Author’s response to reviews

Title: Large-scale, prospective, observational studies in patients with psoriasis and psoriatic arthritis: A systematic and critical review.

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Author's response to reviews: see over
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Dear Editors,

Thank you for sending us the reviewers’ comments on our paper ‘Large-scale, prospective, observational studies in patients with psoriasis and psoriatic arthritis: A systematic and critical review’.

We have made some changes to the manuscript (highlighted in yellow) corresponding to the reviewers comments and below have given a point by point response to the issues raised.

**Reviewer 1**

**Comment 1:** Why limit to at least 100 patients: please add motivation (Unfortunately, data of De Groot M, Appelman M, Spuls PhI, De Rie MA, Bos JD. Initial experience with routine administration of etanercept in psoriasis. Br J Dermatol 2006, 155:808-14, will be missed)

**Response to comment 1:** The focus of our systematic review was on large-scale, prospective, observational studies in patients with psoriasis and psoriatic arthritis. Our review included both ‘treatment’ studies that focused on a particular intervention, drug or group of drugs with any comparison and ‘non-treatment’ studies that assessed the impact on psoriasis or psoriatic arthritis on morbidity, mortality, resource use or HRQOL. Obviously the sample size for each of these studies will depend on the outcome being measured assuming they employed adequate techniques to determine sample size. We employed a cut-off of 100 patients to define large scale because (a) a recent HTA psoriasis systematic review employed this cut-off for observational studies[1] and (b) other studies have used this as a cut-off to define large scale studies[2]. In terms of studies we may have missed by employing such a cut-off, we only excluded one study based on small sample size[3]. De Groot 2006 was not excluded on the basis of sample size, rather on the basis that it was a retrospective analysis and our aim for our systematic review was to include only prospective analyses (see methods).

**Other comments:**

- Page 6 1st alinea, what is resource use?? **Our response:** Resource use corresponds to the goods and services used by patients with psoriasis (e.g. medication, hospitalisation etc).

- Excluded all studies with “an experimental element to them: please formulate different. **Our response:** We have clarified what we mean by experimental by adding the types of studies we excluded on this basis (RCTs, open-label studies and open-label extensions).
• Page 7 TRIP does not include ongoing/planned studies. Our response: TRIP includes systematic reviews which are a useful reference source.

• Add motivation why limit to English language. Add later as a limitation and describe the effect. Our response: It is common systematic review practice to limit papers to English language only. This has been outlined in the methods section to ensure the reader knows that this systematic review is limited to English language papers only.

• Page 11: sentence: Also, in some countries …: what do the authors mean? Our response: The sentence in question is: ‘Also, in some countries these agents are registered for use in specific target groups of patients where evidence of efficacy and safety are not provided by currently published clinical trials.’ Here we are referring to the fact that in some countries around the world biological agents are only registered for use in a specific target group of patients. This is not the case in all countries where the registered use of a biological agent may not be restricted in this way. Our point is that in these specific target groups of patients where clinical efficacy data do not exist it would be useful to have evidence of the impact of biological agents from observational ‘real life’ studies.

• The discussion should be shortened. Too long. Our response: We feel the discussion adequately describes the implications of the systematic review and by shortening its length would detract from the paper.

• Figure 1: Eligible studies 35 # eligible studies 16????? Our response: There are 35 papers covering 16 cohorts. Some cohorts have more than one publication covering different time-scales and different outcomes.

Reviewer 2:

Comment 1: Excluding studies with less than 100 participants seems arbitrary—please include the methodological reasoning (with references) behind this decision.

Our response to comment 1: Please see response 1 for reviewer 1 where this point is covered.

Comment: Please revise the nonsensical abstract sentence "Quality ranged from 41% to 89%.” to say something more meaningful.

Response to comment 2: We have taken out the percentages from the abstract and stated: ‘The quality of the assessed studies varied widely’. This is then backed up with the quality assessment criteria that the studies do well on and those that they don’t.

Comment 3: Revise the conclusion: the study may show a lack of high quality cohort studies but it does not demonstrate a need for high quality cohort studies if there are other feasible study designs with more merit (e.g. RCTs that minimize the effect of bias).
Response to comment 3: We feel that there is a need for high quality cohort studies to measure outcomes that are better measured in observational studies compared to RCTs, for example real-life effectiveness, patient reported outcomes and resource use. The restrictive nature of RCTs would not necessarily highlight the outcomes that would be seen in usual clinical practice where patients are often exposed to a number of different treatment regimes before response is achieved.

Comment 4: Please discuss comparative effectiveness research (CER) and how this study's results relate to CER.

Response to comment 4: We have added a couple of sentences into the introduction section of the paper:

‘In the United States comparative effectiveness research (i.e. the direct comparison of existing health care interventions to determine which work best for which patients and which pose the greatest benefits and harms) assesses effectiveness in patients typical of day to day clinical care and therefore the focus is on ‘real life’ studies rather than RCTs. Such comparative effectiveness research is being employed by the government to improve the quality of health care whilst reducing the rising costs.’

Reviewer 3:

Comment 1: This is a review paper dealing with large-scale observational studies of psoriasis. The term "large-scale" can be challenged since, according to entry criteria, studies of at least 100 adults were eligible. Quality was expressed as a percentage. In the absence of further specification, this results in rather cryptic statements (e.g., Abstract: "Quality ranged from 41% to 89").

Response to comment 1: Please refer to our response to reviewer 1, comment 1 for a discussion on the definition of large scale and please refer to reviewer 2, comment 2 for a discussion on quality expressed as a percentage.

We thank both all three reviewers for their comments and look forward to hearing from you about the outcome of our manuscript.

Yours faithfully,

Sue Langham, on behalf of all authors.
