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EDITORIAL

Is It Time to Introduce HPV Self-Sampling for Primary Cervical Cancer Screening?

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Regular Papanicolaou (Pap) testing has been the backbone of the most successful cancer reduction program in the public health system. However, it is not perfect. In high-income countries, more than half of the women who are diagnosed with cervical cancer had never had a Pap test or were infrequently screened (1). In the United Kingdom, recent studies have suggested a decline in the routine screening program participation to below its target rate of 80%, particularly among women aged 25–29 years (2). Factors that may discourage women from going for regular screening are lack of time, discomfort, inconvenience, cultural objections, and poor socioeconomic status. In low-resource regions, additional barriers include lack of knowledge and lack of accessible or appropriate screening facilities as well as the prohibitively high cost of screening. Offering a simple, inexpensive, and convenient self-test that respects individual privacy may improve the participation of women who might be otherwise reluctant to undergo screening and those who live in areas with poor access to health care.

In the last few years, we have learned that self-collected vaginal specimens from women who have received appropriate instruction produce human papillomavirus (HPV) test results similar to cervical specimens collected by health-care professionals (3). This congruence has supported the concept of introducing HPV self-sampling (Self-HPV) as an alternative means for cervical cancer screening. However, screening is a complex process, and the introduction of a new screening scenario should be carefully evaluated. Fundamental issues that must be addressed regarding the future of Self-HPV as a primary screening method are 1) whether the performance for the detection of cervical intraepithelial neoplasia (CIN) grade 2–3 and cervical cancer (CIN2+) by Self-HPV is (at least) equal or superior to that of the Pap test, 2) whether screening participation rate with Self-HPV will be sufficiently high, and 3) whether comparable results would be obtained outside a research setting.

In this issue of the Journal, Zhao et al. (4) have addressed the first issue. In a pooled analysis of data from five population-based cervical cancer screening studies, including a total of 13 140 rural Chinese women aged 17–56 years, the investigators demonstrated the feasibility of a Self-HPV approach in a context of primary screening. Women were successively screened with Self-HPV, visual inspection with acetic acid (VIA), physician-collected cervical specimens for HPV testing (Physician-HPV), and liquid-based cytology (LBC). Overall 15.6% of Self-HPV and 14.7% of Physician-HPV tests were HPV positive (91.8% agreement, 95% confidence interval [CI] = 84.9% to 95.7%). The clinical sensitivity and specificity with which Self-HPV detected CIN2+ were 86.2% (95% CI = 82.9% to 89.1%) and 80.7% (95% CI = 75.6% to 85.8%), respectively, and the corresponding values for LBC were 80.7% (95% CI = 77.0% to 84.0%) and 94.0% (95% CI = 92.2% to 95.8%), respectively. Overall, this study supports the conclusions that Self-HPV testing is more sensitive than LBC for the detection of CIN2+ and that performance does not depend on the age of the women being screened. These data add to a recent randomized trial in which Self-HPV was demonstrated to be 3.4 times more sensitive than the Pap test in detecting CIN2+ in Mexican women of low socioeconomic status (5).

The problem with Self-HPV is its specificity. A total of 15.6% of the women screened HPV-positive and were referred to colposcopy by the investigators. This approach is impractical in the context of routine screening without triage of HPV-positive women to colposcopy by a more specific test. A randomized trial (6) demonstrated that primary HPV screening with triage by conventional cytology was more sensitive than the Pap test. This strategy is probably one of the most promising for countries that have cytology-based screening programs. Another study (7) showed that triennial primary home-based Self-HPV screening followed by in-clinic cytology triage was sufficiently accurate and cost effective. For countries with a poorly developed cytology-based screening program, VIA may be the more appropriate strategy. It has the advantage to provide immediate results, making it possible to triage and treat without delay during the same visit. Zhao et al. (4) explored both triaging systems and calculated that Self-HPV testing coupled with LBC reduced the referral rate to 4.8% (95% CI = 3.3% to 6.7%) and Self-HPV testing with VIA reduced referrals to 4.5% (95% CI = 3.3% to 6.1%).

Although not evaluated in this study, assessment of women's interest and willingness is crucial before introducing a new screening method. It is unclear if the results obtained by Zhao et al. (4) will be reproducible among patients with limited education and nonuniform instructions about self-sampling technique. An earlier study on patient acceptance in rural China (8) reported that the major barrier encountered was related to the women's educational level. Women generally are receptive to Self-HPV as part of future screening, but many of them are concerned about doing the test properly and have greater confidence in clinician sampling (9–11). Efforts are still needed to increase awareness about HPV and cervical cancer, and more information is needed about the reliability of the method.

The participation rate of women and cost-effectiveness of home-based self-sampling also need to be assessed. In countries with opportunistic screening, few data are currently available.

Studies in Western countries with organized screening programs (12–14) reported that providing self-sampling kits to women who did not participate, particularly when in addition to a reminder letter, may improve their screening adherence. Nevertheless, further investigation is needed to evaluate the response to self-sampling and its cost-effectiveness in different demographic and geographic settings (14). An Italian study (15) found that the effectiveness of mailing self-samplers to nonresponders was context specific and might be expensive in terms of number of Self-HPV tests used per screened woman.

Current literature reinforces the increasing body of evidence that self-collected samples for HPV DNA testing may be an appropriate strategy to increase participation of unscreened women and ultimately promote a decrease in incidence of and mortality from cervical cancer. However, the feasibility and impact of introducing this method outside research settings requires further evaluation. Research should also assess the availability of validated devices and the quality of patient education. Health-care professionals should provide sufficient support to participants to properly interpret their test results, thus avoiding any delay to follow-up and treatment. Self-HPV per se is only a part of a secondary prevention program, and obstacles to program participation might not only result in program failure but also be harmful for women.

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Notes

The authors claim no conflicts of interest.

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