



## Cervical Cancer Screening: The Challenges of Tracking and Follow-up

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### Abstract

The ability of a patient to attend a screening clinic, to return for possible treatment, and to return to clinic for follow-up evaluation ("the patient factor") is an important component to the success of a screening program. The patient factor has not been addressed in the discussion of cervical cancer screening techniques and guidelines. Challenges and barriers to tracking screening results and returning for follow-up include patient factors, limited resources, and inadequate medical infrastructure. The various elements that lead to loss to follow-up in a screened population are discussed. Potential solutions to improve continued surveillance and interventions to prevent the development of cervical cancer are reviewed.

### Keywords

Human papillomavirus; HPV; HPV testing; Cervical cancer screening; Self testing, Compliance; Loss to follow-up; Barriers to screening

### Discussion

In developed countries, regular screening with a Papanicolaou smear has been shown to effectively lower the risk for developing invasive cervical cancer by detecting precancerous changes [1]. However, in developing countries, only approximately 5% of eligible women undergo cytology-based screening in a five-year period, secondary to constraints in technical expertise and health care infrastructure inherent to cytology-based screens [2]. Visual Inspection with Acetic Acid (VIA) is an alternative method that has been shown to overcome these limitations and further, provide opportunity for simultaneous screening and treatment using cryotherapy. This "see and treat" approach provides health care delivery through the primary health system and ensures adherence to treatment soon after diagnosis, and has demonstrated reduction in the incidence of pre-cancerous lesions [3]. Despite its demonstrated efficacy in trial settings, there has been no demonstrable reduction in cervical cancer incidence, raising questions regarding adequacy of screening and treatment provisions to at risk populations [4].

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evaluation ("the patient factor") is an important component to the success of a screening program. The patient factor has not been addressed in the discussion of cervical cancer screening techniques and guidelines. Do women comply with screening recommendations? What are the barriers to getting screened for cervical cancer? Challenges and barriers to tracking screening results and returning for follow-up include patient factors, limited resources, and medical infrastructure. In this brief communication, we examine the various elements that lead to loss of follow-up in a screened population. We also review potential solutions to improve continued surveillance and interventions to prevent the development of cervical cancer.

Published studies regarding cervical cancer screening have been affected by large rates of lost patient follow-up [3,5,6]. For example, a demonstration project published by the World Health Organization in 2012 showed that VIA was feasible in low resource settings, with almost 20,000 women screened in seven countries [7]. However, there was a 10% VIA positive rate and only 65% of these women underwent further treatment. Also, almost 2% of women had invasive cancer at time of initial screening, yet only 30% received adequate follow-up. Among women who delayed care, reasons cited included childcare issues, cost, and the need to seek permission from male partner.

Risks to delayed care in these settings are obvious and well studied. A large prospective cohort screening study in Greece identified that only 30% of women received regular cervical cancer screening [8]. Women who do not present for screening may have a higher rate of preinvasive and invasive cervical lesions. A cohort study of 28,073 women in Amsterdam who did not come in for visits despite two invitations to be screened had increased relative risk of CIN 2 and higher with a RR of 2.04 [9]. In large cohort studies, the loss to follow-up has ranged from 21% to 64% of women who were triaged to repeat testing or follow-up evaluation [10,11]. This data demonstrates the continued challenges to screening pertaining to patient acceptability and follow-up, specifically in areas with limited resources, poor infrastructure, and inability to provide follow-up or treatment. In addition, an unstated risk for the development of cervical cancer has been identified - even when resources for cervical cancer screening exist - which is the inability for women to attend screening clinics and the loss to follow-up after an initial screen [12,13].

Cervical cancer screening with VIA has been an inexpensive intervention that has been used worldwide in resource-poor regions and has a reported 25% decrease in cervical cancer incidence and a 35% reduction in cancer mortality in the VIA group [14]. However, follow-up colposcopy was offered immediately with screen positivity, and only addresses the impact of single interventions and not the consequences of those who did not return for repeat screening. One such program using VIA on 18,586 women in Morocco identified 87 women who needed loop electrosurgical excision procedures (LEEPs) yet only 16 (18.7%) returned for their treatment [15]. This program highlights the

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difficulties of follow-up and treatment of even inexpensive interventions.

Various factors that affect a woman's ability to get screened include knowledge, socioeconomic status, access to healthcare facilities and insurance coverage, age, marital status, lifestyle, family history, and healthcare provider guidance [16]. The new screening guidelines for "low-risk" women may not be appropriate for "high-risk" women who have a history of abnormal cervical cytology, high-risk Human Papillomavirus (HR-HPV) infection, or a history of cervical preinvasive and invasive disease [1,17]. "High-risk" women may also be those who are less likely to come for screening or to follow-up with screening due to complex social and cultural pressures [18]. The certain subgroups that are especially vulnerable to cervical cancer and have reduced access to care range from women over 55 years, incarcerated women, to women with disabilities [18]. Even among well-established cervical cancer screening programs, such as screening within the UK National Health Service, women at highest risk of defaulting from appropriate screening or follow-up include those who lack post-school education, who are not in paid employment, and who report they are not worried about cervical cancer [19]. For those women who live in communities with less well-established medical infrastructure and mechanisms for screening, the risk is even higher. A qualitative study of 198 cervical cancer patients in Ethiopia identified poverty along with other socio-cultural practices such as early marriage, high parity and polygamy as factors that increased the vulnerability of women to cervical cancer [20]. Three types of challenges to coming for screening were identified: psychological, economic, and healthcare based. The identified psychological challenges included fear of recurrence, negative social attitude and psychological distress. In another study of cervical cancer patients in Kenya, patients noted the lack of public education about cervical cancer as a barrier to screening. Additionally, fear of alteration in their body image, sexuality, reduction in fertility, and rejection by their spouse led to avoidance of care until they developed advanced cervical cancer [21]. Similarly, women in parts of Latin America may avoid screening because of fatalistic or religious beliefs [22]. A cross-sectional study from Thailand examined the factors associated with cervical cancer screening adherence [23]. Seven hundred questionnaires to women aged 30 to 60 were administered with a 96.2 % response rate. Only 65.4% of women had undergone at least one screening within a five-year screening interval. Barriers to screening included knowledge base, being divorced or single, and women's perceived fears of screening.

In Columbia, mortality rates from cervical cancer range from 28.7 to 65.5 percent by region in Colombia and did not correlate with screening coverage [4]. These mortality rates were directly related to the inability to provide follow-up and treatment for abnormal results.

Additionally, challenges of the infrastructure of the medical system can limit patient accesses to screening programs. For instance in rural settings, providers are confronted with limited transportation, communication systems, infrastructure, shortages of health professionals, and restricted access to resources for diagnostics, prevention and curative purposes [7]. In the major urban center of Ethiopia, system delay and practitioner delay

were found as the main hurdles within the variable of health care related challenges [20].

Mechanisms to track women who need follow-up must be developed. Various solutions range from improved community health education, patient navigators, and new techniques of self-testing [7,8,24,25].

A survey of over 2000 women in the USA identified cancer risk perceptions to be an indirect factor in reluctance to come for screening [26]. An increase in education around risk factors for cervical cancer at the school and community level is advocated to improve screening compliance. Community based participatory research can be effective to identify cultural and other barriers that limit utilization of screening services [24]. Additionally, trained community health workers can be valuable patient navigators and resources to decrease the numbers lost to follow-up [25,26].

Another alternative, self-screening at home, may be a more acceptable option for these high-risk women. A comparison of self-sampling versus physician swabs using liquid based solutions and PCR HPV testing showed that HPV was detected in 23.2% of patient collected samples compared to 34.9% of physician based samples [27]. Another study of 546 women over age 30 from India showed a 93.8% agreement in HPV identification from self collected and physician collected samples [28].

A cost-effective analysis of 1,665 women supported in-home screening with self collected vaginal swabs for HR-HPV followed by in-clinic cytology every three years [29]. One study evaluated the use of a dry swab versus liquid medium in 722 women who underwent 3 collections [30]. The sensitivity and specificity respectively were 88.7% and 92.5% for dry and 87.4% and 90.9% for liquid concluding that a dry swab was accurate and this is an inexpensive and easily transportable tool.

Overall however, vaginal self-collection for HR HPV is not as sensitive or specific as physician-collected specimens. In a multinational cross-sectional study in three colposcopy clinics, sensitivity and specificity for cervical cytology and PCR based HPV testing, patient versus physician-collected specimens were 55%/84.1% versus 85.2%/73.4% respectively [31]. An evaluation of location of HPV positivity in the lower genital tract revealed that the major cause of the lower HPV yield on self-collected specimens arose because the vagina had differentially lower incidence of HPV positivity compared to the cervical in HPV positive women [32]. This information can lead to better education and guidance for patients who wish to obtain HPV or cytology samples in home screening kits.

In summary, patient factors such as attending screening clinics and returning for follow-up and treatment are crucial challenges to the effectiveness of cervical cancer screening programs. Present data shows significant attrition of patients from screening programs. These patients may be at the highest risk for the development of cervical cancer. Systematic interventions and applications of demonstrated techniques to improve screening should be applied. The World Health Organization endorses a three-stage process for strengthening policies and programmers' in order to establish large scale, sustainable services and effective policy for improved access to and quality of care [2]. Phases I and II involve strategic assessment

and implementation studies, which have been discussed. Phase III moves towards scale up strategies to broaden and support screening strategies. These strategies are directed towards women, providers and health systems.

## Conclusion

This communication highlights areas for improvement in female engagement, specifically the need for well-designed and strategic efforts to motivate women to access cancer preventive services especially those who do not routinely seek health services in the community or those who do seek care yet have never been screened. Interventions such as public information campaigns, education at schools, places of worship, and community centers, results-tracking and patient navigators should be developed. In addition, innovative screening options such as self screening should be considered.

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