Comment on: Modelling the cost effectiveness of TNF-α antagonists in the management of rheumatoid arthritis: results from the British Society for Rheumatology Biologics Registry: reply

SIR, We thank Dr Von Vollenhoven for his interest in our paper. The questions [1] he raises about our article that examined the cost–effectiveness of biologics using the British Society for Rheumatology Biologics Registry (BSRBR) [2] provide an excellent opportunity to describe why decision modelling should be used in calculating a majority of cost–effectiveness ratios.

We refer to an article by Sculpher et al. [3], which eloquently explains many of these points in detail. It should be noted that while the title of the paper refers to trials, much of its content is applicable to a registry like the BSRBR. We summarize the key points:

(i) It is necessary to base cost–effectiveness calculations on the question being addressed—e.g. are biologics in RA a cost-effective use of healthcare resources? rather than what data are available—e.g. the cost-effectiveness of a trial or a registry.

(ii) A trial (or registry) will rarely provide enough information on its own to answer the policy question. The examples given by Sculpher et al. are (i) a failure to compare all relevant options, (ii) a truncated time horizon, (iii) lack of relevance to the decision context, (iv) inadequate quantification of decision uncertainty. The pragmatic nature of the BSRBR means evidence is provided that is superior to nearly all existing clinical trials in RA, which is why a new cost-effectiveness analysis was deemed necessary. However, not all issues are addressed completely. For example, the BSRBR alone could not produce a lifetime estimate as requested by the National Institute for Health and Clinical Excellence (NICE), but rather a 5-yr estimate, which has implications for long-term progression, and treatment switches. Neither is a complete resource utilization history included.

(iii) Sculpher et al. [3] conclude that a combination of evidence synthesis with decision models will be the most appropriate approach for nearly all cost–effectiveness questions. ‘Models have sometimes been characterized as alternatives to trials, but this is to misunderstand their respective roles. The RCT (here the BSRBR) provides estimates of particular parameters in a specific group of patients in a particular healthcare environment. Decision models provide a structure within which evidence from a range of sources can be directed at a specific decision problem for a defined population and context.’

It is for these reasons we used the BSRBR to inform parameters for a specific decision problem. Using the ‘actual’ data whereby only the BSRBR data is utilized, would simply not provide an answer to the question posed by NICE. Unless models are used to extrapolate relatively short-term data to long-term outcomes the potential benefits of many rheumatological interventions may be underestimated. This may mean that, when compared with treatments for other diseases that have more immediate effects (e.g. cancer survival), they do not appear as worthy a use of healthcare resources.

This relates to the first point raised about the type of patients in the DMARD arm, where we believe modelling could actually help. We had too few patients in the control group (at the time of the analysis) to select patients newly starting a DMARD, so we chose to use all patients but adjust for key parameters. It is possible that there would now be sufficient patients to restrict the analysis to those starting a new DMARD or we could use an external data source to provide a new estimate. Only modelling provides a framework for this.

As new evidence emerges from the BSRBR and other registries, it should be included in the modelling to provide new estimates to inform particular policy questions.

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Comment on: Comparing morphometric X-ray absorptiometry and radiography in defining vertebral wedge fractures in patients with ankylosing spondylitis

SIR, we read with interest the paper by Vosse et al. [1] published in your November issue, detailing a comparative study of morphometric X-ray analysis (MXA) and radiography in defining vertebral wedge fractures in patients with AS. We would like to report our experience with general rheumatology patients here.


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Comment on: Comparing morphometric X-ray absorptiometry and radiography in defining vertebral wedge fractures in patients with ankylosing spondylitis

SIR, we read with interest the paper by Vosse et al. [1] published in your November issue, detailing a comparative study of morphometric X-ray analysis (MXA) and radiography in defining vertebral wedge fractures in patients with AS. We would like to report our experience with general rheumatology patients here.

We studied 46 patients referred to the osteoporosis centre at Southampton General Hospital for an MXA scan who had also undergone a lumbar spine X-ray (MRX) (T12–L4) within 6 months of the scan. Using a 6-point semi-quantitative analysis [2], we were able to both compare the intravertebral assessment (IVA) with the plain radiograph and review the X-ray report provided by the radiology department under usual clinical care. The same investigator (A.S.-R.) analysed both the radiographs and MXA, using a cut-off ratio Ha/Hp or Hm/Hp of 0.8 to define fracture.

Among this group, 31 patients had no fracture on either radiograph or MXA, using the aforementioned criteria. However, three of these X-rays had been reported as showing a fracture. The remaining 15 patients had a total of 21 fractures on X-ray analysis of which 20 correlated exactly on MXA and MRX (Table 1). The prevalence of vertebral fracture in our population was 33%.

If we assumed MRX to be the gold standard then the sensitivity, specificity, positive predictive value and negative predictive value of MXA was 95, 88.5, 83 and 97% respectively.

In clinical practice, a doctor frequently relies upon the X-ray report. We went on to look at the correlation between the X-ray report and MRX using the latter as the gold standard (Table 1). The sensitivity, specificity, positive predictive value and negative predictive value of the usual X-ray report was 73, 83, 73 and 83% respectively.

In this pragmatic study, we would reiterate Vosse et al.'s [1] suggestion that the negative predictive value of MXA is high, and therefore if no fracture is found, further imaging is not required, although we would acknowledge that standard radiograph analysis is not necessarily the gold standard in detecting lumbar vertebral fracture, and indeed MXA may pick up some additional fractures. The extent of agreement is dependent on the strictness of the definition of fracture used. We feel MXA has a place aiding quick assessment of fracture risk with less radiation exposure than conventional radiographs, especially in the analysis of the lumbar spine.

**Disclosure statement: the authors have declared no conflicts of interest.**

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Comment on: Comparing morphometric X-ray absorptiometry and radiography in defining vertebral wedge fractures in patients with ankylosing spondylitis: reply

Sir. We appreciate the comments by Scott-Russell et al. [1] and would like to reply to their letter as follows.

They report their experience with morphometry in 46 patients referred to a osteoporosis centre. Using the same definition of a vertebral fracture (deformity of ≥20% in height) as we did, they found similar figures for specificity and negative predictive value, but higher figures for sensitivity and positive predictive value. This could be explained by several differences between the two studies.

The most obvious argument, of course, is the difference between study populations. We have studied AS patients with inherent structural damage of the spine, including processes reflecting bone formation as well as bone loss and destruction, whereas Scott-Russell et al. [1] have studied post-menopausal women. However, there are more arguments.

First, positive and negative predictive values are context-dependent, and the prevalence of fractures in our population is much lower with consequences for the positive predictive value.

Second, we only looked for wedging fractures (Ha:Hp ratio) and not for diabolo fractures (Hm:Hp ratio). It would be interesting to explore if diabolo deformities are easier to recognize, especially in AS patients.

Third, another explanation for the discrepancy could be the poor image quality of vertebrae in the thoracic region (especially in the upper parts).

At last, there is a difference in analysing the fractures on a patient level as compared with a vertebral level. Scott-Russell et al. [1] performed per-patient analyses, whereas we analysed on both levels. Our per-patient analysis showed good agreement between both methods, for the total spine [intraclass correlation coefficient (ICC) = 0.64] as well as for thoracic (ICC = 0.66) and lumbar (ICC = 0.62) parts separately. Analysis on separate vertebrae (n = 335) showed a different pattern of agreement dependent on the part of the spine that was examined. For the total spine (ICC = 0.71) as well as for the lumbar (ICC = 0.76) part, an acceptable level of agreement was achieved. For the thoracic part the level of agreement (ICC = 0.43) was only moderate. All identified fractures, both discrepant and matching, were localized in this thoracic (T6–L1) region. If we recalculate in the same way Scott-Russell et al. [1] did, our results are similar to theirs except for lower sensitivity.

In conclusion, we agree with Scott-Russell et al. [1] that morphometric radiography as well as morphometric X-ray absorptiometry (MXA) are valuable in the assessment of vertebral deformities, especially at the lumbar spine level. In view of the negative predictive value of MXA, we believe that MXA is helpful to select patients in whom X-rays are necessary to verify the degree of vertebral deformities and differentiate them from other causes, such as Scheuerman’s disease or normal variations in height. Further studies will be needed to demonstrate the degree of mutual exchangeability of both techniques.

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The sensitivity, specificity, positive predictive value and negative predictive value of the usual X-ray report was 73, 83, 73 and 83% respectively.

<table>
<thead>
<tr>
<th>Fracture on MXA</th>
<th>Fracture on X-ray report</th>
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<tbody>
<tr>
<td>Yes</td>
<td>No</td>
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<tr>
<td>Yes</td>
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<td>No</td>
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<td>Total</td>
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Of the 25 fractures reported, 20 corresponds to an 80% correlation between MXA and X-ray.