Author's response to reviews

Title: Prevalence of anaemia in older persons: systematic review

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We wish to thank the reviewers for their detailed and helpful comments. Our responses to the points they make are below.

**William Ershler**

The issues of racial differences is dealt with in a new paragraph in the discussion. We are aware that we cannot answer all the questions he sets, but point to some places in the literature that at least open a door, and point out that the racial differences are not confined to older people.

**Andrew Clegg**

1. We have added several sentences to explain why a different review was needed, which included six more years of publications and use of more stringent diagnostic criteria but wider searching. We also examined the importance of setting, and followed up on Beghe & Ershler’s points on consistency of diagnostic criteria. In the circumstances, this review is very different from the previous one, but it was not our intention to disparage what was a good review for its time, and to try and improve using some of the suggestions that Beghe et al suggested. In any event, there is always room for a different point of view on the same subject, especially given the tendency of systematic reviews to be wrong. Even Cochrane reviews, regarded as the best, are known frequently to come to incorrect conclusions. As regards the importance and consequences of prevalence of anaemia in the elderly, we give a raft of references in the discussion, though it would be difficult the summarise these into anything other than the fact is that anaemia is a bad thing and probably quite expensive; there just isn’t the literature to do justice to this.

2. The exclusion of small studies is not arbitrary, but based in evidence. We know, even in fake trials performed by rolling dice, that meta-analysis of the small ones can give statistical significance where there is none (Bandolier 105), and that meta-analysis of small studies gives different answers to large randomised trials, with magnesium and MI as the classic example. In observational studies Ruppen et al (Anesthesiology 2006 105: 394-399) have demonstrated an enormous variation in event rates with small studies, with admittedly low event rates differing by over four orders of magnitude in small studies. There is really quite an extensive literature, but we don’t think this paper is the place to rehearse it. After all, we used data on about 86,000 patients; it would need almost 100 studies of 100 patients or fewer to
contribute another 10%, and we state in the paper that half the studies we actually found only contributed 8% of patients in total. Common sense and experience dictate that small studies are often poor studies, and what use would a prevalence study of 100 patients be except in a special circumstance, and special circumstances were an exclusion criterion? We have added some words to expand on this, and on the decision to restrict searches to 1980 and later, based on formal adoption of the WHO criteria in 1968.

3. We have considerable sympathy with the point about trying to link methodological points to outcomes measured and reported. We have added a section in the discussion to explain why we felt that additional analyses were unsafe because of clinical and methodological heterogeneity, and disparities in size. To make sure that the point gets across the paragraph in the results describing the size of studies is moved earlier and extended to make the point more emphatically before the issue of actual anaemia results is addressed. Re-ordering should help with this.

4. There is no reference for the weighted mean, but we give a sentence in the methods to say how this was done, though we cannot at the moment think of another way of doing it.

5. Quite right, the numbers did not add up. It was 83, not 84 as the total. We have changed this in the paper. We really dislike flow diagrams, despite QUOROM suggesting them. This is especially the case for non-RCTs, for which electronic searches are incredibly insensitive. We and others have shown that fewer than 50% of observational studies are found by conventional electronic searches, and that most are found by diligent reading of papers, reviews, and other sources, and we reference this (Lemeshow et al, Clin Epidemiol 2005 58:867-873; Ruppen et al, Anesthesiology 2006 105: 394-399). Again, we do not think this paper the place to argue over the niceties of how to present this type of systematic review information; the fact is that those studies we looked at are included or referenced as excluded, but have strengthened our discussion a little to make the point a bit more forcefully for readers who may be unaware of this problem.

6. We do not think that there is any possible scope for additional analyses. As we said previously, most studies were relatively small, and small size means little utility because of chance and other factors. No amount of statistical jiggery-pokery can overcome a lack of adequate data, and we feel it would be dangerous. If others feel otherwise, we do provide detailed information in Additional file 2, so that they could do their own analyses if they felt sufficiently brave.

7. We believe that we have given as many references as were needed in the Results section, though we have added a few more, and ensured that all the references that were in Additional File 2 are also in full in the reference section. What we have done is to reference the small number of nursing home or hospital studies, but not the numerous
community studies, since long lists of reference numbers hardly contributes to easy reading. Readers sufficiently interested can find what they want in Additional file 2 and the reference lists

8. We think we have already done discussed heterogeneity sufficiently. In any case, the primary issue is of the smallness of studies, where the effects of random chance may overwhelm other factors, making a discussion of those other factors pointless. We have added a paragraph at the end of the discussion.