

Self-sampling HPV DNA test for cervical cancer screening in Singapore: A prospective study

Dear Editor,

Cervical cancer is known to be the most preventable malignancy through both vaccination and screening. However, it remains the tenth most common cancer among women in Singapore. Cervical cancer screening is opportunistic in Singapore and only 1 in 2 women undergo regular screening in Singapore.¹ Under-screened women are at the highest risk of cervical cancer, and reasons for poor compliance include fear, discomfort and a busy schedule.² The superiority of human papillomavirus (HPV) DNA test compared to cytology screening in detecting pre-invasive cervical disease has been well-established due to its higher sensitivity,^{3,4} resulting in the shift to HPV primary screening in Singapore in 2019.⁵ The self-sampling method of HPV testing has been mooted as a potential strategy to address the issue of poor compliance to cervical cancer screening. International studies have shown a high level of concordance between self- and physician-sampling for the detection of HPV DNA,^{6,7} with strong evidence for women's acceptability for self-sampling.⁸

The primary aim of the study is to establish the acceptability of self-sampling for cervical cancer screening among women attending gynaecological care at a tertiary hospital. Our secondary aim is to compare the concordance between the self-sampling and physician-sampling methods. To our knowledge, there has been no study on HPV self-screening in Singapore. This study would have a considerable impact on future national screening policies that could increase cervical cancer screening uptake by introducing an accessible method to the under-screened population in Singapore.

This was a prospective, randomised crossover study of 300 women attending gynaecology clinics in National University Hospital, Singapore, carried out from April 2019 to September 2020 (online Supplementary Fig. S1). Ethical approval had been obtained from the Domain Specific Review Board (Reference: 2018/00846-SRF0002). The study was registered with ClinicalTrials.gov (identifier: NCT03813576). The inclusion criteria were all women aged 30–69 years who were scheduled to attend cervical screening. The exclusion criteria were women who are pregnant,

with previous total hysterectomy, previous history of cervical cancer, currently menstruating, virgo intactas and women with recent negative cervical cancer screening. We utilised a crossover trial design. Participants were randomised into 2 groups in a 1:1 ratio, with the first arm undergoing the HPV self-sampling before physician-sampling and the second arm in the reverse sequence. All self-sampling and physician-collected swabs were processed using the Cobas 6800 HPV assay (Roche Diagnostics International AG, Rotkreuz, Switzerland). After their experience, participants completed a questionnaire to assess their acceptability of self-sampling. The participants' clinical management was not affected by the study.

The sample size was calculated based on the number of women aged 30–69 in Singapore's population (as of June 2017), using G*Power. All data were analysed using SPSS version 20.0 (SPSS Inc, Chicago, US). Descriptive analyses were done on the survey data, while the agreement of self- and physician-collected specimens were assessed using Cohen's kappa (κ). The 95% confidence interval (CI) was estimated for κ . We also calculated sensitivity and specificity with 95% CIs between the 2 sampling methods.

Table 1 summarises the participants' preferences regarding the type of HPV sampling method, as well as the performance of HPV self-sampling method in cervical cancer screening. The majority of participants found self-sampling easy to perform (79%) with only minimal discomfort (89%). Most participants preferred self-sampling (84%) over physician-sampling (13%), and among those who preferred self-sampling, 86% expressed that they would prefer to perform the self-sampling at home rather than a clinic (14%). If given the option of self-sampling in the future, 90% expressed that they were more likely to participate in cervical cancer screening. About half of the participants also expressed willingness to pay for the self-sampling swab (51%).

A total of 60/300 (20.0%) self-collected samples and 63/300 (21.0%) of physician-collected samples tested positive for high-risk HPV. Two hundred and seventy-seven (92.3%) of 300 self-sampling test results were in

Table 1. Study participants preferences regarding the 2 sampling collection methods and the performance of human papillomavirus self-sampling method in cervical cancer screening

	Yes No. (%)	No No. (%)	Not sure No. (%)		
Do you think that cervical cancer screening is valuable?	286 (95.3)	6 (2.0)	8 (2.7)		
Have you had any cervical cancer vaccinations?	41 (13.7)	236 (78.7)	23 (7.7)		
Have you ever had a PAP test?	287 (95.7)	12 (4.0)	1 (0.3)		
Have you ever used tampons?	93 (31.0)	207 (69)	0 (0)		
Have you ever smoked?	58 (19.3)	242 (80.7)	0 (0)		
Patient experience on HPV self-sampling					
	Strongly disagree No. (%)	Disagree No. (%)	Neutral No. (%)	Agree No. (%)	Strongly agree No. (%)
Did you find it difficult to conduct?	3 (1.0)	11 (3.7)	50 (16.7)	104 (34.7)	132 (44.0)
Did you find the process uncomfortable?	194 (64.7)	74 (24.7)	22 (7.3)	4 (1.3)	6 (2.0)
Did you feel anxious during the procedure?	83 (27.7)	35 (11.7)	99 (33.0)	18 (6.0)	6 (2.0)
Did you feel embarrassed during the procedure?	NA	157 (52.3)	68 (22.7)	16 (5.3)	NA
Did you find the process unpleasant?	141 (47.0)	19 (6.3)	66 (22.0)	12 (4.0)	3 (1.0)
Patient preferences on future cervical cancer screening					
	Self-sampling at home No. (%)	Self-sampling at health centre No. (%)	Physician- sampling No. (%)	Does not matter No. (%)	
Where and how would you prefer to conduct your cervical cancer screening?	217 (72.3%)	36 (12.0%)	39 (13.0%)	8 (2.7%)	
	Yes No. (%)	No No. (%)	Not sure No. (%)		
Are you likely to participate in future cervical cancer screening if you have the option of self-sampling?	271 (90.3)	29 (9.7)	0		
Would you be willing to pay for cervical cancer screening by self-sampling?	153 (51.0)	88 (29.3)	59 (19.7)		
Performance of HPV self-sampling method in cervical cancer screening					
	Value (%)	95% confidence interval			
Specificity	94.6	90.9–97.1			
Sensitivity	83.3	71.5–91.7			
Positive predictive value	79.4	69.1–86.9			
Negative predictive value	95.8	92.8–97.6			
Accuracy	93.3	88.7–95.1			
Cohen’s kappa, κ	0.77, <i>P</i> <0.001		0.67–0.86		

HPV: human papillomavirus; NA: not applicable

concordance with the physician-collected samples, with discordant results observed in only 23 samples (7.7%). The sensitivity and specificity of the self-sampling tests were 83.3% (95% CI, 71.5–91.7) and 94.6% (95% CI 90.9–97.1), respectively. Concordance analysis engendered a kappa of 0.77 (95% CI 0.67–0.86, $P < 0.001$), presenting a substantial agreement between the results of the physician-collected and self-collected samples.

From our study, it was evident the acceptability of the self-sampling swab by the participants was high as the majority found it easy to perform with minimal discomfort, anxiety and embarrassment. Our study also showed substantial agreement between the results from the self-sampling and physician-sampling tests, as corroborated by international meta-analysis.

HPV self-sampling is a potential intervention that can increase cervical cancer screening uptake by overcoming barriers such as fear, discomfort and the inconvenience of visiting a health centre for screening. A randomised clinical trial conducted in the US targeting the under-screened population showed that mailing HPV kits increased screening uptake compared to usual care reminders for in-clinic screening.⁹ This was also reflected in our study where the women were more likely to participate in screening if the self-sampling method was available. The next step moving forward would be to assess the acceptability of HPV self-sampling among women in the community setting.

In view of its high efficacy and acceptability, countries such as Australia and the Netherlands have incorporated HPV self-sampling into their national screening programmes in a move to increase screening uptake. Results from our study are encouraging, and this could pave the way for Singapore to incorporate self-sampling into the national screening programme. Increasing screening uptake is one of the 3-pronged approaches identified by the World Health Organization to achieve the ultimate goal of eradicating cervical cancer.¹⁰ It is our hope that incorporating a self-sampling test would help us move closer to that goal.

Acknowledgements

We would like to thank Dr Ida Ismail-Pratt for her invaluable guidance for this study, and Ms Wan Sin Yee Carrie for assisting with the data collection and study administration.

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