

Emerging role of HPV self-sampling in cervical cancer screening for hard-to-reach women

Focused literature review

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EDITOR'S KEY POINTS

- There are subgroups of women who are less likely to undergo cervical cancer screening (eg, women of low socioeconomic status, immigrant women). Low levels of screening among these women are related to various barriers (eg, lack of a family physician, indirect costs). Self-sampling for human papillomavirus (HPV) is a convenient and cost-effective method to increase screening participation among hard-to-reach women.
- Evidence demonstrates the validity of HPV self-sampling compared with clinician-collected cervical samples. There is also a high acceptance of and positive attitudes toward self-sampling among hard-to-reach women. Important barriers to HPV self-sampling include women's confidence in self-sampling and cultural implications of sexual behaviour. The need for physicians and other community health care professionals to be involved and provide education on sexual health remains pertinent. Barriers to participation could be overcome by addressing disparities in HPV-related knowledge and perceptions about cervical cancer screening and by providing evidence on the ease of use and accuracy of self-sampling kits.

POINTS DE REPÈRE DU RÉDACTEUR

- Le dépistage du cancer du col est moins probable dans certains sous-groupes de femmes (p. ex. celles dont la situation socioéconomique est précaire, les immigrantes). Les faibles taux de dépistage chez ces femmes s'expliquent par divers obstacles (p. ex. sans médecin de famille, coûts indirects). L'auto-prélèvement pour la détection du virus du papillome humain (VPH) est une méthode pratique et rentable pour accroître la participation au dépistage des femmes difficiles à rejoindre.
- Les données probantes démontrent la validité de l'auto-prélèvement pour la détection du VPH lorsqu'il est comparé au prélèvement de spécimens cervicaux par des cliniciens. De plus, les femmes difficiles à rejoindre ont une attitude favorable face à l'auto-prélèvement, et leur taux d'acceptation de cette méthode est élevé. Au nombre des importants obstacles à la détection du VPH par auto-prélèvement figurent la confiance des femmes dans l'auto-prélèvement et les conséquences culturelles du comportement sexuel. Il demeure pertinent que les médecins et d'autres professionnels de la santé s'impliquent et donnent de l'information en matière de santé sexuelle. Il serait possible d'atténuer les obstacles à la participation en comblant le manque de connaissances sur le VPH, en dissipant les perceptions négatives à l'égard du dépistage du cancer du col, et en fournissant des données probantes quant à la facilité d'utiliser les trousseaux d'auto-prélèvement et à leur fiabilité.

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Abstract

Objective To provide a focused critical review of the literature on the acceptability, feasibility, and uptake of human papillomavirus (HPV) self-sampling among hard-to-reach women.

Quality of evidence A focused search to obtain relevant literature published in English between 1997 and 2015 was done using PubMed and EMBASE using search terms including *HPV self-test* or *HPV self-sample* or *HPV kit* in combination with *acceptability* or *feasibility*. Only studies that focused on never-screened or underscreened populations were included in this review.

Main message Human papillomavirus self-sampling was found to be highly acceptable and feasible among these hard-to-reach women across most studies. Mailing of self-sampling kits has been shown to increase participation among hard-to-reach women. Some concerns remain regarding adherence to further follow-up among high-risk women with positive test results for HPV after screening.

Conclusion There is a strong body of evidence to support the usefulness of HPV self-sampling in increasing participation of hard-to-reach women in screening programs (level I evidence). Convenience, privacy, ease of use, and, likely, cost-effectiveness of HPV self-sampling are driving forces in its emerging role in cervical cancer screening among hard-to-reach women. Key barriers to participation could be addressed by overcoming disparities in HPV-related knowledge and perceptions about cervical cancer screening.

Rôle émergent de la détection du VPH par auto-prélèvement pour le dépistage du cancer du col chez les femmes difficiles à rejoindre

Analyse documentaire ciblée

Résumé

Objectif Présenter une revue critique ciblée des ouvrages scientifiques portant sur l'acceptation, la faisabilité et l'adoption de l'auto-prélèvement pour la détection du virus du papillome humain (VPH) chez les femmes difficiles à rejoindre.

Qualité des données Une recension ciblée dans le but de trouver des articles pertinents publiés en anglais entre 1997 et 2015 a été effectuée à l'aide de PubMed et d'EMBASE en se servant des expressions en anglais *HPV self-test* ou *HPV self-sample* ou *HPV kit*, combinées à *acceptability* ou *feasibility*. Seules les études qui portaient spécifiquement sur les populations n'ayant jamais fait l'objet d'un dépistage ou étant sous-représentées dans ces programmes ont été incluses dans cette revue.

Message principal Dans la plupart des études, il a été constaté que la détection du virus du papillome humain par auto-prélèvement était très acceptée et faisable chez ces femmes difficiles à rejoindre. Selon les conclusions, l'envoi d'une trousse d'auto-prélèvement par la poste augmente la participation des femmes difficiles à rejoindre. Certaines préoccupations persistent en ce qui concerne l'acceptation d'un suivi plus approfondi chez les femmes à risque élevé dont les résultats sont positifs pour la présence du VPH après le dépistage.

Conclusion De nombreuses données probantes convaincantes corroborent l'utilité de l'auto-prélèvement pour la détection du VPH chez les femmes difficiles à rejoindre dans les programmes de dépistage (données probantes de niveau I). La nature pratique et confidentielle de l'auto-prélèvement pour la détection du VPH, sa facilité d'usage, et probablement sa rentabilité, sont des forces motrices expliquant son rôle émergent dans le dépistage du cancer du col chez les femmes difficiles à rejoindre. Il serait possible d'atténuer les principaux obstacles à la participation en comblant le manque de connaissances sur le VPH et en dissipant les perceptions négatives relatives au dépistage du cancer du col.

Cervical cancer screening has decreased the incidence of and mortality from cervical cancer.¹ Methods for screening include evaluation with the Papanicolaou test and testing for high-risk types of

human papillomavirus (HPV), the virus that causes cervical cancer. The 2013 Canadian Task Force on Preventive Health Care guidelines for cervical cancer screening recommend routine screening for women aged 25 to 69 every 3 years.² Screening in Canada is largely opportunistic, office-based, and done by a health care professional. Canadian data from 2006 to 2008 showed that the average percentage of women aged 20 to 69 who underwent at least 1 Pap test within a provincial program in a 3-year period was 70.2%.³ However, it is known that certain subgroups of women are less likely to be appropriately screened, particularly women who self-identify as lesbian,⁴ women at both extremes of age within the eligibility criteria,^{5,6} Aboriginal women, women of low socioeconomic status, and immigrant women.⁷⁻¹¹

Grunfeld identified 3 groups of women targeted for cervical cancer screening: women who respond when made aware of the benefits and importance of screening, women who respond to proactive approaches such as reminder letters, and women who are "hard to reach with health promotion messages."¹² Low levels of screening among these hard-to-reach women have been related to such barriers as lack of a family physician, inconvenient clinic hours, forgetting to schedule an appointment, problems with transportation, cultural barriers (eg, modesty, language), and indirect costs (eg, child care, time off work).¹³⁻¹⁵ New methods to address these barriers are necessary to improve screening rates. Self-sampling for HPV has been shown to be a convenient and cost-effective method to increase screening participation among hard-to-reach women.¹⁶ There is a growing body of evidence demonstrating the validity of HPV self-sampling compared with clinician-collected cervical samples; there is also a high acceptance of and positive attitudes toward self-sampling among these women. The purpose of this review is to provide a succinct summary of the literature on the acceptability, feasibility, and uptake of HPV self-sampling among hard-to-reach women.

Quality of evidence

During the literature review, the following broad search terms were used: *HPV self-test*, *HPV self-sample*, *HPV kit*, *hard to reach population*, *immigrants*, *women of low socioeconomic status*, *elderly*, *Aboriginals*, *sexual orientation*, *lesbians*, *women in sex trades*, *Muslim women*, *acceptability*, and *feasibility*. Boolean operators *and*, *or*, and *** were used to ensure a focused and comprehensive list. Only articles that were published in English from 1997 to 2015 in developed and developing countries that focused on hard-to-reach women of all ages within the eligibility criteria were included. A total of 43 relevant published and peer-reviewed articles were found. These included 15 randomized controlled trials (RCTs),^{7,16-29} 2 systematic reviews,^{30,31} and 26 non-experimental quantitative and qualitative studies.^{4,13-15,32-53} A summary of the literature

is available at **CFPlus**.^{*} Most of the studies were done in Europe and North America (**Table 1**).^{4,7,13-29,32-53}

Table 1. Geographic distribution of the RCTs and non-experimental studies included in the literature review

COUNTRY OF STUDY	NO. OF STUDIES
Australia ^{26,47,53}	3
Cameroon ⁵⁰	1
Canada ^{28,38,42,44}	4
Finland ^{7,21}	2
France ²⁴	1
Italy ¹⁸	1
Mexico ^{19,34}	2
Netherlands ^{14,16,23,43,49}	5
Sweden ^{22,25}	2
Taiwan ^{33,45}	2
Thailand ³²	1
UK ^{13,15,20,27,35,39}	6
US ^{4,17,29,36,37,40,41,46,48,51,52}	11

RCT—randomized controlled trial, UK—United Kingdom, US—United States.

Main message

Acceptability. Across most studies, the acceptability of HPV self-sampling was high.^{4,28,30,32,35,39,44,46,50-53} Some attractive features of self-sampling were cost (free in these studies), convenience (home-based),^{14,36} less discomfort (swab vs Pap test), and privacy.^{36,47,53} Women who participated in self-sampling for HPV testing reported less embarrassment, pain, anxiety, or discomfort.^{34,50} An online survey of a US national sample of 418 lesbian and bisexual women between the ages of 21 and 26 (approximately 70% of whom had undergone a Pap test in the past 3 years) found that a little more than half of the women were willing to use the HPV self-sample method. Women were more willing to use self-sampling at home if they were concerned about getting an HPV-related disease (odds ratio=1.28, 95% CI 1.01 to 1.63).⁴ However, focus groups with 28 Muslim women between the ages of 21 and 65 (mean age was 50 years) in London, England, revealed that while these women believed that self-sampling would overcome some of the barriers to screening, they did not trust in their own ability to do the test correctly. Overall, this group preferred screening to be done by a health care worker.¹³ Similarly, sexually active adolescent females between 14 and 21 years of age at an urban teen health centre in Cincinnati, Ohio, underwent both self-sampling and having a vaginal sample collected by a clinician using a speculum for HPV

DNA testing. Both methods were found to be acceptable by the teens; however, there was an overall preference for clinician-collected samples in this group. These young women expressed a lack of confidence in their ability to collect a specimen correctly and had scores reflecting little trust in self-sample results.³⁷

In a telephone survey of 199 noninsured women in the United States, non-participants in cervical cancer screening were found to have low levels of HPV-related knowledge and to perceive the risk of cervical cancer as low.⁴⁶ More important, it has been shown that educational interventions on cervical cancer and HPV before self-sampling were associated with high acceptability.⁵⁰ A study done in Taiwan found that the factors associated with the likelihood of performing HPV self-sampling included having had previous Pap testing, perceiving the risk of cervical cancer to be high, having a high level of HPV-related knowledge, and considering cost to be a priority.⁴⁵

Validity and feasibility. Across many countries and age groups, women were able to carry out the test alone with simple written instructions.^{30,39} When unsupervised self-collected samples were compared with physician-collected samples, there was comparable sensitivity and concordance for identifying high-risk HPV.^{17,22,23,30,33,38,40} Soisson et al demonstrated that in a study of 878 Appalachian women, 775 were able to use a device for self-sampling, and 99% of these samples had an adequate number of epithelial cells for cytologic and HPV testing.⁴¹ In terms of analysis, polymerase chain reaction-based assays for high-risk HPV DNA detection have been shown to be as accurate on self-samples as on clinician-collected samples⁴⁹; however, HPV assays based on signal amplification are less sensitive and specific on self-samples.⁴⁹

In all studies that offered HPV self-sampling tests, there was an increase in participation rates.^{16,22-25,29,31,43} In Sweden, among women who had not participated in an organized screening program for 6 years, self-sampling of vaginal fluid tested for high-risk HPV was more effective for detection of histologic cervical intraepithelial neoplasia (CIN) grades 2 and 3 lesions when compared with advising women to participate in Pap test screening.²² In Finland, combining the interventions (reminder letter and then self-sampling kit) increased total participation from 63% to 78%,^{7,21} suggesting that an affordable self-sampling kit or device that can be included with a reminder letter to screening non-attendees might have a greater effect on participation.⁴⁹ In a 2015 Canadian study done in rural Ontario with 818 women who had not attended for screening, the authors found that women receiving self-sampling kits were 3.7 (95% CI 2.2 to 6.4) times more likely to undergo screening compared with those who received the standard-of-care opportunistic screening, and that this method was more effective than sending reminder letters.²⁸ An RCT completed in Rome, Italy, demonstrated that

^{*}A summary of the literature review is available at www.cfp.ca. Go to the full text of the article online and click on the **CFPlus** tab.

alternative self-sampling strategies, such as offering HPV self-sampling at a clinic or asking non-participants to request a self-sampling kit, had poor compliance or adherence.¹⁸ Directly mailing the self-sampling kit demonstrated the highest compliance; and kits that were small enough to fit in mailboxes were preferred over having to collect a parcel at a post office.⁵³

Studies found a high yield of positive test results for high-risk HPV strains among underscreened women.^{15,16,20,44} In a study of 49 women aged 25 to 59 from a First Nations community in northwestern Ontario, 28.6% of women had positive test results for HPV, 16.3% of whom were infected with a high-risk HPV type.⁴⁴ In 2 studies specifically assessing follow-up (one study looking at 100 immigrant women in Texas and the other at 6000 non-attenders for screening in England), the authors found that a little more than half of self-sampling participants followed up on their HPV-positive test results.^{27,52} Specifically, lack of health care coverage for the women in Texas was identified as a barrier to follow-up. In an RCT done in the Netherlands that studied 26 409 non-attending women who received a self-sampling device, the authors found that 89.1% of the women with positive test results for high-risk HPV adhered to further follow-up with cytology, and 95.8% of those with abnormal test results presented for colposcopy.²³ In this study, sending reminder letters to those women with positive test results for high-risk HPV and having their physicians explain the test results and their consequences increased adherence to follow-up.


In 2007, Bais et al found that in the Netherlands, the cost per CIN grade 2 or higher lesion detected with the self-sampling method was comparable to the cost of conventional screening using the Pap test (€8836 vs €7599 [\$13 134 vs \$11 295]).¹⁶ The overall cost-effectiveness of the HPV self-sampling method still requires further assessment, as it is largely country specific.

Barriers or concerns. A recurrent concern from participants across studies was sampling accuracy.^{15,35,39,42,51} Participants were mostly concerned about performing the procedure correctly.^{4,47,51} Some women also highlighted the need for more nonprocedure-related information, such as when results would be expected and which organization was providing the test.⁵³ For a subgroup of Muslim women, HPV self-sampling was thought to raise issues of trust and fidelity within marriages. The fact that a positive test result for HPV, a sexually transmitted infection, would imply infidelity on the part of the husband or the wife was a potential barrier, as the “consequences of perceived infidelity were seen to be worse for women.”^{13,15} Moreover, a US study showed that the primary barrier to follow-up after a positive test result for high-risk HPV was difficulty in obtaining health care coverage.⁵² Formal and informal

sources of information on HPV were also highlighted. For example, Sewali et al found that among immigrant Somali women in the United States, those who reported having friends or family members to talk to about cancer screening were approximately 3 times more likely to complete any screening test than those who did not.²⁹

Future directions. The value of HPV self-sampling relies on its ability to detect high-grade CIN and early-stage cancer,²⁶ its acceptability to the target population, and women’s willingness to follow up on positive test results. Assessing the compliance of women whose test results are HPV positive with further follow-up, as well as the cost of the self-sampling kit compared with conventional screening, will be important outcomes of future studies. Other studies have also explored the benefit of implementing this strategy for women from rural communities or medically underserved areas where there are fewer medical professionals available and high-sensitivity HPV screening is paramount.^{19,32} In 2016, the Netherlands will be the first to include HPV self-sampling kits as part of their national screening program for women who are overdue for screening.⁴⁹ Other countries might follow this trend in the near future and possibly extend this method to regular screening attendees. Government-supported formal screening programs that include self-sampling as an alternative option have the potential to make important contributions to the success of screening for cervical cancer. These studies suggest that it is not inconceivable that cytology tests might eventually be limited to women with positive test results for high-risk HPV, and HPV self-sampling might become the primary method of screening for cervical cancer.

Conclusion

Interestingly, perceptions of self-sampling for HPV were similar across cultures and countries. The acceptability was high, and both feasibility and uptake were demonstrated. It is unlikely that HPV self-sampling will lead to additional costs^{16,25} for screening programs; however, this might need to be further assessed on a program- and country-specific basis. Important barriers were related to issues of confidence in self-sampling and cultural implications of sexual behaviour and trust within relationships. The need to involve physicians and other members of the community in health care and to include education on sexual health remains pertinent.^{42,44} Key barriers to participation could be overcome by addressing disparities in HPV-related knowledge and perceptions of cervical cancer screening,^{35,46} as well as providing evidence on the ease of use and accuracy of self-sampling kits.⁴⁷ 

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Contributors

All authors contributed to the literature review and interpretation, and to preparing the manuscript for submission.

Competing interests

None declared

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