Letters to the Editor

No evidence-based practice by biased information from systematic reviews: the case of etanercept and infliximab for the treatment of psoriatic arthritis

Sirs,

The danger of a clinical practice increasingly based on opinion dressed up as evidence has already been raised (1). Indeed, a core problem in practising evidence-based medicine is the possibility of different interpretations of the same data sets and, overall, the difficulty in obtaining a consensus in the interpretation of the results of clinical trials (RCTs) and meta-analysis.

Moreover, systematic reviews are thought to be an epistemological change (2) in healthcare knowledge growth, although the same problems could occur. Ole Olson and Peter Gøtzsche, coauthors of the Cochrane Collaboration Breast Cancer Group, published in advance in *The Lancet* the results of their systematic review and meta-analysis of RCTs on the role of mammography in breast cancer screening (3), which were in contrast with those published a few weeks later on the Cochrane Library (4). The two Danish Authors had carried out their analysis only on three of the seven RCTs on the topic, considering the remaining four studies of poor methodological quality. In the same issue of *The Lancet,* an editorial by Richard Horton, editor of the journal at that time, pointed out that even in the best organizations like the Cochrane Collaboration, pure evidence is not sufficient to influence opinions and can develop tensions among colleagues, which might compromise the scientific value of the overview results.

The discussion which followed the controversy and involved experts from all over the world did not allow definite conclusions. However, it was clear that even if the highest standard methodology is used in the collection of data and their analysis (and the Cochrane experience is also the best in this approach) divergent subjective opinions cannot be avoided and the disagreement can negatively influence the soundness of final recommendations.

Another similar problem could be duplicate publication from systematic reviews or technology assessment reports that can misrepresent or omit results. Recently, Woolacott N.F. *et al*. (5) published a health technology assessment (HTA) report on biological agents for the treatment of psoriatic arthritis. This report is a systematic review plus an economic evaluation and is included in the HTA monograph series that publishes work commissioned for the NHS R&D Health Technology Assessment Program of The United Kingdom (6). The findings of the HTA Program directly influence key decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee. Therefore, we can state both the relevance and trustworthiness of such findings. However, the same systematic review was published in the same period in an international specialized journal (7). We have analyzed this duplicate publication that, in this case, could play a role in acquainting the rheumatologist community, possibly unaware or unable to recognize HTA documents. But, the reading of both publication abstracts has allowed us to point out some significant differences that can, themselves, wreck the evidence-based framework on a different basis as above-mentioned. The dataset has not been differently interpreted but has been slightly misinterpreted with some substantial omissions. The facts are as follows. The abstract of the rheumatology journal substantially reports the same results and three topical phrases: 1) “our review indicates that both etanercept and infliximab are efficacious in the treatment of PsA with beneficial effects on both joint and psoriasis symptom and on functional status”; 2) “uncontrolled radiographic assessment data at one year indicated a beneficial effect of both etanercept and infliximab on the progression of joint disease”; 3) “there are limited data indicating that etanercept and infliximab can delay joint disease progression”. Firstly, no mention of contemporaneously HTA publication is made. Secondly, no economic analysis results are presented or mentioned either. Finally, after the abstract reading, one can argue that etanercept and infliximab are both effective and practically superimposable in particular when compared for joint disease progression. On the other hand, the reading of the HTA report abstract points out several different findings. The topical phrases of the HTA abstract are as follows: 1) “Using the York cost-effectiveness model, infliximab was consistently dominated by etanercept because of its higher acquisition and administration costs without superior effectiveness”; 2) “the York model indic-ated that etanercept is more cost-effective than infliximab as it has lower costs with little difference in outcomes”; 3) “short-term data indicated that etanercept can delay joint disease progression, but long-term data are needed”; 4) “There are no controlled data as yet to indicate that infliximab can delay joint disease progression”. Thus, the authors stated the superiority of etanercept because of its minor cost and equal efficacy in the health technology assessment report. Moreover, only etanercept showed some evidence in a short-term controlled study for its efficacy in delaying joint disease progression. The same authors put the two drugs on the same level in the specialized journal, omitting the results of the economic analysis. This could be considered a clear example of scientific information spreading malpractice. All that could induce clinical and managerial decision making with bad resource consumptions and incorrect allocation procedures of economic resources. In conclusion, systematic review is a methodological golden standard but it is not enough for strong conclusions and the best practice. “Evidence” conclusions are strongly affected by the author’s opinion. Therefore, careful discussion and extensive literature search and meta-review is needed for local implementation of evidence. Editors of scientific journals should better control for the quality of publications, starting from abstracts and their conclusions, which easily reach a large audience of readers.

S. Corrao[1]
A. Puleo[2]
G. Pistone[3]
L. Calvo[1]
R. Scaglione[1]
G. Licata[1]

[1]Biomedical Department of Internal Medicine, University of Palermo;
[2]Villa Sofia Hospital Trust, Palermo;
[3]Civico e Benfratelli Hospital Trust of High Specialization and National Relevance, Palermo, Italy.

Address correspondence to:
Prof. Salvatore Corrao, MD,
Biomedical Department of Internal Medicine, University of Palermo, Piazza delle Cliniche 2, 90127 Palermo, Italy.
E-mail: s.corrao@tiscali.it

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Reply

Sirs,

Professor Corrao is correct in stating that there are differences in the conclusions between our paper published in *Clinical and Experimental Rheumatology* and the report of the full technology assessment published as an HTA monograph: the journal article's conclusions do not draw on the results of the economic evaluation and they do draw on additional information relating to radiographic evidence of delay in disease progression with infliximab. However, his suggestion that the results of the review as published in *Clinical and Experimental Rheumatology* are therefore misleading is inaccurate and his suggestion that the conclusions in the journal article are based on the authors' opinion rather than an objective and thorough review of the available trials is unjustified.

Firstly, the journal article is of the systematic review of the clinical data, which was a stand alone piece of work. I disagree with the suggestion that the clinical data are not meaningful or worthy of review without an economic evaluation.

Secondly, the journal article includes some extra data that were not available when the HTA monograph was submitted: one trial of infliximab (IMPACT 2 trial) and some radiographic data (one year data from the IMPACT trial). That both the manuscript and the HTA Monograph were published at the same time is due to differences in the time taken for the publication process.

Thirdly, to compare the conclusions from the clinical data with those of a full economic evaluation based on a model specific to the UK setting is not appropriate. Even so, the conclusions are not incompatible. The clinical data suggest that etanercept and infliximab are effective. The economic evaluation found that despite there being no apparent difference in efficacy between etanercept and infliximab, the higher cost of infliximab made etanercept more cost effective than infliximab.

I would like to add that our failure to cite the full HTA report in the paper was an oversight. That the work was conducted for the HTA is stated in the paper and the publishers can confirm that I stated in my letter to them that the full report of the work was to be published as an HTA monograph.

N.F. WOOLACOTT

Address correspondence to:
Dr. Nerys F. Woolacott, Centre for Reviews and Dissemination, University of York, York, YO10 5DD, UK.
E-mail: nw11@york.ac.uk

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