Author's response to reviews

Title: Systematic review and meta-analysis of the diagnostic accuracy of ultrasonography for deep vein thrombosis

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Author's response to reviews:

Response to reviewer- John Philbrick

Thank you for your helpful comments.

Minor essential revisions:
1. Amended as suggested.
2. More details of the meta-analysis methods have been added together with three new references to where the methodology is described in detail
3. We have amended this paragraph to highlight the potential effect of study design upon heterogeneity and to highlight that weaknesses in the primary data constitute a weakness in the meta-analysis.

Discretionary revisions:
1. We have added this finding and reference to the discussion.
2. We have added a paragraph to the discussion to describe management studies of US and discuss the implications of these studies, and our meta-analysis, for clinical practice.

Response to reviewer- Miriam Brazzelli

Thank you for your helpful comments.

Major compulsory revisions:
1. Poor reporting in the primary studies limited our ability to investigate the influence of methodological quality. We have amended the discussion to address this and to concede that poor methodological quality in the primary studies constitutes a limitation of this review. We did not look for verification bias in our review because one of the selection criteria for studies was that the reference standard must be venography in all cases. Therefore, apart from exception cases (such as protocol violations, which were rarely reported), verification bias should not affect these studies.
2. Reporting of US frequencies in the original studies was not detailed enough to be included in meta-regression. We have added US frequency to the potential causes of heterogeneity considered in the discussion.
3. This was also poorly reported in the primary studies, but we agree that it is an important potential source of heterogeneity. Again, this has been added to the discussion.
4. Added as suggested (2nd paragraph of results).
5. Although we sympathise with reviewer's sentiment that no pooled estimate should be given, we still include it in the revised version because we need to use it as a starting point in our exploration of between study heterogeneity. However, we do include further emphasis that great caution should be taken when interpreting the pooled result (page 9, paragraph 2).
6. The proportion of patients with previous DVT was not recorded consistently enough to be included in meta-regression. However, a number of studies did record whether patients with previous DVT were excluded. We have added this variable to the meta-regression. Interestingly, exclusion of patients with previous DVT is associated with improved specificity.
7. We have added caveats to the conclusions in the main text and abstract highlighting the need for caution due to remaining heterogeneity. We have added a paragraph highlighting the limitations of the analysis of
repeat US.
8. We have added mention of language restriction in our discussion of the limitations in relation to publication bias.
9. We have amended both the main conclusion and the abstract conclusion to reflect the heterogeneity identified and the limited data to support repeat US.

Minor essential revisions:
1. This whole sentence has been replaced.
2. Amended as suggested.

Discretionary revisions:
1. We agree that diagnostic odds ratios and a SROC model could have been used for meta-regression. However, we felt it was more appropriate to explore sensitivity and specificity separately because: a) There are good theoretical grounds for assuming that some covariates may influence one parameter more than the other, and b) This approach is more likely to be understood by non-statisticians.
2. We have added date of publication to the meta-regression. There is a weak association between data of publication and sensitivity, but no association with specificity.