SUPPLEMENTARY MATERIAL

S1. Research questions

Making a diagnosis of rheumatoid arthritis

Q1- What is the evidence for the differential diagnostic value of individual imaging modalities for RA?

Q2- What is the evidence for the diagnostic value above clinical criteria of individual imaging modalities for RA

Detecting inflammation and damage

Q3- What is the evidence for the added value (sensitivity, specificity etc) of individual imaging modalities in detecting inflammation (synovitis, tenosynovitis, osteitis, bursitis, enthesitis) above clinical evaluation?

Q4- What is the evidence of the added value above clinical examination for the comparative value (sensitivity, specificity etc) of individual imaging modalities in detecting tissue damage (bone, cartilage, tendons, ligaments)?

Predicting prognosis in RA: Outcome

Q5- What is the evidence for the prognostic (prediction of outcome) value of individual imaging modalities for RA?

Q6- What is the evidence for the prognostic (prediction of outcome) value above other known prognostic markers of individual imaging modalities for RA?

(Outcome: activity, damage, QoL, HAQ, mortality, surgery, HE, cumulative/AUC/temporal change)

Predicting prognosis in RA: Response to treatment
Q7- What is the evidence for the prognostic (prediction of therapeutic response) value of individual imaging modalities for RA?

Q8- What is the evidence for the prognostic (prediction of therapeutic response) value above other known prognostic markers of individual imaging modalities for RA?
(Outcome: activity, damage, QoL, HAQ, mortality, surgery, HE, cumulative/AUC/temporal change)

Monitoring disease progression
Q9- When (time and under what clinical circumstances), where (which joints), how (modality specifics) and how often, and with what imaging modality should we monitor RA disease inflammation?

Q10- When (time and under what clinical circumstances), where (which joints), how (modality specifics) and how often, and with what imaging modality should we monitor RA disease damage?

Q11- When (time and under what clinical circumstances), where (which joints), how (modality specifics) how often, and with what imaging modality do we need to image the spine in RA?

Imaging in clinical remission
Q12- What is the relationship between individual imaging modalities and clinical remission in RA?

Q13- What is the impact with respect to outcome of imaging-detected inflammation /damage in the patient in clinical remission?
S2. Details of search strategy performed using EMBASE (1980 to June 2011); MEDLINE (1948 to June 2011); and the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, second quarter 2011) without language restrictions. The Cochrane Database of Systematic Reviews (CDSR) and the Database of Abstracts of Reviews of Effects (DARE) were also searched to ensure all potential studies were identified.

Search strategy, MEDLINE

1. exp arthritis, rheumatoid/
2. ((rheumat$ or reumat$) adj3 (arthrit$ or artrit$ or diseas$ or condition$ or nodule$)).tw.
3. 1 or 2
4. Diagnostic Imaging/
5. Radiography/
6. exp Magnetic Resonance Imaging/
7. magnetic resonance.tw.
8. mri$.tw.
9. exp Ultrasoundography/
10. (ultrasonic adj (diagnos$ or tomography or imaging$)).tw.
11. echotomograph$.tw.
12. echograph$.tw.
13. ultrasonography$.tw.
14. ultrasound.tw.
15. sonograph$.tw.
16. exp Tomography, X-Ray Computed/
17. exp Contrast Media/
18. computed adj2 tomography.tw.
19. cat scan$.tw.
20. ct.tw.
21. X-Rays/
22. xray$.tw.
23. (roentgen adj ray$).tw.
24. Absorptiometry, Photon/
25. Absorptiometr$.tw.
26. ((dxa or dexa) adj scan$).tw.
27. radiogram$.tw.
28. dxr.tw.
29. Radionuclide Imaging/
30. (Scintigraph$ or scintiphotograph$).tw.
31. ((gamma camera or radionuclide) adj imag$).tw.
32. radioisotope scan$.tw.
33. Positron-Emission Tomography/
34. Positron emission tomograp$.tw.
35. pet scan$.tw.
36. or/4-35
37. 3 and 36
38. randomized controlled trial.pt.
39. controlled clinical trial.pt.
40. randomized.ab.
41. placebo.ab.
42. drug therapy.fs.
43. randomly.ab.
44. trial.ab.
45. groups.ab.
46. or/38-45
47. (animals not (humans and animals)).sh.
48. 46 not 47
49. 37 and 48
50. exp cohort studies/
51. cohort$.tw.
52. controlled clinical trial.pt.
53. epidemiologic methods/
54. limit 53 to yr=1966-1989
55. exp case-control studies/
56. (case$ and control$).tw.
57. or/50-52,54-56
58. 37 and 57
59. ("review" or "review academic" or "review tutorial").pt.
60. (medline or medlars or embase or pubmed).tw,sh.
61. (scisearch or psychinfo or psycinfo).tw,sh.
62. (psychlit or psyclit).tw,sh.
63. cinahl.tw,sh.
64. ((hand adj2 search$) or (manual$ adj2 search$)).tw,sh.
65. (electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.
66. (pooling or pooled or mantel haenszel).tw,sh.
67. (retraction of publication or retracted publication).pt.
68. (peto or dersimonian or der simonian or fixed effect).tw,sh.
69. or/60-68
70. 59 and 69
71. meta-analysis.pt.
72. meta-analysis.sh.
73. (meta-analys$ or meta analys$ or metaanalys$).tw,sh.
74. (systematic$ adj5 review$).tw,sh.
75. (systematic$ adj5 overview$).tw,sh.
76. (quantitativ$ adj5 review$).tw,sh.
77. (quantitativ$ adj5 overview$).tw,sh.
78. (quantitativ$ adj5 synthesis$).tw,sh.
79. (methodologic$ adj5 review$).tw,sh.
80. (methodologic$ adj5 overview$).tw,sh.
81. (integrative research review$ or research integration).tw.
82. or/71-81
83. 37 and 82
84. limit 37 to "diagnosis (best balance of sensitivity and specificity)"
85. or/49,58,83-84

**Search strategy, EMBASE**

1. exp rheumatoid arthritis/
2. ((rheumat$ or reumat$) adj3 (arthrit$ or artrit$ or diseas$ or condition$ or nodule$)).tw.
3. 1 or 2
4. diagnostic imaging/
5. radiography/
6. exp nuclear magnetic resonance imaging/
7. magnetic resonance.tw.
8. mri$.tw.
9. exp echography/
10. (ultrasonic adj (diagnos$ or tomography or imaging$)).tw.
11. echotomograph$.tw.
12. echograph$.tw.
13. ultrasonography$.tw.
14. ultrasound.tw.
15. sonograph$.tw.
16. exp computer assisted tomography/
17. exp contrast medium/
18. (computed adj2 tomography).tw.
19. cat scan$.tw.
20. ct.tw.
21. X ray/
22. xray$.tw.
23. (roentgen adj ray$).tw.
24. photon absorptiometry/
25. Absorptiometry.tw.
26. ((dxa or dexas) adj scan$).tw.
27. radiogram$_.tw.
28. dxr.tw.
29. scintiscanning/
30. (Scintigraph$ or scintiphotograph$).tw.
31. ((gamma camera or radionuclide) adj imag$).tw.
32. radioisotope scan$.tw.
33. positron emission tomography/
34. Positron emission tomography$.tw.
35. pet scan$.tw.
36. or/4-35
37. 3 and 36
38. (random$ or placebo$).ti,ab.
39. ((single$ or double$ or triple$ or treble$ and (blind$ or mask$)).ti,ab.
40. controlled clinical trial$.ti,ab.
41. RETRACTED ARTICLE/
42. or/38-41
43. (animal$ not human$).sh,hw.
44. 42 not 43
45. 37 and 44
46. exp cohort analysis/
47. exp longitudinal study/
48. exp prospective study/
49. exp follow up/
50. cohort$.tw.
51. exp case control study/
52. (case$ and control$).tw.
53. or/46-52
54. 37 and 53
55. exp review/
56. (literature adj3 review$).ti,ab.
57. exp meta analysis/
58. exp "Systematic Review"/
59. or/55-58
60. (medline or medlars or embase or pubmed or cinahl or amed or psychlit or psyclit or psychinfo or psycinfo or scisearch or cochrane).ti,ab.
61. RETRACTED ARTICLE/
62. 60 or 61
63. 59 and 62
64. (systematic$ adj2 (review$ or overview)).ti,ab.
65. (meta?anal$ or meta anal$ or meta-anal$ or meta anal$ or metanal$).ti,ab.
66. or/63-65
67. 37 and 66
68. limit 37 to "diagnosis (best balance of sensitivity and specificity)"
69. or/45,54,67-68

**Search strategy, The Cochrane Library**

#1 MeSH descriptor Arthritis, Rheumatoid explode all trees
#2 ((rheumat* or reumat*) near/3 (arthrit* or artrit* or diseas* or condition* or nodule*)):ti,ab
#3 (#1 OR #2)
#4 MeSH descriptor Diagnostic Imaging, this term only
#5 MeSH descriptor Radiography, this term only
#6 MeSH descriptor Magnetic Resonance Imaging explode all trees
#7 "magnetic resonance":ti,ab
#8 mri*:ti,ab
#9 MeSH descriptor Ultrasonography explode all trees
#10 (ultrasonic next (diagnos* or tomography or imaging*)):ti,ab
#11 echotomograph*:ti,ab
#12 echograph*:ti,ab
#13 ultrasonography:ti,ab
#14 ultrasound:ti,ab
#15 sonograph*:ti,ab
#16 MeSH descriptor Tomography, X-Ray Computed explode all trees
#17 MeSH descriptor Contrast Media explode all trees
#18 "computed tomography":ti,ab
#19 "Cat scan*":ti,ab
#20 ct:ti,ab
#21 MeSH descriptor X-Rays, this term only
#22 xray*:ti,ab
#23 (roentgen next ray*):ti,ab
#24 MeSH descriptor Absorptiometry, Photon, this term only
#25 Absorptiometr*:ti,ab
#26 ((dxa or dexe) next scan*):ti,ab
#27 radiogram*:ti,ab
#28 dxr:ti,ab
#29 MeSH descriptor Radionuclide Imaging, this term only
#30 (Scintigraph* or scintiphotograph*):ti,ab
#31 ((gamma camera or radionuclide) next imag*):ti,ab
#32 "radioisotope scan*":ti,ab
#33 MeSH descriptor Positron-Emission Tomography, this term only
#34 "Positron emission tomograp*":ti,ab
#35 "pet scan*":ti,ab
#36 (#4 OR #5 OR #6 OR #7 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35)
#37 (#3 AND #36)
Figure S3. Flowchart showing the literature search of 6888 articles, from which 346 articles were selected for detailed review; 199 articles met the inclusion criteria.
### Table S4. Number of included articles per question

<table>
<thead>
<tr>
<th>Question</th>
<th>Number of included articles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1- What is the evidence for the differential diagnostic value of individual imaging modalities for RA?</td>
<td>3</td>
</tr>
<tr>
<td>Q2- What is the evidence for the diagnostic value above clinical criteria of individual imaging modalities for RA?</td>
<td>15</td>
</tr>
<tr>
<td>Q3- What is the evidence for the added value (sensitivity, specificity etc) of individual imaging modalities in detecting inflammation (synovitis, tenosynovitis, osteitis, bursitis, enthesitis) above clinical evaluation?</td>
<td>51</td>
</tr>
<tr>
<td>Q4- What is the evidence of the added value above clinical examination for the comparative value (sensitivity, specificity etc) of individual imaging modalities in detecting tissue damage (bone, cartilage, tendons, ligaments)?</td>
<td>3</td>
</tr>
<tr>
<td>Q5- What is the evidence for the prognostic (prediction of outcome) value of individual imaging modalities for RA?</td>
<td>12</td>
</tr>
<tr>
<td>Q6- What is the evidence for the prognostic (prediction of outcome) value above other known prognostic markers of individual imaging modalities for RA?</td>
<td>38</td>
</tr>
<tr>
<td>Q7- What is the evidence for the prognostic (prediction of therapeutic response) value of individual imaging modalities for RA?</td>
<td>0</td>
</tr>
<tr>
<td>Q8- What is the evidence for the prognostic (prediction of therapeutic response) value above other known prognostic markers of individual imaging modalities for RA?</td>
<td>2</td>
</tr>
<tr>
<td>Q9- When (time and under what clinical circumstances), where (which joints), how (modality specifics) and how often, and with</td>
<td>23</td>
</tr>
<tr>
<td>Question</td>
<td>Answer</td>
</tr>
<tr>
<td>--------------------------------------------------------------------------</td>
<td>--------</td>
</tr>
<tr>
<td>what imaging modality should we monitor RA disease inflammation?</td>
<td></td>
</tr>
<tr>
<td>Q10- When (time and under what clinical circumstances), where (which joints), how (modality specifics) and how often, and with what imaging modality should we monitor RA disease damage?</td>
<td>55</td>
</tr>
<tr>
<td>Q11- When (time and under what clinical circumstances), where (which joints), how (modality specifics) how often, and with what imaging modality do we need to image the spine in RA?</td>
<td>13</td>
</tr>
<tr>
<td>Q12- What is the relationship between individual imaging modalities and clinical remission in RA?</td>
<td>7</td>
</tr>
<tr>
<td>Q13- What is the impact with respect to outcome of imaging-detected inflammation /damage in the patient in clinical remission?</td>
<td>7</td>
</tr>
</tbody>
</table>
S5. Reference list of included articles per recommendation

**Recommendation 1.** (in patients with at least one joint with definite clinical synovitis)

When there is diagnostic doubt, conventional radiography, US or MRI can be used to improve the certainty of a diagnosis of RA above clinical criteria alone.


**Recommendation 2.** The presence of inflammation seen with US or MRI can be used to predict the progression to clinical RA from undifferentiated inflammatory arthritis


**Recommendation 3.** US and MRI are superior to clinical examination in the detection of joint inflammation; these techniques should be considered for more accurate assessment of inflammation


46. Tannenbaum H, Rosenthall L. A prospective study comparing the clinical examination
of peripheral joints with radionuclide scintigraphy in patients with rheumatoid arthritis.


**Recommendation 4.** Conventional radiography of the hands and feet should be used as the initial imaging technique to detect damage. However, US and/or MRI should be considered if conventional radiographs do not show damage and may be used to detect damage at an earlier time point (especially in early RA)


Recommendation 5. MRI bone oedema is a strong independent predictor of subsequent radiographic progression in early RA and should be considered for use as a prognostic indicator. Joint inflammation (synovitis) detected by MRI or US as well as joint damage detected by conventional radiographs, MRI or US can also be considered for the prediction of further joint damage


10. Dixey J, Solymossy C, Young A. Is it possible to predict radiological damage in early rheumatoid arthritis (RA)? A report on the occurrence, progression, and prognostic factors of radiological erosions over the first 3 years in 866 patients from the early RA study (ERAS). *J Rheumatol* 2004;31:48-54.


31. McQueen FM, Stewart N, Crabbe J, et al. Magnetic resonance imaging of the wrist in


**Recommendation 6.** Inflammation seen on imaging may be more predictive of a therapeutic response than clinical features of disease activity; imaging may be used to predict response to treatment


**Recommendation 7.** Given the improved detection of inflammation by MRI and US than by clinical examination, they may be useful in monitoring disease activity


2. Calisir C, Murat Aynaci Al, Korkmaz C. The accuracy of magnetic resonance imaging of the hands and feet in the diagnosis of early rheumatoid arthritis. *Joint Bone Spine*


**Recommendation 8.** The periodic evaluation of joint damage, usually by radiographs of the hands and feet, should be considered. MRI (and possibly US) is more responsive to change in joint damage and can be used to monitor disease progression


33. Lerch K, Borisch N, Paetzel C, et al. Sonographic evaluation of the elbow in


Recommendation 9. Monitoring of functional instability of the cervical spine by lateral radiograph obtained in flexion and neutral should be performed in patients with clinical suspicion of cervical involvement. When the radiograph is positive or specific neurological symptoms and signs are present, MRI should be performed


Recommendation 10. MRI and US can detect inflammation that predicts subsequent joint damage, even when clinical remission is present and can be used to assess persistent inflammation


