# Suitability of Self-Collected Vaginal Samples for Cervical Cancer Screening in Periurban Villages in Andhra Pradesh, India

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## Abstract

Objectives: Our aim was to determine if (1) Hybrid Capture 2 and a PCR-based method were comparable for detection of high-risk human papillomavirus (HPV) clinician-collected and self-collected samples were equally efficient to detect HPV and cervical cancer precursor lesions, and (3) if participation rates improved with home-based versus clinic-based self collection.

Methods: Samples were selected from women participating in a cervical cancer screening study according to HPV, visual inspection with acetic acid, or Pap smear screening results. From 432 of 892 selected women, split sample aliquots were tested for HPV DNA using both the Hybrid Capture 2 assay and the Roche prototype line blot assay. Women from a subset of villages were recruited at two separate time points for clinic-based self-collection and home-based self-collection, and participation rates were compared.

Results: Pairwise agreement between self- and clinician-collected samples was high by both Hybrid Capture 2 (90.8% agreement, $\kappa = 0.7$) and PCR (92.6% agreement, $\kappa = 0.8$), with significantly increased high-risk HPV detection in clinician-collected specimens (McNemar's $P < 0.01$). Ability to detect precursor lesions was highest by PCR testing of clinician-collected samples and lowest by Hybrid Capture 2 testing of self-collected samples (11 of 11 and 9 of 11 cases of cervical intraepithelial neoplasia grade 2/3 and cancer detected, respectively). Participation in home-based screening was significantly higher than clinic-based screening (71.5% and 53.8%, respectively; $P < 0.001$) among women ages 30 to 45 years.

Conclusion: The combination of improved screening coverage and a high single test sensitivity afforded by HPV DNA testing of home-based self-collected swabs may have a greater programmatic effect on cervical cancer mortality reduction compared with programs requiring a pelvic exam. (Cancer Epidemiol Biomarkers Prev 2009;18(5):1373–8)

## Introduction

Cervical cancer screening through cytology (i.e., Pap smears) and treatment of identified precursor lesions are rightly credited with a marked decrease in cervical cancer incidence in industrialized nations. Although a single Pap smear has relatively low sensitivity, frequent testing over the course of a woman's lifetime assures the identification of the precursor lesions. The requirement for repeat testing and multiple follow-up visits make cytology screening strategies virtually impossible to implement in developing nations, which bear the major burden of cervical cancer.

The recognition that infection of the genital tract with high-risk human papillomaviruses (HPV) is the primary cause of cervical cancer has led to the investigation of using HPV assays as an alternative to cytology in screening for cervical cancer. These studies have found that the presence of high-risk HPV (HR-HPV) in cervical swabs collected from the transformation zone of the cervix in the course of a pelvic examination has a higher sensitivity, but lower specificity, for the detection of cervical cancer precursors when compared with cervical cytology (reviewed in ref. 1). However, screening based on physician-directed cervical sampling still requires a clinic visit by the woman, and a speculum-assisted pelvic exam by a health care provider. These requirements limit broad access to and acceptability of the method in many

regions of the developing world. An alternative strategy is screening for HPV from a vaginal swab taken by the women herself, so that the first stage of screening can occur outside of a clinical setting. Studies evaluating the comparability of self-collected vaginal versus clinician-collected cervical swabs have generally shown good agreement for their ability to detect HPV (2-6), but the two methods have not been adequately compared for their performance in detecting cervical neoplasia in a screening setting.

We are conducting studies on HPV and cervical cancer in Medchal Mandal, a periurban community in Andhra Pradesh, 45 km north of Hyderabad. The Community Access to Cervical Health Study aims to evaluate the effectiveness of several cervical cancer screening methods (conventional Pap smear, visual inspection after application of acetic acid, HPV DNA testing from clinician-collected cervical swabs and from self-collected vaginal swabs) incorporated into a health delivery system. To assess the suitability of self-collected specimens for primary screening, we conducted a nested analysis of paired clinician-collected cervical and self-collected vaginal samples from 432 women enrolled in the Community Access to Cervical Health Study to answer 3 questions: (a) is the detection of HR-HPVs by the commercially available Hybrid Capture 2 (hc2) test comparable with that by the Roche prototype PCR line blot method; (b) are the clinician-collected samples comparable with the self-collected samples with respect to detection of HPV and detection of cervical intraepithelial neoplasia (CIN); and (c) does home-based self-sample collection increase the rate of participation of the rural women.

## Materials and Methods

**Study Design and Population.** Using a census list of the entire Medchal Mandal community in Ranga Reddy District in Andhra Pradesh State, India, we approached all eligible women from 42 villages to participate in the Community Access to Cervical Health Study from January 2005 to July 2007. Individual house-to-house recruitment with personal invitation was conducted in 35 villages; village level invitation was used in the remaining 7 villages. Women were eligible if they were age 25 years or older, had an intact uterus, were mentally competent, and were able and willing to provide informed consent. Information on basic demographics, reproductive, and contraceptive histories, as well as tobacco use, was collected from all consenting women by standardized interviews. Women underwent a standard pelvic examination, which included (in order) collection of a conventional Pap smear using an Ayre's spatula and endocervical swab, collection of a cervical swab sample for HPV testing using the Digene cervical sampler, and visual inspection after application of acetic acid. Pap smears were fixed immediately in ethanol. Women were also asked to provide a 10-cc blood sample and to collect a vaginal self-swab sample for HPV testing. Although provision of the blood and self-collected swab were optional, 98.6% and 99.96% of women agreed to provide blood and self-swab samples, respectively. All study procedures were reviewed and approved by the institutional review boards at all participating institutions in India and the United States.

For the present study, a nested sample enriched for HPV-positive women and women with precursor lesions was selected from the first 892 women enrolled. Selection included all 220 women who had a positive screening test result from 1 or more of the 3 assays compared in the study (i.e., HPV DNA, Pap smear, and visual inspection after application of acetic acid). An additional 250 women who were negative by all 3 tests were randomly selected for a total of 470 women. Of these, 38 were excluded because of missing data ($n$ = 8 for hc2 results; $n$ = 7 for PCR results) or because the sample was inadequate for PCR analysis (i.e., β-globin internal control could not be amplified; $n$ = 23). The final data set represents paired clinician-collected and self-collected samples from 432 women, of whom 87 (20.1%) were positive for hc2, 115 (26.6%) had abnormal Pap and/or visual inspection after application of acetic acid test results but were hc2 negative, and 230 (53.2%) were negative by all 3 screening assays.

**Vaginal Self-Swab Collection.** Women were provided verbal and printed diagrammatic instructions for collecting the vaginal swab by the study nurse. The women were asked to insert the swab into their vagina until it met with resistance, turn it thrice, and remove it. After providing the instructions, the nurse opened the collection kit and handed the swab to the participant, who went unaccompanied into a private room and collected the sample. After sample collection, the participant handed the swab back to the study nurse, who placed it into 1.0 mL of the labeled Digene sample transport medium. The self-swabs used in this analysis were collected immediately before the clinician-collected swabs on the same day.

**Specimen Processing.** Both clinician and self-collected specimens were kept at 4°C until processed within 24 h of collection. After vigorous vortex mixing, the samples were subaliquotted into cryovials and stored at −80°C.

**Table 1. Demographics of study population ($n$ = 432)**

| Age (y) | |
| --- | --- |
| 25-29 | 138 (32.9) |
| 30-34 | 96 (22.9) |
| 35-39 | 50 (11.9) |
| 40-44 | 39 (9.3) |
| 45-49 | 31 (7.4) |
| 50-54 | 32 (7.6) |
| 55+ | 34 (8.1) |
| Religion | |
| Hindu | 386 (89.3) |
| Muslim | 28 (6.5) |
| Christian | 18 (4.2) |
| Educational status (y) | |
| None | 292 (69.4) |
| 1-8 | 73 (17.3) |
| 9+ | 56 (13.3) |
| Marital status | |
| Currently married | 736 (88.5) |
| Currently not married | 49 (11.5) |
| Previous Pap history | |
| No | 413 (95.8) |
| Yes | 9 (2.1) |
| Do not know | 9 (2.1) |

NOTE: Missing data: 12 missing due to age, 11 missing due to educational status, 7 missing due to marital status, and 1 missing due to pap history.

**Table 2.  Agreement in HR-HPV DNA detection: hc2 versus consensus PCR in clinician- and self-collected samples**

|  | n | hc2+ | PCR+ | hc2+/PCR+ | hc2+/PCR− | hc2−/PCR+ | hc2−/PCR− | % agreement | κ | McNemar's P |
|---|---|---|---|---|---|---|---|---|---|---|
| Clinician | 432 | 87 (20.1%) | 89 (20.6%) | 76 (17.6%) | 11 (2.5%) | 13 (3.0%) | 332 (76.9%) | 94.4% | 0.8 | 0.68 |
| Self | 432 | 61 (14.1%) | 71 (16.4%) | 54 (12.5%) | 7 (1.6%) | 17 (3.9%) | 354 (81.9%) | 94.4% | 0.8 | 0.04 |

Abbreviations: CC, clinician-collected specimens; SC, self-collected specimens; HR, high risk.

One 200-μL aliquot of the clinician-collected sample was sent directly to the Center for DNA Fingerprinting and Diagnostics in Hyderabad for immediate hc2 testing. The remaining aliquots were stored at −80°C until removed for batch testing by PCR (both clinician- and self-collected samples) and hc2 (self-collected sample).

**hc2 Testing.** The hc2 test was done according to the manufacturer's instructions except where indicated. To preserve the sample for future DNA analyses, a 70-μL aliquot of each sample was denatured in 35 μL of denaturation solution. Seventy-five microliters of the denatured sample were then used as per manufacturer's instructions. Positive results were defined as samples with relative light units per control sample (RLU/CO) of ≥1.0.

**PCR Testing.** Aliquots were thawed and 90 μL were digested in a proteinase K/laureth-12 solution at 65°C for 1 h. Proteinase was heat inactivated at 95°C for 10 min, and DNA precipitated in an ethanol/ammonium acetate solution overnight at −20°C. DNA was pelleted by centrifugation at maximum rpm for 30 min at 4°C, and supernatant was removed with a disposable fine-tip transfer pipette. DNA was air dried and then resuspended in 50 μL of loTE [20 mmol/L Tris-HCl, 1 mmol/L EDTA (pH 8.5)]. A 5-mL aliquot of the extracted DNA was added to a 100 μL final volume PCR master mix including the PGMY09/11 consensus primers as previously described (7). Amplification products were hybridized to a reverse line blot allowing detection of the presence and discrimination of 37 HPV genotypes, including HPV 6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51 to 56, 58, 59, 61, 62, 64, 66 to 73, 81, 82, 82v, 83, 84, and 89 (8).

**Participation in Home-Based Screening.** Beginning in January 2007, all women, regardless of previous participation in the Community Access to Cervical Health Study, were recruited to provide a home-based self-swab sample from eight randomly selected villages. Women who had not previously enrolled in the study were consented in the field. Effective coverage was estimated on the basis of participation rates for screening (i.e., clinic-based and/or self-sample provision) and follow-up visit of HPV positive participants (i.e., clinic-based colposcopic exam).

**Statistical Analysis.** The hc2 results reflect a binary outcome defined as "positive" if the sample contains one or more HR- HPV types and "negative" if the sample does not contain a HR-HPV. To make the type-specific results for both high- and low-risk HPVs detected by the Roche prototype line blot assay comparable with the hc2 results, the type-specific data were similarly categorized into a binary outcome. Any PCR test result that included one or more of the HPV types targeted by the hc2 kit (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68) and/or HPV 66 were considered to be PCR HR-HPV positive. Samples containing none of these types, regardless of the presence of other low-risk HPV types were defined as PCR HR-HPV negative. HPV66 was included in the definition of HR-HPV by PCR because HPV66 is considered a bona fide HR-HPV and is easily detected by the hc2 assay through probe cross-hybridization (9). Exclusion of HPV66 from the PCR HR-HPV definition did not substantially change the agreement.

We calculated overall agreement in pairwise comparisons of hc2 versus PCR in clinician-collected and in self-collected samples, and in pairwise comparisons of clinician-collected versus self-collected samples tested by hc2 and by PCR for the detection of HR-HPV. In the pairwise comparison of clinician-collected versus self-collected samples by PCR testing, we also calculated the overall agreement in detection of any HPV (including low risk). For all pairwise comparisons, the agreement beyond chance was estimated with the κ statistic and corresponding 95% confidence intervals. We used the McNemar's test to detect significant differences in the discordant results ($P < 0.05$), indicating systematic differences by assay or sample type in the detection of HPV.

The correlation between the relative viral load in clinician-collected and self-collected sample pairs was estimated using Pearson's correlation coefficient from the log-transformed RLU/CO values obtained by hc2 testing, which are a semiquantitative estimate of HPV load. Differences in log viral load in cervical and vaginal samples were tested using a paired t test.

## Results

Table 1 summarizes the demographics of the nested sample selected for this substudy. Women in the

**Table 3.  Agreement in HR-HPV DNA detection: clinician- versus self-collected specimens by hc2 and PCR**

|  | n | CC | SC | CC+/SC+ | CC+/SC− | CC−/SC+ | CC−/SC− | % agreement | κ | McNemar's P |
|---|---|---|---|---|---|---|---|---|---|---|
| hc2 | 432 | 87 (20.1%) | 61 (14.1%) | 53 (12.3%) | 34 (7.9%) | 8 (1.9%) | 337 (78.0%) | 90.3% | 0.7 | <0.01 |
| PCR (HR) | 432 | 89 (20.6%) | 71 (16.4%) | 64 (14.8%) | 25 (5.8%) | 7 (1.6%) | 336 (77.8%) | 92.6% | 0.8 | <0.01 |
| PCR (any type) | 432 | 117 (27.1%) | 112 (25.9%) | 92 (21.3%) | 25 (5.8%) | 20 (4.6%) | 295 (68.3%) | 89.6% | 0.7 | 0.45 |

Abbreviations: CC, clinician-collected specimens; SC, self-collected specimens; HR, high risk.

substudy ranged in age from 25 to 85 years (median age, 32 years), 69% had not received a formal education, 87% were currently married, and 96% reported no history of previous Pap screening. In all these respects, they were very similar to the total population of 892 women from which they were sampled.

The agreement between results of hc2 and consensus PCR assays for the detection of HR-HPV is shown in Table 2 for both clinican- and self-collected samples. The overall agreement between the assays was 94.4% ($\kappa = 0.8$) for both clinician- and self-collected samples. PCR was slightly more likely to be HR-HPV positive in the self-collected samples ($P = 0.04$), but PCR and hc2 were equally likely to result in a positive HPV test from the clinician-collected samples ($P = 0.68$).

The overall agreement between clinician-collected and self-collected samples for detection of HR-HPV was similarly high by both hc2 and consensus PCR [90.3% ($\kappa = 0.7$) and 92.6% ($\kappa = 0.8$), respectively]. However, clinician-collected specimens were more frequently positive for HR-HPV (20.6% by PCR and 20.1% by hc2) than self-collected specimens (16.4% by PCR and 14.1% by hc2; Table 3, McNemar's $P < 0.01$). This difference was not seen when comparing the detection of any high- or low-risk HPV by PCR in the paired samples (McNemar's $P = 0.45$; Table 3). At the type-specific level, the PCR resulted in complete type agreement between the clinician-collected cervical and self-collected vaginal specimens in 82.6% of the PCR-positive pairs, and partial agreement (i.e., multiple infections with at least 1 type in common) in 5.6% of the PCR-positive pairs. There was no agreement in 51 (11.8%) clinician-collected/self-collected pairs.

Figure 1 is a scatterplot of the correlation of the relative viral load (measured by hc2 RLU/CO) in clinician-collected and self-collected sample pairs. These results show good correlation in general between the two viral load measures ($\rho = 0.71$; $P < 0.01$). For specimens that were hc2 positive in both samples ($n = 53$), the median log RLU/CO for cervical specimens was 1.4-fold greater than that for vaginal specimens ($P = 0.004$). There were 12 pairs that had clinician-collected cervical specimens with RLU/COs of >10 (median 69.04 RLU/CO) and self-collected vaginal specimens that were negative (Table 4). There were no pairs in which the vaginal specimen had
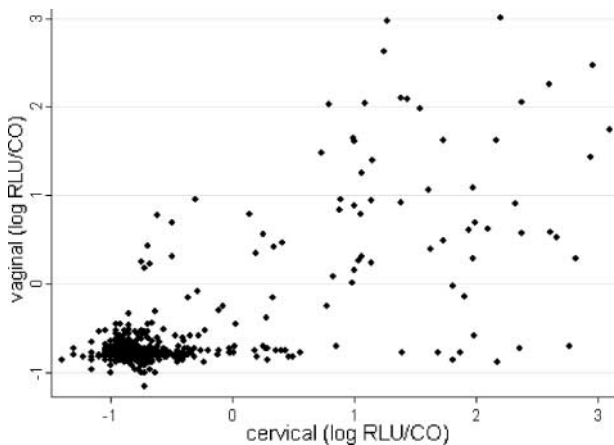


**Figure 1.** Scatterplot correlation of cervical and vaginal RLU/CO values.

**Table 4. Hybrid Capture viral load and genotype signal strength for the 12 clinician-collected cervical positive/self-collected vaginal negative discordant results**

| RLU/CO, cervical | HPV type, cervical | RLU/CO, vaginal | HPV type, vaginal |
|---|---|---|---|
| 24.36 | 52 (3) | 0.17 | HPV negative |
| 31.73 | 31 (4) | 0.49 | 31 (1) |
| 45.4 | IS39 (4) | 0.2 | 51 (1), IS39 (4) |
| 48.19 | 16 (4) | 0.17 | 42 (4) |
| 63.79 | 16 (4) | 0.14 | HPV negative |
| 64.02 | 33 (4) | 0.94 | 33 (2) |
| 74.06 | 16 (3) | 0.17 | HPV negative |
| 80.29 | 16 (3) | 0.72 | 16 (2) |
| 95.74 | 16 (4) | 0.26 | 16 (4) |
| 147.88 | 16 (4) | 0.13 | HPV negative |
| 225.32 | 39 (2) | 0.19 | 64 (2) |
| 582.5 | 35 (4), 70 (1) | 0.2 | HPV negative |

NOTE: RLU/CO indicates a semiquantitative measure of viral load. HPV type indicated; $n$, the relative strength of the hybridization signal; 1, very weak positive; 2, weak positive; 3, strong positive; 4, very strong positive.

an RLU/CO of 10 or greater but had negative cervical specimen.

**Ability to Identify CIN2/3 and Cervical Cancer.** The purpose of screening is to identify high-grade CIN and cervical cancer cases. Among the 432 women participating in this study, a total of 11 cases of biopsy-proven high grade-disease were identified including 4 cases of CIN2, 3 cases of CIN3, and 4 invasive cancers. The majority of cases were detected by any of the combination of sampling and HPV testing methods, ranging from 100% detection of high-grade lesions by PCR from clinician-collected samples to 81.8% detection by hc2 from self-collected samples (Table 5).

**Comparison of Participation in Clinic versus Home-Based Screening.** In the 8 villages where women were recruited to provide a home-based self-collected sample regardless of previous participation, clinic-based screening participation was 45.6% (257 of 564) and home-based participation was 57.5% (324 of 564). Screening participation was dependent on age (Fig. 2); women over the age of 45 years were less likely to participate in either clinic- or home-based screening compared with women 45 years and younger (44.8% versus 76.6%; $P < 0.001$). Among women likely to be targeted for a once- or twice-in-a-lifetime screening program (i.e., those ages 30-45 years), participation in home-based screening (71.5%) was significantly higher than clinic-based screening (53.8%; $P < 0.001$). Total screening coverage for women 30 to 45 years by either clinic- or home-based self-collected swab for HPV DNA testing was 76.3%.

## Discussion

The major aim of this study was to assess the suitability of HPV DNA analysis on home-based self-collected swabs as a primary screening strategy for cervical cancer screening in developing nations. The study was population-based and conducted in a periurban community in Andhra Pradesh, India. The women had virtually no previous history of cervical cancer screening and few had any formal education or financial resources. The self-collected

**Table 5. Hybrid Capture and PCR genotyping results for 11 cases diagnosed with CIN2/3 or invasive cancer**

| Sample | Histology diagnosis | RLU/CO, cervical | HPV type, cervical | RLU/CO, vaginal | HPV type, vaginal |
|---|---|---|---|---|---|
| 1 | CIN2 | 0.32 | 16 (2) | 2.08 | 16 (1) |
| 2 | CIN2 | 97.11 | 16 (4), 18 (4) | 4.88 | 16 (3), 31 (3) |
| 3 | CIN2 | 5.91 | 51 (3) | 0.56 | 51 (3) |
| 4 | CIN2 | 208.55 | 16 (4) | 8.17 | 16 (4) |
| 5 | CIN3 | 406.92 | 16 (3), 82 (4) | 3.9 | 16 (2), 82 (4) |
| 6 | CIN3 | 93.3 | 16 (4) | 12.14 | 16 (4) |
| 7 | CIN3 | 652.46 | 16 (3) | 1.96 | 16 (3) |
| 8 | Invasive cancer | 147.88 | 16 (4) | 0.13 | HPV negative |
| 9 | Invasive cancer | 53.44 | 16 (4) | 42.59 | 16 (3), 56 (4) |
| 10 | Invasive cancer | 157.97 | 16 (4), 52 (1) | 1,008.98 | 16 (4), 51 (1) |
| 11 | Invasive cancer | 2.56 | 16 (3) | 2.96 | 16 (3) |

NOTE: RLU/CO indicates a semiquantitative measure of viral load. HPV type indicated; n, the relative strength of the hybridization signal; 1, very weak positive; 2, weak positive; 3, strong positive; 4, very strong positive.

swabs were taken by the women, without any supervision, in the privacy of their homes or in private in the clinic. The conditions of the study were similar to what will be encountered in implementing any future cervical cancer screening strategy in rural communities in developing nations.

The women showed no hesitation in accepting self-collection; virtually all women who had agreed to clinic-based, physician-directed examination agreed to self-collection, and the laboratory data show that self-collection was successfully done (as indicated by detection of human DNA) by nearly all (96.5%) participants.

One aim of the study was to examine if the more complex PCR assay offers any advantage over the simpler, commercially available hc2 assay. In specimens collected at both vaginal and cervical sites, DNA detection rates by the two assays were very similar, suggesting that either signal or target amplified technologies are compatible with field based self-collection protocols.

Numerous previous studies have concluded that HPV DNA detection in cervical swabs has a high sensitivity for detection of cervical cancer precursor lesions; the sensitivity estimates for HPV DNA detection in the cervix are 66% to 100% compared with 44% to 78% for cervical cytology (1). A second aim of our study was to assess how HPV DNA detection in self-collected swabs compares with HPV DNA detection in clinician-collected swabs. Although there was a good correlation between positive and negative results at the two sites, there were some systematic differences. The DNA detection rate in self-collected specimens was 25% to 42% less than that in clinician-collected specimens, and the amount of virus in HPV-positive self-collected specimens was ~1.4-fold lower than that in the paired HPV-positive clinician-collected specimens. Most of the discordant results could be attributed to Poisson sampling error due to low viral load; 8 of 8 (100%) of hc2-negative clinician-collected/hc2-positive self-collected samples and 21 of 33 (63.6%) of hc2-positive clinician-collected/hc2-negative self-collected samples had an RLU/CO of <10.0. This variability is likely to occur on repeat clinician sampling. However, 36.4% of clearly hc2-positive clinician-collected samples were missed in the self-collected sample (nearly half of which were also PCR negative). These discrepancies represent a systematic difference in the sampling methods, which likely reflect a cervical infection that was insufficiently sampled by the self-collected vaginal swab. The self-collected sample contains a sample of vulvar and vaginal

cells, as well as a sample of cervical cells that are obtained either directly from the brush touching the cervix, or indirectly from pools of exfoliated cervical cells in the vaginal vault. As such, the self-collected specimen is usually, but not always, a good representation of cervical infection (4).

Such ''false negative'' self-collected vaginal samples will affect cervical cancer screening programs only if they are disproportionately occurring in cases of high-grade neoplasia and cancer. In our study, tests of clinician-collected samples of the 11 women who had cervical precursor lesions or cervical cancer, the PCR assay was positive in all instances and the hc2 assay was positive in all but 1 instance; in 1 case of HPV16-positive CIN2, the hc2 assay was negative. When testing the self-collected samples, the viral load was systematically lower compared with the clinician-collected samples; one HPV51 positive CIN2 was missed by hc2 and one invasive cancer was missed by both hc2 and PCR. Although the sample size was small for precise estimation of the test sensitivities, our data suggests that even the least sensitive option (81.8% from self-collected sample tested by hc2) remains significantly better than the Pap reference standard. In addition, a similar number of women screened positive, suggesting that the specificity of the test will remain acceptably high.
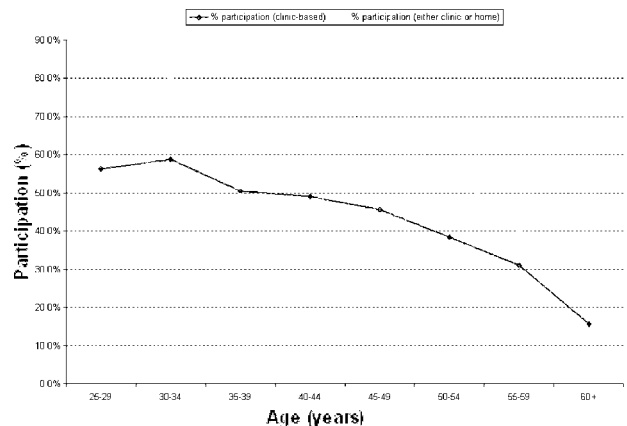


**Figure 2.** Participation in cervical cancer screening among the eight villages where clinic and home-based participation among total eligible population was assessed; clinic-only (circles) versus clinic or home-based (squares).

The absolute reduction in cervical cancer mortality through screening is dependent not only on test sensitivity but also on the population level coverage (i.e., how many women are screened and treated). Coverage among women ages 30 to 45 years increased from 53.8% to 71.5% when offering home-based self-collection versus clinic-based cervical collection in the 8 villages where we examined this question. Using a published model of reduction of lifetime risk of cervical cancer as a function of screening coverage and test sensitivity in twice-in-a-lifetime screening programs (10), our clinic-based program (53.8% coverage, estimated 90.9% sensitivity by hc2) would predict an ∼20% reduction in lifetime risk of cervical cancer. Comparatively, our home-based program using self-collected samples (71.5% coverage, estimated 81.8% sensitivity by hc2) would predict a nearly 30% reduction in lifetime cancer risk. Therefore, a loss in sensitivity combined with significant increases in screening coverage when using self-collected samples for HPV testing may yield comparable, if not improved, reductions in cervical cancer mortality compared with clinic-based HPV screening programs. These results will, of course, be contingent on the ability of such programs to provide appropriate follow-up and treatment of screen-positive women.

At present, the cost of the HPV DNA test is the primary factor prohibiting broader application in cervical cancer screening programs, using either clinician- or self-collected samples. Recently, a new low-cost HPV DNA test, careHPV (Qiagen) showed comparable performance to the hc2 test used in our study in both self- and clinician-collected samples (11). Broader availability of this or other validated and inexpensive HPV tests may make HPV-based screening programs increasingly more feasible. In our population that has a 10% HR-HPV prevalence, 90% of women would provide a simple self-collected sample with no further clinical follow-up. Available resources could be then appropriately targeted to the HPV-positive women at highest risk.

## Disclosure of Potential Conflicts of Interest

P. Gravitt: Roche Molecular Systems, commercial research grant, Roche Molecular Systems, consultant board. The other authors disclosed no potential conflicts of interest.

## Acknowledgments

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