Authors' reply to "Unpacking the Complex Relationship Between Postpartum Haemorrhage and Cardiovascular Disease"

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Dear Dr. Papageorghiou,

We thank Dr May and colleagues for their comments on our paper[1] about the relationship between postpartum haemorrhage (PPH) and cardiovascular disease (CVD).

We agree that it is important to consider potential confounding by hypertensive disorders of pregnancy (HDP) in our study. With this in mind, we adjusted for the presence of HDP prior to PPH in our model. We also explored potential effect modification by HDP of the association between CVD and PPH. These results indicated a slightly stronger association between PPH and CVD among women with HDP. Importantly, we found similar results in our analysis among women with severe PPH (blood loss ≥1500 mL or management of severe PPH). We appreciate the concerns raised about the lack of data about acute-onset coagulopathy or PPH requiring blood transfusion. With the data available to us, we were unable to explore the differences between women who required blood transfusion and those who did not. However, given that blood transfusion was more likely to occur as a result of PPH, i.e. it is on the causal pathway between the main exposure and the outcome, and therefore likely to be a mediator, it would have been inappropriate to adjust for it in our models.[2, 3]

We acknowledge the importance of considering how standards of care for PPH may have changed over time. It was not possible, with the data available to us, to explicitly address such changes, but we adjusted for year of childbirth in all models to account for potential confounding by unmeasured variables such as changes in management of PPH, estimation of blood loss, etc over time, and used extended Cox regression models to allow for time-varying hazard ratios over different follow up periods.

Finally, in terms of appropriately accounting for the effect of past medical history and co-morbidities developing later in life, we would first like to clarify that adjustment for past medical history was conducted for each birth in our model, not just past medical history before the first birth (see footnote to Table S3). Table S4 describes maternal characteristics at the level of the woman and therefore summarised the distribution of past medical history at first birth. A similar table summarising past medical history and other maternal characteristics at the level of births is available upon request. So, while it is possible that some women may have had undiagnosed/unreported co-morbidities, any co-morbidities reported as ‘past medical history’ before any birth were adjusted for in our analyses. We agree that there is a potentially complex interaction between PPH, other co-morbidities, and CVD. Some women may have gone on to develop other comorbidities after their last birth episode and prior to the development of CVD. However, these events would have been potential effect modifiers, not confounders, since they could not have influenced the woman’s risk of PPH.

We value the opportunity to discuss our results in more detail, and hope that our paper and this discussion prompts more consideration of the complex relationship between obstetric complications and CVD.

References

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