BMJ Open HPV self-sampling acceptability in rural and indigenous communities in Guatemala: a cross-sectional study

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ABSTRACT

Introduction Cervical cancer disproportionately burdens low-income 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 the ages of 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 highrisk 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 multiethnic (Afro-Caribbean, indigenous) community of Livingston, of 322 age-eligible participants, 53% chose to self-collect. Among those who took the test, 83% found it comfortable and 95% were willing to use it as a form of screening. In Livingston, literacy (can read and/or write vs cannot read or write) was higher in women who chose to self-collect (prevalence ratio 2.25; 95% Cl 1.38 to 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.

INTRODUCTION

Cervical cancer, primarily caused by human papillomavirus (HPV) infection, has a very good prognosis when detected in

Strengths and limitations of this study

- ► To our knowledge, little is known about the acceptability of self-collection human papillomavirus 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 the sensitive nature of the questions related to sexual history, it is possible that a social desirability bias may have resulted in over-reporting of perceived 'good behaviours', such as screening or use of protection, in addition to under-reporting of perceived 'bad behaviours', such as number of lifetime sexual partners and other sexual behaviour 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.

premalignant or early malignant stages.1 However, it disproportionately burdens low-income and middle-income countries (LMICs), such as Guatemala, compared with 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 programmes 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 programme 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 with 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 programmes, increased participation in cervical cancer screening programmes. However, further work is needed to evaluate acceptable opt-in programmes 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 generalisability 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 civilisation. 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, Sololá 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. 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 women in Santiago Atitlán 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 (CHWs) were involved in the development of the question, design, validation, recruitment and conduct of the study. Local CHWs 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 the development of the research question and study design, organised the laboratory testing, led and assisted with CHW 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 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 multilevel sampling based on maps and population counts of the communities available through the local municipal office and were kept consistent with previous sampling methods. Households in Livingston were selected at



random using convenience sampling due to lack of reliable census data at the neighbourhood 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 minimise 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. 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?'; 'How down 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 returned to the main study office at the end of the day where samples were then processed to stabilise sample life. The brush component of the HerSwab kit was cut into a 15 mL test tube using lab scissors. The lab scissors were sterilised using alcohol and an open flame between each sample. Each tube was filled with 5 mL 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 programme implementation in Guatemala.³⁷ Each sample was labelled with the participant's unique identifier. Time of sample processing and condition of sample were recorded.

Stabilised 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 PCR Hybribio HR-13 kit. Samples were processed according to the manufacturers protocol and modified to use a 10 μ L reaction volume for the real-time PCR and run on an ABI-7000. After testing, samples were labelled 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 μ L 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 could not be reached at the study conclusion were re-contacted either at 6 months or 1 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 analysed 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 Atitlán 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, χ^2 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 behaviour), intrauterine device (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 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 vs Garifuna or Ladino, reflecting a Mayan descent vs 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 five participants missing ethnicity or classified as other ethnicity, one participant missing marital status, one participant missing regular drinking status, three participants missing number of lifetime sexual partners,

one participant missing smoking status, and two participants missing family history of cancer resulting in a final sample size n=309 for analyses evaluating willingness to try self-collection.

Covariates were parameterised 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 do not 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/do not know), continuous age and number of lifetime sexual partners (one versus more than one).

Data cleaning and analyses were carried out using SAS V.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 with 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 HIV, while 56.4% 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 examinations, 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 online supplementary appendix.

Self-collection willingness

When participants were asked if they would be willing to self-collect at home, the majority of women in both



	Santiago Atitlán % (N) or mean (SD)	Livingston N (%) or mean (SD)	P value
N	500	456	
Age (years)	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)	
iteracy			<0.0001
Illiterate (neither read nor write)	48.60% (243)	12.50% (57)	
Literate (either read and/or write)	51.00% (255)	87.28% (398)	
Ever married/united	97.00% (485)	62.50% (285)	<0.0001
Breast examination (heard of)	14.00% (70)	66.45% (303)	<0.0001
Pap (ever)	66.80% (334)	58.11% (265)	0.0056
_ast 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)	
/IA (ever)	6.00% (30)	1.32% (6)	<0.0001
Ever smoke	0.40% (2)	9.65% (44)	<0.0001
Regular drinker	0.60% (3)	9.65% (44)	<0.0001
Jsed IUD (ever)	1.41% (7)	7.89% (36)	<0.0001
Jse 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	90.60% (453)	70.83% (323)	
More than one	6.80% (34)	25.88% (118)	
Refused	2.60% (13)	3.29% (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)	
Do not have daughters	27.60% (138)	8.33% (38)	
Refused	1.80% (9)	2.63% (12)	

CC, cervical cancer; HPV, human papillomavirus; IUD, intrauterine device; VIA, visual inspection with acetic acid .

	Santiago Atitlán % (N)	Livingston % (N)	
N	500 (all participants) 438 (age-eligible)	456 (all participants) 322 (age-eligible)	P value*†
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), among those with previous Pap	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	410 (age-eligible; test-taking participants)	169 (age eligible; test- taking participants)	P value
Comfort of test			†<0.0001
Comfortable	81.22% (333)	83.43% (141)	
Neutral	5.85% (24)	5.33% (9)	
Uncomfortable	12.68% (52)	7.10% (12)	
Unknown	0.24% (1)	4.14% (7)	
Ease of test			0.0241†
Easy	84.63% (347)	83.43% (141)	
Neutral	4.63% (19)	7.10% (12)	
Difficult	10.49% (43)	5.33% (9)	
Unknown	0.24% (1)	4.14% (7)	
Willingness to retake test	98.05% (402)	95.27% (161)	0.3711
Willingriess to retake test	00.0070 (102)	00.21 /0 (101)	0.07 1 1

^{*}P values for means calculated using two-sample t-test; proportions using χ^2 test.

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 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 with 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 are 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 online supplementary 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 with those who did not (crude prevalence ratio (PR) 2.04; 95% CI 1.27 to 3.28; adjusted PR, 2.25; 95% CI 1.38 to 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 to 1.94; adjusted PR 1.43; 95% CI 1.08 to 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 to 1.48; adjusted PR 1.14; 95% CI 0.89 to

[†]Fisher's exact test used to account for low cell counts.

HPV, human papillomavirus; VIA, visual inspection with acetic acid.

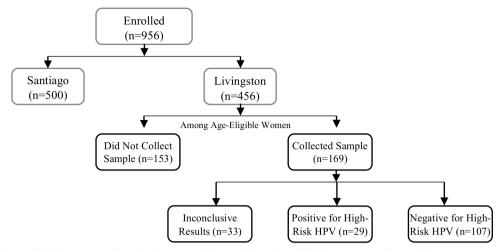


Figure 1 Flow chart of Livingston self-collection sampling and testing. HPV, human papillomavirus.

1.46; never married, crude PR 1.19; 95% CI 0.96 to 1.48; adjusted PR 1.15; 95% CI 0.91 to 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 to 3.68). When stratifying ethnic group (Q'echchi vs 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. Interaction terms between ethnic group (Q'echchi vs 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 to 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 to 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, 81.2% found it comfortable and 84.6% reported that the HerSwab was easy to use. Among Livingston participants who self-collected, 83.4% found it comfortable and 83.4% 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 (98.1% in Santiago and 95.3% in Livingston) (table 2).

HPV prevalence

Overall, 19% of samples tested positive for high-risk HPV (n=549). Furthermore, 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=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 on 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 vs 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 behaviours 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 vs non-Mayan descent) in Livingston. However, high prevalence of literacy among Garifuna

 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†
N	52.48% (169)	47.52% (153)	
Age (years)	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)	
Do not know		100.0% (4)	
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)	

Continued



Table 3 Continued			
	Took the sample % (N) or mean (SD)	Did not take the sample % (N) or mean (SD)	P value†
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)	
Do not have daughters	38.46% (5)	61.54% (8)	
Refused	30.00% (3)	70.00% (7)	

^{*%} calculated for sampling decision by each covariate.

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 programme 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 (ie, positive for HPV). Our results in Livingston suggest that it might be critical that, if implemented, HPV screening and education programmes 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 Atitlán, a community with low literacy levels, as compared with 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 scepticism might be found in places with existing cervical screening programmes, 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 affect women's willingness to try 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.

 $[\]dagger P$ values for means calculated using two-sample t-test; proportions using χ^2 test .

CC, cervical cancer; HPV, human papillomavirus; IUD, intrauterine device; VIA, visual inspection with acetic acid.

sample collection in Livingston among age-eligible women log-binomial regressions: prevalence ratios of sample collection (n=309) Prevalence ratios of

	Exposure covariat	exposure covariates effect on sample collection; PR (95% CI)	collection; PR (95%)	(5				
			Hx of Pap/VIA					Believe at risk for
	Literacy (Y)	Marriage (Never)	(Ever)	Smoking (Y)	Drinking (Y)	IUD use (Y)	Family Hx of CC (Y) CC (Y)	cc (y)
Model ₁ : main Effect	Model ₁ : main Effect 2.04 (1.27 to 3.28) 1.19 (0.96 to 1.48)	1.19 (0.96 to 1.48)	1.18 (0.92 to 1.52)	1.18 (0.92 to 1.52) 1.03 (0.72 to 1.46) 1.18 (0.95 to 1.48) 1.49 (1.15 to 1.94) 1.13 (0.82 to 1.55)	1.18 (0.95 to 1.48)	1.49 (1.15 to 1.94)		1.09 (0.87 to 1.35)
Model ₂ : Main Effect	Model ₂ : Main Effect 2.25 (1.38 to 3.68) 1.15 (0.91 to 1.43)	1.15 (0.91 to 1.43)	1.20 (0.93 to 1.56)	0.94 (0.66 to 1.35) 1.14 (0.89 to 1.46) 1.43 (1.08 to 1.88) 1.15 (0.83 to 1.59)	1.14 (0.89 to 1.46)	1.43 (1.08 to 1.88)	1.15 (0.83 to 1.59)	1.06 (0.85 to 1.32)

partners (more than one) sexual Each exposure was explored independently. M1: unadjusted log-binomial model. M2: adjusted for age, ethnicity and number of lifetime

Table 5 Prevalence ratio of sample collection in Livingston among age-eligible women stratified by ethnic grouping (Mayan descent vs Non-Mayan descent) log-binomial regression: prevalence ratio of sample collection (n=309)

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	Ladino or Garifuna (n=183)	Q'echchi (n=126)
Covariates	PR (95% CI)	PR (95% CI)
Literacy (Y)	2.39 (0.70 to 8.15)	2.08 (1.17 to 3.69)
Age	1.00 (0.98 to 1.02)	0.99 (0.96 to 1.02)
More than One Lifetime Sexual Partner	1.31 (1.00 to 1.73)	1.37 (1.00 to 1.88)

Final stepwise selected model presented, stratified by ethnic group.

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% vs 118.7%). 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 regard 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, generalising the evaluations of a health programme's acceptability and feasibility to the whole country is generally difficult. However, because we evaluated two very different rural multiethnic 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 behaviours', such as screening or use of protection, in addition to under-reporting of perceived 'bad behaviours', such as number of lifetime sexual partners and other sexual behaviour measures. We tried to minimise the possibility of this bias by maintaining confidentiality with participants. Also, women may report their history of screening or utilisation of healthcare 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 Atitlán. 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 the community in terms of ethnic, age and other metrics, suggesting that influential selection bias into the study might be limited. 43

Screening programme 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 need to be considered before programme adoption. 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 might 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 programme may affect attitudes towards new screening modalities. Future research should focus on increasing the generalisability 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 utilising cervical cancer modalities, including HPV self-collection sampling.

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