Self-sampling for cervical cancer screening: Preference, acceptability, convenience and cost-effective

Running title: Self-sampling for cervical cancer screening

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Abstract

Background: Human papillomaviruses (HPVs) are DNA viruses from the *Papillomaviridae* family. These viruses are linked to about 5% of human cancers, significantly related to cervical cancer. Infection of this virus can be screened in women for prevention of cervical cancer.

Methods: This review analyzes articles published in the last two decades regarding self-sampling, the papillomavirus, and cervical cancer. The search for articles was conducted from various scientific databases, and the articles were selected based on their relevance to the topic and their role in understanding and comparing methods. Key results were examined, paying attention to social aspects, economic savings, and participants' satisfaction with the self-sampling method.

Result: One of the most common and effective methods for HPV screening is sampling from the cervix using the Pap smear method and molecular techniques, used in various countries. Currently, the sampling methods for HPV screening in different countries are only performed through clinical sampling. Therefore, this approach cannot cover all urban and rural populations. Self-sampling for HPV screening has been recommended and supported by the World Health Organization as a new strategy.

Conclusion: This mini-review discusses the self-sampling method for HPV screening, its advantages, and its application in different countries. Considering that the self-sampling method can cover all rural and urban areas, it is more economically viable and can help to minimize cultural barriers and public opinion challenges compared to clinical sampling.

The HPV self-sampling strategy can serve as an effective and efficient method for HPV screening focused on preventing cervical cancer caused by the HPV virus in various countries.

Keywords: Self-Sampling, HPV, Healthcare Provider-Collected Samples

Introduction

Cervical cancer is the fourth most common cancer among women, with 570000 new cases every year mostly affecting women around the ages of 30 to 49 (1, 2, 3). According to the World Health Organization, it is predicted that the incidence and mortality of cervical cancer will increase in the upcoming years (4).

In humans, roughly 5% of all cancers are caused by HPV infection, with cervical cancer being one of the most important ones in the global perspective. The papillomaviruses are a widely spread group of non-enveloped epitheliotropic viruses that can cause hyperproliferative lesions of the skin and mucous membranes. Rarely, the viral life cycle of these viruses can get amiss, causing various epithelial malignancies, which can appear as uterine cervix cancer in humans, as well as other types of cancer in the anogenital tract and the upper airway (5). Cervical cancer can be caused by specific types of HPV, with HPV-16 and HPV-18 causing 70% of cervical cancers and lesions (1, 6).

In developing countries, cervical cancer is regarded as more than 90% of HPV-related cancers (7). Widespread cervical cancer screening has reduced cervical cancer incidence worldwide, and the most commonly used cervical cancer screening method is a Pap smear, which involves the harvest of cervical cells to be examined by a cytopathologist (8).

Sampling for HPV screening is often two types, clinical sampling and self-sampling. The most commonly used sampling in the world is clinical sampling, which needs the attendance of the patient, and experienced personnel, and is economically expensive.

On the other hand, HPV samples can be collected by patients themselves which is called self-sampling. Self-sampling for HPV is independent of location, time, and direct involvement of healthcare personnel, which needs low resource setting and may increase screening uptake (8). Additionally, Self-sampling methods have demonstrated high accessibility and acceptability for cervical cancer screening compared to clinician sampling. Self-sampling methods are less invasive and could be more attractive to increase the uptake. It can also overcome barriers of cultural and social beliefs and behaviors (9). Research shows that self-sampling methods are well received, increasing the screening uptake more noticeably compared to traditional clinical methods (2, 10).

A meta-analysis has shown that women with the option of self-sampling were more likely to participate in cervical cancer screening programs, with a reported risk ratio of 2.27 for this increased participation. Although there is a concern about self-sampling accuracy and women's confidence in doing it, demanding clear instructions and support (4). It has been shown that the accuracy of HPV self-sampling for cervical cancer screening is rather similar to the ones taken by healthcare professionals (11). Thus, self-sampling can be a very good alternative method with the potential to increase participation in cervical cancer screening (12, 13). However, while self-sampling has shown promise, both types of testing methods are evaluated to ensure women's health (12).

This mini-review aims to discuss the choice between clinical sampling and self-sampling for HPV testing, their accessibility, comfort, and the effectiveness of these methods. As the healthcare system evolves, it is essential to understand these to improve screening rates and reduce cervical cancer incidence.

Methods

This review is based on the analysis of articles published in the last two decades. For this purpose, scientific databases such as PubMed, Scopus, Web of Science, and Google Scholar were used, and searches were conducted using keywords such as self-sampling, papillomavirus, and cervical cancer. The selected articles were chosen based on their relevance to the topic and their role in better understanding and comparing the methods. Key findings

were combined and categorized, focusing on social insights, cost-effectiveness, and participant satisfaction with the self-sampling method.

Self-sampling for detection of HPV

The usage of new technologies to detect HPV, the necessary cause of cervical cancer, has created new opportunities by allowing women to self-collect cervical cells at home and mail the samples for HPV testing (14). The accuracy and reliability of HPV self-sampling methods have been the subject of multiple studies. A meta-analysis has shown that self-collected samples can be as accurate as clinical samples, providing a reliable alternative for cervical cancer screening. HPV self-sampling can enhance cervical cancer screening uptake, especially in low-and middle-income countries where 89% of cervical cancer cases occur (4).

Although, The World Health Organization (WHO) recommends HPV self-sampling as an additional screening method, for early detection in women aged 30 years and older (1). HPV self-sampling has been effective in reaching women who otherwise delay or opt out. (15) Self-sampling tests have been recommended as an alternative way to improve cervical cancer screening uptake and reduction of disease burden (4).

Many studies have shown that self-sampling is highly accepted by women. Using a standard practice in cervical cancer screening programs is minimally invasive, and associated with women with very low discomfort (16). Due to the physical and psychological discomfort with physician-collected samples, self-sampling can be an acceptable alternative, which is also supported by WHO recommendations on self-care interventions(13). Cervical cancer screening has an opportunity to prevent this invasive cancer, which has contributed to significant reductions in cervical cancer's global burden (14).

Humanity has always sought easier, better, and more cost-effective strategies than traditional methods while ensuring accuracy, efficiency, and convenience. Self-sampling for human papillomavirus to screen cervical cancer, is also one of these strategies that have been used in various communities.

What people particularly liked about HPV self-sampling was the level of privacy, convenience, and overall comfort, especially compared to a Pap Smear .The ability of people to collect a sample in their comfort, and at any time of their choice, reassure some providers about their concerns around access to healthcare. (e.g., wait time, appointment scheduling, transportation) (17). However, it is noteworthy that self-sampling is recommended in 17 countries, primarily to target under-screened populations (4). Figure 1 shows the procedure of self-sampling.

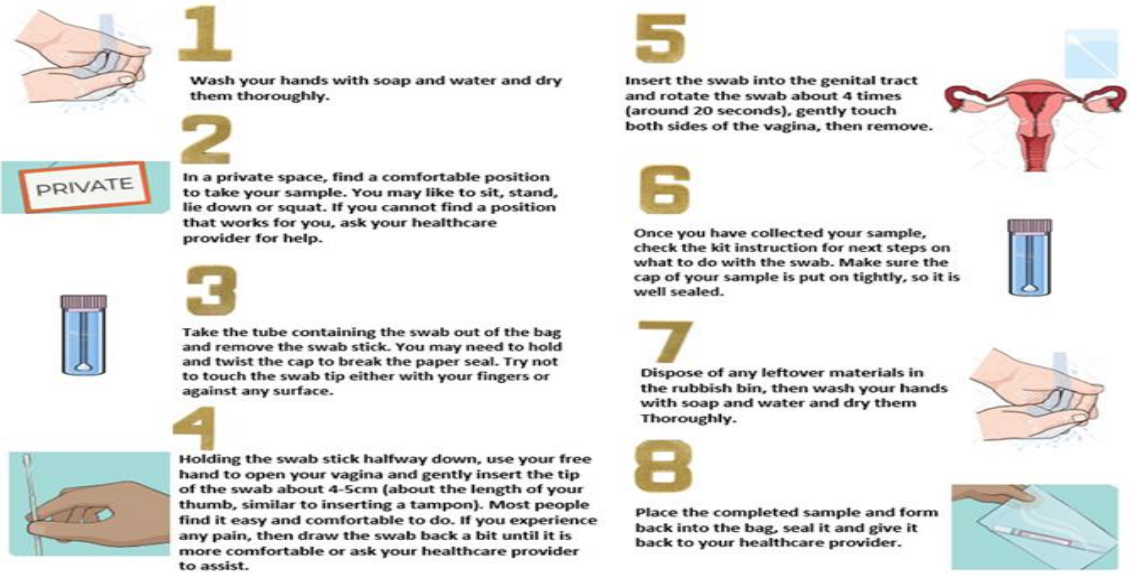

Figure 1. Procedure of self-sampling (Ref. TimeTo CervicalScreen.nz)

HPV self-sampling helps to increase cervical cancer screening coverage

The HPV self-sampling can significantly improve cervical cancer screening uptake, particularly among women who are under or never screened (18).

Self-sampling for HPV testing is one of the most cost-effective, and has been evaluated in several European Populations as well (19). HPV self-sampling has shown efficient and significant improvements in cervical cancer screening rates among women (15). To achieve significant improvements in screening rates, it is essential to develop public health strategies that promote self-sampling as an effective alternative to traditional clinical methods (20). Local public health campaigns can also increase awareness and acceptance of self-sampling methods (21).

Countries, including Australia, Denmark, Malaysia, and the Netherlands, are moving to self-sampling as a screening option (4). In the Netherlands, an observational study has shown that high-risk HPV (hrHPV) testing on self-collected samples performs well in routine primary screening programs, suggesting that self-sampling could be an effective primary screening option (22). Australia was one of the first countries to introduce a national HPV vaccination program in 2007, and it has since achieved high vaccination coverage across both men and women. If the situation is maintained, cervical cancer could be considered eliminated as a public health problem in Australia within the next 20 years (1).

Preferences, acceptability, and economic aspects of HPV self-sampling compared to healthcare provider-collected samples

It is essential to ensure that self-sampling methods are accessible and acceptable to women in low- and middle-income countries. Studies have shown that self-sampling is an acceptable alternative, with women often preferring it because of the privacy and convenience it offers (7). Economic considerations also play a vital role. A systematic review and meta-analysis revealed that HPV self-sampling has the potential to be cost-effective compared to healthcare provider-collected samples(4). However, there are several common concerns and misconceptions about HPV self-sampling. One major concern is the accuracy and reliability of self-collected samples (10). with proper information and effective educational programs, these issues can be solved.

HPV self-sampling is widely accepted; but awareness, experience, and preferences need to improve, it is acceptable and easy to use (2). Acceptability is in developing and developed countries as well, and women prefer to do self-sampling rather than attend the screening with cervical cytology when both methods are available (23). Participants rated more favorably positive test characteristics of self-sampling as compared to cervical cytology (24). Self-sampling tests represent a valid alternative for HPV testing and are widely accepted. Cost-effectiveness is also improved by reducing the cost of HPV self-sampling and attracting never-tested and long-term under-tested women (19).

A systematic review and meta-analysis focusing on low- and middle-income countries pointed out the potential of HPV self-sampling in improving screening uptake (4). A study on African-American women in the Mississippi Delta region of the United States examined the cost-effectiveness of HPV self-sampling. The findings suggest that self-sampling could be a very good strategy for reducing cervical cancer in high-risk populations by making screening more accessible and affordable (25). Insights from federally qualified health centers in the United States have reported that while costs for setting up self-sampling programs might be higher, the long-term savings from increased screening coverage and early detection could benefit much more (26). A cost-effectiveness analysis compared repeated HPV self-sampling with traditional Pap smear cytology. The study reported that HPV self-sampling could enhance participation rates, therefore identifying more women at risk of developing cervical cancer. This increase in participation is likely to reduce the overall costs (19). This is important for

women who live in remote or underserved areas, and who may face logistical and financial barriers to accessing traditional cervical cancer screening methods (12).
Furthermore, Indian women continue to be hesitant and shy about taking a pelvic exam, due to culture (3). Studies of women's positions on HPV self-sampling have indicated that in Western countries they supported the findings that most women are receptive to HPV self-sampling as part of future screening (27).
Studies show that the acceptability of HPV self-sampling was very positive among both women aged 25 to 35 and older than 45, indicating that it could be a solution to overcome the barrier of the Pap smear and feasible to use as an alternative cervical cancer screening method (28). A four-year project in Nicaragua, Guatemala, and Honduras showed high acceptability towards HPV self-sampling among nearly a quarter-million women (29). In Peru, high levels of satisfaction with HPV self-sampling have been documented in the Loreto province, where 74.2% of the users reported feeling at least satisfied with the program and 68.0% preferred the self-sampling compared to healthcare provider sampling (29).
These results can help to adjust public health strategies for the early inclusion of HPV self-sampling as a screening method to prevent cervical cancer in the early stages. Self-collected samples also have high efficiency and acceptability, which can reduce socioeconomic and cultural barriers to increase the screening rate. Currently, primary cervical screening programs in many nations such as Norway, Denmark, and the United Kingdom involve self-sampling (2). Table 1 shows the summary of self-sampling studies in some countries.

Table 1. Summary of self-sampling studies in countries and comparison with clinician collection sampling

Country	Participants	Brief result	Ref.
Denmark	23632	Women participating in self-sampling had a higher XCIN2 (OR ¼ 1.83, 95% CI: 1.21–2.77) and routine screening (OR ¼ 1.03, 95% CI: 0.75–1.40)	(30)
Japan	7653	By sending the HPV test kit to 1,674 women, 953 of them returned the kit and 89 HPV-positive cases was found.	(31)
Botswana	104	Women living with HIV found self-sampling to be comfortable and easy more than 90% of the time, and 95% were willing to try it again.	(32)
Mexico	110	A large proportion of women (42.7%) preferred both methods equally. There was also a strong willingness to use self-sampling and recommend it.	(24)
Nigeria	9406	Overall acceptability of self-sampling was very high (81.2% of women preferring self-sampling over clinician collection.	(33)
Cameroon	540	Participants expressed a high level of acceptance of HPV self-sampling as a screening method. Acceptance of the method did not correlate with education level, knowledge, age, or socio-professional class.	(27)
China	1793	Approximately 88.8% of participants rated the acceptability of self-sampling methods as "high," and 64.2% preferred self-sampling for cervical cancer screening.	(2)
Italy	482271	Self-sampling methods have nearly doubled the likelihood of using cervical cancer screening and show higher rates compared to samples collected by doctors.	(6)

Discussion

Considering the analysis conducted regarding HPVs and the infections it cause, particularly cervical cancer, as well as the importance of the early detection, and complications arising from this virus, for prevention and treatment.
It is expected that all countries, especially developing ones, would adopt measures for self-sampling to increase the coverage of HPV screening in both rural and urban areas, particularly for women who do not participate in regular screening programs or have never been screened.

Conclusion

To minimize the barriers and challenges of sampling by healthcare workers compared to self-sampling for HPV, this method can serve as a highly acceptable and cost-efficient alternative that would be effective across various countries.

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Ethical statement

This study, as a review article written solely based on the research of others, does not require any special ethical permission.

Conflicts of interest

There is no conflict of interest.

Author contributions

AM., SDK., and IM. contributed to the study conception, data analysis, revision, Reading, and confirming the final version of the manuscript.

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