



HHS Public Access

Author manuscript

Sex Transm Dis. Author manuscript; available in PMC 2018 March 12.

Published in final edited form as:

Sex Transm Dis. 2018 January ; 45(1): 42–48. doi:10.1097/OLQ.0000000000000681.

Mailed Human Papillomavirus Self-Collection With Papanicolaou Test Referral for Infrequently Screened Women in the United States

Jennifer S. Smith, PhD, MPH^{*,†}, Andrea C. Des Marais, MPH^{*}, Allison M. Deal, MS[†], Alice R. Richman, PhD, MPH[‡], Carolina Perez-Heydrich, PhD, MPH[§], Belinda Yen-Lieberman, MD[¶], Lynn Barclay, BA^{||}, Jerome Belinson, MD^{**}, Allen Rinas, MS CT (SCT), CM (IAC)^{††}, and Noel T. Brewer, PhD^{*,†}

^{*}Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC

[†]Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC

[‡]College of Health and Human Performance, East Carolina University, Greenville, NC

[§]Department of Biological Science, Meredith College, Raleigh, NC

[¶]Department of Laboratory Medicine, Cleveland Clinic, Cleveland, OH

^{||}American Sexual Health Association, Research Triangle Park, NC

^{**}The Women's Health Institute, Cleveland Clinic, Cleveland, OH

^{††}Department of Allied Health Sciences, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC

Abstract

Background—Testing for high-risk human papillomavirus (HPV) infection using mailed, self-collected samples is a promising approach to increase screening in women who do not attend clinic screening at recommended intervals.

Methods—To assess this intervention among high-risk women in the United States, 429 women without a Papanicolaou (Pap) test in 4 or more years (overdue by US guidelines) were recruited from the general population. Participants aged 30 to 65 years were mailed a kit to self-collect a cervicovaginal sample at home, return the sample by mail, and receive HPV results by telephone, with referral to follow-up cytological Pap testing at a local clinic. Cervicovaginal self-samples were collected with a Viba brush, stored in Scope mouthwash, and tested by Hybrid Capture 2. Data were collected in 2010 to 2011 and analyzed in 2017.

Results—Two-thirds (64%) of participants returned a self-collected sample, of whom 15% tested HPV DNA positive. Human papillomavirus self-test–positive women reported higher rates of

Correspondence: Jennifer S. Smith, PhD, MPH, Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina Chapel Hill, 2103 McGavran-Greenberg CB7435, NC 27599. jennifers@unc.edu.

Conflict of Interest and Sources of Funding: Dr Jennifer S. Smith has received research grants and consultancies from Hologic, Becton Dickinson Corporation, and Trovogene over the past 5 years. Dr Jerome Belinson has served as a speaker and received research funding from Hologic, Becton Dickinson, and QIAGEN. Rovers Medical Devices donated the Viba brushes used for self-collection and QIAGEN donated the Hybrid Capture 2 kits for HPV testing.

follow-up Pap tests (82%) than did those with self-test negative results (51%). No demographic differences were found in self-test return rate or HPV positivity. High acceptability was reported in participant surveys: most women (81%) had “mostly positive” overall thoughts about the self-test, and most reported being comfortable receiving the kit in the mail (99%), returning their self-collected sample by mail (82%), and receiving their test results by telephone (97%).

Conclusions—Conducting HPV self-testing through population-based recruitment, mailed kit delivery and return by mail, and results delivery by telephone has the potential to reach a broad segment of US underscreened women.

In 2017, an estimated 12,820 women in the United States will be diagnosed as having invasive cervical cancer (ICC), and 4210 will die of this preventable disease.¹ More than half of US ICC cases occur among women infrequently or never screened (“underscreened”),² and 15% of women report not completing Papanicolaou (Pap) testing in the preceding 3 years—overdue by national recommendations for Pap alone.³ Barriers to screening include lack of health insurance, poor access to medical services,⁴ and embarrassment or discomfort with pelvic examination.⁵

High-risk (oncogenic) human papillomavirus (HPV) infection is the primary cause of ICC and high-grade precancerous lesions (cervical intraepithelial neoplasia lesions 2 or greater [CIN2+]).⁶ High-risk HPV testing improves sensitivity for the detection of CIN2+, which generally requires treatment.⁷ The US Preventive Services Task Force (USPSTF) recommends HPV testing in conjunction with Pap (co-testing) at 5-year intervals for women 30 years and older.⁸ Primary screening by HPV testing for women 25 years and older was approved by US Food and Drug Administration in 2014⁹ and will be considered by the USPSTF for inclusion in clinical recommendations. However, given that physician-collected HPV and Pap testing remain clinic based, new approaches are needed to address the larger problem of inadequate screening among women facing barriers to clinical services.

Self-collection of cervicovaginal samples for HPV testing, or “self-testing,” may be a viable option for increasing screening uptake in populations with limited access to health care.^{10,11} Studies in both high- and low-resource settings have found HPV self-testing to be well accepted and accurate as an initial screening test, with follow-up of positive self-test results.^{11–14} Large international population-based studies and meta-analyses have found self-testing to be as sensitive as physician-based HPV testing and more sensitive than cytology for CIN2+ detection.^{11,14–16}

In countries with national screening programs, the most appropriate target population for HPV self-testing is women who do not complete in-clinic screening at recommended intervals. Use of self-tests outside clinics (e.g., through mail) could reach patients who do not regularly access preventative clinical care. Studies conducted in Europe and Canada have shown that mailing HPV self-test kits to underscreened women (identified through national screening registries or medical records) increases screening completion compared with in-clinic screening invitations.^{12,17–20} National screening programs in the Netherlands and Denmark will be offering mailed self-test kits to women who do not respond to reminders to complete in-clinic cervical cancer screening.^{21,22}

Given that there is no national screening registry in the United States, identification of underscreened women in the general population is a considerable challenge. US studies have found that women from diverse populations respond positively to HPV self-testing, although most studies delivered self-collection kits and provided instructions in-person to women at clinics,²³ community centers,^{24,25} or their homes for immediate return to health workers.^{26,27} To our knowledge, only 2 US studies have used mailed kits for at-home HPV self-testing.^{28,29} Participants in these studies were not overdue for cervical cancer screening, and most were younger than age 30 years, the current minimum USPSTF-recommended age for HPV testing.

Our study examined feasibility and acceptability of mailing as a method for the distribution and return of HPV self-testing kits among low-income, underscreened women. We assess the feasibility and acceptability among women at high risk for cervical cancer of self-collecting cervicovaginal samples at home, returning samples by mail for HPV testing, and receiving HPV results by telephone. If feasible and acceptable, HPV testing by mail could be a powerful tool to engage women at elevated risk for developing cervical cancer.

MATERIALS AND METHODS

Sample

We recruited low-income, underscreened women in 10 North Carolina counties with relatively high rates of cervical cancer (Wake, Durham, Harnett, Guilford, Wayne, Cumberland, Robeson, Richmond, Hoke, and Scotland counties) between January 2010 and September 2011. Recruitment methods included distribution of flyers and posters, referral of callers from United Way's 2-1-1 social assistance hotline, and direct outreach in locations visited by low-income women. Potential participants were screened for eligibility by calling a toll-free telephone hotline, staffed 24 hours by trained American Sexual Health Association (ASHA) personnel. Women were study eligible if they had not received a Pap test in the previous 4 years, lived in North Carolina, were not pregnant, were aged 30 to 65 years, had not undergone a hysterectomy, and met one of the following income criteria: children qualifying for the federal school lunch program, Medicaid or Medicare Part B insurance, or uninsured and living at or below 200% of the federal poverty level (determined by household income and size). Our study population was largely unvaccinated against HPV: during our data collection period, only the youngest participants would have been 26 (the upper age limit for catch up) when HPV vaccination was recommended to female adolescents by the Advisory Committee on Immunization Practices in 2007.

Design

Eligible women were mailed a self-collection kit containing a brush for collecting a cervicovaginal sample, a vial of preservation media, simple 2-page illustrated instructions for sample collection, informed consent and Health Insurance Portability and Accountability Act authorization forms, and a prepaid mailer to return their self-collected sample for HPV testing. Participants were told at enrollment that the study was based at the University of North Carolina, although study materials were branded as "My Body, My Test." The package contained contact information of local clinics providing low-cost or free Pap tests.

Women who did not promptly return a self-test received a reminder letter at 2 weeks, a reminder telephone call at 3 weeks, and a second reminder letter at 1 month. When HPV laboratory results were available, ASHA call center agents called participants to provide results. The American Sexual Health Association is a national organization that promotes the sexual health of individuals, families, and communities.³⁰ Call center agents were extensively trained in HPV education, counseling on results, and research best practices. At results delivery, agents encouraged participants to obtain a clinic-based Pap test and provided information on where to obtain a free or low-cost Pap in their county. On this call, participants also completed an “acceptability” questionnaire, described later. The American Sexual Health Association called participants an average of 45 days later to complete a “follow-up” questionnaire. Women could report Pap test attendance during either questionnaire, or by returning a postcard with location and date of their appointment. Human papillomavirus self-test–positive women who did not report a Pap test received additional calls to improve compliance. Study participants were informed at enrollment that they would receive gift cards for participation: \$30 for returning the self-test and completing the acceptability questionnaire, \$10 for reporting completion of Pap testing (by postcard or verbally), and \$5 for completing the follow-up questionnaire. Additional effort was made to contact participants who did not return a sample (“nonreturners”) to collect basic acceptability and demographic data approximately 18 months after participants had been sent self-test kits. University of North Carolina Institutional Review Board reviewed and approved the study protocol.

Measures

Sample Self-collection and Testing—Participants collected cervicovaginal samples using a Viba brush (Rovers Medical Devices, BV, Oss, the Netherlands) by inserting the brush to the top of the vaginal canal, rotating 5 times, removing the brush, then removing the brush head and placing it in a 10-mL vial of Scope mouthwash, an acceptable nontoxic preservation medium for HPV DNA testing.³¹ Self-collected samples were returned to study offices at the University of North Carolina in prepaid, preaddressed mailers. Samples were deidentified and shipped in weekly batches to the Cleveland Clinic laboratory (Cleveland, OH) for testing for high-risk HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68 using the Hybrid Capture 2 HPV test (QIAGEN Corp, Gaithersburg, MD).

Questionnaires—The acceptability questionnaire was completed immediately before HPV results were delivered, and assessed HPV knowledge, medical and reproductive history, sociodemographics, and attitudes toward completing HPV self-testing (including clarity of instructions, use of the brush, concerns about the test, returning the sample by mail, and receipt of results by telephone). The follow-up questionnaire assessed completion of in-clinic “follow-up” Pap test and attitudes toward Pap testing, which are being published separately. The nonreturner questionnaire assessed demographics; reasons for not returning the self-test; overall thoughts, likes, and dislikes regarding the self-test; and “follow-up” Pap test completion since study enrollment. Participants could report completion of a follow-up Pap test on any of the questionnaires.

Statistical Analyses

We assessed completion of self-test and follow-up in-clinic Pap testing and predictors of self-test sample return and HPV positivity. Predictors of self-test return (Table 1) and differences in study completion and HPV status by age (Table 2) were assessed by Fisher exact tests that allow for small sample sizes. Unadjusted *P* values are reported. The final population for assessment of HPV positivity included women who returned a self-collected sample (“returners”) and completed informed consent (275; 64% of eligible), and excluded participants with inconclusive HPV self-test results (*n* = 4) or samples that leaked in transit (*n* = 6). Descriptive analyses were performed for measures of acceptability (Table 3) and study completion (Fig. 1). Acceptability measures were assessed in those who returned a self-test and completed the acceptability questionnaire (227; 83% of returners). Logistic regression was used to estimate age-adjusted odds ratios for associations with self-test HPV positivity in 216 participants who received a conclusive (positive or negative) HPV self-test result and completed the acceptability questionnaire. Multivariable analysis adjusting for age, insurance status, self-reported smoking, and HIV status was conducted to assess predictors of HPV positivity among 216 women with conclusive self-test HPV results who completed the acceptability questionnaire (Table 4). Data analyses were completed in 2017 using SAS statistical software version 9.4 (Cary, NC).

RESULTS

Participants

Of 892 women screened for eligibility, 429 (48%) were study eligible and mailed a self-collection kit (Fig. 1). The median age of these 429 women was 42 years (range, 30–65 years; missing 2), and one-fifth lived in rural areas (21%; Table 1). Of 255 women who completed the acceptability questionnaire or nonresponder questionnaire, most had less than a high school education (61%), were unmarried (73%), and were uninsured (67%; data not shown). More than half of participants who returned self-collected samples were black (55%). All participants reported no Pap test in the 4 years before study enrollment. Median time since last Pap was 5 years (range, 4 years to never). A total of 4 women (2%; data not shown) reported that they had never received a Pap test.

Self-Test, Questionnaire, and Pap Test Completion

Of 429 women who were sent a self-test kit, almost two-thirds (64%) returned a self-collected sample, and 83% of those women completed the acceptability questionnaire (Fig. 1). Of 154 nonreturners, 3 completed the acceptability questionnaire (2%) and 27 (18%) completed the nonreturner questionnaire. Among women who returned a sample, the acceptability questionnaire was completed by 79% of women 30 to 45 years of age and 88% of women 45 years and older. Among these women, the follow-up questionnaire was completed by 58% of women 30 to 45 years of age and 71% of women 45 years and older. There were no differences in demographic characteristics or in overall thoughts about self-testing between women who did and did not return a sample (Table 1).

The proportion of women reporting a follow-up Pap test was similar for those who returned a sample and completed the follow-up questionnaire and those who did not return a sample

and completed the nonreturner questionnaire (55% and 48%, respectively; Fig. 1). Older women seemed to report Pap test more frequently than did younger women, although differences were not statistically significant (62% for 45–64 years vs. 49% for 30–44 years, $P = 0.13$; Table 2). Women who tested HPV positive on their self-test reported a higher rate of follow-up in-clinic Pap test completion compared with HPV-negative women (82% vs. 51%, $P < 0.01$). This difference was statistically significant among women 45 years and older (91% vs. 58%, $P < 0.05$), but not in younger women (73% vs. 44%, $P < 0.11$).

Participants' Attitudes and Opinions Regarding the Self-test

Acceptability of mailed, at-home HPV self-testing was very high among the 227 participants who returned a self-test and completed the acceptability questionnaire (Table 2). Most participants (81%) reported mostly positive thoughts about the HPV self-test. Almost all participants reported being comfortable receiving the kit in the mail (99%) and receiving test results by telephone (97%). A large majority (82%) were comfortable returning their sample by mail. Most women (92%) reported willingness to pay for the kit, with 48% willing to pay \$25 or more.

Among 27 participants completing the nonreturner questionnaire (of 154 who did not return a sample), the most commonly reported reasons for nonreturn were misplacing the kit (6; 22%), being too busy (4; 15%), going to the doctor instead (2; 7%), and leaving town for an extended period (2; 7%) (data not shown). Reasons reported by only 1 woman each were house fire, pregnancy, “family problems,” “just forgot,” and concern that the study “would do something” to her. Seven participants (26%) did not remember why or could not provide a specific reason.

HPV Self-Test Results

Of 262 women who returned the self-collected sample and had conclusive results, HPV positivity was 14.9%. Only 10 samples (3.6% of returned) were invalid: 6 leaked in transit and 4 had inconclusive laboratory results. There were no differences in HPV positivity when stratified by age (30–44 vs. 45–65 years; Table 3). Bivariate analysis of predictors of HPV positivity found higher positivity among women with Medicaid, women HIV positive by self-report, and smokers (data not shown). No association was found with age, urbanicity, race, income, educational level, marital status, time since last Pap test, Internet use, religious affiliation, age at first intercourse, parity, literacy, or current use of contraception. No factors for high-risk HPV positivity remained statistically significant in the multivariable analysis adjusting for age, insurance status, self-reported smoking, and HIV status as estimates were relatively imprecise (Table 4).

DISCUSSION

This study of 429 women in North Carolina is, to our knowledge, the first US study to conduct HPV testing using mailed home-based self-collection kits for cervical cancer screening among infrequently screened women. High acceptability indicates that self-collection could be a viable approach to increase screening among this hard-to-reach, high-risk population. No sociodemographic differences were found in self-test return, indicating

that women at particularly high risk for developing ICC, such as black and rural women, may equally benefit from a self-collection intervention. Most participants with positive HPV self-test results completed a follow-up Pap test, an important finding given that screening by HPV self-testing can only prevent ICC if HPV-positive women attend a health care facility for follow-up diagnostics and treatment, if indicated.

Findings of high acceptability of mailed self-collection are consistent with international studies that found that most women were willing to receive the self-test by mail, would complete self-testing again, found self-collection easy, and would recommend the self-test to a friend.^{13,20,32} Our self-test return rate by mail of 64% in this US population was in the middle of the range of rates observed in international studies, which have varied widely by study design and setting (from 8% to 93%).^{11,20,33–37} Our high rates of reported Pap test completion among HPV self-test–positive participants (82%) are consistent with other mailed self-test studies that achieved 41% to 91% completion of follow-up screening among HPV-positive women.^{17,18,32,34–40} Additional research is needed to track completion of follow-up diagnostics and treatment among HPV self-test–positive women to comprehensively assess impact on ICC prevention.

Our study design aimed to approximate a scalable model for increasing coverage among infrequently screened women by incorporating HPV self-testing into a screening program. Several well-conducted US studies have implemented HPV self-testing through community health workers and other direct-interaction approaches.^{23–27,41} Direct one-to-one engagement has many strengths, but requires considerable personnel time and effort. Our approach has the potential to require fewer resources per woman screened. We recruited most participants through population-based advertising, with a relatively lower personnel burden than that in direct recruitment and potential to reach women who might be missed by medical records review.

Furthermore, we delivered kits with illustrated instructions by mail, with personal assistance available as needed by telephone, rather than providing face-to-face kit delivery, coaching, and training. Participants also requested kits and received HPV results by telephone with highly trained agents at the ASHA call center, leveraging an existing resource while still providing high-quality test result delivery and counseling. The nonresearch components of the intervention requiring staff time were recruitment, preparation and mailing of kits and letters, laboratory testing, and delivering results, for which multiple call attempts were sometimes required. Exact time spent on these components is not available for the present study, but is being collected for a current trial of self-collection. In real-world implementation, reminder letters and calls could be automated, further reducing personnel time burden. It is also notable that HPV testing requires considerably less laboratory personnel time and training than cytology. Identification and recruitment of participants, on the other hand, was labor intensive, although it is impossible to know whether aversion to participation in a research study was a barrier. In future implementation, distribution of kits could be done via general advertising, placement in pharmacies, or through medical records review.

Limitations

In terms of study limitations, self-selection into the study could have resulted in a sample of women with higher-than-average positive attitudes toward at-home self-testing and relatively higher motivation to complete cervical cancer screening. However, this approach allowed us to engage hundreds of women from the general population who may not have been reached through alternative approaches requiring *a priori* knowledge of screening status. Offering financial incentives for self-test return may have resulted in higher reported completion rates, although it likely improved our ability to get feedback from women toward self-collection or cervical cancer screening more generally. Low response rate among self-test nonreturners limits our ability to assess reasons for nonreturn, although feedback from the 30 nonreturners reached did not reveal any major concerns regarding the self-test process itself. *P* values should be interpreted with caution because of multiple testing and small sample sizes in some comparisons but can be used to begin to understand differences in groups. Relying on self-report also limited our ability to assess Pap test completion in participants lost to follow-up, and providing an incentive for Pap completion may have motivated overreport. Data were collected several years before analysis; however, we are unaware of any developments or events in recent years that are likely to have affected our key measures by influencing attitudes in the general population toward HPV testing or self-testing more broadly.

Our study could have been strengthened by assessing self-test sample sufficiency (i.e., β -globin testing), although prior studies found high β -globin positivity (97.7%–99.7%) in mailed, self-collected samples with the Viba brush.^{36,39} Given that we did not systematically obtain data on cytology or histology clinical end points, we were unable to assess the sensitivity of home-based HPV self-collection for high-grade cervical detection. Study design also did not permit assessment of intervention efficacy at increasing screening uptake. Future research among under-screened women in the United States will focus on validating results of mailed HPV self-testing against clinical HPV and cytology results, and on evaluating whether offering mailed HPV self-testing increases screening completion in this higher-risk underscreened population.

Our findings have several key programmatic implications. Delivery of self-test kit by mail and delivery of HPV results by telephone were well accepted by almost all participants—approaches that are largely scalable. Providing patients with the option to return their samples by dropping them at a pharmacy, clinic, or laboratory location could provide a more acceptable option for the one-fifth of participants who were uncomfortable returning the sample by mail. Some self-collected samples (2.2%) leaked in transit. Revisions to the instructions emphasizing that women firmly tighten the vial greatly reduced leakage in our current research phases. Current research into “dry” self-collection using retractable brush heads or cards also seeks to reduce damage to samples in transit.^{42,43} Finally, most participants reported that they would pay for the self-test kit, indicating that there could be a market for the self-test kit. However, only 48% indicated willingness to pay more than \$25, suggesting that lower pricing options, insurance coverage, and/or subsidies would be necessary to make the kit attainable to low-income, uninsured women. Feasibility of a widespread self-testing intervention is continually improving owing to considerable

advancements in HPV diagnostics resulting in higher sensitivity and specificity for high-grade lesion detection, and relatively lower future costs per test.^{44,45}

CONCLUSIONS

In conclusion, conducting home-based self-collection for HPV testing was feasible and highly acceptable for a sample of high-risk women recruited by advertising and outreach from the general population in the US South. Future studies in a US setting should evaluate the effect of a mailed HPV self-testing compared with standard of care, or to an evidence-based practice for increasing screening in underscreened women. Our findings contribute to growing evidence that HPV self-testing has the potential to be a powerful tool to engage women at the highest risk for developing cervical cancer into preventative screening.

Acknowledgments

The authors sincerely thank Meredith Kamradt, Rachel Larsen, Kristen Ricchetti, Kelly Murphy, Stephanie Zentz, and Sara B. Smith for their work on study logistics, database, and recruitment; and Florence Paillard, Laura Baker, and Brenda Quincy for their assistance in drafting and editing the manuscript. The authors also thank Meindert Zwartz at Rovers Medical Devices for donating the Viba self-collection brushes and QIAGEN for donating kits for Hybrid Capture 2 HPV testing.

Financial Support: This research was supported by Kate B. Reynolds Charitable Trust. Additional support for staff time came from the NCCU-LCCC Partnership in Cancer Research (5 U54 CA156733) and National Institutes of Health, National Cancer Institute R01 CA183891.

References

1. American Cancer Society. [Accessed March 23, 2017] Cancer Statistics Center [Internet]. Available at: <https://cancerstatisticscenter.cancer.org/#/cancer-site/Cervix>
2. Spence AR, Goggin P, Franco EL. Process of care failures in invasive cervical cancer: Systematic review and meta-analysis. *Prev Med.* 2007; 45:93–106. [PubMed: 17651792]
3. Solomon D, Breen N, McNeel T. Cervical cancer screening rates in the United States and the potential impact of implementation of screening guidelines. *CA Cancer J Clin.* 2007; 57:105–111. [PubMed: 17392387]
4. Centers for Disease Control (CDC). Cancer screening—U.S 2010. *MMWR Morb Mortal Wkly Rep.* 2012; 61:41–45. [PubMed: 22278157]
5. Bukowska-Durawa A, Luszczynska A. Cervical cancer screening and psychosocial barriers perceived by patients: A systematic review. *Contemp Oncol (Pozn).* 2014; 18:153–159. [PubMed: 25520573]
6. Smith JS, Lindsay L, Hoots B, et al. Human papillomavirus type distribution in invasive cervical cancer and high-grade cervical lesions: a meta-analysis update. *Int J Cancer.* 2007; 121:621–632. [PubMed: 17405118]
7. Cuzick J, Arbyn M, Sankaranarayanan R, et al. Overview of human papillomavirus-based and other novel options for cervical cancer screening in developed and developing countries. *Vaccine.* 2008; 26(Suppl 10):K29–K41. [PubMed: 18847555]
8. U.S. Preventive Services Task Force (USPSTF). [Accessed August 06, 2016] Cervical cancer: Screening. Updated July 2015. Available at: <http://www.uspreventiveservicestaskforce.org/uspstf/uspstfcerv.htm>
9. U.S. Food and Drug Administration (FDA). [Accessed August 06, 2016] FDA approves first human papillomavirus test for primary cervical cancer screening. Apr 24, 2014 Available at: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm394773.htm>

10. Stewart DE, Gagliardi A, Johnston M, et al. HPV Self-collection Guidelines Panel. Self-collected samples for testing of oncogenic human papillomavirus: A systematic review. *J Obstet Gynaecol Can.* 2007; 29:817–828. [PubMed: 17915065]
11. Snijders PJ, Verhoef VM, Arbyn M, et al. High-risk HPV testing on self-sampled versus clinician-collected specimens: A review on the clinical accuracy and impact on population attendance in cervical cancer screening. *Int J Cancer.* 2013; 132:2223–2236. [PubMed: 22907569]
12. Racey SC, Withrow DR, Gesink D. Self-collected HPV testing improves participation in cervical cancer screening: A systematic review and meta-analysis. *Can J Public Health.* 2013; 104:159–166.
13. Virtanen A, Nieminen P, Niironen M, et al. Self-sampling experiences among non-attendees to cervical screening. *Gynecol Oncol.* 2014; 135:487–494. [PubMed: 25284037]
14. Arbyn M, Verdoodt F, Snijders PJ, et al. Accuracy of human papilloma-virus testing on self-collected versus clinician-collected samples: a meta-analysis. *Lancet Oncol.* 2014; 15:172–183. [PubMed: 24433684]
15. Zhao FH, Lewkowitz AK, Chen F, et al. Pooled analysis of a self-sampling HPV DNA test as a cervical cancer primary screening method. *J Natl Cancer Inst.* 2012; 104:178–188. [PubMed: 22271765]
16. Taylor S, Wang C, Wright TC, et al. A comparison of human papillomavirus testing of clinician-collected and self-collected samples during follow-up after screen-and-treat. *Int J Cancer.* 2011; 129:879–886. [PubMed: 20957631]
17. Sancho-Garnier H, Tamalet C, Halfon P, et al. HPV self-sampling or the Papsmear: A randomized study among cervical screening non-attenders from lower socioeconomic groups in France. *Int J Cancer.* 2013; 133:2681–2687. [PubMed: 23712523]
18. Haguenoer H, Sengchanh S, Gaudy-Graffin C, et al. Vaginal self-sampling is a cost-effective way to increase participation in a cervical cancer screening programme: a randomised trial. *Br J Cancer.* 2014; 111:2187–2196. [PubMed: 25247320]
19. Broberg G, Gyrd-Hansen D, Jonasson JM, et al. Increasing participation in cervical cancer screening: Offering a HPV self-test to long-term non-attendees as part of RACOMIP, a Swedish randomized controlled trial. *Int J Cancer.* 2014; 134:2223–2230. [PubMed: 24127304]
20. Racey CS, Gesink DC, Burchell AN, et al. Randomized intervention of self-collected sampling for human papillomavirus testing in under-screened rural women: Uptake of screening and acceptability. *J Womens Health (Larchmt).* 2016; 25:489–497. [PubMed: 26598955]
21. Arbyn M, Castle PE. Offering self-sampling kits for HPV testing to reach women who do not attend in the regular cervical cancer screening program. *Cancer Epidemiol Biomarkers Prev.* 2015; 24:769–772. [PubMed: 25713024]
22. Tranberg M, Bech BH, Blaakær J, et al. Study protocol of the CHOICE trial: a three-armed, randomized, controlled trial of home-based HPV self-sampling for non-participants in an organized cervical cancer screening program. *BMC Cancer.* 2016; 16:835. [PubMed: 27809810]
23. Murphy J, Mark H, Anderson J, et al. A randomized trial of human papillomavirus self-sampling as an intervention to promote cervical cancer screening among women with HIV. *J Low Genit Tract Dis.* 2016; 20:139–144. [PubMed: 27015260]
24. Sewali B, Okuyemi KS, Askhir A, et al. Cervical cancer screening with clinic-based Pap test versus home HPV test among Somali immigrant women in Minnesota: a pilot randomized controlled trial. *Cancer Med.* 2015; 4:620–631. [PubMed: 25653188]
25. Crosby RA, Hagensee ME, Vanderpool R, et al. Community-based screening for cervical cancer: a feasibility study of rural Appalachian women. *Sex Transm Dis.* 2015; 42:607–611. [PubMed: 26462184]
26. Castle PE, Rausa A, Walls T, et al. Comparative community outreach to increase cervical cancer screening in the Mississippi Delta. *Prev Med.* 2011; 52:452–455. [PubMed: 21497619]
27. Kobetz E, Kish JK, Campos NG, et al. Burden of human papillomavirus among Haitian immigrants in Miami, Florida: Community-based participatory research in action. *J Oncol.* 2012; 2012:728397. [PubMed: 22619675]

28. Nelson EJ, Hughes J, Oakes JM, et al. Human papillomavirus infection in women who submit self-collected vaginal swabs after internet recruitment. *J Community Health*. 2015; 40:379–386. [PubMed: 25257565]
29. Winer RL, Feng Q, Hughes JP, et al. Concordance of self-collected and clinician-collected swab samples for detecting human papillomavirus DNA in women 18 to 32 years of age. *Sex Transm Dis*. 2007; 34:371–377. [PubMed: 17065848]
30. American Sexual Health Association (ASHA). [Accessed January 16, 2017] Who we are [Internet]. Available at: <http://www.ashalsexualhealth.org/who-we-are/>
31. Castle PE, Sadorra M, Garcia FAR, et al. Mouthwash as a low-cost and safe specimen transport medium for human papillomavirus DNA testing of cervicovaginal specimens. *Cancer Epidemiol Biomarkers Prev*. 2007; 16:840–843. [PubMed: 17416781]
32. Giorgi Rossi P, Marsili LM, Camilloni L, et al. Self-Sampling Study Working Group. The effect of self-sampled HPV testing on participation to cervical cancer screening in Italy: a randomised controlled trial (ISRCTN96071600). *Br J Cancer*. 2011; 104:248–254. [PubMed: 21179038]
33. Tamalet C, Le Retraite L, Leandri FX, et al. Vaginal self-sampling is an adequate means of screening HR-HPV types in women not participating in regular cervical cancer screening. *Clin Microbiol Infect*. 2013; 19:E44–E50. [PubMed: 23137168]
34. Darlin L, Borgfeldt C, Forslund O, et al. Comparison of use of vaginal HPV self-sampling and offering flexible appointments as strategies to reach long-term non-attending women in organized cervical screening. *J Clin Virol*. 2013; 58:155–160. [PubMed: 23867008]
35. Cadman L, Wilkes S, Mansour D, et al. A randomized controlled trial in non-responders from Newcastle upon Tyne invited to return a self-sample for HPV testing versus repeat invitation for cervical screening. *J Med Screen*. 2015; 22:28–37. [PubMed: 25403717]
36. Gok M, Heideman DA, van Kemenade FJ, et al. Offering self-sampling for human papillomavirus testing to non-attendees of the cervical screening programme: characteristics of the responders. *Eur J Cancer*. 2012; 48:1799–1808. [PubMed: 22172570]
37. Szarewski A, Cadman L, Mesher D, et al. HPV self-sampling as an alternative strategy in non-attenders for cervical screening—a randomised controlled trial. *Br J Cancer*. 2011; 104:915–920. [PubMed: 21343937]
38. Wikström I, Lindell M, Sanner K, et al. Self-sampling and HPV testing or ordinary Papsmear in women not regularly attending screening: a randomised study. *Br J Cancer*. 2011; 105:337–339. [PubMed: 21730977]
39. Bais AG, van Kemenade FJ, Berkhof J, et al. Human papillomavirus testing on self-sampled cervicovaginal brushes: An effective alternative to protect nonresponders in cervical screening programs. *Int J Cancer*. 2007; 120:1505–1510. [PubMed: 17205514]
40. Virtanen A, Nieminen P, Luostarinen T, et al. Self-sample HPV Tests as an Intervention for Nonattendees of Cervical Cancer Screening in Finland: A Randomized Trial. *Cancer Epidemiol Biomarkers Prev*. 2011; 20:1960–1969. [PubMed: 21752985]
41. Ilangovan K, Kobetz E, Koru-Sengul T, et al. Acceptability and feasibility of human papilloma virus self-sampling for cervical cancer screening. *J Womens Health (Larchmt)*. 2016; 25:944–945. [PubMed: 26890012]
42. Van Baars R, Bosgraaf RP, ter Harmsel BWA, et al. Dry storage and transport of a cervicovaginal self-sample by use of the Evalyn brush, providing reliable human papillomavirus detection combined with comfort for women. *J Clin Microbiol*. 2012; 50:3937–3943. [PubMed: 23015677]
43. Lenselink CH, de Bie RP, van Hamont D, et al. Detection and genotyping of human papillomavirus in self-obtained cervicovaginal samples by using the FTA cartridge: new possibilities for cervical cancer screening. *J Clin Microbiol*. 2009; 47:2564–2570. [PubMed: 19553570]
44. Belinson JL, Du H, Yang B, et al. Improved sensitivity of vaginal self-collection and high-risk human papillomavirus testing. *Int J Cancer*. 2012; 130:1855–1860. [PubMed: 21630255]
45. Dockter J, Schroder A, Hill C, et al. Clinical performance of the APTIMA HPV Assay for the detection of high-risk HPV and high-grade cervical lesions. *J Clin Virol*. 2009; 45:S55–S61.

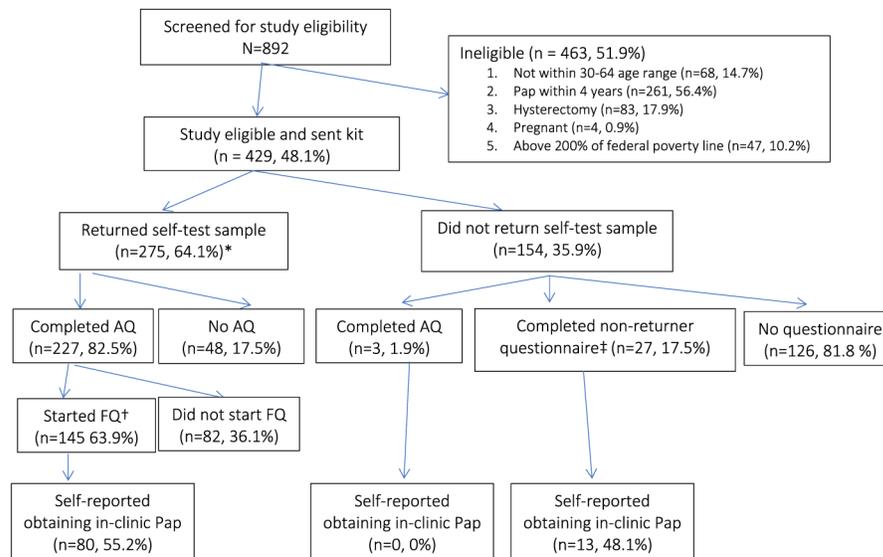


Figure 1. Participant flow diagram. AQ indicates acceptability questionnaire; FQ, follow-up questionnaire. *Six samples leaked in transit; 3 samples could not be run due to incomplete consent forms. †Not all who started FQ completed it. ‡Two non-returned questionnaire respondents also completed AQ.

TABLE 1

Characteristics of Participants Who Did (n = 275) and Did Not (n = 154) Return a Mailed HPV Self-Test

	All Participants, n (%) [*]	Returned Self-test, n (%)	Did Not Return Self-Test, n (%)	P [†]
Age 45 y	174 (40.7)	117 (42.7)	57 (37.3)	0.30
Rural	90 (21.1)	59 (21.5)	31 (20.1)	0.81
Black	160 (55.3)	145 (55.3)	15 (55.6)	1.00
High school education	147 (61.3)	132 (62.0)	15 (55.6)	0.54
Not married	174 (72.8)	153 (72.2)	21 (77.8)	0.65
Thoughts about self-test mostly positive	175 (81.2)	160 (80.8)	15 (83.3)	0.41

* Numerators shown. Denominator varies depending on whether the question was asked at enrollment (denominator for age and rural, n = 429), on a form returned with the self-test (denominator for race, n = 303), or during the acceptability or nonreturner questionnaire (denominator for education, marital status, thoughts about self-test; n = 255). Missing values are as follows: age (n = 2), race (n = 14), education (n = 15), marital status (n = 16), and thoughts on self-test (n = 39).

[†] Difference between women who did and did not return the self-test examined using Fisher's exact test.

TABLE 2

Attitudes Toward the Self-Test Among Participants Who Returned a Self-test and Completed the Acceptability Questionnaire

	n (%)
Overall thoughts about the self-test	
Mostly positive	160 (81)
Neutral	34 (17)
Mostly negative	4 (2)
Refused/don't know/missing	29
Comfortable receiving the self-test kit in the mail *	
Yes	210 (99)
No	3 (1)
Refused/don't know/missing	14
Comfortable returning self-test sample by mail *	
Yes	172 (82)
No	38 (18)
Refused/don't know/missing	17
Comfortable receiving self-test results by telephone *	
Yes	203 (97)
No	6 (3)
Refused/don't know/missing	18
Willing to pay for self-test	
Would not pay for test	18 (9)
<\$25	87 (43)
\$25-\$49	51 (25)
\$50	47 (23)
Refused/don't know/missing	24

* Response scales:

Did you feel comfortable receiving the self-test kit in the mail? Yes/No.

Did you feel uncomfortable sending back your sample in the mail? Yes/No.

I am comfortable getting self-test results by telephone. Strongly agree/ somewhat agree/somewhat disagree/strongly disagree.

TABLE 3

HPV Self-Test Return, Laboratory Results, and Pap Test Completion, Overall and Stratified by Age

	Total	30–44 y, n (%)	45–65 y, n (%)	<i>P</i>
Enrolled (eligible and mailed a self-test kit)*	427	253/427 (59.3)	174/427 (40.8)	
Returned a home self-test by mail	274/427 (64.2)	157/253 (62.1)	117/174 (67.2)	0.31 [†]
HPV test results among women who returned a self-test [‡]				
HPV positive	38/261 (14.6) [‡]	23/148 (15.5)	15/113 (13.3)	0.72 [†]
HPV negative	223/261 (85.4) [‡]	125/148 (84.5)	98/113 (86.7)	
Inconclusive/leaked sample	10/274 (3.6) [§]	6/157 (3.8)	4/113 (3.5)	
Reported a clinic-based Pap test at follow-up questionnaire [¶]	80/145 (55.2)	35/72 (48.6)	45/73 (61.6)	0.13 [†]
HPV positive	18/22 (81.8)	8/11 (72.7)	10/11 (90.9)	
HPV negative	61/119 (51.3)	26/59 (44.1)	35/60 (58.3)	
	<i>P</i> < 0.01 ^{//}	<i>P</i> = 0.11 ^{//}	<i>P</i> < 0.05 ^{//}	

HPV positivity 95% confidence intervals: total, 14.9 (10.8–19.7); 30–44 years, 15.5 (10.1–22.4); 45–65 years, 13.3 (7.6–20.9).

* Excludes 2 participants who were aged 30 to 65 years but did not report specific age.

[†] *P* values using Fisher's exact test for difference in reported Pap test attendance in women younger than 45 years compared with those at least 45 years old.

[‡] n with result over n of valid test results. Inconclusive results excluded from calculation of percentages.

[§] Includes 4 inconclusive lab results and 6 samples that leaked in transit. Not included in calculation of positive and negative result percentages. An additional 3 samples could not be run because of incomplete consent forms.

[¶] n reporting Pap over n completing follow-up questionnaire. Reliable data on follow-up to Pap test were not available from women who did not complete the follow-up questionnaire.

^{//} *P* value using Fisher's exact test for difference in follow-up Pap test between HPV-positive and HPV-negative women within age category.

TABLE 4

Multivariable Associations Between Participant Characteristics and Self-Test HPV Positivity Among 216 Infrequently Screened Women *

Characteristic	Total n *	HPV Positivity, %	Odds Ratio Adjusted for Age [†] (95% CI)
Age, y			
30–44	116	15	Ref.
45	100	14	1.01 (0.45–2.28)
Health insurance			
Uninsured	143	12	Ref.
Medicaid	49	25	1.84 (0.76–4.47)
Military/Blue Cross/other	16	13	1.05 (0.21–5.18)
Missing	8		
Smoking			
Smoker	110	19	1.88 (0.81–4.34)
Nonsmoker	102	10	Ref.
Don't know/ missing	4		
Self-report of HIV positivity			
Yes	13	39	2.93 (0.82–10.40)
No	198	13	Ref.
Missing	5		

Ref. indicates referent group.

* Participants who returned a self-sample, had a valid HPV result, and responded to the acceptability questionnaire.

[†] Adjusted for age using categorical variable: 30–44 versus at least 45 years of age, and all other variables in the table.