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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- 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

1 Cervical cancer, primarily caused by HPV infection, has a very good prognosis when
2 detected in premalignant or early malignant stages¹. However, it disproportionately burdens
3 low- and middle-income countries (LMICs), such as Guatemala, compared to high-income
4 countries (HICs)²⁻⁴. HICs currently use Pap smears to detect abnormal cervical lesions that can
5 be removed, greatly reducing the risk of cervical cancer^{3 5}. However, there are many barriers to
6 implementing successful Pap smear (cytology-based) screening programs in LMICs, including
7 difficulties establishing sustainable laboratory infrastructure, training and retaining adequate
8 numbers of trained pathologists or cytologists, overburdened primary care clinics, and time and
9 travel limitations for women in reaching screening locations^{1 6 7}. Due to these factors and others,
10 the percentage of women in Guatemala who are screened for cervical cancer remains low; in
11 2014, only 49.8% of women (15-49 years of age) reported ever having a Pap smear. Thus,
12 significant improvements in screening or program implementation are paramount to improving
13 cervical cancer outcomes in Guatemala^{3 8 9}.

14 Since more than 90% of cervical cancers are caused by the HPV virus, HPV testing has
15 been suggested as a possible alternative, primary form of cervical cancer screening¹⁰⁻¹². When
16 used in combination with Visual Inspection with Acetic Acid (VIA) or Pap smears in low-
17 income settings, HPV testing has been shown to provide significant improvements in the
18 detection of advanced premalignant lesions and cancer in both sensitivity and specificity as
19 compared to VIA or Pap smear alone, as only women who test positive for HPV need to follow
20 up with further screening¹³⁻¹⁶. Previous studies have also confirmed that HPV self-swab kits are
21 comparable to physician administered samples in their ability to detect carcinogenic, high-risk
22 HPV¹⁷. Thus, at-home HPV sample collection, with referral to further screening for those

23 positive for high-risk HPV, may be both more acceptable within low-income communities and
24 more programmatically feasible^{6 7 18}.

25 Studies have shown that HPV self-sampling is generally acceptable among women in low
26 and high resource settings as well as immigrant, rural, vulnerable populations¹⁹⁻²⁹. To our
27 knowledge, however, little is known about the acceptability of self-collection HPV testing across
28 the diverse communities within Guatemala, and in particular among indigenous populations. In
29 a pilot cross-sectional study assessing the acceptability of HPV self-collection among 200
30 women in the Mayan community of Santiago Atitlán, Guatemala, a self-swab HPV test was
31 found to be a highly acceptable form of screening³⁰. Over 80% of women said that they
32 preferred using a self-swab kit in their home rather than being screened at a doctors' office.
33 However, this pilot study was limited to a relatively small sample in a single, largely
34 homogeneous community, limiting the generalizability of the results. Further research is thus
35 needed to evaluate the acceptability of self-collection testing among more diverse populations
36 within Guatemala, an extremely diverse country ethnically, culturally, and economically. The
37 purpose of this study was to further assess and compare the acceptability of self-collection HPV
38 testing in two rural, ethnically distinct communities in Guatemala: Santiago Atitlán and
39 Livingston, Izabal.

40 **METHODS**

41 **Study Communities**

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

1
2
3 46 language³⁰. The majority of women in Santiago Atitlán have at most a primary education.
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5 47 Additionally, as a conservative, religious community, it is highly uncommon for women to either
6
7 48 drink or smoke, and almost all women in have previously reported having only one lifetime
8
9 49 sexual partner³⁰.

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11
12 50 Livingston, Izabal is located on the Caribbean coast of the country and is a rural
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14 51 community, only accessible by boat, that is the primary Garífuna settlement in Guatemala. The
15
16 52 Garífuna people are considered a unique ethnic group with their own language, culture, and
17
18 53 cuisine. Additionally, there are large populations of other ethnic and cultural groups located in
19
20 54 Livingston including Q'eqchi' (Mayan descent), Ladinos (non-Mayan), and populations of
21
22 55 Indian descent. Most women in Livingston are believed to have at least basic primary education.
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25

26 56 **Patient and Public Involvement**

27
28 57 The patients were not involved in the development of the research questions, outcome measures
29
30 58 or study design. The patients were also not involved in the recruitment and performance of the
31
32 59 study. However, the public, Guatemalan physicians, scientists, and community health workers,
33
34 60 were involved in the development of the question, design, validation, recruitment, and conduct of
35
36 61 the study. Local community health workers were involved in the validation of the survey and
37
38 62 study protocol, recruited participants and conducted the interviews, and assisted in providing test
39
40 63 results to patients. Guatemalan physicians contributed to development of the research question
41
42 64 and study design, organized the laboratory testing, led and assisted with community health
43
44 65 worker training, and provided HPV test results to patients. Local laboratory scientists
45
46 66 contributed to the study design and conducted the HPV laboratory testing. The continued
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48 67 collaborations with these team members will be used to disseminate study results to patients and
49
50 68 Guatemalan officials via publications, presentations, and meetings.
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69 Eligibility and Recruitment

70 Trained community health workers (CHWs) in both communities actively recruited
71 participants through home visits. All CHWs were bilingual and spoke both Spanish and either
72 Tz'utujil, Q'eqchi, or Karif (the language of the Garifuna) depending on the location they were
73 working in. Households in Santiago Atitlán were selected at random using stratified multi-level
74 sampling based upon maps and population counts of the communities available through the local
75 municipal office and were kept consistent with previous sampling methods³⁰. Households in
76 Livingston were selected at random using convenience sampling due to lack of reliable census
77 data at the neighborhood-level. Sampling methods were, however, kept as similar as possible to
78 those in Santiago Atitlán.

79 Selected households that had at least one woman available between the ages of 18 and 60
80 were invited to participate in the survey-component of the study. For households with more than
81 one eligible woman willing to participate, the female in the household whose birthday was
82 closest to the date of the interview was enrolled in the study. Exclusion criteria consisted of past
83 hysterectomy or previous cervical cancer. Only women between the ages of 25 and 54 were
84 asked to provide a sample, in accordance with Guatemala's current screening
85 recommendations³¹. Additionally, pregnant women, women currently menstruating, and women
86 who had never been sexually active were also excluded from providing samples but could
87 participate in the survey component.

88 Survey

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

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2
3 92 selected household together and read a recruitment script to a female household member to
4
5 93 determine the household's eligibility. CHWs administered the survey and provided kits to
6
7
8 94 collect HPV samples only to willing, eligible participants.
9

10 95 The survey questionnaire included 153 questions concerning demographics, risk factors
11
12 96 for cervical cancer and HPV, and knowledge of cervical cancer and HPV. The survey was
13
14 97 developed from the pilot study survey and validated as part of the CHW and translator training to
15
16
17 98 ensure correct translation and cultural relevancy³⁰. Each survey was administered by the CHWs
18
19 99 using electronic tablets and the Qualtrics offline app.
20

21
22 100 All women who participated in the study were compensated with a voucher for a free Pap
23
24 101 smear or VIA at a local health clinic. Women in both communities can access free VIAs
25
26 102 (Santiago) or Pap Smears (Livingston) in the local public health system, but if they chose to use
27
28 103 a private clinic instead of the public clinic, the voucher covered their fees.
29

30 31 104 **HPV Self-Collected Samples** 32

33 105 The HPV samples were collected using HerSwab kits, a self-collection sampling method
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35 106 ^{30 32 33}. If a participant was willing to provide a sample, instructions and graphical materials were
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37
38 107 provided and the participant collected the sample in a separate, private room from the CHWs.
39
40 108 Participants who collected a sample then completed a short post-sample survey with the CHWs
41
42 109 of three questions regarding ease, comfort, and acceptability of the sampling method: "How easy
43
44 110 was the self-collection swab?"; "How comfortable was the self-collection swab?"; and "Would
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46
47 111 you be willing to collect a sample every 2-3 years to detect HPV as a form of cervical cancer
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49 112 screening?".
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51
52 113 After collection, samples were kept in small, refrigerated coolers carried by the CHWs
53
54 114 until they were returned to the main study office at the end of the day where samples were then
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3 115 processed to stabilize sample life. The brush component of the HerSwab kit was cut into a 15-
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5 116 mL test tube using lab scissors. The lab scissors were sterilized using alcohol and an open flame
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7
8 117 between each sample. Each tube was filled with 5mL of Scope mouthwash using a pipette, and
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10 118 tubes were sealed using a cap and parafilm paper³⁴. Each sample was labeled with the
11
12 119 participant's unique identifier. Time of sample processing and condition of sample were
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14
15 120 recorded.

16
17 121 Stabilized samples were sent to a molecular biology laboratory at the Institute of
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19 122 Nutrition of Central America and Panama (INCAP) in Guatemala City for testing. Samples were
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21 123 tested using the real-time polymerase chain reaction (PCR) HybriBio HR-13 kit^{35 36}. Samples
22
23 124 were processed according to the manufacturers protocol and modified to use a 10 ul reaction
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25 125 volume for the real-time PCR and run on an ABI-7000³⁴. After testing, samples were labeled as
26
27 126 positive for HR-HPV, negative, or, if both the HPV probe and the internal control were negative,
28
29 127 inconclusive. If a sample test was inconclusive during the first test, it was run an additional time
30
31 128 using a 20 ul reaction volume, and if no result was obtained, the test was deemed inconclusive.
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34 129 **Follow-Up**

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36 130 A local CHW provided negative and inconclusive results over the phone or through a
37
38 131 home visit. Positive results were provided in-person by a study physician who referred
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40 132 participants to their local community health clinic for follow-up and further cervical cancer
41
42 133 screening. All participants who couldn't be reached at the study conclusion were re-contacted
43
44 134 either at 6 months or one year to provide them with their results. Although women with negative
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46 135 results were not explicitly recommended to attend the clinic, all participants were encouraged to
47
48 136 get screened using the voucher provided at the local clinic to support their engagement with local
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53 137 preventative services.

138 **Outcomes and Statistical Analysis**

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

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

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

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

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

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3 161 literacy, marital status, smoking, alcohol use, IUD use, number of lifetime sexual partners,
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5 162 family history of cervical cancer, and whether a woman believed she was likely to develop
6
7 163 cervical cancer. Statistical analyses were run using log-binomial regression and models were
8
9 164 further adjusted for age, ethnicity, and number of lifetime partners.

10
11 165 Covariates were parameterized as: able to read or write versus unable to read or write
12
13 166 (literacy), ever married versus never married, ever had a Pap or VIA versus never, drinker versus
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15 167 non-drinker, ever had an IUD versus never, ever smoked versus never smoked.

16
17 168 Data cleaning and analyses were carried out using SAS 9.4³⁷.

18 19 169 **RESULTS**

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21
22 170 In total, 956 women were recruited to participate into the study: 500 women in Santiago
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24 171 Atitlán and 456 women in Livingston. Demographic characteristics, health access and
25
26 172 utilization, and knowledge and attitudes towards cervical cancer and HPV screening differed
27
28 173 between the two communities: 69.4% of the participants in Santiago Atitlán had less than
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30 174 primary education and 96.4% were of Tz'tujil ethnicity. In contrast, only 33.9% of the
31
32 175 participants in Livingston had less than primary education and many ethnic groups were
33
34 176 represented: 41.9% Q'echi, 32% Garifuna, and 24.8% mixed ethnicity (Ladino) (Table 1).

35
36 177 Knowledge and attitudes regarding HPV and cervical cancer also differed between the
37
38 178 communities. Only 11.8% of participants in Santiago reported previous knowledge of HPV as
39
40 179 compared to 62.7% of Livingston participants. However, when asked about the seriousness of
41
42 180 cervical cancer, most participants in both communities responded “very” or “extremely” (74.8%
43
44 181 Santiago and 80.9% Livingston) (Appendix).

45
46 182 Self-reported history of access to healthcare appeared higher in Livingston than in
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48 183 Santiago. For example, only 5.0% of participants in Santiago responded that they had ever been
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3 184 tested for HIV while 57.8% of Livingston participants responded that they had been previously
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5 185 tested. Additionally, a higher proportion of participants in Livingston consistently reported using
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7 186 contraception, always using protection during sexual intercourse, and using tobacco and alcohol
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9
10 187 than in Santiago (Table 1).

11 12 188 **Self-Collection Willingness and Acceptability**

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14
15 189 We found significant differences between the communities with respect to willingness to
16
17 190 try self-collection sampling. In Santiago Atitlán, of 438 age-eligible participants, 93.6%
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19 191 (N=410) chose to self-collect. In Livingston, of 322 age-eligible participants, 52.5% (N=169)
20
21 192 chose to self-collect. However, among those who did collect a sample, the self-collection testing
22
23 193 was highly acceptable in both communities. Of Santiago participants who self-collected, 81.4%
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25 194 found it comfortable and 84.8% reported that the HerSwab was easy to use. Among Livingston
26
27 195 participants who self-collected, 87.0% found it comfortable and 87.0% reported it was easy to
28
29 196 use. Among those who chose to self-collect, almost all participants in both locations reported that
30
31 197 they were willing to use it as a form of cervical cancer screening (99.5% in Santiago and 100%
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33 198 in Livingston) (Table 2).

34 35 199 *Willingness to Sample in Livingston*

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37
38 200 We evaluated factors that affected the willingness to try self-collection testing in
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40
41 201 Livingston. Literacy, the use of health services, and beliefs regarding cervical cancer differed
42
43 202 between age-eligible women who self-collected a sample compared to those who did not (Table
44
45 203 3). Additionally, 31.4% of the women who ended up not providing a sample had responded
46
47 204 previously in the questionnaire that they indeed would be willing to collect a self-swab sample at
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49 205 home (Figure 1). While data is unavailable regarding how many age-eligible women were
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206 ineligible to collect a sample due to menstruation or pregnancy, this likely does not entirely
207 account for all women who ultimately chose not to self-collect.

208 Literacy was significantly higher among women who self- collected a sample in
209 Livingston compared to those who did not (crude PR 1.94; 95% CI: 1.23, 3.05; adjusted PR,
210 1.45; 95% CI: 1.07, 1.95) (Table 4 and Appendix). Regular drinking was also higher among
211 women who self-collected (crude PR 1.18; 95% CI: 0.95, 1.46; adjusted PR 1.30; 95% CI: 0.74,
212 2.29) (Table 4 and Appendix). Additionally, IUD use and number of lifetime sexual partners
213 were higher among women who self-collected a sample in Livingston (IUD use, adjusted PR
214 2.09; 95% CI: 0.80, 5.45; lifetime sexual partners, adjusted PR 1.12; 95% CI 0.93, 1.34) (Table
215 4). When stratifying either by indigenous or non-indigenous group or by ethnic group, the
216 association between literacy and actual sample collection remained positive. However, this
217 relationship only remained statistically significant among Q'echchi participants (Appendix).

218 When evaluating how women responded to the survey question, "Would you be willing
219 to collect a sample at home?", literacy and IUD were significantly different among women who
220 responded a priori that they would be willing as compared to women who responded they would
221 not be willing. Characteristics comparing these two populations can be found in the appendix.
222 After adjustment for age, ethnicity, and number of lifetime sexual partners, the association
223 between literacy and a response of willingness to self-collect was no longer significant (crude PR
224 1.51; 95% CI: 1.09, 2.10; adjusted PR, 1.24; 95% CI: 0.96, 1.60) (Appendix). Similarly, the
225 relationship between not using an IUD and a positive willingness survey response was no longer
226 significant after adjustment (crude PR 0.75; 95% CI: 0.62, 0.90; adjusted PR, 0.87; 95% CI:
227 0.69, 1.08) (Appendix).

228 **HPV Prevalence**

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

236 DISCUSSION

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

247 Our study also found, however, that there were differences between communities in
248 willingness to try self-collection. Willingness to try self-collection testing remained consistently
249 high among participants in Santiago Atitlán as reported in the pilot study conducted in 2015
250 (93% in 2015 versus 93.6% in 2016)³⁰. In Livingston, however, even among women who first
251 responded in the survey or consent form that they would be willing to collect a sample, actual

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3 252 self-collection was lower. We found that willingness to self-collect in Livingston was
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6 253 consistently associated with higher levels of literacy. Literacy was also associated in both
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8 254 communities with previous access to cervical cancer screening. In contrast, ethnicity, history of
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10 255 cervical cancer screening, and reproductive history were not associated with willingness to self-
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12 256 collect. Stratified analyses revealed that there were no qualitative differences in the association
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15 257 between literacy and sample collection across ethnic groups in Livingston.

16
17 258 High prevalence of self-collection testing in Santiago Atitlan, a community with low
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19 259 literacy levels, as compared to the low rates of self-collection testing among those with low
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21 260 literacy in Livingston may reflect larger community differences in awareness or access to
22
23 261 screening modalities rather than a lack of effect of literacy in Santiago or an effect of ethnicity.
24
25 262 Santiago Atitlán remains largely deficit in accessible and affordable cervical cancer screening
26
27 263 while Livingston has regular, public or private, screening campaigns in the community. This
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29 264 difference in general community access, then, may be acting as an effect modifier on the
30
31 265 association between literacy and screening between these two communities, suggesting that self-
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33 266 collection might be better received at first in communities that do not have other alternatives,
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35 267 whereas some initial skepticism might be found in places with existing cervical screening
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37 268 programs, independently of their quality and efficacy. The high rates of acceptability and
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39 269 willingness to retake among women who self-collected in both communities suggest that once
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41 270 experienced, self-collection is a valid, and even preferred, alternative to other screening
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43 271 modalities from the women's perspective.

44
45 272 The results suggest thus that HPV self-collection testing program implementation may
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47 273 need to target populations based on levels of literacy or community access, rather than focusing
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49 274 primarily on ethnicity or racial identity. A previous study examining HPV acceptability and
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3 275 intention in the UK similarly found that low education and self-efficacy were associated with
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5 276 low sampling intentions²⁸. The inability to either read or write in Guatemala may negatively
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7
8 277 influence a woman's perceived self-efficacy and her confidence in navigating public health
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10 278 infrastructure or self-collecting a vaginal sample. This population, however, would greatly
11
12 279 benefit from HPV self-collection testing as a primary form of cervical cancer screening due to its
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14 280 strength in concentrating less accessible and more invasive screening modalities towards those
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16 281 that are at high-risk (i.e., positive for HPV). Therefore, our results suggest that it might be
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18 282 critical that, if implemented, HPV screening and education programs are tailored such that they
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20 283 are more accessible to low-literacy populations and, thus, increase perceived self-efficacy in
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22 284 navigating the existing public health infrastructure.

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26 285 Although based on a different HPV test than in our pilot study (HybriBio HR13 vs.
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28 286 Anyplex 28), a similar prevalence of high-risk HPV was found in Santiago between 2015 and
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30 287 2016 (17.4% versus 19.3%)³⁰. Of note, there were no significant differences in high-risk HPV
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32 288 prevalence between ethnic groups in Livingston, and there was not a statistically significant
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34 289 difference between Santiago Atitlán and Livingston with regards to prevalence.

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38 290 Our study provided not only a larger sample size compared with previous studies but was
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40 291 also conducted in two differing communities. This is a strength because Guatemala is an
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42 292 extremely diverse country with over 23 languages, distinct ethnicities, and a history of large
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44 293 economic and social inequalities. Thus, generalizing the evaluations of a health program's
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46 294 acceptability and feasibility to the whole country is generally difficult. However, because we
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48 295 evaluated two very different rural multi-ethnic communities, our results may reflect some of the
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50 296 future obstacles and considerations necessary in implementing self-swab HPV testing in such a
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52 297 diverse country as Guatemala than was previously available. In fact, our results also

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3 298 complement the findings of the ongoing careHPV Scale-Up implementation, which is assessing
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5 299 the performance of HPV testing, including self-collection testing, within urban settings in
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8 300 Guatemala³⁸⁻⁴⁰.

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10 301 There are several limitations to our study. Due to both the sensitive nature of the
11
12 302 questions related to sexual history and the largely religious and conservative environment of the
13
14 303 communities, it may be possible that a social desirability bias may have resulted in over
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16 304 reporting of perceived “good behaviors”, such as screening or use of protection, in addition to
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18 305 under-reporting of perceived “bad behaviors”, such as number of lifetime sexual partners and
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20 306 other sexual behavior measures. We tried to minimize the possibility of this bias by maintaining
21
22 307 confidentiality with participants. Also, women may report their history of screening or
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24 308 utilization of health care resources incorrectly if they had limited information or understanding
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26 309 of these services. This trend may be exaggerated in women with low literacy and thus explain
27
28 310 some of the relationships that were observed in the data. Additionally, because sampling
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30 311 methods differed between the two communities due to the lack of reliable census counts in
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32 312 Livingston, there may be differences between the communities in potential selection bias into the
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34 313 study and more limited comparability of the results. However, our sample in Livingston is
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36 314 reflective of the overall population structure in terms of ethnic, age and other metrics, suggesting
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38 315 that influential selection bias into the study might be limited⁴¹.

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40 316 Due to the ongoing nature of the project, data on follow-up screening are still in process.
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42 317 Future research with our study participants will hopefully elucidate how HPV self-collection
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44 318 testing may affect women’s decisions to pursue further cervical cancer screening and follow-up
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46 319 care in their local communities after HPV testing and receiving their results. Additionally, these
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3 320 data may reveal other downstream facilitators or barriers to screening that will influence the
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5 321 overall success of HPV self-swab testing implementation nationwide.
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8 322 **CONCLUSION**

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10 323 The results of our study add to the literature on the potential of HPV self-collection
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12 324 testing in LMICs, demonstrating its wide acceptability in rural, indigenous, multi-ethnic
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14 325 communities in Latin America. Our findings also suggest that literacy and community access
15
16 326 may affect attitudes towards new screening modalities. It is important, then, that the issue of
17
18 327 literacy is specifically considered when implementing screening programs in Guatemala and
19
20 328 other LMICs through both policy and practice. Additionally, future programs should focus on
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22 329 tailoring messaging and education materials to low literacy versus high literacy women as
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24 330 opposed to specific ethnic or cultural groups. This vulnerable population may need more
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26 331 targeted educational programs that are provided through appropriate mediums to increase
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28 332 screening access in these populations.
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34 334 **LIST OF ABBREVIATIONS**

35
36 335 CC – Cervical Cancer

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38 336 CHW – Community Health Worker

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40 337 CI – Confidence Interval

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42 338 HICs – High-Income Countries

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44 339 HIV – Human Immunodeficiency Virus

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46 340 HPV – Human Papillomavirus

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48 341 HR-HPV – High-Risk Human Papillomavirus

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50 342 INCAP – Institute of Nutrition of Central America and Panama
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3 343 IUD – Intra-Uterine Device
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5 344 LMICs – Low and Middle-Income Countries
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8 345 OR – Odds Ratio
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10 346 PCR – Polymerase Chain Reaction
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12 347 PR – Prevalence Ratio
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15 348 VIA – Visual Inspection with Acetic Acid
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19 350 **DECLARATIONS**

21 351 **Ethics Approval and Consent to Participate**

22 352 The University of Michigan Institutional Review Board (HUM00096559) and the
23
24 353 Institute of Nutrition of Central America and Panama Institutional Review Board (MI-CIE-16-
25
26 354 009) approved study protocols. All participants gave oral and written informed consent prior to
27
28 355 participation in the study. The consent was documented by a signature or fingerprint of the
29
30 356 participant, the surveyors, and a witness.
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33 357 **Consent for Publication**

34 358 The authors of this paper have all reviewed its contents and consent for its publication.
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37 359 **Data Sharing Statement**

38 360 Due to the sensitive nature of the data collected, IRB restrictions, and ongoing data
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40 361 collection, study data is stored at the University of Michigan. Interested parties may contact the
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42 362 corresponding author to request access to de-identified datasets for specific research questions
43
44 363 related to the study. The authors welcome further collaboration but reserve the right to retain data
45
46 364 to protect study participants.
47
48

49 365 **Competing Interests**

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366 The authors have no competing interests to declare.

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376 **Authors' Contributions**

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

383
 37 Audrey Murchland – PIC, DC, SP, SA, W, E
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 43 Gina Ogilvie – PIC, E
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 45 Mark Prince – PIC, SP, E
 46 Michael Dean – PIC, SP, E
 47 Carlos Mendoza-Montano – PIC, SP, E
 48 Alvaro Rivera-Andrade – PIC, DC, SP, E
 49 Rafael Meza – PIC, DC, SP, SA, W, E

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522 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)	

	Santiago Atitlán % (N)	Livingston % (N)	p-value^{a,b}
N	500 (<i>All participants</i>) 438 (<i>age-eligible</i>)	456 (<i>all participants</i>) 322 (<i>age-eligible</i>)	
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 (<i>age-eligible; Test-Taking participants</i>)	169 (<i>age eligible; Test-Taking participants</i>)	
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

^ap-values for means calculated using two-sample t-test; proportions using chi-squared test

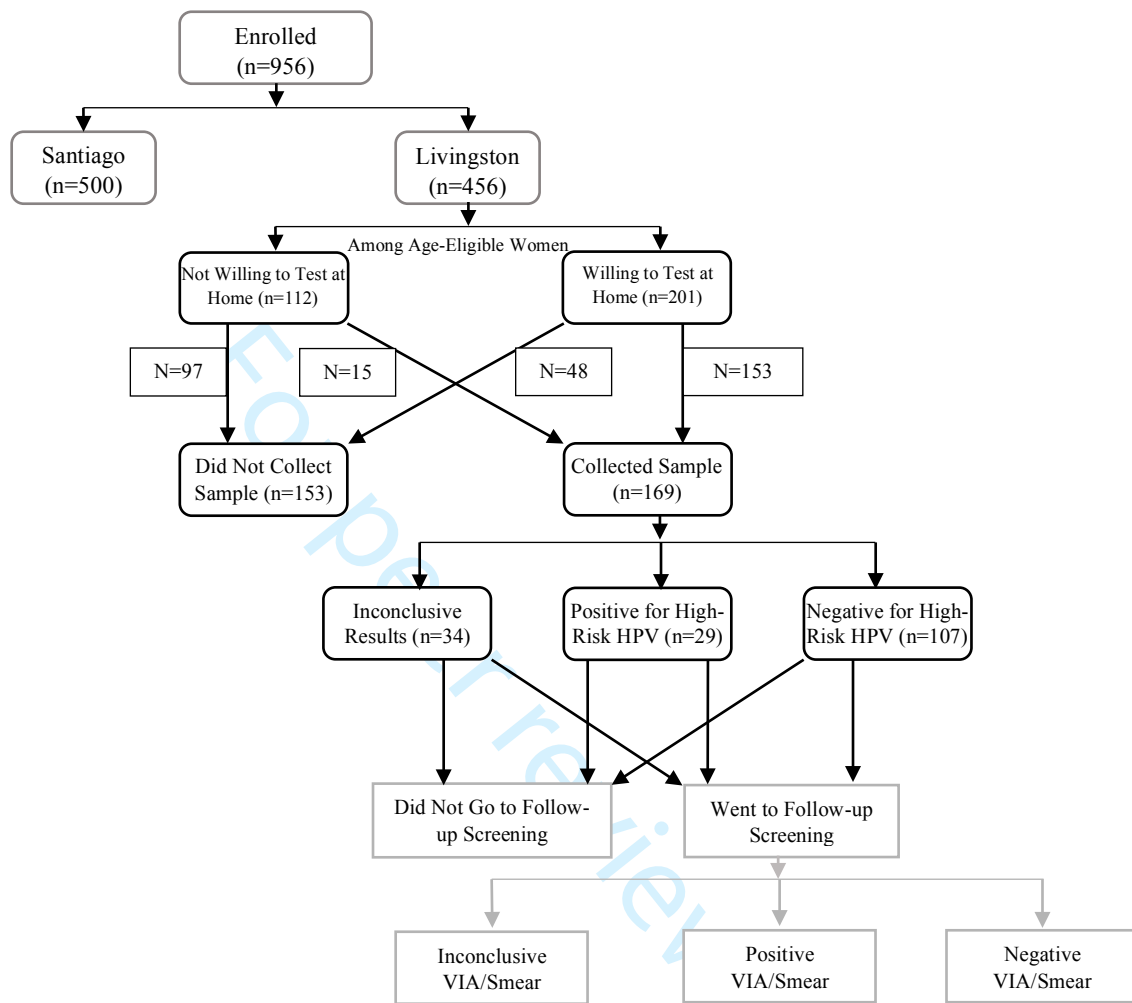
Table 4 Prevalence Ratio of Willingness to Collect a Sample in Livingston
Log-Binomial Regression: Prevalence Ratio of Actual Sample Collection and Willingness to Collect at Home

	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

Table A1 – General Population Characteristics Among All Participants (Continued)

Table A2 – Population Characteristics within Livingston (Continued)

Table A3 – Population Characteristics within Livingston: Comparing Racial/Ethnic Groups

Table A4 - Population Characteristics Comparing HPV Test Result

Table A5 – Differences Among Communities of Age-Eligible Indigenous Mayan Women

Table A6 - High-Risk HPV Prevalence Distribution

Appendix B: Additional Regression Tables

Table B1 – Prevalence Ratio of Willingness to Collect a Sample in Livingston (Continued)

Table B2 – Odds Ratio of Willingness to Collect a Sample in Livingston (Continued)

Table B3 – Odds Ratio of Willingness to Collect a Sample in Livingston: Ethnically Stratified Analysis

Table B4 - Odds Ratio of Willingness to Collect a Sample in Livingston: Stratified Analysis

Table B5 – Odds Ratio of High-Risk HPV

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

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
25 th Percentile	300	600	
50 th Percentile	800	1000	
75 th 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	

	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%)	

^ap-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

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

^bFisher's Exact Test used due to small cell counts

	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 (13.33%)	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

^ap-values for means calculated using two-sample t-test; proportions using chi-squared test

	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

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

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 age²
M3: all variables included and adjusted for age, ethnicity, and age²
- 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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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

1 Cervical cancer, primarily caused by human papillomavirus (HPV) infection, has a very
2 good prognosis when detected in premalignant or early malignant stages¹. However, it
3 disproportionately burdens low- and middle-income countries (LMICs), such as Guatemala,
4 compared to high-income countries (HICs)²⁻⁴. HICs currently use Pap smears to detect abnormal
5 cervical lesions that can be removed, greatly reducing the risk of cervical cancer^{3 5}. However,
6 there are many barriers to implementing successful Pap smear (cytology-based) screening
7 programs in LMICs, including difficulties establishing sustainable laboratory infrastructure,
8 training and retaining adequate numbers of trained pathologists or cytologists, overburdened
9 primary care clinics, and time and travel limitations for women in reaching screening locations^{1 6}
10 ⁷. Due to these factors and others, the percentage of women in Guatemala who are screened for
11 cervical cancer remains low; in 2014, only 49.8% of women (15-49 years of age) reported ever
12 having a Pap smear. Thus, significant improvements in screening or program implementation are
13 paramount to improving cervical cancer outcomes in Guatemala^{3 8 9}.

14 Since more than 90% of cervical cancers are caused by the HPV virus, HPV testing has
15 been suggested as a possible alternative, primary form of cervical cancer screening¹⁰⁻¹². When
16 used in combination with Visual Inspection with Acetic Acid (VIA) or Pap smears in low-
17 income settings, HPV testing has been shown to provide significant improvements in the
18 detection of advanced premalignant lesions and cancer in sensitivity as compared to VIA or Pap
19 smear alone, as only women who test positive for HPV need to follow up with further
20 screening¹³⁻¹⁶. Previous studies have also confirmed¹³⁻¹⁶ that HPV self-swab kits are comparable to
21 physician administered samples in their ability to detect carcinogenic, high-risk HPV ^{17 18}. Thus,
22 at-home HPV sample collection, with referral to further screening for those positive for high-risk

23 HPV, may be both more acceptable within low-income communities and more programmatically
24 feasible^{6 7 19}. Moreover, a 2015 meta-analysis showed that HPV self-sampling, particularly in
25 opt-in programs, increased participation in cervical cancer screening programs. However,
26 further work is needed to evaluate acceptable opt-in programs for women²⁰.

27 Studies have shown that HPV self-sampling is generally acceptable among women in low
28 and high resource settings as well as immigrant, rural, vulnerable populations²¹⁻³¹. To our
29 knowledge, however, little is known about the acceptability of self-collection HPV testing across
30 the diverse communities within Guatemala, and in particular among rural and indigenous
31 populations. In a pilot cross-sectional study assessing the acceptability of HPV self-collection
32 among 200 women in the Mayan community of Santiago Atitlán, Guatemala, a self-swab HPV
33 test was found to be a highly acceptable form of screening³². Over 80% of women said that they
34 preferred using a self-swab kit in their home rather than being screened at a doctors' office.
35 However, this pilot study was limited to a relatively small sample in a single, largely
36 homogeneous community, limiting the generalizability of the results to other rural and
37 indigenous communities in Guatemala. Further research is thus needed to evaluate the
38 acceptability of self-collection testing among more diverse rural and indigenous populations
39 within Guatemala, which is very diverse, with over 23 official languages and many indigenous
40 groups, most but not all descendants from the Mayan civilization. The purpose of this study was
41 to further assess and compare the acceptability of self-collection HPV testing in two rural,
42 ethnically distinct communities in Guatemala: Santiago Atitlán and Livingston, Izabal.

43 **METHODS**

44 **Study Communities**

1
2
3 45 Santiago Atitlán, Sololá is a rural community located on Lake Atitlán, in the southwest
4
5
6 46 region of Guatemala, 75 miles west of Guatemala City. The Tz'utujil, a Mayan descendant
7
8 47 ethnic group, inhabits the region, which surrounds Lake Atitlán. The primary language of
9
10 48 Santiago's inhabitants is Tz'utujil, and over half of the villagers speak Spanish as a second
11
12 49 language³². The majority of women in Santiago Atitlán have at most a primary education.
13
14
15 50 Additionally, as a conservative, religious community, it is highly uncommon for women to either
16
17 51 drink or smoke, and almost all women in have previously reported having only one lifetime
18
19 52 sexual partner³².

21
22 53 Livingston, Izabal is located on the Caribbean coast of the country and is a rural
23
24 54 community, only accessible by boat, that is the primary Garífuna settlement in Guatemala. The
25
26 55 Garífuna people are considered a unique ethnic group with their own language, culture, and
27
28 56 cuisine. Additionally, there are large populations of other ethnic and cultural groups located in
29
30 57 Livingston including Q'eqchi' (Mayan descent), Ladinos (non-Mayan descent), and populations
31
32 58 of Indian descent. Most women in Livingston are believed to have at least basic primary
33
34 59 education.

35 36 37 38 60 **Patient and Public Involvement**

39
40 61 The patients were not involved in the development of the research questions, outcome
41
42 62 measures or study design. The patients were also not involved in the recruitment and
43
44 63 performance of the study. However, the public, Guatemalan physicians, scientists, and
45
46 64 community health workers, were involved in the development of the question, design, validation,
47
48 65 recruitment, and conduct of the study. Local community health workers were involved in the
49
50 66 validation of the survey and study protocol, recruited participants and conducted the interviews,
51
52 67 and assisted in providing test results to patients. Guatemalan physicians contributed to
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2
3 68 development of the research question and study design, organized the laboratory testing, led and
4
5 69 assisted with community health worker training, and provided HPV test results to patients. Local
6
7
8 70 laboratory scientists contributed to the study design and conducted the HPV laboratory testing.
9
10 71 The continued collaborations with these team members will be used to disseminate study results
11
12 72 to patients and Guatemalan officials via publications, presentations, and meetings.
13

14 73 **Eligibility and Recruitment**

15
16
17 74 Trained community health workers (CHWs) in both communities actively recruited
18
19 75 participants through home visits. All CHWs were bilingual and spoke both Spanish and either
20
21 76 Tz'utujil, Q'eqchi, or Karif (the language of the Garifuna) depending on the location they were
22
23 77 working in. Households in Santiago Atitlán were selected at random using stratified multi-level
24
25 78 sampling based upon maps and population counts of the communities available through the local
26
27 79 municipal office and were kept consistent with previous sampling methods³². Households in
28
29 80 Livingston were selected at random using convenience sampling due to lack of reliable census
30
31 81 data at the neighborhood-level. Sampling methods were, otherwise, kept the same as those in
32
33 82 Santiago Atitlán.
34
35
36
37

38 83 Selected households that had at least one woman available between the ages of 18 and 60
39
40 84 were invited to participate in the survey-component of the study. For households with more than
41
42 85 one eligible woman willing to participate, the female in the household whose birthday was
43
44 86 closest to the date of the interview was enrolled in the study. Exclusion criteria consisted of past
45
46 87 hysterectomy or previous cervical cancer. Only women between the ages of 25 and 54 were
47
48 88 asked to provide a sample, in accordance with Guatemala's current screening
49
50 89 recommendations³³. Additionally, pregnant women, women currently menstruating, and women
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52 90 who had never been sexually active were also excluded from providing samples but could
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3 91 participate in the survey component. Approximately 62% and 90% of eligible women contacted
4
5 92 were willing to participate in the study in Santiago and Livingston, respectively. A target sample
6
7
8 93 size of 500 per community was determined to be able to detect a 5% difference in self-sampling
9
10 94 acceptability with 80% power, assuming a 95% acceptability in Santiago Atitlan based on the
11
12 95 pilot.

14 96 **Survey**

16
17 97 Data collection consisted of two main components: the surveys and the HPV self-
18
19 98 collection tests. Local CHWs in each community were trained as interviewers in the appropriate
20
21 99 techniques and protocols before beginning home visits. Two CHWs visited each randomly
22
23 100 selected household together and read a recruitment script to a female household member to
24
25 101 determine the household's eligibility. CHWs administered the survey and provided kits to
26
27 102 collect HPV samples only to willing, eligible participants. Surveys were administered in private
28
29 103 rooms of the participant's house to minimize response bias to sensitive questions.

30
31 104 The survey questionnaire included 153 questions concerning demographics, risk factors
32
33 105 for cervical cancer and HPV, self-reported attitudes towards screening, healthcare service use,
34
35 106 and knowledge of cervical cancer and HPV. The survey was developed from the pilot study
36
37 107 survey and validated as part of the CHW and translator training to ensure correct translation and
38
39 108 cultural relevancy³². Each survey was administered by the CHWs using electronic tablets and
40
41 109 the Qualtrics offline app.

42
43 110 All women who participated in the study were compensated with a voucher for a free Pap
44
45 111 smear or VIA at a local health clinic. Women in both communities can access free VIAs
46
47 112 (Santiago) or Pap Smears (Livingston) in the local public health system, but if they chose to use
48
49 113 a private clinic instead of the public clinic, the voucher covered their fees.

114 HPV Self-Collected Samples

115 The HPV samples were collected using HerSwab kits, a self-collection sampling method
116 ^{32 34 35}. If a participant was willing to provide a sample, instructions and graphical materials were
117 provided and the participant collected the sample in a separate, private room from the CHWs.
118 Participants who collected a sample then completed a short post-sample survey with the CHWs
119 of three questions regarding ease, comfort, and acceptability of the sampling method: “How easy
120 was the self-collection swab?”; “How comfortable was the self-collection swab?”; and “Would
121 you be willing to collect a sample every 2-3 years to detect HPV as a form of cervical cancer
122 screening?”.

123 After collection, samples were kept in small, refrigerated coolers carried by the CHWs
124 until they were returned to the main study office at the end of the day where samples were then
125 processed to stabilize sample life. The brush component of the HerSwab kit was cut into a 15-
126 mL test tube using lab scissors. The lab scissors were sterilized using alcohol and an open flame
127 between each sample. Each tube was filled with 5mL of Scope mouthwash using a pipette, and
128 tubes were sealed using a cap and parafilm paper³⁶. Mouthwash is a reliable, low-cost transport
129 medium for DNA samples and was used to reflect likely standard operating procedures of HPV
130 screening program implementation in Guatemala³⁷. Each sample was labeled with the
131 participant’s unique identifier. Time of sample processing and condition of sample were
132 recorded.

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

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3 137 volume for the real-time PCR and run on an ABI-7000³⁶. After testing, samples were labeled as
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5 138 positive for HR-HPV, negative, or, if both the HPV probe and the internal control were negative,
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7
8 139 inconclusive. If a sample test was inconclusive during the first test, it was run an additional time
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10 140 using a 20 ul reaction volume, and if no result was obtained, the test was deemed inconclusive.

12 141 **Follow-Up**

14 142 A local CHW provided negative and inconclusive results over the phone or through a
15
16
17 143 home visit. Positive results were provided in-person by a study physician who referred
18
19 144 participants to their local community health clinic for follow-up and further cervical cancer
20
21
22 145 screening. All participants who couldn't be reached at the study conclusion were re-contacted
23
24 146 either at 6 months or one year to provide them with their results. Although women with negative
25
26 147 results were not explicitly recommended to attend the clinic, all participants were encouraged to
27
28 148 get screened using the voucher provided at the local clinic to support their engagement with local
29
30
31 149 preventative services. Participants who were found to be positive for advanced lesions as a result
32
33 150 of follow-up screening were referred for care through the free public health infrastructure in
34
35 151 Guatemala, as is currently standard practice. Due to the ongoing nature of the project, data on
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38 152 follow-up screening and care are still in the collection process.

39 153 **Outcomes and Statistical Analysis**

40
41 154 Willingness and acceptability of self-collection testing, knowledge of HPV, and risk
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43 155 factors were evaluated in both communities and across ethnic groups in Livingston, Izabal.
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45 156 Willingness was measured as whether or not a woman chose to self-collect a sample to be tested
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48 157 for HPV (actual self-collection). The acceptability of sample collection was only assessed for
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50
51 158 those who self-collected a sample and was analyzed using the post-self-swab survey questions
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53
54 159 described previously.

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3 160 Due to lower rates of actual self-collection in Livingston, differences between Livingston
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6 161 women willing and those not willing to collect a sample were evaluated using two-sample t-tests
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8 162 for means, chi-squared tests for proportions, and Fisher's Exact test for low cell counts. Most
9
10 163 women tried self-collection in Santiago, so we restrict these analyses to Livingston. Analyses
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12 164 were additionally restricted to age-eligible women in Livingston with complete covariate
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14 165 information (N=134 or 29.4% excluded due to age-ineligibility and N=13 or 2.9% excluded due
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16
17 166 to missing covariates). Specifically, we excluded 1 participant missing marital status, 1
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19 167 participant missing regular drinking status, 4 participants missing IUD use, and 2 participants
20
21 168 missing number of lifetime sexual partners, resulting in a final sample size N=309 for analyses
22
23
24 169 evaluating willingness to try self-collection.

25
26 170 The main exposures explored for willingness to try self-collection included: ethnicity,
27
28 171 literacy, marital status, history of Pap smear or VIA, alcohol use, and IUD use. Statistical
29
30 172 analyses were run using log-binomial regression and models were adjusted for age, ethnicity, and
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32 173 number of lifetime sexual partners. Final models were further stratified across ethnic groups to
33
34 174 evaluate potential effect modification.

35
36 175 Covariates were parameterized as: able to read and/or write (literate) versus unable to
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38 176 either read or write (illiterate), ever married versus never married, ever had a Pap or VIA versus
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40 177 never, regular drinker versus non-regular drinker, ever had an IUD versus never, ever smoked
41
42 178 versus never smoked, continuous age, and number of lifetime sexual partners (one versus more
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44
45 179 than one).

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49 180 Data cleaning and analyses were carried out using SAS 9.4⁴⁰.

50 51 52 181 **RESULTS**

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3 182 In total, 956 women were recruited to participate into the study: 500 women in Santiago
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5 183 Atitlán and 456 women in Livingston. Demographic characteristics differed between the two
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7
8 184 communities: 69.4% of the participants in Santiago Atitlán had less than primary education and
9
10 185 96.4% were of Tz'tujil ethnicity. In contrast, only 33.9% of the participants in Livingston had
11
12 186 less than primary education and three ethnic groups were represented: 41.9% Q'echi, 32%
13
14 187 Garifuna, and 24.8% mixed ethnicity (Ladino) (Table 1).

15
16
17 188 Knowledge and attitudes regarding HPV and cervical cancer also differed between the
18
19 189 communities. Only 11.8% of participants in Santiago reported previous knowledge of HPV as
20
21
22 190 compared to 62.7% of Livingston participants. However, when asked about the seriousness of
23
24 191 cervical cancer, most participants in both communities responded “very” or “extremely” (74.8%
25
26 192 Santiago and 80.9% Livingston) (Appendix).

27
28
29 193 Self-reported history of access to healthcare also appeared higher in Livingston than in
30
31 194 Santiago. For example, only 5.0% of participants in Santiago responded that they had ever been
32
33 195 tested for human immunodeficiency virus ⁴¹ while 57.8% of Livingston participants responded
34
35 196 that they had been previously tested. Additionally, a higher proportion of participants in
36
37 197 Livingston consistently reported using contraception, always using protection during sexual
38
39 198 intercourse, and using tobacco and alcohol than in Santiago (Table 1).

199 **Self-Collection Willingness**

200
201 We found significant differences between the communities with respect to willingness to
202
203 try self-collection sampling. In Santiago Atitlán, of 438 age-eligible participants, 93.6%
204
205 (N=410) chose to self-collect. In Livingston, of 322 age-eligible participants, 52.5% (N=169)
206
207 chose to self-collect (Table 2).

1
2
3 204 We evaluated factors that affected the willingness to try self-collection testing in
4
5
6 205 Livingston. Literacy, the use of health services, and beliefs regarding cervical cancer differed
7
8 206 between age-eligible women who self-collected a sample compared to those who did not (Table
9
10 207 3). Additionally, 31.4% of the women who ended up not providing a sample had responded
11
12 208 previously in the questionnaire that they indeed would be willing to collect a self-swab sample at
13
14 209 home (Figure 1). While data is unavailable regarding how many age-eligible women were
15
16 210 ineligible to collect a sample due to menstruation or pregnancy, this likely does not entirely
17
18 211 account for all women who ultimately chose not to self-collect.

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22 212 Literacy was significantly higher among women who self- collected a sample in
23
24 213 Livingston compared to those who did not (crude PR 2.07; 95% CI: 1.29, 3.35; adjusted PR,
25
26 214 2.28; 95% CI: 1.39, 3.72) (Tables 4-5). Regular drinking was also higher among women who
27
28 215 self-collected but not significant (crude PR 1.19; 95% CI: 0.96, 1.48; adjusted PR 1.16; 95% CI
29
30 216 0.91, 1.49) (Tables 4-5). Additionally, IUD use and never being married were higher among
31
32 217 women who self-collected a sample in Livingston (IUD use, crude PR 1.47; 95% CI: 1.14, 1.91;
33
34 218 adjusted PR 1.42; 95% CI: 1.07, 1.87; never married, crude PR 1.20; 95% CI: 0.97, 1.49;
35
36 219 adjusted PR 1.16; 95% CI: 0.93, 1.45) (Table 4-5). When stratifying either by indigenous or
37
38 220 non-indigenous group or by ethnic group, the association between literacy and actual sample
39
40 221 collection remained positive. However, this relationship only remained statistically significant
41
42 222 among Q'echchi participants.

43 223 **Self-Collection Acceptability and Comfort**

44
45 224 Among those who did collect a sample, the self-collection testing was highly acceptable
46
47 225 in both communities. Of Santiago participants who self-collected, 81.4% found it comfortable
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49 226 and 84.8% reported that the HerSwab was easy to use. Among Livingston participants who self-

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3 227 collected, 87.0% found it comfortable and 87.0% reported it was easy to use. Among those who
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5 228 chose to self-collect, almost all participants in both locations reported that they were willing to
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8 229 use it as a form of cervical cancer screening (99.5% in Santiago and 100% in Livingston) (Table
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11 231 **HPV Prevalence**

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15 232 Overall, 19% of samples tested positive for high-risk HPV (N=549). 18.7% of samples
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17 233 from Santiago Atitlán (N=77) tested positive for high-risk HPV and 21.3% of samples from
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19 234 Livingston (N=29) tested positive, but this difference was not statistically significant (p-
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21 235 value=0.4923). In total, 94% of participants who sampled in Santiago Atitlán and 88.5% of
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23 236 participants who sampled in Livingston were provided with their test results. Overall, 12.3% of
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25 237 HPV tests were found to be inconclusive (N=44 (9.6%) from Santiago Atitlán and N=33 (19.5%)
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27 238 from Livingston).

28 239 **DISCUSSION**

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31 240 In this study, we assessed the acceptability of HPV self-collection testing as an
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33 241 alternative form of primary cervical cancer screening in indigenous and rural communities in
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35 242 Guatemala. We found that self-collection appears to be highly acceptable among women who
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37 243 tried it, independent of community and ethnicity. Most women reported that self-collection was
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39 244 comfortable and easy to use, and almost all women who tried it reported being willing to use it as
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41 245 a form of cervical cancer screening in the future. These results are consistent with other studies
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43 246 looking at self-collection acceptability both within Guatemala and other LMICs^{27 32}. This study
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45 247 was further able to build upon previous studies and provide important information regarding
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47 248 HPV self-collection testing acceptability at the community level, and in a community that had
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49 249 not been previously evaluated.
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3 250 Our study also found, however, that there were differences between communities in
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6 251 willingness to try self-collection. Willingness to try self-collection testing remained consistently
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8 252 high among participants in Santiago Atitlán as reported in the pilot study conducted in 2015
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10 253 (93% in 2015 versus 93.6% in 2016)³². In Livingston, however, even among women who first
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12 254 responded in the survey or consent form that they would be willing to collect a sample, actual
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14 255 self-collection was lower. We found that willingness to self-collect in Livingston was
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17 256 consistently associated with higher levels of literacy and prior IUD use. In contrast, ethnicity,
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19 257 history of cervical cancer screening, and reproductive history were not associated with
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22 258 willingness to self-collect. Stratified analyses revealed that there were no qualitative differences
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24 259 in the association between literacy and sample collection across ethnic groups in Livingston.
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26 260 The results suggest that HPV self-collection testing program implementation may need to
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28 261 target populations based on relative levels of literacy within communities. A previous study
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30 262 examining HPV acceptability and intention in the UK similarly found that low education and
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32 263 self-efficacy were associated with low sampling intentions³⁰. In Guatemala, the inability to
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34 264 either read or write in Spanish may negatively influence a woman's perceived self-efficacy and
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36 265 her confidence in navigating public health infrastructure or self-collecting a vaginal sample,
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38 266 particularly if her surrounding community has high levels of literacy. This population would
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41 267 greatly benefit from HPV self-collection testing as a primary form of cervical cancer screening
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43 268 due to its strength in concentrating less accessible and more invasive screening modalities only
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46 269 towards those that are at high-risk (i.e., positive for HPV). Our results in Livingston suggest that
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48
49 270 it might be critical that, if implemented, HPV screening and education programs are tailored such
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52 271 that they are more accessible to low-literacy populations and, thus, increase perceived self-
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54 272 efficacy in navigating the existing public health infrastructure.
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3 273 High prevalence of self-collection testing in Santiago Atitlan, a community with low
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5 274 literacy levels, as compared to the low rates of self-collection testing among those with low
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8 275 literacy in Livingston may reflect larger community differences in awareness or access to
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10 276 screening modalities rather than a lack of effect of literacy in Santiago or an effect of ethnicity.
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12 277 Although women from Santiago reported slightly higher rates of ever receiving cervical cancer
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14 278 screening than women in Livingston, women in Livingston report much higher rates of recent
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16 279 cervical cancer screening than women in Santiago. Santiago Atitlán remains largely deficit in
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18 280 accessible and affordable cervical cancer screening while Livingston has regular, public or
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20 281 private, screening campaigns in the community. This difference in general community access
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22 282 and infrastructure, then, may be acting as an effect modifier on the association between literacy
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24 283 and screening between these two communities, suggesting that self-collection might be better
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26 284 received at first in communities that do not have other alternatives, whereas some initial
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28 285 skepticism might be found in places with existing cervical screening programs, independently of
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30 286 their quality and efficacy. More research is necessary to evaluate if self-efficacy, relative literacy
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32 287 level, or general community access to healthcare resources and screening play larger barriers for
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34 288 women in trying self-sampling HPV testing. However, the high rates of acceptability and
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36 289 willingness to retake among women who self-collected in both communities suggest that once
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38 290 experienced, self-collection is a valid, and even preferred, alternative to other screening
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40 291 modalities from the women's perspective.

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42 292 Although based on a different HPV test than in our pilot study (HybriBio HR13 vs.
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44 293 Anyplex 28), a similar prevalence of high-risk HPV was found in Santiago between 2015 and
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46 294 2016 (17.4% versus 19.3%)³². Of note, there were no significant differences in high-risk HPV
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3 295 prevalence between ethnic groups in Livingston, and there was not a statistically significant
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5 296 difference between Santiago Atitlán and Livingston with regards to prevalence.
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8 297 Our study provided not only a larger sample size compared with previous studies but was
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10 298 also conducted in two differing communities. This is a strength because Guatemala is an
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12 299 extremely diverse country with over 23 languages, distinct ethnicities, and a history of large
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14 300 economic and social inequalities. Thus, generalizing the evaluations of a health program's
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16 301 acceptability and feasibility to the whole country is generally difficult. However, because we
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18 302 evaluated two very different rural multi-ethnic communities, our results may reflect some of the
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20 303 future obstacles and considerations necessary in implementing self-swab HPV testing in such a
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22 304 diverse country as Guatemala than was previously available. In fact, our results also
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24 305 complement the findings of the ongoing careHPV Scale-Up implementation, which is assessing
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26 306 the performance of HPV testing, including self-collection testing, within urban settings in
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28 307 Guatemala⁴²⁻⁴⁴.
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33 308 There are several limitations to our study. Due to both the sensitive nature of the
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35 309 questions related to sexual history, it may be possible that a social desirability bias may have
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37 310 resulted in over reporting of perceived “good behaviors”, such as screening or use of protection,
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39 311 in addition to under-reporting of perceived “bad behaviors”, such as number of lifetime sexual
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41 312 partners and other sexual behavior measures. We tried to minimize the possibility of this bias by
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43 313 maintaining confidentiality with participants. Also, women may report their history of screening
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45 314 or utilization of health care resources incorrectly if they had limited information or
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47 315 understanding of these services. This may be exaggerated in women with low literacy and thus
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49 316 explain potential over reporting of prior cervical cancer screening in Santiago Atitlan.
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52 317 Additionally, because sampling methods differed between the two communities due to the lack
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3 318 of reliable census counts in Livingston, there may be differences between the communities in
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6 319 potential selection bias into the study and more limited comparability of the results. However,
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8 320 our sample in Livingston is reflective of the overall population structure of Livingston in terms
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10 321 of ethnic, age and other metrics, suggesting that influential selection bias into the study might be
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12 322 limited⁴⁵.

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15 323 Screening program implementation is a major challenge in LMIC settings, HPV self-
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17 324 swab testing may serve as a helpful tool in concentrating less accessible and more expensive and
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19 325 invasive screening modalities only towards those that are at high-risk (i.e., positive for HPV).
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21 326 However, as the results in Livingston showed, there are many complex features related to
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23 327 implementing HPV screening that will need to be evaluated before program adoption of such
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25 328 programs. Due to the longitudinal component of our study, future research with our study
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27 329 participants will hopefully help elucidate how HPV self-collection testing may affect women's
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29 330 decisions to pursue further cervical cancer screening and follow-up care in their local
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31 331 communities after HPV testing and receiving their results. Additionally, these data may reveal
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33 332 other downstream facilitators or barriers to screening that will influence the overall success of
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35 333 HPV self-swab testing implementation in these communities.

36 334 **CONCLUSION**

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39 335 The results of our study add to the literature on the potential of HPV self-collection
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41 336 testing in LMICs, demonstrating its acceptability in two very different communities in rural
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43 337 Guatemala. The high rates of acceptability and willingness to retake among women who self-
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45 338 collected in both communities suggest that once experienced, self-collection is a valid, and even
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47 339 a preferred, alternative to other screening modalities from the women's perspective. However,
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49 340 the difference in willingness to try self-collection between these communities suggests that
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3 341 relative literacy levels and the availability and quality of existing programs may affect attitudes
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6 342 towards new screening modalities. Future research should focus on increasing the
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8 343 generalizability of these findings by evaluating additional communities within Guatemala for
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10 344 differences in willingness to try self-collection sampling and further elucidate the potential
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12 345 barriers to accessing and utilizing cervical cancer modalities, including HPV self-collection
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15 346 sampling.
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19 348 **LIST OF ABBREVIATIONS**

21 349 CC – Cervical Cancer

23 350 CHW – Community Health Worker

25 351 CI – Confidence Interval

27 352 HICs – High-Income Countries

29 353 HIV – Human Immunodeficiency Virus

31 354 HPV – Human Papillomavirus

33 355 HR-HPV – High-Risk Human Papillomavirus

35 356 INCAP – Institute of Nutrition of Central America and Panama

37 357 IUD – Intra-Uterine Device

39 358 LMICs – Low and Middle-Income Countries

41 359 OR – Odds Ratio

43 360 PCR – Polymerase Chain Reaction

45 361 PR – Prevalence Ratio

47 362 VIA – Visual Inspection with Acetic Acid

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364 **DECLARATIONS**

365 **Ethics Approval and Consent to Participate**

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

371 **Consent for Publication**

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

373 **Data Sharing Statement**

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

379 **Competing Interests**

380 The authors have no competing interests to declare.

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390 **Authors' Contributions**

391 PIC - Planning and Key Intellectual Contribution
 392 DC – Data Collection and Project Management
 393 SP – Sample Processing, Laboratory Management, and Test Results
 394 SA – Statistical Analysis and Data Management
 395 W – Writing
 396 E – Editing
 397

Audrey Murchland – PIC, DC, SP, SA, W, E
 Anna Gottschlich – PIC, DC, SP, W, E
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 Alvaro Rivera-Andrade – PIC, DC, SP, E
 Rafael Meza – PIC, DC, SP, SA, W, E

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550 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 (<i>All participants</i>) 438 (<i>age-eligible</i>)	456 (<i>all participants</i>) 322 (<i>age-eligible</i>)	
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 (<i>age-eligible; Test-Taking participants</i>)	169 (<i>age eligible; Test-Taking participants</i>)	
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			

	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)	

^ap-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

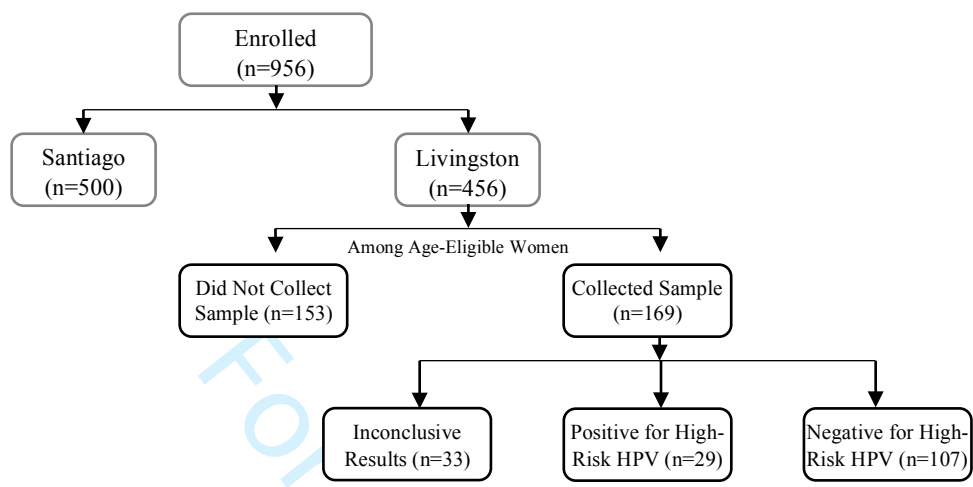
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FIGURE LEGENDS

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



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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

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

Table A2 – General Population Characteristics Among All Participants (Continued)

Table A3 – Population Characteristics within Livingston (Continued)

Table A4 – Population Characteristics within Livingston: Comparing Racial/Ethnic Groups

Table A5 – Differences Among Communities of Age-Eligible Indigenous Mayan Women

Appendix B: Self-reported Willingness to Collect a Sample

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

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			

	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

^ap-values for means calculated using one-way ANOVA or Welch (if equality of variance is rejected); proportions using chi-squared test
^bFisher'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

^ap-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) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		<i>Case-control study</i> —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	
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
Variables	7	(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	11
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Data sources/measurement	8*	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	11
Bias	9	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
Study size	10	Describe any efforts to address potential sources of bias	8
Quantitative variables	11	Explain how the study size was arrived at	8
Statistical methods	12	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	11
		(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) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed	11
<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed			
		<i>Cross-sectional study</i> —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) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —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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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

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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

1 Cervical cancer, primarily caused by human papillomavirus (HPV) infection, has a very
2 good prognosis when detected in premalignant or early malignant stages¹. However, it
3 disproportionately burdens low- and middle-income countries (LMICs), such as Guatemala,
4 compared to high-income countries (HICs)²⁻⁴. HICs currently use Pap smears to detect abnormal
5 cervical lesions that can be removed, greatly reducing the risk of cervical cancer^{3 5}. However,
6 there are many barriers to implementing successful Pap smear (cytology-based) screening
7 programs in LMICs, including difficulties establishing sustainable laboratory infrastructure,
8 training and retaining adequate numbers of trained pathologists or cytologists, overburdened
9 primary care clinics, and time and travel limitations for women in reaching screening locations^{1 6}
10 ⁷. Due to these factors and others, the percentage of women in Guatemala who are screened for
11 cervical cancer remains low; in 2014, only 49.8% of women (15-49 years of age) reported ever
12 having a Pap smear. Thus, significant improvements in screening or program implementation are
13 paramount to improving cervical cancer outcomes in Guatemala^{3 8 9}.

14 Since more than 90% of cervical cancers are caused by the HPV virus, HPV testing has
15 been suggested as a possible alternative, primary form of cervical cancer screening¹⁰⁻¹². When
16 used in combination with Visual Inspection with Acetic Acid (VIA) or Pap smears in low-
17 income settings, HPV testing has been shown to provide significant improvements in the
18 detection of advanced premalignant lesions and cancer in sensitivity as compared to VIA or Pap
19 smear alone, as only women who test positive for HPV need to follow up with further
20 screening¹³⁻¹⁶. Previous studies have also confirmed¹³⁻¹⁶ that HPV self-swab kits are comparable to
21 physician administered samples in their ability to detect carcinogenic, high-risk HPV ^{17 18}. Thus,
22 at-home HPV sample collection, with referral to further screening for those positive for high-risk

23 HPV, may be both more acceptable within low-income communities and more programmatically
24 feasible^{6 7 19}. Moreover, a 2015 meta-analysis showed that HPV self-sampling, particularly in
25 opt-in programs, increased participation in cervical cancer screening programs. However,
26 further work is needed to evaluate acceptable opt-in programs for women²⁰.

27 Studies have shown that HPV self-sampling is generally acceptable among women in low
28 and high resource settings as well as immigrant, rural, vulnerable populations²¹⁻³¹. To our
29 knowledge, however, little is known about the acceptability of self-collection HPV testing across
30 the diverse communities within Guatemala, and in particular among rural and indigenous
31 populations. In a pilot cross-sectional study assessing the acceptability of HPV self-collection
32 among 200 women in the Mayan community of Santiago Atitlán, Guatemala, a self-swab HPV
33 test was found to be a highly acceptable form of screening³². Over 80% of women said that they
34 preferred using a self-swab kit in their home rather than being screened at a doctors' office.
35 However, this pilot study was limited to a relatively small sample in a single, largely
36 homogeneous community, limiting the generalizability of the results to other rural and
37 indigenous communities in Guatemala. Further research is thus needed to evaluate the
38 acceptability of self-collection testing among more diverse rural and indigenous populations
39 within Guatemala, which is very diverse, with over 23 official languages and many indigenous
40 groups, most but not all descendants from the Mayan civilization. The purpose of this study was
41 to evaluate risk factors, knowledge, and attitudes towards cervical cancer and to further assess
42 and compare the acceptability of self-collection HPV testing in two understudied, rural,
43 ethnically distinct communities in Guatemala: Santiago Atitlán and Livingston, Izabal.

44 **METHODS**

45 **Study Communities**

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2
3 46 Santiago Atitlán, Sololá is a rural community located on Lake Atitlán, in the southwest
4
5
6 47 region of Guatemala, 75 miles west of Guatemala City. The Tz'utujil, a Mayan descendant
7
8 48 ethnic group, inhabits the region, which surrounds Lake Atitlán. The primary language of
9
10
11 49 Santiago's inhabitants is Tz'utujil, and over half of the villagers speak Spanish as a second
12
13 50 language³². The majority of women in Santiago Atitlán have at most a primary education.
14
15 51 Additionally, as a conservative, religious community, it is highly uncommon for women to either
16
17 52 drink or smoke, and almost all women in have previously reported having only one lifetime
18
19 53 sexual partner³².

21
22 54 Livingston, Izabal is located on the Caribbean coast of the country and is a rural
23
24 55 community, only accessible by boat, that is the primary Garífuna settlement in Guatemala. The
25
26 56 Garífuna people are considered a unique ethnic group with their own language, culture, and
27
28 57 cuisine. Additionally, there are large populations of other ethnic and cultural groups located in
29
30 58 Livingston including Q'eqchi' (Mayan descent), Ladinos (non-Mayan descent), and populations
31
32 59 of Indian descent. Most women in Livingston are believed to have at least basic primary
33
34 60 education.

37 38 61 **Patient and Public Involvement**

39
40 62 The patients were not involved in the development of the research questions, outcome
41
42 63 measures or study design. The patients were also not involved in the recruitment and
43
44 64 performance of the study. However, the public, Guatemalan physicians, scientists, and
45
46 65 community health workers, were involved in the development of the question, design, validation,
47
48 66 recruitment, and conduct of the study. Local community health workers were involved in the
49
50 67 validation of the survey and study protocol, recruited participants and conducted the interviews,
51
52 68 and assisted in providing test results to patients. Guatemalan physicians contributed to
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69 development of the research question and study design, organized the laboratory testing, led and
70 assisted with community health worker training, and provided HPV test results to patients. Local
71 laboratory scientists contributed to the study design and conducted the HPV laboratory testing.
72 The continued collaborations with these team members will be used to disseminate study results
73 to patients and Guatemalan officials via publications, presentations, and meetings.

74 **Eligibility and Recruitment**

75 Trained community health workers (CHWs) in both communities actively recruited
76 participants through home visits. All CHWs were bilingual and spoke both Spanish and either
77 Tz'utujil, Q'eqchi, or Karif (the language of the Garifuna) depending on the location they were
78 working in. Households in Santiago Atitlán were selected at random using stratified multi-level
79 sampling based upon maps and population counts of the communities available through the local
80 municipal office and were kept consistent with previous sampling methods³². Households in
81 Livingston were selected at random using convenience sampling due to lack of reliable census
82 data at the neighborhood-level. Sampling methods were, otherwise, kept the same as those in
83 Santiago Atitlán.

84 Selected households that had at least one woman available between the ages of 18 and 60
85 were invited to participate in the survey-component of the study to assess risk factors for,
86 attitudes towards, and knowledge of cervical cancer in these communities. For households with
87 more than one eligible woman willing to participate, the female in the household whose birthday
88 was closest to the date of the interview was enrolled in the study. Exclusion criteria consisted of
89 past hysterectomy or previous cervical cancer. Women between the ages of 25 and 54 were also
90 asked to provide a sample, in accordance with Guatemala's current screening
91 recommendations³³. Additionally, pregnant women, women currently menstruating, and women

1
2
3 92 who had never been sexually active were also excluded from providing samples but could
4
5 93 participate in the survey component. Approximately 62% and 90% of eligible women contacted
6
7
8 94 were willing to participate in the study in Santiago and Livingston, respectively. All participants
9
10 95 in the study provided both oral and written informed consent prior to participation in the study.
11
12 96 The consent was documented by a signature or fingerprint of the participant, the surveyors, and a
13
14
15 97 witness to the consent process.
16

17 98 **Survey**

19 99 Data collection consisted of two main components: the surveys and the HPV self-
20
21
22 100 collection tests. Local CHWs in each community were trained as interviewers in the appropriate
23
24 101 techniques and protocols before beginning home visits. Two CHWs visited each randomly
25
26 102 selected household together and read a recruitment script to a female household member to
27
28 103 determine the household's eligibility. CHWs administered the survey and provided kits to
29
30 104 collect HPV samples only to willing, eligible participants. Surveys were administered in private
31
32 105 rooms of the participant's house to minimize response bias to sensitive questions.
33
34

35 106 The survey questionnaire included 153 questions concerning demographics, risk factors
36
37 107 for cervical cancer and HPV, self-reported attitudes towards screening, healthcare service use,
38
39 108 and knowledge of cervical cancer and HPV. The survey was developed from the pilot study
40
41
42 109 survey and validated as part of the CHW and translator training to ensure correct translation and
43
44 110 cultural relevancy³². Each survey was administered by the CHWs using electronic tablets and
45
46
47 111 the Qualtrics offline app.
48

49 112 All women who participated in the study were compensated with a voucher for a free Pap
50
51 113 smear or VIA at a local health clinic. Women in both communities can access free VIAs
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1
2
3 114 (Santiago) or Pap Smears (Livingston) in the local public health system, but if they chose to use
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5
6 115 a private clinic instead of the public clinic, the voucher covered their fees.
7

8 116 **HPV Self-Collected Samples**

9
10 117 The HPV samples were collected using HerSwab kits, a self-collection sampling method
11
12 118 ^{32 34 35}. If a participant was willing to provide a sample, instructions and graphical materials were
13
14
15 119 provided and the participant collected the sample in a separate, private room from the CHWs.
16
17 120 Participants who collected a sample then completed a short post-sample survey with the CHWs
18
19 121 of three questions regarding ease, comfort, and acceptability of the sampling method: “How easy
20
21 122 was the self-collection swab?”; “How comfortable was the self-collection swab?”; and “Would
22
23 123 you be willing to collect a sample every 2-3 years to detect HPV as a form of cervical cancer
24
25 124 screening?”.

26
27
28 125 After collection, samples were kept in small, refrigerated coolers carried by the CHWs
29
30 126 until they were returned to the main study office at the end of the day where samples were then
31
32 127 processed to stabilize sample life. The brush component of the HerSwab kit was cut into a 15-
33
34 128 mL test tube using lab scissors. The lab scissors were sterilized using alcohol and an open flame
35
36 129 between each sample. Each tube was filled with 5mL of Scope mouthwash using a pipette, and
37
38 130 tubes were sealed using a cap and parafilm paper³⁶. Mouthwash is a reliable, low-cost transport
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40 131 medium for DNA samples and was used to reflect likely standard operating procedures of HPV
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42 132 screening program implementation in Guatemala³⁷. Each sample was labeled with the
43
44 133 participant’s unique identifier. Time of sample processing and condition of sample were
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46 134 recorded.
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50
51 135 Stabilized samples were sent to a molecular biology laboratory at the Institute of
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53 136 Nutrition of Central America and Panama (INCAP) in Guatemala City for testing. Samples were
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2
3 137 tested using the real-time polymerase chain reaction (PCR) HybriBio HR-13 kit^{38 39}. Samples
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5 138 were processed according to the manufacturers protocol and modified to use a 10 ul reaction
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7 139 volume for the real-time PCR and run on an ABI-7000³⁶. After testing, samples were labeled as
8
9 140 positive for HR-HPV, negative, or, if both the HPV probe and the internal control were negative,
10
11 141 inconclusive. If a sample test was inconclusive during the first test, it was run an additional time
12
13 142 using a 20 ul reaction volume, and if no result was obtained, the test was deemed inconclusive.
14

17 143 **Follow-Up**

18
19 144 A local CHW provided negative and inconclusive results over the phone or through a
20
21 145 home visit. Positive results were provided in-person by a study physician who referred
22
23 146 participants to their local community health clinic for follow-up and further cervical cancer
24
25 147 screening. All participants who couldn't be reached at the study conclusion were re-contacted
26
27 148 either at 6 months or one year to provide them with their results. Although women with negative
28
29 149 results were not explicitly recommended to attend the clinic, all participants were encouraged to
30
31 150 get screened using the voucher provided at the local clinic to support their engagement with local
32
33 151 preventative services. Participants who were found to be positive for advanced lesions as a result
34
35 152 of follow-up screening were referred for care through the free public health infrastructure in
36
37 153 Guatemala, as is currently standard practice. Due to the ongoing nature of the project, data on
38
39 154 follow-up screening and care are still in the collection process.
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43

45 155 **Outcomes and Statistical Analysis**

46
47 156 Willingness and acceptability of self-collection testing, knowledge of HPV, and risk
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49 157 factors were evaluated in both communities and across ethnic groups in Livingston, Izabal.
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51 158 Willingness was measured as whether or not a woman chose to self-collect a sample to be tested
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53 159 for HPV (actual self-collection). The acceptability of sample collection was only assessed for
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2
3 160 those who self-collected a sample and was analyzed using the post-self-swab survey questions
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5
6 161 described previously.

7
8 162 A target sample size of 500 per community was determined to be able to detect a 5%
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10 163 difference in self-sampling acceptability with 80% power, assuming a 95% acceptability in
11
12 164 Santiago Atitlan based on the pilot.

13
14
15 165 Due to lower rates of actual self-collection in Livingston, differences between Livingston
16
17 166 women willing and those not willing to collect a sample were evaluated using two-sample t-tests
18
19 167 for means, chi-squared tests for proportions, and Fisher's Exact test for low cell counts. Most
20
21 168 women tried self-collection in Santiago, so we restrict these analyses to Livingston.

22
23
24 169 The main exposures explored for willingness to try self-collection included: literacy,
25
26 170 marital status, history of Pap smear or VIA, smoking status, alcohol use (a potential proxy for
27
28 171 risky behavior), IUD use, family history of cervical cancer, and belief of being at risk for
29
30 172 cervical cancer. Statistical analyses were run using log-binomial regression. In model set 1, the
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32 173 relationship between each exposure and sampling decision was unadjusted for other covariates.
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34 174 In model set 2, models were additionally adjusted for age, ethnicity, and number of lifetime
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36 175 sexual partners. In model set 3, we used stepwise selection to select significant the exposure
37
38 176 covariates ($\alpha=0.05$) when adjusting for age, ethnicity, and number of lifetime sexual
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40 177 partners. Finally, in model set 4, we included all exposure covariates and the adjustment
41
42 178 covariates together in a fully adjusted model. The stepwise selected model was further stratified
43
44 179 across ethnic groups to evaluate potential effect modification. Due to high prevalence of literacy
45
46 180 in Garifuna and Ladino, these groups were combined for stratification to prevent positivity
47
48 181 violations (Q'echchi versus Garifuna or Ladino, reflecting a Mayan descent versus non-Mayan
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50 182 descent comparison).
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3 183 Analyses were restricted to age-eligible women in Livingston with complete covariate
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5 184 information (N=134 or 29.4% excluded due to age-ineligibility and N=13 or 3.5% excluded due
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8 185 to missing covariates). Specifically, we excluded 5 participant missing ethnicity or classified as
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10 186 other ethnicity, 1 participant missing marital status, 1 participant missing regular drinking status,
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12 187 and 3 participants missing number of lifetime sexual partners, 1 participant missing smoking
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14
15 188 status, and 2 participants missing family history of cancer resulting in a final sample size N=309
16
17 189 for analyses evaluating willingness to try self-collection.

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20 190 Covariates were parameterized as: able to read and/or write (literate) versus unable to
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22 191 either read or write (illiterate), ever married versus never married, ever had a Pap or VIA versus
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24 192 never, ever smoked versus never smoked, regular drinker versus non-regular drinker, ever had an
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26 193 IUD versus never or don't know/refused, family history of cervical cancer present versus absent,
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28 194 and believe at risk for developing cervical cancer ("strongly agree"/"agree" versus neutral,
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30 195 disagree, strongly disagree, or unsure/don't know), continuous age, and number of lifetime
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32 196 sexual partners (one versus more than one).

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35 197 Data cleaning and analyses were carried out using SAS 9.4⁴⁰.

36 198 **RESULTS**

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40 199 In total, 956 women were recruited to participate into the study: 500 women in Santiago
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42 200 Atitlán and 456 women in Livingston. Demographic characteristics differed between the two
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44 201 communities: 69.4% of the participants in Santiago Atitlán had less than primary education and
45
46 202 96.6% were of Tz'tujil ethnicity. In contrast, only 33.9% of the participants in Livingston had
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48 203 less than primary education and three ethnic groups were represented: 41.9% Q'echi, 32%
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50 204 Garifuna, and 24.8% mixed ethnicity (Ladino) (Table 1).
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205 Knowledge and attitudes regarding HPV and cervical cancer also differed between the
206 communities. Only 11.8% of participants in Santiago reported previous knowledge of HPV as
207 compared to 62.7% of Livingston participants. However, when asked about the seriousness of
208 cervical cancer, most participants in both communities responded “very” or “extremely” (74.8%
209 Santiago and 80.9% Livingston).

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

219 **Self-Collection Willingness**

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

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

1
2
3 228 3). Additionally, 31.4% of the women who ended up not providing a sample had responded
4
5 229 previously in the questionnaire that they indeed would be willing to collect a self-swab sample at
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7 230 home. While data is unavailable regarding how many age-eligible women were ineligible to
8
9 231 collect a sample due to menstruation or pregnancy, this likely does not entirely account for all
10
11 232 women who ultimately chose not to self-collect. Characteristics of women not willing to collect
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13 233 (both reported in the survey and actual sample collection) can be found in the appendix. It is
14
15 234 interesting to also note that women from Santiago, who reported less prior use of healthcare,
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17 235 were more likely to self-collect.
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22 236 Literacy was significantly higher among women who self- collected a sample in
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24 237 Livingston compared to those who did not (crude PR 2.04; 95% CI: 1.27, 3.28; adjusted PR,
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26 238 2.25; 95% CI: 1.38, 3.68) (Table 4). IUD use was also higher among women who self-collected
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28 239 a sample in Livingston (crude PR 1.49; 95% CI: 1.15, 1.94; adjusted PR 1.43; 95% CI: 1.08,
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30 240 1.88) (Table 4). Additionally, regular drinking and never being married were higher among
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32 241 women who self-collected but not significant (regular drinking, crude PR 1.18; 95% CI: 0.95,
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34 242 1.48; adjusted PR 1.14; 95% CI 0.89, 1.46; never married, crude PR 1.19; 95% CI: 0.96, 1.48;
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36 243 adjusted PR 1.15; 95% CI: 0.91, 1.43) (Table 4).
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40 244 Using stepwise selection with adjustment for age, ethnicity, and more than one lifetime
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42 245 sexual partner, only literacy was selected as an exposure covariate (PR 2.25; 95% CI: 1.38,
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44 246 3.68). When stratifying ethnic group (Q'echchi versus Garifuna and Ladino), the association
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46 247 between literacy and actual sample collection remained positive (Table 5). However, this
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48 248 relationship only remained statistically significant among Q'echchi participants. However,
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50 249 interaction terms between ethnic group (Q'echchi versus not) and literacy revealed that the effect
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250 of literacy among the Q'echchi was not significantly different from the Ladinos and Garifunas
251 (interaction term PR 0.94; 95% CI: 0.25, 3.59).

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

254 **Self-Collection Acceptability and Comfort**

255 Among those who did collect a sample, the self-collection testing was highly acceptable
256 in both communities. Of Santiago participants who self-collected, 81.4% found it comfortable
257 and 84.8% reported that the HerSwab was easy to use. Among Livingston participants who self-
258 collected, 87.0% found it comfortable and 87.0% reported it was easy to use. Among those who
259 chose to self-collect, almost all participants in both locations reported that they were willing to
260 use it as a form of cervical cancer screening (98.0% in Santiago and 100% in Livingston) (Table
261 2).

262 **HPV Prevalence**

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

270 **DISCUSSION**

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

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3 273 Guatemala. We found that self-collection appears to be highly acceptable among women who
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5 274 tried it, independent of community and ethnicity. Most women reported that self-collection was
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8 275 comfortable and easy to use, and almost all women who tried it reported being willing to use it as
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10 276 a form of cervical cancer screening in the future. These results are consistent with other studies
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12 277 looking at self-collection acceptability both within Guatemala and other LMICs^{27 32}. This study
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14 278 was further able to build upon previous studies and provide important information regarding
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17 279 HPV self-collection testing acceptability at the community level, and in a community that had
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19 280 not been previously evaluated.

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22 281 Our study also found, however, that there were differences between communities in
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24 282 willingness to try self-collection. Willingness to try self-collection testing remained consistently
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26 283 high among participants in Santiago Atitlán as reported in the pilot study conducted in 2015
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28 284 (93% in 2015 versus 93.6% in 2016)³². In Livingston, however, even among women who first
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30 285 responded in the survey or consent form that they would be willing to collect a sample, actual
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32 286 self-collection was lower. We found that willingness to self-collect in Livingston was
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34 287 consistently associated with higher levels of literacy and prior IUD use. In contrast, ethnicity,
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36 288 history of cervical cancer screening, and health behaviors were not associated with willingness to
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38 289 self-collect. Stratified analyses suggested that there were no qualitative differences in the
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41 290 association between literacy and sample collection across ethnic groupings (Mayan descent
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43 291 versus non-Mayan descent) in Livingston. However, high prevalence of literacy among Garifuna
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45 292 made it difficult to evaluate differences between Ladinos and Garifunas in the association
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47 293 between literacy and sampling decision.

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52 294 The results suggest that HPV self-collection testing program implementation may need to
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54 295 target populations based on relative levels of literacy within communities. A previous study

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3 296 examining HPV acceptability and intention in the UK similarly found that low education and
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5 297 self-efficacy, defined as an individual's belief in their capability to exercise control over
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7 298 challenging demands, were associated with low sampling intentions³⁰. In Guatemala, the
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9 299 inability to either read or write in Spanish may negatively influence a woman's perceived self-
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11 300 efficacy and her confidence in navigating public health infrastructure or self-collecting a vaginal
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13 301 sample, particularly if her surrounding community has high levels of literacy. This population
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15 302 would greatly benefit from HPV self-collection testing as a primary form of cervical cancer
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17 303 screening due to its strength in concentrating less accessible and more invasive screening
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19 304 modalities only towards those that are at high-risk (i.e., positive for HPV). Our results in
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21 305 Livingston suggest that it might be critical that, if implemented, HPV screening and education
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23 306 programs are tailored such that they are more accessible to low-literacy populations and, thus,
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25 307 increase perceived self-efficacy in navigating the existing public health infrastructure.
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31 308 High prevalence of self-collection testing in Santiago Atitlan, a community with low
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33 309 literacy levels, as compared to the low rates of self-collection testing among those with low
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35 310 literacy in Livingston may reflect larger community differences in awareness or access to
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37 311 screening modalities rather than a lack of effect of literacy in Santiago or an effect of ethnicity.
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39 312 Although women from Santiago reported slightly higher rates of ever receiving cervical cancer
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41 313 screening than women in Livingston, women in Livingston report much higher rates of recent
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43 314 cervical cancer screening than women in Santiago. Santiago Atitlán remains largely deficit in
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45 315 accessible and affordable cervical cancer screening while Livingston has regular, public or
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47 316 private, screening campaigns in the community. This difference in general community access
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49 317 and infrastructure, then, may be acting as an effect modifier on the association between literacy
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51 318 and screening between these two communities, suggesting that self-collection might be better
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3 319 received at first in communities that do not have other alternatives, whereas some initial
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5 320 skepticism might be found in places with existing cervical screening programs, independently of
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7 321 their quality and efficacy. More research is necessary to evaluate if self-efficacy, relative literacy
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9 322 level, or general community access to healthcare resources and screening play larger barriers for
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11 323 women in trying self-sampling HPV testing. However, the high rates of acceptability and
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13 324 willingness to retake among women who self-collected in both communities suggest that once
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15 325 experienced, self-collection is a valid, and even preferred, alternative to other screening
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17 326 modalities from the women's perspective.

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21 327 Although based on a different HPV test than in our pilot study (HybriBio HR13 vs.
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23 328 Anyplex 28), a similar prevalence of high-risk HPV was found in Santiago between 2015 and
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25 329 2016 (17.4% versus 19.3%)³². Of note, there were no significant differences in high-risk HPV
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27 330 prevalence between ethnic groups in Livingston, and there was not a statistically significant
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29 331 difference between Santiago Atitlán and Livingston with regards to prevalence.

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33 332 Our study provided not only a larger sample size compared with previous studies but was
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35 333 also conducted in two differing communities. This is a strength because Guatemala is an
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37 334 extremely diverse country with over 23 languages, distinct ethnicities, and a history of large
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39 335 economic and social inequalities. Thus, generalizing the evaluations of a health program's
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41 336 acceptability and feasibility to the whole country is generally difficult. However, because we
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43 337 evaluated two very different rural multi-ethnic communities, our results may reflect some of the
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45 338 future obstacles and considerations necessary in implementing self-swab HPV testing in such a
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47 339 diverse country as Guatemala than was previously available. In fact, our results also
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49 340 complement the findings of the ongoing careHPV Scale-Up implementation, which is assessing
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3 341 the performance of HPV testing, including self-collection testing, within urban settings in
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5 342 Guatemala⁴²⁻⁴⁴.

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8 343 There are several limitations to our study. Due to both the sensitive nature of the
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10 344 questions related to sexual history, it may be possible that a social desirability bias may have
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12 345 resulted in over reporting of perceived “good behaviors”, such as screening or use of protection,
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14 346 in addition to under-reporting of perceived “bad behaviors”, such as number of lifetime sexual
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16 347 partners and other sexual behavior measures. We tried to minimize the possibility of this bias by
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18 348 maintaining confidentiality with participants. Also, women may report their history of screening
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20 349 or utilization of health care resources incorrectly if they had limited information or
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22 350 understanding of these services. This may be exaggerated in women with low literacy and thus
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24 351 explain potential over reporting of prior cervical cancer screening in Santiago Atitlan.
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26 352 Additionally, because sampling methods differed between the two communities due to the lack
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28 353 of reliable census counts in Livingston, there may be differences between the communities in
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30 354 potential selection bias into the study and more limited comparability of the results. However,
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32 355 our sample in Livingston is reflective of the overall population structure of Livingston in terms
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34 356 of ethnic, age and other metrics, suggesting that influential selection bias into the study might be
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36 357 limited⁴⁵.

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38 358 Screening program implementation is a major challenge in LMIC settings, HPV self-
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40 359 swab testing may serve as a helpful tool in concentrating less accessible and more expensive and
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42 360 invasive screening modalities only towards those that are at high-risk (i.e., positive for HPV).
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44 361 However, as the results in Livingston showed, there are many complex features related to
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46 362 implementing HPV screening that will need to be evaluated before program adoption of such
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48 363 programs. Due to the longitudinal component of our study, future research with our study
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3 364 participants will hopefully help elucidate how HPV self-collection testing may affect women's
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5 365 decisions to pursue further cervical cancer screening and follow-up care in their local
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8 366 communities after HPV testing and receiving their results. Additionally, these data may reveal
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10 367 other downstream facilitators or barriers to screening that will influence the overall success of
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12 368 HPV self-swab testing implementation in these communities.

14 369 **CONCLUSION**

16
17 370 The results of our study add to the literature on the potential of HPV self-collection
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19 371 testing in LMICs, demonstrating its acceptability in two very different communities in rural
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21 372 Guatemala. The high rates of acceptability and willingness to retake among women who self-
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23 373 collected in both communities suggest that once experienced, self-collection is a valid, and even
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25 374 a preferred, alternative to other screening modalities from the women's perspective. However,
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27 375 the difference in willingness to try self-collection between these communities suggests that
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29 376 relative literacy levels and the availability and quality of existing healthcare programs may affect
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31 377 attitudes towards new screening modalities. Future research should focus on increasing the
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33 378 generalizability of these findings by evaluating additional communities within Guatemala for
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35 379 differences in willingness to try self-collection sampling and further elucidate the potential
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37 380 barriers to accessing and utilizing cervical cancer modalities, including HPV self-collection
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39 381 sampling.

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43 383 **LIST OF ABBREVIATIONS**

44
45 384 CC – Cervical Cancer

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47 385 CHW – Community Health Worker

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49 386 CI – Confidence Interval

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3 387 HICs – High-Income Countries
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5 388 HIV – Human Immunodeficiency Virus
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8 389 HPV – Human Papillomavirus
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10 390 HR-HPV – High-Risk Human Papillomavirus
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12 391 INCAP – Institute of Nutrition of Central America and Panama
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14 392 IUD – Intra-Uterine Device
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17 393 LMICs – Low and Middle-Income Countries
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19 394 OR – Odds Ratio
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21 395 PCR – Polymerase Chain Reaction
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23 396 PR – Prevalence Ratio
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25 397 VIA – Visual Inspection with Acetic Acid
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31 399 **DECLARATIONS**

33 400 **Ethics Approval and Consent to Participate**

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35 401 The University of Michigan Institutional Review Board (HUM00096559) and the
36
37 402 Institute of Nutrition of Central America and Panama Institutional Review Board (MI-CIE-16-
38
39 403 009) approved study protocols. All participants gave oral and written informed consent prior to
40
41 404 participation in the study. The consent was documented by a signature or fingerprint of the
42
43 405 participant, the surveyors, and a witness.
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47 406 **Consent for Publication**

48
49 407 The authors of this paper have all reviewed its contents and consent for its publication.
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51 408 **Data Sharing Statement**

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3 409 Due to the sensitive nature of the data collected, IRB restrictions, and ongoing data
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6 410 collection, study data is stored at the University of Michigan. Interested parties may contact the
7
8 411 corresponding author to request access to de-identified datasets for specific research questions
9
10 412 related to the study. The authors welcome further collaboration but reserve the right to retain data
11
12 413 to protect study participants.

14 414 **Competing Interests**

16
17 415 The authors have no competing interests to declare.

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39 425 **Authors' Contributions**

41
42 426 PIC - Planning and Key Intellectual Contribution
43 427 DC – Data Collection and Project Management
44 428 SP – Sample Processing, Laboratory Management, and Test Results
45 429 SA – Statistical Analysis and Data Management
46 430 W – Writing
47 431 E – Editing
48
49 432

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9 Alvaro Rivera-Andrade – PIC, DC, SP, E
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14

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581 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)	

	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^aAge-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			

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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)

M₁: unadjusted log-binomial model
M₂: 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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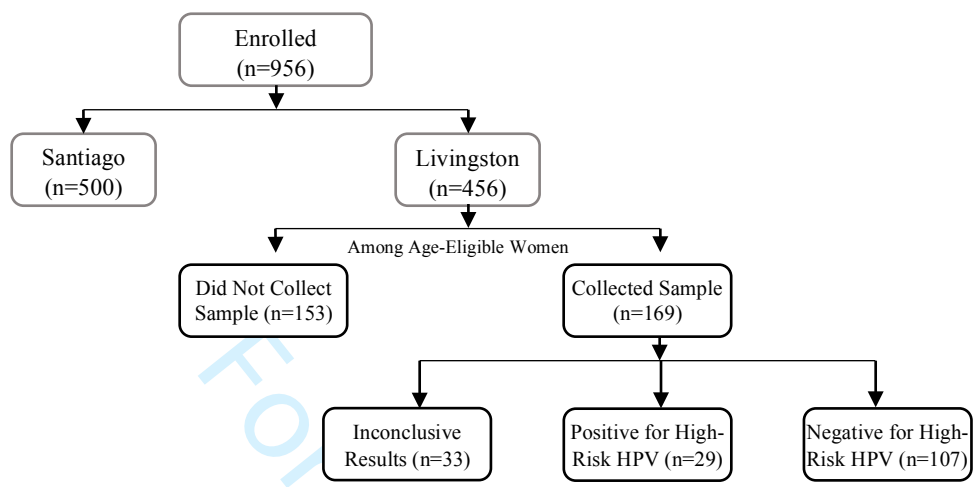
FIGURE LEGENDS

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



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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

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

Table A2 – General Population Characteristics Among All Participants (Continued)

Table A3 – Population Characteristics within Livingston (Continued)

Table A4 – Population Characteristics within Livingston: Comparing Racial/Ethnic Groups

Table A5 – Differences Among Communities of Age-Eligible Indigenous Mayan Women

Appendix B: Self-reported Willingness to Collect a Sample

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

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	

	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)	

^ap-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

^ap-values for means calculated using one-way ANOVA or Welch (if equality of variance is rejected); proportions using chi-squared test
^bFisher'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

^ap-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) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		<i>Case-control study</i> —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	
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
Variables	7	(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	12
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
		Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	
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) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed	11
		<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(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) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —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

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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

1 Cervical cancer, primarily caused by human papillomavirus (HPV) infection, has a very
2 good prognosis when detected in premalignant or early malignant stages¹. However, it
3 disproportionately burdens low- and middle-income countries (LMICs), such as Guatemala,
4 compared to high-income countries (HICs)²⁻⁴. HICs currently use Pap smears to detect abnormal
5 cervical lesions that can be removed, greatly reducing the risk of cervical cancer^{3,5}. However,
6 there are many barriers to implementing successful Pap smear (cytology-based) screening
7 programs in LMICs, including difficulties establishing sustainable laboratory infrastructure,
8 training and retaining adequate numbers of trained pathologists or cytologists, overburdened
9 primary care clinics, and time and travel limitations for women in reaching screening locations^{1,6}
10 ⁷. Due to these factors and others, the percentage of women in Guatemala who are screened for
11 cervical cancer remains low; in 2014, only 49.8% of women (15-49 years of age) reported ever
12 having a Pap smear. Thus, significant improvements in screening or program implementation are
13 paramount to improving cervical cancer outcomes in Guatemala^{3,8,9}.

14 Since more than 90% of cervical cancers are caused by the HPV virus, HPV testing has
15 been suggested as a possible alternative, primary form of cervical cancer screening¹⁰⁻¹². When
16 used in combination with Visual Inspection with Acetic Acid (VIA) or Pap smears in low-
17 income settings, HPV testing has been shown to provide significant improvements in the
18 detection of advanced premalignant lesions and cancer in sensitivity as compared to VIA or Pap
19 smear alone, as only women who test positive for HPV need to follow up with further
20 screening¹³⁻¹⁶. Previous studies have also confirmed that HPV self-swab kits are comparable to
21 physician administered samples in their ability to detect carcinogenic, high-risk HPV^{17,18}. Thus,
22 at-home HPV sample collection, with referral to further screening for those positive for high-risk

23 HPV, may be both more acceptable within low-income communities and more programmatically
24 feasible^{6 7 19}. Moreover, a 2015 meta-analysis showed that HPV self-sampling, particularly in
25 opt-in programs, increased participation in cervical cancer screening programs. However,
26 further work is needed to evaluate acceptable opt-in programs for women²⁰.

27 Studies have shown that HPV self-sampling is generally acceptable among women in low
28 and high resource settings as well as immigrant, rural, vulnerable populations²¹⁻³¹. To our
29 knowledge, however, little is known about the acceptability of self-collection HPV testing across
30 the diverse communities within Guatemala, and in particular among rural and indigenous
31 populations. In a pilot cross-sectional study assessing the acceptability of HPV self-collection
32 among 200 women in the Mayan community of Santiago Atitlán, Guatemala, a self-swab HPV
33 test was found to be a highly acceptable form of screening³². Over 80% of women said that they
34 preferred using a self-swab kit in their home rather than being screened at a doctors' office.
35 However, this pilot study was limited to a relatively small sample in a single, largely
36 homogeneous community, limiting the generalizability of the results to other rural and
37 indigenous communities in Guatemala. Further research is thus needed to evaluate the
38 acceptability of self-collection testing among more diverse rural and indigenous populations
39 within Guatemala, which is very diverse, with over 23 official languages and many indigenous
40 groups, most but not all descendants from the Mayan civilization. The purpose of this study was
41 to evaluate risk factors, knowledge, and attitudes towards cervical cancer and to further assess
42 and compare the acceptability of self-collection HPV testing in two understudied, rural,
43 ethnically distinct communities in Guatemala: Santiago Atitlán and Livingston, Izabal.

44 **METHODS**

45 **Study Communities**

1
2
3 46 Santiago Atitlán, Sololá is a rural community located on Lake Atitlán, in the southwest
4
5
6 47 region of Guatemala, 75 miles west of Guatemala City. The Tz'utujil, a Mayan descendant
7
8 48 ethnic group, inhabits the region, which surrounds Lake Atitlán. The primary language of
9
10
11 49 Santiago's inhabitants is Tz'utujil, and over half of the villagers speak Spanish as a second
12
13 50 language³². The majority of women in Santiago Atitlán have at most a primary education.
14
15 51 Additionally, as a conservative, religious community, it is highly uncommon for women to either
16
17 52 drink or smoke, and almost all women in have previously reported having only one lifetime
18
19 53 sexual partner³².

21
22 54 Livingston, Izabal is located on the Caribbean coast of the country and is a rural
23
24 55 community, only accessible by boat, that is the primary Garífuna settlement in Guatemala. The
25
26 56 Garífuna people are considered a unique ethnic group with their own language, culture, and
27
28 57 cuisine. Additionally, there are large populations of other ethnic and cultural groups located in
29
30 58 Livingston including Q'eqchi' (Mayan descent), Ladinos (non-Mayan descent), and populations
31
32 59 of Indian descent. Most women in Livingston are believed to have at least basic primary
33
34 60 education.

37 38 61 **Patient and Public Involvement**

39
40 62 The patients were not involved in the development of the research questions, outcome
41
42 63 measures or study design. The patients were also not involved in the recruitment and
43
44 64 performance of the study. However, the public, Guatemalan physicians, scientists, and
45
46 65 community health workers, were involved in the development of the question, design, validation,
47
48 66 recruitment, and conduct of the study. Local community health workers were involved in the
49
50 67 validation of the survey and study protocol, recruited participants and conducted the interviews,
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52 68 and assisted in providing test results to patients. Guatemalan physicians contributed to
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3 69 development of the research question and study design, organized the laboratory testing, led and
4
5 70 assisted with community health worker training, and provided HPV test results to patients. Local
6
7 71 laboratory scientists contributed to the study design and conducted the HPV laboratory testing.
8
9
10 72 The continued collaborations with these team members will be used to disseminate study results
11
12 73 to patients and Guatemalan officials via publications, presentations, and meetings.
13
14

15 74 **Eligibility and Recruitment**

16
17 75 Trained community health workers (CHWs) in both communities actively recruited
18
19 76 participants through home visits. All CHWs were bilingual and spoke both Spanish and either
20
21 77 Tz'utujil, Q'eqchi, or Karif (the language of the Garifuna) depending on the location they were
22
23 78 working in. Households in Santiago Atitlán were selected at random using stratified multi-level
24
25 79 sampling based upon maps and population counts of the communities available through the local
26
27 80 municipal office and were kept consistent with previous sampling methods³². Households in
28
29 81 Livingston were selected at random using convenience sampling due to lack of reliable census
30
31 82 data at the neighborhood-level. Sampling methods were, otherwise, kept the same as those in
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33 83 Santiago Atitlán.
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38 84 Selected households that had at least one woman available between the ages of 18 and 60
39
40 85 were invited to participate in the survey-component of the study to assess risk factors for,
41
42 86 attitudes towards, and knowledge of cervical cancer in these communities. For households with
43
44 87 more than one eligible woman willing to participate, the female in the household whose birthday
45
46 88 was closest to the date of the interview was enrolled in the study. Exclusion criteria consisted of
47
48 89 past hysterectomy or previous cervical cancer. Women between the ages of 25 and 54 were also
49
50 90 asked to provide a sample, in accordance with Guatemala's current screening
51
52 91 recommendations³³. Additionally, pregnant women, women currently menstruating, and women
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3 92 who had never been sexually active were also excluded from providing samples but could
4
5 93 participate in the survey component. Approximately 62% and 90% of eligible women contacted
6
7
8 94 were willing to participate in the study in Santiago and Livingston, respectively. All participants
9
10 95 in the study provided both oral and written informed consent prior to participation in the study.
11
12 96 The consent was documented by a signature or fingerprint of the participant, the surveyors, and a
13
14
15 97 witness to the consent process.

17 98 **Survey**

19 99 Data collection consisted of two main components: the surveys and the HPV self-
20
21 100 collection tests. Local CHWs in each community were trained as interviewers in the appropriate
22
23
24 101 techniques and protocols before beginning home visits. Two CHWs visited each randomly
25
26 102 selected household together and read a recruitment script to a female household member to
27
28
29 103 determine the household's eligibility. CHWs administered the survey and provided kits to
30
31 104 collect HPV samples only to willing, eligible participants. Surveys were administered in private
32
33 105 rooms of the participant's house to minimize response bias to sensitive questions.

35 106 The survey questionnaire included 153 questions concerning demographics, risk factors
36
37
38 107 for cervical cancer and HPV, self-reported attitudes towards screening, healthcare service use,
39
40 108 and knowledge of cervical cancer and HPV. The survey was developed from the pilot study
41
42 109 survey and validated as part of the CHW and translator training to ensure correct translation and
43
44
45 110 cultural relevancy³². Each survey was administered by the CHWs using electronic tablets and
46
47 111 the Qualtrics offline app.

49 112 All women who participated in the study were compensated with a voucher for a free Pap
50
51 113 smear or VIA at a local health clinic. Women in both communities can access free VIAs
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1
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3 114 (Santiago) or Pap Smears (Livingston) in the local public health system, but if they chose to use
4
5
6 115 a private clinic instead of the public clinic, the voucher covered their fees.
7

8 116 **HPV Self-Collected Samples**

9
10 117 The HPV samples were collected using HerSwab kits, a self-collection sampling method
11
12 118 ^{32 34 35}. If a participant was willing to provide a sample, instructions and graphical materials were
13
14
15 119 provided and the participant collected the sample in a separate, private room from the CHWs.
16
17 120 Participants who collected a sample then completed a short post-sample survey with the CHWs
18
19 121 of three questions regarding ease, comfort, and acceptability of the sampling method: “How easy
20
21 122 was the self-collection swab?”; “How comfortable was the self-collection swab?”; and “Would
22
23
24 123 you be willing to collect a sample every 2-3 years to detect HPV as a form of cervical cancer
25
26 124 screening?”.

27
28 125 After collection, samples were kept in small, refrigerated coolers carried by the CHWs
29
30 126 until they were returned to the main study office at the end of the day where samples were then
31
32 127 processed to stabilize sample life. The brush component of the HerSwab kit was cut into a 15-
33
34 128 mL test tube using lab scissors. The lab scissors were sterilized using alcohol and an open flame
35
36 129 between each sample. Each tube was filled with 5mL of Scope mouthwash using a pipette, and
37
38 130 tubes were sealed using a cap and parafilm paper³⁶. Mouthwash is a reliable, low-cost transport
39
40 131 medium for DNA samples and was used to reflect likely standard operating procedures of HPV
41
42 132 screening program implementation in Guatemala³⁷. Each sample was labeled with the
43
44 133 participant’s unique identifier. Time of sample processing and condition of sample were
45
46 134 recorded.
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50
51 135 Stabilized samples were sent to a molecular biology laboratory at the Institute of
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53 136 Nutrition of Central America and Panama (INCAP) in Guatemala City for testing. Samples were
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3 137 tested using the real-time polymerase chain reaction (PCR) HybriBio HR-13 kit^{38 39}. Samples
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5 138 were processed according to the manufacturers protocol and modified to use a 10 ul reaction
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7
8 139 volume for the real-time PCR and run on an ABI-7000³⁶. After testing, samples were labeled as
9
10 140 positive for HR-HPV, negative, or, if both the HPV probe and the internal control were negative,
11
12 141 inconclusive. If a sample test was inconclusive during the first test, it was run an additional time
13
14
15 142 using a 20 ul reaction volume, and if no result was obtained, the test was deemed inconclusive.
16

17 143 **Follow-Up**

18
19 144 A local CHW provided negative and inconclusive results over the phone or through a
20
21 145 home visit. Positive results were provided in-person by a study physician who referred
22
23 146 participants to their local community health clinic for follow-up and further cervical cancer
24
25 147 screening. All participants who couldn't be reached at the study conclusion were re-contacted
26
27 148 either at 6 months or one year to provide them with their results. Although women with negative
28
29 149 results were not explicitly recommended to attend the clinic, all participants were encouraged to
30
31 150 get screened using the voucher provided at the local clinic to support their engagement with local
32
33 151 preventative services. Participants who were found to be positive for advanced lesions as a result
34
35 152 of follow-up screening were referred for care through the free public health infrastructure in
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37 153 Guatemala, as is currently standard practice. Due to the ongoing nature of the project, data on
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39 154 follow-up screening and care are still in the collection process.
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44 155 **Outcomes and Statistical Analysis**

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46 156 Willingness and acceptability of self-collection testing, knowledge of HPV, and risk
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48 157 factors were evaluated in both communities and across ethnic groups in Livingston, Izabal.
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50 158 Willingness was measured as whether or not a woman chose to self-collect a sample to be tested
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52 159 for HPV (actual self-collection). The acceptability of sample collection was only assessed for
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3 160 those who self-collected a sample and was analyzed using the post-self-swab survey questions
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6 161 described previously.

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8 162 A target sample size of 500 per community was determined to be able to detect a 5%
9
10 163 difference in self-sampling acceptability with 80% power, assuming a 95% acceptability in
11
12 164 Santiago Atitlan based on the pilot.

13
14
15 165 Due to lower rates of actual self-collection in Livingston, differences between Livingston
16
17 166 women willing and those not willing to collect a sample were evaluated using two-sample t-tests
18
19 167 for means, chi-squared tests for proportions, and Fisher's Exact test for low cell counts. Most
20
21 168 women tried self-collection in Santiago, so we restrict these analyses to Livingston.

22
23
24 169 The main exposures explored for willingness to try self-collection included: literacy,
25
26 170 marital status, history of Pap smear or VIA, smoking status, alcohol use (a potential proxy for
27
28 171 risky behavior), IUD use, family history of cervical cancer, and belief of being at risk for
29
30 172 cervical cancer. Statistical analyses were run using log-binomial regression. In model set 1, the
31
32 173 relationship between each exposure and sampling decision was unadjusted for other covariates.
33
34 174 In model set 2, models were additionally adjusted for age, ethnicity, and number of lifetime
35
36 175 sexual partners. In model set 3, we used stepwise selection to select significant the exposure
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38 176 covariates ($\alpha=0.05$) when adjusting for age, ethnicity, and number of lifetime sexual
39
40 177 partners. Finally, in model set 4, we included all exposure covariates and the adjustment
41
42 178 covariates together in a fully adjusted model. The stepwise selected model was further stratified
43
44 179 across ethnic groups to evaluate potential effect modification. Due to high prevalence of literacy
45
46 180 in Garifuna and Ladino, these groups were combined for stratification to prevent positivity
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48 181 violations (Q'echchi versus Garifuna or Ladino, reflecting a Mayan descent versus non-Mayan
49
50 182 descent comparison).
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3 183 Analyses were restricted to age-eligible women in Livingston with complete covariate
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5 184 information (N=134 or 29.4% excluded due to age-ineligibility and N=13 or 3.5% excluded due
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7
8 185 to missing covariates). Specifically, we excluded 5 participant missing ethnicity or classified as
9
10 186 other ethnicity, 1 participant missing marital status, 1 participant missing regular drinking status,
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12 187 and 3 participants missing number of lifetime sexual partners, 1 participant missing smoking
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14
15 188 status, and 2 participants missing family history of cancer resulting in a final sample size N=309
16
17 189 for analyses evaluating willingness to try self-collection.

18
19 190 Covariates were parameterized as: able to read and/or write (literate) versus unable to
20
21 191 either read or write (illiterate), ever married versus never married, ever had a Pap or VIA versus
22
23 192 never, ever smoked versus never smoked, regular drinker versus non-regular drinker, ever had an
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26 193 IUD versus never or don't know/refused, family history of cervical cancer present versus absent,
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28 194 and believe at risk for developing cervical cancer ("strongly agree"/"agree" versus neutral,
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30 195 disagree, strongly disagree, or unsure/don't know), continuous age, and number of lifetime
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33 196 sexual partners (one versus more than one).

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35
36 197 Data cleaning and analyses were carried out using SAS 9.4.

37 38 198 **RESULTS**

39
40 199 In total, 956 women were recruited to participate into the study: 500 women in Santiago
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42 200 Atitlán and 456 women in Livingston. Demographic characteristics differed between the two
43
44 201 communities: 69.4% of the participants in Santiago Atitlán had less than primary education and
45
46 202 96.6% were of Tz'tujil ethnicity. In contrast, only 33.9% of the participants in Livingston had
47
48
49 203 less than primary education and three ethnic groups were represented: 41.9% Q'echchi, 32%
50
51 204 Garifuna, and 24.8% mixed ethnicity (Ladino) (Table 1).

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

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

219 **Self-Collection Willingness**

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

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

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2
3 228 3). Additionally, 31.4% of the women who ended up not providing a sample had responded
4
5 229 previously in the questionnaire that they indeed would be willing to collect a self-swab sample at
6
7 230 home. While data is unavailable regarding how many age-eligible women were ineligible to
8
9 231 collect a sample due to menstruation or pregnancy, this likely does not entirely account for all
10
11 232 women who ultimately chose not to self-collect. Characteristics of women not willing to collect
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13 233 (both reported in the survey and actual sample collection) can be found in the appendix. It is
14
15 234 interesting to also note that women from Santiago, who reported less prior use of healthcare,
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17 235 were more likely to self-collect.
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22 236 Literacy was significantly higher among women who self- collected a sample in
23
24 237 Livingston compared to those who did not (crude PR 2.04; 95% CI: 1.27, 3.28; adjusted PR,
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26 238 2.25; 95% CI: 1.38, 3.68) (Table 4). IUD use was also higher among women who self-collected
27
28 239 a sample in Livingston (crude PR 1.49; 95% CI: 1.15, 1.94; adjusted PR 1.43; 95% CI: 1.08,
29
30 240 1.88) (Table 4). Additionally, regular drinking and never being married were higher among
31
32 241 women who self-collected but not significant (regular drinking, crude PR 1.18; 95% CI: 0.95,
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34 242 1.48; adjusted PR 1.14; 95% CI 0.89, 1.46; never married, crude PR 1.19; 95% CI: 0.96, 1.48;
35
36 243 adjusted PR 1.15; 95% CI: 0.91, 1.43) (Table 4).
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40 244 Using stepwise selection with adjustment for age, ethnicity, and more than one lifetime
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42 245 sexual partner, only literacy was selected as an exposure covariate (PR 2.25; 95% CI: 1.38,
43
44 246 3.68). When stratifying ethnic group (Q'echchi versus Garifuna and Ladino), the association
45
46 247 between literacy and actual sample collection remained positive (Table 5). However, this
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48 248 relationship only remained statistically significant among Q'echchi participants. However,
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50 249 interaction terms between ethnic group (Q'echchi versus not) and literacy revealed that the effect
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250 of literacy among the Q'echchi was not significantly different from the Ladinos and Garifunas
251 (interaction term PR 0.94; 95% CI: 0.25, 3.59).

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

254 **Self-Collection Acceptability and Comfort**

255 Among those who did collect a sample, the self-collection testing was highly acceptable
256 in both communities. Of Santiago participants who self-collected, 81.4% found it comfortable
257 and 84.8% reported that the HerSwab was easy to use. Among Livingston participants who self-
258 collected, 87.0% found it comfortable and 87.0% reported it was easy to use. Among those who
259 chose to self-collect, almost all participants in both locations reported that they were willing to
260 use it as a form of cervical cancer screening (98.0% in Santiago and 100% in Livingston) (Table
261 2).

262 **HPV Prevalence**

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

270 **DISCUSSION**

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

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3 273 Guatemala. We found that self-collection appears to be highly acceptable among women who
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5 274 tried it, independent of community and ethnicity. Most women reported that self-collection was
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8 275 comfortable and easy to use, and almost all women who tried it reported being willing to use it as
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10 276 a form of cervical cancer screening in the future. These results are consistent with other studies
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12 277 looking at self-collection acceptability both within Guatemala and other LMICs^{27 32}. This study
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14 278 was further able to build upon previous studies and provide important information regarding
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16 279 HPV self-collection testing acceptability at the community level, and in a community that had
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19 280 not been previously evaluated.

21
22 281 Our study also found, however, that there were differences between communities in
23
24 282 willingness to try self-collection. Willingness to try self-collection testing remained consistently
25
26 283 high among participants in Santiago Atitlán as reported in the pilot study conducted in 2015
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28 284 (93% in 2015 versus 93.6% in 2016)³². In Livingston, however, even among women who first
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30 285 responded in the survey or consent form that they would be willing to collect a sample, actual
31
32 286 self-collection was lower. We found that willingness to self-collect in Livingston was
33
34 287 consistently associated with higher levels of literacy and prior IUD use. In contrast, ethnicity,
35
36 288 history of cervical cancer screening, and health behaviors were not associated with willingness to
37
38 289 self-collect. Stratified analyses suggested that there were no qualitative differences in the
39
40 290 association between literacy and sample collection across ethnic groupings (Mayan descent
41
42 291 versus non-Mayan descent) in Livingston. However, high prevalence of literacy among Garifuna
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44 292 made it difficult to evaluate differences between Ladinos and Garifunas in the association
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46 293 between literacy and sampling decision.

51 294 The results suggest that HPV self-collection testing program implementation may need to
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53 295 target populations based on relative levels of literacy within communities. A previous study
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3 296 examining HPV acceptability and intention in the UK similarly found that low education and
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5 297 self-efficacy, defined as an individual's belief in their capability to exercise control over
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7 298 challenging demands, were associated with low sampling intentions³⁰. In Guatemala, the
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9 299 inability to either read or write in Spanish may negatively influence a woman's perceived self-
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11 300 efficacy and her confidence in navigating public health infrastructure or self-collecting a vaginal
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13 301 sample, particularly if her surrounding community has high levels of literacy. This population
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15 302 would greatly benefit from HPV self-collection testing as a primary form of cervical cancer
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17 303 screening due to its strength in concentrating less accessible and more invasive screening
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19 304 modalities only towards those that are at high-risk (i.e., positive for HPV). Our results in
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21 305 Livingston suggest that it might be critical that, if implemented, HPV screening and education
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23 306 programs are tailored such that they are more accessible to low-literacy populations and, thus,
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25 307 increase perceived self-efficacy in navigating the existing public health infrastructure.
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31 308 High prevalence of self-collection testing in Santiago Atitlan, a community with low
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33 309 literacy levels, as compared to the low rates of self-collection testing among those with low
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35 310 literacy in Livingston may reflect larger community differences in awareness or access to
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37 311 screening modalities rather than a lack of effect of literacy in Santiago or an effect of ethnicity.
38
39 312 Although women from Santiago reported slightly higher rates of ever receiving cervical cancer
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41 313 screening than women in Livingston, women in Livingston report much higher rates of recent
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43 314 cervical cancer screening than women in Santiago. Santiago Atitlán remains largely deficit in
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45 315 accessible and affordable cervical cancer screening while Livingston has regular, public or
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47 316 private, screening campaigns in the community. This difference in general community access
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49 317 and infrastructure, then, may be acting as an effect modifier on the association between literacy
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51 318 and screening between these two communities, suggesting that self-collection might be better
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3 319 received at first in communities that do not have other alternatives, whereas some initial
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5 320 skepticism might be found in places with existing cervical screening programs, independently of
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7 321 their quality and efficacy. More research is necessary to evaluate if self-efficacy, relative literacy
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9 322 level, or general community access to healthcare resources and screening play larger barriers for
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11 323 women in trying self-sampling HPV testing. However, the high rates of acceptability and
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13 324 willingness to retake among women who self-collected in both communities suggest that once
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15 325 experienced, self-collection is a valid, and even preferred, alternative to other screening
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17 326 modalities from the women's perspective.
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22 327 Although based on a different HPV test than in our pilot study (HybriBio HR13 vs.
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24 328 Anyplex 28), a similar prevalence of high-risk HPV was found in Santiago between 2015 and
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26 329 2016 (17.4% versus 19.3%)³². Of note, there were no significant differences in high-risk HPV
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28 330 prevalence between ethnic groups in Livingston, and there was not a statistically significant
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30 331 difference between Santiago Atitlán and Livingston with regards to prevalence.
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33 332 Our study provided not only a larger sample size compared with previous studies but was
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35 333 also conducted in two differing communities. This is a strength because Guatemala is an
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37 334 extremely diverse country with over 23 languages, distinct ethnicities, and a history of large
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39 335 economic and social inequalities. Thus, generalizing the evaluations of a health program's
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41 336 acceptability and feasibility to the whole country is generally difficult. However, because we
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43 337 evaluated two very different rural multi-ethnic communities, our results may reflect some of the
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45 338 future obstacles and considerations necessary in implementing self-swab HPV testing in such a
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47 339 diverse country as Guatemala than was previously available. In fact, our results also
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49 340 complement the findings of the ongoing careHPV Scale-Up implementation, which is assessing
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3 341 the performance of HPV testing, including self-collection testing, within urban settings in
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5 342 Guatemala⁴⁰⁻⁴².

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7
8 343 There are several limitations to our study. Due to both the sensitive nature of the
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10 344 questions related to sexual history, it may be possible that a social desirability bias may have
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12 345 resulted in over reporting of perceived “good behaviors”, such as screening or use of protection,
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14 346 in addition to under-reporting of perceived “bad behaviors”, such as number of lifetime sexual
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16 347 partners and other sexual behavior measures. We tried to minimize the possibility of this bias by
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18 348 maintaining confidentiality with participants. Also, women may report their history of screening
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20 349 or utilization of health care resources incorrectly if they had limited information or
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22 350 understanding of these services. This may be exaggerated in women with low literacy and thus
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24 351 explain potential over reporting of prior cervical cancer screening in Santiago Atitlan.

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26 352 Additionally, because sampling methods differed between the two communities due to the lack
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28 353 of reliable census counts in Livingston, there may be differences between the communities in
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30 354 potential selection bias into the study and more limited comparability of the results. However,
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32 355 our sample in Livingston is reflective of the overall population structure of Livingston in terms
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34 356 of ethnic, age and other metrics, suggesting that influential selection bias into the study might be
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36 357 limited⁴³.

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38 358 Screening program implementation is a major challenge in LMIC settings, HPV self-swab
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40 359 testing may serve as a helpful tool in concentrating less accessible and more expensive and
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42 360 invasive screening modalities only towards those that are at high-risk (i.e., positive for HPV).
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44 361 However, as the results in Livingston showed, there are many complex features related to
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46 362 implementing HPV screening that will need to be evaluated before program adoption of such
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48 363 programs. Due to the longitudinal component of our study, future research with our study
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3 364 participants will hopefully help elucidate how HPV self-collection testing may affect women's
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5 365 decisions to pursue further cervical cancer screening and follow-up care in their local
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7 366 communities after HPV testing and receiving their results. Additionally, these data may reveal
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10 367 other downstream facilitators or barriers to screening that will influence the overall success of
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12 368 HPV self-swab testing implementation in these communities.

14 369 **CONCLUSION**

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17 370 The results of our study add to the literature on the potential of HPV self-collection
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19 371 testing in LMICs, demonstrating its acceptability in two very different communities in rural
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21 372 Guatemala. The high rates of acceptability and willingness to retake among women who self-
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23 373 collected in both communities suggest that once experienced, self-collection is a valid, and even
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25 374 a preferred, alternative to other screening modalities from the women's perspective. However,
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27 375 the difference in willingness to try self-collection between these communities suggests that
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29 376 relative literacy levels and the availability and quality of existing healthcare programs may affect
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31 377 attitudes towards new screening modalities. Future research should focus on increasing the
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33 378 generalizability of these findings by evaluating additional communities within Guatemala for
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35 379 differences in willingness to try self-collection sampling and further elucidate the potential
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37 380 barriers to accessing and utilizing cervical cancer modalities, including HPV self-collection
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39 381 sampling.

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43 383 **LIST OF ABBREVIATIONS**

44
45 384 CC – Cervical Cancer

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47 385 CHW – Community Health Worker

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49 386 CI – Confidence Interval

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3 387 HICs – High-Income Countries
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5 388 HIV – Human Immunodeficiency Virus
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7 389 HPV – Human Papillomavirus
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10 390 HR-HPV – High-Risk Human Papillomavirus
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12 391 INCAP – Institute of Nutrition of Central America and Panama
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14 392 IUD – Intra-Uterine Device
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16 393 LMICs – Low and Middle-Income Countries
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18 394 OR – Odds Ratio
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20 395 PCR – Polymerase Chain Reaction
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22 396 PR – Prevalence Ratio
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24 397 VIA – Visual Inspection with Acetic Acid
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31 399 **DECLARATIONS**

32 33 400 **Ethics Approval and Consent to Participate**

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35 401 The University of Michigan Institutional Review Board (HUM00096559) and the
36
37 402 Institute of Nutrition of Central America and Panama Institutional Review Board (MI-CIE-16-
38
39 403 009) approved study protocols. All participants gave oral and written informed consent prior to
40
41 404 participation in the study. The consent was documented by a signature or fingerprint of the
42
43 405 participant, the surveyors, and a witness.
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47 406 **Consent for Publication**

48
49 407 The authors of this paper have all reviewed its contents and consent for its publication.
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51 408 **Data Sharing Statement**

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

414 **Competing Interests**

415 The authors have no competing interests to declare.

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425 **Authors' Contributions**

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

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704 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	Livingston	p-value^{a,b}
	% (N)	% (N)	
N	500 (<i>all participants</i>) 438 (<i>age-eligible</i>)	456 (<i>all participants</i>) 322 (<i>age-eligible</i>)	
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 (<i>age-eligible; test-taking participants</i>)	169 (<i>age eligible; test-taking participants</i>)	
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^aAge-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.

M₁: unadjusted log-binomial model

M₂: 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

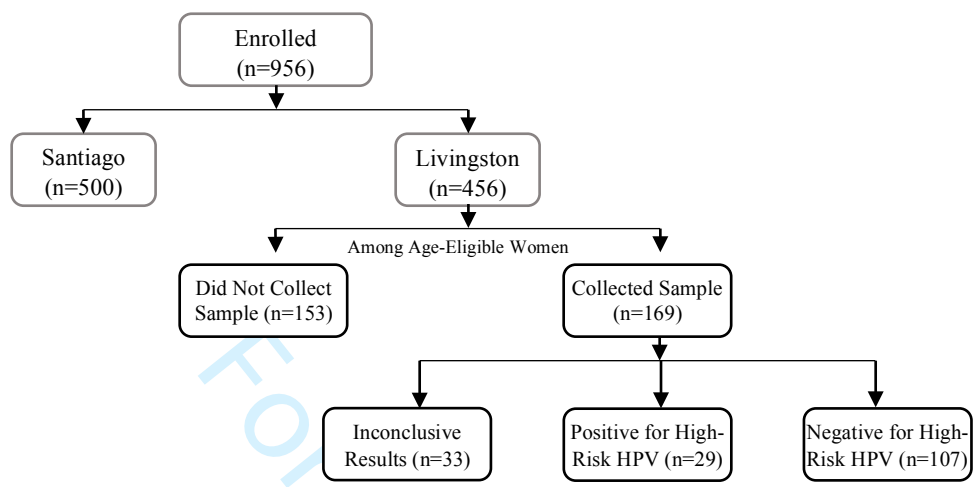
Figure 1. Flow Chart of Livingston Self-Collection Sampling and Testing

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



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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

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

Table A2 – General Population Characteristics Among All Participants (Continued)

Table A3 – Population Characteristics within Livingston (Continued)

Table A4 – Population Characteristics within Livingston: Comparing Racial/Ethnic Groups

Table A5 – Differences Among Communities of Age-Eligible Indigenous Mayan Women

Appendix B: Self-reported Willingness to Collect a Sample

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

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	

	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)	

^ap-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

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

^bFisher'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

^ap-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.

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) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		<i>Case-control study</i> —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	
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
Variables	7	(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	12
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
		Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	
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) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed	11
		<i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(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) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —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.