Evaluating the Feasibility of Self-sampling using CareHPV™ and Treatment with Cryotherapy in Haiti

by

Allia Vaez

Global Health Institute
Duke University

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Approved:

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David Walmer, Supervisor

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Joe Egger

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Megan Huchko

Thesis submitted in partial fulfillment of
the requirements for the degree of
Master of Science in the Global Health Institute in the Graduate School
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ABSTRACT

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Abstract

Introduction: Cervical cancer is one of the leading causes of death for women in Haiti. The purpose of this study was to evaluate the feasibility of HPV self-sampling using CareHPV™ and subsequent treatment with cryotherapy in urban and rural areas of Haiti. CareHPV™ is a vaginal self-sample HPV testing kit used to detect 14 types of high-risk HPV and cryotherapy is a form of treatment that freezes precancerous lesions with CO_2 or nitrous oxide. Methods: The study took place in Port-au-Prince and three rural communities within the suburban commune of Leogane. Screening took place at clinics, community centers, and churches. Participants were given consent forms to sign, as well as a demographic questionnaire and an acceptability survey. If their HPV test result was positive, they were called up to three times to go the community clinic for treatment. The number of women that returned for treatment following a positive HPV test result were compared in the urban and rural communities with a chi square test of association and a prevalence rate ratio. Acceptability was measured quantitatively on the Likert Scale. Results: Feasibility was defined as 80% acceptability and 80% treatment uptake. Other factors related to feasibility such as screening numbers and geographical barriers were discussed. Eighty percent acceptability was reached in both rural and urban communities. Eighty percent treatment uptake was only reached in the rural communities, with a treatment uptake of 83.3%. Eighty percent treatment uptake was

not reached in the urban communities, with a treatment uptake of 42.1%. The prevalence rate ratio of 1.98 indicates that rural participants were found to be nearly twice as likely to return for treatment than urban participants. The chi square test of association shows that this difference in treatment uptake is significant with an estimated p-value of 0.01 at an alpha of 0.05. Further research is needed to investigate the reasons for higher loss to follow-up for treatment in urban communities to further efforts to establish a national HPV screening program in Haiti.

Dedication

This thesis is dedicated to the women of Tom Gato, Canaan, Bosan, and Port-au-Prince for taking part in this study and contributing to the advancement of efforts to prevent cervical cancer in Haiti.

Contents

List of Tables

List of Figures

Acknowledgements

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1. Introduction

Cervical cancer is one of the leading causes of cancers and death among women in Haiti, with an annual incidence rate of 93.9 per 100,000 cases, compared to an annual incidence rate of 7.4 per 100,000 in the United States, and an annual mortality rate of 53.5 per 100,000 cases, compared to 2.3 per 100,000 in the United States.[1,2,3] In 1996, the World Health Association along with the European Research Organization on Genital Infection and Neoplasia and the National Institutes of Health Consensus Conference recognized human papillomavirus (HPV) as the causative agent of cervical cancer.[4] Since then, extensive research has been done on prevention of cervical cancer through the treatment of premalignant HPV-related cervical dysplasia.

1.1 HPV Screening

For decades, the global standard of care for preventing cervical cancer has been the Papanicolaou test, a cytological test, designed to detect cervical dysplasia.[5] The use of cytology has contributed to a major decline in cervical cancer in the developed world, but has not been feasible in low-resource communities due to a lack of infrastructure,

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[1] Merle Lewis, *A situational analysis of cervical cancer in Latin America and the Caribbean,* (Washington, D.C.: PAHO, 2004)
[2] Silvina Arrossi and Rengaswamy Sankaranarayanan and Donald Parkin, "Incidence and mortality of cervical cancer in Latin America." 45, 3 (2003), 306-314.
[3] National Cancer Institute, Cancer Stat Facts: Cervical Cancer, https://seer.cancer.gov/statfacts/html/cervix.html.
[4] Eileen Burd, "Human Papillomavirus and Cervical Cancer." 16, 1 (2003), 1-17
[5] National Cervical Cancer Coalition, *Cervical Cancer Screening: Pap and HPV Tests*, http://www.nccc-online.org/hpvcervical-cancer/cervical-cancer-screening/, (accessed Jan. 15, 2018).

trained healthcare and laboratory providers, and a high false negative rate associated with testing.[6] In the United States and other high-income countries that use the Pap test, frequent testing and closer examination of the cervix is typically available and accessible for patients that have a positive test result for abnormal cells. Frequent testing every six months to one year reduces the chances of receiving a false negative result and prevents the development of cervical cancer.[7] The use of the HPV vaccine has become more widely used in the past few years in the developed world but is currently not feasible in low-income countries mainly due to the high cost.[8]

Studies have shown that a more cost-effective and feasible strategy than cytology for identifying cervical dysplasia in low-resource settings is Visual Inspection with Acetic Acid (VIA). VIA involves applying dilute 5% acetic acid (vinegar) to the cervix and viewing the cervix with the naked eye to identify any color changes; abnormal tissue usually appears white when exposed to acetic acid.[9] VIA can be used in nearly any setting; however, while cost-effective, it is not ideal because it has both a high false positive and a false negative error rate for detecting cervical dysplasia.[6] With both low specificity and sensitivity, VIA must be done as frequently as Pap testing is done in

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[6] PATH, *Cervical Cancer Screening and Treatment in Low-Resource Settings,* (Seattle.: RHO Cervical Cancer Library, 2013)
[7] National Cancer Institute, Pap and HPV Testing, https://www.cancer.gov/types/cervical/pap-hpv-testing-fact-sheet, (accessed Jan. 31st, 2018)
[8] Mark Kane et al., "HPV Use in the Developing World", 24, 3 (2006), 132-139.
[9] *Alliance for Cervical Cancer Prevention*, http://screening.iarc.fr/doc/RH_via_evidence.pdf, (accessed Jan. 15 2018)

high-income countries, and in low-resource settings without proper infrastructure and skilled health professionals, frequent testing may not be feasible. Since HPV is known to be the causative agent of cervical cancer, research has shown that HPV DNA testing may be the most effective way to identify women who are at risk of developing cervical cancer, detecting the presence of the HPV infection rather than examining the cervical cells for abnormalities. Although each HPV DNA test is more expensive than other screening methods, the long-term cost of HPV DNA testing is lower than other screening methods due to the ability to focus on the 20% population at risk. Other benefits of HPV DNA testing include its high sensitivity, reproducibility, and ease of interpretation.[10] Studies have shown that screening for HPV and treating precancerous lesions every three to five years significantly reduces the risk of cervical cancer.[11] The WHO also recommends HPV DNA testing for screening and treatment with cryotherapy in their guidelines for preventing cervical cancer in low-income countries.[12]

1.2 CareHPV™

Qiagen has been working on developing a low-cost HPV assay for many years, creating the CareHPV™ kit, with funding from PATH and the Gates Foundation, which is now approved for use in low resource countries around the world.[8] DGHI-affiliate,

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[10] PATH, *Cervical Cancer Screening and Treatment in Low-Resource Settings*
[11] Nicole Campos, et al., "When and How Often to Screen for Cervical Cancer in Three Low and Middle Income Countries: A Cost-Effective Analysis," 1, (2015), 38-58
[12] World Health Organization, *Sexual and Reproductive Health*, http://www.who.int/reproductivehealth/topics/cancers/guidelines/en/, (accessed Jan. 15 2018)

Family Health Ministries, has partnered with Qiagen over the last 11 years to provide clinical specimens that were used to assess implementation feasibility of CareHPV™ in Haiti. This led to the screening of over 20,000 women in Haiti and the opening of Haiti's first HPV laboratories. CareHPV™ uses a DNA detection method that captures specific target HPV nucleic acid sequences using a chemiluminescence signal. It can detect 14 types of high-risk HPV and can process 10 controls and 90 clinical specimens in about two hours, allowing for quick screening and follow-up.[13]

1.3 HPV Treatment

There are many different types of treatment for HPV or cervical precancer, including cryotherapy, loop electrosurgical excision procedure (LEEP), and laser conization. Methods like LEEP and laser conization can be expensive and require the use of skilled professionals and equipment that may not be practical and feasible in low-resource settings.[14] Cryotherapy involves freezing lesions or abnormal cells on the cervix using compressed carbon dioxide or nitrous oxide. This method is relatively low-cost and requires less equipment than other methods, making it the most used and feasible treatment in low-resource settings.[15] Moreover, treatment with cryotherapy is low-cost, safe and effective. Therefore, treatment based on HPV infection alone in low-resource settings is recommended by the World Health Organization (WHO) based on current

[13] Jose Jeronimo et al., "A Multicountry Evaluation of *care*HPV Testing, Visual Inspection with Acetic Acid, and Papanicolaou Testing for the Detection of Cervical Cancer." 24, 3 (2014), 576-585.
[14] PATH, *Cervical Cancer Screening and Treatment in Low-Resource Settings*
[15] Ibid.

available evidence. Cryotherapy, while the most ideal treatment method in low-resource settings, is only effective if there is adequate access to nitrous or CO_2 gas. Other gasless methods of cryotherapy such as the CryoPen™ and thermoablation are currently being developed and evaluated with research trials.[16]

1.4 HPV in Haiti

A recent study in Haiti reported the prevalence of high-risk HPV genotypes to be 18.5% in Port-au-Prince and Leogane, ranging from 15% to 25% in different communities.[17] The same study also found that approximately 67% of precancerous lesions and 80% of invasive cervical cancers were positive for HPV genotypes 16 or 18, the two most common types of high-risk HPV.[18] It is estimated that Haitian women are 25 times more likely to die from this preventable disease than women in the United States.[19] The Haitian Ministry of Health has officially recognized cervical cancer as an important public health issue and it has determined that preventing cervical cancer is one of its national health priorities. The NGO community in Haiti has come alongside the Haitian Ministry of Health by forming an umbrella organization called Haiti Sans Cervical Cancer (HsCC) to unify the cervical cancer prevention efforts within Haiti. This

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[16] The Cleveland Clinic, An Innovative Treatment for Cervical Precancer, Government Trial, https://clinicaltrials.gov/ct2/show/NCT03084081,
[17] David Walmer et al., "Human Papillomavirus Prevalence in a Population of Women Living in Port-au-Prince and Leogane, Haiti." 8, 10 (2013).
[18] Ibid.
[19] Merle Lewis, *A situational analysis of cervical cancer in Latin America and the Caribbean*

alliance was created in the hopes of assisting the Haitian Ministry of Health to create a national cervical cancer screening program.[20]

1.5 Study Aims and Goals

The study reported here was initiated by two of the HsCC partners, Basic Health International and Family Health Ministries, as a feasibility study to evaluate the challenges of initiating a national screen and treat cervical cancer prevention program in rural and urban Haiti based on HPV testing followed by cryotherapy of all HPV positive women. The study also served as a tool to specifically assess the feasibility of delivering an HPV screening program to women in hard-to-reach areas of Haiti; rural areas have traditionally presented with many barriers and obstacles to receiving treatment. The goal of this feasibility study was to screen 1000 women from a rural area of Haiti and 1000 women from an urban area, comparing rates of treatment and acceptability to determine program feasibility.

Feasibility was defined as 80% treatment uptake and 80% acceptability. Treatment uptake was defined as HPV+ participants that returned to the clinic for treatment with cryotherapy. Loss to follow-up was defined as HPV positive participants that did not return to the clinic for treatment after three contact attempts. Acceptability was defined as an assessment of the HPV DNA test kit from the patient perspective, measured quantitatively on the Likert Scale, ranging from one to five, with one being

[20] Haiti Sans Cervical Cancer, https://haitisanscervicalcancer.org, (accessed Jan. 15 2018).

"strongly agree" and five being "strongly disagree." Results from this feasibility study will be presented to the Ministry of Health to advance efforts towards a national cervical cancer screening program in Haiti.

2. Methods

2.1 Settings

This study took place in four communities that represent urban, suburban and rural areas of Haiti's Ouest Department. Port-au-Prince is urban, the capital city of Haiti. The rural communities of Tom Gato, Bosan, and Canaan reside within the suburban commune of Leogane. Tom Gato is a rural mountainous community while Bosan and Canaan are rural coastal communities. For simplicity, "rural" will refer to the communities of Tom Gato, Bosan, and Canaan, and "urban" will refer to the community of Port-au-Prince within this report. Approximately 50% of Haitians live in poverty, while approximately 25% live in extreme poverty. The primary industry in this part of Haiti is agriculture, with sugar and coffee serving as the crops of most vital importance. Most inhabitants of this area work as laborers in sugar cane fields or peasant farmers, selling their fruits, vegetables, and other goods at local markets. Screening in the three rural communities within the Leogane commune took place in community centers, churches, at the Carmelle Voltaire Women's Health Center and at the Fondwa Clinic. Treatment took place at the Carmelle Voltaire Women's Health Center in Tom Gato. Port-au-Prince is the capital city and chief port of Haiti, with a population of about two million.[1] While less agricultural, Haitians in Port-au-Prince mainly make their living

[1] Encyclopedia Britannica, *Port-au-Prince*, https://www.britannica.com/place/Port-au-Prince, (accessed Jan 15 2018).

through selling goods. Screening and treatment in Port-au-Prince took place at the Manitane Clinic. The HPV laboratory where all the samples from both rural and urban communities were tested for HPV is located in Port-au-Prince at the Blanchard Clinic near the airport.

2.1.1 Participants

Participants of the study included sexually active women aged 30-49 with no prior hysterectomy or active vaginal bleeding. In Tom Gato, women were recruited through word-of-mouth, announcements at the market, informing church and community leaders, and going door-to-door. In Bosan and Canaan, community leaders helped to recruit women to attend screening sessions at a predetermined time, date, and location by meeting with them in their homes, when they saw them in the community, and while at church and other community events. Recruitment in Port-au-Prince took place at the Manitane Clinic.

2.2 Procedure

Eligibility to participate in the study was determined when women arrived at the screening location with the assistance of a bilingual Haitian translator trained in research procedures. Once participants were found to be eligible, consent forms were read and signed. A demographic questionnaire designed by Family Health Ministries and Basic Health International was modified for the aims of this study. After information on the demographic questionnaire was collected, the translator then explained the procedure

for obtaining a vaginal swab with diagrams. Once the women had a sufficient understanding of how to use the test kit, they were led to the private testing space to complete the procedure. When self-sampling was complete, their samples were collected outside the room and they were led back to the translator to complete the acceptability survey. Acceptability surveys from Basic Health International and Family Health Ministries were also adapted for this study. Once the acceptability survey was completed, they were given the Haitian Creole consent forms to keep and reminded that they would receive a phone call with their test results and be advised if they needed to return to the clinic for treatment. Once a full box of samples (50) were collected, the box was sent to the HPV DNA testing laboratory in Port-au-Prince for analysis. Once analysis was complete, the HPV results were sent to the physicians in each clinic, Carmelle Voltaire Women's Health Center for rural participants and Manitane Clinic for urban participants. The physicians and/or their assistants then called each HPV positive participant, informing them of their results and asking them to return to the clinic for treatment. All HPV positive participants were called up to three times. If they did not come to the clinic for treatment within two weeks after three contact attempts, they were considered lost to follow-up. All study procedures were approved by the institutional review boards at Duke University in the US and the DHHS-registered Haitian IRB (Misyon Sante Fanmi Ayisyen) IRB 6585/FWA 13290.

2.3 Measures

Data for each participant were collected using demographic questionnaires, HPV result, treatment data for HPV positive participants, and participant acceptability of self-collection. Questions on the demographic questionnaires included age, address, occupation, highest level of education, religion, and marital status, as well as questions related to menstrual, sexual, and obstetric history. The demographic questionnaire served as a tool to collect data about the study population as well as a medical history for the physician administering the cryotherapy treatment. Questions on the acceptability survey specifically designed to determine acceptability of the test kit included asking about the level of discomfort they felt with the screening procedure, whether they felt embarrassed, if they felt they had collected the sample correctly, and whether they would recommend the test kit to friends and family. These questions were measured quantitatively, on the Likert Scale, with options one and two being "strongly agree" and "agree," representing high acceptability and options four and five being "disagree" and "strongly disagree," representing low acceptability. Other questions on the survey such as screening location preference and whether participants felt the results will be accurate were analyzed as factors related to feasibility. Secondary analyses included comparing screening numbers, demographic characteristics, and prevalence of HPV among the rural and urban communities.

2.3 Analysis

The study reported here is an interim analysis of the full feasibility study. Feasibility was defined as 80% treatment uptake and 80% high acceptability. A p-value for difference in treatment uptake between the rural and urban communities was estimated using a chi square test of association and a prevalence rate ratio was calculated to estimate a rate ratio for treatment uptake, comparing the rural and urban study populations. Acceptability percentages were compared among the two communities and analyzed to determine if they met the feasibility criteria. Demographic tables show characteristic differences among the urban and rural communities. Daily screening numbers in the rural and urban communities were compared and differences were noted as factors related to feasibility.

3. Results

The originally intended 2,000 participants (1,000 in each community), was not reached. In the first ten weeks, 203 participants visited screening locations in the rural communities. Two of those women were found to be outside of the age range of the study and were not enrolled. One of the women did not complete the acceptability survey and was excluded from the acceptability portion of the data analysis. In the urban Port-au-Prince community, 171 women visited screening locations in the first ten weeks, and two were not enrolled for not meeting the study criteria.

3.1 Screening

Table 1. Screening with CareHPV, HPV Positive, and Loss to Follow-up Numbers in Rural and Urban Haiti

Rural n(%)			Urban n(%)		
Overall	HPV+	LTFU	Overall	HPV+	LTFU
201	36 (17.9)	6 (16.7)	169	38 (22.5)	22 (57.9)

Table 1 shows the number of women screened in each community, the number of HPV positive women in each community, and the number of women that were lost to follow-up for treatment. The study aim of 80% treatment uptake was met in the rural communities, with a treatment uptake of about 83.3%, but not in the urban community, with a treatment uptake of 42.1%. The prevalence of HPV in both communities was comparable to the literature. Screening numbers were much lower than expected, with

more variation in screening numbers per day in the rural communities than the urban community.

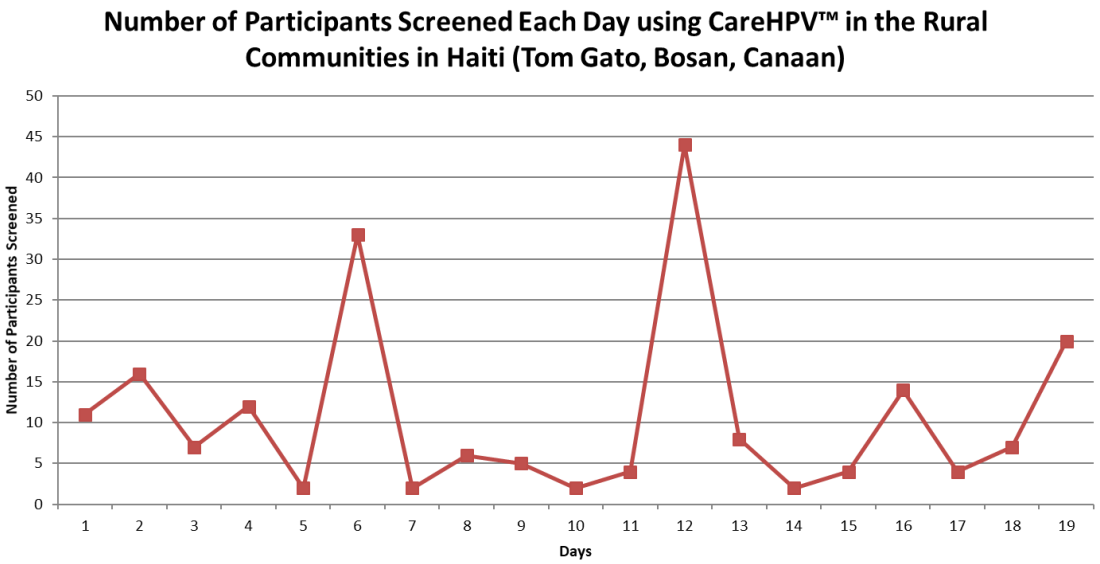

Figure 1: Number of Participants Screened Each Day using CareHPV™ in the Rural Communities in Haiti (Tom Gato, Bosan, Canaan)

Figure 1 shows the number of participants screened on each screening day in the three rural communities. Screening on days one through five, seven through eleven, thirteen through fifteen, seventeen and eighteen took place at the Carmelle Voltaire Clinic in Tom Gato. Screening on day six took place at the Fondwa Clinic in Tom Gato. Screening on days twelve and nineteen took place at a community center in Bosan. Screening on day fifteen took place in a community center in Canaan. Screening numbers were high, with 15 to 16 participants, at the start of the study in Tom Gato, dropping to an average of two participants per day. Screening days were not consecutive.

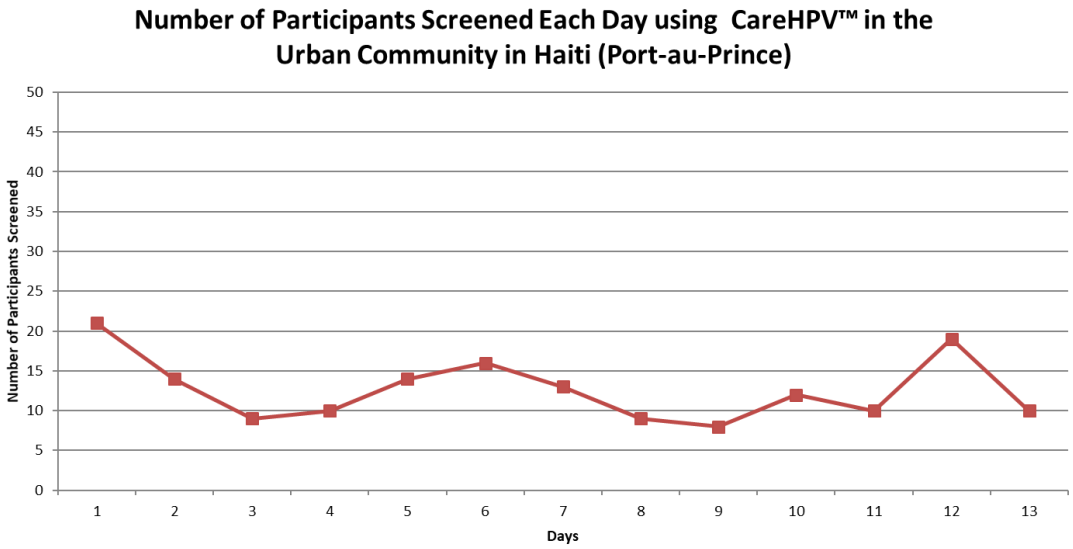

Figure 2: Number of Participants Screened Each Day using CareHPV™ in the Urban Community in Haiti (Port-au-Prince)

Figure 2 shows the number of participants screened on each screening day in the urban community of Port-au-Prince. An average number of twelve participants were screened each day in the Manitane Clinic. There was only one screening site in the Port-au-Prince community and the screening was done by physicians, nurses, or assistants working at the clinic. Screening took place about three days per week and the days were not consecutive.

3.2 Chi Square Test of Association

Loss to follow-up was significantly below the study aim in the urban community. A chi square test of association was used to estimate a p-value for the difference in loss to follow-up numbers in the urban and rural communities. The

estimated p-value of 0.01 at an alpha level of 0.05 with a X^2 value of 3.84 suggests that the difference in loss to follow-up numbers of 22 and 6 in the urban and rural communities, respectively, is significant.

3.2.1 Prevalence Rate Ratio

Since the chi square test of association estimated a significant difference in treatment uptake between the two communities, a prevalence rate ratio was calculated to estimate the rate ratio of treatment uptake in the rural communities compared to the urban communities. The estimated rate ratio was 1.98, indicating that rural participants were almost twice as likely to return to the clinic for treatment than urban participants.

3.3 Acceptability

Table 2. Results of CareHPV™ Acceptability Survey

	Rural		Urban	
	Overall (n=200)	Loss to Follow-up (n=6)	Overall (n=169)	Loss to Follow-up (n=22)
Discomfort				
None	127 (63.5)	5 (83.3)	134 (79.3)	20 (90.9)
A little	49 (24.5)	1 (16.7)	30 (17.8)	2 (9.1)
A lot	23 (11.5)	0 (0.0)	2 (1.2)	0 (0.0)
Don't know/No answer	1 (0.5)	0 (0.0)	3 (1.8)	0 (0.0)
Self-sampling preference				
At home	2 (1.0)	1 (16.7)	9 (5.3)	1 (4.5)
At the clinic	61 (30.5)	2 (33.3)	134 (79.3)	19 (86.4)
No preference	135 (67.5)	3 (50.0)	24 (14.2)	2 (9.1)
Don't know/No answer	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)
Understood procedure				
High	199 (99.5)	6 (100.0)	168 (99.4)	22 (100.0)

Low	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Neutral	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Don't know/No answer	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Instructions were clear				
High	200 (100.0)	6 (100.0)	168 (99.4)	22 (100.0)
Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neutral	0 (0.)	0 (0.0)	1 (0.6)	0 (0.0)
Don't know/ No answer	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Collected sample correctly				
High	193 (96.5)	5 (83.3)	168 (99.4)	22 (100.0)
Low	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Neutral	4 (2.0)	1 (16.7)	1 (0.6)	0 (0.0)
Don't Know/ No answer	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
Did not feel embarrassed				
High	186 (93.0)	6 (100.0)	168 (99.4)	22 (100.0)
Low	10 (5.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neutral	4 (2.0)	0 (0.0)	1 (0.6)	0 (0.0)
Don't know/No answer	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Result will be accurate				
High	16 (8.0)	1 (16.7)	168 (99.4)	22 (100.0)
Low	6 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neutral	178 (89.0)	5 (83.3)	1 (0.6)	0 (0.0)
Don't know/No answer	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Would recommend to friends and family				
High	199 (99.5)	6 (100.0)	168 (99.4)	22 (100.0)
Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neutral	1 (0.5)	0 (0.0)	1 (0.6)	0 (0.0)
Don't know/ No answer	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Table 2 shows responses to the acceptability survey used to assess participants' comfort level with using the HPV self-sampling kit. Questions directly related to acceptability included asking about the level of discomfort felt while collecting the

sample, whether they felt they had collected the sample correctly, whether they felt embarrassed, and if they would recommend the test to friends and family. The majority in both rural and urban communities reported no discomfort, at 63.5% and 79.3%, respectively. No discomfort was also reported among the majority of those lost to follow-up in both urban and rural communities. None of the lost to follow-up participants in either group reported high discomfort. The other questions related to acceptability indicated overwhelmingly high, nearly 100% acceptability. Questions on the survey asking about screening location preference, whether they understood the procedure, if instruction were clear, and if they felt the results will be accurate were analyzed as factors related to feasibility. Sixty-seven percent of the participants in the rural communities reported no preference for self-sampling location while 79.3% of participants in the urban community reported a preference for self-sampling in the clinic. Responses to understanding the instructions and feeling as if the sample had been collected correctly were almost 100% “strongly agree” or “agree.” Accuracy of results, however, was “neutral” for 89% of the rural participants and “strongly agree” or “agree” for 99.4% of the urban participants.

3.4 Demographic Characteristics

Table 3. Demographic Characteristics of All Participants, HPV Positive Participants, and Participants Lost to Follow-up in the Rural and Urban Study Populations

	Rural n(%)			Urban n(%)		
	Overall (n=201)	HPV + (n=36)	Loss to Follow-up (n=6)	Overall (n=169)	HPV + (n=38)	Loss to Follow-up (n=22)
Age						
30 - 35 y	70 (34.8)	18 (50.0)	1 (16.7)	47 (27.8)	9 (23.7)	8 (36.4)
36 - 40 y	61 (30.3)	7 (19.4)	1 (16.7)	42 (24.9)	9 (23.7)	4 (18.3)
41 - 45 y	37 (18.4)	8 (22.2)	2 (33.3)	44 (26.0)	13 (34.2)	6 (27.3)
46 - 49 y	30 (14.9)	3 (8.3)	2 (33.3)	30 (17.8)	6 (15.8)	4 (18.3)
Median	38	35.5	42	39	41	39.5
IQR	9	10	6	10	8.5	10.75
Location						
Tom Gato	114 (56.7)	23 (63.9)	2 (33.3)	--	--	--
Bosan	76 (37.8)	9 (25.0)	2 (33.3)	--	--	--
Canaan	11 (5.5)	4 (30.6)	2 (33.3)	--	--	--
Occupation						
None	11 (5.5)	4 (11.1)	2 (33.3)	20 (11.8)	5 (13.2)	3 (13.6)
Clothes maker	14 (7.0)	3 (8.3)	0 (0.0)	1 (0.6)	1 (2.6)	0 (0.0)
Nurse	3 (1.5)	1 (2.8)	0 (0.0)	4 (2.4)	2 (5.3)	2 (9.1)
Student	1 (0.5)	1 (2.8)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)
Teacher	10 (5.0)	2 (5.6)	0 (0.0)	10 (6.0)	1 (2.6)	0 (0.0)
Business owner	139 (69.2)	19 (52.8)	2 (33.3)	101 (59.8)	23 (60.5)	15 (68.2)
Laboratory technician	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
Cook/Chef	3 (1.5)	0 (0.0)	0 (0.0)	3 (1.8)	0 (0.0)	0 (0.0)
Cosmetologist	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
Manager	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.6)	1 (2.6)	0 (0.0)
Nurses Aide	1 (0.5)	1 (2.8)	1 (16.7)	2 (1.2)	0 (0.0)	0 (0.0)
Secretary	1 (0.5)	0 (0.0)	0 (0.0)	3 (1.8)	0 (0.0)	0 (0.0)
Agronomist	16 (8.0)	5 (13.9)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)
Housewife	0 (0.0)	0 (0.0)	0 (0.0)	5 (3.0)	1 (2.6)	1 (4.5)

Other/No answer	1 (0.5)	0 (0.0)	0 (0.0)	15 (8.9)	4 (10.5)	1 (4.5)
Education						
None	34 (16.9)	3 (8.3)	1 (16.7)	23 (13.6)	4 (10.5)	2 (9.1)
Elementary	82 (40.8)	15 (41.7)	2 (33.3)	46 (27.2)	11 (28.9)	5 (22.7)
Middle	23 (11.4)	3 (8.3)	0 (0.0)	79 (46.7)	21 (55.3)	13 (59.1)
High	62 (30.8)	15 (41.7)	3 (50.0)	21 (12.4)	2 (5.3)	2 (9.1)
Religion						
Roman Catholic	86 (42.8)	13 (36.1)	1 (16.7)	28 (16.6)	5 (13.2)	3 (13.6)
Protestant	52 (25.9)	7 (19.4)	1 (16.7)	129 (76.3)	26 (68.4)	16 (72.7)
Voodoo	4 (0.2)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
Other	58 (28.9)	15 (41.7)	3 (50.0)	3 (1.8)	1 (2.6)	0 (0.0)
Don't know/No answer	1 (0.5)	1 (2.8)	1 (16.7)	8 (4.7)	6 (15.8)	3 (13.6)
Marital Status						
Single	19 (9.5)	6 (16.7)	1 (16.7)	36 (21.3)	11 (28.9)	6 (27.3)
Married	68 (33.5)	9 (25.0)	1 (16.7)	98 (58.0)	21 (55.3)	10 (45.5)
Domestic Partner	109 (54.2)	19 (52.8)	3 (50.0)	32 (18.9)	5 (13.2)	5 (22.7)
Divorced	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.2)	1 (2.6)	1 (4.5)
Widowed	5 (2.5)	2 (5.6)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)
Partner Has Children Outside Marriage						
No	102 (50.7)	20 (55.6)	2 (33.3)	145 (85.8)	31 (81.6)	18 (81.8)
Yes	99 (49.3)	16 (44.4)	4 (66.7)	20 (11.8)	5 (13.2)	3 (13.6)
Don't know/No Answer	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.4)	2 (5.3)	1 (4.5)
Age of 1st Menstruation						
10 or younger	1 (0.5)	0 (0.0)	0 (0.0)	3 (1.8)	1 (2.6)	1 (4.5)
11-15 y	135 (67.2)	24 (66.7)	4 (66.7)	115 (68.0)	25 (65.8)	13 (59.1)

16-20 y	42 (20.9)	11 (30.6)	2 (33.3)	41 (24.3)	9 (23.7)	6 (27.3)
21 or older	2 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Don't know/No answer	22 (10.9)	1 (2.8)	0 (0.0)	10 (5.9)	3 (7.9)	2 (9.1)
Age of 1st sexual relationship						
12 or younger	5 (2.5)	0 (0.0)	0 (0.0)	2 (1.2)	1 (2.6)	1 (4.5)
13-20 y	103 (51.2)	19 (52.8)	1 (16.7)	93 (55.0)	24 (63.2)	14 (63.6)
21-30 y	38 (18.9)	7 (19.4)	4 (66.7)	53 (31.4)	9 (23.7)	4 (18.2)
31 or older	5 (2.5)	1 (2.8)	0 (0.0)	7 (4.1)	1 (2.6)	1 (4.5)
Don't know/no answer	50 (24.9)	9 (25.0)	1 (16.7)	14 (8.3)	3 (7.9)	2 (9.1)
Age of 1st pregnancy						
15 or younger	7 (3.5)	1 (2.8)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)
16-20 y	76 (37.8)	14 (38.9)	2 (33.3)	43 (25.4)	12 (31.6)	7 (31.8)
21-25 y	47 (23.4)	12 (33.3)	2 (33.3)	49 (29.0)	11 (28.9)	6 (27.3)
26-30 y	32 (15.9)	1 (2.8)	0 (0.0)	37 (21.9)	5 (13.2)	3 (13.6)
31-35 y	14 (7.0)	5 (13.9)	1 (16.7)	14 (8.3)	2 (5.3)	1 (4.5)
36-40 y	3 (1.5)	0 (0.0)	0 (0.0)	1 (0.6)	1 (2.6)	1 (4.5)
41 or older	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.2)	1 (2.6)	0 (0.0)
No children	22 (10.9)	3 (8.3)	1 (16.7)	19 (11.2)	6 (15.8)	4 (18.2)
Number of sexual partners						
1 or 2	108 (53.7)	19 (52.8)	4 (66.7)	104 (61.5)	21 (55.3)	11 (50.0)
3 or 4	39 (19.4)	7 (19.4)	0 (0.0)	48 (28.4)	12 (31.6)	6 (27.3)
5 or more	7 (3.5)	1 (2.8)	1 (16.7)	14 (8.3)	5 (13.2)	5 (22.7)
Don't know/No answer	47 (23.4)	9 (25.0)	1 (16.7)	3 (1.8)	0 (0.0)	0 (0.0)

The median age of the rural participants that came in for screening was 38 (IQR=9), and the median age of the urban participants that came in for screening was 39

(IQR=10). The median age for HPV positive rural participants was 35.5 (IQR=10) and for the HPV positive urban participants, 41 (IQR=8.5). The Protestant religion was more prominent in the urban community, with 76.3% of participants practicing the protestant faith, which Roman Catholicism was more prominent in the rural communities, with 42.8% practicing Roman Catholicism. The category "other" in response to the question about religion was chosen more often in the rural communities than urban communities, 28.9% and 1.8%, respectively. Participants in the rural communities were more likely to have domestic partners and have partners with children from other women. Fifty-four percent of participants in the rural communities were in domestic partnerships compared to 18.9% of the Port-au-Prince community. The difference between communities in participants having partners with children from other women was large, with 49.3% of the rural participants having partners with children from other women compared to 11.8% of the urban participants. The education level of most rural participants was lower than that of urban participants. 40.8% of rural participants attended up to elementary school while 46.7% of urban participants attended up to middle school. While still a lower percentage than participants that attended only elementary school, a larger percentage of participants attended high school in the rural communities than the urban community, at 30.8% and 12.4%, respectively. Among both rural and urban communities, business owner was the most common profession, at 69.2% for rural participants and 59.8% for urban participants. There was a larger variety

of professions in the urban community, falling under the "other" category, at 8.9% compared to 0.5% of the urban community. Loss to follow-up, defined as HPV positive participants that did not return for treatment, was 16.7% in the rural communities and 57.9% in the urban community. Loss to follow-up was spread equally among the three rural communities, with two participants lost in each for a total of six participants lost to follow-up. Non-response was higher in the rural communities than urban communities for questions, "Age of 1st sexual encounter," "Age of 1st menstruation," and "How many sexual partners have you had," at 24.9%, 10,9%, and 23.4%, respectively. For the urban community, those questions had 8.3%, 5.9%, and 1.8% non-response rates, respectively. The percentage of women with no children was comparable, at 10.9% for rural and 11.2% for urban. Due to the convenience sampling in the study, these percentages can only be applied to the study population and are not necessarily representative of the underlying population.

3.5 Prevalence

Table 4. HPV Prevalence Among Different Groups Within the Urban and Rural Study Populations

	Rural			Urban		
	n	Prevalence (%)	95% CI	n	Prevalence (%)	95% CI
Overall	201	36 (17.9)	0.124 - 0.23	169	38 (22.5)	0.162 - 0.288
Age						
30-39	125	25 (20.0)	0.13 - 0.27	82	17 (20.7)	0.119 - 0.295
40-49	73	11 (15.1)	0.069 - 0.233	81	20 (24.7)	0.153 - 0.341

Location						
Tom Gato	114	23 (20.2)	0.128 - 0.276	--	--	--
Bossan	76	9 (11.8)	0.045 - 0.191	--	--	--
Canaan	11	4 (36.4)	--	--	--	--
Children Outside Marriage						
Yes	99	16 (16.2)	0.089 - 0.235	20	5 (25.0)	--
No	102	20 (19.6)	0.119 - 0.273	145	31 (21.4)	0.147 - 0.281
Marital Status						
Married	68	9 (13.2)	0.052 - 0.213	98	21 (21.4)	0.133 - 0.295
Single	19	6 (31.6)	--	36	11 (30.6)	0.155 - 0.457
Domestic Partner	109	19 (17.4)	0.103 - 0.245	32	5 (15.6)	0.030 - 0.282
Education						
Elementary School	82	15 (18.3)	0.099 - 0.267	46	11 (23.9)	0.116 - 0.362
Middle School	23	3 (13.0)	--	79	21 (26.6)	0.169 - 0.363
High School	62	15 (24.2)	0.135 - 0.349	21	2 (9.5)	--

HPV prevalence was calculated for each of the groups in Table 4. Within each group, prevalence is comparable to the literature and there are no major differences between the urban and rural study populations. Prevalence of HPV within each group only applies to this study population as participants were recruited through convenience sampling. This study population is not necessarily representative of the underlying population.

4. Discussion

4.1 Implications for Policy and Practice

The study aim of 80% high acceptability was met in both study populations. From this data, we can conclude that the HPV self-sampling kit used in the study does not cause significant discomfort or embarrassment, is easy to use, and is likely to be recommended to friends and family among the women in this study population. However, the study aim of 80% treatment uptake was not met in the urban study population at the time of this interim analysis. This has significant implications for feasibility of self-sampling in Haiti and must be addressed prior to the implementation of a national screening program.

4.1.1 Factors Contributing to Low Screening Numbers

While treatment uptake was 83.3% in the rural study population, higher than the study aim of 80%, screening numbers were much lower than expected. Over the course of a four-and-a-half-week study period, only 201 participants were screened over nineteen days, with the majority screened on the first day of screening in each rural community. Previous studies using HPV self-sampling kits in Leogane have brought in thousands of women in equally short time periods, which is one reason treatment uptake was chosen as a study aim and not screening numbers. However, downtown Leogane, where previous studies have taken place, is considered suburban, and while the rural communities chosen for this study are located within the Leogane commune,

they are a distance away from downtown Leogane and less populated. Another point to consider is the difference in geography within the rural areas. Tom Gato is a mountainous community, with absolutely no flat land; even a short walk through the community is a strenuous hike. Participants that were physically and/or financially able to come up to the clinic in these conditions were also able to return for treatment. This geographic barrier may have been excluding women that were unable to walk long distances on mountainous terrain or did not have money to pay for a mototaxi ride. Age and occupation may also be factors for low screening numbers. Older women may be less likely to travel long, difficult distances for screening. While there is no evidence that older women have a higher prevalence of HPV, precancerous lesions may take up to twenty years to develop into cervical cancer, leaving HPV positive women in their forties at risk of developing cervical cancer. Occupation is also an important factor and may have contributed to low screening numbers; most women in Tom Gato work as peasant farmers, and on days where significant rainfall has occurred the night before (which is often), they do not leave their homes and spend the entire day tending to their crops. In the coastal communities of Bosan and Canaan, there is less mountainous terrain and it is easier to walk to community centers for testing. However, the distance between the communities of Bosan and Canaan and the Carmelle Voltaire Clinic where treatment took place is significant. This presents the same limitations as screening in Tom Gato. Screening may be higher in these coastal communities, but treatment uptake

may decrease as screening increases, due to this distance and difficulty in reaching the treatment clinic. These barriers pose two implications for policy and practice. Due to the factors that contributed to low screening numbers, we can conclude that it may be beneficial to use community health workers in going door-to-door to screen women in their homes rather than using a central location for screening in rural communities. On the acceptability survey, a majority of rural women indicated that they had no preference for screening location. The second implication is the need for more treatment clinics closer to each community in which screening is taking place to eliminate the risk of high loss to follow-up for treatment.

4.1.2 Education Before Screening

The acceptability survey used in this study asked participants to indicate whether they felt the results of the self-sampling kit would be accurate. Ninety-nine percent of the urban participants responded, "strongly agree" or "agree," while 89% of rural participants responded "neutral." The reason for the high "neutral" responses are unclear, but most of the rural participants that answered "neutral" did not seem to understand the questions and the translator did not seem to know how to translate "accuracy" properly enough for participants to understand. This may have been a difference in the understanding of the translators, their translation, or the education level of the women. While observing the administration of the surveys, it was noted that many participants asked how we would distinguish their CareHPV™ test vial from the

others after we placed it into a box with the remaining vials. The informality of the screening process, the simplicity of the HPV test kit, and being in a community center rather than a clinic, gave some participants doubt that the test would be reliable, and this may have been the cause of the high "neutral" response rate in rural participants. One potential suggestion for a national program would be to distribute educational materials about the accuracy of the test in case women in rural areas are hesitant to undergo screening based on their mistrust that the test will be accurate. "Educational materials" would most likely be given orally by community health workers going door-to-door, as most women in the rural communities that took part in the study were illiterate. Giving information about the kit itself may help with screening rates and treatment uptake if women are not comfortable with the accuracy and reliability of the test.

4.1.3 Urban Loss to Follow-up

At the time of this interim analysis, loss to follow-up in the urban study population was significantly higher than loss to follow-up in the rural communities, with rural study participants almost twice as likely to complete treatment than urban study participants. The reasons for this high, unexpected loss to follow-up are unknown, and must be investigated further before beginning a national screening program. Because the study reported here is an interim analysis, it allows time for changes and modifications to the study before a final report or final conclusions are made. It was

recently determined that the cryogun in Port-au-Prince had to be sent out for repair, which caused the clinical staff to get behind in treating the HPV positive women. This may explain the apparent loss to follow up in the urban community. However, as a result of this report, the clinic in Port-au-Prince is reviewing the protocol to ensure that study protocol is being followed and that each participant is being contacted up to three times. If these measures do not completely address the high loss to follow-up for the remainder of the study, a more in-depth investigation will be initiated to uncover the explanation for this paradoxical finding.

4.2 Implications for Future Research

The study reported here is an interim analysis of the overall feasibility study. The study is currently in continuation in both the rural and urban communities, with the suggested changes and improvements incorporated. Perhaps for future studies, particularly if the high urban loss to follow-up is not addressed within this study, a qualitative component may be helpful to assess potential reasons for the high loss to follow-up. Future studies may also be necessary in other regions and communities in Haiti since feasibility could differ among different communities with their unique characteristics.

4.3 Strengths and Limitations

This study has many strengths and limitations. Strengths include the study being a realistic simulation of a national screening program, use of two different types of communities (rural and urban), and that it is an interim analysis, with the opportunity to make changes and improvements before making final conclusions.

As previously mentioned, one of the limitations of the study was the geographic barriers in the Tom Gato community that may have inhibited women from coming for screening that were physically and/or financially unable to. Another limitation of the study is that it took place in only four communities. While these communities do represent rural and urban Haiti, the test kit may not produce the same feasibility results as seen in this study. More information about other communities may be needed during the implementation of a national screening program. The rural communities in this study are also familiar with research efforts, which serves as the third limitation of the study. Family Health Ministries is very active in these communities, regularly conducting research and engaging the community in health-related programs. The high treatment uptake in the rural communities may have been due to the familiarity with research efforts, which does not represent all of Haiti; most Haitians are not familiar with research efforts and this may affect screening numbers, treatment uptake, and even acceptability of the test kit itself. One last limitation was the high non-response rate of some questions on the demographic questionnaire in the rural communities. Many

women in the rural communities declined to answer questions related to sexual and menstrual history, seeming embarrassed for the remainder of the screening time. This may have been due to using a male translator and a non-Haitian, non-Creole speaking researcher. While it did not seem to affect treatment uptake or responses on the acceptability survey, it may have impacted their decision to recommend friends and family to screen. It also suggests that perhaps other questions on the demographic questionnaire were not answered honestly, particularly those relating to stigmatized habits or illnesses, such as smoking or being HIV positive. A female, Haitian researcher has been employed for the continuation of this study. Perhaps if participants are still showing aversion to answering these personal questions in an informal setting, these medical history questions could be asked at the time of treatment for HPV positive participants.

5. Conclusion

Cervical cancer is one of the number one causes of death of women in Haiti and the need for a national cervical cancer screening program is evident from the high prevalence of high-risk HPV infection. Feasibility criteria as defined prior to the study were met in the rural communities but not in the urban community. While treatment uptake of 80% was met in the rural communities, low screening numbers were found to be an important factor of feasibility as well. Acceptability of the test kit was found to be overwhelmingly high in both rural and urban communities. Prevalence of HPV in both types of communities were comparable to the literature. Due to geographic barriers in the rural communities as well as participants having no preference for screening location, it may be best to screen women in their homes using community health workers for the remainder of the study as well as in a national screening program. The transient delay in treatment in the urban clinic due to malfunctioning equipment raises the importance of having back-up systems in place. Further studies, as well as the continuation of this study will contribute to presenting a strong case to the Ministry of Health for a national cervical cancer screening program in Haiti.

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