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Complete List of Authors:	Murchland, Audrey; University of Michigan School of Public Health, Epidemiology Gottschlich, Anna; University of Michigan School of Public Health, Epidemiology Bevilacqua, Kristin; University of Michigan School of Public Health, Epidemiology Pineda, Andres; Instituto de Nutricion de Centroamerica y Panama Sandoval-Ramírez, Berner Andrée; Universitat Rovira i Virgili, Hospital Universitari Sant Joan, Functional Nutrition, Oxidation, and Cardiovascular Diseases Group (NFOC-Salut) Alvarez, Christian; University of Michigan School of Public Health, Epidemiology Ogilvie, Gina; BC Centre for Disease Control, Clinical Prevention Services Carey, Thomas E; University of Michigan, Department of Otolaryngology-Head and Neck Surgery and Department of Pharmacology Prince, Mark; University of Michigan Department of Otolaryngology Head and Neck Surgery Dean, Michael; National Cancer Institute, Laboratory of Translational Genomics, Division of Cancer, Epidemiology and Genetics Montano, Carlos; Instituto de Nutricion de Centroamerica y Panama Rivera-Andrade, Alvaro; Instituto de Nutricion de Centroamerica y Panama Meza, Rafael; University of Michigan School of Public Health, Epidemiology
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HPV Self-Sampling Acceptability in Rural and Indigenous Communities in Guatemala: A Cross-Sectional Study

Audrey Murchland[1], Anna Gottschlich[1], Kristin Bevilacqua[1], Andres Pineda[2], Berner Andrée Sandoval-Ramírez[3], Christian S. Alvarez[1], Gina Ogilvie[4], Thomas E Carey[5], Mark Prince[6], Michael Dean[7], Carlos Mendoza-Montano[2], Alvaro Rivera-Andrade[2], Rafael Meza[1]

1. Department of Epidemiology, School of Public Health, University of Michigan, 1415 Washington Heights, Ann Arbor, Michigan 48103

2. Institute of Nutrition of Central America and Panama-INCAP, Calzada Roosevelt 6-25 zona 11, Apartado Postal 1188 Guatemala City, Guatemala 01011

3. Functional Nutrition, Oxidation, and Cardiovascular Diseases Group (NFOC-Salut), Universitat Rovira i Virgili, Hospital Universitari Sant Joan (HUSJR), Sant Llorenç, 21, 43201, Reus, Spain

4. Clinical Prevention Services, BC Centre for Disease Control, 655 W 12th Ave, Vancouver, British Columbia V5Z4R4, Canada

5. Department of Otolaryngology-Head and Neck Surgery and Department of Pharmacology, University of Michigan, 5311 Medical Science Unit I 1301 Catherine St., Ann Arbor, Michigan 48109

6. Department of Otolaryngology, University of Michigan, 1500 E Medical Center Dr SPC 5312, Ann Arbor, Michigan 48109

7. Laboratory of Translational Genomics, Division of Cancer, Epidemiology and Genetics, National Cancer Institute, Gaithersburg, MD USA

Corresponding Author:
Rafael Meza, Ph.D.
SPH II, Room 5033, 1415 Washington Heights
Ann Arbor, MI 48109-2029
E-mail: rmeza@umich.edu
Telephone: +1 (734) 763-1946

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ABSTRACT

Introduction: Cervical cancer disproportionately burdens low- and middle-income countries (LMICs) such as Guatemala. Self-collection testing for human papillomavirus (HPV) has been suggested as a form of cervical cancer screening to facilitate access in LMICs. This study assessed and compared the acceptability of self-collection HPV testing in two rural, indigenous and ethnically distinct communities in Guatemala: Santiago Atitlán, Solola and Livingston, Izabal.

Methods: All participants, women between ages 18 and 60, completed a questionnaire. Eligible participants were also asked to self-collect a vaginal sample and complete a questionnaire regarding comfort and acceptability. Self-collected samples were tested for high-risk HPV using the real-time PCR Hybribio kit.

Results: In the indigenous community of Santiago Atitlán, of 438 age-eligible participants, 94% completed self-collection. Of those, 81% found it comfortable and 99% were willing to use it as a form of screening. In the multi-ethnic (Afro-Caribbean, indigenous) community of Livingston, of 322 age-eligible participants, 53% chose to self-collect. Among those who took the test, 87% found it comfortable and 100% were willing to use it as a form of screening. In Livingston, literacy was higher in women who chose to self-collect (prevalence ratio, 1.45; 95% CI, 1.07 to 1.95). Ethnicity, history of screening, and reproductive history were not associated with willingness to self-collect. Overall, 19% (87/549) of samples tested positive for high-risk HPV.

Conclusion: Among women willing to self-collect in rural and indigenous communities in Guatemala, self-collection for HPV testing appears to be highly acceptable. However, willingness to try self-collection might vary across communities and settings. Literacy, in particular, may affect attitudes towards new screening modalities in rural, multi-ethnic communities in Latin America, and should then be considered when designing and implementing self-collection based cervical cancer screening programs in the region.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- To our knowledge, little is known about the acceptability of self-collection HPV testing across the diverse communities within Guatemala, and in particular among indigenous populations.
- Our study provided not only a larger sample size compared with previous studies but was also conducted in two differing communities, increasing the generalizability of the study across Guatemala.
- Due to both the sensitive nature of the questions related to sexual history and the largely religious and conservative environment of the communities, it may be possible that a social desirability bias may have resulted in over reporting of perceived "good behaviors", such as screening or use of protection, in addition to under-reporting of perceived "bad behaviors", such as number of lifetime sexual partners and other sexual behavior measures.
- Women may report their history of screening or utilization of health care resources incorrectly if they had limited information or understanding of these services. This trend may be exaggerated in women with low literacy.
- Sampling methods differed between the two communities due to the lack of reliable census counts in one community, but our sample in this community is reflective of the overall population structure in terms of ethnic, age and other metrics, suggesting that influential selection bias into the study might be limited.

INTRODUCTION

Cervical cancer, primarily caused by HPV infection, has a very good prognosis when detected in premalignant or early malignant stages[1]. However, it disproportionately burdens low- and middle-income countries (LMICs), such as Guatemala, compared to high-income countries (HICs)[2-4]. HICs currently use Pap smears to detect abnormal cervical lesions that can be removed, greatly reducing the risk of cervical cancer[3 5]. However, there are many barriers to implementing successful Pap smear (cytology-based) screening programs in LMICs, including difficulties establishing sustainable laboratory infrastructure, training and retaining adequate numbers of trained pathologists or cytologists, overburdened primary care clinics, and time and travel limitations for women in reaching screening locations[1 6 7]. Due to these factors and others, the percentage of women in Guatemala who are screened for cervical cancer remains low; in 2014, only 49.8% of women (15-49 years of age) reported ever having a Pap smear. Thus, significant improvements in screening or program implementation are paramount to improving cervical cancer outcomes in Guatemala[3 8 9].

Since more than 90% of cervical cancers are caused by the HPV virus, HPV testing has been suggested as a possible alternative, primary form of cervical cancer screening[10-12]. When used in combination with Visual Inspection with Acetic Acid (VIA) or Pap smears in low-income settings, HPV testing has been shown to provide significant improvements in the detection of advanced premalignant lesions and cancer in both sensitivity and specificity as compared to VIA or Pap smear alone, as only women who test positive for HPV need to follow up with further screening[13-16]. Previous studies have also confirmed that HPV self-swab kits are comparable to physician administered samples in their ability to detect carcinogenic, high-risk HPV[17]. Thus, at-home HPV sample collection, with referral to further screening for those

positive for high-risk HPV, may be both more acceptable within low-income communities and more programmatically feasible[6 7 18].

Studies have shown that HPV self-sampling is generally acceptable among women in low and high resource settings as well as immigrant, rural, vulnerable populations[19-29]. To our knowledge, however, little is known about the acceptability of self-collection HPV testing across the diverse communities within Guatemala, and in particular among indigenous populations. In a pilot cross-sectional study assessing the acceptability of HPV self-collection among 200 women in the Mayan community of Santiago Atitlán, Guatemala, a self-swab HPV test was found to be a highly acceptable form of screening[30]. Over 80% of women said that they preferred using a self-swab kit in their home rather than being screened at a doctors' office. However, this pilot study was limited to a relatively small sample in a single, largely homogeneous community, limiting the generalizability of the results. Further research is thus needed to evaluate the acceptability of self-collection testing among more diverse populations within Guatemala, an extremely diverse country ethnically, culturally, and economically. The purpose of this study was to further assess and compare the acceptability of self-collection HPV testing in two rural, ethnically distinct communities in Guatemala: Santiago Atitlán and Livingston, Izabal.

METHODS

Study Communities

Santiago Atitlán, Solola is a rural community located on Lake Atitlán, in the southwest region of Guatemala, 75 miles west of Guatemala City. The Tz'utujil, a Mayan descendant ethnic group, inhabits the region, which surrounds Lake Atitlán. The primary language of Santiago's inhabitants is Tz'utujil, and over half of the villagers speak Spanish as a second

language[30]. The majority of women in Santiago Atitlán have at most a primary education. Additionally, as a conservative, religious community, it is highly uncommon for women to either drink or smoke, and almost all women in have previously reported having only one lifetime sexual partner[30].

Livingston, Izabal is located on the Caribbean coast of the country and is a rural community, only accessible by boat, that is the primary Garífuna settlement in Guatemala. The Garífuna people are considered a unique ethnic group with their own language, culture, and cuisine. Additionally, there are large populations of other ethnic and cultural groups located in Livingston including Q'eqchi' (Mayan descent), Ladinos (non-Mayan), and populations of Indian descent. Most women in Livingston are believed to have at least basic primary education.

Patient and Public Involvement

The patients were not involved in the development of the research questions, outcome measures or study design. The patients were also not involved in the recruitment and performance of the study. However, the public, Guatemalan physicians, scientists, and community health workers, were involved in the development of the question, design, validation, recruitment, and conduct of the study. Local community health workers were involved in the validation of the survey and study protocol, recruited participants and conducted the interviews, and assisted in providing test results to patients. Guatemalan physicians contributed to development of the research question and study design, organized the laboratory testing, led and assisted with community health worker training, and provided HPV test results to patients. Local laboratory scientists contributed to the study design and conducted the HPV laboratory testing. The continued collaborations with these team members will be used to disseminate study results to patients and Guatemalan officials via publications, presentations, and meetings.

Eligibility and Recruitment

Trained community health workers (CHWs) in both communities actively recruited participants through home visits. All CHWs were bilingual and spoke both Spanish and either Tz'utujil, Q'eqchi, or Karif (the language of the Garifuna) depending on the location they were working in. Households in Santiago Atitlán were selected at random using stratified multi-level sampling based upon maps and population counts of the communities available through the local municipal office and were kept consistent with previous sampling methods[30]. Households in Livingston were selected at random using convenience sampling due to lack of reliable census data at the neighborhood-level. Sampling methods were, however, kept as similar as possible to those in Santiago Atitlán.

Selected households that had at least one woman available between the ages of 18 and 60 were invited to participate in the survey-component of the study. For households with more than one eligible woman willing to participate, the female in the household whose birthday was closest to the date of the interview was enrolled in the study. Exclusion criteria consisted of past hysterectomy or previous cervical cancer. Only women between the ages of 25 and 54 were asked to provide a sample, in accordance with Guatemala's current screening recommendations[31]. Additionally, pregnant women, women currently menstruating, and women who had never been sexually active were also excluded from providing samples but could participate in the survey component.

Survey

Data collection consisted of two main components: the surveys and the HPV self-collection tests. Local CHWs in each community were trained as interviewers in the appropriate techniques and protocols before beginning home visits. Two CHWs visited each randomly

selected household together and read a recruitment script to a female household member to determine the household's eligibility. CHWs administered the survey and provided kits to collect HPV samples only to willing, eligible participants.

The survey questionnaire included 153 questions concerning demographics, risk factors for cervical cancer and HPV, and knowledge of cervical cancer and HPV. The survey was developed from the pilot study survey and validated as part of the CHW and translator training to ensure correct translation and cultural relevancy[30]. Each survey was administered by the CHWs using electronic tablets and the Qualtrics offline app.

All women who participated in the study were compensated with a voucher for a free Pap smear or VIA at a local health clinic. Women in both communities can access free VIAs (Santiago) or Pap Smears (Livingston) in the local public health system, but if they chose to use a private clinic instead of the public clinic, the voucher covered their fees.

HPV Self-Collected Samples

The HPV samples were collected using HerSwab kits, a self-collection sampling method [30 32 33]. If a participant was willing to provide a sample, instructions and graphical materials were provided and the participant collected the sample in a separate, private room from the CHWs. Participants who collected a sample then completed a short post-sample survey with the CHWs of three questions regarding ease, comfort, and acceptability of the sampling method: "How easy was the self-collection swab?"; "How comfortable was the self-collection swab?"; and "Would you be willing to collect a sample every 2-3 years to detect HPV as a form of cervical cancer screening?".

After collection, samples were kept in small, refrigerated coolers carried by the CHWs until they were returned to the main study office at the end of the day where samples were then

processed to stabilize sample life. The brush component of the HerSwab kit was cut into a 15-mL test tube using lab scissors. The lab scissors were sterilized using alcohol and an open flame between each sample. Each tube was filled with 5mL of Scope mouthwash using a pipette, and tubes were sealed using a cap and parafilm paper[34]. Each sample was labeled with the participant's unique identifier. Time of sample processing and condition of sample were recorded.

Stabilized samples were sent to a molecular biology laboratory at the Institute of Nutrition of Central America and Panama (INCAP) in Guatemala City for testing. Samples were tested using the real-time polymerase chain reaction (PCR) Hybribio HR-13 kit[35 36]. Samples were processed according to the manufacturers protocol and modified to use a 10 ul reaction volume for the real-time PCR and run on an ABI-7000[34]. After testing, samples were labeled as positive for HR-HPV, negative, or, if both the HPV probe and the internal control were negative, inconclusive. If a sample test was inconclusive during the first test, it was run an additional time using a 20 ul reaction volume, and if no result was obtained, the test was deemed inconclusive.

Follow-Up

A local CHW provided negative and inconclusive results over the phone or through a home visit. Positive results were provided in-person by a study physician who referred participants to their local community health clinic for follow-up and further cervical cancer screening. All participants who couldn't be reached at the study conclusion were re-contacted either at 6 months or one year to provide them with their results. Although women with negative results were not explicitly recommended to attend the clinic, all participants were encouraged to get screened using the voucher provided at the local clinic to support their engagement with local preventative services.

Outcomes and Statistical Analysis

Willingness and acceptability of self-collection testing, knowledge of HPV, and risk factors were compared between communities and across ethnic groups in Livingston, Izabal. Willingness was measured using two metrics: the first was if a woman chose to self-collect a sample to be tested for HPV (actual self-collection), and the second was how a woman responded to a question of willingness to self-collect in the initial survey (self-reported willingness).

Due to lower rates of actual self-collection and self-reported willingness in Livingston, differences between Livingston women willing and those not willing to collect a sample were evaluated using two-sample t-tests for means, chi-squared tests for proportions, and Fisher's Exact test for low cell counts. Most women tried self-collection in Santiago, so we restrict these analyses to Livingston.

The main exposures explored for willingness to try self-collection included: ethnicity, literacy, marital status, history of Pap smear or VIA, alcohol use, and IUD use. Statistical analyses were run using log-binomial regression and models were adjusted for age, ethnicity, and number of lifetime sexual partners. Final models were further stratified across ethnic groups to evaluate potential effect modification.

The acceptability of sample collection was only assessed for those who self-collected a sample and was analyzed using the post-self-swab survey questions. These questions included "How comfortable was the test?", "How easy was the test?", and "Would you be willing to continue using this test periodically as a form of cervical cancer screening?"

Prevalence of high-risk HPV and history of previous Pap smear or VIA were also evaluated for both communities. The main exposures explored for these outcomes included:

literacy, marital status, smoking, alcohol use, IUD use, number of lifetime sexual partners, family history of cervical cancer, and whether a woman believed she was likely to develop cervical cancer. Statistical analyses were run using log-binomial regression and models were further adjusted for age, ethnicity, and number of lifetime partners.

Covariates were parameterized as: able to read or write versus unable to read or write (literacy), ever married versus never married, ever had a Pap or VIA versus never, drinker versus non-drinker, ever had an IUD versus never, ever smoked versus never smoked.

Data cleaning and analyses were carried out using SAS 9.4[37].

RESULTS

In total, 956 women were recruited to participate into the study: 500 women in Santiago Atitlán and 456 women in Livingston. Demographic characteristics, health access and utilization, and knowledge and attitudes towards cervical cancer and HPV screening differed between the two communities: 69.4% of the participants in Santiago Atitlán had less than primary education and 96.4% were of Tz'tujil ethnicity. In contrast, only 33.9% of the participants in Livingston had less than primary education and many ethnic groups were represented: 41.9% Q'echi, 32% Garifuna, and 24.8% mixed ethnicity (Ladino) (Table 1).

Knowledge and attitudes regarding HPV and cervical cancer also differed between the communities. Only 11.8% of participants in Santiago reported previous knowledge of HPV as compared to 62.7% of Livingston participants. However, when asked about the seriousness of cervical cancer, most participants in both communities responded "very" or "extremely" (74.8% Santiago and 80.9% Livingston) (Appendix).

Self-reported history of access to healthcare appeared higher in Livingston than in Santiago. For example, only 5.0% of participants in Santiago responded that they had ever been

tested for HIV while 57.8% of Livingston participants responded that they had been previously tested. Additionally, a higher proportion of participants in Livingston consistently reported using contraception, always using protection during sexual intercourse, and using tobacco and alcohol than in Santiago (Table 1).

Self-Collection Willingness and Acceptability

We found significant differences between the communities with respect to willingness to try self-collection sampling. In Santiago Atitlán, of 438 age-eligible participants, 93.6% (N=410) chose to self-collect. In Livingston, of 322 age-eligible participants, 52.5% (N=169) chose to self-collect. However, among those who did collect a sample, the self-collection testing was highly acceptable in both communities. Of Santiago participants who self-collected, 81.4% found it comfortable and 84.8% reported that the HerSwab was easy to use. Among Livingston participants who self-collected, 87.0% found it comfortable and 87.0% reported it was easy to use. Among those who chose to self-collect, almost all participants in both locations reported that they were willing to use it as a form of cervical cancer screening (99.5% in Santiago and 100% in Livingston) (Table 2).

Willingness to Sample in Livingston

We evaluated factors that affected the willingness to try self-collection testing in Livingston. Literacy, the use of health services, and beliefs regarding cervical cancer differed between age-eligible women who self-collected a sample compared to those who did not (Table 3). Additionally, 31.4% of the women who ended up not providing a sample had responded previously in the questionnaire that they indeed would be willing to collect a self-swab sample at home (Figure 1). While data is unavailable regarding how many age-eligible women were

ineligible to collect a sample due to menstruation or pregnancy, this likely does not entirely account for all women who ultimately chose not to self-collect.

Literacy was significantly higher among women who self- collected a sample in Livingston compared to those who did not (crude PR 1.94; 95% CI: 1.23, 3.05; adjusted PR, 1.45; 95% CI: 1.07, 1.95) (Table 4 and Appendix). Regular drinking was also higher among women who self-collected (crude PR 1.18; 95% CI: 0.95, 1.46; adjusted PR 1.30; 95% CI: 0.74, 2.29) (Table 4 and Appendix). Additionally, IUD use and number of lifetime sexual partners were higher among women who self-collected a sample in Livingston (IUD use, adjusted PR 2.09; 95% CI: 0.80, 5.45; lifetime sexual partners, adjusted PR 1.12; 95% CI 0.93, 1.34) (Table 4). When stratifying either by indigenous or non-indigenous group or by ethnic group, the association between literacy and actual sample collection remained positive. However, this relationship only remained statistically significant among Q'echchi participants (Appendix).

When evaluating how women responded to the survey question, "Would you be willing to collect a sample at home?", literacy and IUD were significantly different among women who responded a priori that they would be willing as compared to women who responded they would not be willing. Characteristics comparing these two populations can be found in the appendix. After adjustment for age, ethnicity, and number of lifetime sexual partners, the association between literacy and a response of willingness to self-collect was no longer significant (crude PR 1.51; 95% CI: 1.09, 2.10; adjusted PR, 1.24; 95% CI: 0.96, 1.60) (Appendix). Similarly, the relationship between not using an IUD and a positive willingness survey response was no longer significant after adjustment (crude PR 0.75; 95% CI: 0.62, 0.90; adjusted PR, 0.87; 95% CI: 0.69, 1.08) (Appendix).

HPV Prevalence

Overall, 19% of samples tested positive for high-risk HPV (N=549). 18.7% of samples from Santiago Atitlán tested positive for high-risk HPV and 21.3% of samples from Livingston tested positive, but this difference was not statistically significant (Appendix). Additional tables exploring the differences between women who test positive for high-risk HPV and those that did not can also be found in the appendix. In total, 94% of participants who sampled in Santiago Atitlán and 88.5% of participants who sampled in Livingston were provided with their test results.

DISCUSSION

In this study, we assessed the acceptability of HPV self-collection testing as an alternative form of primary cervical cancer screening in indigenous and rural communities in Guatemala. We found that self-collection appears to be highly acceptable among women who tried it, independent of community and ethnicity. Most women reported that self-collection was comfortable and easy to use, and almost all women who tried it reported being willing to use it as a form of cervical cancer screening in the future. These results are consistent with other studies looking at self-collection acceptability both within Guatemala and other LMICs[25 30]. This study was further able to build upon previous studies and provide important information regarding HPV self-collection testing acceptability at the community level, and in a community that had not been previously evaluated.

Our study also found, however, that there were differences between communities in willingness to try self-collection. Willingness to try self-collection testing remained consistently high among participants in Santiago Atitlán as reported in the pilot study conducted in 2015 (93% in 2015 versus 93.6% in 2016)[30]. In Livingston, however, even among women who first responded in the survey or consent form that they would be willing to collect a sample, actual

self-collection was lower. We found that willingness to self-collect in Livingston was consistently associated with higher levels of literacy. Literacy was also associated in both communities with previous access to cervical cancer screening. In contrast, ethnicity, history of cervical cancer screening, and reproductive history were not associated with willingness to self-collect. Stratified analyses revealed that there were no qualitative differences in the association between literacy and sample collection across ethnic groups in Livingston.

High prevalence of self-collection testing in Santiago Atitlan, a community with low literacy levels, as compared to the low rates of self-collection testing among those with low literacy in Livingston may reflect larger community differences in awareness or access to screening modalities rather than a lack of effect of literacy in Santiago or an effect of ethnicity. Santiago Atitlán remains largely deficit in accessible and affordable cervical cancer screening while Livingston has regular, public or private, screening campaigns in the community. This difference in general community access, then, may be acting as an effect modifier on the association between literacy and screening between these two communities, suggesting that self-collection might be better received at first in communities that do not have other alternatives, whereas some initial skepticism might be found in places with existing cervical screening programs, independently of their quality and efficacy. The high rates of acceptability and willingness to retake among women who self-collected in both communities suggest that once experienced, self-collection is a valid, and even preferred, alternative to other screening modalities from the women's perspective.

The results suggest thus that HPV self-collection testing program implementation may need to target populations based on levels of literacy or community access, rather than focusing primarily on ethnicity or racial identity. A previous study examining HPV acceptability and

intention in the UK similarly found that low education and self-efficacy were associated with low sampling intentions[28]. The inability to either read or write in Guatemala may negatively influence a woman's perceived self-efficacy and her confidence in navigating public health infrastructure or self-collecting a vaginal sample. This population, however, would greatly benefit from HPV self-collection testing as a primary form of cervical cancer screening due to its strength in concentrating less accessible and more invasive screening modalities towards those that are at high-risk (i.e., positive for HPV). Therefore, our results suggest that it might be critical that, if implemented, HPV screening and education programs are tailored such that they are more accessible to low-literacy populations and, thus, increase perceived self-efficacy in navigating the existing public health infrastructure.

Although based on a different HPV test than in our pilot study (Hybribio HR13 vs. Anyplex 28), a similar prevalence of high-risk HPV was found in Santiago between 2015 and 2016 (17.4% versus 19.3%)[30]. Of note, there were no significant differences in high-risk HPV prevalence between ethnic groups in Livingston, and there was not a statistically significant difference between Santiago Atitlán and Livingston with regards to prevalence.

Our study provided not only a larger sample size compared with previous studies but was also conducted in two differing communities. This is a strength because Guatemala is an extremely diverse country with over 23 languages, distinct ethnicities, and a history of large economic and social inequalities. Thus, generalizing the evaluations of a health program's acceptability and feasibility to the whole country is generally difficult. However, because we evaluated two very different rural multi-ethnic communities, our results may reflect some of the future obstacles and considerations necessary in implementing self-swab HPV testing in such a diverse country as Guatemala than was previously available. In fact, our results also

complement the findings of the ongoing careHPV Scale-Up implementation, which is assessing the performance of HPV testing, including self-collection testing, within urban settings in Guatemala[38-40].

There are several limitations to our study. Due to both the sensitive nature of the questions related to sexual history and the largely religious and conservative environment of the communities, it may be possible that a social desirability bias may have resulted in over reporting of perceived "good behaviors", such as screening or use of protection, in addition to under-reporting of perceived "bad behaviors", such as number of lifetime sexual partners and other sexual behavior measures. We tried to minimize the possibility of this bias by maintaining confidentiality with participants. Also, women may report their history of screening or utilization of health care resources incorrectly if they had limited information or understanding of these services. This trend may be exaggerated in women with low literacy and thus explain some of the relationships that were observed in the data. Additionally, because sampling methods differed between the two communities due to the lack of reliable census counts in Livingston, there may be differences between the communities in potential selection bias into the study and more limited comparability of the results. However, our sample in Livingston is reflective of the overall population structure in terms of ethnic, age and other metrics, suggesting that influential selection bias into the study might be limited[41].

Due to the ongoing nature of the project, data on follow-up screening are still in process. Future research with our study participants will hopefully elucidate how HPV self-collection testing may affect women's decisions to pursue further cervical cancer screening and follow-up care in their local communities after HPV testing and receiving their results. Additionally, these

data may reveal other downstream facilitators or barriers to screening that will influence the overall success of HPV self-swab testing implementation nationwide.

CONCLUSION

The results of our study add to the literature on the potential of HPV self-collection testing in LMICs, demonstrating its wide acceptability in rural, indigenous, multi-ethnic communities in Latin America. Our findings also suggest that literacy and community access may affect attitudes towards new screening modalities. It is important, then, that the issue of literacy is specifically considered when implementing screening programs in Guatemala and other LMICs through both policy and practice. Additionally, future programs should focus on tailoring messaging and education materials to low literacy versus high literacy women as opposed to specific ethnic or cultural groups. This vulnerable population may need more targeted educational programs that are provided through appropriate mediums to increase screening access in these populations.

LIST OF ABBREVIATIONS

CC – Cervical Cancer

CHW – Community Health Worker

CI – Confidence Interval

HICs – High-Income Countries

HIV – Human Immunodeficiency Virus

HPV – Human Papillomavirus

HR-HPV – High-Risk Human Papillomavirus

INCAP – Institute of Nutrition of Central America and Panama

IUD – Intra-Uterine Device

LMICs – Low and Middle-Income Countries

OR – Odds Ratio

PCR – Polymerase Chain Reaction

PR – Prevalence Ratio

VIA – Visual Inspection with Acetic Acid

DECLARATIONS

Ethics Approval and Consent to Participate

The University of Michigan Institutional Review Board (HUM00096559) and the Institute of Nutrition of Central America and Panama Institutional Review Board (MI-CIE-16-009) approved study protocols. All participants gave oral and written informed consent prior to participation in the study. The consent was documented by a signature or fingerprint of the participant, the surveyors, and a witness.

Consent for Publication

The authors of this paper have all reviewed its contents and consent for its publication.

Data Sharing Statement

Due to the sensitive nature of the data collected, IRB restrictions, and ongoing data collection, study data is stored at the University of Michigan. Interested parties may contact the corresponding author to request access to de-identified datasets for specific research questions related to the study. The authors welcome further collaboration but reserve the right to retain data to protect study participants.

Competing Interests

The authors have no competing interests to declare.

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Authors' Contributions

PIC - Planning and Key Intellectual Contribution
DC – Data Collection and Project Management
SP – Sample Processing, Laboratory Management, and Test Results
SA – Statistical Analysis and Data Management
W – Writing
E – Editing

Audrey Murchland – PIC, DC, SP, SA, W, E
Anna Gottschlich – PIC, DC, SP, W, E
Kristin Bevilacqua – PIC, DC, SP, E
Andres Pineda – PIC, DC, SP, E
Andree Berner Sandoval-Ramírez – PIC, DC, SP, E
Christian Alvarez – PIC, E
Gina Ogilvie – PIC, E
Thomas E Carey – PIC, SP, E
Mark Prince – PIC, SP, E
Michael Dean – PIC, SP, E
Carlos Mendoza-Montano – PIC, SP, E
Alvaro Rivera-Andrade – PIC, DC, SP, E
Rafael Meza – PIC, DC, SP, SA, W, E

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TABLES

Table 1. General Population Characteristics Among All Participants			
	Santiago Atitlán % (N) or Mean (SD)	Livingston N (%) or Mean (SD)	p-value
Age (y)	34.78 (8.44)	32.97 (10.38)	**0.003**
Ethnicity			**<0.0001**
Tz'tujil	96.60% (483)	0	
Ladino	1.80% (9)	24.78% (113)	
Garifuna	0	31.80% (145)	
Q'echchi	0	41.89% (191)	
Other	1.40% (7)	1.32% (6)	
Education			**<0.0001**
Less than Primary	69.40% (347)	33.92% (153)	
Primary or Secondary	20.12% (100)	34.37% (155)	
More than Secondary	10.06% (50)	31.71% (143)	
Literacy			**<0.0001**
Illiterate	48.60% (243)	12.53% (57)	
Literate	51.20% (255)	87.47% (398)	
Ever Married/United	97.00% (485)	62.50% (285)	**<0.0001**
Breast exam (Heard of)	14.08% (70)	66.59% (303)	**<0.0001**
Pap (Ever)	66.80% (334)	58.11% (265)	**0.0056**
Last pap			**<0.0001**
Less than 6 months	9.28% (31)	23.77% (63)	
6 months to a year	19.76% (66)	26.79% (71)	
1 to 5 years	51.2% (171)	35.1% (93)	
More than 5 years	14.97% (50)	13.21% (35)	
VIA (ever)	6.04% (30)	1.32% (6)	**<0.0001**
Ever Smoke	0.40% (2)	9.65% (44)	**<0.0001**
Drink Alcohol (Regularly)	11.54% (3)	33.85% (44)	**0.0080**
Used IUD (Ever)	1.41% (7)	8.09% (36)	**<0.0001**
Use Protection			**<0.0001**
Always	7.93% (39)	12.81% (57)	
Almost always	2.21% (11)	7.64% (34)	
Sometimes	4.82% (24)	12.13% (54)	
Rarely	1.81% (9)	5.62% (25)	
Never	68.07% (339)	42.70% (190)	
Family Member with Cervical Cancer	2.65% (13)	11.28% (51)	**<0.0001**
Age at First Sexual Relation	19.63 (4.29)	17.24 (2.77)	**<0.0001**
Number of Lifetime Sexual Partners	1.08 (0.31)	1.61 (1.43)	**<0.0001**
Knowledge of HPV	11.80% (59)	62.72% (286)	**<0.0001**
Believe at Risk for CC			**<0.0001**
Strongly Agree	24.80% (124)	14.47% (66)	
Agree	13.20% (66)	41.23% (188)	
Neutral	13.60% (68)	5.26% (24)	
Disagree	9.00% (45)	8.55% (39)	
Strongly Disagree	19.00% (95)	8.99% (41)	
Willing to Vaccinate Daughters for HPV if Available			**<0.0001**
Yes	69.60% (348)	82.24% (375)	
No	1.00% (5)	6.80% (31)	
Don't Have Daughters	27.60% (138)	8.33% (38)	

Table 2: Acceptability of Self-Collection HPV Tests Among Age-Eligible Women (25-54 years of age)			
	Santiago Atitlán % (N)	**Livingston % (N)**	**p-value[a,b]**
N	500 *(All participants)* *438 (age-eligible)*	*456 (all participants)* *322 (age-eligible)*	
HPV knowledge	10.05% (44)	63.98% (206)	**<0.0001**
Self-Reported Previous Pap (Ever)	71.46% (313)	69.88% (225)	0.6348
Abnormal Pap (Ever)	16.61% (52)	36.89% (83)	**<0.0001**
Knowledge of VIA	6.85% (30)	1.86% (6)	**0.0023**
Willing to Collect Sample at Home	93.38% (409)	62.42% (201)	**<0.0001**
Intent to Self-Collect	94.75% (415)	70.19% (226)	**<0.0001**
Collected Sample	93.61% (410)	52.48% (169)	**<0.0001**
Prefer Home Screening	94.06% (412)	44.41% (143)	**<0.0001**
Prefer Self-Collection	91.10% (399)	41.61% (134)	**<0.0001**
Collected Sample, Among Those Who Said They Were Willing to Collect at Home	96.82% (396)	76.12% (153)	**<0.0001**
	% (N)	**% (N)**	
N	410 *(age-eligible; Test-Taking participants)*	*169 (age eligible; Test-Taking participants)*	
Comfort of test			**0.0013[b]**
Comfortable	81.4% (333)	87.0% (141)	
Neutral	5.87% (24)	5.56% (9)	
Uncomfortable	12.7% (52)	7.4% (12)	
Ease of test			**0.0241[b]**
Easy	84.8% (347)	87.0% (141)	
Neutral	4.65% (19)	7.41% (12)	
Difficult	10.5% (43)	5.55% (9)	
Willingness to retake test	99.50% (402)	100% (169)	1.00[b]
[a]p-values for means calculated using two-sample t-test; proportions using chi-squared test [b]Fisher's exact test used to account for low cell counts			

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Table 3. Population Characteristics within Livingston Age-Eligible Women Who Sampled vs. Age-Eligible Women Who Did Not Sample			
	Took the Sample % (N) or Mean (SD)	**Did Not Take the Sample % (N) or Mean (SD)**	**p-value[a]**
N	52.48% (169)	47.52% (153)	
Age (y)	34.98 (7.76)	36.35 (7.66)	0.1141
Ethnicity			0.6986
Ladino	25.44% (43)	27.45% (42)	
Garifuna	33.14% (56)	30.72% (47)	
Q'echchi	39.64% (67)	40.52% (62)	
Other	1.78% (3)	0.65% (1)	
Declined	0	0.65% (1)	
Education			0.0784
Less than Primary	33.73% (57)	43.14% (66)	
Primary or Secondary	35.50% (60)	29.41% (45)	
More than Secondary	29.59% (50)	25.49% (39)	
Literacy			**0.0005**
Illiterate	8.54% (14)	21.52% (34)	
Literate	91.72% (155)	77.78% (119)	
Ever Married/United	66.27% (112)	73.86% (113)	0.2365
No. Health Locations Used	1.51 (0.86)	1.32 (0.71)	**0.0324**
Pap or VIA (Ever)	72.78% (123)	66.67% (102)	0.2324
Ever Smoke	9.47% (16)	9.15% (14)	0.6309
Drink (regularly)	32.08% (17)	35.14% (13)	0.7619
Used IUD	11.24% (19)	4.58% (7)	**0.0295**
Use Protection			0.3998
Always	11.24% (19)	10.46% (16)	
Almost always	8.88% (15)	5.23% (8)	
Sometimes	14.20% (24)	11.11% (17)	
Rarely	5.92% (10)	5.88% (9)	
Never	44.97% (76)	42.48% (65)	
Unknown	15.24% (25)	24.0% (38)	
Family Member with CC	11.83% (20)	8.50% (13)	0.6143
Age at First Sexual Relation	17.20 (2.97)	17.56 (2.96)	0.4102
Number of Lifetime Partners	1.83 (1.73)	1.51 (1.31)	0.0670
Knowledge of HPV	68.05% (115)	59.48% (91)	0.1097
Believe at Risk for CC			**0.0398**
Strongly Agree	21.89% (37)	11.76% (18)	
Agree	38.46% (65)	42.48% (65)	
Neutral	5.92% (10)	1.96% (3)	
Disagree	7.69% (13)	6.54% (10)	
Strongly Disagree	7.69% (13)	10.46% (16)	
Unsure	18.34% (31)	26.80% (41)	
Vaccinate Daughters for HPV			0.4024
Yes	189.35% (151)	83.01% (127)	
No	5.92% (10)	7.19% (11)	
Don't Have Daughters	2.96% (5)	5.23% (8)	
Willing to Collect Sample at Home	90.53% (153)	31.37% (48)	**<0.0001**
Intent to Collect Sample	94.67% (160)	43.14% (66)	**<0.0001**
[a]p-values for means calculated using two-sample t-test; proportions using chi-squared test			

Table 4 Prevalence Ratio of Willingness to Collect a Sample in Livingston

Log-Binomial Regression: Prevalence Ratio of Actual Sample Collection and Willingness to Collect at Home

	Literacy (Y)		Marriage (Never)		Hx of Pap/VIA (Never)		Drinking (Ever)		IUD Use	
	PR	95% CI	PR	95% CI	PR	95% CI	PR	95% CI	PR	95% CI
Actual Sample Collection	1.45	(1.07, 1.95)	1.10	(0.94, 1.30)	0.97	(0.80, 1.16)	1.12	(0.93, 1.34)	2.09	(0.80, 5.45)
Willingness to Collect at Home	1.24	(0.96, 1.60)	1.09	(0.95, 1.25)	0.93	(0.79, 1.09)	1.06	(0.90, 1.25)	1.16	(0.93, 1.44)

Models additionally adjusted for age, ethnicity, and number of lifetime sexual partners

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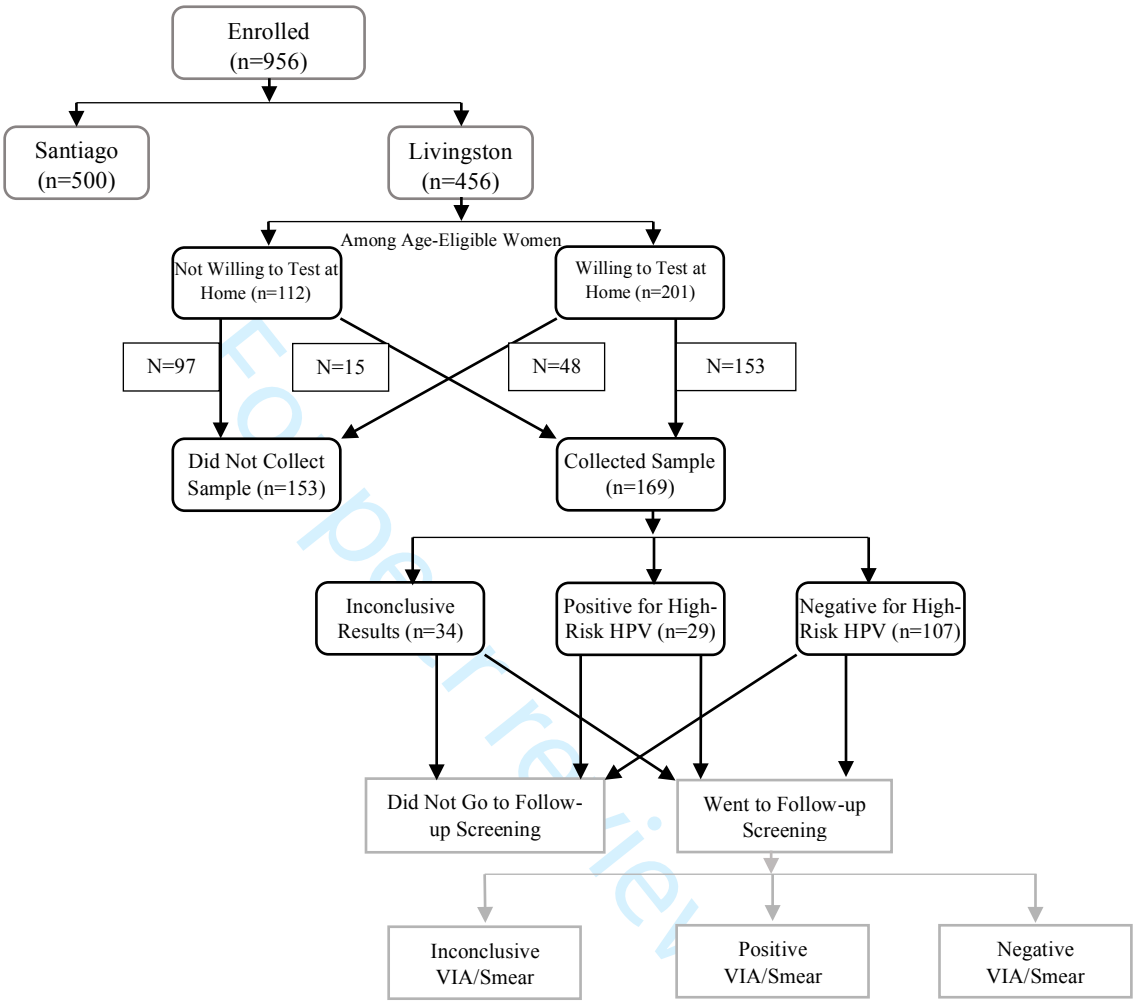
Figure 1. Flow Chart of Livingston Self-Collection Sampling and Testing



HPV Self-Sampling Acceptability in Rural and Indigenous Communities in Guatemala: A Cross-Sectional Study

Audrey Murchland, Anna Gottschlich, Kristin Bevilacqua, Andres Pineda, Berner Andrée Sandoval-Ramírez, Christian S. Alvarez, Gina Ogilvie, Thomas E Carey, Mark Prince, Michael Dean, Carlos Mendoza-Montano, Alvaro Rivera-Andrade, Rafael Meza

Supplementary Appendix

Appendix A: Additional Reference Tables

Appendix B: Additional Regression Tables

Appendix A – Additional Reference Tables

Table A1. General Population Characteristics Among All Participants (Continued)			
	Santiago Atitlan N (%) or Mean (SD)	**Livingston N (%) or Mean (SD)**	**p-value[a]**
N	500	456	
Monthly Income (Quetzals)	1392 (1484)	2428 (5266)	0.3159
25th Percentile	300	600	
50th Percentile	800	1000	
75th Percentile	2500	2000	
Current Marital Status			**<0.0001**
Single	3 (0.62%)	30 (10.53%)	
Married	311 (64.12%)	101 (35.44%)	
Separated	28 (5.77%)	2 (0.70%)	
Divorced	5 (1.03%)	0	
Widowed	15 (3.09%)	1 (0.35%)	
Common Law	120 (24.74%)	151 (52.98%)	
Refused	3 (0.62%)	0	
Age at Marriage	19.8 (4.31)	19.74 (5.82)	0.8771
Use Health Services	451 (90.2%)	421 (92.32%)	0.2465
Mammogram (Ever)	10 (2.01%)	40 (8.77%)	**<0.0001**
Pap or VIA (Ever)	337 (67.40%)	265 (58.11%)	0.7592
Used Birth Control Injections	215 (43.17%)	173 (38.88%)	0.3459
Used Oral Contraceptives	54 (10.84%)	123 (27.64%)	**<0.0001**
Number of Pregnancies	2.81 (1.93)	3.19 (2.49)	**0.0082**
Number of Children	2.54 (1.65)	3.20 (2.12)	**<0.0001**
Age at First Child	20.18 (5.80)	18.88 (3.74%)	**0.0001**
Currently Sexually Active	171 (79.53%)	121 (63.68%)	**0.0035**
Severity of CC			**<0.0001**
Not	6 (1.20%)	18 (3.95%)	
A little	6 (1.20%)	38 (8.33%)	
Moderate	114 (22.80%)	31 (6.80%)	
Very	234 (46.80%)	274 (60.09%)	
Extremely	140 (28.0%)	95 (20.83%)	
Likely to Get CC			**<0.0001**
No Chance	135 (27%)	152 (33.33%)	
Low	97 (19.40%)	175 (38.38%)	
Moderate	32 (6.40%)	13 (2.85%)	
High	22 (4.40%)	7 (1.54%)	
Certain	17 (3.40%)	6 (1.32%)	
Unsure	0	103 (22.59%)	
Refused	197 (39.40%)	0	

Table A2. Population Characteristics within Livingston (Continued)
Age-Eligible Women Who Sampled vs. Age-Eligible Women Who Did Not Sample

	Took the Sample N (%) or Mean (SD)	Did Not Take the Sample N (%) or Mean (SD)	p-value[a]
N	169 (52.48%)	153 (47.52%)	
Monthly Income (Quetzals)	3083.5 (5485.0)	3166.7 (7444.5)	0.9565
Current Marital Status			0.4399
Single	12 (10.71%)	13 (11.50%)	
Married	36 (32.14%)	47 (41.59%)	
Separated	1 (0.89%)	1 (0.88%)	
Divorced	0	0	
Widowed	0	1 (0.88%)	
Common Law	63 (56.25%)	51 (45.13%)	
Age at First Marriage	19.67 (4.51)	20.90 (7.35)	0.1506
Use Health Services	159 (94.08%)	140 (91.50%)	0.3694
No. Health Services Received	2.33 (1.44)	2.26 (1.56)	0.6754
Breast Exam (Heard Of)	30 (17.75%)	26 (16.99%)	0.3473
Mammogram (Ever)	16 (9.47%)	16 (10.46%)	0.7668
Pap (Ever)	123 (72.78%)	102 (66.67%)	0.2324
Last Pap			0.7520
Less than 6 months	28 (22.76%)	25 (24.51%)	
Within the last year	32 (27.12%)	24 (22.43%)	
Within the last 2-5 years	47 (38.21%)	37 (36.27%)	
More than 5 years	16 (13.56%)	13 (12.75%)	
VIA (Ever)	5 (2.96%)	1 (0.65%)	0.1050
Used Birth Control Injections	78 (46.15%)	61 (39.87%)	0.2292
Used Oral Contraceptives	60 (35.50%)	43 (28.10%)	0.1336
Number of Pregnancies	3.49 (2.27)	3.74 (2.30)	0.3346
Number of Children	3.20 (1.78)	3.61 (2.14)	0.1712
Age at First Pregnancy	18.87 (3.50)	19.27 (4.41)	0.3853
Currently Sexually Active	45 (62.50%)	24 (33.33%)	0.2068
Severity of CC			0.4191
Not	4 (2.37%)	7 (4.58%)	
A little	15 (8.88%)	7 (4.58%)	
Moderate	13 (7.69%)	10 (6.54%)	
Very	102 (60.36%)	92 (60.13%)	
Extremely	35 (20.71%)	37 (24.18%)	
Likely to Get CC			0.0612
No Chance	67 (39.64%)	47 (30.72%)	
Low	55 (32.54%)	57 (37.25%)	
Moderate	6 (2.96%)	1 (0.65%)	
High	5 (2.96%)	1 (0.65%)	
Certain	2 (1.18%)	2 (1.31%)	
Unsure	34 (20.12%)	45 (29.41%)	

[a]p-values for means calculated using two-sample t-test; proportions using chi-squared test

Table A3: Population Characteristics within Livingston
Comparing Racial/Ethnic Groups in Livingston Including All Women

	Ladino N (%) or Mean (SD)	Garifuna N (%) or Mean (SD)	Q'echchi N (%) or Mean (SD)	p-value[a]
N	113 (25.17%)	145 (32.29%)	191 (42.54%)	
Age (y)	34.49 (10.32)	33.23 (10.54)	31.91 (10.19)	0.1022
Education				**<0.0001**
Less than primary	35 (30.97%)	12 (8.28%)	104 (54.45%)	
Primary	39 (34.51%)	69 (47.59%)	45 (23.56%)	
More than primary	38 (33.63%)	62 (42.76%)	40 (20.94%)	
Monthly Income (Quetzal)	4388 (9434)	2771 (4624)	58101 (9548)	0.5123
Literacy				**<0.0001**
Neither	8 (7.08%)	3 (2.07%)	45 (23.56%)	
Read Only	1 (0.88%)	0	3 (1.57%)	
Read and Write	104 (92.04%)	142 (97.93%)	142 (74.35%)	
Married/United (Ever)	87 (76.99%)	63 (43.45%)	128 (67.02%)	**<0.0001**
Use Health Services	105 (92.925%)	136 (93.79%)	174 (91.10%)	0.6354
Breast Exam (Heard of)	88 (77.88%)	112 (77.24%)	98 (51.31%)	**<0.0001**
Mammogram (Ever)	11 (9.73%)	21 (14.48%)	8 (4.19%)	**0.0043**
Pap (Ever)	70 (61.95%)	107 (73.79%)	83 (43.46%)	**<0.0001**
Last pap				**0.0212[b]**
Less than 6 months	14 (20%)	34 (31.78%)	13 (15.66%)	
Within the last year	18 (25.71%)	37 (34.58%)	16 (19.28%)	
Within the last 2-5 years	27 (38.57%)	28 (26.19%)	36 (43.37%)	
More than 5 years	10 (14.29%)	6 (5.61%)	18 (21.69%)	
VIA (Ever)	2 (1.77%)	1 (0.69%)	3 (1.57%)	0.6142
Ever Smoke	15 (13.27%)	27 (18.62%)	2 (1.05%)	**<0.0001[b]**
Ever Drink	30 (26.55%)	74 (51.03%)	24 (12.57%)	**<0.0001[b]**
Used Birth Control Injections	46 (41.44%)	59 (41.55%)	66 (35.68%)	0.8213
Used Oral Contraceptives	30 (27.03%)	64 (45.07%)	28 (15.14%)	**<0.0001[b]**
Used IUD	9 (8.11%)	22 (15.49%)	4 (2.16%)	**<0.0001[b]**
Use protection				**<0.0001[b]**
Always	11 (9.91%)	36 (25.35%)	9 (4.86%)	
Almost always	11 (9.91%)	15 (10.56%)	8 (4.32%)	
Sometimes	8 (7.215)	30 (21.13%)	14 (7.57%)	
Rarely	5 (4.50%)	9 (6.34%)	11 (5.95%)	
Never	62 (55.865)	41 (28.87%)	85 (45.95%)	
Unknown	14 (12.61%)	11 (7.75%)	58 (31.35%)	
Family Member with CC	21 (18.58%)	19 (13.10%)	10 (5.24%)	**<0.0001[b]**
Knowledge of HPV	78 (69.03%)	112 (77.24%)	90 (47.12%)	**<0.0001**
Believe They Are at Risk for CC				
Strongly Agree	11 (9.73%)	30 (20.69%)	25 (13.09%)	
Agree	51 (45.13%)	49 (33.79%)	87 (45.55%)	
Neutral	6 (5.31%)	7 (4.83%)	10 (5.24%)	
Disagree	15 (13.27%)	17 (11.72%)	6 (3.14%)	
Strongly Disagree	10 (8.85%)	22 (15.17%)	9 (4.71%)	
Unsure	20 (17.70%)	19 (13.10%)	54 (28.27%)	
Vaccinate Daughters for HPV				0.4056
Yes	94 (83.19%)	120 (82.70%)	156 (81.68%)	
No	10 (8.85%)	5 (3.45%)	15 (7.85%)	
Don't Have Daughters	8 (7.08%)	15 (10.34%)	14 (7.33%)	
Willing to Collect Sample at Home	61 (53.98%)	94 (64.83%)	104 (54.45%)	0.2802
Collected Sample	44 (38.94%)	56 (38.62%)	67 (35.08%)	0.7264

[a]p-values for means calculated using one-way ANOVA or Welch (if equality of variance is rejected); proportions using chi-squared test

[b]Fisher's Exact Test used due to small cell counts

Table A4: Population Characteristics Comparing HPV Test Result
Among Women Who Provided a Sample in Livingston and Santiago Atitlan

	HPV Negative N (%) or Mean (SD)	HPV Positive N (%) or Mean (SD)	p-value[a]
N	443	106	
Age (y)	34.96 (8.03)	34.67 (8.28)	0.7364
Ethnicity			0.0891
T'zutujil	289 (70.83%)	69 (70.41%)	
Ladino	32 (7.84%)	11 (11.22%)	
Garifuna	29 (7.11%)	12 (12.24%)	
Q'echchi	49 (12.01%)	6 (6.12%)	
Other	8 (1.96%)	0	
Education			**0.0262**
Less Than Primary	266 (65.68%)	54 (55.67%)	
Primary (at least some)	75 (18.52%)	30 (30.93%)	
More than primary	64 (15.80%)	13 (13.40%)	
Monthly Income (Q)	572.3 (117.4)	358.2 (685.8)	0.0869
Literacy			0.5610
Neither	173 (42.51%)	36 (36.73%)	
Read Only	5 (1.23%)	1 (1.02%)	
Read and Write	229 (56.27%)	61 (62.24%)	
Age at Marriage	19.98 (4.48)	19.13 (4.07)	0.0930
Use Health Services	372 (91.18%)	91 (92.86%)	0.5921
Breast exam (heard of)	120 (29.63%)	29 (29.90%)	0.9587
Mammogram (Ever)	17 (4.18%)	2 (2.04%)	0.3184
Pap (Ever)	293 (71.81%)	71 (72.45%)	0.9000
Last pap			0.9873
Less than 6 months	38 (13.335)	8 (11.76%)	
Within the last year	58 (20.35%)	16 (23.53%)	
Within the last 2-5 years	144 (50.5%)	35 (51.48%)	
More than 5 years	10 (13.51%)	9 (13.24%)	
VIA (Ever)	24 (5.91%)	6 (6.12%)	0.9368
Ever Smoke	8 (1.99%)	3 (3.13%)	0.4966
Ever Drink	37 (9.11%)	15 (15.63%)	**0.0597**
Use protection			0.2534
Always	38 (11.21%)	4 (4.82%)	
Almost always	19 (5.60%)	4 (4.82%)	
Sometimes	27 (7.96%)	11 (13.25%)	
Rarely	11 (3.24%)	4 (4.82%)	
Never	244 (71.98%)	60 (72.29%)	
Number of pregnancies	3.00 (2.07)	2.91 (1.78)	0.6500
Number of children	2.73 (1.74)	2.68 (1.59)	0.8097
Age at first pregnancy	19.90 (5.40)	19.72 (5.37)	0.7637
Family Member with Cervical Cancer	19 (4.73%)	9 (9.38%)	0.0757
Age at First Sexual Relation	19.26 (4.10)	18.48 (4.15)	0.1021
Number of Lifetime Partners	1.29 (1.10)	1.23 (0.66)	0.3982
Knowledge of HPV	104 (25.49%)	26 (26.53%)	0.8324

[a]p-values for means calculated using one-way ANOVA or Welch (if equality of variance is rejected); proportions using chi-squared test

Table A5: Differences Among Communities of Age-Eligible Indigenous Mayan Women
Age-Eligible Tz'tujil Women vs. Age-Eligible Q'echchi Women

	Tz'tujil - Santiago N (%) or Mean (SD)	Q'echchi - Livingston N (%) or Mean (SD)	p-value[a]
N	420 (68.74%)	191 (31.26%)	
Age (y)	36.25 (7.46)	31.91 (10.19)	**<0.0001**
Education			**<0.0001**
Less than primary	314 (75.12%)	104 (54.45%)	
Primary	64 (15.31%)	45 (23.56%)	
More than primary	40 (9.57%)	40 (20.94%)	
Monthly Income (Quetzals)	1433 (1547.3)	644.5 (2916.9)	**0.0135**
Literacy			**<0.0001**
Neither	225 (53.57%)	45 (23.56%)	
Read Only	7 (1.67%)	3 (1.57%)	
Read and Write	188 (44.76%)	142 (74.35%)	
Ever Married/United	412 (98.10%)	128 (67.02%)	**<0.0001**
Age at marriage	29.85 (137.8)	24.46 (20.33)	0.4463
Use health services	379 (90.24%)	174 (91.10%)	**0.7363**
Breast exam (Heard of)	53 (12.68%)	98 (51.31%)	**<0.0001**
Mammogram (Ever)	10 (2.38%)	8 (4.19%)	0.2206
Pap (Ever)	296 (70.48%)	83 (43.46%)	**<0.0001**
Last pap			0.2751
Less than 6 months	26 (9.25%)	13 (15.66%)	
Within the last year	57 (20.28%)	16 (19.28%)	
Within the last 2-5 years	153 (54.44%)	36 (43.37%)	
More than 5 years	45 (16.01%)	18 (21.69%)	
VIA (ever)	28 (6.70%)	3 (1.57%)	**0.0076**
Pap or VIA (Ever)	299 (71.19%)	83 (43.46%)	**<0.0001**
Ever Smoke	1 (0.24%)	2 (1.05%)	0.1907
Drink (regularly)	3 (14.29%)	1 (4.17%)	0.2341
Used BC injections	186 (44.71%)	66 (35.68%)	**0.0786**
Used Oral Contraceptives	47 (11.33%)	28 (15.14%)	0.1349
Used IUD	5 (1.20%)	4 (2.16%)	0.1497
Use protection			**<0.0001**
Always	29 (8.33%)	9 (4.86%)	
Almost always	11 (3.16%)	8 (4.32%)	
Sometimes	20 (5.75%)	14 (7.57%)	
Rarely	9 (2.59%)	11 (5.95%)	
Never	279 (80.17%)	85 (45.95%)	
Family Member with CC	12 (2.01%)	10 (5.24%)	**0.0408**
Age at First Sexual Relation	20.00 (4.48)	16.64 (2.45)	**<0.0001**
Currently Sexually Active	138 (82.63%)	42 (64.62%)	**0.0025**
Number of Lifetime Partners	1.08 (0.27)	1.19 (9.56)	**0.0061**
Knowledge of HPV	37 (8.81%)	90 (47.12%)	**<0.0001**
Believe At Risk for CC			**<0.0001**
Strongly Agree	105 (31.82%)	25 (13.09%)	
Agree	51 (15.45%)	87 (45.55%)	
Neutral	61 (18.48%)	10 (5.24%)	
Disagree	41 (12.42%)	6 (3.14%)	
Strongly Disagree	72 (21.82%)	9 (4.71%)	
Unsure	0	54 (28.27%)	
Vaccinate Daughters for HPV			**<0.0001**
Yes	301 (73.24%)	156 (81.68%)	
No	4 (0.97%)	15 (7.85%)	
Don't Have Daughters	106 (25.79%)	14 (7.33%)	
Willing to Sample in Home	394 (95.63%)	104 (54.45%)	**<0.0001**
Collected Sample	395 (94.05%)	67 (35.08%)	**<0.0001**

[a]p-values for means calculated using two-sample t-test; proportions using chi-squared test

Table A6. High-Risk HPV Prevalence Distribution		
	Total Sample N	**High-Risk HPV Positive % (N)**
Total	549	19.31% (106)
Santiago Atitlán	413	18.64% (77)
Livingston	136	21.32% (29)
Chi-Squared=0.4715; p-value=0.4923		

Appendix B – Additional Regression Tables

Table B1. Prevalence Ratio of Actual Sample Collection in Livingston

Log-Binomial Regression: Prevalence Ratio of Sample Collection

Variable	**PR^{M1}**	**95% CI**		**PR^{M2}**	**95% CI**		**PR^{M3}**	**95% CI**	
Literacy (Y)	**1.94**	**1.23**	**3.05**	**1.91**	**1.23**	**1.91**	**1.42**	**1.01**	**2.00**
Marriage (Never)	1.17	0.95	1.42	1.11	0.94	1.32	1.08	0.91	1.30
Hx of Pap/VIA (Never)	**0.87**	0.68	1.10	0.83	0.64	1.07	0.97	0.78	1.20
Smoking (Y)	**0.98**	0.69	1.39	1.10	0.76	1.60	1.11	0.80	1.55
Drinking (Y)	**1.18**	**1.18**	**1.47**	**1.14**	**1.14**	**1.48**	1.11	0.89	1.38
IUD Use (Y)	1.42	1.10	1.84	1.24	0.91	1.69	1.30	0.94	1.81
Family Hx of CC (N)	**0.85**	**0.63**	**1.15**	**0.85**	**0.62**	**1.15**	**0.98**	**0.74**	**1.59**
Believe at Risk for CC (Y)	1.00	0.78	1.30	1.00	0.76	1.32	1.01	0.82	1.24

M1: unadjusted log-binomial model
M2: adjusted for age, ethnicity, and number of lifetime sexual partners
M3: all variables included and adjusted for age, ethnicity, and number of lifetime sexual partners

Table B2. Odds Ratio of Willingness to Collect a Sample in Livingston: Stratified Analysis

Logistic Regression: Prevalence Ratio of Actual Sample Collection Stratified Across Ethnic Groups

Sample Collection Group	**Literacy (Y)**		**Marriage (Never)**		**Hx of Pap/VIA (Never)**	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
All Ethnic Groups	**3.21**	**(1.52, 6.75)**	1.57	(0.93, 2.64)	0.76	(0.45, 1.32)
Ladino	3.81	(0.57, 25.48)	1.10	(0.32, 3.74)	2.27	(0.69, 7.45)
Garifuna	2.86	(0.24, 34.17)	1.45	(0.65, 3.22)	0.85	(0.28, 2.57)
Q'echchi	**2.77**	**(1.10, 7.02)**	1.85	(0.76, 4.50)	0.46	(0.21, 1.02)

Models additionally adjusted for age and number of lifetime sexual partners

Table B3. Odds Ratio of Willingness to Collect a Sample in Livingston

Logistic Regression: Odds Ratio of Actual Sample Collection

Sample Collection Group	Literacy (Y)		Marriage (Never)		Hx of Pap/VIA (Never)		Drinking (Ever)		IUD Use	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Non-Indigenous	5.18	(0.95, 28.30)	1.39	(0.73, 2.65)	1.75	(0.75, 4.06)	1.29	(0.67, 2.45)	2.32	(0.82, 6.52)
Indigenous	2.53	(0.98, 6.52)	1.79	(0.73, 4.39)	0.44	(0.20, 0.99)	1.93	(0.57, 6.50)	-	-

Models additionally adjusted for age and number of lifetime sexual partners

Table B4. Prevalence Ratio of Willingness to Collect at Home in Livingston

Log-Binomial Regression: Prevalence Ratio of Willingness to Sample at Home

Variable	PR^{M1}	95% CI		PR^{M2}	95% CI		PR^{M3}	95% CI	
Literacy (Y)	**1.51**	**1.09**	**2.10**	**1.45**	**1.02**	**2.06**	**1.08**	**0.85**	**1.36**
Marriage (Never)	1.15	0.97	1.36	1.12	0.94	1.34	1.09	0.93	1.28
Hx of Pap/VIA (Never)	0.83	0.68	1.02	0.82	0.67	1.01	0.95	0.81	1.12
Smoking (Y)	1.17	0.92	1.49	1.11	0.83	1.49	1.06	0.80	1.39
Drinking (Y)	1.17	0.99	1.38	1.13	0.93	1.38	1.00	0.85	1.19
IUD Use (Y)	**1.34**	**1.11**	**1.61**	1.23	0.99	1.54	1.13	0.86	1.48
Family Hx of CC (N)	0.87	0.69	1.09	0.89	0.72	1.11	0.98	0.78	1.23
Belief CC is Likely (Y)	1.14	0.86	1.51	1.22	0.89	1.67	0.97	0.83	1.13

M1: unadjusted log-binomial model
M2: adjusted for age, ethnicity, and number of lifetime sexual partners
M3: all variables included and adjusted for age, ethnicity, and number of lifetime sexual partners

Table B5. Odds Ratio of High-Risk HPV

Logistic Regression: HPV Prevalence in Livingston and Santiago

Variable	OR^{M1}	95% CI		OR^{M2}	95% CI		OR^{M3}	95% CI	
Education									
Less than Primary	Ref.			Ref.			Ref.		
Primary	1.26	0.78	2.03	1.11	0.64	1.09	0.87	0.14	5.26
More than Primary	0.95	0.49	1.84	0.76	0.35	1.65	0.84	0.14	5.26
Marriage (Never)	0.93	0.43	1.98	0.74	0.31	1.78	0.37	0.12	1.20
Hx of Pap/VIA (Y)	1.01	0.62	1.65	1.03	0.61	1.73	2.42	0.64	9.09
Smoking (Y)	1.59	0.41	6.10	1.28	0.30	5.43	0.93	0.15	5.81
Drinking (Y)	1.85	0.97	3.52	1.59	0.74	3.44	1.79	0.53	6.06
IUD Use (Y)	1.03	0.34	3.12	1.36	0.43	4.35	7.40	0.82	67.20
Family Hx of CC (N)	0.48	0.21	1.10	0.57	0.24	1.36	1.64	0.39	6.86
Number of Lifetime	1.81	0.89	3.65	1.13	0.58	2.20	1.47	0.54	4.02

Sexual Partners (more than one)									
Belief CC is Likely (Y)	1.26	0.64	2.46	0.69	0.40	1.17	-	-	-

M1: unadjusted logistic regression model
M2: adjusted for age, ethnicity, and age^2
M3: all variables included and adjusted for age, ethnicity, and age^2
- variable not included in model

Table B6. Prevalence Ratio of Ever Being Screened for Cervical Cancer in Livingston

Log-Binomial Regression: If a Woman Has Never Been Screened in Livingston with Either VIA or Pap Smear

Variable	**PR^{M1}**	**95% CI**		**PR^{M2}**	**95% CI**		**PR^{M3}**	**95% CI**	
Literacy (Y)	**1.70**	**1.23**	**2.36**	**1.58**	**1.13**	**2.22**	1.14	0.92	1.42
Marriage (Never)	0.95	0.81	1.12	0.96	0.82	1.12	0.99	0.84	1.17
Smoking (Y)	**1.21**	**1.02**	**1.45**	1.01	0.85	1.21	0.97	0.78	1.22
Drinking (Y)	**1.29**	**1.13**	**1.48**	1.09	0.97	1.23	1.07	0.91	1.25
IUD Use (Y)	**1.23**	**1.03**	**1.47**	1.08	0.88	1.32	1.08	0.85	1.37
Family Hx of CC (N)	0.87	0.72	1.06	0.98	0.79	1.20	0.99	0.84	1.18
Belief CC is Likely (Y)	1.11	0.88	1.41	1.01	0.81	1.24	1.02	0.78	1.32

M1: unadjusted log-binomial model
M2: adjusted for age, ethnicity, and number of lifetime sexual partners
M3: all variables included and adjusted for age and ethnicity

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HPV Self-Sampling Acceptability in Rural and Indigenous Communities in Guatemala: A Cross-Sectional Study

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HPV Self-Sampling Acceptability in Rural and Indigenous Communities in Guatemala: A Cross-Sectional Study

Audrey Murchland[1], Anna Gottschlich[1], Kristin Bevilacqua[1], Andres Pineda[2], Berner Andrée Sandoval-Ramírez[3], Christian S. Alvarez[1], Gina Ogilvie[4], Thomas E Carey[5], Mark Prince[6], Michael Dean[7], Carlos Mendoza-Montano[2], Alvaro Rivera-Andrade[2], Rafael Meza[1]

1. Department of Epidemiology, School of Public Health, University of Michigan, 1415 Washington Heights, Ann Arbor, Michigan 48103

2. Institute of Nutrition of Central America and Panama-INCAP, Calzada Roosevelt 6-25 zona 11, Apartado Postal 1188 Guatemala City, Guatemala 01011

3. Functional Nutrition, Oxidation, and Cardiovascular Diseases Group (NFOC-Salut), Universitat Rovira i Virgili, Hospital Universitari Sant Joan (HUSJR), Sant Llorenç, 21, 43201, Reus, Spain

4. Clinical Prevention Services, BC Centre for Disease Control, 655 W 12th Ave, Vancouver, British Columbia V5Z4R4, Canada

5. Department of Otolaryngology-Head and Neck Surgery and Department of Pharmacology, University of Michigan, 5311 Medical Science Unit I 1301 Catherine St., Ann Arbor, Michigan 48109

6. Department of Otolaryngology, University of Michigan, 1500 E Medical Center Dr SPC 5312, Ann Arbor, Michigan 48109

7. Laboratory of Translational Genomics, Division of Cancer, Epidemiology and Genetics, National Cancer Institute, Gaithersburg, MD USA

Corresponding Author:
Rafael Meza, Ph.D.
SPH II, Room 5033, 1415 Washington Heights
Ann Arbor, MI 48109-2029
E-mail: rmeza@umich.edu
Telephone: +1 (734) 763-1946

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ABSTRACT

Introduction: Cervical cancer disproportionately burdens low- and middle-income countries (LMICs) such as Guatemala. Self-collection testing for human papillomavirus (HPV) has been suggested as a form of cervical cancer screening to facilitate access in LMICs. This study assessed and compared the acceptability of self-collection HPV testing in two rural, indigenous and ethnically distinct communities in Guatemala: Santiago Atitlán, Sololá and Livingston, Izabal.

Methods: All participants, women between ages 18 and 60, completed a questionnaire. Eligible participants were also asked to self-collect a vaginal sample and complete a questionnaire regarding comfort and acceptability. Self-collected samples were tested for high-risk HPV using the real-time PCR Hybribio kit.

Results: In the indigenous community of Santiago Atitlán, of 438 age-eligible participants, 94% completed self-collection. Of those, 81% found it comfortable and 99% were willing to use it as a form of screening. In the multi-ethnic (Afro-Caribbean, indigenous) community of Livingston, of 322 age-eligible participants, 53% chose to self-collect. Among those who took the test, 87% found it comfortable and 100% were willing to use it as a form of screening. In Livingston, literacy (can read and/or write versus cannot read or write) was higher in women who chose to self-collect (prevalence ratio, 2.28; 95% CI: 1.39, 3.72). Ethnicity, history of screening, and reproductive history were not associated with willingness to self-collect in Livingston. Overall, 19% (87/549) of samples tested positive for high-risk HPV.

Conclusion: Among women willing to self-collect in rural and indigenous communities in Guatemala, self-collection for HPV testing is highly acceptable. However, willingness to try self-collection might vary across communities and settings. Further research is necessary to determine what factors influence a woman's choice to self-collect.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- To our knowledge, little is known about the acceptability of self-collection HPV testing across the diverse communities within Guatemala and Latin America, and in particular among indigenous populations.
- Our study provided not only a larger sample size compared with previous studies but was also conducted in two differing communities.
- Due to both the sensitive nature of the questions related to sexual history, it may be possible that a social desirability bias may have resulted in over reporting of perceived "good behaviors", such as screening or use of protection, in addition to under-reporting of perceived "bad behaviors", such as number of lifetime sexual partners and other sexual behavior measures.
- Sampling methods differed between the two communities due to the lack of reliable census counts in one community, but our sample in this community is reflective of the overall population structure in terms of ethnic, age and other metrics, suggesting that influential selection bias into the study might be limited.

INTRODUCTION

Cervical cancer, primarily caused by human papillomavirus (HPV) infection, has a very good prognosis when detected in premalignant or early malignant stages[1]. However, it disproportionately burdens low- and middle-income countries (LMICs), such as Guatemala, compared to high-income countries (HICs)[2-4]. HICs currently use Pap smears to detect abnormal cervical lesions that can be removed, greatly reducing the risk of cervical cancer[3 5]. However, there are many barriers to implementing successful Pap smear (cytology-based) screening programs in LMICs, including difficulties establishing sustainable laboratory infrastructure, training and retaining adequate numbers of trained pathologists or cytologists, overburdened primary care clinics, and time and travel limitations for women in reaching screening locations[1 6 7]. Due to these factors and others, the percentage of women in Guatemala who are screened for cervical cancer remains low; in 2014, only 49.8% of women (15-49 years of age) reported ever having a Pap smear. Thus, significant improvements in screening or program implementation are paramount to improving cervical cancer outcomes in Guatemala[3 8 9].

Since more than 90% of cervical cancers are caused by the HPV virus, HPV testing has been suggested as a possible alternative, primary form of cervical cancer screening[10-12]. When used in combination with Visual Inspection with Acetic Acid (VIA) or Pap smears in low-income settings, HPV testing has been shown to provide significant improvements in the detection of advanced premalignant lesions and cancer in sensitivity as compared to VIA or Pap smear alone, as only women who test positive for HPV need to follow up with further screening[13-16]. Previous studies have also confirmed that HPV self-swab kits are comparable to physician administered samples in their ability to detect carcinogenic, high-risk HPV [17 18]. Thus, at-home HPV sample collection, with referral to further screening for those positive for high-risk

HPV, may be both more acceptable within low-income communities and more programmatically feasible[6 7 19]. Moreover, a 2015 meta-analysis showed that HPV self-sampling, particularly in opt-in programs, increased participation in cervical cancer screening programs. However, further work is needed to evaluate acceptable opt-in programs for women[20].

Studies have shown that HPV self-sampling is generally acceptable among women in low and high resource settings as well as immigrant, rural, vulnerable populations[21-31]. To our knowledge, however, little is known about the acceptability of self-collection HPV testing across the diverse communities within Guatemala, and in particular among rural and indigenous populations. In a pilot cross-sectional study assessing the acceptability of HPV self-collection among 200 women in the Mayan community of Santiago Atitlán, Guatemala, a self-swab HPV test was found to be a highly acceptable form of screening[32]. Over 80% of women said that they preferred using a self-swab kit in their home rather than being screened at a doctors' office. However, this pilot study was limited to a relatively small sample in a single, largely homogeneous community, limiting the generalizability of the results to other rural and indigenous communities in Guatemala. Further research is thus needed to evaluate the acceptability of self-collection testing among more diverse rural and indigenous populations within Guatemala, which is very diverse, with over 23 official languages and many indigenous groups, most but not all descendants from the Mayan civilization. The purpose of this study was to further assess and compare the acceptability of self-collection HPV testing in two rural, ethnically distinct communities in Guatemala: Santiago Atitlán and Livingston, Izabal.

METHODS

Study Communities

Santiago Atitlán, Sololá is a rural community located on Lake Atitlán, in the southwest region of Guatemala, 75 miles west of Guatemala City. The Tz'utujil, a Mayan descendant ethnic group, inhabits the region, which surrounds Lake Atitlán. The primary language of Santiago's inhabitants is Tz'utujil, and over half of the villagers speak Spanish as a second language[32]. The majority of women in Santiago Atitlán have at most a primary education. Additionally, as a conservative, religious community, it is highly uncommon for women to either drink or smoke, and almost all women in have previously reported having only one lifetime sexual partner[32].

Livingston, Izabal is located on the Caribbean coast of the country and is a rural community, only accessible by boat, that is the primary Garífuna settlement in Guatemala. The Garífuna people are considered a unique ethnic group with their own language, culture, and cuisine. Additionally, there are large populations of other ethnic and cultural groups located in Livingston including Q'eqchi' (Mayan descent), Ladinos (non-Mayan descent), and populations of Indian descent. Most women in Livingston are believed to have at least basic primary education.

Patient and Public Involvement

The patients were not involved in the development of the research questions, outcome measures or study design. The patients were also not involved in the recruitment and performance of the study. However, the public, Guatemalan physicians, scientists, and community health workers, were involved in the development of the question, design, validation, recruitment, and conduct of the study. Local community health workers were involved in the validation of the survey and study protocol, recruited participants and conducted the interviews, and assisted in providing test results to patients. Guatemalan physicians contributed to

development of the research question and study design, organized the laboratory testing, led and assisted with community health worker training, and provided HPV test results to patients. Local laboratory scientists contributed to the study design and conducted the HPV laboratory testing. The continued collaborations with these team members will be used to disseminate study results to patients and Guatemalan officials via publications, presentations, and meetings.

Eligibility and Recruitment

Trained community health workers (CHWs) in both communities actively recruited participants through home visits. All CHWs were bilingual and spoke both Spanish and either Tz'utujil, Q'eqchi, or Karif (the language of the Garifuna) depending on the location they were working in. Households in Santiago Atitlán were selected at random using stratified multi-level sampling based upon maps and population counts of the communities available through the local municipal office and were kept consistent with previous sampling methods[32]. Households in Livingston were selected at random using convenience sampling due to lack of reliable census data at the neighborhood-level. Sampling methods were, otherwise, kept the same as those in Santiago Atitlán.

Selected households that had at least one woman available between the ages of 18 and 60 were invited to participate in the survey-component of the study. For households with more than one eligible woman willing to participate, the female in the household whose birthday was closest to the date of the interview was enrolled in the study. Exclusion criteria consisted of past hysterectomy or previous cervical cancer. Only women between the ages of 25 and 54 were asked to provide a sample, in accordance with Guatemala's current screening recommendations[33]. Additionally, pregnant women, women currently menstruating, and women who had never been sexually active were also excluded from providing samples but could

participate in the survey component. Approximately 62% and 90% of eligible women contacted were willing to participate in the study in Santiago and Livingston, respectively. A target sample size of 500 per community was determined to be able to detect a 5% difference in self-sampling acceptability with 80% power, assuming a 95% acceptability in Santiago Atitlan based on the pilot.

Survey

Data collection consisted of two main components: the surveys and the HPV self-collection tests. Local CHWs in each community were trained as interviewers in the appropriate techniques and protocols before beginning home visits. Two CHWs visited each randomly selected household together and read a recruitment script to a female household member to determine the household's eligibility. CHWs administered the survey and provided kits to collect HPV samples only to willing, eligible participants. Surveys were administered in private rooms of the participant's house to minimize response bias to sensitive questions.

The survey questionnaire included 153 questions concerning demographics, risk factors for cervical cancer and HPV, self-reported attitudes towards screening, healthcare service use, and knowledge of cervical cancer and HPV. The survey was developed from the pilot study survey and validated as part of the CHW and translator training to ensure correct translation and cultural relevancy[32]. Each survey was administered by the CHWs using electronic tablets and the Qualtrics offline app.

All women who participated in the study were compensated with a voucher for a free Pap smear or VIA at a local health clinic. Women in both communities can access free VIAs (Santiago) or Pap Smears (Livingston) in the local public health system, but if they chose to use a private clinic instead of the public clinic, the voucher covered their fees.

HPV Self-Collected Samples

The HPV samples were collected using HerSwab kits, a self-collection sampling method [32 34 35]. If a participant was willing to provide a sample, instructions and graphical materials were provided and the participant collected the sample in a separate, private room from the CHWs. Participants who collected a sample then completed a short post-sample survey with the CHWs of three questions regarding ease, comfort, and acceptability of the sampling method: "How easy was the self-collection swab?"; "How comfortable was the self-collection swab?"; and "Would you be willing to collect a sample every 2-3 years to detect HPV as a form of cervical cancer screening?".

After collection, samples were kept in small, refrigerated coolers carried by the CHWs until they were returned to the main study office at the end of the day where samples were then processed to stabilize sample life. The brush component of the HerSwab kit was cut into a 15-mL test tube using lab scissors. The lab scissors were sterilized using alcohol and an open flame between each sample. Each tube was filled with 5mL of Scope mouthwash using a pipette, and tubes were sealed using a cap and parafilm paper[36]. Mouthwash is a reliable, low-cost transport medium for DNA samples and was used to reflect likely standard operating procedures of HPV screening program implementation in Guatemala[37]. Each sample was labeled with the participant's unique identifier. Time of sample processing and condition of sample were recorded.

Stabilized samples were sent to a molecular biology laboratory at the Institute of Nutrition of Central America and Panama (INCAP) in Guatemala City for testing. Samples were tested using the real-time polymerase chain reaction (PCR) Hybribio HR-13 kit[38 39]. Samples were processed according to the manufacturers protocol and modified to use a 10 ul reaction

volume for the real-time PCR and run on an ABI-7000[36]. After testing, samples were labeled as positive for HR-HPV, negative, or, if both the HPV probe and the internal control were negative, inconclusive. If a sample test was inconclusive during the first test, it was run an additional time using a 20 ul reaction volume, and if no result was obtained, the test was deemed inconclusive.

Follow-Up

A local CHW provided negative and inconclusive results over the phone or through a home visit. Positive results were provided in-person by a study physician who referred participants to their local community health clinic for follow-up and further cervical cancer screening. All participants who couldn't be reached at the study conclusion were re-contacted either at 6 months or one year to provide them with their results. Although women with negative results were not explicitly recommended to attend the clinic, all participants were encouraged to get screened using the voucher provided at the local clinic to support their engagement with local preventative services. Participants who were found to be positive for advanced lesions as a result of follow-up screening were referred for care through the free public health infrastructure in Guatemala, as is currently standard practice. Due to the ongoing nature of the project, data on follow-up screening and care are still in the collection process.

Outcomes and Statistical Analysis

Willingness and acceptability of self-collection testing, knowledge of HPV, and risk factors were evaluated in both communities and across ethnic groups in Livingston, Izabal. Willingness was measured as whether or not a woman chose to self-collect a sample to be tested for HPV (actual self-collection). The acceptability of sample collection was only assessed for those who self-collected a sample and was analyzed using the post-self-swab survey questions described previously.

Due to lower rates of actual self-collection in Livingston, differences between Livingston women willing and those not willing to collect a sample were evaluated using two-sample t-tests for means, chi-squared tests for proportions, and Fisher's Exact test for low cell counts. Most women tried self-collection in Santiago, so we restrict these analyses to Livingston. Analyses were additionally restricted to age-eligible women in Livingston with complete covariate information (N=134 or 29.4% excluded due to age-ineligibility and N=13 or 2.9% excluded due to missing covariates). Specifically, we excluded 1 participant missing marital status, 1 participant missing regular drinking status, 4 participants missing IUD use, and 2 participants missing number of lifetime sexual partners, resulting in a final sample size N=309 for analyses evaluating willingness to try self-collection.

The main exposures explored for willingness to try self-collection included: ethnicity, literacy, marital status, history of Pap smear or VIA, alcohol use, and IUD use. Statistical analyses were run using log-binomial regression and models were adjusted for age, ethnicity, and number of lifetime sexual partners. Final models were further stratified across ethnic groups to evaluate potential effect modification.

Covariates were parameterized as: able to read and/or write (literate) versus unable to either read or write (illiterate), ever married versus never married, ever had a Pap or VIA versus never, regular drinker versus non-regular drinker, ever had an IUD versus never, ever smoked versus never smoked, continuous age, and number of lifetime sexual partners (one versus more than one).

Data cleaning and analyses were carried out using SAS 9.4[40].

RESULTS

In total, 956 women were recruited to participate into the study: 500 women in Santiago Atitlán and 456 women in Livingston. Demographic characteristics differed between the two communities: 69.4% of the participants in Santiago Atitlán had less than primary education and 96.4% were of Tz'tujil ethnicity. In contrast, only 33.9% of the participants in Livingston had less than primary education and three ethnic groups were represented: 41.9% Q'echi, 32% Garifuna, and 24.8% mixed ethnicity (Ladino) (Table 1).

Knowledge and attitudes regarding HPV and cervical cancer also differed between the communities. Only 11.8% of participants in Santiago reported previous knowledge of HPV as compared to 62.7% of Livingston participants. However, when asked about the seriousness of cervical cancer, most participants in both communities responded "very" or "extremely" (74.8% Santiago and 80.9% Livingston) (Appendix).

Self-reported history of access to healthcare also appeared higher in Livingston than in Santiago. For example, only 5.0% of participants in Santiago responded that they had ever been tested for human immunodeficiency virus [41] while 57.8% of Livingston participants responded that they had been previously tested. Additionally, a higher proportion of participants in Livingston consistently reported using contraception, always using protection during sexual intercourse, and using tobacco and alcohol than in Santiago (Table 1).

Self-Collection Willingness

We found significant differences between the communities with respect to willingness to try self-collection sampling. In Santiago Atitlán, of 438 age-eligible participants, 93.6% (N=410) chose to self-collect. In Livingston, of 322 age-eligible participants, 52.5% (N=169) chose to self-collect (Table 2).

We evaluated factors that affected the willingness to try self-collection testing in Livingston. Literacy, the use of health services, and beliefs regarding cervical cancer differed between age-eligible women who self-collected a sample compared to those who did not (Table 3). Additionally, 31.4% of the women who ended up not providing a sample had responded previously in the questionnaire that they indeed would be willing to collect a self-swab sample at home (Figure 1). While data is unavailable regarding how many age-eligible women were ineligible to collect a sample due to menstruation or pregnancy, this likely does not entirely account for all women who ultimately chose not to self-collect.

Literacy was significantly higher among women who self- collected a sample in Livingston compared to those who did not (crude PR 2.07; 95% CI: 1.29, 3.35; adjusted PR, 2.28; 95% CI: 1.39, 3.72) (Tables 4-5). Regular drinking was also higher among women who self-collected but not significant (crude PR 1.19; 95% CI: 0.96, 1.48; adjusted PR 1.16; 95% CI 0.91, 1.49) (Tables 4-5). Additionally, IUD use and never being married were higher among women who self-collected a sample in Livingston (IUD use, crude PR 1.47; 95% CI: 1.14, 1.91; adjusted PR 1.42; 95% CI: 1.07, 1.87; never married, crude PR 1.20; 95% CI: 0.97, 1.49; adjusted PR 1.16; 95% CI: 0.93, 1.45) (Table 4-5). When stratifying either by indigenous or non-indigenous group or by ethnic group, the association between literacy and actual sample collection remained positive. However, this relationship only remained statistically significant among Q'echchi participants.

Self-Collection Acceptability and Comfort

Among those who did collect a sample, the self-collection testing was highly acceptable in both communities. Of Santiago participants who self-collected, 81.4% found it comfortable and 84.8% reported that the HerSwab was easy to use. Among Livingston participants who self-

collected, 87.0% found it comfortable and 87.0% reported it was easy to use. Among those who chose to self-collect, almost all participants in both locations reported that they were willing to use it as a form of cervical cancer screening (99.5% in Santiago and 100% in Livingston) (Table 2).

HPV Prevalence

Overall, 19% of samples tested positive for high-risk HPV (N=549). 18.7% of samples from Santiago Atitlán (N=77) tested positive for high-risk HPV and 21.3% of samples from Livingston (N=29) tested positive, but this difference was not statistically significant (p-value=0.4923). In total, 94% of participants who sampled in Santiago Atitlán and 88.5% of participants who sampled in Livingston were provided with their test results. Overall, 12.3% of HPV tests were found to be inconclusive (N=44 (9.6%) from Santiago Atitlán and N=33 (19.5%) from Livingston).

DISCUSSION

In this study, we assessed the acceptability of HPV self-collection testing as an alternative form of primary cervical cancer screening in indigenous and rural communities in Guatemala. We found that self-collection appears to be highly acceptable among women who tried it, independent of community and ethnicity. Most women reported that self-collection was comfortable and easy to use, and almost all women who tried it reported being willing to use it as a form of cervical cancer screening in the future. These results are consistent with other studies looking at self-collection acceptability both within Guatemala and other LMICs[27 32]. This study was further able to build upon previous studies and provide important information regarding HPV self-collection testing acceptability at the community level, and in a community that had not been previously evaluated.

Our study also found, however, that there were differences between communities in willingness to try self-collection. Willingness to try self-collection testing remained consistently high among participants in Santiago Atitlán as reported in the pilot study conducted in 2015 (93% in 2015 versus 93.6% in 2016)[32]. In Livingston, however, even among women who first responded in the survey or consent form that they would be willing to collect a sample, actual self-collection was lower. We found that willingness to self-collect in Livingston was consistently associated with higher levels of literacy and prior IUD use. In contrast, ethnicity, history of cervical cancer screening, and reproductive history were not associated with willingness to self-collect. Stratified analyses revealed that there were no qualitative differences in the association between literacy and sample collection across ethnic groups in Livingston.

The results suggest that HPV self-collection testing program implementation may need to target populations based on relative levels of literacy within communities. A previous study examining HPV acceptability and intention in the UK similarly found that low education and self-efficacy were associated with low sampling intentions[30]. In Guatemala, the inability to either read or write in Spanish may negatively influence a woman's perceived self-efficacy and her confidence in navigating public health infrastructure or self-collecting a vaginal sample, particularly if her surrounding community has high levels of literacy. This population would greatly benefit from HPV self-collection testing as a primary form of cervical cancer screening due to its strength in concentrating less accessible and more invasive screening modalities only towards those that are at high-risk (i.e., positive for HPV). Our results in Livingston suggest that it might be critical that, if implemented, HPV screening and education programs are tailored such that they are more accessible to low-literacy populations and, thus, increase perceived self-efficacy in navigating the existing public health infrastructure.

High prevalence of self-collection testing in Santiago Atitlan, a community with low literacy levels, as compared to the low rates of self-collection testing among those with low literacy in Livingston may reflect larger community differences in awareness or access to screening modalities rather than a lack of effect of literacy in Santiago or an effect of ethnicity. Although women from Santiago reported slightly higher rates of ever receiving cervical cancer screening than women in Livingston, women in Livingston report much higher rates of recent cervical cancer screening than women in Santiago. Santiago Atitlán remains largely deficit in accessible and affordable cervical cancer screening while Livingston has regular, public or private, screening campaigns in the community. This difference in general community access and infrastructure, then, may be acting as an effect modifier on the association between literacy and screening between these two communities, suggesting that self-collection might be better received at first in communities that do not have other alternatives, whereas some initial skepticism might be found in places with existing cervical screening programs, independently of their quality and efficacy. More research is necessary to evaluate if self-efficacy, relative literacy level, or general community access to healthcare resources and screening play larger barriers for women in trying self-sampling HPV testing. However, the high rates of acceptability and willingness to retake among women who self-collected in both communities suggest that once experienced, self-collection is a valid, and even preferred, alternative to other screening modalities from the women's perspective.

Although based on a different HPV test than in our pilot study (Hybribio HR13 vs. Anyplex 28), a similar prevalence of high-risk HPV was found in Santiago between 2015 and 2016 (17.4% versus 19.3%)[32]. Of note, there were no significant differences in high-risk HPV

prevalence between ethnic groups in Livingston, and there was not a statistically significant difference between Santiago Atitlán and Livingston with regards to prevalence.

Our study provided not only a larger sample size compared with previous studies but was also conducted in two differing communities. This is a strength because Guatemala is an extremely diverse country with over 23 languages, distinct ethnicities, and a history of large economic and social inequalities. Thus, generalizing the evaluations of a health program's acceptability and feasibility to the whole country is generally difficult. However, because we evaluated two very different rural multi-ethnic communities, our results may reflect some of the future obstacles and considerations necessary in implementing self-swab HPV testing in such a diverse country as Guatemala than was previously available. In fact, our results also complement the findings of the ongoing careHPV Scale-Up implementation, which is assessing the performance of HPV testing, including self-collection testing, within urban settings in Guatemala[42-44].

There are several limitations to our study. Due to both the sensitive nature of the questions related to sexual history, it may be possible that a social desirability bias may have resulted in over reporting of perceived "good behaviors", such as screening or use of protection, in addition to under-reporting of perceived "bad behaviors", such as number of lifetime sexual partners and other sexual behavior measures. We tried to minimize the possibility of this bias by maintaining confidentiality with participants. Also, women may report their history of screening or utilization of health care resources incorrectly if they had limited information or understanding of these services. This may be exaggerated in women with low literacy and thus explain potential over reporting of prior cervical cancer screening in Santiago Atitlan. Additionally, because sampling methods differed between the two communities due to the lack

of reliable census counts in Livingston, there may be differences between the communities in potential selection bias into the study and more limited comparability of the results. However, our sample in Livingston is reflective of the overall population structure of Livingston in terms of ethnic, age and other metrics, suggesting that influential selection bias into the study might be limited[45].

Screening program implementation is a major challenge in LMIC settings, HPV self-swab testing may serve as a helpful tool in concentrating less accessible and more expensive and invasive screening modalities only towards those that are at high-risk (i.e., positive for HPV). However, as the results in Livingston showed, there are many complex features related to implementing HPV screening that will need to be evaluated before program adoption of such programs. Due to the longitudinal component of our study, future research with our study participants will hopefully help elucidate how HPV self-collection testing may affect women's decisions to pursue further cervical cancer screening and follow-up care in their local communities after HPV testing and receiving their results. Additionally, these data may reveal other downstream facilitators or barriers to screening that will influence the overall success of HPV self-swab testing implementation in these communities.

CONCLUSION

The results of our study add to the literature on the potential of HPV self-collection testing in LMICs, demonstrating its acceptability in two very different communities in rural Guatemala. The high rates of acceptability and willingness to retake among women who self-collected in both communities suggest that once experienced, self-collection is a valid, and even a preferred, alternative to other screening modalities from the women's perspective. However, the difference in willingness to try self-collection between these communities suggests that

relative literacy levels and the availability and quality of existing programs may affect attitudes towards new screening modalities. Future research should focus on increasing the generalizability of these findings by evaluating additional communities within Guatemala for differences in willingness to try self-collection sampling and further elucidate the potential barriers to accessing and utilizing cervical cancer modalities, including HPV self-collection sampling.

LIST OF ABBREVIATIONS

CC – Cervical Cancer

CHW – Community Health Worker

CI – Confidence Interval

HICs – High-Income Countries

HIV – Human Immunodeficiency Virus

HPV – Human Papillomavirus

HR-HPV – High-Risk Human Papillomavirus

INCAP – Institute of Nutrition of Central America and Panama

IUD – Intra-Uterine Device

LMICs – Low and Middle-Income Countries

OR – Odds Ratio

PCR – Polymerase Chain Reaction

PR – Prevalence Ratio

VIA – Visual Inspection with Acetic Acid

DECLARATIONS

Ethics Approval and Consent to Participate

The University of Michigan Institutional Review Board (HUM00096559) and the Institute of Nutrition of Central America and Panama Institutional Review Board (MI-CIE-16-009) approved study protocols. All participants gave oral and written informed consent prior to participation in the study. The consent was documented by a signature or fingerprint of the participant, the surveyors, and a witness.

Consent for Publication

The authors of this paper have all reviewed its contents and consent for its publication.

Data Sharing Statement

Due to the sensitive nature of the data collected, IRB restrictions, and ongoing data collection, study data is stored at the University of Michigan. Interested parties may contact the corresponding author to request access to de-identified datasets for specific research questions related to the study. The authors welcome further collaboration but reserve the right to retain data to protect study participants.

Competing Interests

The authors have no competing interests to declare.

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Authors' Contributions

PIC - Planning and Key Intellectual Contribution
DC – Data Collection and Project Management
SP – Sample Processing, Laboratory Management, and Test Results
SA – Statistical Analysis and Data Management
W – Writing
E – Editing

Audrey Murchland – PIC, DC, SP, SA, W, E
Anna Gottschlich – PIC, DC, SP, W, E
Kristin Bevilacqua – PIC, DC, SP, E
Andres Pineda – PIC, DC, SP, E
Berner Andrée Sandoval-Ramírez – PIC, DC, SP, E
Christian Alvarez – PIC, E
Gina Ogilvie – PIC, E
Thomas E Carey – PIC, SP, E
Mark Prince – PIC, SP, E
Michael Dean – PIC, SP, E
Carlos Mendoza-Montano – PIC, SP, E
Alvaro Rivera-Andrade – PIC, DC, SP, E
Rafael Meza – PIC, DC, SP, SA, W, E

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TABLES

Table 1. General Population Characteristics Among All Participants			
	Santiago Atitlán % (N) or Mean (SD)	Livingston N (%) or Mean (SD)	p-value
Age (y)	34.78 (8.44)	32.97 (10.38)	**0.003**
Ethnicity			**<0.0001**
Tz'tujil	96.60% (483)	0	
Ladino	1.80% (9)	24.78% (113)	
Garifuna	0	31.80% (145)	
Q'echchi	0	41.89% (191)	
Other	1.40% (7)	1.32% (6)	
Education			**<0.0001**
Less than Primary	69.40% (347)	33.92% (153)	
Primary or Secondary	20.12% (100)	34.37% (155)	
More than Secondary	10.06% (50)	31.71% (143)	
Literacy			**<0.0001**
Illiterate (Neither Read nor Write)	48.60% (243)	12.53% (57)	
Literate (Either Read and/or Write)	51.20% (255)	87.47% (398)	
Ever Married/United	97.00% (485)	62.50% (285)	**<0.0001**
Breast exam (Heard of)	14.08% (70)	66.59% (303)	**<0.0001**
Pap (Ever)	66.80% (334)	58.11% (265)	**0.0056**
Last Pap			**<0.0001**
Less than 6 months	9.28% (31)	23.77% (63)	
6 months to a year	19.76% (66)	26.79% (71)	
1 to 5 years	51.2% (171)	35.1% (93)	
More than 5 years	14.97% (50)	13.21% (35)	
VIA (Ever)	6.04% (30)	1.32% (6)	**<0.0001**
Ever Smoke	0.40% (2)	9.65% (44)	**<0.0001**
Regular Drinker	11.54% (3)	33.85% (44)	**0.0080**
Used IUD (Ever)	1.41% (7)	8.09% (36)	**<0.0001**
Use Protection			**<0.0001**
Always	7.93% (39)	12.81% (57)	
Almost always	2.21% (11)	7.64% (34)	
Sometimes	4.82% (24)	12.13% (54)	
Rarely	1.81% (9)	5.62% (25)	
Never	68.07% (339)	42.70% (190)	
Family Member with Cervical Cancer	2.65% (13)	11.28% (51)	**<0.0001**
Age at First Sexual Relation	19.63 (4.29)	17.24 (2.77)	**<0.0001**
Number of Lifetime Sexual Partners			**<0.0001**
One	90.6% (453)	70.8% (323)	
More than One	6.8% (34)	25.9% (118)	
Refused	2.6% (13)	3.3% (15)	
Knowledge of HPV	11.80% (59)	62.72% (286)	**<0.0001**
Believe at Risk for CC			**<0.0001**
Strongly Agree	24.80% (124)	14.47% (66)	
Agree	13.20% (66)	41.23% (188)	
Neutral	13.60% (68)	5.26% (24)	
Disagree	9.00% (45)	8.55% (39)	
Strongly Disagree	19.00% (95)	8.99% (41)	
Willing to Vaccinate Daughters for HPV if Available			**<0.0001**

Yes	69.60% (348)	82.24% (375)	
No	1.00% (5)	6.80% (31)	
Don't Have Daughters	27.60% (138)	8.33% (38)	
Refused	1.8% (9)	2.6% (12)	

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Table 2: Acceptability of Self-Collection HPV Tests
Among Age-Eligible Women (25-54 years of age)

	Santiago Atitlán % (N)	**Livingston % (N)**	**p-value[a,b]**
N	500 *(All participants)* *438 (age-eligible)*	*456 (all participants)* *322 (age-eligible)*	
HPV knowledge	10.05% (44)	63.98% (206)	**<0.0001**
Self-Reported Previous Pap (Ever)	71.46% (313)	69.88% (225)	0.6348
Abnormal Pap (Ever)	16.61% (52)	36.89% (83)	**<0.0001**
Knowledge of VIA	6.85% (30)	1.86% (6)	**0.0023**
Collected Sample	93.61% (410)	52.48% (169)	**<0.0001**
Prefer Home Screening	94.06% (412)	44.41% (143)	**<0.0001**
Prefer Self-Collection	91.10% (399)	41.61% (134)	**<0.0001**
	% (N)	**% (N)**	
N	410 *(age-eligible; Test-Taking participants)*	*169 (age eligible; Test-Taking participants)*	
Comfort of test			**0.0013[b]**
Comfortable	81.4% (333)	87.0% (141)	
Neutral	5.87% (24)	5.56% (9)	
Uncomfortable	12.7% (52)	7.4% (12)	
Ease of test			**0.0241[b]**
Easy	84.8% (347)	87.0% (141)	
Neutral	4.65% (19)	7.41% (12)	
Difficult	10.5% (43)	5.55% (9)	
Willingness to retake test	99.50% (402)	100% (169)	1.00[b]

[a]p-values for means calculated using two-sample t-test; proportions using chi-squared test
[b]Fisher's exact test used to account for low cell counts

Table 3. Population Characteristics within Livingston Age-Eligible Women Who Sampled vs. Age-Eligible Women Who Did Not Sample			
	Took the Sample % (N) or Mean (SD)	**Did Not Take the Sample % (N) or Mean (SD)**	**p-value[a]**
N	52.48% (169)	47.52% (153)	
Age (y)	34.98 (7.76)	36.35 (7.66)	0.1141
Ethnicity			0.6986
Ladino	25.44% (43)	27.45% (42)	
Garifuna	33.14% (56)	30.72% (47)	
Q'echchi	39.64% (67)	40.52% (62)	
Other	1.78% (3)	0.65% (1)	
Declined	0	0.65% (1)	
Education			0.0784
Less than Primary	33.73% (57)	43.14% (66)	
Primary or Secondary	35.50% (60)	29.41% (45)	
More than Secondary	29.59% (50)	25.49% (39)	
Literacy			**0.0005**
Illiterate (Neither Read nor Write)	8.54% (14)	21.52% (34)	
Literate (Either Read and/or Write)	91.72% (155)	77.78% (119)	
Ever Married/United	66.27% (112)	73.86% (113)	0.2365
No. Health Locations Used	1.51 (0.86)	1.32 (0.71)	**0.0324**
Pap or VIA (Ever)	72.78% (123)	66.67% (102)	0.2324
Ever Smoke	9.47% (16)	9.15% (14)	0.6309
Regular Drinker	32.08% (17)	35.14% (13)	0.7619
Used IUD	11.24% (19)	4.58% (7)	**0.0295**
Use Protection			0.3998
Always	11.24% (19)	10.46% (16)	
Almost always	8.88% (15)	5.23% (8)	
Sometimes	14.20% (24)	11.11% (17)	
Rarely	5.92% (10)	5.88% (9)	
Never	44.97% (76)	42.48% (65)	
Unknown	15.24% (25)	24.0% (38)	
Family Member with CC	11.83% (20)	8.50% (13)	0.6143
Age at First Sexual Relation	17.20 (2.97)	17.56 (2.96)	0.4102
Number of Lifetime Partners	1.83 (1.73)	1.51 (1.31)	0.0670
One	65.7% (111)	75.2% (115)	
More than One	33.7% (57)	23.5% (36)	
Refused	0.6% (1)	1.3% (2)	
Knowledge of HPV	68.05% (115)	59.48% (91)	0.1097
Believe at Risk for CC			**0.0398**
Strongly Agree	21.89% (37)	11.76% (18)	
Agree	38.46% (65)	42.48% (65)	
Neutral	5.92% (10)	1.96% (3)	
Disagree	7.69% (13)	6.54% (10)	
Strongly Disagree	7.69% (13)	10.46% (16)	
Unsure	18.34% (31)	26.80% (41)	
Vaccinate Daughters for HPV			0.4024
Yes	89.35% (151)	83.01% (127)	
No	5.92% (10)	7.19% (11)	
Don't Have Daughters	2.96% (5)	5.23% (8)	
Refused	1.78% (3)	4.58% (7)	

[a]p-values for means calculated using two-sample t-test; proportions using chi-squared test

Table 4. Prevalence Ratio of Sample Collection in Livingston among Age-Eligible Women
Log-Binomial Regression: Prevalence Ratio of Sample Collection (N=309)

Variable	PR^{M1}	95% CI		PR^{M2}	95% CI		PR^{M3}	95% CI	
Literacy (Y)	**2.07**	**1.29**	**3.35**	**2.28**	**1.39,**	**3.72**	**1.62**	**1.03**	**2.56**
Marriage (Never)	1.20	0.97	1.49	1.16	0.93	1.45	1.12	0.90	1.39
Hx of Pap/VIA (Never)	0.86	0.67	1.10	0.84	0.65	1.08	0.96	0.73	1.26
Smoking (Y)	0.98	0.69	1.40	1.07	0.75	1.53	1.16	0.76	1.74
Drinking (Y)	1.19	0.96	1.48	1.16	0.91	1.49	1.15	0.88	1.49
IUD Use (Y)	**1.47**	**1.14**	**1.91**	**1.42**	**1.07**	**1.87**	1.46	0.98	2.17
Family Hx of CC (N)	0.89	0.64	1.19	0.87	0.63	1.19	0.98	0.69	1.39
Believe at Risk for CC (Y)	0.99	0.77	1.29	1.01	0.77	1.33	1.01	0.78	1.32

M1: unadjusted log-binomial model
M2: adjusted for age, ethnicity, and number of lifetime sexual partners
M3: all variables included and adjusted for age, ethnicity, and number of lifetime sexual partners

Table 5. Prevalence Ratio of Sample Collection in Livingston among Age-Eligible Women
Log-Binomial Regression: Prevalence Ratio of Sample Collection (N=309)

	Literacy (Y)		Marriage (Never)		Hx of Pap/VIA (Never)		Drinking (Regular)		IUD Use	
	PR	95% CI	PR	95% CI	PR	95% CI	PR	95% CI	PR	95% CI
Actual Sample Collection	2.28	(1.39, 3.72)	1.16	(0.93, 1.45)	0.84	(0.65, 1.08)	1.16	(0.91, 1.49)	1.42	(1.07, 1.87)
Age	0.99	(0.98, 1.01)	0.99	(0.97, 1.00)	0.98	(0.97, 1.00)	0.99	(0.97, 1.00)	0.99	(0.98, 1.00)
Ethnicity										
Ladino (Ref)	-	-								
Garifuna	1.22	(0.93, 1.59)	1.02	0.78, 1.33	1.06	(0.76, 1.31)	1.04	(0.80, 1.37)	1.05	(0.81, 1.38)
Q'echchi	0.98	(0.75, 1.28)	0.97	0.73, 1.27	1.00	(0.76, 1.31)	0.96	(0.72, 1.27)	0.96	(0.73, 1.25)
More than One Lifetime Sexual Partners	1.31	(1.06, 1.63)	1.20	0.96, 1.50	1.21	(0.97, 1.50)	1.20	0.95, 1.50	1.21	(0.97, 1.49)

Models additionally adjusted for age, ethnicity, and number of lifetime sexual partners

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FIGURE LEGENDS

Figure 1. Flow Chart of Livingston Self-Collection Sampling and Testing

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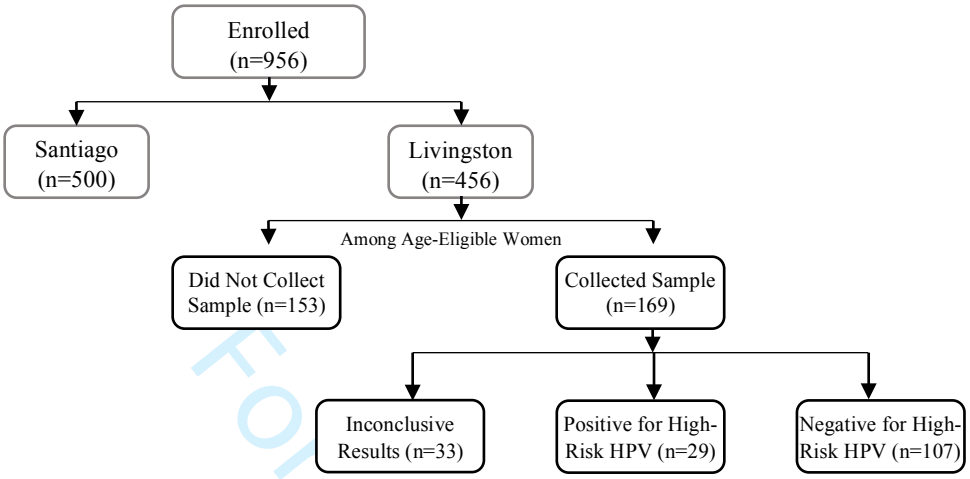
Figure 1. Flow Chart of Livingston Self-Collection Sampling and Testing



HPV Self-Sampling Acceptability in Rural and Indigenous Communities in Guatemala: A Cross-Sectional Study

Audrey Murchland, Anna Gottschlich, Kristin Bevilacqua, Andres Pineda, Berner Andrée Sandoval-Ramírez, Christian S. Alvarez, Gina Ogilvie, Thomas E Carey, Mark Prince, Michael Dean, Carlos Mendoza-Montano, Alvaro Rivera-Andrade, Rafael Meza

Supplementary Appendix

Appendix A: Additional Reference Tables

Appendix B: Self-reported Willingness to Collect a Sample

Appendix A – Additional Reference Tables

Table A1: Population Characteristics within Livingston
Age-Eligible Women Who Declined At Home Sampling vs. Age-Eligible Women Who Did Not Sample

	Did Not Want to Collect Sample (Survey Response) N (%) or Mean (SD)	Did Not Collect Sample N (%) or Mean (SD)
N	112	169
Age (y)	36.51 (7.88)	36.3 (7.66)
Education		
Less than primary	24 (21.43%)	21 (12.43%)
Primary	57 (50.89%)	96 (56.80%)
More than primary	31 (27.68%)	52 (30.77%)
Literacy		
Neither	26 (23.21%)	14 (8.28%)
Read Only or Read and Write	86 (76.79%)	155 (91.72%)
Married/United (Ever)	84 (75.00%)	112 (49.78%)
Ever Drink	87 (77.68%)	115 (68.45%)
Use Health Services	103 (91.96%)	159 (94.08%)

Table A2. General Population Characteristics Among All Participants (Continued)			
	Santiago Atitlan N (%) or Mean (SD)	**Livingston N (%) or Mean (SD)**	**p-value[a]**
N	500	456	
Current Marital Status			**<0.0001**
Single	3 (0.62%)	30 (10.53%)	
Married	311 (64.12%)	101 (35.44%)	
Separated	28 (5.77%)	2 (0.70%)	
Divorced	5 (1.03%)	0	
Widowed	15 (3.09%)	1 (0.35%)	
Common Law	120 (24.74%)	151 (52.98%)	
Refused	3 (0.62%)	0	
Age at Marriage	19.8 (4.31)	19.74 (5.82)	0.8771
Use Health Services	451 (90.2%)	421 (92.32%)	0.2465
Mammogram (Ever)	10 (2.01%)	40 (8.77%)	**<0.0001**
Pap or VIA (Ever)	337 (67.40%)	265 (58.11%)	0.7592
Used Birth Control Injections	215 (43.17%)	173 (38.88%)	0.3459
Used Oral Contraceptives	54 (10.84%)	123 (27.64%)	**<0.0001**
Number of Pregnancies	2.81 (1.93)	3.19 (2.49)	**0.0082**
Number of Children	2.54 (1.65)	3.20 (2.12)	**<0.0001**
Age at First Child	20.18 (5.80)	18.88 (3.74%)	**0.0001**
Currently Sexually Active	171 (79.53%)	121 (63.68%)	**0.0035**
Severity of CC			**<0.0001**
Not	6 (1.20%)	18 (3.95%)	
A little	6 (1.20%)	38 (8.33%)	
Moderate	114 (22.80%)	31 (6.80%)	
Very	234 (46.80%)	274 (60.09%)	
Extremely	140 (28.0%)	95 (20.83%)	
Likely to Get CC			**<0.0001**
No Chance	135 (27%)	152 (33.33%)	
Low	97 (19.40%)	175 (38.38%)	
Moderate	32 (6.40%)	13 (2.85%)	
High	22 (4.40%)	7 (1.54%)	
Certain	17 (3.40%)	6 (1.32%)	
Unsure	0	103 (22.59%)	
Refused	197 (39.40%)	0	

Table A3. Population Characteristics within Livingston (Continued)
Age-Eligible Women Who Sampled vs. Age-Eligible Women Who Did Not Sample

	Took the Sample N (%) or Mean (SD)	Did Not Take the Sample N (%) or Mean (SD)	p-value[a]
N	169 (52.48%)	153 (47.52%)	
Current Marital Status			0.4399
Single	12 (10.71%)	13 (11.50%)	
Married	36 (32.14%)	47 (41.59%)	
Separated	1 (0.89%)	1 (0.88%)	
Divorced	0	0	
Widowed	0	1 (0.88%)	
Common Law	63 (56.25%)	51 (45.13%)	
Age at First Marriage	19.67 (4.51)	20.90 (7.35)	0.1506
Use Health Services	159 (94.08%)	140 (91.50%)	0.3694
No. Health Services Received	2.33 (1.44)	2.26 (1.56)	0.6754
Breast Exam (Heard Of)	30 (17.75%)	26 (16.99%)	0.3473
Mammogram (Ever)	16 (9.47%)	16 (10.46%)	0.7668
Pap (Ever)	123 (72.78%)	102 (66.67%)	0.2324
Last Pap			0.7520
Less than 6 months	28 (22.76%)	25 (24.51%)	
Within the last year	32 (27.12%)	24 (22.43%)	
Within the last 2-5 years	47 (38.21%)	37 (36.27%)	
More than 5 years	16 (13.56%)	13 (12.75%)	
VIA (Ever)	5 (2.96%)	1 (0.65%)	0.1050
Used Birth Control Injections	78 (46.15%)	61 (39.87%)	0.2292
Used Oral Contraceptives	60 (35.50%)	43 (28.10%)	0.1336
Number of Pregnancies	3.49 (2.27)	3.74 (2.30)	0.3346
Number of Children	3.20 (1.78)	3.61 (2.14)	0.1712
Age at First Pregnancy	18.87 (3.50)	19.27 (4.41)	0.3853
Currently Sexually Active	45 (62.50%)	24 (33.33%)	0.2068
Severity of CC			0.4191
Not	4 (2.37%)	7 (4.58%)	
A little	15 (8.88%)	7 (4.58%)	
Moderate	13 (7.69%)	10 (6.54%)	
Very	102 (60.36%)	92 (60.13%)	
Extremely	35 (20.71%)	37 (24.18%)	
Likely to Get CC			0.0612
No Chance	67 (39.64%)	47 (30.72%)	
Low	55 (32.54%)	57 (37.25%)	
Moderate	6 (2.96%)	1 (0.65%)	
High	5 (2.96%)	1 (0.65%)	
Certain	2 (1.18%)	2 (1.31%)	
Unsure	34 (20.12%)	45 (29.41%)	

[a]p-values for means calculated using two-sample t-test; proportions using chi-squared test

Table A4: Population Characteristics within Livingston
Comparing Racial/Ethnic Groups in Livingston Including All Women

	Ladino N (%) or Mean (SD)	Garifuna N (%) or Mean (SD)	Q'echchi N (%) or Mean (SD)	p-value[a]
N	113 (25.17%)	145 (32.29%)	191 (42.54%)	
Age (y)	34.49 (10.32)	33.23 (10.54)	31.91 (10.19)	0.1022
Education				**<0.0001**
Less than primary	35 (30.97%)	12 (8.28%)	104 (54.45%)	
Primary	39 (34.51%)	69 (47.59%)	45 (23.56%)	
More than primary	38 (33.63%)	62 (42.76%)	40 (20.94%)	
Literacy				**<0.0001**
Neither	8 (7.08%)	3 (2.07%)	45 (23.56%)	
Read Only	1 (0.88%)	0	3 (1.57%)	
Read and Write	104 (92.04%)	142 (97.93%)	142 (74.35%)	
Married/United (Ever)	87 (76.99%)	63 (43.45%)	128 (67.02%)	**<0.0001**
Use Health Services	105 (92.925%)	136 (93.79%)	174 (91.10%)	0.6354
Breast Exam (Heard of)	88 (77.88%)	112 (77.24%)	98 (51.31%)	**<0.0001**
Mammogram (Ever)	11 (9.73%)	21 (14.48%)	8 (4.19%)	**0.0043**
Pap (Ever)	70 (61.95%)	107 (73.79%)	83 (43.46%)	**<0.0001**
Last pap				**0.0212[b]**
Less than 6 months	14 (20%)	34 (31.78%)	13 (15.66%)	
Within the last year	18 (25.71%)	37 (34.58%)	16 (19.28%)	
Within the last 2-5 years	27 (38.57%)	28 (26.19%)	36 (43.37%)	
More than 5 years	10 (14.29%)	6 (5.61%)	18 (21.69%)	
VIA (Ever)	2 (1.77%)	1 (0.69%)	3 (1.57%)	0.6142
Ever Smoke	15 (13.27%)	27 (18.62%)	2 (1.05%)	**<0.0001[b]**
Ever Drink	30 (26.55%)	74 (51.03%)	24 (12.57%)	**<0.0001[b]**
Used Birth Control Injections	46 (41.44%)	59 (41.55%)	66 (35.68%)	0.8213
Used Oral Contraceptives	30 (27.03%)	64 (45.07%)	28 (15.14%)	**<0.0001[b]**
Used IUD	9 (8.11%)	22 (15.49%)	4 (2.16%)	**<0.0001[b]**
Use protection				**<0.0001[b]**
Always	11 (9.91%)	36 (25.35%)	9 (4.86%)	
Almost always	11 (9.91%)	15 (10.56%)	8 (4.32%)	
Sometimes	8 (7.215)	30 (21.13%)	14 (7.57%)	
Rarely	5 (4.50%)	9 (6.34%)	11 (5.95%)	
Never	62 (55.865)	41 (28.87%)	85 (45.95%)	
Unknown	14 (12.61%)	11 (7.75%)	58 (31.35%)	
Family Member with CC	21 (18.58%)	19 (13.10%)	10 (5.24%)	**<0.0001[b]**
Knowledge of HPV	78 (69.03%)	112 (77.24%)	90 (47.12%)	**<0.0001**
Believe They Are at Risk for CC				
Strongly Agree	11 (9.73%)	30 (20.69%)	25 (13.09%)	
Agree	51 (45.13%)	49 (33.79%)	87 (45.55%)	
Neutral	6 (5.31%)	7 (4.83%)	10 (5.24%)	
Disagree	15 (13.27%)	17 (11.72%)	6 (3.14%)	
Strongly Disagree	10 (8.85%)	22 (15.17%)	9 (4.71%)	
Unsure	20 (17.70%)	19 (13.10%)	54 (28.27%)	
Vaccinate Daughters for HPV				0.4056
Yes	94 (83.19%)	120 (82.70%)	156 (81.68%)	
No	10 (8.85%)	5 (3.45%)	15 (7.85%)	
Don't Have Daughters	8 (7.08%)	15 (10.34%)	14 (7.33%)	
Willing to Collect Sample at Home	61 (53.98%)	94 (64.83%)	104 (54.45%)	0.2802
Collected Sample	44 (38.94%)	56 (38.62%)	67 (35.08%)	0.7264

[a]p-values for means calculated using one-way ANOVA or Welch (if equality of variance is rejected); proportions using chi-squared test
[b]Fisher's Exact Test used due to small cell counts

Table A5: Differences Among Communities of Age-Eligible Indigenous Mayan Women Age-Eligible Tz'tujil Women vs. Age-Eligible Q'echchi Women			
	Tz'tujil - Santiago N (%) or Mean (SD)	**Q'echchi - Livingston N (%) or Mean (SD)**	**p-value[a]**
N	420 (68.74%)	191 (31.26%)	
Age (y)	36.25 (7.46)	31.91 (10.19)	**<0.0001**
Education			**<0.0001**
Less than primary	314 (75.12%)	104 (54.45%)	
Primary	64 (15.31%)	45 (23.56%)	
More than primary	40 (9.57%)	40 (20.94%)	
Literacy			**<0.0001**
Neither	225 (53.57%)	45 (23.56%)	
Read Only	7 (1.67%)	3 (1.57%)	
Read and Write	188 (44.76%)	142 (74.35%)	
Ever Married/United	412 (98.10%)	128 (67.02%)	**<0.0001**
Age at marriage	29.85 (137.8)	24.46 (20.33)	0.4463
Use health services	379 (90.24%)	174 (91.10%)	**0.7363**
Breast exam (Heard of)	53 (12.68%)	98 (51.31%)	**<0.0001**
Mammogram (Ever)	10 (2.38%)	8 (4.19%)	0.2206
Pap (Ever)	296 (70.48%)	83 (43.46%)	**<0.0001**
Last pap			0.2751
Less than 6 months	26 (9.25%)	13 (15.66%)	
Within the last year	57 (20.28%)	16 (19.28%)	
Within the last 2-5 years	153 (54.44%)	36 (43.37%)	
More than 5 years	45 (16.01%)	18 (21.69%)	
VIA (ever)	28 (6.70%)	3 (1.57%)	**0.0076**
Pap or VIA (Ever)	299 (71.19%)	83 (43.46%)	**<0.0001**
Ever Smoke	1 (0.24%)	2 (1.05%)	0.1907
Drink (regularly)	3 (14.29%)	1 (4.17%)	0.2341
Used BC injections	186 (44.71%)	66 (35.68%)	**0.0786**
Used IUD	5 (1.20%)	4 (2.16%)	0.1497
Use protection			**<0.0001**
Always	29 (8.33%)	9 (4.86%)	
Almost always	11 (3.16%)	8 (4.32%)	
Sometimes	20 (5.75%)	14 (7.57%)	
Rarely	9 (2.59%)	11 (5.95%)	
Never	279 (80.17%)	85 (45.95%)	
Family Member with CC	12 (2.01%)	10 (5.24%)	**0.0408**
Age at First Sexual Relation	20.00 (4.48)	16.64 (2.45)	**<0.0001**
Currently Sexually Active	138 (82.63%)	42 (64.62%)	**0.0025**
Knowledge of HPV	37 (8.81%)	90 (47.12%)	**<0.0001**
Believe At Risk for CC			**<0.0001**
Strongly Agree	105 (31.82%)	25 (13.09%)	
Agree	51 (15.45%)	87 (45.55%)	
Neutral	61 (18.48%)	10 (5.24%)	
Disagree	41 (12.42%)	6 (3.14%)	
Strongly Disagree	72 (21.82%)	9 (4.71%)	
Unsure	0	54 (28.27%)	
Vaccinate Daughters for HPV			**<0.0001**
Yes	301 (73.24%)	156 (81.68%)	
No	4 (0.97%)	15 (7.85%)	
Don't Have Daughters	106 (25.79%)	14 (7.33%)	
Willing to Sample in Home	394 (95.63%)	104 (54.45%)	**<0.0001**
Collected Sample	395 (94.05%)	67 (35.08%)	**<0.0001**
[a]p-values for means calculated using two-sample t-test; proportions using chi-squared test			

Appendix B – Self-Reported Willingness to Self-Collect Sample

As a final sensitivity analysis, we present results evaluating potential predictors of self-reported willingness to self-collect a vaginal sample as reported in the survey.

Table B1. Prevalence Ratio of Willingness to Collect at Home in Livingston

Log-Binomial Regression: Prevalence Ratio of Willingness to Sample at Home

Variable	PR^{M1}	95% CI		PR^{M2}	95% CI		PR^{M3}	95% CI	
Literacy (Y)	**1.51**	**1.09**	**2.10**	**1.45**	**1.02**	**2.06**	**1.08**	**0.85**	**1.36**
Marriage (Never)	1.15	0.97	1.36	1.12	0.94	1.34	1.09	0.93	1.28
Hx of Pap/VIA (Never)	0.83	0.68	1.02	0.82	0.67	1.01	0.95	0.81	1.12
Smoking (Y)	1.17	0.92	1.49	1.11	0.83	1.49	1.06	0.80	1.39
Drinking (Y)	1.17	0.99	1.38	1.13	0.93	1.38	1.00	0.85	1.19
IUD Use (Y)	**1.34**	**1.11**	**1.61**	1.23	0.99	1.54	1.13	0.86	1.48
Family Hx of CC (N)	0.87	0.69	1.09	0.89	0.72	1.11	0.98	0.78	1.23
Belief CC is Likely (Y)	1.14	0.86	1.51	1.22	0.89	1.67	0.97	0.83	1.13

M1: unadjusted log-binomial model
M2: adjusted for age, ethnicity, and number of lifetime sexual partners
M3: all variables included and adjusted for age, ethnicity, and number of lifetime sexual partners

STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	11
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	11
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	11
		(*b*) Describe any methods used to examine subgroups and interactions	11
		(*c*) Explain how missing data were addressed	11
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	11
		(*e*) Describe any sensitivity analyses	

Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11-12
		(b) Indicate number of participants with missing data for each variable of interest	11
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	12
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	13
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18
Generalisability	21	Discuss the generalisability (external validity) of the study results	16,17
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	20

**Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.*

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Complete List of Authors:	Murchland, Audrey; University of Michigan School of Public Health, Epidemiology Gottschlich, Anna; University of Michigan School of Public Health, Epidemiology Bevilacqua, Kristin; University of Michigan School of Public Health, Epidemiology Pineda, Andres; Instituto de Nutricion de Centroamerica y Panama Sandoval-Ramírez, Berner Andrée; Universitat Rovira i Virgili, Hospital Universitari Sant Joan, Functional Nutrition, Oxidation, and Cardiovascular Diseases Group (NFOC-Salut) Alvarez, Christian; University of Michigan School of Public Health, Epidemiology Ogilvie, Gina; BC Centre for Disease Control, Clinical Prevention Services Carey, Thomas E; University of Michigan, Department of Otolaryngology-Head and Neck Surgery and Department of Pharmacology Prince, Mark; University of Michigan Department of Otolaryngology Head and Neck Surgery Dean, Michael; National Cancer Institute, Laboratory of Translational Genomics, Division of Cancer, Epidemiology and Genetics Montano, Carlos; Instituto de Nutricion de Centroamerica y Panama Rivera-Andrade, Alvaro; Instituto de Nutricion de Centroamerica y Panama Meza, Rafael; University of Michigan School of Public Health, Epidemiology
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HPV Self-Sampling Acceptability in Rural and Indigenous Communities in Guatemala: A Cross-Sectional Study

Audrey Murchland[1], Anna Gottschlich[1], Kristin Bevilacqua[1], Andres Pineda[2], Berner Andrée Sandoval-Ramírez[3], Christian S. Alvarez[1], Gina Ogilvie[4], Thomas E Carey[5], Mark Prince[6], Michael Dean[7], Carlos Mendoza-Montano[2], Alvaro Rivera-Andrade[2], Rafael Meza[1]

1. Department of Epidemiology, School of Public Health, University of Michigan, 1415 Washington Heights, Ann Arbor, Michigan 48103

2. Institute of Nutrition of Central America and Panama-INCAP, Calzada Roosevelt 6-25 zona 11, Apartado Postal 1188 Guatemala City, Guatemala 01011

3. Functional Nutrition, Oxidation, and Cardiovascular Diseases Group (NFOC-Salut), Universitat Rovira i Virgili, Hospital Universitari Sant Joan (HUSJR), Sant Llorenç, 21, 43201, Reus, Spain

4. Clinical Prevention Services, BC Centre for Disease Control, 655 W 12th Ave, Vancouver, British Columbia V5Z4R4, Canada

5. Department of Otolaryngology-Head and Neck Surgery and Department of Pharmacology, University of Michigan, 5311 Medical Science Unit I 1301 Catherine St., Ann Arbor, Michigan 48109

6. Department of Otolaryngology, University of Michigan, 1500 E Medical Center Dr SPC 5312, Ann Arbor, Michigan 48109

7. Laboratory of Translational Genomics, Division of Cancer, Epidemiology and Genetics, National Cancer Institute, Gaithersburg, MD USA

Corresponding Author:
Rafael Meza, Ph.D.
SPH II, Room 5033, 1415 Washington Heights
Ann Arbor, MI 48109-2029
E-mail: rmeza@umich.edu
Telephone: +1 (734) 763-1946

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ABSTRACT

Introduction: Cervical cancer disproportionately burdens low- and middle-income countries (LMICs) such as Guatemala. Self-collection testing for human papillomavirus (HPV) has been suggested as a form of cervical cancer screening to facilitate access in LMICs. This study assessed and compared the acceptability of self-collection HPV testing in two rural, indigenous and ethnically distinct communities in Guatemala: Santiago Atitlán, Sololá and Livingston, Izabal.

Methods: All participants, women between ages 18 and 60, completed a questionnaire. Eligible participants were also asked to self-collect a vaginal sample and complete a questionnaire regarding comfort and acceptability. Self-collected samples were tested for high-risk HPV using the real-time PCR Hybribio kit.

Results: In the indigenous community of Santiago Atitlán, of 438 age-eligible participants, 94% completed self-collection. Of those, 81% found it comfortable and 98% were willing to use it as a form of screening. In the multi-ethnic (Afro-Caribbean, indigenous) community of Livingston, of 322 age-eligible participants, 53% chose to self-collect. Among those who took the test, 87% found it comfortable and 100% were willing to use it as a form of screening. In Livingston, literacy (can read and/or write versus cannot read or write) was higher in women who chose to self-collect (prevalence ratio, 2.25; 95% CI: 1.38, 3.68). Ethnicity, history of screening, and reproductive history were not associated with willingness to self-collect in Livingston. Women in Santiago reported less prior use of healthcare than women in Livingston. Overall, 19% (106/549) of samples tested positive for high-risk HPV.

Conclusion: Among women willing to self-collect in rural and indigenous communities in Guatemala, self-collection for HPV testing is highly acceptable. However, willingness to try self-collection might vary across communities and settings. Women from a community that used less healthcare were more likely to choose self-collection. Further research is necessary to determine what factors influence a woman's choice to self-collect.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- To our knowledge, little is known about the acceptability of self-collection HPV testing across the diverse communities within Guatemala and Latin America, and in particular among indigenous populations.
- Our study provided not only a larger sample size compared with previous studies but was also conducted in two differing communities.
- Due to both the sensitive nature of the questions related to sexual history, it may be possible that a social desirability bias may have resulted in over reporting of perceived "good behaviors", such as screening or use of protection, in addition to under-reporting of perceived "bad behaviors", such as number of lifetime sexual partners and other sexual behavior measures.
- Sampling methods differed between the two communities due to the lack of reliable census counts in one community, but our sample in this community is reflective of the overall population structure in terms of ethnic, age and other metrics, suggesting that influential selection bias into the study might be limited.

INTRODUCTION

Cervical cancer, primarily caused by human papillomavirus (HPV) infection, has a very good prognosis when detected in premalignant or early malignant stages[1]. However, it disproportionately burdens low- and middle-income countries (LMICs), such as Guatemala, compared to high-income countries (HICs)[2-4]. HICs currently use Pap smears to detect abnormal cervical lesions that can be removed, greatly reducing the risk of cervical cancer[3 5]. However, there are many barriers to implementing successful Pap smear (cytology-based) screening programs in LMICs, including difficulties establishing sustainable laboratory infrastructure, training and retaining adequate numbers of trained pathologists or cytologists, overburdened primary care clinics, and time and travel limitations for women in reaching screening locations[1 6 7]. Due to these factors and others, the percentage of women in Guatemala who are screened for cervical cancer remains low; in 2014, only 49.8% of women (15-49 years of age) reported ever having a Pap smear. Thus, significant improvements in screening or program implementation are paramount to improving cervical cancer outcomes in Guatemala[3 8 9].

Since more than 90% of cervical cancers are caused by the HPV virus, HPV testing has been suggested as a possible alternative, primary form of cervical cancer screening[10-12]. When used in combination with Visual Inspection with Acetic Acid (VIA) or Pap smears in low-income settings, HPV testing has been shown to provide significant improvements in the detection of advanced premalignant lesions and cancer in sensitivity as compared to VIA or Pap smear alone, as only women who test positive for HPV need to follow up with further screening[13-16]. Previous studies have also confirmed that HPV self-swab kits are comparable to physician administered samples in their ability to detect carcinogenic, high-risk HPV [17 18]. Thus, at-home HPV sample collection, with referral to further screening for those positive for high-risk

HPV, may be both more acceptable within low-income communities and more programmatically feasible[6 7 19]. Moreover, a 2015 meta-analysis showed that HPV self-sampling, particularly in opt-in programs, increased participation in cervical cancer screening programs. However, further work is needed to evaluate acceptable opt-in programs for women[20].

Studies have shown that HPV self-sampling is generally acceptable among women in low and high resource settings as well as immigrant, rural, vulnerable populations[21-31]. To our knowledge, however, little is known about the acceptability of self-collection HPV testing across the diverse communities within Guatemala, and in particular among rural and indigenous populations. In a pilot cross-sectional study assessing the acceptability of HPV self-collection among 200 women in the Mayan community of Santiago Atitlán, Guatemala, a self-swab HPV test was found to be a highly acceptable form of screening[32]. Over 80% of women said that they preferred using a self-swab kit in their home rather than being screened at a doctors' office. However, this pilot study was limited to a relatively small sample in a single, largely homogeneous community, limiting the generalizability of the results to other rural and indigenous communities in Guatemala. Further research is thus needed to evaluate the acceptability of self-collection testing among more diverse rural and indigenous populations within Guatemala, which is very diverse, with over 23 official languages and many indigenous groups, most but not all descendants from the Mayan civilization. The purpose of this study was to evaluate risk factors, knowledge, and attitudes towards cervical cancer and to further assess and compare the acceptability of self-collection HPV testing in two understudied, rural, ethnically distinct communities in Guatemala: Santiago Atitlán and Livingston, Izabal.

METHODS

Study Communities

Santiago Atitlán, Sololá is a rural community located on Lake Atitlán, in the southwest region of Guatemala, 75 miles west of Guatemala City. The Tz'utujil, a Mayan descendant ethnic group, inhabits the region, which surrounds Lake Atitlán. The primary language of Santiago's inhabitants is Tz'utujil, and over half of the villagers speak Spanish as a second language[32]. The majority of women in Santiago Atitlán have at most a primary education. Additionally, as a conservative, religious community, it is highly uncommon for women to either drink or smoke, and almost all women in have previously reported having only one lifetime sexual partner[32].

Livingston, Izabal is located on the Caribbean coast of the country and is a rural community, only accessible by boat, that is the primary Garífuna settlement in Guatemala. The Garífuna people are considered a unique ethnic group with their own language, culture, and cuisine. Additionally, there are large populations of other ethnic and cultural groups located in Livingston including Q'eqchi' (Mayan descent), Ladinos (non-Mayan descent), and populations of Indian descent. Most women in Livingston are believed to have at least basic primary education.

Patient and Public Involvement

The patients were not involved in the development of the research questions, outcome measures or study design. The patients were also not involved in the recruitment and performance of the study. However, the public, Guatemalan physicians, scientists, and community health workers, were involved in the development of the question, design, validation, recruitment, and conduct of the study. Local community health workers were involved in the validation of the survey and study protocol, recruited participants and conducted the interviews, and assisted in providing test results to patients. Guatemalan physicians contributed to

development of the research question and study design, organized the laboratory testing, led and assisted with community health worker training, and provided HPV test results to patients. Local laboratory scientists contributed to the study design and conducted the HPV laboratory testing. The continued collaborations with these team members will be used to disseminate study results to patients and Guatemalan officials via publications, presentations, and meetings.

Eligibility and Recruitment

Trained community health workers (CHWs) in both communities actively recruited participants through home visits. All CHWs were bilingual and spoke both Spanish and either Tz'utujil, Q'eqchi, or Karif (the language of the Garifuna) depending on the location they were working in. Households in Santiago Atitlán were selected at random using stratified multi-level sampling based upon maps and population counts of the communities available through the local municipal office and were kept consistent with previous sampling methods[32]. Households in Livingston were selected at random using convenience sampling due to lack of reliable census data at the neighborhood-level. Sampling methods were, otherwise, kept the same as those in Santiago Atitlán.

Selected households that had at least one woman available between the ages of 18 and 60 were invited to participate in the survey-component of the study to assess risk factors for, attitudes towards, and knowledge of cervical cancer in these communities. For households with more than one eligible woman willing to participate, the female in the household whose birthday was closest to the date of the interview was enrolled in the study. Exclusion criteria consisted of past hysterectomy or previous cervical cancer. Women between the ages of 25 and 54 were also asked to provide a sample, in accordance with Guatemala's current screening recommendations[33]. Additionally, pregnant women, women currently menstruating, and women

who had never been sexually active were also excluded from providing samples but could participate in the survey component. Approximately 62% and 90% of eligible women contacted were willing to participate in the study in Santiago and Livingston, respectively. All participants in the study provided both oral and written informed consent prior to participation in the study. The consent was documented by a signature or fingerprint of the participant, the surveyors, and a witness to the consent process.

Survey

Data collection consisted of two main components: the surveys and the HPV self-collection tests. Local CHWs in each community were trained as interviewers in the appropriate techniques and protocols before beginning home visits. Two CHWs visited each randomly selected household together and read a recruitment script to a female household member to determine the household's eligibility. CHWs administered the survey and provided kits to collect HPV samples only to willing, eligible participants. Surveys were administered in private rooms of the participant's house to minimize response bias to sensitive questions.

The survey questionnaire included 153 questions concerning demographics, risk factors for cervical cancer and HPV, self-reported attitudes towards screening, healthcare service use, and knowledge of cervical cancer and HPV. The survey was developed from the pilot study survey and validated as part of the CHW and translator training to ensure correct translation and cultural relevancy[32]. Each survey was administered by the CHWs using electronic tablets and the Qualtrics offline app.

All women who participated in the study were compensated with a voucher for a free Pap smear or VIA at a local health clinic. Women in both communities can access free VIAs

(Santiago) or Pap Smears (Livingston) in the local public health system, but if they chose to use a private clinic instead of the public clinic, the voucher covered their fees.

HPV Self-Collected Samples

The HPV samples were collected using HerSwab kits, a self-collection sampling method [32 34 35]. If a participant was willing to provide a sample, instructions and graphical materials were provided and the participant collected the sample in a separate, private room from the CHWs. Participants who collected a sample then completed a short post-sample survey with the CHWs of three questions regarding ease, comfort, and acceptability of the sampling method: "How easy was the self-collection swab?"; "How comfortable was the self-collection swab?"; and "Would you be willing to collect a sample every 2-3 years to detect HPV as a form of cervical cancer screening?".

After collection, samples were kept in small, refrigerated coolers carried by the CHWs until they were returned to the main study office at the end of the day where samples were then processed to stabilize sample life. The brush component of the HerSwab kit was cut into a 15-mL test tube using lab scissors. The lab scissors were sterilized using alcohol and an open flame between each sample. Each tube was filled with 5mL of Scope mouthwash using a pipette, and tubes were sealed using a cap and parafilm paper[36]. Mouthwash is a reliable, low-cost transport medium for DNA samples and was used to reflect likely standard operating procedures of HPV screening program implementation in Guatemala[37]. Each sample was labeled with the participant's unique identifier. Time of sample processing and condition of sample were recorded.

Stabilized samples were sent to a molecular biology laboratory at the Institute of Nutrition of Central America and Panama (INCAP) in Guatemala City for testing. Samples were

tested using the real-time polymerase chain reaction (PCR) Hybribio HR-13 kit[38 39]. Samples were processed according to the manufacturers protocol and modified to use a 10 ul reaction volume for the real-time PCR and run on an ABI-7000[36]. After testing, samples were labeled as positive for HR-HPV, negative, or, if both the HPV probe and the internal control were negative, inconclusive. If a sample test was inconclusive during the first test, it was run an additional time using a 20 ul reaction volume, and if no result was obtained, the test was deemed inconclusive.

Follow-Up

A local CHW provided negative and inconclusive results over the phone or through a home visit. Positive results were provided in-person by a study physician who referred participants to their local community health clinic for follow-up and further cervical cancer screening. All participants who couldn't be reached at the study conclusion were re-contacted either at 6 months or one year to provide them with their results. Although women with negative results were not explicitly recommended to attend the clinic, all participants were encouraged to get screened using the voucher provided at the local clinic to support their engagement with local preventative services. Participants who were found to be positive for advanced lesions as a result of follow-up screening were referred for care through the free public health infrastructure in Guatemala, as is currently standard practice. Due to the ongoing nature of the project, data on follow-up screening and care are still in the collection process.

Outcomes and Statistical Analysis

Willingness and acceptability of self-collection testing, knowledge of HPV, and risk factors were evaluated in both communities and across ethnic groups in Livingston, Izabal. Willingness was measured as whether or not a woman chose to self-collect a sample to be tested for HPV (actual self-collection). The acceptability of sample collection was only assessed for

those who self-collected a sample and was analyzed using the post-self-swab survey questions described previously.

A target sample size of 500 per community was determined to be able to detect a 5% difference in self-sampling acceptability with 80% power, assuming a 95% acceptability in Santiago Atitlan based on the pilot.

Due to lower rates of actual self-collection in Livingston, differences between Livingston women willing and those not willing to collect a sample were evaluated using two-sample t-tests for means, chi-squared tests for proportions, and Fisher's Exact test for low cell counts. Most women tried self-collection in Santiago, so we restrict these analyses to Livingston.

The main exposures explored for willingness to try self-collection included: literacy, marital status, history of Pap smear or VIA, smoking status, alcohol use (a potential proxy for risky behavior), IUD use, family history of cervical cancer, and belief of being at risk for cervical cancer. Statistical analyses were run using log-binomial regression. In model set 1, the relationship between each exposure and sampling decision was unadjusted for other covariates. In model set 2, models were additionally adjusted for age, ethnicity, and number of lifetime sexual partners. In model set 3, we used stepwise selection to select significant the exposure covariates (alpha=0.05) when adjusting for age, ethnicity, and number of lifetime sexual partners. Finally, in model set 4, we included all exposure covariates and the adjustment covariates together in a fully adjusted model. The stepwise selected model was further stratified across ethnic groups to evaluate potential effect modification. Due to high prevalence of literacy in Garifuna and Ladino, these groups were combined for stratification to prevent positivity violations (Q'echchi versus Garifuna or Ladino, reflecting a Mayan descent versus non-Mayan descent comparison).

Analyses were restricted to age-eligible women in Livingston with complete covariate information (N=134 or 29.4% excluded due to age-ineligibility and N=13 or 3.5% excluded due to missing covariates). Specifically, we excluded 5 participant missing ethnicity or classified as other ethnicity, 1 participant missing marital status, 1 participant missing regular drinking status, and 3 participants missing number of lifetime sexual partners, 1 participant missing smoking status, and 2 participants missing family history of cancer resulting in a final sample size N=309 for analyses evaluating willingness to try self-collection.

Covariates were parameterized as: able to read and/or write (literate) versus unable to either read or write (illiterate), ever married versus never married, ever had a Pap or VIA versus never, ever smoked versus never smoked, regular drinker versus non-regular drinker, ever had an IUD versus never or don't know/refused, family history of cervical cancer present versus absent, and believe at risk for developing cervical cancer ("strongly agree"/"agree" versus neutral, disagree, strongly disagree, or unsure/don't know), continuous age, and number of lifetime sexual partners (one versus more than one).

Data cleaning and analyses were carried out using SAS 9.4[40].

RESULTS

In total, 956 women were recruited to participate into the study: 500 women in Santiago Atitlán and 456 women in Livingston. Demographic characteristics differed between the two communities: 69.4% of the participants in Santiago Atitlán had less than primary education and 96.6% were of Tz'tujil ethnicity. In contrast, only 33.9% of the participants in Livingston had less than primary education and three ethnic groups were represented: 41.9% Q'echi, 32% Garifuna, and 24.8% mixed ethnicity (Ladino) (Table 1).

Knowledge and attitudes regarding HPV and cervical cancer also differed between the communities. Only 11.8% of participants in Santiago reported previous knowledge of HPV as compared to 62.7% of Livingston participants. However, when asked about the seriousness of cervical cancer, most participants in both communities responded "very" or "extremely" (74.8% Santiago and 80.9% Livingston).

Self-reported history of access to healthcare also appeared higher in Livingston than in Santiago. For example, only 5.0% of participants in Santiago responded that they had ever been tested for human immunodeficiency virus while 57.8% of Livingston participants responded that they had been previously tested. Furthermore, statistically significantly higher proportions of women from Livingston reported knowledge of breast exams, receiving more recent Pap testing, and regular use of contraceptives. Additionally, a higher proportion of participants in Livingston consistently reported always using protection during sexual intercourse and using tobacco and alcohol than in Santiago (Table 1). Additional comparisons of population characteristics can be found in the appendix.

Self-Collection Willingness

When participants were asked if they would be willing to self-collect at home, the majority of women in both communities responded they would be willing (93.4% in Santiago and 62.4% in Livingston, Table 2). However, a lower percentage of women in Livingston who actually tried self-collection sampling (93.6% in Santiago and 52.5% in Livingston, Table 2 and Figure 1), as opposed to simply stating willingness in the survey.

We evaluated factors that affected the willingness to try self-collection testing in Livingston. Literacy, the use of health services, and beliefs regarding cervical cancer differed between age-eligible women who self-collected a sample compared to those who did not (Table

3). Additionally, 31.4% of the women who ended up not providing a sample had responded previously in the questionnaire that they indeed would be willing to collect a self-swab sample at home. While data is unavailable regarding how many age-eligible women were ineligible to collect a sample due to menstruation or pregnancy, this likely does not entirely account for all women who ultimately chose not to self-collect. Characteristics of women not willing to collect (both reported in the survey and actual sample collection) can be found in the appendix. It is interesting to also note that women from Santiago, who reported less prior use of healthcare, were more likely to self-collect.

Literacy was significantly higher among women who self- collected a sample in Livingston compared to those who did not (crude PR 2.04; 95% CI: 1.27, 3.28; adjusted PR, 2.25; 95% CI: 1.38, 3.68) (Table 4). IUD use was also higher among women who self-collected a sample in Livingston (crude PR 1.49; 95% CI: 1.15, 1.94; adjusted PR 1.43; 95% CI: 1.08, 1.88) (Table 4). Additionally, regular drinking and never being married were higher among women who self-collected but not significant (regular drinking, crude PR 1.18; 95% CI: 0.95, 1.48; adjusted PR 1.14; 95% CI 0.89, 1.46; never married, crude PR 1.19; 95% CI: 0.96, 1.48; adjusted PR 1.15; 95% CI: 0.91, 1.43) (Table 4).

Using stepwise selection with adjustment for age, ethnicity, and more than one lifetime sexual partner, only literacy was selected as an exposure covariate (PR 2.25; 95% CI: 1.38, 3.68). When stratifying ethnic group (Q'echchi versus Garifuna and Ladino), the association between literacy and actual sample collection remained positive (Table 5). However, this relationship only remained statistically significant among Q'echchi participants. However, interaction terms between ethnic group (Q'echchi versus not) and literacy revealed that the effect

of literacy among the Q'echchi was not significantly different from the Ladinos and Garifunas (interaction term PR 0.94; 95% CI: 0.25, 3.59).

Finally, when fully adjusting for all exposure covariates, the effect of literacy continued to remain significant (PR 1.68; 95% CI: 1.12, 2.51).

Self-Collection Acceptability and Comfort

Among those who did collect a sample, the self-collection testing was highly acceptable in both communities. Of Santiago participants who self-collected, 81.4% found it comfortable and 84.8% reported that the HerSwab was easy to use. Among Livingston participants who self-collected, 87.0% found it comfortable and 87.0% reported it was easy to use. Among those who chose to self-collect, almost all participants in both locations reported that they were willing to use it as a form of cervical cancer screening (98.0% in Santiago and 100% in Livingston) (Table 2).

HPV Prevalence

Overall, 19% of samples tested positive for high-risk HPV (N=549). 18.7% of samples from Santiago Atitlán (N=77) tested positive for high-risk HPV and 21.3% of samples from Livingston (N=29) tested positive, but this difference was not statistically significant (p-value=0.4923). In total, 94% of participants who sampled in Santiago Atitlán and 88.5% of participants who sampled in Livingston were provided with their test results. Overall, 12.3% of HPV tests were found to be inconclusive (N=44 (9.6%) from Santiago Atitlán and N=33 (19.5%) from Livingston).

DISCUSSION

In this study, we assessed the acceptability of HPV self-collection testing as an alternative form of primary cervical cancer screening in indigenous and rural communities in

Guatemala. We found that self-collection appears to be highly acceptable among women who tried it, independent of community and ethnicity. Most women reported that self-collection was comfortable and easy to use, and almost all women who tried it reported being willing to use it as a form of cervical cancer screening in the future. These results are consistent with other studies looking at self-collection acceptability both within Guatemala and other LMICs[27 32]. This study was further able to build upon previous studies and provide important information regarding HPV self-collection testing acceptability at the community level, and in a community that had not been previously evaluated.

Our study also found, however, that there were differences between communities in willingness to try self-collection. Willingness to try self-collection testing remained consistently high among participants in Santiago Atitlán as reported in the pilot study conducted in 2015 (93% in 2015 versus 93.6% in 2016)[32]. In Livingston, however, even among women who first responded in the survey or consent form that they would be willing to collect a sample, actual self-collection was lower. We found that willingness to self-collect in Livingston was consistently associated with higher levels of literacy and prior IUD use. In contrast, ethnicity, history of cervical cancer screening, and health behaviors were not associated with willingness to self-collect. Stratified analyses suggested that there were no qualitative differences in the association between literacy and sample collection across ethnic groupings (Mayan descent versus non-Mayan descent) in Livingston. However, high prevalence of literacy among Garifuna made it difficult to evaluate differences between Ladinos and Garifunas in the association between literacy and sampling decision.

The results suggest that HPV self-collection testing program implementation may need to target populations based on relative levels of literacy within communities. A previous study

examining HPV acceptability and intention in the UK similarly found that low education and self-efficacy, defined as an individual's belief in their capability to exercise control over challenging demands, were associated with low sampling intentions[30]. In Guatemala, the inability to either read or write in Spanish may negatively influence a woman's perceived self-efficacy and her confidence in navigating public health infrastructure or self-collecting a vaginal sample, particularly if her surrounding community has high levels of literacy. This population would greatly benefit from HPV self-collection testing as a primary form of cervical cancer screening due to its strength in concentrating less accessible and more invasive screening modalities only towards those that are at high-risk (i.e., positive for HPV). Our results in Livingston suggest that it might be critical that, if implemented, HPV screening and education programs are tailored such that they are more accessible to low-literacy populations and, thus, increase perceived self-efficacy in navigating the existing public health infrastructure.

High prevalence of self-collection testing in Santiago Atitlan, a community with low literacy levels, as compared to the low rates of self-collection testing among those with low literacy in Livingston may reflect larger community differences in awareness or access to screening modalities rather than a lack of effect of literacy in Santiago or an effect of ethnicity. Although women from Santiago reported slightly higher rates of ever receiving cervical cancer screening than women in Livingston, women in Livingston report much higher rates of recent cervical cancer screening than women in Santiago. Santiago Atitlán remains largely deficit in accessible and affordable cervical cancer screening while Livingston has regular, public or private, screening campaigns in the community. This difference in general community access and infrastructure, then, may be acting as an effect modifier on the association between literacy and screening between these two communities, suggesting that self-collection might be better

received at first in communities that do not have other alternatives, whereas some initial skepticism might be found in places with existing cervical screening programs, independently of their quality and efficacy. More research is necessary to evaluate if self-efficacy, relative literacy level, or general community access to healthcare resources and screening play larger barriers for women in trying self-sampling HPV testing. However, the high rates of acceptability and willingness to retake among women who self-collected in both communities suggest that once experienced, self-collection is a valid, and even preferred, alternative to other screening modalities from the women's perspective.

Although based on a different HPV test than in our pilot study (Hybribio HR13 vs. Anyplex 28), a similar prevalence of high-risk HPV was found in Santiago between 2015 and 2016 (17.4% versus 19.3%)[32]. Of note, there were no significant differences in high-risk HPV prevalence between ethnic groups in Livingston, and there was not a statistically significant difference between Santiago Atitlán and Livingston with regards to prevalence.

Our study provided not only a larger sample size compared with previous studies but was also conducted in two differing communities. This is a strength because Guatemala is an extremely diverse country with over 23 languages, distinct ethnicities, and a history of large economic and social inequalities. Thus, generalizing the evaluations of a health program's acceptability and feasibility to the whole country is generally difficult. However, because we evaluated two very different rural multi-ethnic communities, our results may reflect some of the future obstacles and considerations necessary in implementing self-swab HPV testing in such a diverse country as Guatemala than was previously available. In fact, our results also complement the findings of the ongoing careHPV Scale-Up implementation, which is assessing

the performance of HPV testing, including self-collection testing, within urban settings in Guatemala[42-44].

There are several limitations to our study. Due to both the sensitive nature of the questions related to sexual history, it may be possible that a social desirability bias may have resulted in over reporting of perceived "good behaviors", such as screening or use of protection, in addition to under-reporting of perceived "bad behaviors", such as number of lifetime sexual partners and other sexual behavior measures. We tried to minimize the possibility of this bias by maintaining confidentiality with participants. Also, women may report their history of screening or utilization of health care resources incorrectly if they had limited information or understanding of these services. This may be exaggerated in women with low literacy and thus explain potential over reporting of prior cervical cancer screening in Santiago Atitlan. Additionally, because sampling methods differed between the two communities due to the lack of reliable census counts in Livingston, there may be differences between the communities in potential selection bias into the study and more limited comparability of the results. However, our sample in Livingston is reflective of the overall population structure of Livingston in terms of ethnic, age and other metrics, suggesting that influential selection bias into the study might be limited[45].

Screening program implementation is a major challenge in LMIC settings, HPV self-swab testing may serve as a helpful tool in concentrating less accessible and more expensive and invasive screening modalities only towards those that are at high-risk (i.e., positive for HPV). However, as the results in Livingston showed, there are many complex features related to implementing HPV screening that will need to be evaluated before program adoption of such programs. Due to the longitudinal component of our study, future research with our study

participants will hopefully help elucidate how HPV self-collection testing may affect women's decisions to pursue further cervical cancer screening and follow-up care in their local communities after HPV testing and receiving their results. Additionally, these data may reveal other downstream facilitators or barriers to screening that will influence the overall success of HPV self-swab testing implementation in these communities.

CONCLUSION

The results of our study add to the literature on the potential of HPV self-collection testing in LMICs, demonstrating its acceptability in two very different communities in rural Guatemala. The high rates of acceptability and willingness to retake among women who self-collected in both communities suggest that once experienced, self-collection is a valid, and even a preferred, alternative to other screening modalities from the women's perspective. However, the difference in willingness to try self-collection between these communities suggests that relative literacy levels and the availability and quality of existing healthcare programs may affect attitudes towards new screening modalities. Future research should focus on increasing the generalizability of these findings by evaluating additional communities within Guatemala for differences in willingness to try self-collection sampling and further elucidate the potential barriers to accessing and utilizing cervical cancer modalities, including HPV self-collection sampling.

LIST OF ABBREVIATIONS

CC – Cervical Cancer

CHW – Community Health Worker

CI – Confidence Interval

HICs – High-Income Countries

HIV – Human Immunodeficiency Virus

HPV – Human Papillomavirus

HR-HPV – High-Risk Human Papillomavirus

INCAP – Institute of Nutrition of Central America and Panama

IUD – Intra-Uterine Device

LMICs – Low and Middle-Income Countries

OR – Odds Ratio

PCR – Polymerase Chain Reaction

PR – Prevalence Ratio

VIA – Visual Inspection with Acetic Acid

DECLARATIONS

Ethics Approval and Consent to Participate

The University of Michigan Institutional Review Board (HUM00096559) and the Institute of Nutrition of Central America and Panama Institutional Review Board (MI-CIE-16-009) approved study protocols. All participants gave oral and written informed consent prior to participation in the study. The consent was documented by a signature or fingerprint of the participant, the surveyors, and a witness.

Consent for Publication

The authors of this paper have all reviewed its contents and consent for its publication.

Data Sharing Statement

Due to the sensitive nature of the data collected, IRB restrictions, and ongoing data collection, study data is stored at the University of Michigan. Interested parties may contact the corresponding author to request access to de-identified datasets for specific research questions related to the study. The authors welcome further collaboration but reserve the right to retain data to protect study participants.

Competing Interests

The authors have no competing interests to declare.

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Authors' Contributions

PIC - Planning and Key Intellectual Contribution
DC – Data Collection and Project Management
SP – Sample Processing, Laboratory Management, and Test Results
SA – Statistical Analysis and Data Management
W – Writing
E – Editing

Audrey Murchland – PIC, DC, SP, SA, W, E
Anna Gottschlich – PIC, DC, SP, W, E
Kristin Bevilacqua – PIC, DC, SP, E
Andres Pineda – PIC, DC, SP, E
Berner Andrée Sandoval-Ramírez – PIC, DC, SP, E

Christian Alvarez – PIC, E
Gina Ogilvie – PIC, E
Thomas E Carey – PIC, SP, E
Mark Prince – PIC, SP, E
Michael Dean – PIC, SP, E
Carlos Mendoza-Montano – PIC, SP, E
Alvaro Rivera-Andrade – PIC, DC, SP, E
Rafael Meza – PIC, DC, SP, SA, W, E

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TABLES

Table 1. General Population Characteristics Among All Participants

	Santiago Atitlán % (N) or Mean (SD)	Livingston N (%) or Mean (SD)	p-value
N	500	456	
Age (y)	34.78 (8.44)	32.97 (10.38)	**0.003**
Ethnicity			**<0.0001**
Tz'tujil	96.60% (483)	0	
Ladino	1.80% (9)	24.78% (113)	
Garifuna	0	31.80% (145)	
Q'echchi	0	41.89% (191)	
Other	1.40% (7)	1.32% (6)	
Education			**<0.0001**
Less than Primary	69.40% (347)	33.92% (153)	
Primary or Secondary	20.12% (100)	34.37% (155)	
More than Secondary	10.06% (50)	31.71% (143)	
Unknown	0.60% (3)	1.09% (5)	
Literacy			**<0.0001**
Illiterate (Neither Read nor Write)	48.60% (243)	12.53% (57)	
Literate (Either Read and/or Write)	51.20% (255)	87.47% (398)	
Ever Married/United	97.00% (485)	62.50% (285)	**<0.0001**
Breast exam (Heard of)	14.08% (70)	66.59% (303)	**<0.0001**
Pap (Ever)	66.80% (334)	58.11% (265)	**0.0056**
Last Pap			**<0.0001**
Never or Unknown	36.40% (182)	42.54% (194)	
Less than a year	19.40% (97)	29.39% (134)	
More than a year	44.20% (221)	28.07% (128)	
VIA (Ever)	6.04% (30)	1.32% (6)	**<0.0001**
Ever Smoke	0.40% (2)	9.65% (44)	**<0.0001**
Regular Drinker	11.54% (3)	33.85% (44)	**0.0080**
Used IUD (Ever)	1.41% (7)	8.09% (36)	**<0.0001**
Use Protection			**<0.0001**

Always or Almost always	10.00% (50)	19.96% (91)	
Sometimes	4.80% (24)	11.84% (54)	
Rarely or Never	69.60% (348)	47.15% (215)	
Unknown or Refused	15.60% (78)	21.05% (96)	
Number of Lifetime Sexual Partners			**<0.0001**
One	90.6% (453)	70.8% (323)	
More than One	6.8% (34)	25.9% (118)	
Refused	2.6% (13)	3.3% (15)	
Knowledge of HPV	11.80% (59)	62.72% (286)	**<0.0001**
Severity of CC			**<0.0001**
Not or A Little	2.40% (12)	12.28% (56)	
Moderate	22.80% (114)	6.80% (31)	
Very or Extremely	74.80% (374)	80.92% (369)	
Willing to Vaccinate Daughters for HPV if Available			**<0.0001**
Yes	69.60% (348)	82.24% (375)	
No	1.00% (5)	6.80% (31)	
Don't Have Daughters	27.60% (138)	8.33% (38)	
Refused	1.8% (9)	2.6% (12)	

Table 2: Acceptability of Self-Collection HPV Tests
Among Age-Eligible Women (25-54 years of age)

	Santiago Atitlán % (N)	**Livingston % (N)**	**p-value[a,b]**
N	500 *(all participants)* 438 *(age-eligible)*	*456 (all participants)* *322 (age-eligible)*	
HPV knowledge	10.05% (44)	63.98% (206)	**<0.0001**
Self-Reported Previous Pap (Ever)	71.46% (313)	69.88% (225)	0.6348
Abnormal Pap (Ever)	16.61% (52)	36.89% (83)	**<0.0001**
Knowledge of VIA	6.85% (30)	1.86% (6)	**0.0023**
Willing to Collect Sample at Home	93.38% (409)	62.42% (201)	**<0.0001**
Collected Sample	93.61% (410)	52.48% (169)	**<0.0001**
Prefer Home Screening	94.06% (412)	44.41% (143)	**<0.0001**
Prefer Self-Collection	91.10% (399)	41.61% (134)	**<0.0001**
Collected Sample, Among Those Who Said They Were Willing to Collect at Home	96.82% (396)	76.12% (153)	**<0.0001**
	% (N)	**% (N)**	
N	410 *(age-eligible; test-taking participants)*	*169 (age eligible; test-taking participants)*	
Comfort of test			**0.0013[b]**
Comfortable	81.4% (333)	87.0% (141)	
Neutral	5.87% (24)	5.56% (9)	
Uncomfortable	12.7% (52)	7.4% (12)	
Ease of test			**0.0241[b]**

Easy	84.8% (347)	87.0% (141)	
Neutral	4.65% (19)	7.41% (12)	
Difficult	10.5% (43)	5.55% (9)	
Willingness to retake test	98.0% (402)	100% (169)	1.00[b]

[a]p-values for means calculated using two-sample t-test; proportions using chi-squared test
[b]Fisher's exact test used to account for low cell counts

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Table 3. Population Characteristics within Livingston [a]Age-Eligible Women Who Sampled vs. Age-Eligible Women Who Did Not Sample			
	Took the Sample % (N) or Mean (SD)	**Did Not Take the Sample % (N) or Mean (SD)**	**p-value[b]**
N	52.48% (169)	47.52% (153)	
Age (y)	34.98 (7.76)	36.35 (7.66)	0.1141
Ethnicity			0.6986
Ladino	50.59% (43)	49.41% (42)	
Garifuna	54.37% (56)	45.63% (47)	
Q'echchi	51.94% (67)	48.06% (62)	
Other	75.0% (3)	25.00% (1)	
Declined	0	100.0% (1)	
Education			0.0784
Less than Primary	46.34% (57)	53.66% (66)	
Primary or Secondary	57.14% (60)	42.86% (45)	
More than Secondary	56.18% (50)	43.82% (39)	
Unknown	40.00% (2)	60.00% (3)	
Literacy			**0.0005**
Illiterate (Neither Read nor Write)	29.17% (14)	70.83% (34)	
Literate (Either Read and/or Write)	56.57% (155)	43.43% (119)	
Married/United			0.2365
Ever	49.78% (112)	50.22% (113)	
Never	50.22% (56)	41.67% (40)	
Unknown	100.0% (1)	0	
Pap or VIA			0.2324
Ever	54.67% (123)	45.33% (102)	
Never	47.42% (46)	52.58% (51)	
Ever Smoke			0.6309
Ever	53.33% (16)	46.67% (14)	
Never	52.23% (152)	47.77% (139)	
Unknown	100.0% (1)	0	
Regular Drinker			0.7619
Yes	56.67% (17)	43.33% (13)	
No	51.89% (151)	48.11% (140)	
Unknown	100.0% (1)	0	
Used IUD			**0.0112**
Ever	73.08% (19)	26.92% (7)	
Never	51.37% (150)	48.63% (142)	
Don't know	100.0% (4)	0	
Use Protection			0.1260
Always or Almost always	58.62% (34)	41.38% (24)	
Sometimes	58.54% (24)	41.46% (17)	
Rarely or Never	53.75% (86)	46.25% (74)	
Unknown	39.68% (25)	60.32% (38)	
Number of Lifetime Partners			0.0670
One	49.12% (111)	50.88% (115)	
More than One	61.29% (57)	38.71% (36)	
Refused	33.33% (1)	66.66% (2)	
Knowledge of HPV	55.83% (115)	44.17% (91)	0.1097
Severity of CC			0.4191
Not	36.36% (4)	63.64% (7)	

A little	68.18% (15)	31.82% (7)	
Moderate	56.52% (13)	43.48% (10)	
Very	52.58% (102)	47.42% (92)	
Extremely	48.61% (35)	51.39% (37)	
Believe at risk of CC			0.2684
Strongly Agree or Agree	55.14% (102)	44.86% (83)	
Other	48.91% (67)	51.09% (70)	
Willing to Vaccinate Daughters for HPV if Available			0.4024
Yes	54.32% (151)	45.68% (127)	
No	47.62% (10)	52.38% (11)	
Don't Have Daughters	38.46% (5)	61.54% (8)	
Refused	30.00% (3)	70.00% (7)	

[a]% calculated for sampling decision by each covariate
[b] p-values for means calculated using two-sample t-test; proportions using chi-squared test

Table 4. Prevalence Ratio of Sample Collection in Livingston among Age-Eligible Women

Log-Binomial Regression: Prevalence Ratio of Sample Collection (N=309)

	Exposure Covariates Effect on Sample Collection; PR (95% CI)							
	Literacy (Y)	Marriage (Never)	Hx of Pap/VIA (Ever)	Smoking (Y)	Drinking (Y)	IUD Use (Y)	Family Hx of CC (Y)	Believe at Risk for CC (Y)
$Model_1$: Main Effect	**2.04 (1.27, 3.28)**	1.19 (0.96, 1.48)	1.18 (0.92, 1.52)	1.02 (0.71, 1.46)	1.18 (0.95, 1.48)	**1.49 (1.15, 1.94)**	1.13 (0.81, 1.55)	1.09 (0.87, 1.35)
$Model_2$: Main Effect	**2.25 (1.38, 3.68)**	1.15 (0.91, 1.43)	1.20 (0.93, 1.56)	0.94 (0.66, 1.35)	1.14 (0.89, 1.46)	**1.43 (1.08, 1.88)**	1.15 (0.83, 1.58)	1.06 (0.85, 1.32)
Age	1.00 (0.98, 1.01)	0.99 (0.97, 1.00)	0.99 (0.97, 1.00)	0.99 (0.97, 1.00)	0.99 (0.97, 1.00)	0.99 (0.98, 1.01)	0.99 (0.97, 1.00)	0.99 (0.97, 1.00)
Ethnicity								
Ladino (Ref.)	---	---	---	---	---	---	---	---
Garifuna	0.98 (0.75, 1.28)	0.97 (0.73, 1.28)	0.99 (0.75, 1.31)	1.00 (0.75, 1.32)	0.96 (0.72, 1.28)	0.96 (0.73, 1.25)	1.00 (0.76, 1.32)	0.99 (0.75, 1.31)
Q'echchi	1.22 (0.93, 1.60)	1.02 (0.78, 1.33)	1.06 (0.81, 1.39)	1.01 (0.76, 1.32)	1.04 (0.79, 1.37)	1.05 (0.80, 1.38)	1.04 (0.79, 1.38)	1.00 (0.77, 1.32)
More than One Lifetime Sexual Partners	1.31 (1.06, 1.63)	1.22 (0.98, 1.53)	1.23 (0.99, 1.53)	1.25 (1.00, 1.56)	1.22 (0.98, 1.54)	1.23 (0.99, 1.52)	1.25 (1.00, 1.56)	1.23 (0.99, 1.54)

M_1: unadjusted log-binomial model

M_2: adjusted for age, ethnicity, and number of lifetime sexual partners (more than one)

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Table 5. Prevalence Ratio of Sample Collection in Livingston among Age-Eligible Women Stratified by Ethnic Grouping (Mayan descent versus Non-Mayan descent)

Log-Binomial Regression: Prevalence Ratio of Sample Collection (N=309)

Covariates	Ladino or Garifuna (N=183)	Q'echchi (N=126)
	PR (95% CI)	PR (95% CI)
Literacy (Y)	2.39 (0.70, 8.15)	2.08 (1.17, 3.69)
Age	1.00 (0.98, 1.02)	0.99 (0.96, 1.02)
More than One Lifetime Sexual Partner	1.31 (1.00, 1.72)	1.37 (1.00, 1.88)

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FIGURE LEGENDS

Figure 1. Flow Chart of Livingston Self-Collection Sampling and Testing

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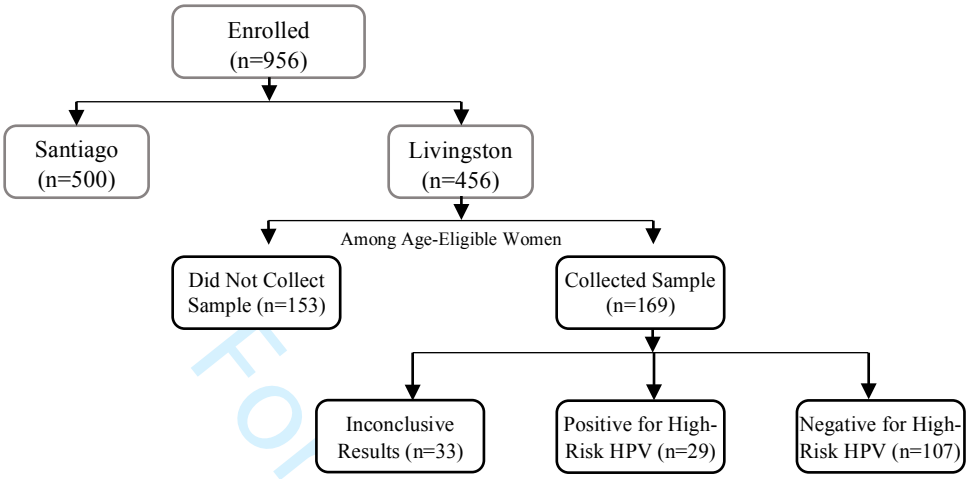
Figure 1. Flow Chart of Livingston Self-Collection Sampling and Testing



HPV Self-Sampling Acceptability in Rural and Indigenous Communities in Guatemala: A Cross-Sectional Study

Audrey Murchland, Anna Gottschlich, Kristin Bevilacqua, Andres Pineda, Berner Andrée Sandoval-Ramírez, Christian S. Alvarez, Gina Ogilvie, Thomas E Carey, Mark Prince, Michael Dean, Carlos Mendoza-Montano, Alvaro Rivera-Andrade, Rafael Meza

Supplementary Appendix

Appendix A: Additional Reference Tables

Appendix B: Self-reported Willingness to Collect a Sample

Appendix A – Additional Reference Tables

Table A1: Population Characteristics within Livingston
Age-Eligible Women Who Declined At Home Sampling vs. Age-Eligible Women Who Did Not Sample

	Did Not Want to Collect Sample (Survey Response) N (%) or Mean (SD)	Did Not Collect Sample N (%) or Mean (SD)
N	121	153
Age (y)	36.7 (7.80)	36.3 (7.66)
Education		
Less than primary	51 (42.15%)	66 (43.14%)
Primary	34 (28.10%)	45 (29.41%)
More than primary	33 (27.27%)	39 (25.49%)
Unknown	3 (2.48%)	3 (1.96%)
Literacy		
Illiterate (Neither Read nor Write)	27 (22.31%)	34 (22.22%)
Literate (Either Read and/or Write)	94 (77.69%)	119 (77.78%)
Married/United (Ever)	92 (76.03%)	113 (73.9%)
Regular Drinking	8 (6.61%)	13 (8.50%)
Use Health Services	112 (92.56%)	140 (91.50%)

Table A2. General Population Characteristics Among All Participants (Continued)			
	Santiago Atitlan N (%) or Mean (SD)	**Livingston N (%) or Mean (SD)**	**p-value[a]**
N	500	456	
Current Marital Status			**<0.0001**
Single	3 (0.62%)	30 (10.53%)	
Married	311 (64.12%)	101 (35.44%)	
Separated	28 (5.77%)	2 (0.70%)	
Divorced	5 (1.03%)	0	
Widowed	15 (3.09%)	1 (0.35%)	
Common Law	120 (24.74%)	151 (52.98%)	
Refused	3 (0.62%)	0	
Age at Marriage	19.8 (4.31)	19.74 (5.82)	0.8771
Mammogram (Ever)	10 (2.01%)	40 (8.77%)	**<0.0001**
Pap or VIA (Ever)	337 (67.40%)	265 (58.11%)	0.7592
Last Pap			**<0.0001**
Never	33.20% (166)	41.9% (191)	
Less than 6 months	6.20% (31)	13.82% (63)	
6 months to a year	13.20% (66)	15.57% (71)	
1 to 5 years	34.20% (171)	20.39% (93)	
More than 5 years	10.00% (50)	7.68% (35)	
Unknown	3.20% (16)	0.66% (3)	
Used Birth Control Injections	215 (43.17%)	173 (38.88%)	0.3459
Used Oral Contraceptives	54 (10.84%)	123 (27.64%)	**<0.0001**
Number of Pregnancies	2.81 (1.93)	3.19 (2.49)	**0.0082**
Number of Children	2.54 (1.65)	3.20 (2.12)	**<0.0001**
Age at First Child	20.18 (5.80)	18.88 (3.74%)	**0.0001**
Currently Sexually Active	171 (79.53%)	121 (63.68%)	**0.0035**
Age at First Sexual Relation	19.63 (4.29)	17.24 (2.77)	**<0.0001**
Family Member with Cervical Cancer	2.65% (13)	11.28% (51)	**<0.0001**
Believe at Risk for CC			**<0.0001**
Strongly Agree	24.80% (124)	14.47% (66)	
Agree	13.20% (66)	41.23% (188)	
Neutral	13.60% (68)	5.26% (24)	
Disagree	9.00% (45)	8.55% (39)	
Strongly Disagree	19.00% (95)	8.99% (41)	
Likely to Get CC			**<0.0001**
No Chance	135 (27%)	152 (33.33%)	
Low	97 (19.40%)	175 (38.38%)	
Moderate	32 (6.40%)	13 (2.85%)	
High	22 (4.40%)	7 (1.54%)	
Certain	17 (3.40%)	6 (1.32%)	
Unsure	0	103 (22.59%)	
Refused	197 (39.40%)	0	

Table A3. Population Characteristics within Livingston (Continued)
Age-Eligible Women Who Sampled vs. Age-Eligible Women Who Did Not Sample

	Took the Sample % (N) or Mean (SD)	Did Not Take the Sample % (N) or Mean (SD)	p-value[a]
N	52.48% (169)	47.52% (153)	
Current Marital Status			0.4399
Never Married	58.76% (57)	41.24% (40)	
Single	48.00% (12)	52.00% (13)	
Married	43.37% (36)	56.63% (47)	
Separated	50.00% (1)	50.00% (1)	
Divorced	0.00% (0)	0.00% (0)	
Widowed	0.00% (0)	100.00% (1)	
Common Law	55.26% (63)	44.74% (51)	
Age at First Marriage	19.67 (4.51)	20.90 (7.35)	0.1506
Breast Exam (Heard Of)	55.66% (123)	44.34% (98)	0.1325
Mammogram (Ever)	50.00% (16)	50.00% (16)	0.7668
Pap (Ever)	54.67% (123)	45.33% (102)	0.2324
Last Pap			0.7520
Less than 6 months	52.83% (28)	47.17% (25)	
Within the last year	57.14% (32)	42.86% (24)	
Within the last 2-5 years	55.95% (47)	44.05% (37)	
More than 5 years	55.17% (16)	44.83% (13)	
VIA (Ever)	83.33% (5)	16.67% (1)	0.1050
Used Birth Control Injections	56.12% (78)	43.88% (61)	0.2292
Used Oral Contraceptives	58.25% (60)	41.75% (43)	0.1336
Number of Pregnancies	3.49 (2.27)	3.74 (2.30)	0.3346
Number of Children	3.20 (1.78)	3.61 (2.14)	0.1712
Age at First Pregnancy	18.87 (3.50)	19.27 (4.41)	0.3853
Currently Sexually Active	52.94% (45)	47.06% (40)	0.2068
Age at First Sexual Relation	17.20 (2.97)	17.56 (2.96)	0.4102
Family Member with CC	60.61% (20)	39.39% (13)	0.6143
Believe at Risk for CC			**0.0398**
Strongly Agree	67.27% (37)	32.73% (18)	
Agree	50.00% (65)	50.00% (65)	
Neutral	76.92% (10)	23.08% (3)	
Disagree	56.52% (13)	43.48% (10)	
Strongly Disagree	44.83% (13)	55.17% (16)	
Unsure	43.06% (31)	56.94% (41)	
Likely to Get CC			0.0612
No Chance	58.77% (67)	41.25% (47)	
Low	49.11% (55)	50.89% (57)	
Moderate	85.71% (6)	12.49% (1)	
High	83.33% (5)	16.67% (1)	
Certain	50.00% (2)	50.00% (2)	
Unsure	43.04% (34)	56.96% (45)	

[a]p-values for means calculated using two-sample t-test; proportions using chi-squared test

Table A4: Population Characteristics within Livingston
Comparing Racial/Ethnic Groups in Livingston Including All Women

	Ladino N (%) or Mean (SD)	Garifuna N (%) or Mean (SD)	Q'echchi N (%) or Mean (SD)	p-value[a]
N	113 (25.17%)	145 (32.29%)	191 (42.54%)	
Age (y)	34.49 (10.32)	33.23 (10.54)	31.91 (10.19)	0.1022
Education				**<0.0001**
Less than primary	35 (30.97%)	12 (8.28%)	104 (54.45%)	
Primary	39 (34.51%)	69 (47.59%)	45 (23.56%)	
More than primary	38 (33.63%)	62 (42.76%)	40 (20.94%)	
Literacy				**<0.0001**
Neither	8 (7.08%)	3 (2.07%)	45 (23.56%)	
Read Only	1 (0.88%)	0	3 (1.57%)	
Read and Write	104 (92.04%)	142 (97.93%)	142 (74.35%)	
Married/United (Ever)	87 (76.99%)	63 (43.45%)	128 (67.02%)	**<0.0001**
Breast Exam (Heard of)	88 (77.88%)	112 (77.24%)	98 (51.31%)	**<0.0001**
Mammogram (Ever)	11 (9.73%)	21 (14.48%)	8 (4.19%)	**0.0043**
Pap (Ever)	70 (61.95%)	107 (73.79%)	83 (43.46%)	**<0.0001**
Last pap				**0.0212[b]**
Less than 6 months	14 (20%)	34 (31.78%)	13 (15.66%)	
Within the last year	18 (25.71%)	37 (34.58%)	16 (19.28%)	
Within the last 2-5 years	27 (38.57%)	28 (26.19%)	36 (43.37%)	
More than 5 years	10 (14.29%)	6 (5.61%)	18 (21.69%)	
VIA (Ever)	2 (1.77%)	1 (0.69%)	3 (1.57%)	0.6142
Ever Smoke	15 (13.27%)	27 (18.62%)	2 (1.05%)	**<0.0001[b]**
Ever Drink	30 (26.55%)	74 (51.03%)	24 (12.57%)	**<0.0001[b]**
Used Birth Control Injections	46 (41.44%)	59 (41.55%)	66 (35.68%)	0.8213
Used Oral Contraceptives	30 (27.03%)	64 (45.07%)	28 (15.14%)	**<0.0001[b]**
Used IUD	9 (8.11%)	22 (15.49%)	4 (2.16%)	**<0.0001[b]**
Use protection				**<0.0001[b]**
Always	11 (9.91%)	36 (25.35%)	9 (4.86%)	
Almost always	11 (9.91%)	15 (10.56%)	8 (4.32%)	
Sometimes	8 (7.215)	30 (21.13%)	14 (7.57%)	
Rarely	5 (4.50%)	9 (6.34%)	11 (5.95%)	
Never	62 (55.865)	41 (28.87%)	85 (45.95%)	
Unknown	14 (12.61%)	11 (7.75%)	58 (31.35%)	
Family Member with CC	21 (18.58%)	19 (13.10%)	10 (5.24%)	**<0.0001[b]**
Knowledge of HPV	78 (69.03%)	112 (77.24%)	90 (47.12%)	**<0.0001**
Believe They Are at Risk for CC				
Strongly Agree	11 (9.73%)	30 (20.69%)	25 (13.09%)	
Agree	51 (45.13%)	49 (33.79%)	87 (45.55%)	
Neutral	6 (5.31%)	7 (4.83%)	10 (5.24%)	
Disagree	15 (13.27%)	17 (11.72%)	6 (3.14%)	
Strongly Disagree	10 (8.85%)	22 (15.17%)	9 (4.71%)	
Unsure	20 (17.70%)	19 (13.10%)	54 (28.27%)	
Vaccinate Daughters for HPV				0.4056
Yes	94 (83.19%)	120 (82.70%)	156 (81.68%)	
No	10 (8.85%)	5 (3.45%)	15 (7.85%)	
Don't Have Daughters	8 (7.08%)	15 (10.34%)	14 (7.33%)	
Willing to Collect Sample at Home	61 (53.98%)	94 (64.83%)	104 (54.45%)	0.2802
Collected Sample	44 (38.94%)	56 (38.62%)	67 (35.08%)	0.7264

[a]p-values for means calculated using one-way ANOVA or Welch (if equality of variance is rejected); proportions using chi-squared test
[b]Fisher's Exact Test used due to small cell counts

Table A5: Differences Among Communities of Age-Eligible Indigenous Mayan Women
Age-Eligible Tz'tujil Women vs. Age-Eligible Q'echchi Women

	Tz'tujil - Santiago N (%) or Mean (SD)	Q'echchi - Livingston N (%) or Mean (SD)	p-value[a]
N	420 (68.74%)	191 (31.26%)	
Age (y)	36.25 (7.46)	31.91 (10.19)	**<0.0001**
Education			**<0.0001**
Less than primary	314 (75.12%)	104 (54.45%)	
Primary	64 (15.31%)	45 (23.56%)	
More than primary	40 (9.57%)	40 (20.94%)	
Literacy			**<0.0001**
Neither	225 (53.57%)	45 (23.56%)	
Read Only	7 (1.67%)	3 (1.57%)	
Read and Write	188 (44.76%)	142 (74.35%)	
Ever Married/United	412 (98.10%)	128 (67.02%)	**<0.0001**
Age at marriage	29.85 (137.8)	24.46 (20.33)	0.4463
Breast exam (Heard of)	53 (12.68%)	98 (51.31%)	**<0.0001**
Mammogram (Ever)	10 (2.38%)	8 (4.19%)	0.2206
Pap (Ever)	296 (70.48%)	83 (43.46%)	**<0.0001**
Last pap			0.2751
Less than 6 months	26 (9.25%)	13 (15.66%)	
Within the last year	57 (20.28%)	16 (19.28%)	
Within the last 2-5 years	153 (54.44%)	36 (43.37%)	
More than 5 years	45 (16.01%)	18 (21.69%)	
VIA (ever)	28 (6.70%)	3 (1.57%)	**0.0076**
Pap or VIA (Ever)	299 (71.19%)	83 (43.46%)	**<0.0001**
Ever Smoke	1 (0.24%)	2 (1.05%)	0.1907
Drink (regularly)	3 (14.29%)	1 (4.17%)	0.2341
Used BC injections	186 (44.71%)	66 (35.68%)	**0.0786**
Used IUD	5 (1.20%)	4 (2.16%)	0.1497
Use protection			**<0.0001**
Always	29 (8.33%)	9 (4.86%)	
Almost always	11 (3.16%)	8 (4.32%)	
Sometimes	20 (5.75%)	14 (7.57%)	
Rarely	9 (2.59%)	11 (5.95%)	
Never	279 (80.17%)	85 (45.95%)	
Family Member with CC	12 (2.01%)	10 (5.24%)	**0.0408**
Age at First Sexual Relation	20.00 (4.48)	16.64 (2.45)	**<0.0001**
Currently Sexually Active	138 (82.63%)	42 (64.62%)	**0.0025**
Knowledge of HPV	37 (8.81%)	90 (47.12%)	**<0.0001**
Believe At Risk for CC			**<0.0001**
Strongly Agree	105 (31.82%)	25 (13.09%)	
Agree	51 (15.45%)	87 (45.55%)	
Neutral	61 (18.48%)	10 (5.24%)	
Disagree	41 (12.42%)	6 (3.14%)	
Strongly Disagree	72 (21.82%)	9 (4.71%)	
Unsure	0	54 (28.27%)	
Vaccinate Daughters for HPV			**<0.0001**
Yes	301 (73.24%)	156 (81.68%)	
No	4 (0.97%)	15 (7.85%)	
Don't Have Daughters	106 (25.79%)	14 (7.33%)	
Willing to Sample in Home	394 (95.63%)	104 (54.45%)	**<0.0001**
Collected Sample	395 (94.05%)	67 (35.08%)	**<0.0001**

[a]p-values for means calculated using two-sample t-test; proportions using chi-squared test

Appendix B – Self-Reported Willingness to Self-Collect Sample

As a final sensitivity analysis, we present results evaluating potential predictors of self-reported willingness to self-collect a vaginal sample as reported in the survey.

Table B1. Prevalence Ratio of Willingness to Collect at Home in Livingston

Log-Binomial Regression: Prevalence Ratio of Willingness to Sample at Home (N=309)

Variable	PR^{M1}	95% CI		PR^{M2}	95% CI		PR^{M3}	95% CI	
Literacy (Y)	**1.55**	**1.10**	**2.19**	**1.55**	**1.08**	**2.23**	1.15	0.94	1.41
Marriage (Never)	**1.20**	**1.01**	**1.42**	1.11	0.98	1.34	1.08	0.94	1.22
Hx of Pap/VIA (Ever)	1.23	0.99	1.52	**1.24**	**1.01**	**1.52**	1.06	0.93	1.21
Smoking (Y)	1.08	0.82	1.41	1.01	0.98	1.29	1.01	0.80	1.27
Drinking (Y)	1.18	0.99	1.40	1.09	0.90	1.32	1.02	0.89	1.17
IUD Use (Y)	**1.38**	**1.12**	**1.68**	1.22	0.97	1.53	1.11	0.88	1.40
Family Hx of CC (Y)	1.16	0.90	1.47	1.18	0.93	1.48	1.03	0.84	1.26
Believe at Risk for CC (Y)	**1.24**	**1.03**	**1.49**	1.19	0.99	1.43	1.08	0.96	1.22

M1: unadjusted log-binomial model
M2: adjusted for age, ethnicity, and number of lifetime sexual partners
M3: all variables included and adjusted for age, ethnicity, and number of lifetime sexual partners

STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	12
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	11
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	11
		(*b*) Describe any methods used to examine subgroups and interactions	11
		(*c*) Explain how missing data were addressed	11
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	11
		(*e*) Describe any sensitivity analyses	

Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12-13
		(b) Indicate number of participants with missing data for each variable of interest	12
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	13, 15
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	14
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	14
Discussion			
Key results	18	Summarise key results with reference to study objectives	15,16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17
Generalisability	21	Discuss the generalisability (external validity) of the study results	18,19
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

**Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.*

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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HPV Self-Sampling Acceptability in Rural and Indigenous Communities in Guatemala: A Cross-Sectional Study

Audrey R. Murchland[1], Anna Gottschlich[1], Kristin Bevilacqua[1], Andres Pineda[2], Berner Andrée Sandoval-Ramírez[3], Christian S. Alvarez[1], Gina Ogilvie[4], Thomas E Carey[5], Mark Prince[6], Michael Dean[7], Carlos Mendoza-Montano[2], Alvaro Rivera-Andrade[2], Rafael Meza[1]

1. Department of Epidemiology, School of Public Health, University of Michigan, 1415 Washington Heights, Ann Arbor, Michigan 48103

2. Institute of Nutrition of Central America and Panama-INCAP, Calzada Roosevelt 6-25 zona 11, Apartado Postal 1188 Guatemala City, Guatemala 01011

3. Functional Nutrition, Oxidation, and Cardiovascular Diseases Group (NFOC-Salut), Universitat Rovira i Virgili, Hospital Universitari Sant Joan (HUSJR), Sant Llorenç, 21, 43201, Reus, Spain

4. Clinical Prevention Services, BC Centre for Disease Control, 655 W 12th Ave, Vancouver, British Columbia V5Z4R4, Canada

5. Department of Otolaryngology-Head and Neck Surgery and Department of Pharmacology, University of Michigan, 5311 Medical Science Unit I 1301 Catherine St., Ann Arbor, Michigan 48109

6. Department of Otolaryngology, University of Michigan, 1500 E Medical Center Dr SPC 5312, Ann Arbor, Michigan 48109

7. Laboratory of Translational Genomics, Division of Cancer, Epidemiology and Genetics, National Cancer Institute, Gaithersburg, MD USA

Corresponding Author:
Rafael Meza, Ph.D.
SPH II, Room 5033, 1415 Washington Heights
Ann Arbor, MI 48109-2029
E-mail: rmeza@umich.edu
Telephone: +1 (734) 763-1946

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ABSTRACT

Introduction: Cervical cancer disproportionately burdens low- and middle-income countries (LMICs) such as Guatemala. Self-collection testing for human papillomavirus (HPV) has been suggested as a form of cervical cancer screening to facilitate access in LMICs. This study assessed and compared the acceptability of self-collection HPV testing in two rural, indigenous and ethnically distinct communities in Guatemala: Santiago Atitlán, Sololá and Livingston, Izabal.

Methods: All participants, women between ages 18 and 60, completed a questionnaire. Eligible participants were also asked to self-collect a vaginal sample and complete a questionnaire regarding comfort and acceptability. Self-collected samples were tested for high-risk HPV using the real-time PCR Hybribio kit.

Results: In the indigenous community of Santiago Atitlán, of 438 age-eligible participants, 94% completed self-collection. Of those, 81% found it comfortable and 98% were willing to use it as a form of screening. In the multi-ethnic (Afro-Caribbean, indigenous) community of Livingston, of 322 age-eligible participants, 53% chose to self-collect. Among those who took the test, 87% found it comfortable and 100% were willing to use it as a form of screening. In Livingston, literacy (can read and/or write versus cannot read or write) was higher in women who chose to self-collect (prevalence ratio, 2.25; 95% CI: 1.38, 3.68). Ethnicity, history of screening, and reproductive history were not associated with willingness to self-collect in Livingston. Women in Santiago reported less prior use of healthcare than women in Livingston. Overall, 19% (106/549) of samples tested positive for high-risk HPV.

Conclusion: Among women willing to self-collect in rural and indigenous communities in Guatemala, self-collection for HPV testing is highly acceptable. However, willingness to try self-collection might vary across communities and settings. Women from a community that used less healthcare were more likely to choose self-collection. Further research is necessary to determine what factors influence a woman's choice to self-collect.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- To our knowledge, little is known about the acceptability of self-collection HPV testing across the diverse communities within Guatemala and Latin America, and in particular among indigenous populations.
- Our study provided not only a larger sample size compared with previous studies but was also conducted in two differing communities.
- Due to both the sensitive nature of the questions related to sexual history, it may be possible that a social desirability bias may have resulted in over reporting of perceived "good behaviors", such as screening or use of protection, in addition to under-reporting of perceived "bad behaviors", such as number of lifetime sexual partners and other sexual behavior measures.
- Sampling methods differed between the two communities due to the lack of reliable census counts in one community, but our sample in this community is reflective of the overall population structure in terms of ethnic, age and other metrics, suggesting that influential selection bias into the study might be limited.

INTRODUCTION

Cervical cancer, primarily caused by human papillomavirus (HPV) infection, has a very good prognosis when detected in premalignant or early malignant stages[1]. However, it disproportionately burdens low- and middle-income countries (LMICs), such as Guatemala, compared to high-income countries (HICs)[2-4]. HICs currently use Pap smears to detect abnormal cervical lesions that can be removed, greatly reducing the risk of cervical cancer[3 5]. However, there are many barriers to implementing successful Pap smear (cytology-based) screening programs in LMICs, including difficulties establishing sustainable laboratory infrastructure, training and retaining adequate numbers of trained pathologists or cytologists, overburdened primary care clinics, and time and travel limitations for women in reaching screening locations[1 6 7]. Due to these factors and others, the percentage of women in Guatemala who are screened for cervical cancer remains low; in 2014, only 49.8% of women (15-49 years of age) reported ever having a Pap smear. Thus, significant improvements in screening or program implementation are paramount to improving cervical cancer outcomes in Guatemala[3 8 9].

Since more than 90% of cervical cancers are caused by the HPV virus, HPV testing has been suggested as a possible alternative, primary form of cervical cancer screening[10-12]. When used in combination with Visual Inspection with Acetic Acid (VIA) or Pap smears in low-income settings, HPV testing has been shown to provide significant improvements in the detection of advanced premalignant lesions and cancer in sensitivity as compared to VIA or Pap smear alone, as only women who test positive for HPV need to follow up with further screening[13-16]. Previous studies have also confirmed that HPV self-swab kits are comparable to physician administered samples in their ability to detect carcinogenic, high-risk HPV [17 18]. Thus, at-home HPV sample collection, with referral to further screening for those positive for high-risk

HPV, may be both more acceptable within low-income communities and more programmatically feasible[6 7 19]. Moreover, a 2015 meta-analysis showed that HPV self-sampling, particularly in opt-in programs, increased participation in cervical cancer screening programs. However, further work is needed to evaluate acceptable opt-in programs for women[20].

Studies have shown that HPV self-sampling is generally acceptable among women in low and high resource settings as well as immigrant, rural, vulnerable populations[21-31]. To our knowledge, however, little is known about the acceptability of self-collection HPV testing across the diverse communities within Guatemala, and in particular among rural and indigenous populations. In a pilot cross-sectional study assessing the acceptability of HPV self-collection among 200 women in the Mayan community of Santiago Atitlán, Guatemala, a self-swab HPV test was found to be a highly acceptable form of screening[32]. Over 80% of women said that they preferred using a self-swab kit in their home rather than being screened at a doctors' office. However, this pilot study was limited to a relatively small sample in a single, largely homogeneous community, limiting the generalizability of the results to other rural and indigenous communities in Guatemala. Further research is thus needed to evaluate the acceptability of self-collection testing among more diverse rural and indigenous populations within Guatemala, which is very diverse, with over 23 official languages and many indigenous groups, most but not all descendants from the Mayan civilization. The purpose of this study was to evaluate risk factors, knowledge, and attitudes towards cervical cancer and to further assess and compare the acceptability of self-collection HPV testing in two understudied, rural, ethnically distinct communities in Guatemala: Santiago Atitlán and Livingston, Izabal.

METHODS

Study Communities

Santiago Atitlán, Sololá is a rural community located on Lake Atitlán, in the southwest region of Guatemala, 75 miles west of Guatemala City. The Tz'utujil, a Mayan descendant ethnic group, inhabits the region, which surrounds Lake Atitlán. The primary language of Santiago's inhabitants is Tz'utujil, and over half of the villagers speak Spanish as a second language[32]. The majority of women in Santiago Atitlán have at most a primary education. Additionally, as a conservative, religious community, it is highly uncommon for women to either drink or smoke, and almost all women in have previously reported having only one lifetime sexual partner[32].

Livingston, Izabal is located on the Caribbean coast of the country and is a rural community, only accessible by boat, that is the primary Garífuna settlement in Guatemala. The Garífuna people are considered a unique ethnic group with their own language, culture, and cuisine. Additionally, there are large populations of other ethnic and cultural groups located in Livingston including Q'eqchi' (Mayan descent), Ladinos (non-Mayan descent), and populations of Indian descent. Most women in Livingston are believed to have at least basic primary education.

Patient and Public Involvement

The patients were not involved in the development of the research questions, outcome measures or study design. The patients were also not involved in the recruitment and performance of the study. However, the public, Guatemalan physicians, scientists, and community health workers, were involved in the development of the question, design, validation, recruitment, and conduct of the study. Local community health workers were involved in the validation of the survey and study protocol, recruited participants and conducted the interviews, and assisted in providing test results to patients. Guatemalan physicians contributed to

development of the research question and study design, organized the laboratory testing, led and assisted with community health worker training, and provided HPV test results to patients. Local laboratory scientists contributed to the study design and conducted the HPV laboratory testing. The continued collaborations with these team members will be used to disseminate study results to patients and Guatemalan officials via publications, presentations, and meetings.

Eligibility and Recruitment

Trained community health workers (CHWs) in both communities actively recruited participants through home visits. All CHWs were bilingual and spoke both Spanish and either Tz'utujil, Q'eqchi, or Karif (the language of the Garifuna) depending on the location they were working in. Households in Santiago Atitlán were selected at random using stratified multi-level sampling based upon maps and population counts of the communities available through the local municipal office and were kept consistent with previous sampling methods[32]. Households in Livingston were selected at random using convenience sampling due to lack of reliable census data at the neighborhood-level. Sampling methods were, otherwise, kept the same as those in Santiago Atitlán.

Selected households that had at least one woman available between the ages of 18 and 60 were invited to participate in the survey-component of the study to assess risk factors for, attitudes towards, and knowledge of cervical cancer in these communities. For households with more than one eligible woman willing to participate, the female in the household whose birthday was closest to the date of the interview was enrolled in the study. Exclusion criteria consisted of past hysterectomy or previous cervical cancer. Women between the ages of 25 and 54 were also asked to provide a sample, in accordance with Guatemala's current screening recommendations[33]. Additionally, pregnant women, women currently menstruating, and women

who had never been sexually active were also excluded from providing samples but could participate in the survey component. Approximately 62% and 90% of eligible women contacted were willing to participate in the study in Santiago and Livingston, respectively. All participants in the study provided both oral and written informed consent prior to participation in the study. The consent was documented by a signature or fingerprint of the participant, the surveyors, and a witness to the consent process.

Survey

Data collection consisted of two main components: the surveys and the HPV self-collection tests. Local CHWs in each community were trained as interviewers in the appropriate techniques and protocols before beginning home visits. Two CHWs visited each randomly selected household together and read a recruitment script to a female household member to determine the household's eligibility. CHWs administered the survey and provided kits to collect HPV samples only to willing, eligible participants. Surveys were administered in private rooms of the participant's house to minimize response bias to sensitive questions.

The survey questionnaire included 153 questions concerning demographics, risk factors for cervical cancer and HPV, self-reported attitudes towards screening, healthcare service use, and knowledge of cervical cancer and HPV. The survey was developed from the pilot study survey and validated as part of the CHW and translator training to ensure correct translation and cultural relevancy[32]. Each survey was administered by the CHWs using electronic tablets and the Qualtrics offline app.

All women who participated in the study were compensated with a voucher for a free Pap smear or VIA at a local health clinic. Women in both communities can access free VIAs

(Santiago) or Pap Smears (Livingston) in the local public health system, but if they chose to use a private clinic instead of the public clinic, the voucher covered their fees.

HPV Self-Collected Samples

The HPV samples were collected using HerSwab kits, a self-collection sampling method [32 34 35]. If a participant was willing to provide a sample, instructions and graphical materials were provided and the participant collected the sample in a separate, private room from the CHWs. Participants who collected a sample then completed a short post-sample survey with the CHWs of three questions regarding ease, comfort, and acceptability of the sampling method: "How easy was the self-collection swab?"; "How comfortable was the self-collection swab?"; and "Would you be willing to collect a sample every 2-3 years to detect HPV as a form of cervical cancer screening?".

After collection, samples were kept in small, refrigerated coolers carried by the CHWs until they were returned to the main study office at the end of the day where samples were then processed to stabilize sample life. The brush component of the HerSwab kit was cut into a 15-mL test tube using lab scissors. The lab scissors were sterilized using alcohol and an open flame between each sample. Each tube was filled with 5mL of Scope mouthwash using a pipette, and tubes were sealed using a cap and parafilm paper[36]. Mouthwash is a reliable, low-cost transport medium for DNA samples and was used to reflect likely standard operating procedures of HPV screening program implementation in Guatemala[37]. Each sample was labeled with the participant's unique identifier. Time of sample processing and condition of sample were recorded.

Stabilized samples were sent to a molecular biology laboratory at the Institute of Nutrition of Central America and Panama (INCAP) in Guatemala City for testing. Samples were

tested using the real-time polymerase chain reaction (PCR) Hybribio HR-13 kit[38 39]. Samples were processed according to the manufacturers protocol and modified to use a 10 ul reaction volume for the real-time PCR and run on an ABI-7000[36]. After testing, samples were labeled as positive for HR-HPV, negative, or, if both the HPV probe and the internal control were negative, inconclusive. If a sample test was inconclusive during the first test, it was run an additional time using a 20 ul reaction volume, and if no result was obtained, the test was deemed inconclusive.

Follow-Up

A local CHW provided negative and inconclusive results over the phone or through a home visit. Positive results were provided in-person by a study physician who referred participants to their local community health clinic for follow-up and further cervical cancer screening. All participants who couldn't be reached at the study conclusion were re-contacted either at 6 months or one year to provide them with their results. Although women with negative results were not explicitly recommended to attend the clinic, all participants were encouraged to get screened using the voucher provided at the local clinic to support their engagement with local preventative services. Participants who were found to be positive for advanced lesions as a result of follow-up screening were referred for care through the free public health infrastructure in Guatemala, as is currently standard practice. Due to the ongoing nature of the project, data on follow-up screening and care are still in the collection process.

Outcomes and Statistical Analysis

Willingness and acceptability of self-collection testing, knowledge of HPV, and risk factors were evaluated in both communities and across ethnic groups in Livingston, Izabal. Willingness was measured as whether or not a woman chose to self-collect a sample to be tested for HPV (actual self-collection). The acceptability of sample collection was only assessed for

those who self-collected a sample and was analyzed using the post-self-swab survey questions described previously.

A target sample size of 500 per community was determined to be able to detect a 5% difference in self-sampling acceptability with 80% power, assuming a 95% acceptability in Santiago Atitlan based on the pilot.

Due to lower rates of actual self-collection in Livingston, differences between Livingston women willing and those not willing to collect a sample were evaluated using two-sample t-tests for means, chi-squared tests for proportions, and Fisher's Exact test for low cell counts. Most women tried self-collection in Santiago, so we restrict these analyses to Livingston.

The main exposures explored for willingness to try self-collection included: literacy, marital status, history of Pap smear or VIA, smoking status, alcohol use (a potential proxy for risky behavior), IUD use, family history of cervical cancer, and belief of being at risk for cervical cancer. Statistical analyses were run using log-binomial regression. In model set 1, the relationship between each exposure and sampling decision was unadjusted for other covariates. In model set 2, models were additionally adjusted for age, ethnicity, and number of lifetime sexual partners. In model set 3, we used stepwise selection to select significant the exposure covariates (alpha=0.05) when adjusting for age, ethnicity, and number of lifetime sexual partners. Finally, in model set 4, we included all exposure covariates and the adjustment covariates together in a fully adjusted model. The stepwise selected model was further stratified across ethnic groups to evaluate potential effect modification. Due to high prevalence of literacy in Garifuna and Ladino, these groups were combined for stratification to prevent positivity violations (Q'echchi versus Garifuna or Ladino, reflecting a Mayan descent versus non-Mayan descent comparison).

Analyses were restricted to age-eligible women in Livingston with complete covariate information (N=134 or 29.4% excluded due to age-ineligibility and N=13 or 3.5% excluded due to missing covariates). Specifically, we excluded 5 participant missing ethnicity or classified as other ethnicity, 1 participant missing marital status, 1 participant missing regular drinking status, and 3 participants missing number of lifetime sexual partners, 1 participant missing smoking status, and 2 participants missing family history of cancer resulting in a final sample size N=309 for analyses evaluating willingness to try self-collection.

Covariates were parameterized as: able to read and/or write (literate) versus unable to either read or write (illiterate), ever married versus never married, ever had a Pap or VIA versus never, ever smoked versus never smoked, regular drinker versus non-regular drinker, ever had an IUD versus never or don't know/refused, family history of cervical cancer present versus absent, and believe at risk for developing cervical cancer ("strongly agree"/"agree" versus neutral, disagree, strongly disagree, or unsure/don't know), continuous age, and number of lifetime sexual partners (one versus more than one).

Data cleaning and analyses were carried out using SAS 9.4.

RESULTS

In total, 956 women were recruited to participate into the study: 500 women in Santiago Atitlán and 456 women in Livingston. Demographic characteristics differed between the two communities: 69.4% of the participants in Santiago Atitlán had less than primary education and 96.6% were of Tz'tujil ethnicity. In contrast, only 33.9% of the participants in Livingston had less than primary education and three ethnic groups were represented: 41.9% Q'echchi, 32% Garifuna, and 24.8% mixed ethnicity (Ladino) (Table 1).

Knowledge and attitudes regarding HPV and cervical cancer also differed between the communities. Only 11.8% of participants in Santiago reported previous knowledge of HPV as compared to 62.7% of Livingston participants. However, when asked about the seriousness of cervical cancer, most participants in both communities responded "very" or "extremely" (74.8% Santiago and 80.9% Livingston).

Self-reported history of access to healthcare also appeared higher in Livingston than in Santiago. For example, only 5.0% of participants in Santiago responded that they had ever been tested for human immunodeficiency virus while 57.8% of Livingston participants responded that they had been previously tested (HIV data not shown in Tables due to low cell counts). Furthermore, statistically significantly higher proportions of women from Livingston reported knowledge of breast exams, receiving more recent Pap testing, and regular use of contraceptives. Additionally, a higher proportion of participants in Livingston consistently reported always using protection during sexual intercourse and using tobacco and alcohol than in Santiago (Table 1). Additional comparisons of population characteristics can be found in the appendix.

Self-Collection Willingness

When participants were asked if they would be willing to self-collect at home, the majority of women in both communities responded they would be willing (93.4% in Santiago and 62.4% in Livingston, Table 2). However, a lower percentage of women in Livingston who actually tried self-collection sampling (93.6% in Santiago and 52.5% in Livingston, Table 2 and Figure 1), as opposed to simply stating willingness in the survey.

We evaluated factors that affected the willingness to try self-collection testing in Livingston. Literacy, the use of health services, and beliefs regarding cervical cancer differed between age-eligible women who self-collected a sample compared to those who did not (Table

3). Additionally, 31.4% of the women who ended up not providing a sample had responded previously in the questionnaire that they indeed would be willing to collect a self-swab sample at home. While data is unavailable regarding how many age-eligible women were ineligible to collect a sample due to menstruation or pregnancy, this likely does not entirely account for all women who ultimately chose not to self-collect. Characteristics of women not willing to collect (both reported in the survey and actual sample collection) can be found in the appendix. It is interesting to also note that women from Santiago, who reported less prior use of healthcare, were more likely to self-collect.

Literacy was significantly higher among women who self- collected a sample in Livingston compared to those who did not (crude PR 2.04; 95% CI: 1.27, 3.28; adjusted PR, 2.25; 95% CI: 1.38, 3.68) (Table 4). IUD use was also higher among women who self-collected a sample in Livingston (crude PR 1.49; 95% CI: 1.15, 1.94; adjusted PR 1.43; 95% CI: 1.08, 1.88) (Table 4). Additionally, regular drinking and never being married were higher among women who self-collected but not significant (regular drinking, crude PR 1.18; 95% CI: 0.95, 1.48; adjusted PR 1.14; 95% CI 0.89, 1.46; never married, crude PR 1.19; 95% CI: 0.96, 1.48; adjusted PR 1.15; 95% CI: 0.91, 1.43) (Table 4).

Using stepwise selection with adjustment for age, ethnicity, and more than one lifetime sexual partner, only literacy was selected as an exposure covariate (PR 2.25; 95% CI: 1.38, 3.68). When stratifying ethnic group (Q'echchi versus Garifuna and Ladino), the association between literacy and actual sample collection remained positive (Table 5). However, this relationship only remained statistically significant among Q'echchi participants. However, interaction terms between ethnic group (Q'echchi versus not) and literacy revealed that the effect

of literacy among the Q'echchi was not significantly different from the Ladinos and Garifunas (interaction term PR 0.94; 95% CI: 0.25, 3.59).

Finally, when fully adjusting for all exposure covariates, the effect of literacy continued to remain significant (PR 1.68; 95% CI: 1.12, 2.51).

Self-Collection Acceptability and Comfort

Among those who did collect a sample, the self-collection testing was highly acceptable in both communities. Of Santiago participants who self-collected, 81.4% found it comfortable and 84.8% reported that the HerSwab was easy to use. Among Livingston participants who self-collected, 87.0% found it comfortable and 87.0% reported it was easy to use. Among those who chose to self-collect, almost all participants in both locations reported that they were willing to use it as a form of cervical cancer screening (98.0% in Santiago and 100% in Livingston) (Table 2).

HPV Prevalence

Overall, 19% of samples tested positive for high-risk HPV (N=549). 18.7% of samples from Santiago Atitlán (N=77) tested positive for high-risk HPV and 21.3% of samples from Livingston (N=29) tested positive, but this difference was not statistically significant (p-value=0.4923). In total, 94% of participants who sampled in Santiago Atitlán and 88.5% of participants who sampled in Livingston were provided with their test results. Overall, 12.3% of HPV tests were found to be inconclusive (N=44 (9.6%) from Santiago Atitlán and N=33 (19.5%) from Livingston).

DISCUSSION

In this study, we assessed the acceptability of HPV self-collection testing as an alternative form of primary cervical cancer screening in indigenous and rural communities in

Guatemala. We found that self-collection appears to be highly acceptable among women who tried it, independent of community and ethnicity. Most women reported that self-collection was comfortable and easy to use, and almost all women who tried it reported being willing to use it as a form of cervical cancer screening in the future. These results are consistent with other studies looking at self-collection acceptability both within Guatemala and other LMICs[27 32]. This study was further able to build upon previous studies and provide important information regarding HPV self-collection testing acceptability at the community level, and in a community that had not been previously evaluated.

Our study also found, however, that there were differences between communities in willingness to try self-collection. Willingness to try self-collection testing remained consistently high among participants in Santiago Atitlán as reported in the pilot study conducted in 2015 (93% in 2015 versus 93.6% in 2016)[32]. In Livingston, however, even among women who first responded in the survey or consent form that they would be willing to collect a sample, actual self-collection was lower. We found that willingness to self-collect in Livingston was consistently associated with higher levels of literacy and prior IUD use. In contrast, ethnicity, history of cervical cancer screening, and health behaviors were not associated with willingness to self-collect. Stratified analyses suggested that there were no qualitative differences in the association between literacy and sample collection across ethnic groupings (Mayan descent versus non-Mayan descent) in Livingston. However, high prevalence of literacy among Garifuna made it difficult to evaluate differences between Ladinos and Garifunas in the association between literacy and sampling decision.

The results suggest that HPV self-collection testing program implementation may need to target populations based on relative levels of literacy within communities. A previous study

examining HPV acceptability and intention in the UK similarly found that low education and self-efficacy, defined as an individual's belief in their capability to exercise control over challenging demands, were associated with low sampling intentions[30]. In Guatemala, the inability to either read or write in Spanish may negatively influence a woman's perceived self-efficacy and her confidence in navigating public health infrastructure or self-collecting a vaginal sample, particularly if her surrounding community has high levels of literacy. This population would greatly benefit from HPV self-collection testing as a primary form of cervical cancer screening due to its strength in concentrating less accessible and more invasive screening modalities only towards those that are at high-risk (i.e., positive for HPV). Our results in Livingston suggest that it might be critical that, if implemented, HPV screening and education programs are tailored such that they are more accessible to low-literacy populations and, thus, increase perceived self-efficacy in navigating the existing public health infrastructure.

High prevalence of self-collection testing in Santiago Atitlan, a community with low literacy levels, as compared to the low rates of self-collection testing among those with low literacy in Livingston may reflect larger community differences in awareness or access to screening modalities rather than a lack of effect of literacy in Santiago or an effect of ethnicity. Although women from Santiago reported slightly higher rates of ever receiving cervical cancer screening than women in Livingston, women in Livingston report much higher rates of recent cervical cancer screening than women in Santiago. Santiago Atitlán remains largely deficit in accessible and affordable cervical cancer screening while Livingston has regular, public or private, screening campaigns in the community. This difference in general community access and infrastructure, then, may be acting as an effect modifier on the association between literacy and screening between these two communities, suggesting that self-collection might be better

received at first in communities that do not have other alternatives, whereas some initial skepticism might be found in places with existing cervical screening programs, independently of their quality and efficacy. More research is necessary to evaluate if self-efficacy, relative literacy level, or general community access to healthcare resources and screening play larger barriers for women in trying self-sampling HPV testing. However, the high rates of acceptability and willingness to retake among women who self-collected in both communities suggest that once experienced, self-collection is a valid, and even preferred, alternative to other screening modalities from the women's perspective.

Although based on a different HPV test than in our pilot study (Hybribio HR13 vs. Anyplex 28), a similar prevalence of high-risk HPV was found in Santiago between 2015 and 2016 (17.4% versus 19.3%)[32]. Of note, there were no significant differences in high-risk HPV prevalence between ethnic groups in Livingston, and there was not a statistically significant difference between Santiago Atitlán and Livingston with regards to prevalence.

Our study provided not only a larger sample size compared with previous studies but was also conducted in two differing communities. This is a strength because Guatemala is an extremely diverse country with over 23 languages, distinct ethnicities, and a history of large economic and social inequalities. Thus, generalizing the evaluations of a health program's acceptability and feasibility to the whole country is generally difficult. However, because we evaluated two very different rural multi-ethnic communities, our results may reflect some of the future obstacles and considerations necessary in implementing self-swab HPV testing in such a diverse country as Guatemala than was previously available. In fact, our results also complement the findings of the ongoing careHPV Scale-Up implementation, which is assessing

the performance of HPV testing, including self-collection testing, within urban settings in Guatemala[40-42].

There are several limitations to our study. Due to both the sensitive nature of the questions related to sexual history, it may be possible that a social desirability bias may have resulted in over reporting of perceived "good behaviors", such as screening or use of protection, in addition to under-reporting of perceived "bad behaviors", such as number of lifetime sexual partners and other sexual behavior measures. We tried to minimize the possibility of this bias by maintaining confidentiality with participants. Also, women may report their history of screening or utilization of health care resources incorrectly if they had limited information or understanding of these services. This may be exaggerated in women with low literacy and thus explain potential over reporting of prior cervical cancer screening in Santiago Atitlan. Additionally, because sampling methods differed between the two communities due to the lack of reliable census counts in Livingston, there may be differences between the communities in potential selection bias into the study and more limited comparability of the results. However, our sample in Livingston is reflective of the overall population structure of Livingston in terms of ethnic, age and other metrics, suggesting that influential selection bias into the study might be limited[43].

Screening program implementation is a major challenge in LMIC settings, HPV self-swab testing may serve as a helpful tool in concentrating less accessible and more expensive and invasive screening modalities only towards those that are at high-risk (i.e., positive for HPV). However, as the results in Livingston showed, there are many complex features related to implementing HPV screening that will need to be evaluated before program adoption of such programs. Due to the longitudinal component of our study, future research with our study

participants will hopefully help elucidate how HPV self-collection testing may affect women's decisions to pursue further cervical cancer screening and follow-up care in their local communities after HPV testing and receiving their results. Additionally, these data may reveal other downstream facilitators or barriers to screening that will influence the overall success of HPV self-swab testing implementation in these communities.

CONCLUSION

The results of our study add to the literature on the potential of HPV self-collection testing in LMICs, demonstrating its acceptability in two very different communities in rural Guatemala. The high rates of acceptability and willingness to retake among women who self-collected in both communities suggest that once experienced, self-collection is a valid, and even a preferred, alternative to other screening modalities from the women's perspective. However, the difference in willingness to try self-collection between these communities suggests that relative literacy levels and the availability and quality of existing healthcare programs may affect attitudes towards new screening modalities. Future research should focus on increasing the generalizability of these findings by evaluating additional communities within Guatemala for differences in willingness to try self-collection sampling and further elucidate the potential barriers to accessing and utilizing cervical cancer modalities, including HPV self-collection sampling.

LIST OF ABBREVIATIONS

CC – Cervical Cancer

CHW – Community Health Worker

CI – Confidence Interval

HICs – High-Income Countries

HIV – Human Immunodeficiency Virus

HPV – Human Papillomavirus

HR-HPV – High-Risk Human Papillomavirus

INCAP – Institute of Nutrition of Central America and Panama

IUD – Intra-Uterine Device

LMICs – Low and Middle-Income Countries

OR – Odds Ratio

PCR – Polymerase Chain Reaction

PR – Prevalence Ratio

VIA – Visual Inspection with Acetic Acid

DECLARATIONS

Ethics Approval and Consent to Participate

The University of Michigan Institutional Review Board (HUM00096559) and the Institute of Nutrition of Central America and Panama Institutional Review Board (MI-CIE-16-009) approved study protocols. All participants gave oral and written informed consent prior to participation in the study. The consent was documented by a signature or fingerprint of the participant, the surveyors, and a witness.

Consent for Publication

The authors of this paper have all reviewed its contents and consent for its publication.

Data Sharing Statement

Due to the sensitive nature of the data collected, IRB restrictions, and ongoing data collection, study data is stored at the University of Michigan. Interested parties may contact the corresponding author to request access to de-identified datasets for specific research questions related to the study. The authors welcome further collaboration but reserve the right to retain data to protect study participants.

Competing Interests

The authors have no competing interests to declare.

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Authors' Contributions

PIC - Planning and Key Intellectual Contribution
DC – Data Collection and Project Management
SP – Sample Processing, Laboratory Management, and Test Results
SA – Statistical Analysis and Data Management
W – Writing
E – Editing

Audrey Murchland – PIC, DC, SP, SA, W, E
Anna Gottschlich – PIC, DC, SP, W, E
Kristin Bevilacqua – PIC, DC, SP, E
Andres Pineda – PIC, DC, SP, E
Berner Andrée Sandoval-Ramírez – PIC, DC, SP, E

Christian Alvarez – PIC, E
Gina Ogilvie – PIC, E
Thomas E Carey – PIC, SP, E
Mark Prince – PIC, SP, E
Michael Dean – PIC, SP, E
Carlos Mendoza-Montano – PIC, SP, E
Alvaro Rivera-Andrade – PIC, DC, SP, E
Rafael Meza – PIC, DC, SP, SA, W, E

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TABLES

Table 1. General Population Characteristics Among All Participants			
	Santiago Atitlán % (N) or Mean (SD)	Livingston N (%) or Mean (SD)	p-value
N	500	456	
Age (y)	34.78 (8.44)	32.97 (10.38)	**0.003**
Ethnicity			**<0.0001**
Tz'tujil	96.60% (483)	0	
Ladino	1.80% (9)	24.78% (113)	
Garifuna	0	31.80% (145)	
Q'echchi	0	41.89% (191)	
Other	1.40% (7)	1.32% (6)	
Education			**<0.0001**
Less than Primary	69.40% (347)	33.92% (153)	
Primary or Secondary	20.12% (100)	34.37% (155)	
More than Secondary	10.06% (50)	31.71% (143)	
Unknown	0.60% (3)	1.09% (5)	
Literacy			**<0.0001**
Illiterate (Neither Read nor Write)	48.60% (243)	12.53% (57)	
Literate (Either Read and/or Write)	51.20% (255)	87.47% (398)	
Ever Married/United	97.00% (485)	62.50% (285)	**<0.0001**
Breast exam (Heard of)	14.08% (70)	66.59% (303)	**<0.0001**
Pap (Ever)	66.80% (334)	58.11% (265)	**0.0056**
Last Pap			**<0.0001**
Never or Unknown	36.40% (182)	42.54% (194)	
Less than a year	19.40% (97)	29.39% (134)	
More than a year	44.20% (221)	28.07% (128)	
VIA (Ever)	6.04% (30)	1.32% (6)	**<0.0001**
Ever Smoke	0.40% (2)	9.65% (44)	**<0.0001**
Regular Drinker	11.54% (3)	33.85% (44)	**0.0080**
Used IUD (Ever)	1.41% (7)	8.09% (36)	**<0.0001**
Use Protection			**<0.0001**
Always or Almost always	10.00% (50)	19.96% (91)	
Sometimes	4.80% (24)	11.84% (54)	
Rarely or Never	69.60% (348)	47.15% (215)	
Unknown or Refused	15.60% (78)	21.05% (96)	
Number of Lifetime Sexual Partners			**<0.0001**
One	90.6% (453)	70.8% (323)	
More than One	6.8% (34)	25.9% (118)	
Refused	2.6% (13)	3.3% (15)	
Knowledge of HPV	11.80% (59)	62.72% (286)	**<0.0001**
Severity of CC			**<0.0001**
Not or A Little	2.40% (12)	12.28% (56)	
Moderate	22.80% (114)	6.80% (31)	
Very or Extremely	74.80% (374)	80.92% (369)	

Willing to Vaccinate Daughters for HPV if Available			**<0.0001**
Yes	69.60% (348)	82.24% (375)	
No	1.00% (5)	6.80% (31)	
Don't Have Daughters	27.60% (138)	8.33% (38)	
Refused	1.8% (9)	2.6% (12)	

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Table 2: Acceptability of Self-Collection HPV Tests
Among Age-Eligible Women (25-54 years of age)

	Santiago Atitlán % (N)	**Livingston % (N)**	**p-value[a,b]**
N	500 *(all participants)* *438 (age-eligible)*	*456 (all participants)* *322 (age-eligible)*	
HPV knowledge	10.05% (44)	63.98% (206)	**<0.0001**
Self-Reported Previous Pap (Ever)	71.46% (313)	69.88% (225)	0.6348
Abnormal Pap (Ever)	16.61% (52)	36.89% (83)	**<0.0001**
Knowledge of VIA	6.85% (30)	1.86% (6)	**0.0023**
Willing to Collect Sample at Home	93.38% (409)	62.42% (201)	**<0.0001**
Collected Sample	93.61% (410)	52.48% (169)	**<0.0001**
Prefer Home Screening	94.06% (412)	44.41% (143)	**<0.0001**
Prefer Self-Collection	91.10% (399)	41.61% (134)	**<0.0001**
Collected Sample, Among Those Who Said They Were Willing to Collect at Home	96.82% (396)	76.12% (153)	**<0.0001**
	% (N)	**% (N)**	
N	410 *(age-eligible; test-taking participants)*	*169 (age eligible; test-taking participants)*	
Comfort of test			**0.0013[b]**
Comfortable	81.4% (333)	87.0% (141)	
Neutral	5.87% (24)	5.56% (9)	
Uncomfortable	12.7% (52)	7.4% (12)	
Ease of test			**0.0241[b]**
Easy	84.8% (347)	87.0% (141)	
Neutral	4.65% (19)	7.41% (12)	
Difficult	10.5% (43)	5.55% (9)	
Willingness to retake test	98.0% (402)	100% (169)	1.00[b]

[a]p-values for means calculated using two-sample t-test; proportions using chi-squared test
[b]Fisher's exact test used to account for low cell counts

Table 3. Population Characteristics within Livingston

[a]Age-Eligible Women Who Sampled vs. Age-Eligible Women Who Did Not Sample

	Took the Sample % (N) or Mean (SD)	Did Not Take the Sample % (N) or Mean (SD)	p-value[b]
N	52.48% (169)	47.52% (153)	
Age (y)	34.98 (7.76)	36.35 (7.66)	0.1141
Ethnicity			0.6986
Ladino	50.59% (43)	49.41% (42)	
Garifuna	54.37% (56)	45.63% (47)	
Q'echchi	51.94% (67)	48.06% (62)	
Other	75.0% (3)	25.00% (1)	
Declined	0	100.0% (1)	
Education			0.0784
Less than Primary	46.34% (57)	53.66% (66)	
Primary or Secondary	57.14% (60)	42.86% (45)	
More than Secondary	56.18% (50)	43.82% (39)	
Unknown	40.00% (2)	60.00% (3)	
Literacy			**0.0005**
Illiterate (Neither Read nor Write)	29.17% (14)	70.83% (34)	
Literate (Either Read and/or Write)	56.57% (155)	43.43% (119)	
Married/United			0.2365
Ever	49.78% (112)	50.22% (113)	
Never	50.22% (56)	41.67% (40)	
Unknown	100.0% (1)	0	
Pap or VIA			0.2324
Ever	54.67% (123)	45.33% (102)	
Never	47.42% (46)	52.58% (51)	
Ever Smoke			0.6309
Ever	53.33% (16)	46.67% (14)	
Never	52.23% (152)	47.77% (139)	
Unknown	100.0% (1)	0	
Regular Drinker			0.7619
Yes	56.67% (17)	43.33% (13)	
No	51.89% (151)	48.11% (140)	
Unknown	100.0% (1)	0	
Used IUD			**0.0112**
Ever	73.08% (19)	26.92% (7)	
Never	51.37% (150)	48.63% (142)	
Don't know	100.0% (4)	0	
Use Protection			0.1260
Always or Almost always	58.62% (34)	41.38% (24)	
Sometimes	58.54% (24)	41.46% (17)	
Rarely or Never	53.75% (86)	46.25% (74)	
Unknown	39.68% (25)	60.32% (38)	
Number of Lifetime Partners			0.0670

One	49.12% (111)	50.88% (115)	
More than One	61.29% (57)	38.71% (36)	
Refused	33.33% (1)	66.66% (2)	
Knowledge of HPV	55.83% (115)	44.17% (91)	0.1097
Severity of CC			0.4191
Not	36.36% (4)	63.64% (7)	
A little	68.18% (15)	31.82% (7)	
Moderate	56.52% (13)	43.48% (10)	
Very	52.58% (102)	47.42% (92)	
Extremely	48.61% (35)	51.39% (37)	
Believe at risk of CC			0.2684
Strongly Agree or Agree	55.14% (102)	44.86% (83)	
Other	48.91% (67)	51.09% (70)	
Willing to Vaccinate Daughters for HPV if Available			0.4024
Yes	54.32% (151)	45.68% (127)	
No	47.62% (10)	52.38% (11)	
Don't Have Daughters	38.46% (5)	61.54% (8)	
Refused	30.00% (3)	70.00% (7)	

[a] % calculated for sampling decision by each covariate

[b] p-values for means calculated using two-sample t-test; proportions using chi-squared test

Table 4. Prevalence Ratios of Sample Collection in Livingston among Age-Eligible Women

Log-Binomial Regressions: Prevalence Ratios of Sample Collection (N=309)

	Exposure Covariates Effect on Sample Collection; PR (95% CI)							
	Literacy (Y)	Marriage (Never)	Hx of Pap/VIA (Ever)	Smoking (Y)	Drinking (Y)	IUD Use (Y)	Family Hx of CC (Y)	Believe at Risk for CC (Y)
$Model_1$: Main Effect	**2.04 (1.27, 3.28)**	1.19 (0.96, 1.48)	1.18 (0.92, 1.52)	1.02 (0.71, 1.46)	1.18 (0.95, 1.48)	**1.49 (1.15, 1.94)**	1.13 (0.81, 1.55)	1.09 (0.87, 1.35)
$Model_2$: Main Effect	**2.25 (1.38, 3.68)**	1.15 (0.91, 1.43)	1.20 (0.93, 1.56)	0.94 (0.66, 1.35)	1.14 (0.89, 1.46)	**1.43 (1.08, 1.88)**	1.15 (0.83, 1.58)	1.06 (0.85, 1.32)

Each exposure was explored independently.

M_1: unadjusted log-binomial model

M_2: adjusted for age, ethnicity, and number of lifetime sexual partners (more than one)

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Table 5. Prevalence Ratio of Sample Collection in Livingston among Age-Eligible Women Stratified by Ethnic Grouping (Mayan descent versus Non-Mayan descent) Log-Binomial Regression: Prevalence Ratio of Sample Collection (N=309)		
Covariates	Ladino or Garifuna (N=183)	Q'echchi (N=126)
	PR (95% CI)	PR (95% CI)
Literacy (Y)	2.39 (0.70, 8.15)	**2.08 (1.17, 3.69)**
Age	1.00 (0.98, 1.02)	0.99 (0.96, 1.02)
More than One Lifetime Sexual Partner	1.31 (1.00, 1.72)	1.37 (1.00, 1.88)
Final stepwise selected model presented, stratified by ethnic group.		

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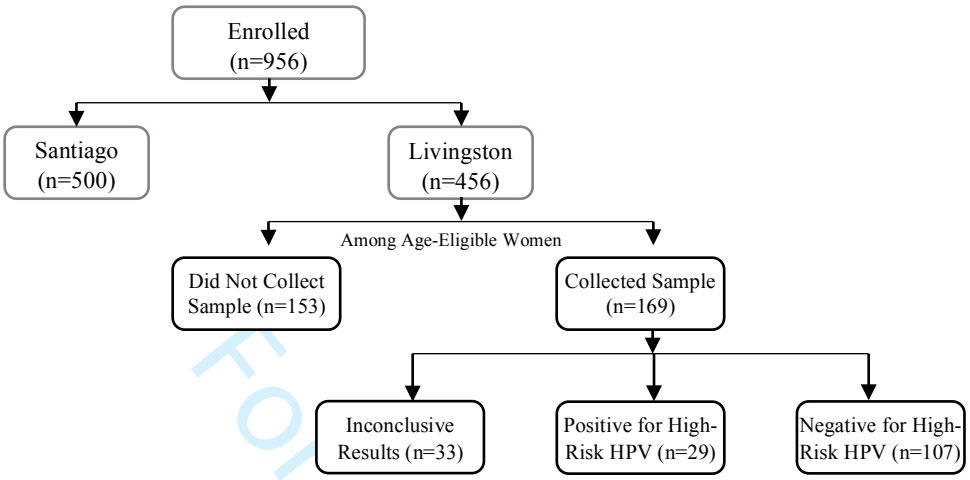
FIGURE LEGENDS

Figure 1. Flow Chart of Livingston Self-Collection Sampling and Testing

Figure 1. Flow Chart of Livingston Self-Collection Sampling and Testing



HPV Self-Sampling Acceptability in Rural and Indigenous Communities in Guatemala: A Cross-Sectional Study

Audrey R. Murchland, Anna Gottschlich, Kristin Bevilacqua, Andres Pineda, Berner Andrée Sandoval-Ramírez, Christian S. Alvarez, Gina Ogilvie, Thomas E Carey, Mark Prince, Michael Dean, Carlos Mendoza-Montano, Alvaro Rivera-Andrade, Rafael Meza

Supplementary Appendix

Appendix A: Additional Reference Tables

Appendix B: Self-reported Willingness to Collect a Sample

Appendix A – Additional Reference Tables

Table A1: Population Characteristics within Livingston
Age-Eligible Women Who Declined At Home Sampling vs. Age-Eligible Women Who Did Not Sample

	Did Not Want to Collect Sample (Survey Response) N (%) or Mean (SD)	Did Not Collect Sample N (%) or Mean (SD)
N	121	153
Age (y)	36.7 (7.80)	36.3 (7.66)
Education		
Less than primary	51 (42.15%)	66 (43.14%)
Primary	34 (28.10%)	45 (29.41%)
More than primary	33 (27.27%)	39 (25.49%)
Unknown	3 (2.48%)	3 (1.96%)
Literacy		
Illiterate (Neither Read nor Write)	27 (22.31%)	34 (22.22%)
Literate (Either Read and/or Write)	94 (77.69%)	119 (77.78%)
Married/United (Ever)	92 (76.03%)	113 (73.9%)
Regular Drinking	8 (6.61%)	13 (8.50%)
Use Health Services	112 (92.56%)	140 (91.50%)

Table A2. General Population Characteristics Among All Participants (Continued)			
	Santiago Atitlan N (%) or Mean (SD)	**Livingston N (%) or Mean (SD)**	**p-value[a]**
N	500	456	
Current Marital Status			**<0.0001**
Single	3 (0.62%)	30 (10.53%)	
Married	311 (64.12%)	101 (35.44%)	
Separated	28 (5.77%)	2 (0.70%)	
Divorced	5 (1.03%)	0	
Widowed	15 (3.09%)	1 (0.35%)	
Common Law	120 (24.74%)	151 (52.98%)	
Refused	3 (0.62%)	0	
Age at Marriage	19.8 (4.31)	19.74 (5.82)	0.8771
Mammogram (Ever)	10 (2.01%)	40 (8.77%)	**<0.0001**
Pap or VIA (Ever)	337 (67.40%)	265 (58.11%)	0.7592
Last Pap			**<0.0001**
Never	33.20% (166)	41.9% (191)	
Less than 6 months	6.20% (31)	13.82% (63)	
6 months to a year	13.20% (66)	15.57% (71)	
1 to 5 years	34.20% (171)	20.39% (93)	
More than 5 years	10.00% (50)	7.68% (35)	
Unknown	3.20% (16)	0.66% (3)	
Used Birth Control Injections	215 (43.17%)	173 (38.88%)	0.3459
Used Oral Contraceptives	54 (10.84%)	123 (27.64%)	**<0.0001**
Number of Pregnancies	2.81 (1.93)	3.19 (2.49)	**0.0082**
Number of Children	2.54 (1.65)	3.20 (2.12)	**<0.0001**
Age at First Child	20.18 (5.80)	18.88 (3.74%)	**0.0001**
Currently Sexually Active	171 (79.53%)	121 (63.68%)	**0.0035**
Age at First Sexual Relation	19.63 (4.29)	17.24 (2.77)	**<0.0001**
Family Member with Cervical Cancer	2.65% (13)	11.28% (51)	**<0.0001**
Believe at Risk for CC			**<0.0001**
Strongly Agree	24.80% (124)	14.47% (66)	
Agree	13.20% (66)	41.23% (188)	
Neutral	13.60% (68)	5.26% (24)	
Disagree	9.00% (45)	8.55% (39)	
Strongly Disagree	19.00% (95)	8.99% (41)	
Likely to Get CC			**<0.0001**
No Chance	135 (27%)	152 (33.33%)	
Low	97 (19.40%)	175 (38.38%)	
Moderate	32 (6.40%)	13 (2.85%)	
High	22 (4.40%)	7 (1.54%)	
Certain	17 (3.40%)	6 (1.32%)	
Unsure	0	103 (22.59%)	
Refused	197 (39.40%)	0	

Table A3. Population Characteristics within Livingston (Continued)
Age-Eligible Women Who Sampled vs. Age-Eligible Women Who Did Not Sample

	Took the Sample % (N) or Mean (SD)	Did Not Take the Sample % (N) or Mean (SD)	p-value[a]
N	52.48% (169)	47.52% (153)	
Current Marital Status			0.4399
Never Married	58.76% (57)	41.24% (40)	
Single	48.00% (12)	52.00% (13)	
Married	43.37% (36)	56.63% (47)	
Separated	50.00% (1)	50.00% (1)	
Divorced	0.00% (0)	0.00% (0)	
Widowed	0.00% (0)	100.00% (1)	
Common Law	55.26% (63)	44.74% (51)	
Age at First Marriage	19.67 (4.51)	20.90 (7.35)	0.1506
Breast Exam (Heard Of)	55.66% (123)	44.34% (98)	0.1325
Mammogram (Ever)	50.00% (16)	50.00% (16)	0.7668
Pap (Ever)	54.67% (123)	45.33% (102)	0.2324
Last Pap			0.7520
Less than 6 months	52.83% (28)	47.17% (25)	
Within the last year	57.14% (32)	42.86% (24)	
Within the last 2-5 years	55.95% (47)	44.05% (37)	
More than 5 years	55.17% (16)	44.83% (13)	
VIA (Ever)	83.33% (5)	16.67% (1)	0.1050
Used Birth Control Injections	56.12% (78)	43.88% (61)	0.2292
Used Oral Contraceptives	58.25% (60)	41.75% (43)	0.1336
Number of Pregnancies	3.49 (2.27)	3.74 (2.30)	0.3346
Number of Children	3.20 (1.78)	3.61 (2.14)	0.1712
Age at First Pregnancy	18.87 (3.50)	19.27 (4.41)	0.3853
Currently Sexually Active	52.94% (45)	47.06% (40)	0.2068
Age at First Sexual Relation	17.20 (2.97)	17.56 (2.96)	0.4102
Family Member with CC	60.61% (20)	39.39% (13)	0.6143
Believe at Risk for CC			**0.0398**
Strongly Agree	67.27% (37)	32.73% (18)	
Agree	50.00% (65)	50.00% (65)	
Neutral	76.92% (10)	23.08% (3)	
Disagree	56.52% (13)	43.48% (10)	
Strongly Disagree	44.83% (13)	55.17% (16)	
Unsure	43.06% (31)	56.94% (41)	
Likely to Get CC			0.0612
No Chance	58.77% (67)	41.25% (47)	
Low	49.11% (55)	50.89% (57)	
Moderate	85.71% (6)	12.49% (1)	
High	83.33% (5)	16.67% (1)	
Certain	50.00% (2)	50.00% (2)	
Unsure	43.04% (34)	56.96% (45)	

[a]p-values for means calculated using two-sample t-test; proportions using chi-squared test

Table A4: Population Characteristics within Livingston
Comparing Racial/Ethnic Groups in Livingston Including All Women

	Ladino N (%) or Mean (SD)	Garifuna N (%) or Mean (SD)	Q'echchi N (%) or Mean (SD)	p-value[a]
N	113 (25.17%)	145 (32.29%)	191 (42.54%)	
Age (y)	34.49 (10.32)	33.23 (10.54)	31.91 (10.19)	0.1022
Education				**<0.0001**
Less than primary	35 (30.97%)	12 (8.28%)	104 (54.45%)	
Primary	39 (34.51%)	69 (47.59%)	45 (23.56%)	
More than primary	38 (33.63%)	62 (42.76%)	40 (20.94%)	
Literacy				**<0.0001**
Neither	8 (7.08%)	3 (2.07%)	45 (23.56%)	
Read Only	1 (0.88%)	0	3 (1.57%)	
Read and Write	104 (92.04%)	142 (97.93%)	142 (74.35%)	
Married/United (Ever)	87 (76.99%)	63 (43.45%)	128 (67.02%)	**<0.0001**
Breast Exam (Heard of)	88 (77.88%)	112 (77.24%)	98 (51.31%)	**<0.0001**
Mammogram (Ever)	11 (9.73%)	21 (14.48%)	8 (4.19%)	**0.0043**
Pap (Ever)	70 (61.95%)	107 (73.79%)	83 (43.46%)	**<0.0001**
Last pap				**0.0212[b]**
Less than 6 months	14 (20%)	34 (31.78%)	13 (15.66%)	
Within the last year	18 (25.71%)	37 (34.58%)	16 (19.28%)	
Within the last 2-5 years	27 (38.57%)	28 (26.19%)	36 (43.37%)	
More than 5 years	10 (14.29%)	6 (5.61%)	18 (21.69%)	
VIA (Ever)	2 (1.77%)	1 (0.69%)	3 (1.57%)	0.6142
Ever Smoke	15 (13.27%)	27 (18.62%)	2 (1.05%)	**<0.0001[b]**
Ever Drink	30 (26.55%)	74 (51.03%)	24 (12.57%)	**<0.0001[b]**
Used Birth Control Injections	46 (41.44%)	59 (41.55%)	66 (35.68%)	0.8213
Used Oral Contraceptives	30 (27.03%)	64 (45.07%)	28 (15.14%)	**<0.0001[b]**
Used IUD	9 (8.11%)	22 (15.49%)	4 (2.16%)	**<0.0001[b]**
Use protection				**<0.0001[b]**
Always	11 (9.91%)	36 (25.35%)	9 (4.86%)	
Almost always	11 (9.91%)	15 (10.56%)	8 (4.32%)	
Sometimes	8 (7.215)	30 (21.13%)	14 (7.57%)	
Rarely	5 (4.50%)	9 (6.34%)	11 (5.95%)	
Never	62 (55.865)	41 (28.87%)	85 (45.95%)	
Unknown	14 (12.61%)	11 (7.75%)	58 (31.35%)	
Family Member with CC	21 (18.58%)	19 (13.10%)	10 (5.24%)	**<0.0001[b]**
Knowledge of HPV	78 (69.03%)	112 (77.24%)	90 (47.12%)	**<0.0001**
Believe They Are at Risk for CC				
Strongly Agree	11 (9.73%)	30 (20.69%)	25 (13.09%)	
Agree	51 (45.13%)	49 (33.79%)	87 (45.55%)	
Neutral	6 (5.31%)	7 (4.83%)	10 (5.24%)	
Disagree	15 (13.27%)	17 (11.72%)	6 (3.14%)	
Strongly Disagree	10 (8.85%)	22 (15.17%)	9 (4.71%)	
Unsure	20 (17.70%)	19 (13.10%)	54 (28.27%)	
Vaccinate Daughters for HPV				0.4056
Yes	94 (83.19%)	120 (82.70%)	156 (81.68%)	
No	10 (8.85%)	5 (3.45%)	15 (7.85%)	
Don't Have Daughters	8 (7.08%)	15 (10.34%)	14 (7.33%)	
Willing to Collect Sample at Home	61 (53.98%)	94 (64.83%)	104 (54.45%)	0.2802
Collected Sample	44 (38.94%)	56 (38.62%)	67 (35.08%)	0.7264

[a]p-values for means calculated using one-way ANOVA or Welch (if equality of variance is rejected); proportions using chi-squared test
[b]Fisher's Exact Test used due to small cell counts

Table A5: Differences Among Communities of Age-Eligible Indigenous Mayan Women
Age-Eligible Tz'tujil Women vs. Age-Eligible Q'echchi Women

	Tz'tujil - Santiago N (%) or Mean (SD)	Q'echchi - Livingston N (%) or Mean (SD)	p-value[a]
N	420 (68.74%)	191 (31.26%)	
Age (y)	36.25 (7.46)	31.91 (10.19)	**<0.0001**
Education			**<0.0001**
Less than primary	314 (75.12%)	104 (54.45%)	
Primary	64 (15.31%)	45 (23.56%)	
More than primary	40 (9.57%)	40 (20.94%)	
Literacy			**<0.0001**
Neither	225 (53.57%)	45 (23.56%)	
Read Only	7 (1.67%)	3 (1.57%)	
Read and Write	188 (44.76%)	142 (74.35%)	
Ever Married/United	412 (98.10%)	128 (67.02%)	**<0.0001**
Age at marriage	29.85 (137.8)	24.46 (20.33)	0.4463
Breast exam (Heard of)	53 (12.68%)	98 (51.31%)	**<0.0001**
Mammogram (Ever)	10 (2.38%)	8 (4.19%)	0.2206
Pap (Ever)	296 (70.48%)	83 (43.46%)	**<0.0001**
Last pap			0.2751
Less than 6 months	26 (9.25%)	13 (15.66%)	
Within the last year	57 (20.28%)	16 (19.28%)	
Within the last 2-5 years	153 (54.44%)	36 (43.37%)	
More than 5 years	45 (16.01%)	18 (21.69%)	
VIA (ever)	28 (6.70%)	3 (1.57%)	**0.0076**
Pap or VIA (Ever)	299 (71.19%)	83 (43.46%)	**<0.0001**
Ever Smoke	1 (0.24%)	2 (1.05%)	0.1907
Drink (regularly)	3 (14.29%)	1 (4.17%)	0.2341
Used BC injections	186 (44.71%)	66 (35.68%)	**0.0786**
Used IUD	5 (1.20%)	4 (2.16%)	0.1497
Use protection			**<0.0001**
Always	29 (8.33%)	9 (4.86%)	
Almost always	11 (3.16%)	8 (4.32%)	
Sometimes	20 (5.75%)	14 (7.57%)	
Rarely	9 (2.59%)	11 (5.95%)	
Never	279 (80.17%)	85 (45.95%)	
Family Member with CC	12 (2.01%)	10 (5.24%)	**0.0408**
Age at First Sexual Relation	20.00 (4.48)	16.64 (2.45)	**<0.0001**
Currently Sexually Active	138 (82.63%)	42 (64.62%)	**0.0025**
Knowledge of HPV	37 (8.81%)	90 (47.12%)	**<0.0001**
Believe At Risk for CC			**<0.0001**
Strongly Agree	105 (31.82%)	25 (13.09%)	
Agree	51 (15.45%)	87 (45.55%)	
Neutral	61 (18.48%)	10 (5.24%)	
Disagree	41 (12.42%)	6 (3.14%)	
Strongly Disagree	72 (21.82%)	9 (4.71%)	
Unsure	0	54 (28.27%)	
Vaccinate Daughters for HPV			**<0.0001**
Yes	301 (73.24%)	156 (81.68%)	
No	4 (0.97%)	15 (7.85%)	
Don't Have Daughters	106 (25.79%)	14 (7.33%)	
Willing to Sample in Home	394 (95.63%)	104 (54.45%)	**<0.0001**
Collected Sample	395 (94.05%)	67 (35.08%)	**<0.0001**

[a]p-values for means calculated using two-sample t-test; proportions using chi-squared test

Appendix B – Self-Reported Willingness to Self-Collect Sample

As a final sensitivity analysis, we present results evaluating potential predictors of self-reported willingness to self-collect a vaginal sample as reported in the survey.

Table B1. Prevalence Ratio of Willingness to Collect at Home in Livingston
Log-Binomial Regression: Prevalence Ratio of Willingness to Sample at Home (N=309)

Variable	PR^{M1}	95% CI		PR^{M2}	95% CI		PR^{M3}	95% CI	
Literacy (Y)	**1.55**	**1.10**	**2.19**	**1.55**	**1.08**	**2.23**	1.15	0.94	1.41
Marriage (Never)	**1.20**	**1.01**	**1.42**	1.11	0.98	1.34	1.08	0.94	1.22
Hx of Pap/VIA (Ever)	1.23	0.99	1.52	**1.24**	**1.01**	**1.52**	1.06	0.93	1.21
Smoking (Y)	1.08	0.82	1.41	1.01	0.98	1.29	1.01	0.80	1.27
Drinking (Y)	1.18	0.99	1.40	1.09	0.90	1.32	1.02	0.89	1.17
IUD Use (Y)	**1.38**	**1.12**	**1.68**	1.22	0.97	1.53	1.11	0.88	1.40
Family Hx of CC (Y)	1.16	0.90	1.47	1.18	0.93	1.48	1.03	0.84	1.26
Believe at Risk for CC (Y)	**1.24**	**1.03**	**1.49**	1.19	0.99	1.43	1.08	0.96	1.22

M1: unadjusted log-binomial model
M2: adjusted for age, ethnicity, and number of lifetime sexual partners
M3: all variables included and adjusted for age, ethnicity, and number of lifetime sexual partners

STROBE Statement

Checklist of items that should be included in reports of observational studies

Section/Topic	Item No	Recommendation	Reported on Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	12
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	11
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	11
		(*b*) Describe any methods used to examine subgroups and interactions	11
		(*c*) Explain how missing data were addressed	11
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	11
		(*e*) Describe any sensitivity analyses	

Section/Topic	Item No	Recommendation	Reported on Page No
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12-13
		(b) Indicate number of participants with missing data for each variable of interest	12
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	13, 15
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	14
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	14
Discussion			
Key results	18	Summarise key results with reference to study objectives	15,16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17
Generalisability	21	Discuss the generalisability (external validity) of the study results	18,19
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

**Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.*

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.