



# Cross-Sectional Study of HPV Self-Sampling among Indian Women—A Way Forward

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## Abstract

Molecular human papillomavirus (HPV) DNA is a recommended test for any country planning cervical cancer screening as a national policy. The emerging literature proposes HPV self-sampling (HPV-SS) as a feasible implementing strategy in low-income settings. The success of this strategy would depend on developing impactful health education materials, understanding modalities toward generating awareness, and precision in performing the screening test among beneficiaries. The current paper is an interim analysis of ongoing research undertaken to understand the acceptability of HPV-SS among Indian women across different community settings. The study design has two modalities for generating awareness: (1) health education arm wherein the awareness and steps of collecting self-sample are explained by health personnel, and (2) the pamphlet arm wherein pictorial illustrations depicting the steps to conduct HPV-SS are distributed among women. The quality of samples is compared with primary health worker samples (PHW-S). Initial results of this study support the acceptance of HPV-SS (97%) among urban slum settings. An agreement between HPV-SS and PHW-S was demonstrated to be 95.1%. The results of the pamphlet arm were comparable to the health education arm in every aspect. The art-based strategy seems like a promising communication modality for generating awareness toward cervical cancer screening using HPV-SS in low-resource settings.

## Keywords

- cervical cancer screening
- HPV test
- HPV self-sampling
- art-based strategy
- low-resource settings

## Introduction

India reports a high burden of cervical cancer.<sup>1,2</sup> The factors contributing to a high burden of disease are the lack of health care infrastructure and access to available facilities. Among social determinants, low literacy level, lack of awareness of cervical cancer symptoms and lack of priority of women's

health issues are some of the contributing factors.<sup>3</sup> These factors together have a potential to lead to a global disparity in terms of population coverage for cervical cancer screening in India. A population-based survey conducted across 57 countries reported cervical cancer screening coverage of 19% on an average in developing countries compared with

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63% in developed countries. The author commented that older and poor women, who are at the highest risk of developing cervical cancer, are least likely to be screened.<sup>4</sup>

Currently, India does not have an organized screening program. Although visual inspection with acetic acid (VIA) is a recommended screening test, it is challenging to sustain and scale up the program due to repeated training, quality control, and screening rounds needed.<sup>5</sup> To avail VIA test, women need to visit health care facilities with trained health personnel to perform the test. This scenario represents programmatic barriers for screening in terms of accessibility and human resources. Currently, there is sufficient evidence from epidemiological studies about the causal role of persistent oncogenic human papillomavirus (HPV) infection and cervical cancer.<sup>6,7</sup> The direct detection of HPV in cervical specimens by a molecular test can offer an alternative for cytology/VIA-based screening. Among the various emerging HPV molecular tests, the hybrid capture-2 test (HC2) has been extensively evaluated in various health care settings.<sup>8,9</sup> The test identifies women at the risk of developing cervical cancer, needing a close follow-up.<sup>10,11</sup> The advantages of HPV-DNA molecular test are high sensitivity (reported from developing countries), longer screening intervals if tested negative, the potential of self-collection, reproducibility, and standardization of the test.<sup>10,12,13</sup> HPV self-sampling (HPV-SS) is posed to be a viable option to increase the uptake of cervical cancer screening among women. At the national level implementation strategy, the test has the additional advantage of reducing the human resources in terms of empowering the women to undertake their own test.<sup>14</sup>

Among all the above factors, the current study mainly explores the potential of acceptance of HPV-SS as a preferred screening method by Indian women. India is a country with diversities. Promoting HPV-SS shall need effective information, education, and communication materials (IEC) in generating awareness toward screening and performing the HPV-SS test with confidence among the beneficiaries. This is crucial in settings where illiteracy is a key barrier in undertaking cervical cancer screening tests.

The current paper discusses interim results of the main study in terms of acceptability of self-sampling as a screening modality to increase the coverage for cervical cancer screening, the impact of communication modalities of IEC materials (the health education arm versus pamphlet arm) to increase the uptake of HPV-SS, and quality of HPV-SS measured in terms of agreement rates between the HPV-SS and primary health care worker collected HPV samples (HPV-PHW) among women in the slum settings in Mumbai, Maharashtra.

Quality of HPV-SS measured in terms of agreement rates between the self-sampling and HPV-PHW among women in the slum setting was considered as a primary objective of the study.

## Materials and Methods

### Inclusion Criteria

Inclusion criteria were sexually active non-pregnant women in the age group of 30 to 55 years with no previous history of cervical cancer.

### Exclusion Criteria

Exclusion criteria were women not sexually active, who underwent total hysterectomy, with prior treatment history for cervical cancer, and pregnant or postpartum 6 months.

### Study Design

The main study was a cross-sectional study proposed to be implemented across three communities: namely (1) urban slum area, (2) urban non-slum area, and (3) rural area (►Fig. 1). Herein, we tried to understand if HPV-SS would be similarly or preferentially accepted by specific groups. For each setting, three clusters were identified and one of the clusters under each setting was selected by a lottery method for implementation. The current study presents the results of urban slum community settings collected during the study period of 12th April 2021 to 24th June 2021.

As per our hypothesis, the modality of communication may influence cervical cancer screening uptake and quality of self-sampling. To address this, the current study was designed with two interventional arms—(1) health education arm and (2) pamphlet arm. Each selected cluster was then demarcated for two interventions using geographical landmarks. In the health education arm, primary awareness for cervical cancer (risk factors, types of screening tests, and advantage of early diagnosis and prevention) and steps demonstrating the method to collect HPV-SS was explained in the local language using flip charts/posters by medical social workers (MSW). In the pamphlet arm, art-based strategy pamphlets with self-explanatory pictorial illustrations demonstrating the steps of the procedure of collecting HPV-SS were distributed by MSW.

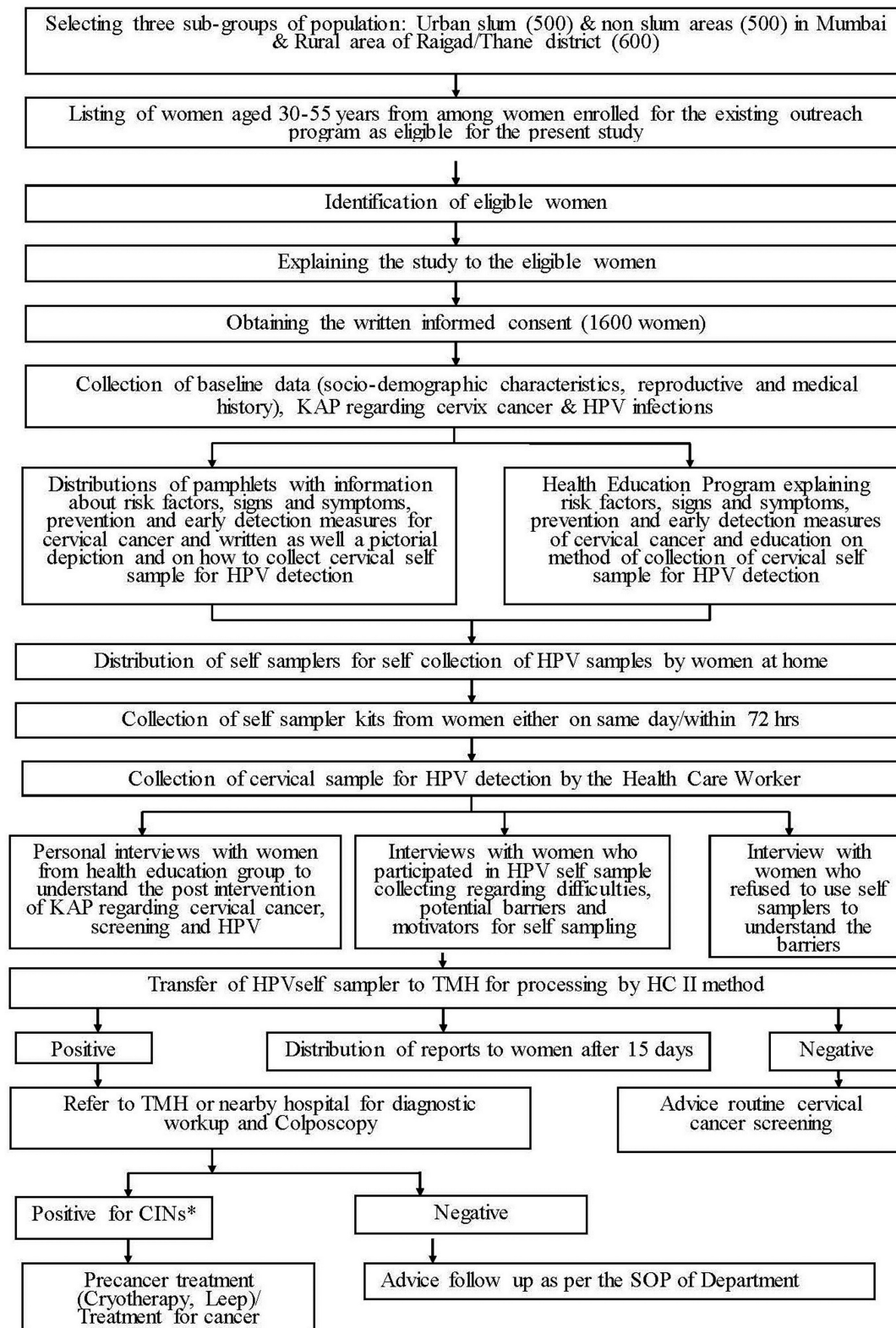
## Methodology

As per the literature, the prevalence of HPV in self-sample is assumed to be 7 to 10%. To get a concordance rate of 80%, at 95% confidence interval (CI) and power of 80%, estimated sample size comprised 1,600 women (500 under urban slum settings, 500 under urban non-slum settings, and 600 under rural settings) to undergo HPV testing by both the methods for the main study.

Under the current study, a total of 500 women, 250 women in the health education arm and 250 women in the pamphlet arm, were enrolled. After the detailed mapping of the area, door-to-door survey was conducted by trained MSWs to register eligible women and invite them to participate in the study. Eligible women were enrolled following informed consent, and the study questionnaires were completed.

After the awareness session as per the arm assigned, HPV-SS kits were distributed to women in both groups. Used/unused kits were collected either on the same day or within 72 hours by the MSWs. All women enrolled in the study were invited for HPV-PHW samples. The women who tested positive on either HPV tests were referred to the tertiary care center for further diagnostic workup.

The MSWs and the PHWs recruited under this trial received intensive training on delivering the standard

**Study Algorithm (Figure 1)****Fig. 1** Demonstrates the detailed methodology of study. \*Cervical intraepithelial neoplasia.

health education on cervical cancer for 4 weeks. MSWs were additionally trained for conducting survey, mapping, and HPV-SS test. PHWs received hands-on training in collecting HPV samples using the HC2 test for an additional period of 4 weeks in the institutional department as per the standard operating protocols (SOPs). The audit for quality control was planned every month.

### Screen Positivity Criteria for the HC2 Test

To diagnose HPV infection, samples were processed by the HC2 test which has probes for 13 recognized oncogenic HPV types. The relative light unit/cut-off ratio  $\geq 1$ , corresponding to 5,000 or more copies of virus in a sample, is considered a positive test. The transportation of the samples from the field to institute was as per the SOPs of the Institutional Department of Microbiology.<sup>8,9</sup>

### Statistical Analysis

The quantitative data related to the study's objective were captured and analyzed using IBM SPSS statistics for windows, version 25.0 (IBM Corp, Armonk, NY, United States). For the current paper, agreement between the HPV-SS and HPV-PHW samples using the molecular HPV test was analyzed using Kappa statistics for the probability of chance along with 95% CI.

### Ethics

The female participants were enrolled only after informed written consent was obtained. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practices as defined by the International Conference on Harmonization. The study received clearance of the Tata Memorial Hospital Institutional Review Board on 2nd March 2017, Project No- 1686.

### Results

The overall acceptance of HPV-SS was 97% (485) in the target population (► **Table 1**). The acceptance of HPV-SS was 100% (250) in the health education arm and 94% (235) in the pamphlet arm for all those receiving the instructions in both formats. The agreement between the HPV-PHW sample and the HPV-SS was demonstrated to be 94.69% (232) and 95.61% (196) in the health education arm and pamphlet arm, respectively. Overall, the agreement rate was 95.11% (428). The kappa value demonstrated moderate agreement between the two samples readings by the HC2 test,  $k=0.55$  (95% CI = 0.34–0.77),  $p < 0.001$ .

### Discussion

In India, cervical cancer is a vivid indicator of health inequality within the country with the burden of disease reported high among rural and low-income areas.<sup>15</sup> Hence, all efforts should be made to cover this hard-to-reach population to reduce the incidence and mortality rates for the country. The current article reports interim data on acceptability and quality of HPV-SS among women in urban slum settings using a camp-based approach. Only slum women were selected for the current paper as they face challenges such as non-availability of washrooms in the household and lack of privacy for collecting self-samples.

This setting was high risk for HPV infections in terms of low economy, risky behavior, sharing common toilets, and low vaginal hygiene. The women enrolled in the study were in the median age group of 38 years which is a recognized age for the persistence of oncogenic HPV infection. A single round of screening in this age group has the advantage of prevention and downstaging of the disease.<sup>14,15</sup> The study overall demonstrated high acceptability (97%) of HPV-SS among this group of women (► **Table 1**).

**Table 1** Acceptability and agreements between HPV self-sampling and health worker collected HPV samples between the health education arm and pamphlet education arm as modalities of communications

Variable		Health education arm n = 250			Pamphlet education arm n = 250			Total n = 500		
1. a. Acceptance of self-sampling										
Acceptance of self-sampling n(%)		250 (100%)			235 (94%)			485 (97%)		
1. b. Agreements between samples										
		Health worker collected sample			Health worker collected sample			Health worker collected sample		
HPV test result		+ ve	– ve	Total	+ve	– ve	Total	+ ve	– ve	Total
Women self- collected sample	+ ve	9	7	16	7	4	11	16	11	27
	– ve	6	223	229	5	189	194	11	412	423
	Total	15	230	245 <sup>a</sup>	12	193	205 <sup>a</sup>	27	423	450 <sup>a</sup>
Agreement		232 (94.69%)			196 (95.61%)			428 (95.11%)		
Kappa (95% CI)		0.55 (0.34–0.77)			0.58 (0.34–0.83)			0.57 (0.40–0.73)		

Abbreviations: HPV, human papilloma virus; –ve, negative for HPV in cervical sample; + ve, positive for HPV in cervical sample.

<sup>a</sup>Women gave self-collected sample and health worker sample was also collected.

Moreover, beyond acceptance of the test, it is crucial that women perform the test with precision. There are numerous studies that have reported comparable performance of self-sampling to clinician collected samples.<sup>16,17</sup> To our knowledge, this is the first study that compares the performance between the self-collected and trained PHWs collected HPV samples. Our study also demonstrates comparable agreements between HPV-SS and HPV-PHW samples. Understanding that the majority of Indian population resides in rural areas with illiteracy and social stigmatization<sup>18</sup> being a major barrier in taking the test, it becomes important to understand, develop, and evaluate appropriate IEC materials to raise awareness toward cervical cancer and the screening test to be implemented. The educative materials also need to be effective in de-stigmatizing and facilitating the undertaking of screening. Prior knowledge of the screening test helps women to do so confidently. Currently, resources are needed for one-to-one counseling for women before preparing them to undertake HPV-SS.<sup>16,17,19</sup> This strategy may not be feasible in human-resource-constrained countries like India. The art-based health promotion strategies have been proven effective in facilitating and mobilizing women among diverse settings. These strategies are warranted in low-resource settings.<sup>19,20</sup> The strength of our study design is the use of two modalities of communication in two groups, which shall help us understand the effective communication modality. The current study demonstrates an equally good acceptance of HPV-SS by women in the pamphlet arm comparable to the health education arm (► **Table 1**). Recruiting and training MSWs and PHWs as project staff for implementation shall help us understand the time needed for capacity building and quality of deliverables with the goal of transferrable skills. This is an attempt to understand the feasibility of integrating HPV-SS in public health systems.

## Conclusion

The initial findings of the study support the acceptability of HPV-SS as a primary screening test in the targeted population. In resources constraint settings, the current finding demonstrates the potential of art-based strategy as a modality in facilitating HPV-SS among women. The study also supports the feasibility of rapidly training para-medical staff in implementing the test at ground levels. These findings are encouraging toward building a sustainable and operational cervical cancer screening model for the country.

### Work to be Credited

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### Approval by all Authors

This manuscript has been read and approved by all the authors and represents honest work.

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### Conflict of Interests

None declared.

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