plato CC, Tobin JD. Appendicular bone mass and osteoarthritis of the hands in women: Data from the Baltimore longitudinal study of aging. *Journal of Rheumatology* 1994; 21(8):1532-1536.
- (41) Marcelli C, Favier F, Kotzki PO, Ferrazzi V, Picot MC, Simon L. The relationship between osteoarthritis of the hands, bone mineral density, and osteoporotic fractures in elderly women. *Osteoporosis International* 1995; 5(5):382-388.
- (42) Schneider DL, Barrett-Connor E, Morton DJ, Weisman M. Bone mineral density and clinical hand osteoarthritis in elderly men and women: the Rancho Bernardo study. *Journal of Rheumatology* 2002; 29(7):1467-1472.
- (43) Sowers M, Hochberg M, Crabbe JP, Muhich A, Crutchfield M, Updike S. Association of bone mineral density and sex hormone levels with osteoarthritis and the hand and knee in premenopausal women. *American Journal of Epidemiology* 1996; 143(1):38-47.

- (44) Jonsson H, Manolescu I, Stefansson SE, Ingvarsson T, Jonsson HH, Manolescu A et al. The inheritance of hand osteoarthritis in Iceland. *Arthritis & Rheumatism* 2003; 48(2):391-395.
- (45) Riyazi N, Meulenbelt I, Kroon HM, Roday KH, Helliö LG, Rosendaal FR et al. Evidence for familial aggregation of hand, hip, and spine but not knee osteoarthritis in siblings with multiple joint involvement: The GARP study. *Ann-Rheum-Dis* 2005; 64(3):438-443.
- (46) Spector TD, MacGregor AJ. Risk factors for osteoarthritis: genetics. *Osteoarthritis & Cartilage* 2004; 12:Suppl-44.
- (47) Zhang W, Doherty M. How important are genetic factors in osteoarthritis? Contributions from family studies. *Journal of Rheumatology* 2005; 32(6):1139-1142.
- (48) Bagge E, Bjelle A, Eden S, Svanborg A. Factors associated with radiographic osteoarthritis: Results from the population study 70-year-old people in Goteborg. *Journal of Rheumatology* 1991; 18(8):1218-1222.
- (49) Carman WJ, Sowers M, Hawthorne VM, Weissfeld LA. Obesity as a risk factor for osteoarthritis of the hand and wrist: a prospective study. *American Journal of Epidemiology* 1994; 139(2):119-129.
- (50) Cicuttini FM, Baker JR, Spector TD. The association of obesity with osteoarthritis of the hand and knee in women: a twin study. *Journal of Rheumatology* 1996; 23(7):1221-1226.
- (51) Haara MM, Manninen P, Kroger H, Arokoski JP, Karkkainen A, Knekt P et al. Osteoarthritis of finger joints in Finns aged 30 or over: prevalence, determinants, and association with mortality. *Ann-Rheum-Dis* 2003; 62(2):151-158.
- (52) Oliveria SA, Felson DT, Cirillo PA, Reed JI, Walker AM. Body weight, body mass index, and incident symptomatic osteoarthritis of the hand, hip, and knee. *Epidemiology* 1999; 10(2):161-166.
- (53) Chaisson CE, Zhang Y, Sharma L, Kannel W, Felson DT. Grip strength and the risk of developing radiographic hand osteoarthritis: Results from the Framingham study. *Arthritis & Rheumatism* 1999; 42(1):33-38.
- (54) Huskisson EC, Dieppe PA, Tucker AK, Cannell LB. Another look at osteoarthritis. *Ann-Rheum-Dis* 1979; 38(5):423-428.
- (55) Niu J, Zhang Y, La Valley M, Chaisson CE, Aliabadi P, Felson DT. Symmetry and clustering of symptomatic hand osteoarthritis in elderly men and women: The Framingham Study. *Rheumatology* 2003; 42(2):343-348.
- (56) Plato CC, Norris AH. Osteoarthritis of the hand: age-specific joint-digit prevalence rates. *Am J Epidemiol* 1979; 109(2):169-180.
- (57) Chaisson CE, Zhang Y, McAlindon TE, Hannan MT, Aliabadi P, Naimark A et al. Radiographic hand osteoarthritis: Incidence, patterns, and influence of pre-existing disease in a population based sample. *Journal of Rheumatology* 1997; 24(7):1337-1343.
- (58) Poole J, Sayer AA, Hardy R, Wadsworth M, Kuh D, Cooper C. Patterns of interphalangeal hand joint involvement of osteoarthritis among men and women: a British cohort study. *Arthritis & Rheumatism* 2003; 48(12):3371-3376.

- (59) Egger P, Cooper C, Hart DJ, Doyle DV, Coggon D, Spector TD. Patterns of joint involvement in osteoarthritis of the hand: the Chingford Study. *J Rheumatol* 1995; 22(8):1509-1513.
- (60) Neame R, Zhang W, Deighton C, Doherty M, Doherty S, Lanyon P et al. Distribution of radiographic osteoarthritis between the right and left hands, hips, and knees. *Arthritis & Rheumatism* 2004; 50(5):1487-1494.
- (61) Caspi D, Flusser G, Farber I, Ribak J, Leibovitz A, Habot B et al. Clinical, radiologic, demographic, and occupational aspects of hand osteoarthritis in the elderly. *Seminars in Arthritis & Rheumatism* 2001; 30(5):321-331.
- (62) Cicuttini FM, Baker J, Hart DJ, Spector TD. Relation between Heberden's nodes and distal interphalangeal joint osteophytes and their role as markers of generalised disease. *Ann-Rheum-Dis* 1998; 57(4):246-248.
- (63) Thaper A, Zhang W, Wright G, Doherty M. Relationship between Heberden's nodes and underlying radiographic changes of osteoarthritis. *Ann-Rheum-Dis* 2005; 64(8):1214-1216.
- (64) O'Reilly S, Johnson S, Doherty S, Muir K, Doherty M. Screening for hand osteoarthritis (OA) using a postal survey. *Osteoarthritis & Cartilage* 1999; 7(5):461-465.
- (65) Dreiser R-L, Maheu E, Guillou GB, Caspard H, Grouin J-M. Validation of an algofunctional index for osteoarthritis of the hand. *Revue du Rhumatisme (English Edition)* 1995; 62(6 SUPPL. 1):43S-53S.
- (66) Kjekken I, Dagfinrud H, Slatkowsky-Christensen B, Mowinckel P, Uhlig T, Kvien TK et al. Activity limitations and participation restrictions in women with hand osteoarthritis: patients' descriptions and associations between dimensions of functioning. *Ann-Rheum-Dis* 2005; 64(11):1633-1638.
- (67) Ricci JA, Stewart WF, Chee E, Leotta C, Foley K, Hochberg MC. Pain exacerbation as a major source of lost productive time in US workers with arthritis. *Arthritis & Rheumatism* 2005; 53(5):673-681.
- (68) Jones G, Cooley HM, Bellamy N. A cross-sectional study of the association between Heberden's nodes, radiographic osteoarthritis of the hands, grip strength, disability and pain. *Osteoarthritis & Cartilage* 2001; 9(7):606-611.
- (69) Bagis S, Sahin G, Yapici Y, Cimen OB, Erdogan C. The effect of hand osteoarthritis on grip and pinch strength and hand function in postmenopausal women. *Clinical Rheumatology* 2003; 22(6):420-424.
- (70) Patrick 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(12):978-982.
- (71) Leeb BF, Sautner J, Andel I, Rintelen B. SACRAH: a score for assessment and quantification of chronic rheumatic affections of the hands. *Rheumatology* 2003; 42(10):1173-1178.
- (72) Ziebland S, Fitzpatrick R, Jenkinson C, Mowat A, Mowat A. Comparison of two approaches to measuring change in health status in rheumatoid arthritis: the Health Assessment Questionnaire (HAQ) and modified HAQ. *Ann-Rheum-Dis* 1992; 51(11):1202-1205.
- (73) Backman C, Mackie H. Arthritis Hand Function Test: inter-rater reliability among self-trained raters. *Arthritis Care and Research* 1995; 8(1):10-15.

- (74) 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 & Rheumatism* 1992; 35(1):1-10.
- (75) Duruoz MT, Poiraudau S, Fermanian J, Menkes CJ, Amor B, Dougados M et al. Development and validation of a rheumatoid hand functional disability scale that assesses functional handicap. *Journal of Rheumatology* 1996; 23(7):1167-1172.
- (76) Sautner J, Andel I, Rintelen B, Leeb BF. Development of the M-SACRAH, a modified, shortened version of SACRAH (Score for the Assessment and Quantification of Chronic Rheumatoid Affections of the Hands). *Rheumatology* 2004; 43(11):1409-1413.
- (77) Bellamy N, Campbell J, Haraoui B, Gerez-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(11):863-869.
- (78) Dziedzic KS, Thomas E, Hay EM. A systematic search and critical review of measures of disability for use in a population survey of hand osteoarthritis (OA). *Osteoarthritis & Cartilage* 2005; 13(1):1-12.
- (79) Englund M, Paradowski PT, Lohmander LS. Association of Radiographic Hand Osteoarthritis with Radiographic Knee Osteoarthritis after Meniscectomy. *Arthritis & Rheumatism* 2004; 50(2):469-475.
- (80) Hochberg MC, Lane NE, Pressman AR, Genant HK, Scott JC, Nevitt M. The association of radiographic changes of osteoarthritis of the hand and hip in elderly women. *J Rheumatol* 1995; 22(12):2291-2294.
- (81) Mannoni A, Briganti MP, Di Bari M, Ferrucci L, Serni U, Masotti G et al. Prevalence of symptomatic hand osteoarthritis in community-dwelling older persons: The ICARE Dicomano study. *Osteoarthritis & Cartilage* 2000; 8(SUPPL. A):S11-S13.
- (82) Jonsson H, Valtysdottir ST, Kjartansson O, Brekkan A. Hypermobility associated with osteoarthritis of the thumb base: A clinical and radiological subset of hand osteoarthritis. *Ann-Rheum-Dis* 1996; 55(8):540-543.
- (83) Kraus VB, Li YJ, Martin ER, Jordan JM, Renner JB, Doherty M et al. Articular hypermobility is a protective factor for hand osteoarthritis. *Arthritis & Rheumatism* 2004; 50(7):2178-2183.
- (84) Spacek E, Poiraudau S, Fayad F, Lefevre-Colau MM, Beaudreuil J, Rannou F et al. Disability induced by hand osteoarthritis: are patients with more symptoms at digits 2-5 interphalangeal joints different from those with more symptoms at the base of the thumb? *Osteoarthritis & Cartilage* 2004; 12(5):366-373.
- (85) Smith D, Braunstein EM, Brandt KD, Katz BP. A radiographic comparison of erosive osteoarthritis and idiopathic nodal osteoarthritis. *Journal of Rheumatology* 1992; 19(6):896-904.
- (86) Verbruggen G, Goemaere S, Veys EM. Systems to assess the progression of finger joint osteoarthritis and the effects of disease modifying osteoarthritis drugs. *Clinical Rheumatology* 2002; 21(3):231-243.
- (87) Verbruggen G, Veys EM. Erosive and non-erosive hand osteoarthritis. Use and limitations of two scoring systems. *Osteoarthritis & Cartilage* 2000; 8(Suppl A):S45-S54.

- (88) Cobby M, Cushnaghan J, Creamer P, Dieppe P, Watt I. Erosive osteoarthritis: is it a separate disease entity? *Clinical Radiology* 1990; 42(4):258-263.
- (89) Fioravanti A, Tofi C, Cerase A, Priolo F, Marcolongo R. Capillaroscopic findings in erosive and nodal osteoarthritis of the hands. *Clinical Rheumatology* 2001; 20(3):174-176.
- (90) Punzi L, Ramonda R, Oliviero F, Sfriso P, Mussap M, Plebani M et al. Value of C reactive protein in the assessment of erosive osteoarthritis of the hand. *Ann-Rheum-Dis*.
- (91) Silvestri T, Pulsatelli L, Dolzani P, Punzi L, Meliconi R. Analysis of cartilage biomarkers in erosive and non-erosive osteoarthritis of the hands. *Osteoarthritis & Cartilage* 2004; 12(10):843-845.
- (92) Riestra JL, Sanchez A, Rodriques-Valverde V. Roentgenographic features of the arthropathy associated with CPPD crystal deposition disease. A comparative study with primary osteoarthritis. *Journal of Rheumatology* 1985; 12(6):1154-1158.
- (93) Fam AG, Stein J, Rubenstein J. Gouty arthritis in nodal osteoarthritis. *Journal of Rheumatology* 1996; 23(4):684-689.
- (94) Gerster JC, Rappoport G, Ginalski JM. Prevalence of periarticular calcifications in pyrophosphate arthropathy and their relation to nodal osteoarthritis. *Ann-Rheum-Dis* 1984; 43(2):255-257.
- (95) Erturk H, Bal S, Aydin M, Ugur O, Celiker R. The predictive value of bone scintigraphy in osteoarthritis relationship with age and severity of the disease. *Journal of Rheumatology & Medical Rehabilitation* 2002; 13(1):25-29.
- (96) Falsetti P, Frediani B, Fioravanti A, Acciai C, Baldi F, Filippou G et al. Sonographic study of calcaneal entheses in erosive osteoarthritis, nodal osteoarthritis, rheumatoid arthritis and psoriatic arthritis. *Scandinavian Journal of Rheumatology* 2003; 32(4):229-234.
- (97) Tan AL, Grainger AJ, Tanner SF, Shelley DM, Pease C, Emery P et al. High-resolution magnetic resonance imaging for the assessment of hand osteoarthritis. *Arthritis & Rheumatism* 2005; 52(8):2355-2365.
- (98) Tan AL, Grainger AJ, Tanner SF, Emery P, McGonagle D. A high-resolution magnetic resonance imaging study of distal interphalangeal joint arthropathy in psoriatic arthritis and osteoarthritis: are they the same? *Arthritis & Rheumatism* 2006; 54(4):1328-1333.
- (99) Bellamy N, Klestov A, Muirden K, Kuhnert P, Do KA, O'Gorman L et al. Perceptual variation in categorizing individuals according to American College of Rheumatology classification criteria for hand, knee, and hip osteoarthritis (OA): observations based on an Australian Twin Registry study of OA. *Journal of Rheumatology* 1999; 26(12):2654-2658.
- (100) Kessler S, Dieppe P, Fuchs J, Sturmer T, Gunther KP. Assessing the prevalence of hand osteoarthritis in epidemiological studies. The reliability of a radiological hand scale. *Ann-Rheum-Dis* 2000; 59(4):289-292.
- (101) Maheu E, Cadet C, Gueneugues S, Ravaud P, Dougados M. Reproducibility and sensitivity to change of four scoring methods for the radiological assessment of osteoarthritis of the hand. *Ann-Rheum-Dis* 2007; 66(4):464-469.
- (102) McCarthy C, Cushnaghan J, Dieppe P. The predictive role of scintigraphy in radiographic osteoarthritis of the hand. *Osteoarthritis & Cartilage* 1994; 2(1):25-28.

- (103) Punzi L, Ramonda R, Oliviero F, Sfriso P, Mussap M, Plebani M et al. Value of C reactive protein in the assessment of erosive osteoarthritis of the hand. *Ann-Rheum-Dis*.
- (104) Zhang W, Doherty M. EULAR recommendations for knee and hip osteoarthritis: a critique of the methodology. *Br J Sports Med* 2006; 40(8):664-669.

## Figure legends

Figure 1. Diagnostic tests or elements examined in hand osteoarthritis

Figure 2. “Gold” standards used in the assessment of the diagnostic tests or elements

Figure 3. Types of studies for the assessment of the diagnostic tests or elements

Figure 4. Likelihood ratio (LR) and 95%confidence interval (CI) of different diagnostic makers or features (useful ruled in cut-off level LR=10)

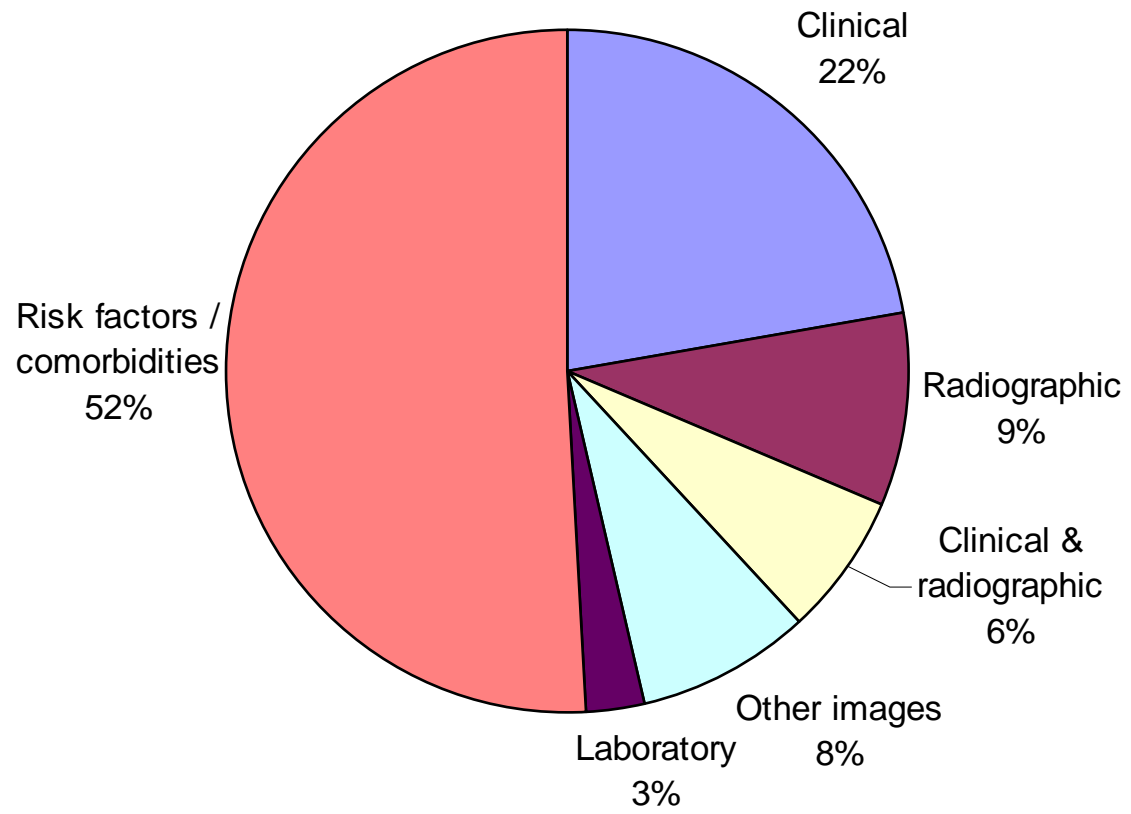
Figure 5. Diagnostic ladder of hand OA (source population prevalence 10%)

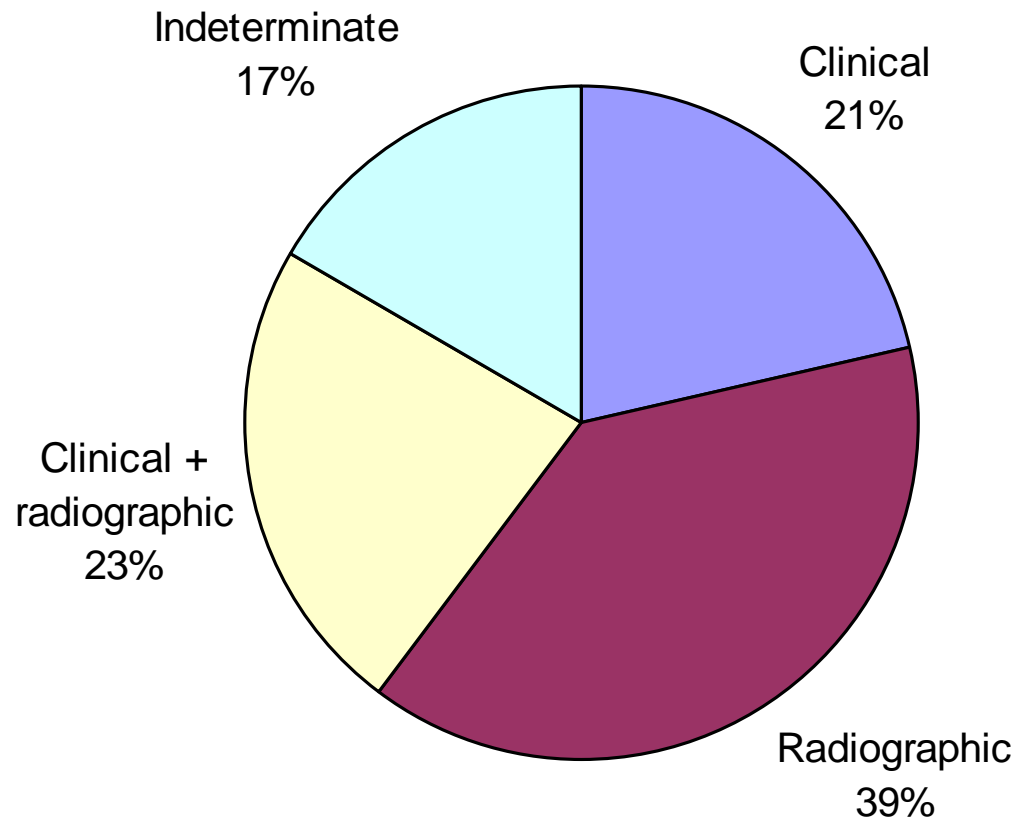
Figure 6. Incidence of hand osteoarthritis by age and sex 1991-1992

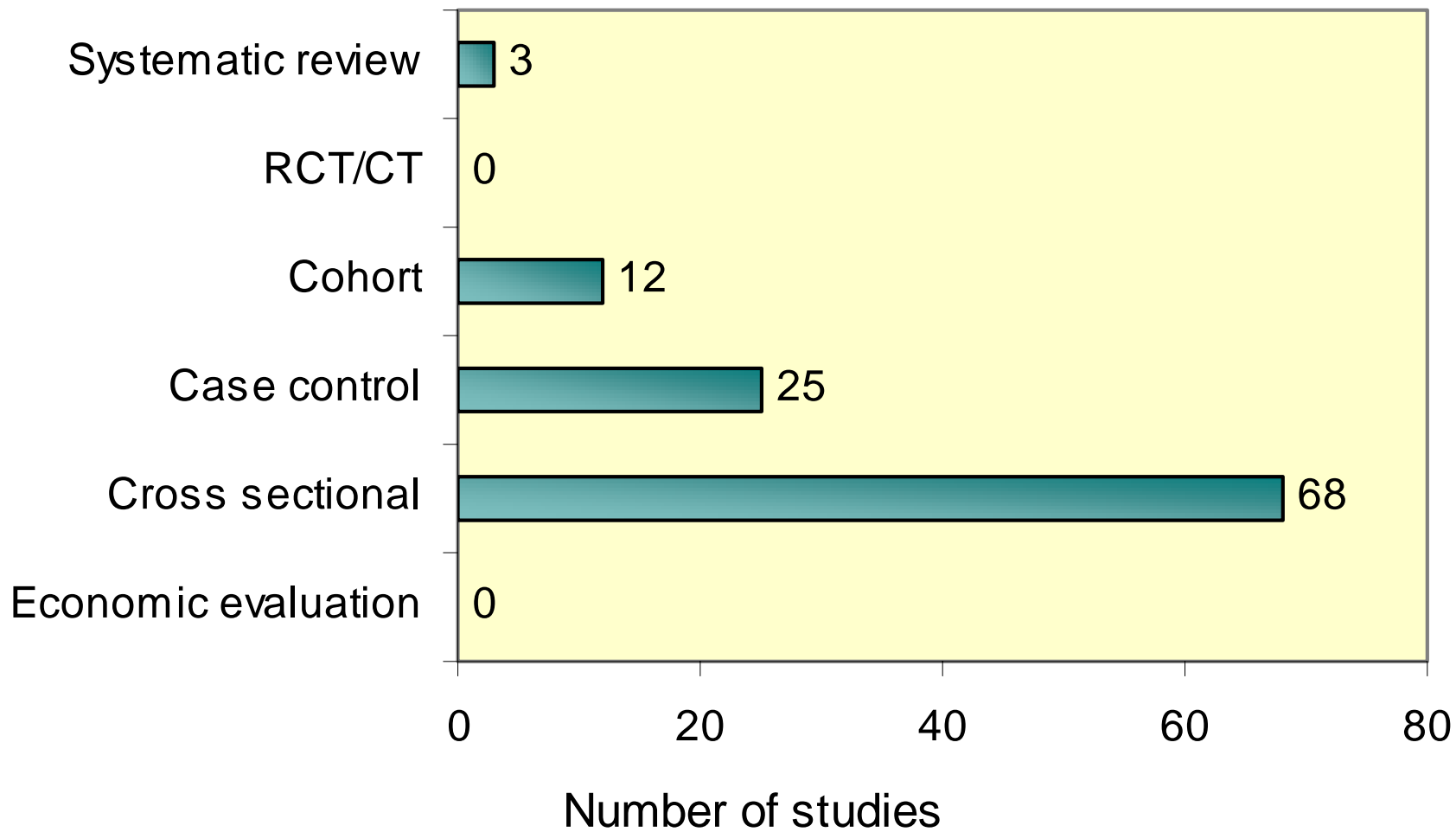
Figure 7. Target sites of involvement with hand OA, erosive OA, psoriatic arthritis, rheumatoid arthritis and haemochromatosis

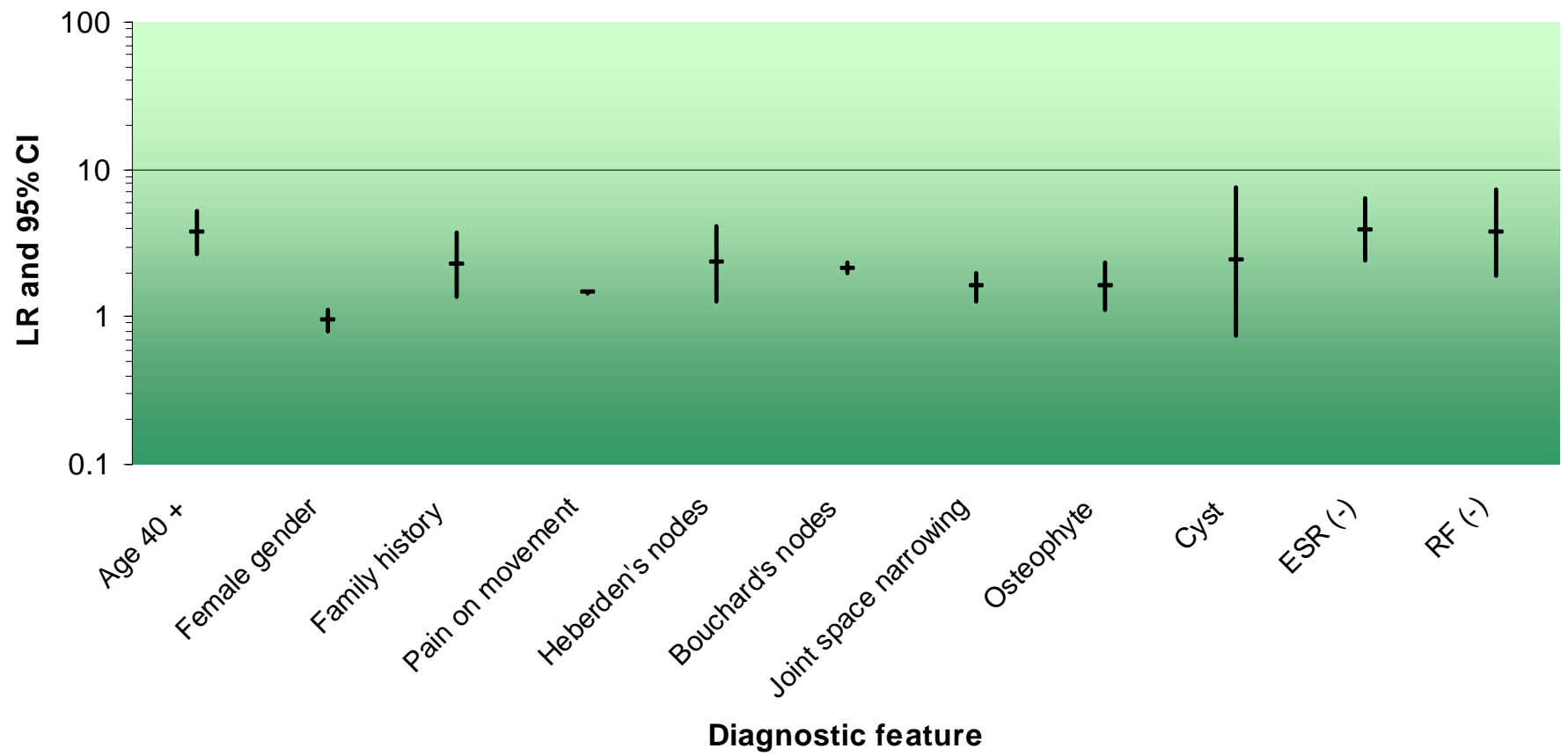
Figure 8. Contrasting radiographic features at IPJs of: (A) OA - focal narrowing, marginal osteophyte, sclerosis, osteochondral bodies; (B) erosive OA - subchondral erosion; (C) psoriasis - proliferative marginal erosion, retained or increased bone density; and (D) rheumatoid arthritis – non-proliferative marginal erosion, osteopenia.

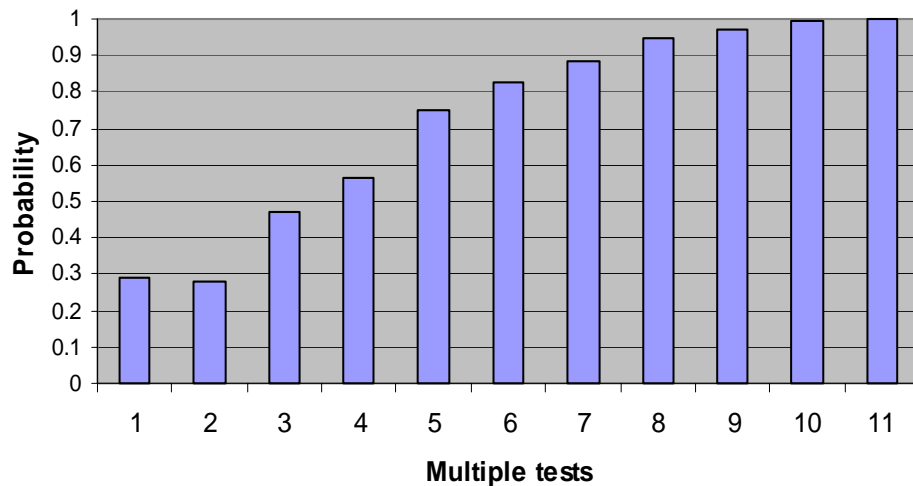
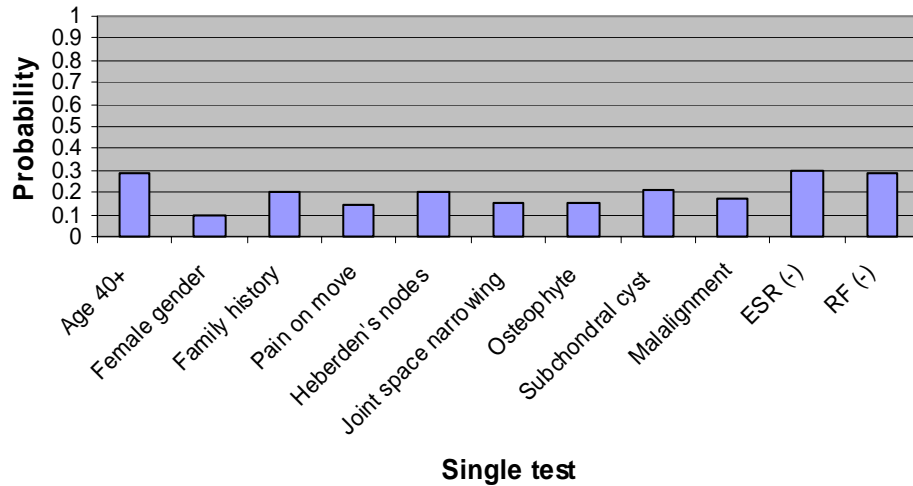




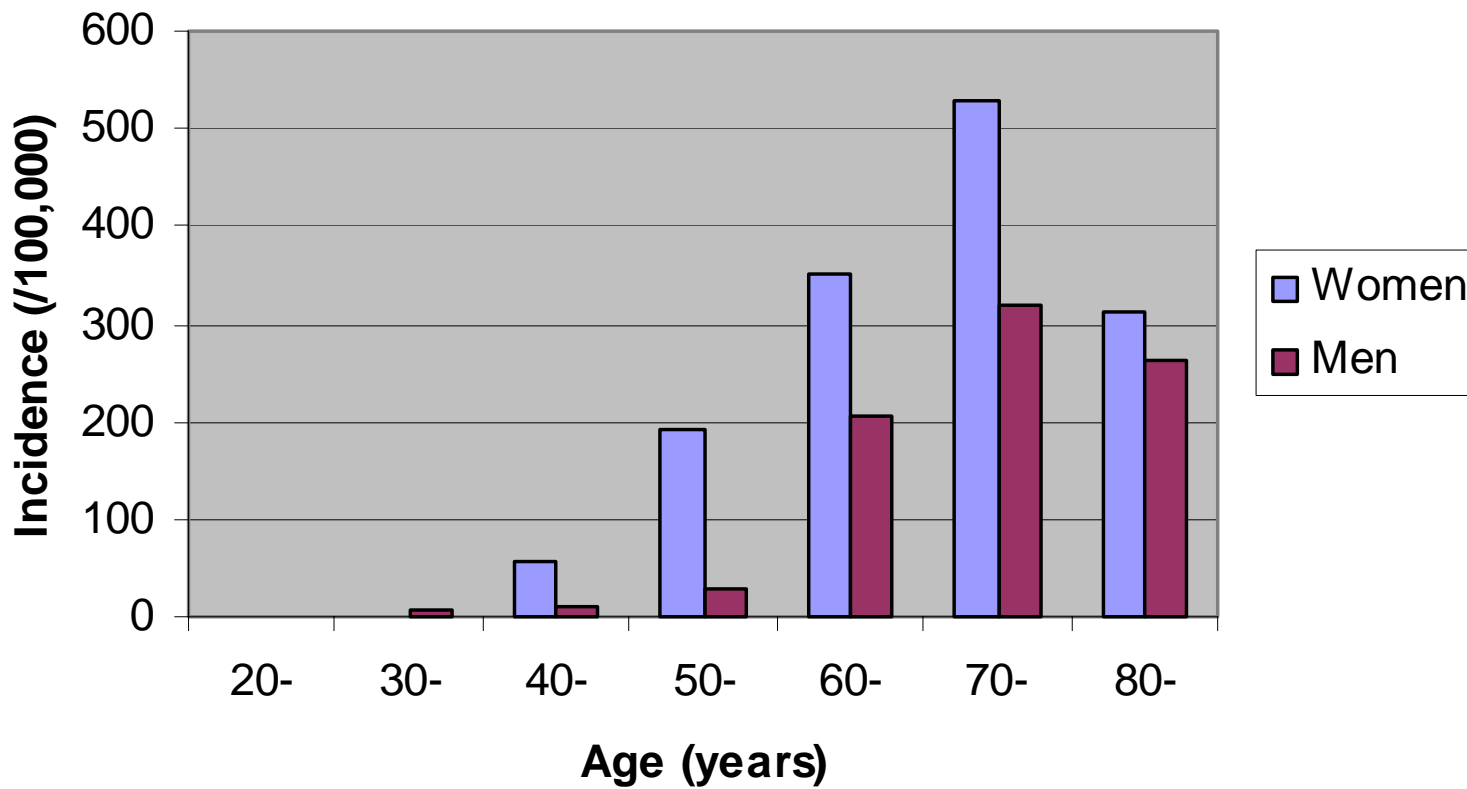


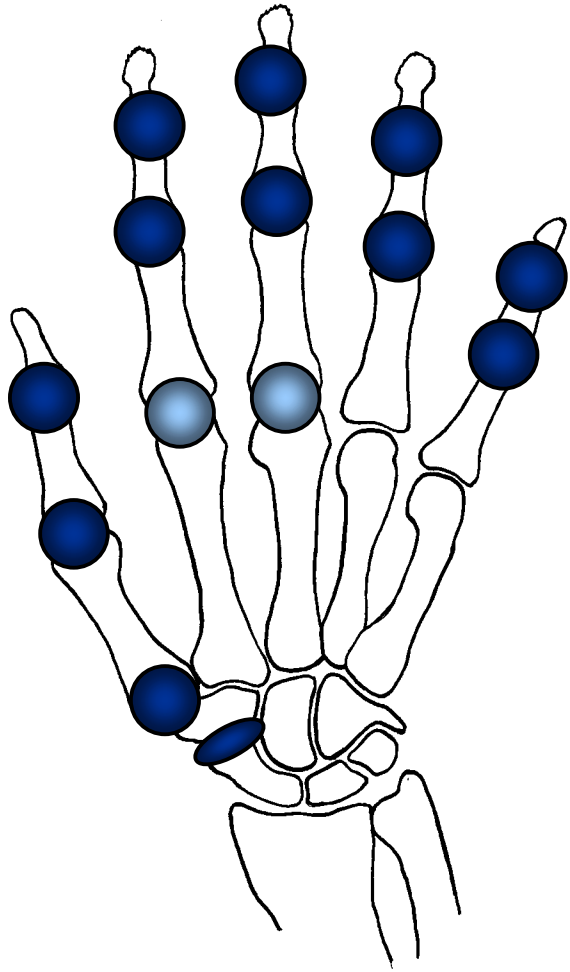




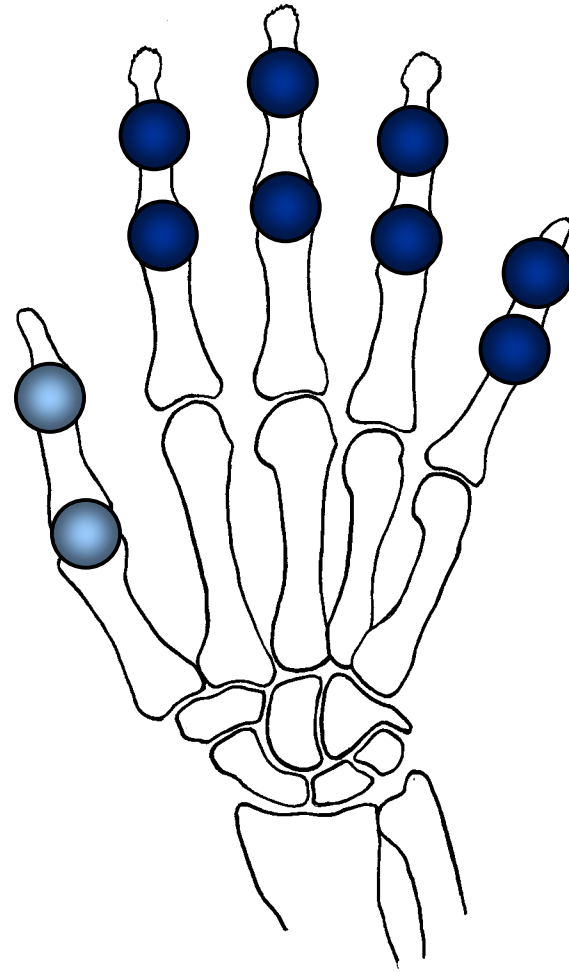


- Composite 1: Age > 40 yrs
- Composite 2: Age > 40 yrs and female gender
- Composite 3: Age > 40 yrs, female gender and family history
- Composite 4: Age > 40 yrs, female gender, family history and pain on move
- Composite 5: Age > 40 yrs, female gender, family history, pain on move and Heberden's nodes
- Composite 6: Age > 40 yrs, female gender, family history, pain on move, Heberden's nodes and joint space narrowing
- Composite 7: Age > 40 yrs, female gender, family history, pain on move, Heberden's nodes, joint space narrowing and osteophytes
- Composite 8: Age > 40 yrs, female gender, family history, pain on move, Heberden's nodes, joint space narrowing, osteophytes and subchondral cysts
- Composite 9: Age > 40 yrs, female gender, family history, pain on move, Heberden's nodes, joint space narrowing, osteophytes, subchondral cysts and malalignment
- Composite 10: Age > 40 yrs, female gender, family history, pain on move, Heberden's nodes, joint space narrowing, osteophytes, subchondral cysts, malalignment and ESR (-)
- Composite 11: Age > 40 yrs, female gender, family history, pain on move, Heberden's nodes, joint space narrowing, osteophytes, subchondral cysts, malalignment, ESR (-) and RF (-)

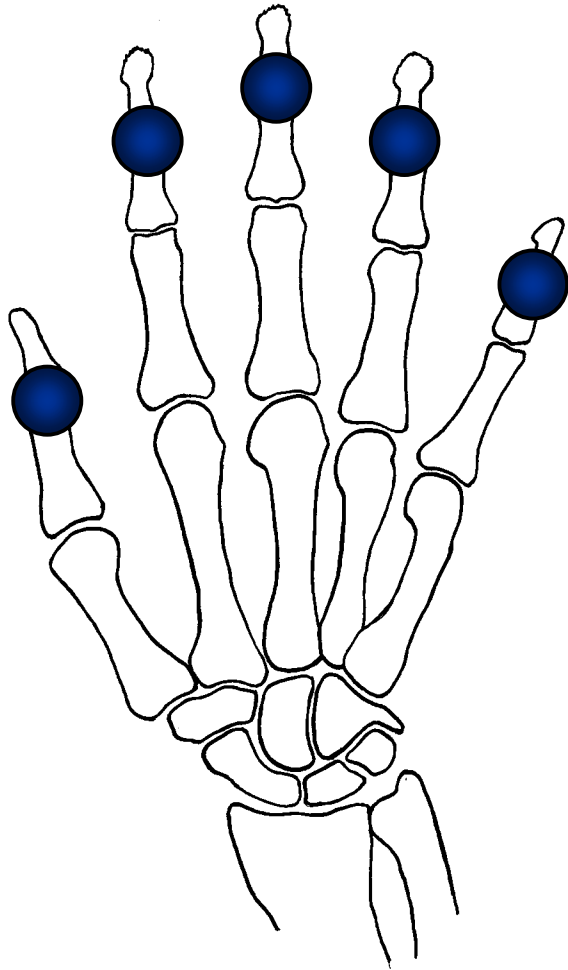




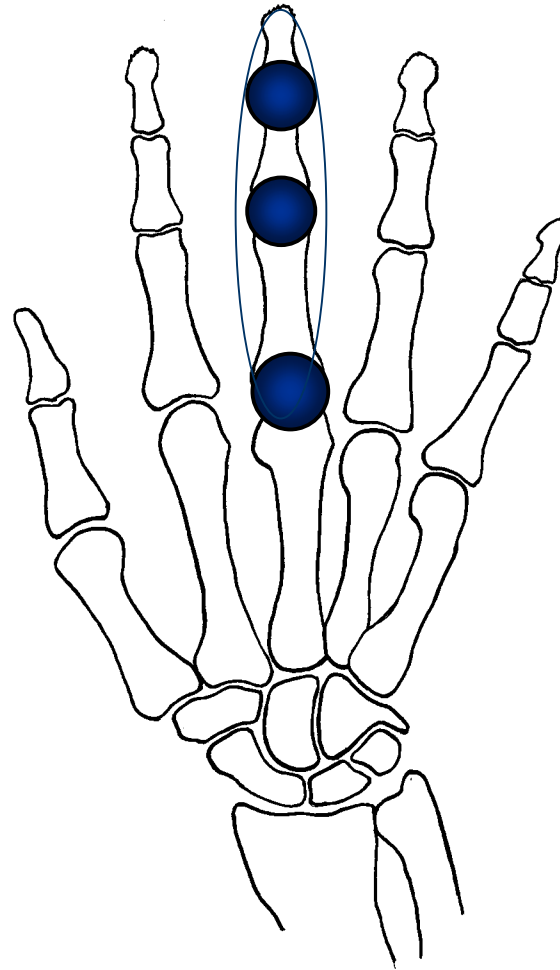
Hand OA



Erosive OA

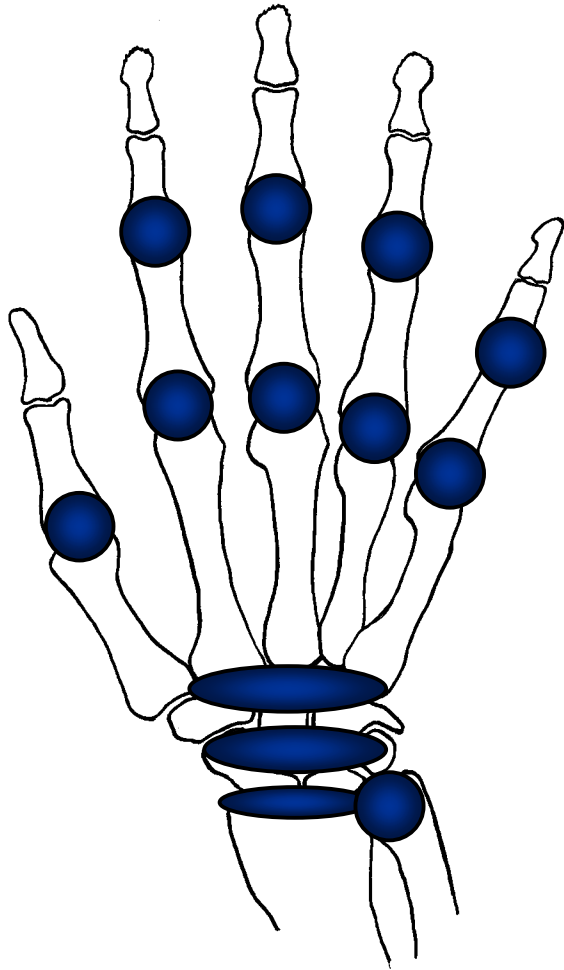


Psoriatic arthritis –  
DIPJ pattern

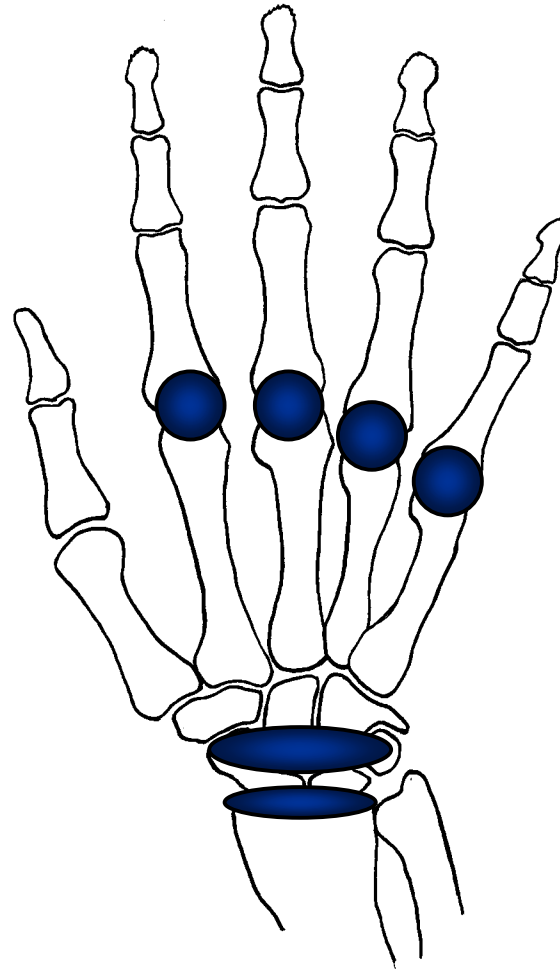


Psoriatic arthritis – dactylitis pattern  
(arthritis, osteitis, adjacent peri-  
articular inflammation)

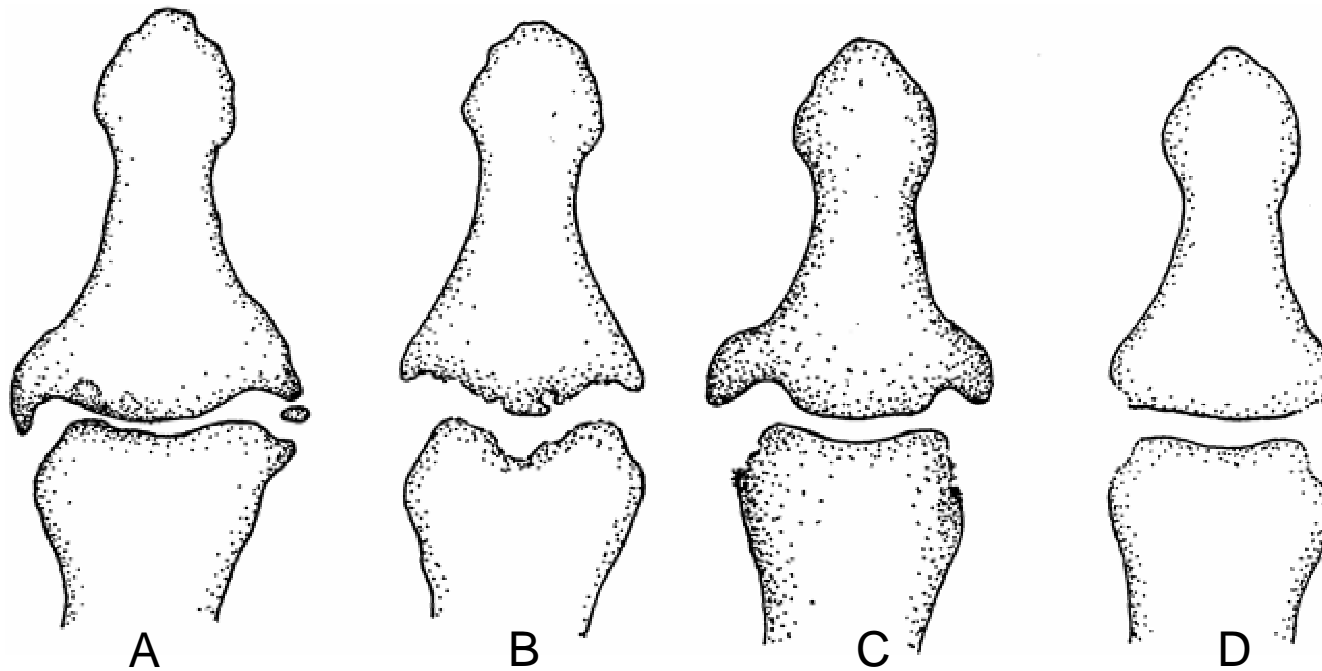




Rheumatoid arthritis



Haemochromatosis



Contrasting radiographic features at IPJs of: (A) OA - focal narrowing, marginal osteophyte, sclerosis, osteochondral bodies; (B) erosive OA - subchondral erosion; (C) psoriasis - proliferative marginal erosion, retained or increased bone density; and (D) rheumatoid arthritis – non-proliferative marginal erosion, osteopenia.