Reviewer’s report

Title: Protocol for assessing maternal, environmental and epigenetic risk factors for dental caries in a population of Queensland children

Version: 1 Date: 08 Sep 2015

Reviewer: Deborah Polk


The purpose of this paper is to describe the research protocol for a study examining maternal, environmental, and epigenetic risk factors for dental caries. This study is part of a larger longitudinal study of children and their families, "Environments for Healthy Living - the Griffin Birth Cohort study," in Queensland, Australia.

The writing is generally clear and the topic is relevant for the BMC Oral Health audience. The level of detail provided in most of the sections was appropriate and sufficient.

Major Points

1. Please provide a rationale for why we need more risk factors for oral health. At lines 85 through 93, you list many risk factors for oral health. If the purpose of the study is to identify additional risk factors, you should provide an explanation for why the existing risk factors are not sufficient.
2. Please provide a conceptual model. There are many, many variables being assessed in this study. I need to see how you think they all fit together. You may decide to narrow the focus of the study to address things that can cause methylation and relationships between methylated genes and disease.
3. Please provide more detail in data analysis section. The data analysis section needs a lot more detail. See examples of published protocols (listed below) for examples of data analysis sections. I think having a conceptual model will help with this section. Once you have a conceptual model, then you can think about mediators and moderators/confounders and make sure your analysis treats them appropriately. I'm also really concerned about the number of analyses that could potentially be conducted. Will p-values be adjusted to account for this? Or will some other strategy be adopted?

Minor points

1. In the Abstract, lines 38-39. The sentence describing the birth cohort beginning in 2012 and six year old children is unclear because children born in 2012 are not yet six. The language
used at lines 145 and 154 later in the manuscript is clearer, stating that the children were six in 2012.

2. Lines 49 to 52, Discussion. The Discussion section of the Abstract is written as though this manuscript is a proposal and not a protocol.

3. Somewhere in the Abstract, perhaps in the Methods section after the first sentence, it should be stated clearly that this is a cross-sectional study.

4. Line 90. I'm not sure "Conversely" is the right word. Perhaps "Additionally?"

5. Line 106, inherited alterations in sugar metabolism. Although I agree that there probably are inherited differences in sugar metabolism, I think the direct, topical effect of sugar on the oral flora is far more important for the caries process.


7. Line 153, Sample recruitment. This section also describes the examination study participants undergo. You might add that to the section title. What happens if you see disease during the examination? Do you give referrals for treatment? Please address this.

8. Lines 154 through 157. Do you have any information about differences between families that accepted and families that declined to participate? Also, has the representativeness of the study sample relative to the population been retained?

9. Line 166, Figures 1a and 1b. I think you can combine boxes and reduce the flow chart to one figure. See examples of published protocols (listed below) for examples of flow charts.

10. Lines 173 to 182, Sample size. This gets back to my major concern about the lack of information about the statistical analyses. You say the sample size is based on multivariate regression model with up to five variables, but in the data analysis section, you don't commit to this analysis. Also, would this sample size be true even if you conducted 100 regression
models with up to five variables? Or is it true only if you conduct one regression model with up to five variables? Given all the analyses you presumably will be conducting, this sample size seems surprisingly small to me.

11. Lines 183 to 192, Primary outcome variable. As written, you don't actually commit to a primary outcome variable. Also, how is the severity of restored lesions determined? It doesn't seem like it can be determined. So then untreated caries severity is primarily a measure of how long the carious lesions have been around. Do you have any hypotheses about reversible versus nonreversible lesions?

12. Lines 194 to 196, Main explanatory variables and Lines 197 to 200, Oral health knowledge and practice. Please provide more information about these measures. See examples of published protocols (listed below) for examples of the level of detail for measures. With respect to oral health practices, specifically what is being measured? Oral hygiene, sugar consumption? Other factors?

13. Lines 202 to 207, Anthropometric measurements and Lines 218 to 224, Periodontal status. Please provide a rationale for why these measures are being taken. Do you have hypotheses about weight and timing of tooth eruption, for example?

14. Lines 226 to 238, Demographic and environmental data. How will you handle it in the data analyses if families change over time, such as if mother's educational status changes for example?

15. Lines 240 to 257, Genetic and epigenetic markers. As I understand it, this manuscript is describing the study protocol. If the protocol hasn't yet been determined for the genetic and epigenetic markers, then it may be premature to publish. It seems like this manuscript should describe the final protocol. And it also states that results from the pilot study will be used to define a sample size for a large scale future study. Yet in the Sample size section earlier in the manuscript, the case was made for a sample size of 147. This is confusing.

16. Table 1. How are the data in this table organized? It might make sense to organize them by caries experience. And if you have data about the caries experience of study participants, you could add that as another column.

Protocols published in BMC Oral Health that can be used as examples.

1. The midwifery initiated oral health-dental service protocol: an intervention to improve oral health outcomes for pregnant women
Maree Johnson, Ajesh George, Hannah Dahlen, Shilpi Ajwani, Sameer Bhole, Anthony Blinkhorn, Sharon Ellis, Anthony Yeo BMC Oral Health 2015, 15:2 (15 January 2015)

I liked the "Aims and hypotheses" section and the "Data analysis" section.

I also liked in the "Development of the intervention" section how the authors informed the reader that the intervention was developed using a developmental framework for complex interventions, with citations.

2. Developing Effective and Efficient care pathways in chronic Pain: DEEP study protocol

3. Protocol for diagnostic test accuracy study: the efficacy of screening for common dental diseases by Dental Care Professionals
Richard Macey, Tanya Walsh, Anne-Marie Glenny, Helen Worthington, Martin Tickle, James Ashley, Paul Brocklehurst BMC Oral Health 2013, 13:45 (21 September 2013)

4. The FiCTION dental trial protocol - filling children's teeth: indicated or not?
Nicola PT Innes, Jan E Clarkson, Chris Speed, Gail VA Douglas, Anne Maguire, FiCTION Trial Collaboration BMC Oral Health 2013, 13:25 (1 June 2013)

I like the "Trial purpose and objectives" section and the "Basis for the study design and setting" section. I like Figure 2, how it combines in the same box everything done at the same visit. I like how they distinguish primary from secondary outcomes. I like the level of detail in the "Statistical methods" section.

5. Protocol for "Seal or Varnish?" (SoV) trial: a randomised controlled trial to measure the relative cost and effectiveness of pit and fissure sealants and fluoride varnish in preventing dental decay
Ivor Gordon Chestnutt, Barbara Lesley Chadwick, Simon Hutchings, Rebecca Playle, Timothy Pickles, Catherine Lisles, Nigel Kirkby, Maria Zeta Morgan, Lindsay Hunter, Ceri Hodell, Beverly Withers, Simon Murphy, Sarah Morgan-Trimmer, Deborah Fitzsimmons, Ceri Phillips, Jacqueline Nuttall, Kerenza Hood BMC Oral Health 2012, 12:51 (20 November 2012)
I like the "Trial aim" and "Trial objectives" sections. I like Figure 2 of participant flow through the trial. I like the "Statistical analysis" section. I like its breadth, though I wish it had greater detail about what analyses were going to be conducted.

6. Protocol for Northern Ireland Caries Prevention in Practice Trial (NIC-PIP) trial: a randomised controlled trial to measure the effects and costs of a dental caries prevention regime for young children attending primary care dental services

   Martin Tickle, Keith M Milsom, Michael Donaldson, Seamus Killough, Ciaran O'Neill, Grainne Crealey, Matthew Sutton, Solveig Noble, Margaret Greer, Helen V Worthington
   BMC Oral Health 2011, 11:27 (10 October 2011)

   I like the "Statistical analysis" section.

7. Study protocol of the Center for Oral Health Research in Appalachia (COHRA) etiology study
   Deborah E Polk, Robert J Weyant, Richard J Crout, Daniel W McNeil, Ralph E Tarter, John G Thomas, Mary L Marazita
   BMC Oral Health 2008, 8:18 (3 June 2008)

   Are the methods appropriate and well described?
   If not, please specify what is required in your comments to the authors.

   No

   Does the work include the necessary controls?
   If not, please specify which controls are required in your comments to the authors.

   Unable to assess

   Are the conclusions drawn adequately supported by the data shown?
   If not, please explain in your comments to the authors.

   Unable to assess

   Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
   If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

   I recommend additional statistical review

   Quality of written English
   Please indicate the quality of language in the manuscript:
Acceptable

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