The Society for Colposcopy & Cervical Pathology of Singapore

SCCPS Scientific Committee Position Paper on HPV Self-sampling Test

Abstract

In order to achieve the World Health Organisation (WHO) goal of cervical cancer elimination, there is a crucial need to increase screening uptake. HPV self-sampling has been shown to be well-accepted amongst women, making it a viable tool to encourage more women to participate in screening. It has been determined to be a reliable alternative to physician sampling with equivalent sensitivity to physician-sampling. The most effective implementation methods include direct mailing, community mobilisation and offering at healthcare services. There are numerous vaginal self-sampling tools available on the market with little evidence over which tools are superior. The optimal self-sampling tool should generally be decided in conjunction with consideration of type of setting it will be implemented in. HPV self-sampling is a promising strategy to overcome the multiple barriers to cervical cancer screening and has the potential in increasing attendance in under-screened women in countries with well-established screening programmes. As a result, it can increase screening participation in the community and is potentially a cost-effective strategy. With increased screening uptake, we aim to be one step closer to cervical cancer elimination in our community.

Introduction

Cervical cancer is a highly preventable malignancy through both vaccination and screening. However, it remains the tenth most common cancer among Singaporean women[1], accounting for 2.6% of all cancer-related mortality[1]. This is likely due to the poor uptake of cervical cancer screening among Singaporean women. Women who do not go for regular cervical screening are at the highest risk of developing cervical cancer[2]. The National Population Health Survey 2019 report revealed that only 48.2% of women were up to date in their cervical cancer screening[3]. A systemic review in South East Asia identified barriers to cervical cancer screening include the lack of time, cost of screening, embarrassment, and fear[4].

Singapore has adopted Human Papillomavirus (HPV) primary screening for cervical cancer since 2019 into our national guidelines. The self-sampling method for HPV screening may overcome barriers to screening by avoiding the need for a pelvic exam or clinic visit, hence improving access to and uptake

of screening, especially among under-screened women. HPV self-sampling is a non-invasive method that involves the woman collecting her own vaginal sample with a device and subsequently submitting it for HPV testing. The World Health Organisation (WHO) has recommended that HPV self-sampling should be made available as an additional approach in cervical cancer screening services[5]. As of the year 2022, 17 countries have already introduced self-sampling into their national screening programmes either as a primary screening option (Albania, Kenya, Guatemala, Honduras, Malaysia, Netherlands, Peru, Rwanda and Uganda) or for under-screened populations (Argentina, Australia, Denmark, Ecuador, Finland, France, Myanmar and Sweden)[6]. There are eight more countries that are planning to pilot self-sampling in the next few years[6].

Introducing HPV self-sampling in Singapore has the potential to increase the uptake of cervical cancer screening for early detection of cervical cancer or pre-invasive disease. The purpose of this consensus statement is to provide a succinct summary of the diagnostic accuracy, acceptability, and cost effectiveness of HPV self-sampling.

Accuracy of HPV self-sampling for cervical cancer screening

HPV self-sampling has been shown in international studies to have comparable sensitivity and specificity to provider samples, and this is a robust outcome that is consistent throughout different clinical settings. A meta-analysis by Petignat et al involving more than 5000 women in 18 studies revealed a high level of concordance of 0.87 (95%CI, 0.82 to 0.91) between self- and physician-sampling for the detection of HPV DNA[7]. These results have been validated in our local multi-ethnic population as well. In a study conducted at a tertiary hospital in Singapore of 300 women, sensitivity and specificity of the self-sampling tests compared to physician-sampling tests were 83.3% (95% CI, 71.5-91.7) and 94.6% 95% CI, 90.9-97.1), respectively[8].

In addition, diagnostic accuracy of HPV self-samples has been established for clinical outcomes of high grade cervical intraepithelial neoplasia (HGCIN) when polymerase chain reaction (PCR) based tests are used. Arbyn et al conducted a meta-analysis of 81 studies, which showed similar sensitivity (pooled ratio 0.99, 95% CI 0.97 to 1.02) and slightly lower specificity pooled ratio 0.85, 95% confidence interval 0.80 to 0.89) of self-sampling compared to clinician-sampling for detecting HGCIN with PCR-based assays[9]. In contrast, HPV assays based on signal amplification, have lower sensitivity to detect HGCIN

and are less specific to exclude CIN when applied to self-samples[9]. mRNA testing was also less sensitive but as specific on self-samples compared with clinician samples[9].

Acceptability of HPV self-sampling

Studies have shown high acceptability of approximately 90% for the self-sampling method[8,10-12] and a preference for HPV self-sampling over the traditional physician-directed cervical sampling ranging from 34% to 90%[10,11,13-16]. The majority of study participants found that the self-sampling was easy to perform[8,11,17,18] and up to 90% felt that self-collection would increase their likelihood of participation in cervical cancer screening[8]. Self-sampling showed higher participation compared to receiving reminder letters to attend a Pap test for under-screened and never-screened women[18,19].

Majority of the participants were amenable to future HPV screening by self-sampling[11,17,20,21]. This was independent of age, educational status or previous history of an abnormal Pap in an under-screened population[21]. Self-sampling was highlighted to be a promising strategy for under-screened women who were reluctant or unable to have clinic-based cervical screening[22] as well as for increasing attendance in countries with well-established screening programs[6].

Reasons for favouring self-collection include privacy, comfort, easiness, reliability, user-friendliness and less pain and embarrassment[13,15,17,23]. A majority of study participants reported self-sampling to be acceptable, easy to use, convenient with increased privacy particularly when performed within a home setting[24-26]. For those who did not want to self-sample, their reasons included a perception that clinical professionals were more skilled in the sampling as well as doubts about performing the self-collection themselves properly[13,17].

Implementation methods of HPV self-sampling

HPV self-sampling has the potential to overcome barriers to cervical cancer screening and improve rates of screening. Methods to disseminate self-sampling kits include direct mailing, offering door-to-door by a healthcare worker, community mobilisation and outreach, offering at healthcare services and on-demand strategy.

Combining all methods of self-sampling kit dissemination strategies, a meta-analysis found that women were twice as likely to participate in cervical cancer screening programmes through HPV self-sampling compared with standard of care screening practices.[27] All self-sampling invitation scenarios have also been found to be more effective in reaching under-screened women regardless of strategy.[28]

Comparing the methods of dissemination, it appeared that mail-to-all, community mobilisation and offering at healthcare service all had higher screening uptake compared to the opt-in method.[26,28] While the on-demand approach returned a lower response rate compared to the direct mail strategy, this strategy has the advantage of reducing device wastes and cost.[29] Regarding preferred method for requesting the test kit, Tranberg et al found that the most common method was by website followed by text messaging.[30]

Cost effectiveness of HPV self-sampling

It has been shown that HPV self-sampling can be cost-effective either as an addition to existing screening programmes[31-38] or as a primary screening strategy. The main driver of this is a reduction of clinic visits in women who test HPV-negative, potential decreases in colposcopy referrals and subsequent treatments.[39,40] Cost-effectiveness was most marked when HPV-SS resulted in a significant increase in screening attendance[34-36,41,42] especially in never-screened or long-term underscreened women[34,35], unvaccinated populations, lower costs of HPV-SS materials and testing[31,38,42], and a higher relative sensitivity to detect CIN2+[34,35].

In terms of outreach strategy, direct mail resulted in a better screening uptake than opt-in and is hence likely to be more cost-effective[36,37]. A triage strategy suited to population needs for HPV positivity on HPV-SS, either via cytology, colposcopy or HPV genotyping will further improve cost-effectiveness. HPV-SS through direct mail with PAP triage resulted in improved incremental cost-effectiveness ratios (ICER) – cost/QALY gained or cost/life-year[34-37,43-45].

Types of swabs and assays

Specific to HPV DNA vaginal self-sampling, there are numerous tools available[46] on the market such as swabs, brushes, lavage, wands, with ongoing development of novel tools. Based on the literature, the most common tools used are brushes and swabs. However, the current evidence is heterogenous and there is limited comparative data on the different vaginal self-sampling tools. Furthermore, results may be affected by a multitude of factors including HPV assay type, time to processing, choice of wet or dry mediums, etc. Hence, there is little evidence over which tools are superior. Jentschke[47], Leinonen[48], Cadman et al.[49] found no significant difference in efficacy of detecting hrHPV strains using various self-sampling tools compared to physician sampling. Conversely, some authors found higher degrees of agreement between self and physician sampling with flocked swabs[50,51] and Evalyn brushes[52]. Of note, study methodology was not standardised, and the sample sizes were small.

External factors such as cost, accessibility, mode of dissemination of self-sampling tools may influence choice of self-sampling tool. Further standardised, large scale, multi-centred studies are required to evaluate the differences in efficacies between self-sampling tools. The optimal self-sampling tool should also be decided in conjunction with consideration of type of setting it will be implemented in.

Conclusion

HPV self-sampling has been determined to be a reliable alternative to physician sampling as recommended by the WHO. It has been proven to have equivalent sensitivity to physician-sampling and is well-accepted amongst the screening population. It is a promising strategy to overcome the multiple barriers to cervical cancer screening and has the potential in increasing attendance in under-screened women in countries with well-established screening programmes. As a result, it can increase screening participation in the community and is potentially a cost-effective strategy. With increased screening uptake, we aim to be one step closer to cervical cancer elimination in our community.

In conclusion, SCCPS supports the adoption of HPV self-testing into screening algorithms based on the current evidence.

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