Author's response to reviews

Title: Meta-analysis of efficacy and safety of intravenous ferric carboxymaltose (Ferinject) from clinical trial reports and published trial data

Authors:

R Andrew Moore (andrew.moore@pru.ox.ac.uk)
Helen Gaskell (helen.gaskell@pru.ox.ac.uk)
Peter Rose (peter.rose@swft.nhs.uk)
Jonathan Allan (Jonathan.allan@ggc.scot.nhs.uk)

Version: 3 Date: 8 August 2011

Author's response to reviews: see over
Response to reviewer 2 (Munoz)

Changes in the text are highlighted in red. Some renumbering of references has also been necessary. Additional or changed references are highlighted in red in the reference list, but not in numbering in the text.

Major compulsory revisions

1. They included data from unpublished clinical trial reports. How was the quality of these reports assessed? Why were they not published when some one were performed as far as 2004? This reviewer has some doubts on the use of data from unpublished, not peer-reviewed reports.

Randomised trials were scored using the Oxford Quality Scale, and the results are given in trial details in Additional file 2. We have also added some sentences in Results and Discussion that deal with the issue, and in the latter case referring to how CTR data has been used to investigate both new outcomes, and to look more closely at adverse events.

2. Time period for identification of studies is not given. However, there is an important study (FERGIcor) comparing ferric carboxymaltose with iron sucrose in more than 400 IBD patients which is missing (It was presented at the EUGW Barcelona October 2010, and just published in Gastroenterology June 12 PMID 21699794).

This CTR for this study was not finalized when we began the review, and only published after submission. It is an important study, and it is now included in the paper. We have updates results, discussion, and numbers to include it. This has let to some changes in the way in which the Results section is constructed.

There is not any comment or analysis on the economical implications of the use of ferric carboxymaltose.

Frankly, this is difficult, but the 2011 Estatiev trial has economic information that is now included in the results, and we have made some comments in the discussion also. It is almost a separate paper to make a thorough economic argument, and that is not the point of this paper.

Minor essential revisions.
Abstract.

3. Intravenous ferric carboxymaltose was given up to the calculated iron deficit (up to 1,000 mg in one week) for iron deficiency anaemia …..
Change made

4. The final sentence of the conclusion (It increases the evidence available to
support recommendations given for intravenous iron treatment, but direct comparison trials between different intravenous iron preparations are lacking) is not accurate. 
Change made

Background
5. Page 4, paragraph 2. Cost of blood products, but not mention to cost of different IV iron preparations, nor comparison between IV iron and transfusion.
That is true, but we felt that we made enough of a point without going into too great a detail, and because economic was not the main thrust of the paper.

6. Page 5, paragraph 2. “Intravenous iron preparations typically involve iron as high or low molecular weight iron dextran, iron gluconate, or iron sucrose, and require multiple administrations of low doses to replenish iron stores”.
This does not apply to HMWID, LMWID, or Ferinject.
We have re-written this to read:

“Intravenous iron preparations have included iron as high or low molecular weight iron dextran, iron gluconate, or iron sucrose, and ferric carboxymaltose; differences include the number of administrations required to replenish iron stores.”

7. Page 6, paragraph 2. Please, check reference 28 (Iron dextran or Ferinject?)
References 27 and 28 were wrongly numbered. They have been corrected.

Methods
8. Which was the time period for identification of studies?
This is not added.

Discussion
7. The reader would benefit for a more complete discussion on death.
We have added a new section in the results looking at the number, frequency, and cause of deaths. With a relatively few deaths there is not much more we can do, but we have also changed the Discussion a little.

8. Why ferinject-induced hypophosphatemia, and its possible clinical consequences, has not been commented?
Because we didn’t find it mentioned in the trials. Right now we only know of one case report in Transplantation last year.

9. Again, some comments on comparative cost-effectiveness will be much well come.
We have commented on this.

Direct comparison between iron preparations are few, but not lacking
We have made changes to this point.