Author's response to reviews

Title: Outcomes when Congenital Heart Disease is diagnosed antenatally versus postnatally in the UK: a retrospective population-based study

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Author's response to reviews: see over
Dear Editor,

RE: Cover Letter for Manuscript Re-Submission

Thank you for considering our original research manuscript, entitled “Outcomes when Congenital Heart Disease is diagnosed antenatally versus postnatally in the UK: a retrospective population-based study”, for submission to your Journal.

We are appreciative of the positive feedback from both peer-reviewers, as well as the pertinent questions they have raised. As requested, we have endeavoured to address the comments from the Editor and both peer-reviewers as outlined below.

**Reviewer 1:** Could the authors comment on why data on patients operated at other centres could not be obtained? Have they considered widening / enlarging the dataset?

**Our Response:** The study was undertaken as part of an Intercalated BSc and thus had limited time for data collection. This impacted on the ability to collect information on cases operated on outside the county. It would certainly be interesting to utilise other regional anomaly registers to increase our data set and, time allowing, this is something we may look to do in the future. Regardless, we feel the limited amount of similar data available for British populations in the literature justifies submission at our study’s current scope.

**Reviewer 1:** The paper is set up so that you have to get to the tables at the end before you know [what the outcome measures were] or else jump back and forth once you find out where they have been put. Would the authors consider changing this element of the structure of the report?

**Our Response:** The tables outlining the outcome measures were put at the end as per the manuscript submission guidelines. It is anticipated that if the report was to be accepted for publication these tables would be inserted close to the text where the outcome measures are first referenced and should therefore eliminate this problem.

**Reviewer 1:** My understanding is that the authors have chosen to use PH<7.35 to define presence of acidosis...Why limit the scope of this aspect of the analysis to such a blunt comparison?

**Our Response:** The proforma that was used for data collection focused simply on the presence of acidosis (pH<7.35) in the post-natal period. We did not anticipate that so many of the cases would meet this criterion. Regretfully, as this information was collected quantitatively, levels of acidosis cannot be commented on. We decided to still include this data in the report as there was a difference (albeit non-significantly) between acidosis reported in pre and post-natally diagnosed TGA.
Reviewer 1: “Can the authors comment on the indication for intubation? If these were mainly emergency intubations or done for instability then certainly this is important.”

Our Response: Unfortunately, as stated in the previous question, a lot of the data was collected quantitatively (intubated post-natally: Yes or No) and as such indications for intubation cannot be commented on.

Reviewer 1: “Given the small numbers the study may be underpowered to detect a difference [in survival], can the authors comment on this? Has any power calculation been done?”

Our Response: This study has provided preliminary data which will facilitate a more definitive epidemiological study and because of its nature a power calculation was not performed.

Reviewer 1: In babies and small children with CHD neurological and developmental abnormalities are under detected...an objective test such as Bayley, Mullen or other standard test at a given age is more likely to determine whether or not there is a difference in neuro-developmental outcome between the two groups. Given the retrospective nature of the data this type of assessment is unavailable. Can the authors comment on any potential bias in their approach to this element of outcome?”

Our Response: The assessment of neuro-developmental outcome depends on a diagnosis being referenced in the individual case notes. It is possible that the cases which are more medically unstable (and therefore have more frequent follow up) will have a greater opportunity to have a negative outcome diagnosed and recorded if present, than those cases that are reviewed less frequently. This potential source of bias has now been included in the discussion.

Reviewer 1: “Ongoing cardiac problem’s is partly evidenced by the need for medication. Do the authors have any concerns about the objectivity of this assessment?”

Our Response: It is possible that variations in long-term management of isolated TGA or HLHS may be managed differently amongst clinicians. These figures may therefore be impacted upon by individual clinician practices. However, it is hoped that as the majority of these cases were followed up by a single clinical department, prescribing practices will have been consistent throughout. In addition, the use of medication does provide an objective measure of the need for on-going cardiac ‘support’.

Reviewer 2: “In abstract, line 19: ‘a large but non-significant increase’ is misleading.”

Our Response: This line has been altered.

Reviewer 2: “Please remove the limitation of retrospective study in previous literature. Your study is also one retrospective study.”

Our Response: The sentence explaining the limitations of retrospective studies has been removed. We do however believe our data differs from other similar reports by the way in which our cases were identified.

Reviewer 2: “If you have follow-up period data, you can use a method of survival analysis by Cox proportional hazards model.”

Our Response: As mentioned in the response to Reviewer 1, this study has provided preliminary data which will facilitate a more definitive epidemiological study. Given the small numbers in the study, statistical advice was not to over analyse this data set.

Editor: “Further statistical input should be by the authors with the help of a statistical consultant”

Our Response: Statistical advice was sought and the calculations re-checked. As stated previously,
the advice given was to not over analyse the data set and that the existing calculations went far enough to present the findings.

**Editor:** “We recommend that you copyedit the paper to improve the style of written English.”

**Our Response:** The paper has been reviewed again by the authors, with small changes made throughout in an effort to improve the written style.

We hope the revisions are sufficient for your continued consideration of our research paper.

Kind regards,

Lewis Peake