Author's response to reviews

Title: Protocol for a scoping review to map evidence from randomised controlled trials on paediatric eye disease to disease burden.

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Author's response to reviews:

Point 1:

Based on the requirements of a systematic review, for example dual screening, data extraction and the objectives of your review, I don't believe this review is correctly categorised within the evidence synthesis space. Objectives 1, 2, 3 and 5 discuss the how many trials and the distribution of these trials by disease. It appears you are not interested in the effectiveness of any of the interventions you are reviewing. For example you aren't doing any meta-analysis or looking at the quality of your evidence (GRADE). As such I would recommend the authors consider revising the methods of this review as a scoping study, gap mapping or an evidence mapping review and making the appropriate changes. Or include appropriate information on the effectiveness of the interventions they are collecting (eg statistical analysis) and change the screening and data extraction parts of the protocol to include two people for all stages.

Response to point 1:

Thank you. We have clarified that we are not investigating therapeutic effectiveness or disease outcomes, and that the planned work is a 'scoping review' as our primary objective is to identify gaps in the evidence base.

We have changed the title of the protocol to reflect this:

“Where's the evidence for interventions to prevent or treat childhood visual impairment and blindness? Protocol for a systematic scoping review to map evidence from randomised controlled trials on paediatric eye disease and disease burden.”

We will also include a bubble chart as our evidence map to illustrate the distribution of clinical trial research across SVI/BL diseases in one figure. This way all SVI/BL diseases can be plotted against burden of disease, with the size of the bubble proportional to the total number of participants with each bubble coded to match an anatomical site.
The following has been added under the new heading “Evidence Map” within the Analysis section:

“A bubble chart will be used to map the quantity of trial evidence (total RCTs) against the burden of disease (relative frequency of disease), with the size of each bubble proportional to the total number of paediatric participants. Each bubble will be coded to identify the anatomical site affected.”

Point 2:

Also I don’t think the screening and data extraction procedure is enough to reduce error and bias. Other than the 20% FT screen check by a second author all other processes are completed by one person. This may result in many errors during the process and is not strict enough for a systematic or scoping review. I would recommend dual FT screen and data extraction at the minimum for the scoping review and if the authors still keep the systematic review method then dual screening and data extraction at all stages.

Response to point 2:

Thank you.

We have changed our proposed methods, which are now as follows:

Dual full-text screening of trials

• Dual data extraction of the main outcomes to measure clinical trial activity: number of paediatric trials and number of paediatric participants included in each trial.

• In addition the second reviewer (ALS) will check 10 data points extracted from a random sample of 33% of all included trials.

These changes have been made under the sub-heading “Study selection”.

Point 3:

Objective 4 and Determining the distribution of burden of disease: I am unclear how this occurs. The explanation given in lines 26-31 do not adequately explain how this is going to be achieved. What will you be doing with the data you collect to the UK reference? When you mean distribution is this for age, disease, geography? More information is needed in this section.

Response to point 3:

Thank you for providing this feedback for objective 4.
We have changed the “Determining the distribution of burden of disease” subtitle to “Burden of paediatric eye disease” in order to clarify this, as the point of this section is to highlight the source of data we use to obtain the paediatric burden of SVI/BL which is the UK reference mentioned.

We have modified this adding this section below:

“The relative frequency (%) of each disorder causing SVI/BL in children in the UK (reported in the only national surveillance study of SVI/BL in children [9]) will be used as the proportional measure of burden for each eye condition, in the absence of global burden of disease data in children. RCTs will be grouped according to the primary anatomical site affected (e.g. Retina for retinopathy of prematurity) in order to assess the distribution of evidence across all SVI/BL diseases, as per the WHO taxonomy for causes of childhood blindness.”

We also clarified this in objective 4 by including “distribution of research activity by disease”.

Point 4:

Search strategy: Will you be looking at reference lists of included studies?

Types of studies: Will you be including quasi-RCTs (i.e. in which allocation is not truly random - such as alternative walk-in into the clinic) in the review?

Primary outcomes: Are there ways that the primary outcomes will be measured? Are there unacceptable ways that you would not include in this review?

Data extraction: You mention secondary outcomes as part of the data extraction, however, there are no secondary outcomes mentioned. Can you please clarify whether there are secondary outcomes and if so what will these be.

Response to point 4:

Thank you for listing these pertinent points of clarification.

We will be looking at reference lists from included trials in order to confirm that pertinent trials are not missed.

The following has been added under ‘Search methods’ to reflect this:

“Reference lists from eligible trials will be checked to ensure no pertinent trials were missed.”

Types of studies
We will not be including quasi-RCTs in this review and thus have amended the text under ‘Types of studies’ to reflect this.

Primary outcomes

In line with our re-designation as a scoping review we have removed this section as well as the Intervention section as we do not have exclusion criteria for primary outcome measures and our review encompasses all interventions that attempt to prevent or treat eye or vision disorders in children. We will be extracting data on primary outcomes and intervention type and will present this in evidence tables as outlined in the charting the data section.

Data extraction

As cerebral visual impairment (CVI) is a neurodevelopmental outcome secondary to mortality in neonatal trials, we will include secondary outcome measures in data extraction only for CVI trials as they will not include a primary ophthalmic outcome measure.

We have clarified this point by amending this line to the data point #8 (Data extraction):

“Primary ophthalmic outcome measure (or secondary outcome measure for CVI trials)”

Point 5:

Discussion: In the discussion you have the following sentence. What do you mean by 'level of RCT evidence'?

'No study has investigated this question of the association between the level of RCT evidence on interventions and the burden of disorders that cause visual disability.'

Response to point 5:

Thank you for highlighting this point in need of a more detailed description. We have clarified this by changing ‘level’ to ‘quantity and distribution’ as we are interested in the total number of RCTs in all paediatric eye diseases but also the distribution across diseases and anatomical sites.

Point 6:

In the discussion you also discuss mention: 'Therefore the aim of this review is to ascertain whether randomised trials of interventions to prevent or treat eye and vision disorders that cause SVI/BL in children, actually reflect the burden of disease in industrialised countries for whom the necessary data on burden of disease are available.'
I'm not clear how you are doing this in the methods. I understand this is about the 'distribution of burden of disease' however the methods don't clearly articulate how this is going to be achieved. As mentioned before this needs to be made clearer.

Response to point 6

We apologise for not providing a clear explanation for our approach to assessing the distribution of burden of disease across SVI/BL disorders.

We have adjusted the wording in both the abstract and analysis section to clarify that we will be measuring how well the distribution of RCT evidence aligns with the burden of eye disease through a statistical test of association (Spearman’s correlation coefficient).

The following has be added to the methods section of the abstract and under the Analysis section to clarify this:

“The degree of alignment between paediatric trial activity and burden of SVI/BL disease (relative proportion) will be measured using a test of association (Spearman’s correlation coefficient).”

Point 7:

PRISMA statement 15d: You need to describe the data synthesis even if it's not quantitative. I believe you do this under the 'analysis' heading.

Response to point 7:

Thank you for pointing out this PRISMA requirement. 15d has now been completed by referencing the ‘analysis’ section.