Reviewer’s report

Title: Seeking consent to genetic and genomic research in a rural Ghanaian setting: the MalariaGEN experience

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Reviewer: Gail Davey

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General. This is a very welcome addition to the literature on research ethics in low-resource settings. The authors are to be congratulated for preceding a study on malaria genetics with this thorough assessment of issues relevant to the ethics of conducting the study in the Kassena-Nankana District, northern Ghana. Many issues identified will be highly relevant to other groups taking forward genetic and genomic research in similar settings (in particular, but not limited to, new studies arising through the H3Africa initiative, as noted by the authors).

The research aims are well defined, and the methodology is appropriate to meet these aims. Data appear sound, and the manuscript adheres to the relevant standards for reporting and data deposition. However, I have a few comments on how this manuscript builds on earlier research that may help the authors focus on what makes the research reported here genuinely novel.

1. Major Compulsory Revisions

Tindana, Kass & Akweongo’s 2006 study based in the same two communities is an important foundation for further ethics research in the Kassena-Nankana District. Although this is referenced in the third paragraph of the Introduction (reference 11), it is not referred to again in the Discussion. I feel the authors could explain more clearly how the present study builds on this research. The earlier study clearly established preferred routes for permission-seeking, the vital role that trust in NHRC/VAST plays, preferred consent processes and issues relating to the benefits of research. The present study reiterates some of this (the consent process, routes of permission-seeking, trust in NHRC/VAST), which is fine, but where the present study goes beyond the earlier one, this should be emphasized in the Discussion. Perhaps more importantly, the areas that are new in the present study should receive even more attention: difficulties related to enhancing community understanding of genetics and genomics; the ethics of requesting consent in an emergency setting and issues relating to international data sharing. These are new areas, explored for the first time in these communities, and more could be made of them. For example, mothers agreed that it was acceptable to take blood samples prior to fuller discussion of the research project. This is hugely important information. Similarly, there is a general view that researchers could conduct ongoing studies with 'leftover' samples without seeking additional permission from donors. This is more nuanced, and needs further exploration, but again is very relevant to many other studies that may consider this approach. Giving more weight to some of these
issues is likely to require re-structuring of the Introduction and Discussion (and also be reflected in the Abstract).

2. Minor Essential Revisions
A. Please be more precise in the penultimate sentence under ‘Study site’. ‘... with up to 57% of the population having never been to school’ could mean only 1% of the population ...or 56.9% of the population. The Kassenas and Nankanis may differ in school attendance; if so, please give a precise figure for each group.
B. Under ‘Sampling’, the idea of mothers of cases and controls is introduced rather abruptly. It would be useful to add a sentence into para 5 of the introduction (where the MalariaGEN project is mentioned) to briefly explain the study design.
C. (Minor Issue not for Review) This is probably very pedantic, but I was taught that data are plural. This comes up in the Methods (para 1), under ‘Data collection’ (first line).

3. Discretionary Revisions
One very interesting area that is not fully explored is that of conveying genetic concepts to groups with little background in science. The authors note the difficulty of getting across ideas about malaria genetics towards the end of the section ‘Enrolling cases in the hospital’ and throughout the section ‘Knowledge and understanding of genetic and genomic research’. Views of fieldworkers are quoted, but I wonder if mothers’ conceptions of ‘familial-ness’ were explored at any stage. It would be valuable to know if there is any community familiarity with issues of heredity that are expressed in terms other than those about ‘the blood’. If the authors have any more information on this, they may wish to consider adding it.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
No financial competing interests.
I co-authored an article with one of the manuscript's authors 2 years ago.