**Reviewer’s report**

**Title:** Hereditary gynaecologic cancers in Nepal: A proposed model of care to serve high risk populations in developing countries

**Version:** 0  **Date:** 26 Jul 2017

**Reviewer:** Finlay Macrae

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The paper is a very good attempt to introduce a model of delivery of hereditary gynaecological cancer care to developing countries such as Nepal. There are obvious issues, touched on, of competing priorities for the limited health dollar which is likely the major block to implementation. A range of other cultural, geographic and process barriers are well described. There is a suggestion that a pilot program might be the way forward is perhaps not emphasized enough. Some idea of what the QALY value that can be afforded in Nepal would help to underpin the argument made for introduction of genetic testing in Nepal.

The paper could make reference to the debate as to whether all endometrial cancers (diagnosed at any age) or only those diagnosed under 60 or 70 should be tested for Lynch Syndrome - and the need for reflex methylation testing for those tumours with loss of MLH1, to relieve the downstream burden gene testing and counselling.

There are already molecular diagnostic services in Kathmandu. That should be mentioned, and any barriers to collaboration with these services described be they professional, financial or organizational. I think that it would be important that such an enthusiastic gynaecological oncology group is linked in to these resources. [I can assist in that introduction - for example, there is a Nepalese Country Node of the Human Variome Project]

Mainstreaming can be the only way forward for countries like Nepal and this is well promoted in this manuscript. There is little mention of any culturally-specific issues relating to informed consent. When would such consent be done in the context of a service in Nepal? At tumour testing? After methylation testing (is negative)? Before germline testing?

The need to establish the extent of founder mutations is a clear priority in Nepal given the endogamous society - as well recognized in the manuscript.
The paper gives no hint, even from case series or anecdotal experience, that there is burden of hereditary gynaecological cancers - though doubtless there is.

In the overall, the paper does not give sufficient credence to the broader role of familial cancer diagnosis, and management. Notwithstanding the enthusiasm of the gynaecological oncologists represented in the authorship, a model that included familial breast, colorectal, and other cancers including gynaecological cancers would seem a better strategy given the need to address barriers (eg educational, geographic, cultural) all these syndromic presentations. Let alone a broader clinical genetics service model.

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