number of swollen joints, and C reactive protein over two years. However 18 patients reported high pain scores despite no evidence of C reactive protein or swollen joint activity. On the other hand 10 patients reported no pain despite active disease. The difference could not be explained on the grounds of joint deformity. Thompson and Carr do not set out to explain their finding.

However their previous writings on subjects such as handicap[2] indicate they are well aware of the importance of psychosocial factors in the manifestations of disease and, by implication, the weakness of rigid application of the medical model to chronic disease. Only a small proportion of patients with the mechanical low back pain or tender fibromyalgic spots develops chronic pain syndromes and becomes severely disabled. Psychosocial factors rather than clinical findings or treatment prescribed are the strongest predictors of chronicity in mechanical low back pain.[3] In patients with fibromyalgia Wolff *et al* have demonstrated that the number of tender spots is proportional to the degree of distress. They suggest that the tender point count could be considered as the erythrocyte sedimentation rate of distress.[4]

Even in osteoarthritis, disease severity accounts for only a proportion of the individual variability in clinical outcome. After controlling for disease severity, psychological variables remain strong predictors of individual differences in functional impairment and pain.[5]

Thus it is well established that psychosocial factors are important predictors of ongoing pain in non-inflammatory musculoskeletal conditions. There is no reason to anticipate that people will behave differently whether responding to pain of an inflammatory or non-inflammatory nature. Thus it can be assumed that a proportion of those with rheumatoid arthritis will develop a chronic pain syndrome. This is almost certainly what has happened in the 18% of Thompson and Carr's patients with high pain scores in the presence of inactive disease.

The appropriate treatment of these patients is not by first, second or third line drugs combined or otherwise but by paying attention to self management strategies, coping skills, etc, etc. No doubt a proportion of those with active disease will also have developed chronic pain behaviours and associated disability that require as much attention as the raised C reative protein and number of swollen joints.

And what are we to make of the 10% of RA patients who do not express pain despite active disease? Although they are a delight for the rheumatologist to deal with, such pain related behaviour may also be pathological. It is well recognised that a proportion of patients with rheumatoid arthritis battle on regardless and develop what has been called arthritis robustus with rapid aggressive joint destruction. Might these patients be found among Thompson and Carr's pain free 10% with active joints?

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Authors' reply

We agree with Dr Jones that psychological factors are likely to be important in self reported pain and disability in chronic musculoskeletal conditions. However, the available clinical data are controversial in this area. Current studies variously report an absent[1] or only weak[2] correlation between disease activity and pain scores, that disease activity is a strong predictor of pain[3] and that disease activity influences pain indirectly via depression.[4]

Therefore we feel that the cause and effect relation between psychosocial distress and self reported pain and disability remains a hypothesis that would explain our findings rather than a conclusion of the findings themselves.

We are currently studying these relations in more detail.

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What about IgA rheumatoid factor in rheumatoid arthritis?

We read with interest the editorial by Soltys and colleagues about rheumatoid factors (RFs).[1] They correctly stated that most naturally occurring RFs were of the IgM isotype while IgG RFs were thought to be associated with rhematoid arthritis (RA). It should be pointed out in this context that it is very difficult to measure IgG RF and this RF isotype can only be detected in approximately 50% of RA patients whereas IgA RF, usually in combination with IgM RF, can be detected in most patients with seropositive RA.[2–4] It should also be noted that increased IgA RF is associated with severe manifestations in RA and this has been extensively reported by several different groups in the last 15 years.[5–10]

Furthermore, several reports have shown that RFs may be increased in serum many months or even years before clinical symptoms of RA appear,[11–13] and it has also been reported that symptom free people with an increase in IgA RF or IgG RF have an increased risk of developing RA.[14] This indicates that both IgA RF and IgG RF may have a primary role in the pathogenesis of RA.

Recent studies have shown that a combined increase in IgM and IgA RF, with or without IgG RF, is the most common RF pattern found in patients with RA.[2–4 14] Thus, a combined increase in IgM and IgA RF is very specific for RA and rarely found in symptom free people or patients with other rheumatic disorders.[3 15] It should also be noted that IgG RF and IgM RF are more frequently raised than IgA RF in symptom free members of families with multicase RA.[16] This indicates that an increase in IgA RF is more specific for RA than an increase in IgM RF or IgG RF. Thus, switching from IgM RF to IgA RF may be at least as important in the pathogenesis of RA as switching to the IgG class.

Several studies have shown that RA patients with an increase in IgA RF develop a more severe disease, with bone erosions or extra-articular manifestations, or both, than patients without IgA RF.[5–10 17–21] Table 1 summarises some published studies on the association between disease manifestations in

*Table 1 Associations between individual RF isotypes and disease manifestations as reported in 14 studies on RA**

Disease manifestations	*Association observed between RF isotypes and disease manifestations*	
Report (reference)	*Yes*	*No*
Bone erosions		
Tarkowski *et al*[5]	IgA RF	IgM RF, IgG RF
Teitsson *et al*[6]	IgA RF	IgM RF, IgG RF
Árnason *et al*[17]	IgA RF	IgM RF, IgG RF
Gioud Paquet *et al*[18]		IgM RF, IgG RF, IgA RF, IgE RF
Brik *et al*[19]	IgA RF	IgM RF
Winska-Willoch *et al*[8]	IgA RF	
Eberhardt *et al*[2]	IgG RF	IgM RF, IgA RF
Eggelmeijer *et al*[7]	IgA RF	IgM RF, IgG RF
Van Zeben *et al*[9]	IgA RF>IgG RF>IgM RF	
Jorgensen *et al*[10]	IgA RF>IgM RF	
Extra-articular manifestations		
Tarkowski *et al*[5]	IgG RF>IgA RF>IgM RF	
Gioud-Paquet *et al*[18]	IgA RF, IgE RF	IgM RF, IgG RF
Elkon *et al*[20]	IgA RF	IgM RF, IgG RF
Lúðvíksson *et al*[21]	IgA RF	IgM RF
Elson *et al*[22]	IgG RF	
Jónsson *et al*[23]	IgA RF	IgM RF, IgG RF
Jorgensen *et al*[10]	IgA RF	IgM RF

*Not a complete literature survey.

RA and different RF isotypes. Not all studies have agreed[2 18] but different findings can at least in part be explained by technical differences in RF testing.[24 25]

Measurement of individual RF isotypes is clinically useful, both in terms of diagnostic and prognostic evaluation of patients with RA. Furthermore, it is probable that RF has a primary role in the pathogenesis of RA and this may apply even more to IgA RF than IgG RF.

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Authors' reply

We are most grateful to Drs Jonsson and Valdimarsson for their additional comments with regard to rheumatoid factors and their definite pathogenic associations with disease mechanisms in rheumatoid arthritis.

Their take home message is that perhaps we should be measuring other rheumatoid factor isotypes, as well as IgM, as they may be more prognostically relevant. This may indeed be the case but, at present, IgM rheumatoid factor is the only isotype that can be precisely measured using techniques such as nepholometry where additionally there is an accepted primary (WHO) standard. IgG and IgA rheumatoid factors are often measured by enzyme linked immunosorbent assay and this is where problems may occur. IgM rheumatoid factors can interfere with the assay by binding to the antigen and then subsequently to the detection antibody to give false positive results. Use of $F(ab)_2$ gets over this to some extent, but IgM can still form complexes that may interfere. Currently there is no agreed international reference standard to make assays comparable between laboratories and in the UK there is no national quality assurance programme; other than for IgM. This means that there can be no independent assessment of laboratory performance of IgG and IgA rheumatoid factors if these were to be applied to clinical samples. The advice from Professor Pam Riches of the Protein Reference Unit at St George's Hospital Medical School is that, at present, she would not recommend the use of non-standardised unvalidated assays other than for research.

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