LETTER TO THE EDITOR

Human papillomavirus assay design is a crucial consideration for self-collection based cervical screening

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Dear Editors,

Tan and colleagues recently published an interesting study [1] which used self-collection in a remote region of Malaysia during the first wave of the COVID19 pandemic in May, 2020. The study design involved participants collecting their own specimen which was then transported to the Universiti Malaysia Sarawak for testing using the careHPV test. The primary finding of the study was that only one out of 55 (1.82%) participants returned a positive high-risk Human papillomavirus (HPV) result. The incorporation of self-collection into the testing paradigm should be applauded but there are some critical technical issues which the authors didn't address. careHPV has met the World Health Organization (WHO) standard for pre-qualification with a positive agreement of 74.42%, however wasn't able to meet international standards for clinical validation, primarily due to a lack of sensitivity compared to a reference assay (0.86 (95%CI 0.79 – 0.94)) for cervical intraepithelial neoplasia grade 2+ (CIN2+).[2] careHPV has an European claim for self-collection, however independent studies have shown that it, along with other signal amplification assays, are not suitable for self-collection due to insufficient sensitivity.[3]

Another aspect of careHPV, which the authors acknowledge as a limitation, is the lack of a control for sample adequacy. Pragmatically, this means that if a collection device is returned without any specimen being collected, careHPV would produce a negative result, rather than an error noting insufficient material to test. If participants in a study didn't engage with the process it may produce samples which lack any clinical specimen.

The authors have previously undertaken a study in the same region of Sarawak which used the careHPV test, but with clinician-collected specimens. The oncogenic HPV positivity rate for this earlier study was 8% (6/75). The obvious difference in protocol between these two studies is that of clinician-collected vs self-collected specimens. The author's highlight this as a possible limitation but provided citations to suggest that other studies have shown strong concordance between self- and clinician collected specimens for the same patient. As no clinician-collected specimens were obtained during the current study it is difficult to draw the same conclusions on concordance between sample types when they are taken from different people. Another outcome of this study was that only 10 participants completed the self-sampling perception survey, compared with 55 who undertook the initial HPV literacy study. This raises the possibility that participants may not have been engaged with the self-collection process.

The evidence highlighted above provides a rationale for why this study found so few positive results. A combination of participants returning swabs without clinical specimens, and the use of a HPV test which is less sensitive and lacks a sample adequacy control, could produce an outcome which underestimates the prevalence of oncogenic HPV.

REFERENCES

1. Tan CS, Hamzah ND, Ismail ZHF, Jerip AR, Kipli M. Self-sampling in Human Papillomavirus screening during and post-COVID-19 pandemic. Med J Malaysia 2021; 76(3): 298-303.
2. Arbyn M, Simon M, Peeters E, Xu L, Meijer CJLM, Berkhof J, et al. 2020 list of human papillomavirus assays suitable for primary cervical cancer screening. Clin Microbiol Infect 2021; 27(8): 1083-95.
3. Arbyn M, Smith SB, Temin S, Sultana F, Castle P, Testing CoS-SaH. Detecting cervical precancer and reaching underscreened women by using HPV testing on self samples: updated meta-analyses. BMJ 2018; 363: k4823.

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