Reviewer's report

Title: Prevalence of HPV16, 18, 52, 58 and 59 in cervical cancer in Sichuan province, China

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Reviewer: Gary M Clifford

Reviewer's report:

The authors present a study of the importance of certain high-risk HPV types in a case series of cervical cancer from Sichuan province China, which in itself is worthwhile. However, the paper also attempts to be a validation exercise comparing three different PCR techniques, which identifies many more multiple infections, and which complicates the message considerably.

Major Compulsory Revisions

1) There are already a lot of similar data available from China. The authors should at least reference and discuss "Human papillomavirus type-distribution in the cervix of Chinese women: a meta-analysis. Int J STD AIDS. 2008" including more than 2000 Chinese cancer cases, and "Human papillomavirus type distribution in invasive cervical cancer and high-grade cervical lesions: a meta-analysis update. Int J Cancer. 2007" that summarises all the Chinese data in the published appendix.

2) The long and similar names of the three different PCR techniques makes for very difficult reading. Please at least define some simpler terminology in the methods to be used throughout e.g. MY09/11, One step TS, nested TS.

3) In addition, to help the reader through the comparisons of the different tests, please describe in which order the 3 tests were performed, and try, as much as possible, to keep the same order when describing the tests in the different parts of the manuscript. For example, it was not clear to me which of the three tests were performed on all samples, or which were used only when the other two were negative.

4) Is One-step a commercial product? Why is the capital letter always used?

5) Multiple infections - The authors describe that nested TS PCR improves the sensitivity for HPV52, HPV58 and HPV 59 but, importantly, predominantly in multiple infections with HPV16. The conclusion of the abstract is then that 52, 58 and 59 are more important than HPV18 in this population. However, if one looks at single infections, 18 remains by far the most important type after 16, suggesting that the additional gain in types are just benign passenger infections with low copy number.

The authors should clarify that the identification of HPV DNA does not necessarily link the infection with the tumour, especially in the presence of
multiple infections. This caveat is completely missing at present.

6) The discussion should not simply repeat the findings reported in the results, and could be made much more concise if concentrating on comparisons with other data.

7) The definition of optimal sensitivity - the authors refer to the nested PCR as an improvement on the sensitivity of other methods. However, many would argue that the optimal HPV test has "clinical sensitivity", namely only picking up the one HPV type that is clonally related to the tumour, whilst ignoring passenger infections at extremely low copy number. The identification of many multiple infections can thus hinder rather than help the interpretation of results. This issue should be clarified, at least in the discussion.

Minor Essential Revisions

The authors quote two meta-analyses in the introduction (refs 7 and 8) to report geographical differences in HPV type distribution. However, these two analyses refer to women with normal cytology and LSIL. We know that the geographical differences reduce greatly with increasing severity of cervical lesions, so that the differences at the level of cancer are much less (Smith et al, International Journal of Cancer, 2007).

Discretionary Revisions

**Level of interest:** An article of limited interest

**Quality of written English:** Not suitable for publication unless extensively edited

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

**Declaration of competing interests:**

I declare that I have no competing interests