Infectious Disease: *Original Research*

Home Self-Collection by Mail to Test for Human Papillomavirus and Sexually Transmitted Infections

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OBJECTIVE: To evaluate the validity and acceptability of at-home self-collection to test for high-risk human papillomavirus (HPV) and sexually transmitted infections among women overdue for cervical cancer screening by national guidelines.

METHODS: Low-income, infrequently screened women were recruited from the general population in North Carolina to participate in an observational study. Participants provided two self-collected cervicovaginal samples (one at home and one in the clinic) and a clinician-collected cervical sample. Samples were tested for high-risk HPV, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, and *Mycoplasma genitalium*. Cervical samples were also tested by liquid-based cytology.

RESULTS: Overall, 193 women had conclusive high-risk HPV results for all three samples and cytology results. Prevalence of high-risk HPV within self-home samples (12.4%) was not different from that within clinician samples (11.4%; $P=.79$) and from that within self clinic samples (15.5%; $P=.21$). Positivity for high-risk HPV in all sample types increased with increasing grades of cervical abnormality ($P<.001$). Self-home samples detected high-risk HPV in all identified cases of high-grade squamous intraepithelial lesions and of cervical intraepithelial neoplasia 2 or worse. Detection was comparable across sample types for *T vaginalis* (range 10.2–10.8%), *M genitalium* (3.3–5.5%), *C trachomatis* (1.1–2.1%), and *N gonorrhoeae* (0–0.5%). Kappa values between sample types ranged from 0.56 to 0.66 for high-risk HPV, 0.86–0.91 for *T vaginalis*, and 0.65–0.83 for *M genitalium*. Most participants reported no difficulty understanding self-collection instructions (93.6%) and were willing to use self-collection in the future (96.3%).

CONCLUSION: Mail-based, at-home self-collection for high-risk HPV and sexually transmitted infection detection was valid and well accepted among infrequently screened women in our study. These findings support the future use of high-risk HPV self-collection to increase

cervical cancer screening rates among higher risk women in the United States.

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Cervical cancer is preventable with regular screening and treatment.[1] However, an estimated 13,240 women in the United States will develop and 4,170 will die from cervical cancer in 2018.[2] Almost 20% of eligible U.S. women report not having received a Pap test within the previous 3 years,[3] the maximum interval recommended for Pap testing alone.[4]

High-risk human papillomavirus (HPV) is the primary cause of high-grade precancerous lesions and cervical cancer.[5] Testing for high-risk HPV is usually performed on cervical samples collected by a clinician. The development of new collection devices and sensitive molecular diagnostic assays have made it possible to conduct high-risk HPV testing on cervicovaginal samples self-collected by women.[6] Studies in Europe and Canada found that offering at-home high-risk HPV self-collection by mail to women overdue for screening increases screening completion compared with invitation to in-clinic screening.[7,8] Self-collection for high-risk HPV testing with sensitive amplification tests has a similar sensitivity and specificity as clinician collection for high-grade cervical precancerous detection, although most studies have evaluated samples self-collected in clinical settings.[6,9,10]

Few studies have assessed validity of self-collection for high-risk HPV testing conducted by mail.[11,12] Assessing validity of mail-based self-collection for high-risk HPV and sexually transmitted infection (STI) testing among women overdue for screening is key, because a self-collection intervention conducted by mail may be more scalable than in-person distribution of kits with face-to-face instruction, with potential to reach women not in regular clinical care.

MATERIALS AND METHODS

Our primary aim was to examine the clinical performance of high-risk HPV testing on self-collected cervicovaginal samples for cervical intraepithelial neoplasia (CIN) 2 or worse detection in a population of U.S. women at elevated risk of cervical cancer as a result of underscreening. We also examined detection of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, and *Mycoplasma genitalium* in the self-collected compared with clinician-collected samples.

Data presented here are from the second phase of the My Body, My Test observational study. The first phase of the My Body, My Test study found that using samples self-collected at home and returned by mail for high-risk HPV testing was feasible and well accepted among underscreened low-income women in North Carolina.[13,14]

Women were eligible to participate in the My Body, My Test-2 study if they were 30–64 years of age; reported no history of Pap testing in the past 4 years (overdue for screening by national guidelines at the start of the study); had a household income below 250% of the poverty level; were not pregnant; had not had a hysterectomy; and were uninsured, underinsured, or had Medicaid insurance. Eligibility measures were assessed by self-report. Income and insurance criteria were defined to ensure eligibility for free cervical cancer screening services through collaborating safety net clinics and programs.

From February 2012 to October 2014, participants were recruited from the general population in five counties in North Carolina: Alamance, Buncombe, Chatham, Durham, and Orange. Recruitment was conducted by direct outreach by study personnel and collaborators; referral from the United Way 2-1-1 social assistance hotline; word of mouth; and posters and flyers distributed in social service agencies, shelters, churches, supermarkets, and other locations likely to reach low-income women. Women were screened by phone for eligibility by a call center run by the American Sexual Health Association or in person at the time of recruitment.

Participants were asked to provide three types of genital samples: 1) a cervicovaginal sample self-collected by brush at home and returned by mail (self-home sample), 2) a cervicovaginal sample self-collected by brush in a clinic and handed to a nurse (self-clinic sample), and 3) a cervical sample collected by brush by a clinician during a pelvic examination (clinician sample). On determination of a woman's eligibility, study personnel mailed each woman a packet containing a self-collection kit, an informed consent form, and Health Insurance Portability and Accountability Act authorization for the study to access participant medical records related to cervical cancer screening and treatment. At the time of enrollment, all participants were also scheduled for an appointment at a collaborating clinic for collection of the self-clinic and clinician samples, which were collected before self-home results were known. At study completion, participants completed a questionnaire eliciting feedback on their experiences of and attitudes toward self- and clinician-collection. Self-collection was referred to as the "self-test" on the questionnaire for participant comprehension. All

participants were referred to in-clinic screening and were provided an incentive of $35 for returning the self-home sample and attending an appointment for collection of the self-clinic, and for clinician samples, and $10 for completing the questionnaire.

Self-collection of the cervicovaginal samples was performed by using a Viba brush. Participants were instructed to introduce the brush into the vagina as far as it could comfortably go and rotate five times, remove the brush head, and place it into a collection tube containing 4.3 mL of Aptima sample transport media. The sample was then mailed in a prepaid, preaddressed envelope to study staff at the University of North Carolina. Illustrated instructions for completing self-collection instructions were pilot-tested for comprehension by low-literacy populations before use. Instructions were slightly revised during project implementation to emphasize that vials should be closed tightly, which resolved an emergent issue of a few samples leaking in transit. Home self-collected samples were returned an average of 15 days before the clinic appointment.

At the study clinic appointment, participants self-collected a second cervicovaginal sample using the same brush, preservation solution, and instructions used for at-home self-collection. Participants then underwent a standard pelvic examination, during which a clinician collected a cervical sample using an endocervical brush and spatula preserved in PreservCyt media for high-risk HPV and cytology testing. The in-clinic self- and clinician-collected cervical samples were then mailed or hand-delivered to study staff.

On receipt, study staff deidentified the self-collected samples. The self-home and self-clinic samples were shipped at ambient temperature to Hologic laboratories in San Diego, California, for high-risk HPV and STI testing. Two 1-mL aliquots were taken from the clinician-collected sample and each placed into a vial containing 2.9 mL of Aptima sample transport media. One of these vials was sent at ambient temperature to Hologic Laboratories for high-risk HPV and STI testing, and the other vial was stored at the University of North Carolina in case of the need for confirmatory testing by the Microbiology Core Laboratory of the Southeastern Sexually Transmitted Diseases Cooperative Research Center. The remainder of the clinician sample was delivered to the McLendon laboratory at University of North Carolina Hospitals for liquid-based cytology testing on a ThinPrep processor.

Testing for high-risk HPV was performed using the Aptima HPV assay, a molecular amplification assay that detects qualitatively E6/E7 mRNA of 14 high-risk HPV genotypes (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68). Testing procedures were identical for self-collected samples and aliquots from clinician samples. Samples testing positive for the high-risk HPV panel according to manufacturer's instructions[15] were then tested for types 16 and for 18/45 as part of standard of care using the U.S. Food and Drug Administration–approved Aptima 16 18/45 assay. Testing for STIs was performed using the Aptima Combo2 assay for *C trachomatis* and *N gonorrhoeae*, the Aptima *T vaginalis* assay, and the Aptima analyte-specific reagent-based assay for *M genitalium* (all from Hologic, Inc). Testing was performed on the automated Panther system by a trained operator, according to the manufacturer's instructions. Cytology samples were analyzed using the ThinPrep 2000 Processor and classified according to the 2001 Bethesda System. If any cytologic cervical abnormality or high-risk HPV infection was identified by a clinician-collected cervical sample, the clinician referred the participant to follow-up diagnostics and treatment per standard guidelines.[16]

Participants attending in-clinic appointments received the results of their clinician-collected tests from clinic staff per standard protocols. Participants who did not attend an in-clinic appointment received at-home self-collection results from study staff by phone or letter along with information to schedule a clinic appointment with a local clinic offering low-cost cervical cancer screening. The University of North Carolina institutional review board approved the study protocol.

We used the McNemar test to assess differences in detection rates between sample collection methods and in participants' attitudes toward self-collection as compared with Pap testing. Wilson score intervals were calculated for high-risk HPV and STI detection by sample type. Agreement between sample collection methods was measured by pairwise calculation of the κ statistic. A κ value of 0.41–0.60 is considered moderate agreement, 0.61–0.80 good agreement, and 0.81–0.99 excellent agreement.[17] Difference in high-risk HPV prevalence across cytology grades was assessed by Fisher exact test. Sensitivity and specificity of high-risk HPV testing for the detection of high-grade squamous intraepithelial lesions (HSIL) and of CIN 2 or worse were computed for each sample type.

Of the 675 women screened, 42.1% (n=284) were eligible for the study and were sent home self-collection kits by mail (Fig. 1). Of these 284 women, 80.3% (n=228) returned a self-home sample and 70.4% (n=200) also attended a clinic appointment. Of the

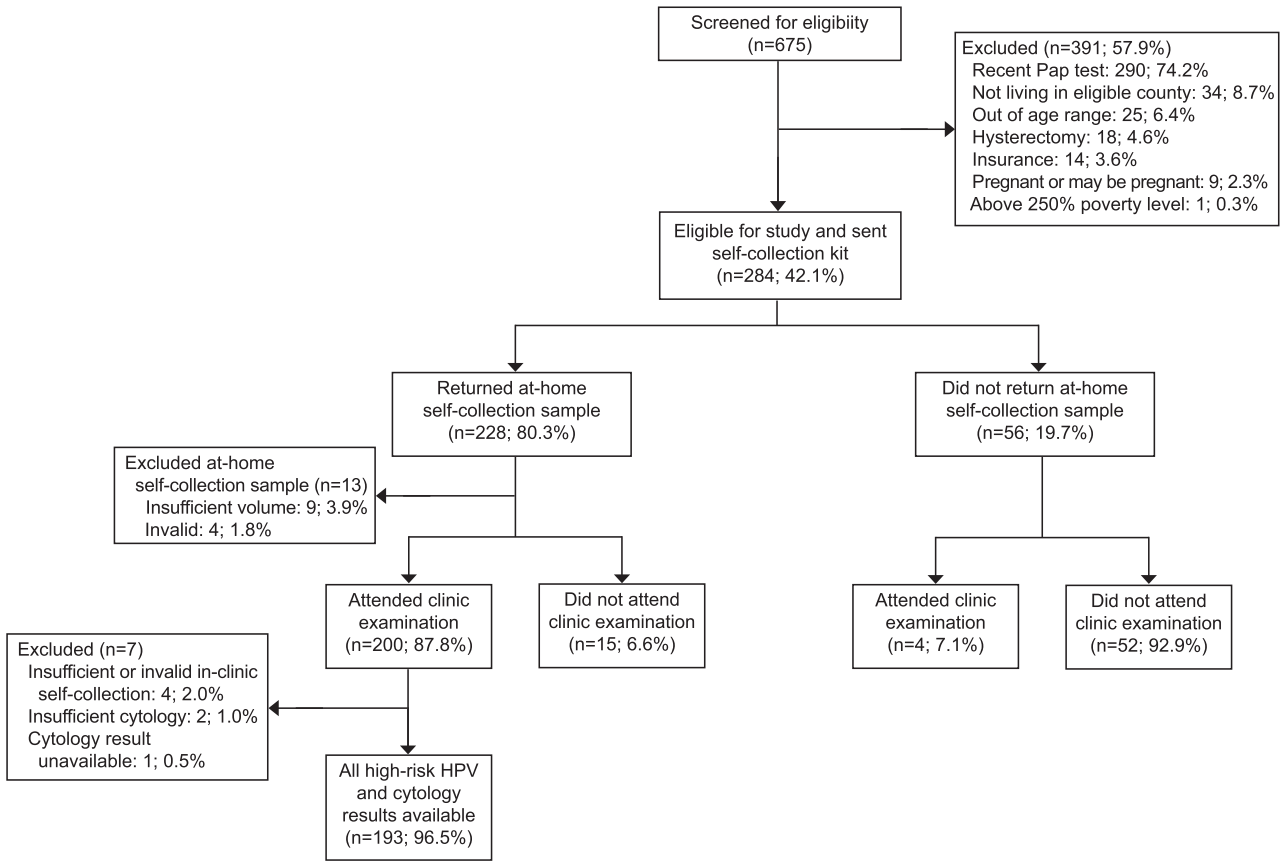

Fig. 1. Study flowchart of My Body, My Test-2 participants. HPV, human papillomavirus.
Des Marais. Home Self-Collection to Detect HPV and STIs. Obstet Gynecol 2018.

228 self-home samples returned, 94.3% (n=215) had valid high-risk HPV results, after excluding 13 samples: nine (3.9%) with insufficient volume and four (1.8%) with inconclusive high-risk HPV results. Four women who tested high-risk HPV positive by self-collection and one woman who tested positive for trichomonas by self-collection were lost to follow-up. Of the 200 self-clinic samples collected, 98.1% (n=196) had valid high-risk HPV results, after excluding four samples: three (1.5%) with insufficient volume and one (0.5%) with an inconclusive high-risk HPV result. All clinician samples resulted in valid high-risk HPV results. Two clinician samples (0.9%) contained insufficient cells for cytology diagnosis, and one cytology result (0.4%) was unavailable as a result of a processing error. Thus, a final analytic sample of 193 women with conclusive high-risk HPV results for the three different sample types and corresponding cytology results were included in data analyses. No demographic differences were found between the included (n=193) and excluded (n=91) women (data not shown).

Women were referred to colposcopy or repeat cytology based on the clinician sample results according to national consensus guidelines.[16] We tracked attendance of recommended follow-up among women with abnormal cytology until follow-up procedures had been completed or, in the case of participant nonattendance, until the patient was lost to follow-up. Of 11 women referred to colposcopy, eight (72.7%) attended. The three colposcopy referrals lost to follow-up were excluded from histology analysis, leaving an analytic sample of 190 for CIN 2 or worse calculations. Six women were referred to treatment for biopsy-confirmed CIN 2 or worse by loop electrosurgical excision procedure or cold-knife conization, of whom five (83.3%) completed treatment and one was lost to follow-up.

RESULTS

The median age of the 193 participants was 45 years (range 30–63 years; Table 1). The median time since previous Pap test was 5 years (range 4–20 years). Approximately half of the participants (45%) were white, 26% were black, 26% were Hispanic, and 4% reported another race. The majority had no post–high school education (61%). Most participants lived on

Table 1. Sociodemographic Characteristics and Attitudes of 193 Low-Income, Underscreened Women*

Characteristics and Attitudes	Value
Age (y)	45 (30–63)
Time since previous Pap test (y)	5 (4–20)
Race	
White	85 (44.5)
Black	49 (25.7)
Hispanic	49 (25.7)
Other†	8 (4.2)
Education	
High school diploma or less	101 (61.2)
Some college or more	64 (38.8)
Income	
100% of FPL or more	47 (26.0)
Below 100% FPL	134 (74.0)
Current health insurance	
No insurance or underinsured	154 (80.2)
Medicaid or Medicare	38 (19.8)
Overall thoughts about the self-test	
Mostly positive	127 (67.6)
Neutral	42 (22.3)
Mostly negative	18 (9.6)
Do not know	1 (0.5)
Willing to use the self-test again	
Yes	182 (96.3)
No	6 (3.2)
Do not know	1 (0.5)
Preference for receiving self-test or Pap results	
Phone	39 (20.5)
Mail	84 (44.2)
No preference	67 (35.3)
Trusts the self-test is safe	
Completely	116 (62.0)
A moderate amount	42 (22.5)
A little	17 (9.1)
Not at all	5 (2.7)
Do not know	7 (3.7)
Hard to understand the self-test instructions	
No	175 (93.6)
Yes	12 (6.4)
Physical discomfort when using the self-test	
None	126 (66.3)
A little	59 (31.1)
A lot	5 (2.6)
Pain when using the self-test	
None	157 (82.2)
A little	32 (16.8)
A lot	2 (1.0)
Bleeding when using the self-test	
None	173 (92.0)
A little	15 (8.0)

FPL, federal poverty level.
Data are median (range) or n (%).
* Includes 193 participants with complete high-risk human papillomavirus and cytology results. Counts may not total 193 as a result of missing values: race=2; education=28, income=10, health insurance=1, overall thoughts about the self-test=5, willing to use the self-test again=4, preference for receiving self-test or Pap results=3, trusts the self-test is safe=6, hard to understand the self-test instructions=6, physical discomfort when using the self-test=3, pain when using the self-test=2, bleeding when using the self-test=5.
† Other includes: Asian (n=1), Native American or Alaska Native (n=1), "mixed" (n=3), and other not specified (n=3).

income at or below 100% of the federal poverty level (74%) and were uninsured or underinsured (80%).

Prevalence of high-risk HPV within self-home samples (12.4%) was not different from that within clinician samples (11.4%; P=.79) and with that within self-clinic samples (15.5%; P=.21) (Table 2). Detection of *T vaginalis* was nearly identical across sample types: 10.2% for self-home, 10.8% for self-clinic, and 10.2% for clinician samples. Detection of *M genitalium* in self-home (5%) and self-clinic (5.5%) samples was not statistically different from clinician samples (3.3%; P=.38 and P=.13, respectively). Detection of *C trachomatis* and *N gonorrhoeae* was less common, with four (2.1%) *C trachomatis* infections and one (0.5%) *N gonorrhoeae* infection detected by any sample type (Table 2).

For high-risk HPV detection, agreement was good between self-home and self-clinic (κ=0.66) and between self-home and clinician samples (κ=0.66); agreement was moderate between self-clinic and clinician samples (κ=0.56) (Table 3). For *T vaginalis* detection, agreement between all sample types was excellent (range of κ=0.86–0.91). For *M genitalium* detection, agreement was excellent between self-home and self-clinic samples (κ=0.83) and was good between self-home and clinician samples (κ=0.65) and between self-clinic and clinician samples (κ=0.74). *C trachomatis* and *N gonorrhoeae* prevalence was too low to assess agreement.

Overall prevalence of atypical squamous cells of undetermined significance or worse cytology in the study population was 7.8% (n=15/193 participants), and that of HSIL was 1.6% (n=3/193) (Table 4). Histologically confirmed CIN 2 or worse was detected in six women referred to colposcopy based on abnormal cytology, representing an overall CIN 2 or worse prevalence of 3.2% in our population.

Positivity for high-risk HPV in all sample types increased with increasing grades of cervical abnormality (P<.001). Among the 165 women with normal cytology and high-risk HPV-negative clinician-collected samples, 4.8% (n=8/165) of the self-home and 8.5% (n=14/165) of the self-clinic samples were high-risk HPV-positive. Six of 13 women with normal cytology and high-risk HPV-positive clinician results had high-risk HPV-negative self-home samples. Among the 24 self-home high-risk HPV-positive samples, prevalence of abnormal cytology was 37.5% (n=9/24) and of HSIL was 12.5% (n=3/24) compared with 3.6% (n=6/169) and 0%, respectively, among self-home high-risk HPV-negative samples. Prevalence of CIN 2 or worse was 0% among the 168 self-home high-risk HPV-negative samples and

Table 2. Prevalence of High-Risk Human Papillomavirus and Other Sexually Transmitted Infections Stratified by Sample Type

		Home Self-Collection		Clinic Self-Collection		Clinician Collection	
Sample Type	Overall*	Positive	Percent (95% CI)	Positive	Percent (95% CI)	Positive	Percent (95% CI)
High-risk HPV	193	24	12.4 (8.1–17.9)	30	15.5 (10.9–21.2)	22	11.4 (7.3–16.5)
CT	189	2	1.1 (0.1–3.8)	4	2.1 (0.6–5.3)	3	1.6 (0.3–4.6)
NG	189	0	0.0 (0.0–1.9)	1	0.5 (0.0–2.9)	0	0.0 (0.0–1.9)
TV	186	19	10.2 (6.3–15.5)	20	10.8 (6.7–16.1)	19	10.2 (6.3–15.5)
MG	181	9	5.0 (2.3–9.2)	10	5.5 (2.7–9.9)	6	3.3 (1.2–7.1)

HPV, human papillomavirus; CT, *Chlamydia trachomatis*; NG, *Neisseria gonorrhoeae*; TV, *Trichomonas vaginalis*; MG, *Mycoplasma genitalium*.
Data are unless otherwise specified.
* Overall number defined for each infection by participants with conclusive results for all sample types. Missing data included n=4 each for CT and NG, n=7 for TV, and n=12 for MG.

27.3% (n=6/22) among self-home high-risk HPV-positive samples with histologic status.

All identified cases of HSIL and CIN 2 or worse tested high-risk HPV-positive by self-home samples (Table 4). Self-home sampling sensitivity was 100% for HSIL and 100% for CIN 2 or worse, and specificity was 88.9% (95% CI 83.6–93%) for HSIL and 91.1% (95% CI 86–94.8%) for CIN 2 or worse. Self-clinic sensitivity was 100% for HSIL and 83.3% (95% CI 35.9–99.6%) for CIN 2 or worse, and specificity was 85.8% (95% CI 80–90.4%) for HSIL and 87.2% (95% CI 81.5–91.7%) for CIN 2 or worse. Clinician sample sensitivity was 100% for HSIL and 100% for CIN 2 or worse, and specificity was 90% (95% CI 84.8–93.9%) for HSIL and 92.2% (95% CI 87.3–95.7%) for CIN 2 or worse.

The prevalence of high-risk HPV type 16 was 2.6% (n=5) in self-home, 2.1% (n=4) in self-clinic, and 2.1% (n=4) in clinician samples, respectively, and the prevalence of high-risk HPV types 18/45 was 1% (n=2), 0.5% (n=1), and 1.6% (n=3), respectively. High-risk HPV type 16 was not detected in any HSIL case by any sample type and was detected in one (16.7%) case of CIN 2 or worse by all sample types. High-risk HPV types 18/45 were detected in one (33.3%) case of HSIL by all sample types, in two (33.3%) cases of CIN 2 or worse by self-home and clinician samples, and in one (16.7%) case by a self-clinic sample.

Nearly all participants reported being willing to do the self-collection again (96.3%) and reported that it was not hard to understand the self-collection instructions (93.6%) (Table 1). The majority had mostly positive (67.6%) or neutral (22.3%) "overall thoughts" about the self-collection. Most participants reported no or little physical discomfort (97.4%) or

Table 3. Kappa Agreement of Infection Detection Between Sample Types

			Result (Sample 1/Sample 2)					
Sample Type	Sample 1	Sample 2	Positive/ Positive	Positive/ Negative	Negative/ Positive	Negative/ Negative	κ	95% CI
High-risk HPV (n=193)	Self-home*	Self-clinic†	19	5	11	158	0.66	0.49–0.80
	Self-home	Clinician‡	16	8	6	163	0.66	0.46–0.80
	Self-clinic	Clinician	16	14	6	157	0.56	0.36–0.73
TV (n=186)	Self-home	Self-clinic	17	2	3	164	0.86	0.71–0.96
	Self-home	Clinician	17	2	2	165	0.88	0.74–0.98
	Self-clinic	Clinician	18	2	1	165	0.91	0.80–1.00
MG (n=181)	Self-home	Self-clinic	8	1	2	170	0.83	0.59–1.00
	Self-home	Clinician	5	4	1	171	0.65	0.27–0.92
	Self-clinic	Clinician	6	4	0	171	0.74	0.44–0.94

HPV, human papillomavirus; TV, *Trichomonas vaginalis*; MG, *Mycoplasma genitalium*.
Data are unless otherwise specified.
Analyses for each infection among women with available results for all three sample types.
* Self-home=cervicovaginal sample self-collected at home.
† Self-clinic=cervicovaginal sample self-collected in clinic.
‡ Clinician=cervical sample collected by clinician.

Table 4. High-Risk Human Papillomavirus Prevalence Stratified by Cytology and Histology Results

		Home-Based Self-Collection		Clinic Self-Collection		Clinician Collection	
	Total	High-Risk HPV (%)	95% CI	High-Risk HPV (%)	95% CI	High-Risk HPV (%)	95% CI
Cytology (n=193)*							
Normal	178	8.4	5.2–13.4	12.4	8.3–18.0	7.3	4.3–12.1
ASC-US	6	33.3	9.7–70.0	16.7	3.0–56.4	33.3	9.7–70.0
LSIL	3	66.7	20.8–93.9	66.7	20.8–93.9	66.7	20.8–93.9
ASC-H	3	66.7	20.8–93.9	66.7	20.8–93.9	66.7	20.8–93.9
HSIL or worse	3	100	43.9–100	100	43.9–100	100	43.9–100
Histology (n=190)†							
Normal‡	184	8.7	5.4–13.7	12.5	8.5–18.1	7.6	4.6–12.4
CIN 2 or worse§	6	100	61.0–100	83.3	43.7–97.0	100	61.0–100

HPV, human papillomavirus; ASC-US, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion; ASC-H, atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion; HSIL or worse, high-grade squamous intraepithelial lesion or worse; CIN, cervical intraepithelial neoplasia.

Data are unless otherwise specified.

* Analyses limited to participants with conclusive cytology and high-risk HPV results on all three sample types.

† Excludes 1 ASC-US high-risk HPV-positive, 1 ASC-H, and 1 LSIL referred to colposcopy but lost to follow-up. No CIN 1 cases were detected.

‡ Includes women with normal cytology for whom colposcopy was not recommended and thus histology not conducted.

§ Histology results: three cases of CIN 2–3, two cases of CIN 3, one case of CIN 3–carcinoma in situ.

pain (99%) during self-collection; however, two (1%) reported "a lot" of pain. Five participants reported that they "hurt or injured" themselves during self-collection, of whom two provided a response when asked what had happened: "I had some bleeding," and "both the Pap and the self-test were uncomfortable." A small proportion of participants reported "a lot of pain" from the Pap test (n=5 [2.9%]) or from the self-collection (n=2 [1%]) (P=.37). Most participants were willing to do the Pap test (97.9%) and the self-collection (96.3%) again (P=.72). Participants reported similar levels of overall positive thoughts about the Pap test (60.7%) and the self-collection (67.6%; P=.15). Five women (2.7%) reported lack of trust in the safety of self-collection. More participants expressed preference for receiving their self-collection results by mail (n=84 [44.2%]) than by phone (n=39 [20.5%]) (P<.001), and 67 (35.3%) expressed no preference.

DISCUSSION

High-risk HPV testing on samples self-collected at home and returned by mail detected high-risk HPV infection in all histologically confirmed CIN 2 or worse cases among approximately 200 infrequently screened women. The study population had a relatively high CIN 2 or worse prevalence (3.2%). At-home self-collection was comparable with clinician-based collection for high-risk HPV, *T vaginalis*, and *M genitalium* detection. Participants responded positively to conducting self-collection at home using simple illustrated instructions and reported high willingness to do self-collection again.

These results provide evidence that high-risk HPV RNA testing on samples self-collected by brush at home, placed in preservation solution, and returned by mail may be as accurate as testing on clinician-collected samples for high-grade lesion detection. Self-collected samples returned by mail and clinician-collected samples showed comparable sensitivity for CIN 3 or worse detection among Swedish patients referred for cervical precancer treatment[11] and identical sensitivity for CIN 2 or worse detection in a Chinese population.[12] Other studies have found high concordance of high-risk HPV detection in mailed self-collected and clinician-collected samples, although study designs did not generally allow for assessment of sensitivity and specificity given that only self-collection high-risk HPV-positive women were referred to in-clinic screening.[18,19]

Home-based self-collection to test for STIs (eg, *C trachomatis* and *N gonorrhoeae*) has been found highly feasible and well accepted with comparable sensitivity and specificity to clinician-collected samples[20–22] and could be a good option for those unable or unwilling to attend in-clinic screening. We found comparable *T vaginalis* detection rates between self- and clinician-collected samples, consistent with findings in other populations.[23–25] *M genitalium* infection was detected more often in self-collected cervicovaginal samples than clinician-collected cervical samples, although this difference was relatively imprecise, consistent with

findings from our recent study conducted in Kenya.[26] Higher *M genitalium* detection in self-collected samples may be attributable to differences in the type and volume of media used for sample preservation or the relatively low *M genitalium* load in cervical cells of infected women.[27] Further research is needed to determine whether sample type affects sensitivity for *M genitalium* infection.

An important study strength is that all self-collection results were paired with standard-of-care high-risk HPV and cytology cotesting. Our focus on validation of self-collection among infrequently screened women is novel for U.S.-based studies. Estimated CIN 2 or worse prevalence of 3.2% among our participants, compared with a prevalence of much less than 1% in the general U.S. screening population,[28] indicates that we successfully identified a population of women at elevated risk for high-grade lesions and cervical cancer. All identified CIN 2 or worse cases were detected by high-risk HPV testing on home self-collected samples, indicating the safety of a home-based high-risk HPV self-collection approach with referral of self-collection high-risk HPV-positive women to in-clinic screening.

This study could have been strengthened by assessing self-collected sample adequacy (ie β-globin testing), although very high adequacy has been previously found in mailed samples self-collected by the Viba brush with liquid preservation solution (97.7–99.7%).[18,29] A larger sample with more cases of CIN 2 or worse would provide more robust assessment of sensitivity and specificity estimates and detection of smaller differences between sample types. Self-home and clinician-collected samples showed good agreement ($\kappa = 0.66$) among all women tested and complete agreement in CIN 2 or worse cases, although power was limited for definitive assessment. Our population-based recruitment approach, essential to identifying medically underserved women who might fall outside regular care, made confirmation of eligibility through medical records review infeasible. Because participants self-selected into the study, our sample may not be representative of the overall U.S. population of infrequently screened women. Financial incentives for screening completion and lack of a comparator group prevented assessment of behavioral outcomes such as effect on screening uptake or follow-up to further care.

Almost all women in our study were willing to perform self-collection again and found the instructions not difficult to understand. These findings add to evidence of high acceptability of mailed self-collection among infrequently screened women[30] including diverse groups of U.S. women.[30–33] Broad acceptability is critical if this practice is to be implemented in national screening programs as has been done in the Netherlands and Denmark.[34,35]

In conclusion, we found at-home self-collection for high-risk HPV and STI detection to be valid and well accepted among this population of infrequently screened women in North Carolina. Although findings are promising for the future use of self-collection in U.S. screening programs to improve access and coverage of cervical cancer screening in infrequently screened women, future implementation research is needed on program efficacy and cost-effectiveness, including a comprehensive assessment of continuity from screening to treatment.

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