EULAR-PReS points to consider for the use of imaging in the diagnosis and management of juvenile idiopathic arthritis in clinical practice

A N Colebatch-Bourn,1,2 C J Edwards,1,3 P Collado,4 M-A D’Agostino,5,6 R Hemke,7 S Jousse-Joulin,8 M Maas,7 A Martini,9,10 E Naredo,11 M Østergaard,12,13 M Rooney,14 N Tzaribachev,15 M A van Rossum,16,17 J Vojinovic,18 P G Conaghan,19 C Malattia9,10

ABSTRACT
To develop evidence based points to consider the use of imaging in the diagnosis and management of juvenile idiopathic arthritis (JIA) in clinical practice. The task force comprised a group of paediatric rheumatologists, rheumatologists experienced in imaging, radiologists, methodologists and patients from nine countries. Eleven questions on imaging in JIA were generated using a process of discussion and consensus. Research evidence was searched systematically for each question using MEDLINE, EMBASE and Cochrane CENTRAL. Imaging modalities included were conventional radiography, ultrasound, MRI, CT, scintigraphy and positron emission tomography. The experts used the evidence obtained from the relevant studies to develop a set of points to consider. The level of agreement of each question to consider was assessed using a numerical rating scale. A total of 13 277 references were identified from the search process, from which 204 studies were included in the systematic review. Nine points to consider were produced, taking into account the heterogeneity of JIA, the lack of normative data and consequent difficulty identifying pathology. These encompassed the role of imaging in making a diagnosis of JIA, detecting and monitoring inflammation and damage, predicting outcome and response to treatment, use of guided therapies, progression and remission. Level of agreement for each proposition varied according to the research evidence and expert opinion. Nine points to consider and a related research agenda for the role of imaging in the management of JIA were developed using published evidence and expert opinion.

INTRODUCTION
Juvenile idiopathic arthritis (JIA) is a heterogeneous group of conditions with onset under the age of 16 years with unknown aetiology and persistence of symptoms for over 6 weeks. Imaging plays an important role in diagnosis and monitoring of patients with JIA, but until recently there were few studies in this area.

A European League against Rheumatism (EULAR) —Pediatric Rheumatology European Society (PReS) task force was convened to produce evidence and consensus-based recommendations on the use of imaging in the diagnosis and management of JIA in clinical practice for use by secondary care professionals caring for children with JIA, to help define standards of care for appropriate imaging.

METHODS
An expert group of paediatric rheumatologists, rheumatologists with imaging expertise, radiologists, methodologists and a fellow (16 people, representing 9 countries) participated. The task force used a rigorous procedure as described in the updated EULAR standardised operating procedures. Full methodological details are given in the online supplementary material S1.

At an initial meeting, members developed questions relevant to key aspects of the use of imaging in JIA. Eleven research questions were agreed by consensus, encompassing the role of imaging in making a diagnosis, detecting inflammation and damage, predicting outcome and response to treatment, the use of guided treatment, monitoring disease progression, and remission (see online supplementary text research questions S2). A detailed systematic search of the published literature was performed on studies involving the use of imaging in children with JIA. Imaging modalities included were X-ray described as conventional radiography (CR), ultrasound (US), MRI, CT, scintigraphy and positron emission tomography. Included studies were evaluated for risk of bias and applicability using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 tool. Following presentation of the literature review at a second meeting, experts produced points to consider (PTC) with final agreement by a process of discussion and consensus. The available evidence for each recommendation was scored according to the Oxford Centre for Evidence-Based Medicine level of evidence. The experts anonymously scored their level of agreement for each proposition using a 0–10 numerical rating scale (0=do not agree at all, 10=fully agree). Scores reflected research evidence and clinical expertise. An agenda for future research was also agreed upon following presentation of the literature review.

Three patient representatives (one child and two young adults with a diagnosis of JIA) and two parents of children with JIA participated in the development of the PTC at a Patient and Public Involvement event; further details are given in the online supplementary material S1.

RESULTS
The database search (November 2013) resulted in 13 277 records leaving 10 925 articles after...
deduplication. Four hundred and thirty-three articles were included for detailed review once exclusions were made based on title or abstract. All full text articles written in English were retrieved for review, of which 244 articles were excluded leaving 189 articles for inclusion. The hand search identified 15 additional articles, resulting in a total of 204 articles for inclusion (see flow chart in the online supplementary figure S4). Articles that were relevant to multiple research questions were included in the review as necessary. The number of articles included per question is shown in the online supplementary table S5.

The task force produced nine PTC which are presented with the level of evidence, grade of recommendation and level of agreement in Table 1. The task force felt that the supporting data was not sufficient to produce ‘recommendations’ so they were categorised as ‘points to consider’. Scores for risk of bias and applicability of the included studies according to QUADAS-2, a full reference list for articles included in each recommendation, and feedback given at the Patient and Public Involvement meeting are given in the online supplementary text S6 S7 and S8.

### Points to consider

#### Making a diagnosis of JIA

**PTC 1:** US and MRI are superior to clinical examination in the evaluation of joint inflammation; these techniques should be considered for more accurate detection of inflammation, in diagnosis and assessing extent of joint involvement.

- There is a paucity of data on the joint-specific imaging features present during growth and skeletal development in healthy children. Understanding normative data is essential for interpretation of imaging abnormalities. For example, some physiological features of recently ossified bones can be misinterpreted as cortical erosions, cartilage thickness may vary with skeletal maturation and vascularity of epiphyses will change with ageing.
- Joint inflammation at certain developmental time points may cause specific structural changes, further challenging imaging assessment.
- The appropriateness and feasibility of different imaging modalities differs with age, related to radiation exposure and requirement for sedation. Every effort should be made to avoid unnecessary radiation exposure. However, there is a long established experience with the use of CR to demonstrate damage.
- Patient experience with different imaging modalities is affected by their age and development. It is important to provide a ‘child friendly’ environment.

#### Overarching principles

The task force produced general statements that should be considered when interpreting the PTC. These principles cover the imaging needs of inflammatory arthritis is children and assume that other important differentials such as infection have been ruled out.

- JIA is an umbrella term for all forms of inflammatory arthritis that begins before the age of 16 years, persists for more than 6 weeks and is of unknown origin. This heterogeneous group of diseases is currently classified according to the International League of Associations for Rheumatology classification. There is a lack of information on imaging related to JIA categories at present.

<table>
<thead>
<tr>
<th>Point to consider</th>
<th>Level of evidence</th>
<th>Grade of recommendation</th>
<th>Level of agreement, mean NRS 0–10 (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 US and MRI are superior to clinical examination in the evaluation of joint inflammation; these techniques should be considered for more accurate detection of inflammation, in diagnosis and assessing extent of joint involvement.</td>
<td>3b</td>
<td>C</td>
<td>9.07 (6–10)</td>
</tr>
<tr>
<td>2 When there is clinical diagnostic doubt, CR, US or MRI can be used to improve the certainty of a diagnosis of JIA above clinical features alone.</td>
<td>3b</td>
<td>C</td>
<td>9.43 (9–10)</td>
</tr>
<tr>
<td>3 If detection of structural abnormalities or damage is required, CR can be used. However MRI or US may be used to detect damage at an earlier time point than CR.</td>
<td>3b</td>
<td>C</td>
<td>8.71 (5–10)</td>
</tr>
<tr>
<td>4 In JIA imaging may be of particular benefit over routine clinical evaluation when assessing certain joints, particularly the use of MRI in detecting inflammation of the TMJ and axial involvement.</td>
<td>3b</td>
<td>C</td>
<td>9.64 (8–10)</td>
</tr>
<tr>
<td>5 Imaging in JIA may be considered for use as a prognostic indicator. Damage on CR can be used for the prediction of further joint damage. Persistent inflammation on US or MRI may be predictive of subsequent joint damage.</td>
<td>4</td>
<td>C</td>
<td>9.07 (5–10)</td>
</tr>
<tr>
<td>6 In JIA, US and MRI can be useful in monitoring disease activity given their sensitivity over clinical examination and good responsiveness. MRI should be considered for monitoring axial disease and TMJ.</td>
<td>3b</td>
<td>C</td>
<td>9.07 (7–10)</td>
</tr>
<tr>
<td>7 The periodic evaluation of joint damage should be considered. The imaging modality used may be joint dependent.</td>
<td>3b</td>
<td>C</td>
<td>8.29 (5–10)</td>
</tr>
<tr>
<td>8 US can be used for accurate placement of intra-articular injections.</td>
<td>3b</td>
<td>C</td>
<td>9.64 (8–10)</td>
</tr>
<tr>
<td>9 US and MRI can detect inflammation when clinically inactive disease is present; this may have implications for monitoring.</td>
<td>3b</td>
<td>C</td>
<td>8.86 (5–10)</td>
</tr>
</tbody>
</table>

The level of evidence and grade of recommendation are based on the Oxford Centre for Evidence-Based Medicine system. Level of evidence scale, 1a–5; grade of recommendation scale; A–D. NRS, numerical rating scale (0=do not agree at all, 10=fully agree).

CR, conventional radiography; JIA, juvenile idiopathic arthritis; TMJ, temporomandibular joint; US, ultrasound.
### Table 2  Point to consider 1: Summary of included studies comparing imaging with CE in the detection of joint inflammation

<table>
<thead>
<tr>
<th>Ultrasound</th>
<th>MRI</th>
<th>CR</th>
</tr>
</thead>
<tbody>
<tr>
<td>US knees vs CE</td>
<td>MRI knees vs CE</td>
<td>CR knees vs CE</td>
</tr>
<tr>
<td>13 studies</td>
<td>13-15 36 72 84-87</td>
<td>3 studies</td>
</tr>
<tr>
<td>Detection rate, mean (range)</td>
<td>Detection rate, mean (range)</td>
<td>Detection rate, mean (range)</td>
</tr>
<tr>
<td>US vs CE</td>
<td>MRI vs CE</td>
<td>CR vs CE</td>
</tr>
<tr>
<td>Synovitis/effusion (12 studies)</td>
<td>Synovitis vs clinical swelling (3 studies)</td>
<td>Joint distension vs swelling (3 studies)</td>
</tr>
<tr>
<td>13 14 34 36 76-83</td>
<td>13 14 36 86</td>
<td>13 15 85</td>
</tr>
<tr>
<td>1.19-fold (0.14–3.67-fold)</td>
<td>1.02-fold (0.96–1.12-fold)</td>
<td>0.69-fold (0.45–1.0-fold)</td>
</tr>
<tr>
<td>Effusion (1 study)</td>
<td>Effusion vs swelling (5 studies)</td>
<td>Effusion vs pain (1 study)</td>
</tr>
<tr>
<td>Agreement k=0.54</td>
<td>1.07-fold (0.75–1.33-fold)</td>
<td>1.45-fold (1.33–1.57-fold)</td>
</tr>
<tr>
<td>PD vascularity (2 studies)</td>
<td>Synovial volume vs CRP (1 study)</td>
<td>Joint distension vs pain (1 study)</td>
</tr>
<tr>
<td>13 15 84-87</td>
<td>n=0.51–0.80</td>
<td>1.57-fold</td>
</tr>
<tr>
<td>1.63-fold (0.96–2.71-fold)</td>
<td>p=0.000–0.036</td>
<td></td>
</tr>
<tr>
<td>Synovitis/effusion (5 studies)</td>
<td>Synovial hypertrophy vs pain (1 study)</td>
<td>MRI inflammation (4 studies)</td>
</tr>
<tr>
<td>MRI vs CE</td>
<td>13 15 90-91</td>
<td>13 15 90-91</td>
</tr>
<tr>
<td>0.85-fold (0.13–1.39-fold)</td>
<td>0.88-fold (0.50–1.78-fold)</td>
<td>0.80-fold</td>
</tr>
<tr>
<td>Synovitis/effusion vs pain (1 study)</td>
<td>Association p=0.006</td>
<td>Joint distension vs clinical effusion (1 study)</td>
</tr>
<tr>
<td>13 15 85</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.03-fold</td>
<td></td>
<td>15</td>
</tr>
<tr>
<td>Synovitis/effusion vs LOM (1 study)</td>
<td>Synovitis volume vs total hand swelling score (1 study)</td>
<td></td>
</tr>
<tr>
<td>13 15 85</td>
<td>MRI score significantly higher with higher swelling score p&lt;0.00001</td>
<td></td>
</tr>
<tr>
<td>0.93-fold (0.47–1.33-fold)</td>
<td>r=0.52–0.72 p&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>PD vascularity (2 studies)</td>
<td>Synovitis volume vs LOM (1 study)</td>
<td></td>
</tr>
<tr>
<td>13 15 85</td>
<td>r=0.76 p&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>0.96-fold</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GS synovitis had weaker correlation with clinical disease activity than PD</td>
<td>Synovitis score vs wrist swelling score (1 study)</td>
<td></td>
</tr>
<tr>
<td>13 15 85</td>
<td>MRI score significantly higher with higher swelling score p&lt;0.00001</td>
<td></td>
</tr>
<tr>
<td>Flexor/extensor tenosynovitis (1 study)</td>
<td>Synovitis score vs wrist swelling score (1 study)</td>
<td></td>
</tr>
<tr>
<td>13 15 85</td>
<td>MRI score significantly higher with higher swelling score p&lt;0.00001</td>
<td></td>
</tr>
<tr>
<td>Significant association with clinical disease activity</td>
<td>MRI score significantly higher with higher swelling score p&lt;0.00001</td>
<td></td>
</tr>
<tr>
<td>US hands/wrists vs CE</td>
<td>MRI hands/wrists vs CE</td>
<td>CR hands/wrists vs CE</td>
</tr>
<tr>
<td>4 studies</td>
<td>2 studies</td>
<td>1 study</td>
</tr>
<tr>
<td>Synovitis/effusion (3 studies)</td>
<td>Synovitis volume vs total hand swelling score (1 study)</td>
<td></td>
</tr>
<tr>
<td>13 15 85-94</td>
<td>MRI score significantly higher with higher swelling score p&lt;0.00001</td>
<td></td>
</tr>
<tr>
<td>0.93-fold (0.47–1.33-fold)</td>
<td>MRI score significantly higher with higher swelling score p&lt;0.00001</td>
<td></td>
</tr>
<tr>
<td>PD vascularity (2 studies)</td>
<td>Synovitis volume vs LOM (1 study)</td>
<td></td>
</tr>
<tr>
<td>13 15 85</td>
<td>Synovitis score vs wrist swelling score (1 study)</td>
<td></td>
</tr>
<tr>
<td>0.96-fold</td>
<td>MRI score significantly higher with higher swelling score p&lt;0.00001</td>
<td></td>
</tr>
<tr>
<td>GS synovitis had weaker correlation with clinical disease activity than PD</td>
<td>MRI score significantly higher with higher swelling score p&lt;0.00001</td>
<td></td>
</tr>
<tr>
<td>US ankles/feet vs CE</td>
<td>MRI ankles/feet vs CE</td>
<td>CR hands/wrists vs CE</td>
</tr>
<tr>
<td>5 studies</td>
<td>1 study</td>
<td>1 study</td>
</tr>
<tr>
<td>Synovitis/effusion (3 studies)</td>
<td>Tibiotalar synovitis (1 study)</td>
<td></td>
</tr>
<tr>
<td>13 15 85-96</td>
<td>MRI score significantly higher with higher swelling score p&lt;0.00001</td>
<td></td>
</tr>
<tr>
<td>0.97-fold (0.86–1.04-fold)</td>
<td>1.00-fold</td>
<td></td>
</tr>
<tr>
<td>PD vascularity (1 study)</td>
<td>MRI score significantly higher with higher swelling score p&lt;0.00001</td>
<td></td>
</tr>
<tr>
<td>13 15 85-96</td>
<td>MRI score significantly higher with higher swelling score p&lt;0.00001</td>
<td></td>
</tr>
<tr>
<td>0.57-fold</td>
<td>MRI score significantly higher with higher swelling score p&lt;0.00001</td>
<td></td>
</tr>
<tr>
<td>US TMJ vs CE3</td>
<td>MRI TMJ vs CE</td>
<td>CR hands/wrists vs CE</td>
</tr>
<tr>
<td>8 studies</td>
<td>1 study</td>
<td>1 study</td>
</tr>
<tr>
<td>Synovitis/effusion (2 studies)</td>
<td>Synovitis volume vs LOM (1 study)</td>
<td></td>
</tr>
<tr>
<td>25 100 101</td>
<td>MRI score significantly higher with higher swelling score p&lt;0.00001</td>
<td></td>
</tr>
<tr>
<td>11.7-fold (0.35–23.0-fold)</td>
<td>Synovitis score vs wrist swelling score (1 study)</td>
<td></td>
</tr>
<tr>
<td>25 100 101</td>
<td>Acute changes (1 study)</td>
<td></td>
</tr>
<tr>
<td>2.46-fold (1.10–5.91-fold)</td>
<td>MRI score significantly higher with higher swelling score p&lt;0.00001</td>
<td></td>
</tr>
<tr>
<td>Significantly correlated</td>
<td>Acute changes (1 study)</td>
<td></td>
</tr>
<tr>
<td>Reduced MIO best predictor of active MRA changes</td>
<td>Acute changes (1 study)</td>
<td></td>
</tr>
<tr>
<td>71% asymptomatic</td>
<td>3.33-fold</td>
<td></td>
</tr>
<tr>
<td>63% normal CE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Recommendation**

<table>
<thead>
<tr>
<th>US enthesis vs CE</th>
<th>MRI enthesis vs CE</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 studies(^{107-109})</td>
<td>1 study(^{110})</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>US enthesis vs CE</th>
<th>MRI enthesis vs CE</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 studies(^{107-109})</td>
<td>1 study(^{110})</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Enthesitis (3 studies)(^{107-109})</th>
<th>Enthesitis (1 study)(^{110})</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.79-fold (0.53–1.09-fold)</td>
<td>0.50-fold</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>US VARIOUS MULTIPLE JOINTS vs CE</th>
<th>MRI VARIOUS MULTIPLE JOINTS vs CE</th>
<th>CR VARIOUS MULTIPLE JOINTS vs CE</th>
</tr>
</thead>
<tbody>
<tr>
<td>9 studies(^{48 50 64 111-117})</td>
<td>1 study(^{110})</td>
<td>1 study(^{118})</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Synovitis/effusion (6 studies)(^{48 111-114 116})</th>
<th>Synovitis/effusion (1 study)(^{110})</th>
<th>Soft tissue swelling vs clinical swelling (1 study)(^{118})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.85-fold (1.00–3.33-fold)</td>
<td>1.08-fold</td>
<td>1.05-fold</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Association US changes vs swelling (1 study)(^{48})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swelling: (r=0.50)</td>
</tr>
<tr>
<td>LOM: (r=0.40)</td>
</tr>
<tr>
<td>Pain: (r=0.21)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Association synovitis vs CE (2 studies)(^{10 117})</th>
</tr>
</thead>
<tbody>
<tr>
<td>CE missed inflammation in 25.2% joints</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Synovitis/SH (1 study)(^{20})</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.25-fold</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MRI cervical spine vs CE 1 study(^{20})</th>
</tr>
</thead>
<tbody>
<tr>
<td>SynovitisSH (1 study)(^{20})</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MRI SIJ vs CE 2 studies(^{23 118})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sacroiliitis (2 studies)(^{23 119})</td>
</tr>
</tbody>
</table>

| CE was normal in 22.9% patients with MRI sacroiliitis |


Table 2  Continued

---

---
the mean (range) detection rate for synovitis and effusion at the knee was 1.19-fold (0.14–3.67-fold) for US and 1.02-fold (0.96–1.12-fold) for MRI knee synovitis.

PTC 2: When there is clinical diagnostic doubt, CR, US or MRI can be used to improve the certainty of a diagnosis of JIA above clinical features alone.

The diagnosis of JIA is mainly based on clinical features and the exclusion of other causes of chronic arthritis. However this point illustrates the role of imaging when there is diagnostic doubt; no specific imaging signatures for JIA have been described yet, but imaging is helpful to narrow the differential diagnosis. Four studies compared imaging features in suspected/proven JIA with either controls or other disease entities, including infectious arthritis, acute lymphoblastic leukaemia and haemophilia.2–10 US detected more joint inflammation than clinical examination; two studies specifically described US improving the diagnostic certainty in subjects with suspected JIA.11–12

Detecting damage
PTC 3: If detection of structural abnormalities or damage is required, CR can be used. However MRI or US may be used to detect damage at an earlier time point than CR.

Thirty-seven studies compared joint damage (erosions, joint space narrowing (JSN), deformity) detected by imaging with clinical findings suggestive of underlying damage, such as tenderness, limitation of movement and crepitus. In general, all imaging modalities appeared to detect less joint damage than suggested by clinical examination; for example the mean (range) detection rate for cartilage loss at the knee was 0.32-fold for US, 0.63-fold (0.20–1.0-fold) for MRI and 0.46-fold (0.23–0.71-fold) for CR when compared with pain.11–15 This reflects the poor sensitivity of pain as an indicator of underlying damage.

When the imaging modalities are directly compared MRI and US detected more joint damage than CR, particularly at the hip (MRI vs CR detection rate, mean (range) 1.54-fold (1.08–2.0-fold); US vs CR detection rate, mean 2.29-fold), and at the wrist (MRI vs CR detection rate, 1.36-fold (1.0–2.0-fold)).13–15–19

Imaging specific joints
PTC 4: In JIA imaging may be of particular benefit over routine clinical evaluation when assessing certain joints, particularly the use of MRI in detecting inflammation of the temporomandibular joint (TMJ) and axial involvement.

Cervical spine MRI appears better at detecting inflammation than clinical examination; one study showed 20% of patients had pain and/or limitation of movement whereas 85% had MRI inflammatory changes suggesting that cervical spine involvement in JIA is often clinically silent.20 MRI and CR have shown better detection rates than clinical examination for structural changes in the cervical spine (4.5-fold and mean, range 2.29 (1.58–3.0-fold), respectively).21–22 Abnormal sacroiliac joint (SIJ) imaging is also demonstrated despite a high rate of normal examination; for example, normal SIJ examination in 42.9% and 22.9%, in patients with CR and MRI sacroilitis, respectively.23–24

Muller et al25 compared TMJ clinical examination and US with MRI changes, and found that examination correctly identified 58% patients with active MRI TMJ arthritis compared with 33% for US, and missed inflammation in 42% and 67%, respectively. They described reduced maximal incisal opening to be the best predictor of active MRI changes.26 Full data comparing the various imaging modalities with clinical examination of the TMJ is given in the online supplementary text S9.

Prognosis
PTC 5: Imaging in JIA may be considered for use as a prognostic indicator. Damage on CR can be used for the prediction of further joint damage. Persistent inflammation on US or MRI may be predictive of subsequent joint damage.

Thirteen observational studies examined the relationship between baseline imaging and subsequent radiographic and clinical outcome; 11 with CR and 2 with MRI at baseline. The statement on US inflammation is therefore based on expert opinion; the findings are given in full in table 3. In general, CR damage in the 1st year has a moderate correlation with functional deterioration according to Steinbocker class, Childhood Health Assessment Questionnaire and physician/parent disability scores at 3 years, as well as with CR progression at 5 years.22–25 A baseline CR wrist adapted Sharp van der Heijde score >1 was shown to be predictive of CR progression at 5 years (OR, 8.2), and patients with erosions and/or JSN in the first 6 months of the study spent more time with clinically active disease and were less likely to achieve clinical remission on medication.30–31 Just one study described the correlation of baseline MRI wrist synovial volume with MRI erosive progression at 1 year; this found a moderate correlation, and all patients with high synovial volume at baseline had erosive progression.32

Monitoring inflammation
PTC 6: In JIA, US and MRI can be useful in monitoring disease activity given their sensitivity over clinical examination and good responsiveness. MRI should be considered for monitoring axial disease and TMJ.

Data comparing imaging with clinical examination in detecting joint inflammation is discussed in PTC 1, and specific information on imaging the TMJ and for axial involvement is summarised in PTC 4. This section will consider the comparison of the ability of imaging to detect inflammation, responsiveness of imaging to change in inflammation, and which joints should be assessed.

Comparison of the ability of imaging to detect inflammation
Several studies compared US with MRI in the detection of inflammation, particularly at the knee.13–14 33 34 These studies have shown MRI to be better in detecting knee inflammation than US (mean detection rate 1.20-fold, range 0.63–1.56-fold) and in particular MRI was better than US in differentiating pannus from effusion.13 Knee MRI with contrast enhancement was more reliable at localising and differentiating synovial hypertrophy from synovial fluid particularly when there was <5 mm of synovial hypertrophy, but the addition of contrast did not provide additional information in the assessment of inflammatory bone marrow lesions.35–37 Comparison of power Doppler with grey-scale wrist US has resulted in conflicting results, whereas the use of contrast significantly increased knee US synovial pixel intensity in those with symptomatic disease (p=0.004) and asymptomatic disease (p=0.0001), but not in those in clinical remission.38–40

Studies comparing TMJ US with MRI have shown a poor correlation between these modalities, with US missing 67–75% of TMJ MRI inflammation.23 41 The use of MRI contrast enhancement improved the detection of MRI TMJ inflammation from 35.7% to 86.7%.42 One study examined the CR findings in patients with TMJ MRI synovitis and found significant correlation with abnormal condyle morphology and accentuated antegonial notching on CR, and joints with both of these changes
<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of subjects</th>
<th>Duration of follow-up (months)</th>
<th>Radiological or clinical assessment</th>
<th>Outcome assessed</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline CR predictive factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Susic et al&lt;sup&gt;10&lt;/sup&gt;</td>
<td>87</td>
<td>48</td>
<td>Wrist involvement</td>
<td>CHAQ-DI</td>
<td>Significant correlation p&lt;0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hip involvement</td>
<td>Significant correlation p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>JADI-A</td>
<td>Significant correlation p&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Ravelli et al&lt;sup&gt;19&lt;/sup&gt;</td>
<td>96</td>
<td>min. 60</td>
<td>CR wrist changes at baseline in 1st year in 1st 5 years</td>
<td>No. of joints with LOM</td>
<td>Baseline: low r=0.16 1st year: low r=0.35 1st 5 years: moderate r=0.59</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1st year: moderate r=0.53 1st 5 years: moderate r=0.60</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1st 5 years: moderate r=0.60</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1st year: moderate r=0.48 1st 5 years: moderate r=0.55</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1st 5 years: moderate r=0.61</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1st 5 years: high r=0.89</td>
</tr>
<tr>
<td>Pederzoli et al&lt;sup&gt;20&lt;/sup&gt;</td>
<td>130</td>
<td>min. 60</td>
<td>CR wrist a SH score &gt; 1</td>
<td>CR progression at 5 years</td>
<td>Significant predictor OR 8.2</td>
</tr>
<tr>
<td>Magni-Manzoni et al&lt;sup&gt;28&lt;/sup&gt;</td>
<td>94</td>
<td>54</td>
<td>Baseline Poznanski score</td>
<td>Yearly CR progression</td>
<td>Baseline Poznanski score r=0.88 p=0.47</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>OR 14.32 p&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CR wrist progression in 1st year</td>
<td>Final Poznanski score</td>
<td>r=0.58 p&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>OR 6.49 p=0.0006</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1st year: moderate r=0.39 1st 5 years: moderate r=0.61</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1st 5 years: moderate r=0.60</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1st year: moderate r=0.48 1st 5 years: moderate r=0.55</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1st 5 years: moderate r=0.61</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1st 5 years: high r=0.89</td>
</tr>
<tr>
<td>Bertamino et al&lt;sup&gt;12&lt;/sup&gt;</td>
<td>148</td>
<td>max. 132</td>
<td>CR hip progression in 1st year</td>
<td>CHAQ</td>
<td>r=0.24 p=0.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SJC</td>
<td>r=0.03 p=0.86</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>TJC</td>
<td>r=0.06 p=0.65</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No. of joints with LOM</td>
<td>r=0.46 p=0.0005</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Steinbocker functional class</td>
<td>r=0.50 p=0.005</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>JADI-A</td>
<td>r=0.45 p=0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Physician disability score</td>
<td>r=0.40 p=0.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Parent disability score</td>
<td>r=0.53 p=0.007</td>
</tr>
<tr>
<td>Oen et al&lt;sup&gt;21&lt;/sup&gt;</td>
<td>136</td>
<td>min. 60</td>
<td>Early (&lt;2 years) erosions/JSN</td>
<td>CHAQ</td>
<td>No correlation</td>
</tr>
<tr>
<td>Selvaag et al&lt;sup&gt;22&lt;/sup&gt;</td>
<td>197</td>
<td>36</td>
<td>Baseline swelling/osteopenia</td>
<td>CR erosive progression</td>
<td>OR 7.95 p&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Less patients with CR progression had CHAQ of 0, p=0.045</td>
</tr>
</tbody>
</table>

Continued
<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of subjects</th>
<th>Duration of follow-up (months)</th>
<th>Radiological or clinical assessment</th>
<th>Outcome assessed</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ringold et al⁶¹</td>
<td>104</td>
<td>29.9</td>
<td>Early (&lt;6 months) erosions/JSN vs normal</td>
<td>Time with active disease CRM</td>
<td>More time with active disease p&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>RF +ve vs −ve</td>
<td></td>
<td>Less chance of CRM, RR=0.34, p&lt;0.001</td>
</tr>
<tr>
<td>Oen et al⁶⁴</td>
<td>88</td>
<td>Early (&lt;2 years) Late (1–20.8 years)</td>
<td>Late vs early JSN Joint pain</td>
<td>CHAQ</td>
<td>Significant correlation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Explains 17.7% of variation in CHAQ</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Explains 32.4% of variation in CHAQ</td>
</tr>
<tr>
<td>Habib et al⁶³</td>
<td>68</td>
<td>–</td>
<td>ACPA</td>
<td>CR erosions</td>
<td>Significant correlation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>p=0.004</td>
</tr>
<tr>
<td>Arvidsson et al⁶⁴</td>
<td>103</td>
<td>324</td>
<td>Baseline/early TMJ involvement</td>
<td>Micronathia</td>
<td>66.7% patients with micronathia had baseline TMJ involvement; 33.3% had CR TMJ involvement within 2 years</td>
</tr>
<tr>
<td>Baseline MRI predictive factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malattia et al⁶⁵</td>
<td>58</td>
<td>12</td>
<td>Baseline wrist synovial volume</td>
<td>MRI erosive progression</td>
<td>Correlation r=0.42 p&lt;0.02 All patients with high synovial volume had erosive progression</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Correlation r=0.40 p&lt;0.02</td>
</tr>
<tr>
<td>Gardner-Medvin et al⁶⁶</td>
<td>10</td>
<td>12</td>
<td>Baseline synovial hypertrophy in a clinically normal joint</td>
<td>Disease extension from monoarthritis</td>
<td>100% patients developed clinical arthritis in other joints</td>
</tr>
</tbody>
</table>

ACPA, anticyclic citrullinated peptide antibody; aSH, adapted Sharp van der Heijde score; CHAQ-DI, Childhood Health Assessment Questionnaire disability index; CR, conventional radiography; CRM, clinical remission on medication; CRP, C reactive protein; JADI-A, Juvenile Arthritis Damage Index for articular damage; JSN, joint space narrowing; LOM, limitation of movement; RF, rheumatoid factor; +ve, positive; −ve, negative; RR, relative risk; SJC, swollen joint count; TJC, tender joint count; TMJ, temporomandibular joint.
on CR were 7.5 times more likely to have MRI synovitis (OR 7.55, 95% CI 1.66 to 34.4, p=0.009).43

Responsiveness of imaging to change in inflammation
US and MRI have been shown to have good responsiveness to change in inflammation, as measured by standardised response means (SRM, ≥0.20 small change, ≥0.50 moderate, ≥0.80 good). The mean (range) SRM for MRI wrist synovitis was good at 1.27 (0.51 to 1.69) and demonstrated ability to discriminate between different levels of clinical responder categories, whereas the SRM for MRI wrist bone marrow oedema was small at 0.22.19 32 44 Similar levels of SRM have been described for MRI knee synovial hypertrophy (0.68–0.70) and bone marrow oedema (0.15).45 46 A comparison of MRI wrist synovitis score with US showed higher MRI responsiveness (1.61) when compared with US grey-scale (0.87) and US power Doppler (0.71).47

Which joints to assess
Studies describing the frequency of US joint inflammation in JIA have shown these changes to be most common in the knee (39%), with the first metatarsophalangeal joint and second metatarsophalangeal joint (30%) and wrist (20%).48 49 Joint and metatarsophalangeal joint (30%) and wrist (10%) each).48 49 US power Doppler activity was most common in the wrist (35%).48 49 One study examined the frequency of US peripheral synovitis and found changes more commonly in the metatarsophalangeal joint (61.9%) than in the metacarpophalangeal joint (39%), with the first metatarsophalangeal joint and second metatarsophalangeal joint most frequently affected (20% and 13%, respectively).50

Monitoring damage
PTC 7: The periodic evaluation of joint damage should be considered. The imaging modality used may be joint dependent.

As for PTC 6, this section will consider the comparison of the ability of imaging to detect damage, responsiveness of imaging to change in damage, and which joints should be assessed. Data comparing imaging with clinical examination in detecting joint damage and comparing CR with MRI and US in detecting damage is discussed in part in PTC 3.

Comparison of the ability of imaging to detect damage
El-Miedany et al14 examined the role of MRI, US and CR in the detection of knee JSN and described a 3.14-fold detection rate of MRI compared with US, 4.40-fold for MRI compared with CR and 1.4-fold for US compared with CR. The addition of contrast to MRI enhanced the appreciation of depth of cartilage involvement by 1.42-fold. Data describing the detection of wrist erosive changes have shown a detection rate for MRI compared with US of 1.92-fold, MRI compared with CR of 1.36-fold and US compared with CR of 1.0-fold.17–19 40

In terms of detecting damage of the TMJ, Muller et al55 showed that MRI condylar damage was detected in 25% of their cohort, whereas US detected only 17% (1.47-fold). Weiss et al51 also described a poor correlation between these modalities, with only 50% agreement (detection rate 2.44-fold).

Responsiveness of imaging to change in damage
Several studies examined the responsiveness of imaging to detect change in damage at the wrist, particularly with CR and MRI. The rate of change in CR score (Larsen, Sharp, Poznanski) appears to be greatest in the 1st year, which is mainly due to progression in JSN.58 51 This seems to slow after the 1st year, whereas the rate of erosive change is steady from baseline to year 3; the rate of progression overall slows after 3rd third year. In general, the rate of JSN exceeds that of erosions and total score.29 When compared with CR, Malattia et al44 described the relative efficacy of MRI compared with CR erosion score to be <1 at year 1; that is, MRI was less responsive than CR in detecting erosive progression; the fact that cartilage assessment was not included in the MRI scoring systems might explain this result. A study of TMJ condylar changes showed that MRI identified significantly more changes than CR (p≤0.003), and MRI was superior to CR in following condylar changes over time: MRI condylar changes at baseline were found in 58.6% compared with 80% at year 2; CR condylar changes were stable at baseline and year 2 at 30%.52

Which joints to assess
Studies describing the distribution of CR changes in ‘early’ (within 2 years of disease onset) and ‘late’ (up to 20.8 years of follow-up) disease have shown JSN to be most common in early disease in the wrist (20%), hips (16%), cervical spine (5%), ankles (4%) and knees (3%) compared with 34%, 25%, 38%, 15% and 6%, respectively in late disease.13 44 Rostom et al54 observed CR hip disease to start after 4 years of disease, whereas 80% had developed hip disease at 6 years, and 100% after 14 years. Other studies describing radiological features of JIA found most CR changes in the hands (57%), knees (47%), ankles (27%) and feet (36%), with erosions mainly in hands (18%) and feet (25%).55 The hands and feet were the area most likely to show CR damage progression at 6 months and 5 years.56

Guided treatment
PTC 8: US can be used for accurate placement of intra-articular injections.

Studies summarising the role of imaging for guiding intra-articular steroid injections are given in online supplementary text S10, along with additional data on the use of imaging to assess and monitor efficacy of steroid injections. All studies used triamcinolone injections; doses and preparations varied according to the age of the patient and the joint being injected. Young et al46 used US to assess the accuracy of needle placement for steroid injections at various sites (joints and tendon sheaths), and described that US allowed accurate visualisation of the injection point in all 1444 injections. A study by Parra et al49 used CT to establish if US-guided TMJ injections had been accurately placed; needle placement was shown to be acceptable in 91% (75% required no needle adjustment, 16% required minor adjustment) and unacceptable in 9% where the needle required major readjustment. A study of the efficacy of TMJ injections used MRI to assess needle placement accuracy according to the location (intra-articular or extra-articular) of the injected material on MRI acquired after injection; MRI confirmed that 65% of injections were accurately placed.51 A similar study using postinjection MRI of the SIJ described technical success in 100%.52

Remission
PTC 9: US and MRI can detect inflammation when clinically inactive disease is present; this may have implications for monitoring.

Several studies addressed the discrepancy between clinical remission and inflammation seen on US and MRI; these are summarised in the online supplementary text S11. Evidence of ongoing US synovitis has been described in 56.1–94.1% of patients with clinically inactive joints, and 32% of patients with

inactive disease showed US signs of synovial hypertrophy, effusion and power Doppler activity. In clinical remission, US grey-scale synovitis was seen in up to 84.1% of joints, and power Doppler activity in up to 48.6% of joints, with a non-significant trend to more US inflammation in clinical remission on medication compared with clinical remission off medication.\(^\text{39 66–71}\) MRI knee inflammation has been demonstrated in up to 50% of patients in clinical remission and bone marrow oedema in 33.3% patients with clinically inactive joints.\(^\text{72–74}\) Recent pilot studies have demonstrated that patients with sub-clinical US or MRI inflammation are more likely to develop active disease and disease progression, even within 6 months of follow-up.\(^\text{64 70 74 75}\)

Research agenda
The group formulated a research agenda based on areas identified with a lack of currently available evidence, shown in box 1.

**DISCUSSION**

These EULAR-PReS considerations for imaging provide important and novel advice for JIA in clinical practice. There is still significant research needed in this field, in particular consensus on understanding normative data to allow the interpretation of imaging abnormalities, agreement on appropriate MRI protocols and definitions of bone marrow oedema, synovitis and erosions, and suitability of the imaging modalities for detecting changes at specific joints. Our data is limited by the lack of specific information for each JIA disease subtype; this is reflected in the research agenda.

There are significant conceptual differences between imaging in adult and paediatric conditions, and consideration must be given to the appropriateness and feasibility of different imaging modalities which differs with age and developmental stage, as well as to economic issues such as the cost-effectiveness of the intervention. Repeated unnecessary exposure to radiation from imaging should also be considered. We appreciate that access to individual imaging modalities may be insufficient to allow full implementation of these PTC; however most of the points include the use of US which is generally readily available. An economic evaluation was not included in the process as the primary aim was to discuss the clinical implications of imaging; overall the cost of implementing the PTC should be low.

After dissemination of the PTC by means of publication and presentation at European meetings, we would propose to perform a survey of awareness and their use, for example:

- Do you have access to musculoskeletal US and MRI routinely?
- Are you aware of and implementing the EULAR-PReS JIA imaging PTC?
- Have the PTC changed your clinical practice?

The task force agreed that it was not appropriate to create audit or implementation tools as the strength of data was only sufficient to develop PTC rather than recommendations.

In summary, we have developed nine PTC on the role of imaging in various clinical aspects in JIA. We would recommend that a similar rigorous process is followed to reassess the available data after an interval of 5 years.

**Author affiliations**
1. NIHR Wellcome Trust Clinical Research Facility, University Hospital Southampton NHS Foundation Trust, Southampton, UK
2. Department of Rheumatology, Yeovil District Hospital, Yeovil, UK
3. MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton General Hospital, Southampton, UK
4. Hospital Universitario Severo Ochoa, Madrid, Spain
5. Rheumatology Department, APHP, Hôpital Ambroise Paré, Boulogne-Billancourt, France
6. Inserm U1173, Laboratoire d’Excellence INFLAMEX, Université Versailles St. Quentin, Montigny-le-Bretonneux, France
7. Academic Medical Centre Amsterdam, University of Amsterdam, Amsterdam, The Netherlands
8. St. Barts University Medical School Hospital, Brest, France
9. Institute Gaslini, Genova, Italy
10. Department of Pediatrics, University of Genova, Genova, Italy
11. Rheumatology Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain
12. Copenhagen Center for Arthritis Research, Center of Rheumatology and Spine Diseases, Rigshospitalet, Glostrup, Denmark
13. Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark
14. Queen’s University Belfast, Belfast, UK
15. Pediatric Rheumatology Research Institute, Bad Bramstedt, Germany
16. Academic Medical Centre, Emma Children’s Hospital, Amsterdam, The Netherlands
17. Department of Rheumatology, Jan van Breemen Research Institute/Reade, Amsterdam, The Netherlands
18. Faculty of Medicine University of Nis, Department of Pediatric Rheumatology, Clinic Center, Nis, Serbia
19. NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, UK

**Acknowledgements** The authors thank Louise Falzon for her work in the development of the literature search strategy and Dr Brian Davidson for his involvement in the PPI event.

**Contributors** ANC-B and CJJE performed the literature review and produced drafts of the manuscript with advice from PGCC and CM. All authors were involved in the production of the recommendations, and have reviewed the final manuscript.

**Funding** EULAR.

**Competing interests** CJJE: Speakers bureau and consultancy for Roche, BMS, Pfizer, Abbott, UCB, Samsung, MSD, GSK; M-AD: A consulting fees and PI of international multicentre study on US for Bristol-Myers Squibb; speakers bureau for Roche, BMS, Pfizer, Abbott and UCB; research grant on US from PHRC; book royalties from Elsevier; PGC: speakers bureau or advisory boards for BMS, Pfizer and Roche.

**Provenance and peer review** Not commissioned; externally peer reviewed.
REFERENCES


Recommendation


124 Anvidsson LZ, Fjeld MG, Smith HJ, et al. Craniofacial growth disturbance is related to temporomandibular joint abnormality in patients with juvenile idiopathic arthritis, but normal facial profile was also found at the 27-year follow-up. Scand J Rheumatol 2010;39:373–9.

SUPPLEMENTARY MATERIAL

S1. Full methodology

At the initial task force meeting, members contributed clinically relevant questions related to key aspects of the use of imaging in JIA. The research questions were agreed by consensus and 11 final research questions were selected which encompassed the role of imaging in making a diagnosis of JIA, detecting inflammation and damage, predicting outcome and response to treatment, the use of guided treatment, monitoring disease progression, and remission (see online supplementary text, research questions, S2).

A systematic search of articles was performed and the bibliographies of included papers were manually searched for evidence of other studies for inclusion. A hand search was performed of the conference proceedings for the American College of Rheumatology (ACR) and the European League against Rheumatism (EULAR) annual general meetings for 2012-13 to identify unpublished studies. Specific medical subject headings (MeSH) and additional keywords were used to identify all relevant studies (see online supplementary text, details of search strategy, S3).

Titles and abstracts of all citations identified were screened, and potentially relevant articles were reviewed in full text using predetermined inclusion and exclusion criteria. Studies, published in English, on the use of imaging in all patients with a clinical diagnosis of JIA were included. Imaging modalities included were X-ray described as conventional radiology (CR), ultrasound (US), magnetic resonance imaging (MRI), computed tomography (CT), scintigraphy and positron emission tomography (PET); study types included randomised controlled trials, controlled clinical trials, cohort studies, case-control studies, diagnostic studies and case series where n≥10. Studies were considered for inclusion when they provided information on the role of imaging in making a diagnosis of JIA, detecting inflammation and damage, predicting outcome and response to treatment, the use of guided treatment, monitoring disease progression, and remission. Included studies were evaluated for risk of bias and applicability using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 tool.

Following presentation of the data from the literature review, the experts produced points to consider (the evidence was not deemed strong enough to produce recommendations) based on the 11 clinical questions with final agreement by a process of discussion and consensus. The available evidence for each recommendation was scored according to the Oxford Centre for Evidence-based medicine (CEBM) level of evidence, which gives studies a score for “level of evidence” (1a-5) and for “grade of recommendation” (A-D). The experts anonymously scored their perceived level of agreement for each proposition using a 0–10 numerical rating scale (0=do not agree at all, 10=fully agree). Scores reflected both research evidence and clinical expertise.
An agenda for future research was agreed by consensus following presentation of the literature review.

Given the unique challenges of asking children or young adults to attend consensus meetings in Zurich with the task force members, a separate Patient and Public Involvement (PPI) event was arranged following the second task force meeting where the process and results were presented and all comments were recorded. The meeting was attended by three patients (one child and two young adults with a diagnosis of JIA), two parents of children with JIA, two consultant rheumatologists including task force epidemiologist CJE and, one with a special interest in paediatric rheumatology, a paediatric rheumatology nurse specialist and a paediatric research senior nurse. At this meeting all proposed points to consider were reviewed by the patients and any alternations made as required.
S2. Research questions

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

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

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 according to age?

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

Q5 - What is the evidence for the prognostic (prediction of therapeutic response) value of individual imaging modalities for JIA?

Q6 - What is the evidence for the prognostic (prediction of outcome) value of individual imaging modalities for JIA?

Q7 - When (time), where (which joints), how often and with what imaging modality should we monitor JIA disease inflammation?

Q8 - When (time), where (which joints), how often and with what imaging modality should we monitor age-related structural abnormalities and damage in JIA?

Q9 - What is the role of imaging for the monitoring of systemic treatment (corticosteroids, synthetic and biological DMARDs) and the targeted delivery of local treatments such as intra-articular injections?

Q10 - What is the relationship between individual imaging modalities and clinical remission in JIA?

Q11 - What is the impact with respect to outcome of imaging-detected inflammation /damage in the patient in clinical remission?
S3. Details of search strategy performed using MEDLINE (1946 to November 2013); EMBASE (1980 to November 2013); and the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, third quarter 2013) 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, Juvenile Rheumatoid/
2. (juvenile$ adj3 arthrit$).tw.
3. jia.tw.
4. or/1-3
5. exp ARTHRITIS/
6. arthrit$.tw.
7. (still$ adj disease).tw.
8. Oligoarthrit$.tw.
10. or/5-9
11. exp Child/
12. Adolescent/
13. child$.tw.
14. adolesc$.tw.
15. juvenile$.tw.
16. teenage$.tw.
17. youth$.tw.
18. or/11-17
19. 10 and 18
20. 4 or 19
21. exp Diagnostic Imaging/
22. magnetic resonance.tw.
23. mri$.tw.
24. (ultrasonic adj (diagnos$ or tomography or imaging$)).tw.
25. echotomograph$.tw.
26. echograph$.tw.
27. ultrasonograph$.tw.
28. ultrasound.tw.
29. sonograph$.tw.
30. exp Contrast Media/
31. (computed adj2 tomography).tw.
32. cat scan$.tw.
33. ct.tw.
34. X-Rays/
35. (xray$ or x-ray$).tw.
36. Arthrogram$.tw.
37. radiograph$.tw.
38. radiolog$.tw.
40. (Scintigraph$ or scintiphotograph$).tw.
41. ((gamma camera or radionuclide) adj imag$).tw.
42. radioisotope scan$.tw.
43. Positron emission tomograp$.tw.
44. (pet scan$ or pet-scan$).tw.
45. or/21-44
46. 20 and 45

Search Strategy, EMBASE

1. juvenile rheumatoid arthritis/
2. (juvenile$ adj3 arthrit$).tw.
3. jia.tw.
4. or/1-3
5. exp arthritis/
6. arthrit$.tw.
7. (still$ adj disease).tw.
8. Oligoarthrit$.tw.
10. or/5-9
11. child/
12. adolescent/
13. child$.tw.
14. adolesc$.tw.
15. juvenile$.tw.
16. teenage$.tw.
17. youth$.tw.
18. or/11-17
19. 10 and 18
20. 4 or 19
21. exp diagnostic imaging/
22. exp joint radiography/
23. exp nuclear magnetic resonance imaging/
24. magnetic resonance.tw.
25. mri$.tw.
26. exp echography/
27. (ultrasonic adj (diagnos$ or tomography or imaging$)).tw.
28. echotomograph$.tw.
29. echograph$.tw.
30. ultrasonograph$.tw.
31. ultrasound.tw.
32. sonograph$.tw.
33. exp computer assisted tomography/
34. exp contrast medium/
35. (computed adj2 tomography).tw.
36. cat scan$.tw.
37. ct.tw.
38. X ray/
39. (xray$ or x-ray$).tw.
40. Arthrograph$.tw.
41. radiograph$.tw.
42. radiolog$.tw.
43. (roentgen adj ray$).tw.
44. scintiscanning/
45. (Scintigraph$ or scintiphotograph$).tw.
46. ((gamma camera or radionuclide) adj imag$).tw.
47. radioisotope scan$.tw.
48. positron emission tomography/
49. Positron emission tomograp$.tw.
50. (pet scan$ or pet-scan$).tw.
51. or/21-50
52. 20 and 51

**Search Strategy, The Cochrane Library**

#1 MeSH descriptor: [Arthritis, Juvenile Rheumatoid] this term only
#2 juvenile* near/3 arthrit*:ti,ab
#3 jia:ti,ab
#4 #1 or #2 or #3
#5 MeSH descriptor: [Arthritis] explode all trees
#6 arthrit*:ti,ab
#7 "still* disease":ti,ab
#8 Oligoarthrit*:ti,ab
#9 Polyarthrit*:ti,ab
#10 #5 or #6 or #7 or #8 or #9
#11 MeSH descriptor: [Child] explode all trees
#12 MeSH descriptor: [Adolescent] this term only
#13 child*:ti,ab
#14 adolesc*:ti,ab
#15 juvenile:ti,ab
#16 teenage*:ti,ab
#17 youth*:ti,ab
#18 #11 or #12 or #13 or #14 or #15 or #16 or #17
#19 #10 and #18
#20 #4 or #19
#21 MeSH descriptor: [Diagnostic Imaging] explode all trees
#22 "magnetic resonance":ti,ab
#23 mri*:ti,ab
(ultrasonic next (diagnosis or tomography or imaging*)):ti,ab
echotomograph*:ti,ab
echograph*:ti,ab
ultrasonograph*:ti,ab
ultrasound:ti,ab
sonograph*:ti,ab
MeSH descriptor: [Contrast Media] explode all trees
computed near/2 tomography:ti,ab
"cat scan**":ti,ab or cat-scan*:ti,ab
c:t:ti,ab
MeSH descriptor: [X-Rays] this term only
xray*:ti,ab or x-ray*:ti,ab
Arthrograph*:ti,ab
radiograph*:ti,ab
radiolog*:ti,ab
"roentgen ray**":ti,ab
(Scintigraph* or scintiphotograph*):ti,ab
("gamma camera" or radionuclide) next imag*:ti,ab
"radioisotope scan**":ti,ab
"Positron emission tomograph**":ti,ab
("pet scan** or pet-scan").ti,ab
#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 or #36
or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44
#20 and #45
Figure S4. Flowchart showing the literature search of 13,277 articles, from which 433 articles were selected for detailed review; 204 articles met the inclusion criteria.
<table>
<thead>
<tr>
<th>Question</th>
<th>No. of included articles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 - What is the evidence for the differential diagnostic value of individual imaging modalities for JIA?</td>
<td>4</td>
</tr>
<tr>
<td>Q2 - What is the evidence for the diagnostic value above clinical criteria of individual imaging modalities for JIA?</td>
<td>2</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 according to age?</td>
<td>65</td>
</tr>
<tr>
<td>Q4 - What is the evidence for the added value above clinical examination for the comparative value (sensitivity, specificity etc) of individual imaging modalities in detecting age-related structural abnormalities and damage in JIA (bone, cartilage, tendons, ligaments)?</td>
<td>37</td>
</tr>
<tr>
<td>Q5 - What is the evidence for the prognostic (prediction of therapeutic response) value of individual imaging modalities for JIA?</td>
<td>1</td>
</tr>
<tr>
<td>Q6 - What is the evidence for the prognostic (prediction of outcome) value of individual imaging modalities for JIA?</td>
<td>13</td>
</tr>
<tr>
<td>Q7 - When (time), where (which joints), how often and with what imaging modality should we monitor JIA disease inflammation?</td>
<td>39</td>
</tr>
<tr>
<td>Q8 - When (time), where (which joints), how often and with what imaging modality should we monitor age-related structural abnormalities and damage in JIA?</td>
<td>57</td>
</tr>
<tr>
<td>Q9 - What is the role of imaging for the monitoring of systemic treatment (corticosteroids, synthetic and biological DMARDs) and the targeted delivery of local treatments such as intra-articular injections?</td>
<td>40</td>
</tr>
<tr>
<td>Q10 - What is the relationship between individual imaging modalities and clinical remission in JIA?</td>
<td>16</td>
</tr>
<tr>
<td>Q11 - What is the impact with respect to outcome of imaging-detected inflammation /damage in the patient in clinical remission?</td>
<td>5</td>
</tr>
<tr>
<td>Point to consider</td>
<td>RoB</td>
</tr>
<tr>
<td>-----------------------------------------------------------------------------------</td>
<td>------------------------------------------</td>
</tr>
<tr>
<td><strong>S6. Scores for risk of bias and applicability of the included studies according to QUADAS-2</strong></td>
<td><strong>Patient</strong></td>
</tr>
<tr>
<td><strong>1</strong> <strong>US and MRI are superior to clinical examination in the evaluation of joint inflammation; these techniques should be considered for more accurate detection of inflammation, both in diagnosis and assessing extent of joint involvement.</strong></td>
<td>Low (%) 43</td>
</tr>
<tr>
<td><strong>High (%) 0</strong></td>
<td>6</td>
</tr>
<tr>
<td><strong>Unclear (%) 56.9</strong></td>
<td>52.3</td>
</tr>
<tr>
<td><strong>2</strong> <strong>When there is clinical diagnostic doubt, CR, US or MRI can be used to improve the certainty of a diagnosis of JIA above clinical features alone.</strong></td>
<td>Low (%) 50</td>
</tr>
<tr>
<td><strong>High (%) 0</strong></td>
<td>0</td>
</tr>
<tr>
<td><strong>Unclear (%) 50</strong></td>
<td>50</td>
</tr>
<tr>
<td><strong>3</strong> <strong>If detection of structural abnormalities or damage is required, CR can be used. However MRI or US may be used to detect damage at an earlier time point than CR.</strong></td>
<td>Low (%) 46.8</td>
</tr>
<tr>
<td><strong>High (%) 0</strong></td>
<td>0</td>
</tr>
<tr>
<td><strong>Unclear (%) 53.2</strong></td>
<td>56.4</td>
</tr>
<tr>
<td><strong>4</strong> <strong>In JIA imaging may be of particular benefit over routine clinical evaluation when assessing certain joints, particularly the use of MRI in detecting inflammation of the TMJ and axial involvement.</strong></td>
<td>Low (%) 38.8</td>
</tr>
<tr>
<td><strong>High (%) 0</strong></td>
<td>2.6</td>
</tr>
<tr>
<td><strong>Unclear (%) 63.2</strong></td>
<td>57.9</td>
</tr>
<tr>
<td><strong>5</strong> <strong>Imaging in JIA may be considered for use as a prognostic indicator. Damage on CR can be used for the prediction of further joint damage. Persistent inflammation on US or MRI may be predictive of subsequent joint damage.</strong></td>
<td>Low (%) 46.2</td>
</tr>
<tr>
<td><strong>High (%) 0</strong></td>
<td>7.7</td>
</tr>
<tr>
<td><strong>Unclear (%) 53.8</strong></td>
<td>46.2</td>
</tr>
<tr>
<td><strong>6</strong> <strong>In JIA, US and MRI can be useful in monitoring disease activity given their sensitivity over clinical examination and good responsiveness. MRI should be considered for monitoring axial disease and TMJ.</strong></td>
<td>Low (%) 43.6</td>
</tr>
<tr>
<td><strong>High (%) 0</strong></td>
<td>12.8</td>
</tr>
<tr>
<td><strong>Unclear (%) 56.4</strong></td>
<td>53.4</td>
</tr>
<tr>
<td><strong>7</strong> <strong>The periodic evaluation of joint damage should be considered. The imaging modality used may be joint dependent.</strong></td>
<td>Low (%) 49.1</td>
</tr>
<tr>
<td><strong>High (%) 0</strong></td>
<td>3.5</td>
</tr>
<tr>
<td><strong>Unclear (%) 50.9</strong></td>
<td>50.9</td>
</tr>
<tr>
<td><strong>8</strong> <strong>US can be used for accurate placement of intra-articular injections.</strong></td>
<td>Low (%) 47.6</td>
</tr>
<tr>
<td><strong>High (%) 0</strong></td>
<td>14.3</td>
</tr>
<tr>
<td><strong>Unclear (%) 52.4</strong></td>
<td>66.7</td>
</tr>
<tr>
<td><strong>9</strong> <strong>US and MRI can detect inflammation when clinically inactive disease is present; this may have implications for monitoring.</strong></td>
<td>Low (%) 29.4</td>
</tr>
<tr>
<td><strong>High (%) 0</strong></td>
<td>5.9</td>
</tr>
<tr>
<td><strong>Unclear (%) 70.6</strong></td>
<td>35.3</td>
</tr>
</tbody>
</table>
S7. Reference list of included articles per point to consider

PTC 1. US and MRI are superior to clinical examination in the evaluation of joint inflammation; these techniques should be considered for more accurate detection of inflammation, both in diagnosis and assessing extent of joint involvement.


PTC 2. When there is clinical diagnostic doubt, CR, US or MRI can be used to improve the certainty of a diagnosis of JIA above clinical features alone.


**PTC 3. If detection of structural abnormalities or damage is required, CR can be used. However MRI or US may be used to detect damage at an earlier time point than CR.**


PTC 4. In JIA imaging may be of particular benefit over routine clinical evaluation when assessing certain joints, particularly the use of MRI in detecting inflammation of the TMJ and axial involvement.


**PTC 5. Imaging in JIA may be considered for use as a prognostic indicator. Damage on CR can be used for the prediction of further joint damage. Persistent inflammation on US or MRI may be predictive of subsequent joint damage.**


PTC 6. In JIA, US and MRI can be useful in monitoring disease activity given their sensitivity over clinical examination and good responsiveness. MRI should be considered for monitoring axial disease and TMJ.


**PTC 7.** The periodic evaluation of joint damage should be considered. The imaging modality used may be joint dependent.


**PTC 8. US can be used for accurate placement of intra-articular injections.**


**PTC 9. US and MRI can detect inflammation when clinically inactive disease is present; this may have implications for monitoring.**


### Specific comments on PTC:

None given. Read all and discussed but thought all sounded reasonable but clearly they were not for patients.

### General comments:

<table>
<thead>
<tr>
<th>Positioning:</th>
<th>Anything with JIA is very awkward and painful due to the positions you have to hold and for the length required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information Giving:</td>
<td>Really important to be talked to as an adult and as someone with understanding of their illness; don't just speak to mum; appropriateness of going to Children's Outpatient Department surrounding by 'kids'; 'I like being talked to about my illness'</td>
</tr>
<tr>
<td>Understanding how a machine works makes it less scary</td>
<td></td>
</tr>
<tr>
<td>Best if imaging and rheumatology in the same physical space</td>
<td></td>
</tr>
<tr>
<td>Delay for appointments and travelling to hospital and within hospital is a problem so try to co-locate</td>
<td></td>
</tr>
<tr>
<td>Technology not worrying i.e. radiation from CR</td>
<td></td>
</tr>
<tr>
<td>Need dedicated imaging area for paediatrics</td>
<td></td>
</tr>
<tr>
<td>One stop shop is best to reduce time wasted</td>
<td></td>
</tr>
<tr>
<td>Always good to be shown scans (always shown US, sometimes CR, almost never shown MRI)</td>
<td></td>
</tr>
<tr>
<td>Need scanning to show joint inflammation as when you have pain for a long time you get used to it and may not notice it anymore</td>
<td></td>
</tr>
<tr>
<td>Having contrast (injection and needle) can be frightening</td>
<td></td>
</tr>
<tr>
<td>Position for CR and MRI can be painful particularly if you have to maintain the same position for a long time</td>
<td></td>
</tr>
<tr>
<td>Climbing onto couch for MRI or CR can be difficult/painful, as the couch is often at adult height.</td>
<td></td>
</tr>
<tr>
<td>CR and MRI environment can look very sparse and clinical for children</td>
<td></td>
</tr>
</tbody>
</table>

### CR specific comments:

- At least this is quick |
- Parents can be frightened by the risk of CR radiation |

### MRI specific comments:

- It can take a long time to have an MRI and it is uncomfortable |
- Need clear information in advance about how long will take, how noisy it is and what it looks like |
- Perceived high value of MRI for some joints (TMJ) |
- Music with MRI helps but is often not loud enough; noise of MRI very scary |
- MRI is often in an environment used by adults and children and can look frightening |
- You can sometimes see the faces of the MRI staff looking ‘puzzled’ at the pictures - this is a worrying experience for children/young people, especially as the staff don’t give any information at the time/after the MRI - you have to wait for your next clinic appointment which causes prolonged worry |
- Sometimes it’s difficult to even get up and off on the MRI ‘bed’, you need a wheelchair and they often don’t have the right equipment to help you get on and off the bed. |

### Parental perspective:

- Would be beneficial to learn about the ‘loudness’ of the noise; it was a shock when first heard the loudness of the MRI; first MRI was a ‘traumatic experience’ but needed to ‘be brave for XXX’; some prior warning of just how loud it was would be very useful - perhaps an audio clip of the sound and of the scanner |

### US specific comments:

- Good because they can show you what’s going on at the time of the scan; you get instant feedback and they can show you the image and inflammation on the screen; even if that joint feels fine; it’s very visual and instant |
- US made guided injections less worrying, helped |
- US is easy to understand |
- Saw benefit of US as showed inflammation when it was not detected by clinical examination |
- US is real time so you can discuss as you go along, often a doctor you know is doing the scan |

---

PTC, points to consider; CR, conventional radiography; US, ultrasound MRI, magnetic resonance imaging; TMJ, temporomandibular joint
S9. PTC 4: Summary of the included studies comparing imaging and CE in the detection of TMJ damage and inflammation (references in S7, PTC 4)

<table>
<thead>
<tr>
<th>TMJ damage:</th>
<th>US TMJ vs. CE</th>
<th>MRI TMJ vs. CE</th>
<th>CR TMJ vs. CE</th>
<th>CT TMJ vs. CE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bony changes vs. abnormal CE</strong></td>
<td>Detection rate, mean (range) US vs. CE</td>
<td>Detection rate, mean (range) MRI vs. CE</td>
<td>Detection rate, mean (range) CR vs. CE</td>
<td>Detection rate, mean (range) CT vs. CE</td>
</tr>
<tr>
<td>(3 studies) [21, 30]</td>
<td>0.52-fold (0.35-0.69-fold)</td>
<td>1.26-fold (0.41-1.69-fold)</td>
<td>Condylar damage in 81.6% asymptomatic joints</td>
<td>Bony changes vs. abnormal CE (4 studies) [3, 14, 27, 31]</td>
</tr>
<tr>
<td>Abnormal translation vs. facial asymmetry</td>
<td>1.20-fold</td>
<td></td>
<td>Bony vs. functional changes (1 study) [19]</td>
<td>1.0-fold</td>
</tr>
<tr>
<td>(1 study) [6]</td>
<td>All pt with asymmetry/micrognathia had abnormal MRI translation</td>
<td></td>
<td>No significant correlation</td>
<td></td>
</tr>
<tr>
<td><strong>Bony changes vs. reduced MIO</strong></td>
<td>5.63-fold p 0.002</td>
<td></td>
<td>Bony changes vs. reduced MIO (4 studies) [15, 19, 23, 27]</td>
<td>1.75-fold (1.39-2.40)</td>
</tr>
<tr>
<td>(2 studies) [11, 23]</td>
<td></td>
<td></td>
<td>r -0.46, p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td><strong>Erosions vs. abnormal CE</strong></td>
<td>Agreement: 81.9% kappa: 0.57</td>
<td>0.86-fold (0.63-1.0-fold)</td>
<td>Erosions in 57.9% asymptomatic joints</td>
<td>Erosions vs. abnormal CE (2 studies) [13, 17]</td>
</tr>
<tr>
<td>(1 study) [24]</td>
<td></td>
<td></td>
<td></td>
<td>1.71-fold (0.67-2.78-fold)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>reduced MIO, mandibular asymmetry, mandibular deviation: positive discriminator when all 3 factors combined in 86%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Correlation: 0.303 p&lt;0.05</td>
</tr>
</tbody>
</table>

**Note:** The table above summarizes the detection rates and correlations for various imaging methods compared to clinical examination (CE) in the detection of TMJ damage and inflammation. The results are based on the studies referenced in S7 and PTC 4.
<table>
<thead>
<tr>
<th></th>
<th>US TMJ vs. CE 3 studies [18, 21, 24]</th>
<th>MRI TMJ vs. CE 8 studies [1, 2, 12, 13, 20, 21, 30, 32]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synovitis/effusion</td>
<td>11.7-fold (0.35-23.0-fold)</td>
<td>2.46-fold (1.10-5.91-fold)</td>
</tr>
<tr>
<td>Synovitis</td>
<td>Synovitis (6 studies) [12, 13, 20, 21, 30, 32]</td>
<td>Significantly correlated Reduced MIO best predictor of active MRI changes</td>
</tr>
<tr>
<td>Synovitis vs.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>reduced MIO</td>
<td>Synovitis vs. reduced MIO (4 studies) [1, 2, 20, 21]</td>
<td></td>
</tr>
<tr>
<td>Acute changes</td>
<td>Acute changes (1 study) [30]</td>
<td>71% asymptomatic 63% normal CE</td>
</tr>
</tbody>
</table>

CE, clinical examination; CR, conventional radiography; MIO, maximal incisal opening; r, correlation coefficient
### S10. Point to consider 8: Summary of included studies describing the role of imaging for guided IA steroid injections (references in S7, PTC 8)

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of subjects</th>
<th>Duration of follow-up (months)</th>
<th>Intervention</th>
<th>Imaging modality</th>
<th>Outcome assessed</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young 2012</td>
<td>198</td>
<td>Not specified</td>
<td>IA various joints</td>
<td>US-guided</td>
<td>Accuracy of needle placement</td>
<td>US allowed visualisation of point for injection for 1444 injections</td>
</tr>
<tr>
<td>Agarwal 2012</td>
<td>23</td>
<td>30</td>
<td>IA hip</td>
<td>US-guided</td>
<td>Clinical response</td>
<td>Clinical response in 71% after 1 injection Mean duration of response (range): 7 (4-15) months</td>
</tr>
<tr>
<td>Boehnke 1994</td>
<td>26</td>
<td>18</td>
<td>IA hip</td>
<td>US-guided</td>
<td>US remission</td>
<td>US remission in 32%</td>
</tr>
<tr>
<td>Neidel 2002</td>
<td>48</td>
<td>24</td>
<td>IA hip</td>
<td>US-guided</td>
<td>Clinical remission</td>
<td>Clinical remission in 76.1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MRI remission</td>
<td>MRI remission in 76.1%</td>
</tr>
<tr>
<td>Tynjala 2004</td>
<td>13</td>
<td>12</td>
<td>IA hip</td>
<td>US</td>
<td>Clinical remission</td>
<td>Clinical and US remission in 70% at 3 and 6 months, 50% at 12 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MRI</td>
<td>MRI inflammation</td>
<td>MRI: Hips - 75% improved; knees - 63.6% improved</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Clinical response in 80%; US response in 91%</td>
</tr>
<tr>
<td>Laurell 2012</td>
<td>11</td>
<td>1</td>
<td>IA wrist</td>
<td>US-guided</td>
<td>Clinical response</td>
<td>US enabled precise location of inflamed compartment which could not be established clinically</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>US response</td>
<td></td>
</tr>
<tr>
<td>Laurell 2011</td>
<td>30</td>
<td>1</td>
<td>IA ankle</td>
<td>US-guided</td>
<td>US inflammation</td>
<td>Improvement in 87% (resolution in 55%, regression in 32%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>US enabled precise location of inflamed compartment which could not be established clinically</td>
</tr>
<tr>
<td>Savage 2012</td>
<td>20</td>
<td>3</td>
<td>IA ankle</td>
<td>US-guided</td>
<td>Clinical response</td>
<td>Clinical resolution in 81.6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>US response</td>
<td>US resolution in 92.1%</td>
</tr>
<tr>
<td>Parra 2010</td>
<td>83</td>
<td>None</td>
<td>IA TMJ</td>
<td>US-guided</td>
<td>Accuracy of needle placement by CT</td>
<td>Acceptable needle placement in 91% (75% required no adjustment, 16% minor adjustment)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Unacceptable needle placement in 9% (i.e. required major readjustment)</td>
</tr>
<tr>
<td>Habibi 2012</td>
<td>39</td>
<td>2</td>
<td>IA TMJ</td>
<td>US-guided</td>
<td>Clinical response</td>
<td>Clinical response in 92.1%</td>
</tr>
<tr>
<td>Arabshahi 2005</td>
<td>14</td>
<td>6-12</td>
<td>IA TMJ</td>
<td>CT-guided</td>
<td>Clinical response</td>
<td>Improvement in pain (77%), jaw locking (67%), MIO 43%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MRI inflammation</td>
<td>Resolution of effusion in 48%</td>
</tr>
<tr>
<td>Study</td>
<td>N</td>
<td>%</td>
<td>Site</td>
<td>Guided</td>
<td>Outcome Description</td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>----</td>
<td>----</td>
<td>-----------------------------</td>
<td>----------</td>
<td>------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Cahill 2007</td>
<td>15</td>
<td>15</td>
<td>IA TMJ</td>
<td>CT-guided</td>
<td>Clinical response in 58.3%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MRI inflammation</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MRI improvement in 73%, stable in 20%, worse in 6.7%</td>
<td></td>
</tr>
<tr>
<td>Lochbuler 2013</td>
<td>33</td>
<td>6-12</td>
<td>IA vs. extra-articular TMJ</td>
<td>MRI</td>
<td>Clinical response in 56% with IA injection, 17% with extra-articular injection</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MRI inflammation</td>
<td></td>
</tr>
<tr>
<td>Saurenmann 2009</td>
<td>33</td>
<td>3</td>
<td>IA vs. extra-articular TMJ</td>
<td>MRI</td>
<td>MRI confirmed injection accurately placed IA in 65%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MRI accuracy of needle placement</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MRI improvement in 73% with IA injection, 15% with extra-articular injection</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MRI inflammation</td>
<td></td>
</tr>
<tr>
<td>Stoll 2012</td>
<td>31</td>
<td>5.3</td>
<td>IA TMJ</td>
<td>MRI</td>
<td>MRI improvement in 38.7% (resolution in 14.5%), deterioration in 24.2%, stable changes 12.9%, stable normal 24.2%</td>
<td></td>
</tr>
<tr>
<td>Fritz 2011</td>
<td>14</td>
<td>22</td>
<td>IA SIJ</td>
<td>MRI-guided</td>
<td>100% of injections were accurately located</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Clinical response in 79%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MRI improvement in 59%</td>
<td></td>
</tr>
<tr>
<td>Huppertz 1995</td>
<td>21</td>
<td>13</td>
<td>IA knee, ankle, elbow</td>
<td>MRI</td>
<td>Clinical response</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MRI inflammation</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>At 7 weeks: clinical resolution in 76.2%, MRI improvement in 100%, resolution in 52.4%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>At 13 months: clinical resolution in 50%, MRI improvement in 100%</td>
<td></td>
</tr>
<tr>
<td>Beukelman 2006</td>
<td>38</td>
<td>1.5</td>
<td>IA ankle</td>
<td>Fluoroscopy-guided</td>
<td>Clinical response in 89%</td>
<td></td>
</tr>
<tr>
<td>Cahill 2007</td>
<td>38</td>
<td>1.5</td>
<td>IA ankle</td>
<td>Fluoroscopy-guided</td>
<td>Clinical response in 89%</td>
<td></td>
</tr>
<tr>
<td>Sparling 1990</td>
<td>30</td>
<td>42</td>
<td>IA various joints</td>
<td>CR</td>
<td>CR deterioration after IA steroid was unusual, but most common at the hip (deterioration in 33% by 2+ grades)</td>
<td></td>
</tr>
</tbody>
</table>

IA, intra-articular; MIO, maximal incisal opening
### S11. Point to consider 9: Summary of included studies describing imaging findings in clinical remission

(references in S7, PTC 9)

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of subjects</th>
<th>Clinical assessment of remission</th>
<th>Imaging modality</th>
<th>Site</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collado 2012</td>
<td>44</td>
<td>CRM CR</td>
<td>US synovitis (GS, PD)</td>
<td>44-joints</td>
<td>GS synovitis: 84.1% jt PD activity: 48.6% jt More in CRM than CR, p NS</td>
</tr>
<tr>
<td>Erik Nielsen 2013</td>
<td>62</td>
<td>Clinically inactive joints</td>
<td>US synovitis</td>
<td>Multiple</td>
<td>Subclinical synovitis: 56.1% pt</td>
</tr>
<tr>
<td>Halbwachs 2012</td>
<td>13</td>
<td>Clinically inactive joints</td>
<td>US synovitis</td>
<td>Multiple</td>
<td>Subclinical synovitis: 94.1% jt</td>
</tr>
<tr>
<td>Magni-Manzoni 2013</td>
<td>39</td>
<td>ID</td>
<td>US inflammation</td>
<td>Multiple</td>
<td>Synovial hyperplasia: 76.9% pt Effusion: 66.7% pt PD activity: 15.4% pt Tenosynovitis: 15.4% pt</td>
</tr>
<tr>
<td>Donati 2012</td>
<td>100</td>
<td>Wallace ID</td>
<td>US synovitis (SH, effusion, PD)</td>
<td>72-joints</td>
<td>US inflammation: 23% pt, 43/7200 (0.06%) jt All 3 US changes: 17/43 (32%) jt</td>
</tr>
<tr>
<td>Silva 2013</td>
<td>35</td>
<td>CRM CR</td>
<td>US synovitis (SH, PD)</td>
<td>17-joints</td>
<td>Subclinical US: 37.8% jt</td>
</tr>
<tr>
<td>Rebollo-Pollo 2011</td>
<td>28</td>
<td>Clinical remission</td>
<td>US synovitis (GS, PD)</td>
<td>Wrist</td>
<td>Pt with prior jt disease (%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ankle</td>
<td>Pt with no prior jt disease (%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>GS: 57.1</td>
<td>GS: 50.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PD: 21.4</td>
<td>PD: 0</td>
</tr>
<tr>
<td>Bugni Miotto E Silva 2013</td>
<td>36</td>
<td>Clinical remission</td>
<td>US synovitis (GS, PD)</td>
<td>Multiple</td>
<td>GS synovitis: 41.7% pt (3.1% jt) PD activity: 19.4% pt Subclinical synovitis more common with older disease onset (p 0.007), and in extended oligoarticular or pJIA (p 0.013)</td>
</tr>
<tr>
<td>Parsa 2011</td>
<td>35</td>
<td>ID, CRM, CR</td>
<td>US inflammation</td>
<td>Knee</td>
<td>Inflammation: 35% pt in ID, CRM or CR</td>
</tr>
<tr>
<td>Molina 2011</td>
<td>11</td>
<td>Clinical remission</td>
<td>US synovitis</td>
<td>Knee</td>
<td>Synovitis: 36% pt</td>
</tr>
<tr>
<td>Doria 2001</td>
<td>22</td>
<td>Clinical remission vs. active disease</td>
<td>US effusion</td>
<td>Knee</td>
<td>Effusion in remission: 20% jt Effusion in active disease: 77.8%</td>
</tr>
<tr>
<td>Hemke 2013</td>
<td>146</td>
<td>Clinically inactive joints</td>
<td>MRI inflammation</td>
<td>Knee</td>
<td>Synovitis: 35.9% pt BM changes: 33.3% pt</td>
</tr>
<tr>
<td>Van Veenendaal 2012</td>
<td>16</td>
<td>CRM CR</td>
<td>MRI synovitis</td>
<td>Knee</td>
<td>Synovitis, CRM: 30% pt Synovitis, CR: 25% pt</td>
</tr>
<tr>
<td>Van Veenendaal 2011</td>
<td>30</td>
<td>CRM CR</td>
<td>MRI synovitis</td>
<td>Knee</td>
<td>Synovitis, CRM: 30% pt Synovitis, CR: 25% pt</td>
</tr>
<tr>
<td>Brown 2012</td>
<td>11</td>
<td>CRM CR</td>
<td>MRI inflammation</td>
<td>Hand/wrist</td>
<td>Any MRI inflammation: 63% pt Synovitis: 45.5% pt BM oedema: 27.3% pt Tenosynovitis: 54.5%</td>
</tr>
<tr>
<td>Zwir 2010</td>
<td>93</td>
<td>Active disease vs. CRM and CR</td>
<td>MRI synovitis</td>
<td>TMJ</td>
<td>Synovitis, active disease: 80% pt Synovitis, CRM: 70% pt Synovitis, CR: 65.6%</td>
</tr>
</tbody>
</table>
CRM, clinical remission on medication; CR, clinical remission off medication; GS, grey scale; PD, power Doppler; NS, not significant; ID, inactive disease; SH, synovial hypertrophy; BM, bone marrow
Imaging may be more important than clinical examination in JIA

A EULAR task force has developed nine key points to consider around the use of imaging children with JIA in clinical practice, and a research agenda to help further the evidence.

INTRODUCTION
Juvenile idiopathic arthritis is more commonly referred to as JIA, and includes most types of arthritis seen in children. JIA is an inflammatory arthritis that causes pain and swelling in one or more joints. Some children develop long-term joint damage from JIA, but most get better and are able to live close to normal lives.

Imaging techniques are a non-invasive way to be able to look inside the joint. There are several imaging techniques available, including MRI (magnetic resonance imaging), ultrasound and radiography (X-ray). These give doctors a picture of the inside of the joint and may be more accurate than clinical examination. But they involve inconvenience for children and we need to know how to use imaging in a way that most benefits children’s care.

WHAT DID THE AUTHORS HOPE TO FIND?
The authors hoped to find evidence about the role of imaging in the diagnosis and treatment of JIA. This included seeing how well the imaging techniques could detect both potentially treatable inflammation and permanent damage in joints, and how imaging could help in monitoring response to treatment. The study also looked for information on the use of imaging to assess the amount of joint involvement and show whether children are really in remission despite how well they might appear.

WHO WAS STUDIED?
The authors looked at studies that had already been published. These all reported the use of imaging techniques in children with JIA.

HOW WAS THE STUDY CONDUCTED?
A systematic review aims to identify all the published evidence on a particular topic and draw it together into one summary. This paper also included a meta-analysis, which means that statistical analyses were performed on the results in order to be sure that the conclusions being drawn are meaningful.

The authors used major electronic databases and clinical trial registries to search for trials and studies that reported studies of imaging techniques in children with JIA. The search gave a long list of 13,277 articles. Of these, 204 had the correct type of information and were included in the review.

WHAT WERE THE MAIN FINDINGS OF THE STUDY?
The authors developed nine key points to consider for the role of imaging in JIA. The findings suggest that imaging techniques are better than simple clinical examinations in evaluating joint inflammation. In particular, the authors highlight the importance of newer techniques such as ultrasound and MRI.

1. MRI and ultrasound are better than clinical examination in detecting joint inflammation.
2. When there is doubt, X-ray, MRI or ultrasound can be used to confirm a diagnosis of JIA.
3. MRI or ultrasound may be able to detect damage to the joints sooner than can be seen on an X-ray.
4. Imaging may be more useful in certain joints, for example in the lower back.
5. Imaging may be used to predict what damage might occur in the future.
6. MRI and ultrasound can be useful to monitor disease activity.
7. Joint damage should be checked for periodically.
8. Ultrasound can be used to guide injections into the joints.
9. MRI and ultrasound can be used for monitoring when the disease shows no clinical symptoms.

The study also helped the authors to develop a research agenda for further studies that are needed in this area.

ARE THESE FINDINGS NEW?
The findings from the individual studies are not new as this is a summary of the available data and evidence that has already been published elsewhere, but they provide an up to date summary of the available evidence in this area and this enabled the expert committee to make new recommendations for everyday care of JIA.
HOW RELIABLE ARE THE FINDINGS?

There were some limitations in the information available. JIA can be complex and not all patients have the same pattern of disease, so comparisons of existing data are not always straightforward.

WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?

The authors have produced a research agenda based on the areas where information is currently lacking, and hope that this will encourage researchers to increase studies in this area. If more studies become available and the issues raised in the research agenda are addressed then it is hoped that this systematic review will be repeated in 5 years.

WHAT DOES THIS MEAN FOR ME?

The last decade has seen a major increase in the use of newer imaging (MRI and ultrasound) for adult arthritis and it is hoped that the new recommendations will provide encouragement and a sensible basis for their use in JIA.

There are differences in imaging for children and adults – for example, some techniques require the patient to lie very still for a long time, and this may not be practical for small children – but more research should help to develop better options. With better imaging techniques, children with JIA may receive better care and treatment that is tailored to their disease.

If you would like to know more about imaging and how it may help you or your child, you should talk to your doctor.

Disclaimer: This is a summary of a scientific article written by a medical professional (“the Original Article”). The Summary is written to assist non medically trained readers to understand general points of the Original Article. It is supplied “as is” without any warranty. You should note that the Original Article (and Summary) may not be fully relevant nor accurate as medical science is constantly changing and errors can occur. It is therefore very important that readers not rely on the content in the Summary and consult their medical professionals for all aspects of their health care and only rely on the Summary if directed to do so by their medical professional. Please view our full Website Terms and Conditions. http://www.bmj.com/company/legal-information/

Date prepared: November 2015

Summary based on research article published on: 5 August 2015.


Copyright © 2015 BMJ Publishing Group Ltd & European League Against Rheumatism. Medical professionals may print copies for their and their patients and students non commercial use. Other individuals may print a single copy for their personal, non commercial use. For other uses please contact our Rights and Licensing Team.