Reviewer's report

Title: Handling Ethical, Legal and Social Issues in Birth Cohort Studies involving Genetic Research: Responses from Studies in Six Countries

Version: 2 Date: 12 February 2010

Reviewer: Laura Beskow

Reviewer's report:

Response to common comments

Both reviewers suggested that additional details about study methods would be helpful. We have expanded this discussion, including points about recruitment of participants (e.g. contacted investigators from 14 studies and six agreed to participate) and conduct of the interviews (e.g. conducted in English, average duration of 45 minutes). The original manuscript noted that the interviews were semi-structured and conducted by co-author JL.

• These are helpful changes.

Response to comments from Dr. Beskow

Dr. Beskow comments on our approach of combining results and discussion. We have maintained this format as it is permissible under the journal guidelines. We prepared an earlier version of the paper that separated these two sections and found that the key findings could be described most efficiently by combining results and discussion. In particular, this structure permits discussion observations to be made immediately after findings have been summarized. To state the findings in one section, then comment on them in a subsequent section flows less effectively and some readers may find that they must jump backward and forward in the text to put the discussion points back in the context of the findings. By combining results and discussion, we eliminate this inefficiency.

Dr. Beskow asked about information we retrieved from publicly available sources about the studies. We looked up study websites where available to search for general background documents explaining the scope and purpose of the study. This information is summarized in Table 1. We also looked for copies of consent documents and any study policies (e.g. about storage of data and samples). We also located several articles in peer-reviewed literature where study investigators reported on their experiences in design, recruitment, etc. We reviewed these resources primarily to help provide us with background information before conducting the interview. Our objective was not to compare interviewee statements with statements in publicly accessible documents (for e.g., to look for discrepancies) and we did not state this as an objective in our invitation letter or during our verbal consent process with interviewees. Therefore, we do include this type of analysis in our paper.

Additionally, we did not obtain consent materials from three of the six studies as
they were not available in English, so we have only included illustrative examples from written sources from the Born in Bradford Study, the CHILD Study and the National Children’s Study. We want to give relatively equal attention to the six studies, so the dominant focus of our paper is on information obtained from interviews, rather than attempting to glean information from written documents from the studies. This also addresses the review comment about whether we studied policies to examine handling of sensitive information.

• I understand your point about not looking at discrepancies because mention of this was not included in the way the project was framed to interviewees. Nonetheless, information that is publicly available could obviously be used to augment your manuscript and help create a more complete view of these studies (without assessing discrepancies). Given that you have done the work of finding and reading this information, it seems a missed opportunity not to make a bit more use of it. Be that as it may, given your explanation above that this material was only used for background, you might consider moving reference to it earlier in the Methods section. Right now it appears near the end, which may lead to some confusion about the role it played in your study.

Dr. Beskow also noted our mention of external researchers in the section on Assent and Consent. Many of the studies do involve a large number of researchers, but they may be affiliated with various institutions involved in the study. In referring to external researchers, we mean researchers who do not have such institutional connections. We include this mention of external researchers in the section on Assent and Consent as we note that some scholars argue that data and samples should not be shared with such researchers until the child is old enough to consent to this disclosure.

• It might be useful to work this explanation into the manuscript. Also, with regard to the argument you present from the Gurwitz paper, you might consider noting the other arguments presented in letters published in response to that paper.

It was also suggested that we could expand on the section on withdrawal. However, the studies were all very consistent in their handling of withdrawal issues. Participants are informed of their right to withdraw without penalty and, if they choose to withdraw, they generally have a choice about how previously collected data and samples are handled. We have revised the paper to clarify that where a participant requests full withdrawal, it is not possible to withdraw samples or data that have already been used or analysed.

• This is a helpful change.

Dr. Beskow suggested caution in using the term “blanket consent.” We concur with this cautionary advice and note that we refer to “blanket consent” as “an approach to consent where participants are asked to give one-time consent to unlimited future use,” which we believe is consistent with how the reviewer uses the term. We note that none of the studies we examined use blanket consent. We had one subsequent reference to “blanket form of consent” on page 18, but have changed this to “general form of consent”.

• This is a helpful change.
Dr. Beskow noted that the issue we raise about failure of anonymisation is an important one, but suggested that we add context about how difficult re-identification actually is. This is a growing area of study and we have cited examples of recent literature. Our principal intent, however, is to highlight this issue, but not to detail the multitude of factors that may facilitate or impede re-identification. We have added a statement that “there continues to be debate about the degree of effort and cost required to re-identify specific individuals from de-identified data and samples” (p. 14).

• My suggestion was not to detail the multitude of factors that may facilitate or impede re-identification, but rather to provide “some context about how difficult re-identification actually is.” The change you made addresses this point.

It was suggested that we consider adding reference to the issue of genetic testing in children. In fact, this issue is central to all the ELS issues we address in the paper and we have cited general literature on the topic of children and genetic research (e.g. notes 4,5,6,22,35). There is also a large body of literature on ELS aspects of genetic testing of children in the health care context, particularly the issue of pre-symptomatic testing of adult-onset conditions. We focus on the research context, so do not incorporate literature that focuses on clinical delivery of health care services to children.

• My comment here was specifically on the “Handling of Results” section, where I don’t find direct reference to the problem of returning research results related to children. Adding a line or two to highlight that the much-debated topic of offering research results is made that much more complex by the involvement of children would address this comment. I absolutely agree with the approach of not mixing clinical delivery of health care services and research—but the issues around discovering significant risk for an adult-onset condition in children still apply in research.

Finally, Dr. Beskow recommends caution around recommending that participants should be offered options about receiving results. We strove to word this recommendation very carefully. We recommend that researchers consider the types of information that may arise (e.g. findings of known clinical significance, incidental findings, etc) and determine an approach to handling these various types of information. Whatever approach researchers decide to follow (and for which they receive ethics approval), we note that this issue should be discussed with participants during the consent process and where researchers propose to return results, participants should have some choice in receiving results. For instance, if researchers propose to return all results (which is not an approach any of the six studies took), we would advocate that participants be able to exercise some choice about whether they want to receive all results, especially as some may not want to receive results of unknown significance. We also note that participants should decide about disclosure of results to their health care providers.

• Personally, I question whether participants can be given enough information to comprehend what kinds of results might be generated, particularly in the context
of a biobank, to make an informed decision at the time of initial consent. However, my comment was primarily that you consider your recommendation carefully and it sounds like you have. One additional note, though, is that there is a difference between offering and receiving results. I would think participants would be approached with an offer to learn specific results, and then there would always be a consent process before actual disclosure—so you might think about whether the choice you recommend is about offering versus receiving.