


Reply

We thank Dr Matsukawa for the interest in our article. In response to the specific points addressed by Dr Matsukawa, we have now made some additional analyses. First, none of the suicide victims in our database had suffered from systemic lupus erythematosus (SLE). However, it has to be remembered that all somatic diagnoses of suicide victims were based on hospital admissions extracted from the National Finnish Hospital Discharge Register. Thus, there remains the possibility that our data included some cases of SLE treated as out-patients, which were missed. Second, Dr Matsukawa wanted to confirm the order of onset of the diseases, i.e. whether rheumatoid arthritis (RA) preceded psychiatric disease, or vice versa. We have now performed further analyses specifically with regard to this question. We used subjects with osteoarthritis (OA) as the control group. However, of all the psychiatric disorders, only the information on hospital-treated depression was used, because depression is known to be a major risk factor in suicidal behaviour. Figure 1 shows the Kaplan–Meier estimates for the temporal relationship between first admission due to RA/OA and subsequent first hospitalization due to depression. In all cases with both RA and depression (n=9), RA always preceded depression. Further, of all the cases with OA and depression, in 9 out of 12 cases depression followed OA. These analyses did not alter the major results of our paper, but actually provided us with important additional information in understanding the connection between RA and suicidal behaviour.

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Infliximab cost-effectiveness/safety?

Sir, There is no question that tumour necrosis factor inhibitors have made a major difference in our ability to control rheumatoid arthritis. Claims [1–4] related to cost-effectiveness of one such inhibitor, infliximab (Remicade), must be more closely examined.

It is ‘bothersome’ to find allegations that one can demonstrate lifetime cost-effectiveness based on limitation of use to only 1 or 2 yr of therapy [1–4] with a medication whose benefits disappear to baseline with its cessation [5, 6]. Kobelt et al.’s [1] recent article must be reconciled with their 2001 American College of Rheumatology meeting presentation [2]. They reported US$6600 extra cost offset the direct costs of methotrexate therapy by $1190, suggesting a cost per ‘quality of life’ gain of $29 900. This study was very difficult to assess, as multiple clinical trials were combined and their listed direct product cost was less than half that in clinical practice in both the UK and the USA. They reported a cost-effectiveness ratio of $38 200 per discounted quality-adjusted life year (QALY). However, this (similar to the present study) was predicated on the use of infliximab for no more than 2 yr! Their more recent study is similarly difficult to interpret, as it uses historical controls of individuals with early rheumatoid arthritis (different catchment group from infliximab group) from a disparate time period (5–15 yr prior). The assumption that treatment approaches were the same for the historical and infliximab groups makes the unwarranted assumption of absence of
For decades, use of other treatments has been limited to only those patients with full prescription coverage or who have sufficient 'disposable income' to afford the $10 000-plus per year expense. I look forward to application of Kobelt et al.'s [1] methodology to calculation of the true cost-effectiveness of medications (including toxicity), use of which is likely to be required for decades.

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Reply

Cost-effectiveness analyses of new treatments of chronic diseases at their launch are difficult, as they have to be based on short-term clinical trials. However, payers in a number of countries request that such analyses be presented for reimbursement decisions. As a consequence, a number of assumptions regarding effectiveness in clinical practice, including the effect beyond the clinical trial, need to be made until post-launch follow-up studies become available several years later. In such models, it is common and accepted practice to combine clinical, epidemiological, economic and quality of life data.

For our analysis, we have used the actual primary clinical data from one trial (ATTRACT) and applied them to the economic model. All four cost-effectiveness analyses mentioned were based on ATTRACT and were performed when infliximab was introduced. Also, all four analyses have merged the active treatment groups, as there was no statistically significant difference between them. While there may be differences for individual patients that might be relevant to the treating physician, such interpretations cannot be included in an economic model that has to be based on available data from the trial. The purpose of merging the groups is to increase the sample size for modelling. Distributing each of the four treatment arms separately into the six disease states of the model carries the risk of estimating transition probabilities based on very few patients or even individual patients in some of these states, making any estimates questionable. It is correct that costs and effects should be based on the same population. However, we believe that using the cost for infliximab of 3 mg/kg for the entire cohort is the correct approach, as it represents the currently recommended dose. Using a different dose will obviously change the cost, and the sensitivity analysis on the price of infliximab (table 6) is indicative on how sensitive the analysis is to the drug cost.

One issue when using epidemiological cohort studies is that generally patients have been followed from onset of disease, and will therefore, seldom correspond to patients in clinical trials. This is particularly true in this case where the ATTRACT trial enrolled patients with advanced disease. However, we have used a novel approach where the demographics and disease parameters of the clinical trial patients are matched to a subsample drawn from the epidemiological cohorts. Thus the extrapolation is not based on the full cohort, but on a group of patients with the same disease severity and duration as the trial patients. The majority of...