Reviewer's report

Title: Erythropoietin, uncertainty principle and cancer related anaemia

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Reviewer: Prof Jos Kleijnen

Level of interest: A paper of considerable general medical or scientific interest

Advice on publication: Unable to decide on acceptance or rejection until the authors have responded to the compulsory revisions

This is in general terms a well performed systematic review, which includes a cumulative meta-analysis that shows that a review in 1995 might already have resolved the uncertainty about the efficacy of this treatment.

I have a number of comments that if addressed would improve this paper considerably. All comments should be considered compulsory revisions.

1) There is little or no attention paid to any potential adverse effects of the treatment. Adverse effects need to be considered and discussed, even if none of the trials reported any.
2) The authors report numbers needed to treat based on meta-analysis. This should be accompanied by an appropriate message of caution. Depending on the rate of the outcome in the individual trials this NNT varies widely in different patient groups.
3) The meta-analysis is done using the Peto odds ratio. The studies included are all randomised trials and allow calculation of relative risks. In many of the included trials the outcome rate is high, which means that the odds ratio gives a more extreme result than the relative risk (if the OR is interpreted as a RR, which I assume to be the case). When doing the analysis using the RR, the pooled estimate is less favourable RR = 0.61 (95%CI 0.54-0.68). More importantly, the RR meta-analysis shows great heterogeneity (p=0.0044)! I wonder what happens if all the sensitivity analyses are done using the RR outcome. Possibly some of the heterogeneity can be explained. In my opinion the analysis needs to be repeated with RR as the outcome statistic.
4) A number of editorial suggestions: on page 3 under 'what does this paper add?' "settings" in stead of "setting"; on page 8 last sentence of 1st para 'Their exclusion could not significantly altered our findings' this sentence doesn't run well.

Competing interests:

None declared.