Cost of community-based human papillomavirus self-sampling in Peru: A micro-costing study

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Summary

Background Cost data of human papillomavirus (HPV) self-sampling programs from low-and-middle-income countries is limited. We estimated the total and unit costs associated with the Hope Project, a community-based HPV self-sampling social entrepreneurship in Peru.

Methods We conducted a micro-costing analysis from the program perspective to determine the unit costs of (1) recruitment/training of community women (Hope Ladies); (2) Hope Ladies distributing HPV self-sampling kits in their communities and the laboratory testing; and (3) Hope Ladies linking screened women with follow-up care. A procedural manual was used to identify the program's activities. A structured questionnaire and in-depth interviews were conducted with administrators to estimate the resource/time associated with activities. We obtained unit costs for each input previously identified from budgets and expenditure reports.

Findings From November 2018 to March 2020, the program recruited and trained 62 Hope Ladies who distributed 4,882 HPV self-sampling kits in their communities. Of the screened women, 586 (12%) tested HPV positive. The annual cost per Hope Lady recruited/trained was $147·51 (2018 USD). The cost per HPV self-sampling kit distributed/tested was $45·39, the cost per woman followed up with results was $55·64, and the cost per HPV-positive woman identified was $378·14. Personnel and laboratory costs represented 56·1% and 24·7% of the total programmatic cost, respectively.

Interpretation Our findings indicate that implementation of a community-based HPV self-sampling has competitive prices, which increases its likelihood to be feasible in Peru. Further economic evaluation is needed to quantify the incremental benefits of HPV self-sampling compared to more established options such as Pap tests.

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Keywords: Micro-costing; HPV self-sampling; Cervical cancer prevention; Peru

Abbreviations: HPV, Human papillomavirus; VIA, Visual inspection with acetic acid; LMICs, Low- and middle- income countries; WHO, World Health Organization; PEN, Peruvian Soles; USD, United States Dollars; CHW, community health worker; FTE, full-time equivalent

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Research in Context

Evidence before this study

We searched PubMed and Web of Science from 1/1/2000 to 3/1/2021 for micro-costing studies or cost-effectiveness studies of HPV self-sampling in low-and-middle-income countries (LMICs) using keywords, "micro-costing" AND "HPV self-sampl*" OR "HPV self-collect*" AND "LMICs." We also referenced Malone et al. for a systematic review of cost-effectiveness studies of HPV self-sampling, who found five studies (out of 16) conducted in the LMICs context and two from Latin American countries (Nicaragua and Mexico). Fourteen of the 16 studies found HPV self-sampling could be cost-effective against the standard of care (e.g., Pap and co-testing with HPV testing, clinician-collected HPV testing, and VIA), either as an addition to existing screening programs or a primary screening strategy. Factors associated with increased cost-effectiveness were lower testing and material cost, higher sensitivity of the test to detect cervical precancer, and longer duration of underscreening among the HPV self-sampling users. Previous studies have documented many barriers to Pap tests in Peru, such as environmental factors, fear of gynaecological exams, and shortage of laboratories and personnel. HPV self-sampling has the potential to overcome these barriers in LMICs; however, the context-specific economic evidence is limited.

Added value of this study

Our study reports on real-world implementation of HPV self-sampling from Peru. We considered three program activities: recruitment and training of the community women to sell HPV self-sampling kits (Hope Ladies); Hope Ladies offering HPV self-sampling kits in their communities and the laboratory testing; and Hope Ladies linking screened women with appropriate follow-up care. Sensitivity analyses identified the cost per kit as the main driver of the cost per person reached for cervical cancer screening. Further, our findings suggest opportunities for increased programmatic efficiency in linking HPV-positive women with appropriate care and treatment.

Implication of all the available evidence

Our findings are consistent with the body of evidence that HPV self-sampling can offer competitive prices for cervical cancer screening. Our study highlights the potential of community-based programs to improve screening coverage and minimize loss to follow-up among HPV-positive women. These findings can be used as the basis for cost-effectiveness analysis of HPV self-sampling to fill the evidence gap from LMICs.

Introduction

Cervical cancer is the fourth most common cause of cancer incidence and mortality in women worldwide, with an estimated 604,000 new cases and 342,000 deaths worldwide in 2020.[1] Nearly 90% of the new cases and deaths occur in low-and-middle-income countries (LMICs).[2] To achieve the World Health Organization (WHO)'s 2018 call for global cervical cancer elimination,[3] high coverage cervical cancer screening of women in LMICs will be essential. Globally, approximately 20% of women in LMICs have ever been screened compared to 60% in high-income countries.[4] This means that we are far from achieving the WHO's target of 70% twice-lifetime screening of women ages 35-45 and 90% treatment of cervical cancer and precancer by 2030.[5]

In Peru, cervical cancer is the leading cause of cancer deaths in women aged 15-44.[6] The age-standardized incidence rate in Peru is 23·2 per 100,000 women per year, compared to the world average of 13·1 per 100,000 women.[6] Although Peruvian women can receive a Pap test free of charge at public health centres,[7] multiple barriers toward achieving high-quality cytology programs have been identified. These include an unequal regional concentration of lab facilities and clinics, inconsistency of procedures, distance, fear of the gynaecological examination, and shame.[8-11] According to the Peruvian Demographic and Family Health Survey from 2015 to 2017, only 52·4% of women aged over 30 reported having had a Pap test in the last two years.[12]

The WHO recommends self-sampling and HPV DNA testing as an approach to increase screening uptake for women aged 30-60 years.[13] HPV self-sampling is an alternative strategy that can overcome barriers to screening because additional providers, facilities, and visits are not required for the initial part of the screening. A meta-analysis of HPV self-sampling across resource settings, ethnicities and countries, found greater screening uptake among HPV self-sampling participants than those who received Pap test, visual inspection with acetic acid (VIA), or clinician-collected HPV testing.[14] HPV self-sampling is especially pertinent in the context of the COVID-19 pandemic because it allows women to receive cervical cancer screening while minimizing their visits to health centres.

The Hope Project is a social entrepreneurship program that was initially started by the Universidad Peruana Cayetano Heredia in 2015 as a pilot project to address the barriers to cervical cancer screening.[15,16] The program now offers HPV self-sampling kits to high-income women (commercial component) at a higher price point to create a sustainable platform to offer subsidized testing (social component) to lower-income women. The commercial component targets women of higher socioeconomic status, who can purchase the HPV self-sampling kits online for 150 Peruvian Soles (PEN), equivalent to 46 US Dollars (USD) in 2018. Each kit contains a cytobrush (careBrush®), a collection vial (careHPV® collection medium, Qiagen), and a simple instruction on how to self-sample. The samples are processed using the careHPV® (Qiagen),

which was specifically developed to lower the cost of HPV DNA testing in low-resource settings.[17] In the social component, the same kit is offered door-to-door for 10 PEN (~3·00 USD) by volunteer women (known as Hope Ladies) from socioeconomically disadvantaged communities, who are trained as community health agents to promote cervical cancer screening through HPV self-sampling and receive 5 PEN (~1·50 USD) as an incentive for each kit they sell.

In Peru, community health workers (CHWs) are referred to as community health agents.[18] The International Labour Organization defines CHWs as those who "provide health education, referral and follow-up, case management, basic preventive health care and home visiting services to specific communities."[19] The traditional CHW model has been deployed along with various points of the cervical cancer screening pathway, such as education, outreach, screening (e.g., HPV self-sampling), specimen transportation, and follow-up.[20] However, many of these approaches have been found to suffer from a lack of financial and programmatic sustainability. The social entrepreneurship model presents an innovative implementation pathway, where each worker has a financial as well as a social incentive to promote health. Unlike the traditional community health worker model, women working in social entrepreneurship programs seek to become financially self-sufficient by promoting health, rather than being dependent on, or being employed by an organization.[21]

Cost is a critical component of determining implementation feasibility, sustainability, and adoption,[22] yet, economic evaluations of HPV self-sampling in LMICs are limited.[23] Estimating the costs associated with the implementation of the Hope Project can address the evidence gap and facilitate future economic evaluations such as budget impact and cost-effectiveness analysis. Further, it can inform future decision-making processes regarding the scale-up and integration of HPV self-sampling into the public health system, especially as active discussions about compensation models for CHWs are taking place in global health.[24] Therefore, we conducted this study to estimate the total and unit costs associated with the social component of the Hope Project that can be used to project impact at a larger scale.

Methods

Study Setting

The social component of the Hope Project was initiated in 2015 in the socioeconomically disadvantaged peri-urban district of Ventanilla in the region of Callao as a pilot to evaluate the feasibility and acceptability of HPV self-sampling promoted by women from the community. After a successful pilot,[25] the program was officially implemented in an additional district within Callao called "Mi Perú" and a special city project within Ventanilla called "Pachacútec" in November 2018.

In the Hope Project, the Hope Ladies initially receive six hours of training spanning two days on topics including cervical cancer, HPV self-sampling and project procedures. Upon completion of the training, the Hope Ladies raise awareness about cervical cancer, promote HPV self-sampling, and sell sampling kits to women in their communities door-to-door at a significantly subsidized price of 10 PEN (~3·00 USD). They make a profit of 5 PEN (~1·50 USD) per kit distributed, which serves as an incentive for wide dissemination. The Hope Ladies pick up the samples from the participants and bring them to a central location, which is then transferred to the laboratory once a week. The participants receive their results via text messages and by paper delivered by the Hope Ladies, and the HPV-positive women follow up for care in the public health clinics. The administrators provide ongoing logistical support to the Hope Ladies through WhatsApp and monthly training on different topics according to the evolving needs of the Hope Ladies (e.g., how to effectively connect HPV-positive women with public health clinics). The micro-costing protocol was approved by the University of Washington Human Subjects Division and the program administrators who participated in in-depth interviews provided oral informed consent. The program output was abstracted from the administrative records from November 1, 2018, to March 30, 2020.

Data source and collection

We estimated the economic cost of HPV self-sampling from the program perspective, guided by the principles of the Global Health Cost Consortium (GHCC) Reference Case.[26] The Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist is available in the supplementary material.[27] The costing source was the Hope Project, which was the only provider considered for the analysis. We used three forms of data: (1) program expense report, (2) in-depth interview with three program administrators, and (3) program procedural manual that described its activities and processes. We considered three program activities: (1) recruitment and training of the Hope Ladies; (2) Hope Ladies offering HPV self-sampling kits in their communities and the laboratory testing of the samples; and (3) Hope Ladies linking screened women with appropriate follow-up care. Due to the COVID-19 pandemic, we conducted in-depth interviews with the three program administrators virtually instead of a time-and-motion study to enumerate the materials and time spent on each activity.

Costs. We categorized costs as either fixed or variable costs. Costs were considered fixed if the amount of the inputs used stayed constant regardless of the program output over one year. Variable costs were defined as those directly related to the program output. We

estimated the financial cost (e.g., as implemented cost) and the economic cost for both fixed and variable costs. The costing data was collected in local currency units (PEN). We applied Gross Domestic Product deflators to adjust all costs to 2018 nominal values and used the 2018 average exchange rate (1·00 USD ~3·29 PEN) to convert them to US Dollars.[28] We used Excel 2018 (Microsoft, Redmond, USA) for our analysis.

Fixed costs consisted of six mutually exclusive input categories: start-up (microplanning and training), supervision and administration, overhead, capital and personnel costs. The first kit sale was made by a Hope Lady in March 2019, hence, we considered the start-up period to be November 2018 to March 2019. The start-up and capital costs were annualized over the expected useful life of the goods, using a 3% discount rate. The input categories of overhead (e.g., buildings and utilities and laboratory facility) and capital (e.g., careHPV® equipment) were shared with the program's commercial component. We assumed the cost incurred by the social sector to be 89·0% in these categories, which was the proportion of the total number of HPV self-sampling kits sold by the social component (n=4,882) compared to the commercial component (n=601).

Variable costs consisted of four mutually exclusive input categories: service delivery, laboratory costs, variable supplies, and personnel costs associated with service delivery. Service delivery referred to costs associated with activities related to HPV self-sampling kit sales, following up with the participants about their results, and helping HPV-positive women to attend their local public health clinics for care. The laboratory costs included the material and service costs associated with HPV self-sampling kits, such as consumables, delivery services, packaging, and careHPV® testing supplies. We divided the cost incurred on the expense report by the number of goods purchased to calculate the financial unit cost of items for supplies and commodity costs.

The personnel costs of persons involved in both the program's social and commercial components were calculated based on the full-time equivalent (FTE) allocated to the social sector in the program's strategic plan. The opportunity costs associated with the Hope Ladies' time and travel was measured based on the administrators' report of daily activities and the use of public transportation based on Peru's climate. We derived the Hope Ladies' time costs by using the minimum wage in Peru as of 2019, which was 930 PEN per month.[29]

We calculated the average cost of study outcome by adding the costs of all activities and dividing it by the program output measures: the number of Hope Ladies recruited and trained HPV self-sampling kits distributed and tested, and HPV-positive women-identified, and the number of participants followed up with their results (HPV-positive and HPV-negative women), and HPV-positive women attending their local public health clinic for care. Fixed costs that were allocated to the program in general (e.g., overhead, capital) were apportioned using the minutes of service producing the program output estimated by the program administrators. While the aggregate costs for each activity were assumed to be mutually exclusive of each other, the unit costs represent all costs incurred during activities along the screening pathway leading up to the output, as described in Figure 1. For example, the "cost per HPV self-sampling kit distributed and tested" was calculated by adding the variable and fixed cost of training the Hope Ladies and HPV self-sampling kit distribution, and dividing by the number of kits sold and tested. Likewise, the "cost per HPV-positive woman successfully linked to care" represents the sum of the cost of training, kit distribution, sample testing and follow-up activities after the screening, divided by the number of HPV-positive women who attended their public clinics for care.

Sensitivity analysis

We explored the impact of HPV self-sampling kit and testing cost and screening volume on the total program cost in a two-way sensitivity analysis to gauge the impact of uncertainty in parameter values. In a systematic review of cost-effectiveness analyses of HPV self-sampling,[23] the combined kit and testing cost (in 2017 USD) in LMICs varied from 9·24 USD (Uganda), 9·70 USD (India), 10·47 USD (China), 14·69 USD (Nicaragua), and 16·11 USD (Mexico).[30-32] To account for uncertainty in the cost per kit in implementation settings, we varied the kit price between 5-35 USD in increments of 5 USD in our analysis. We used this equation:

$$T(v_2\ ,\ y) = F + v_1x\ + v_2y + v_3z$$

Where T represents the total cost, F represents the total fixed costs of the Hope Project, v_1 represents the variable unit cost of recruiting and training of the Hope Ladies, x represents the number of Hope Ladies recruited and trained, v_2 represents the variable unit cost per kit distributed and tested, y represents the number of kits distributed and tested (i.e., potential screening volume), v_3 represents the variable unit cost of follow-up and linkage to care, and z represents the number of women followed up for care. For the sensitivity analysis, the variable unit costs of the three activities were assumed to be mutually exclusive of one another, meaning that the variable cost per kit distributed and tested did not include the cost of recruiting and training the Hope Ladies. The variable cost of the kit distribution (26·09 USD) included the consumable and disposable goods used to assemble and test the kits (e.g., chemical solvents and supplies), services (e.g., freight transport of supplies), and the kit components (e.g., cytobrushes, vials, and boxes). It also included the personnel and overhead costs associated with community outreach and kit distribution, such as the Hope Ladies' time and transportation costs spent

Figure 1. Hope Project Screening Pathway.

on home visits, education, sample collection, and delivery. It did not include the testing machinery, the software platform for uploading the results, or the laboratory personnel salary, as these were accounted for as fixed costs.

We increased the screening volume by 2-5 times in our sensitivity analysis, corresponding to screening coverage of 4·1%, 8·1%, 12·2%, 16·2%, and 20·3% in our catchment area, respectively. The coverage was calculated based on the number of eligible women (n=120,523) in the Callao, and nearby districts Mí Peru, and Ventanilla, ages 30-49 as reported in the 2017 Demographic Census Survey,[33] assuming that women had not been screened previously with HPV testing in these districts. We assumed that the number of Hope Ladies, HPV prevalence, and the proportion of HPV-positive women successfully linked to care stayed constant in the sensitivity analysis.

	Hope Ladies recruitment and training	HPV self-sampling kit distribution and testing	Follow-up	Total annual cost
Total and Unit Costs (2018 USD)	**(n=62)**	**(n=4,882)**	**(n=4,882)**	
Variable				
Personnel (service delivery)	$0·00	$57,806·39	$18,355·09	$76,161·48
Service Delivery	$0·00	$2,406·42	$2,529·43	$4,935·86
Laboratory (e.g. sampling supplies, laboratory consumables, delivery services, packaging, testing kits)	$0·00	$67,144·03	$0·00	$67,144·03
Variable supplies	$234·06	$0·00	$0·00	$234·06
Sub-total	**$234·06**	**$127,356·85**	**$20,884·52**	**$148,475·43**
Fixed				
Microplanning	$37·93	$964·29	$330·32	$1,332·54
Training	$623·86	$0·00	$0·00	$623·86
Supervision and administration	$583·57	$14,837·58	$5,082·70	$20,503·85
Personnel (e.g., microplanning, supervision and administration, training, laboratory)	$6,971·19	$51,614·79	$17,680·93	$76,266·91
Overhead (e.g., buildings and utilities)	$496·27	$12,618·06	$4,322·39	$17,436·72
Capital (e.g., *careHPV*® equipment)	$198·83	$5,055·40	$1,731·75	$6,985·98
Sub-total	**$8,911·66**	**$85,090·12**	**$29,148·08**	**$123,149·86**
Total annual cost (variable + fixed)	**$9,145·72**	**$212,446·97**	**$50,032·60**	**$271,625·29**

***Table 1*: Total cost breakdown by input and activities (2018 USD).**

Role of Funding Source. Thomas Francis Jr. Fellowship provided funding for data collection. The Hope Project was funded by grants from Grand Challenges Canada (TTS-1812-21131), Uniting for Health Innovation, Global Initiative Against HPV and Cervical Cancer, University of Manitoba, and the John E. Fogarty International Center (5D43TW009375-05). None of the funders had any role in the study design, implementation, the process of data collection, data analysis, interpretation, or writing of the report.

Results

During the study period, the program recruited and trained 62 Hope Ladies, who distributed 4,882 HPV self-sampling kits to women in their communities. Of the screened women, 586 (12·0%) tested positive for HPV, and of these, 365 (62·3%) were successfully linked to care at the public health clinic. The total annual program cost was 271,625·29 USD (Table 1).

The average unit cost per Hope Lady recruited and trained was 147·51 USD, and the cost per HPV self-sampling kit distributed and tested was 45·39 USD. The average cost per HPV-positive woman identified was 378·14 USD, the cost per woman successfully linked to care was 744·18 USD. The cost per woman who completed the screening pathway through the Hope Project was 55·64 USD (Table 2).

Costs associated with personnel and HPV DNA self-sampling and testing (e.g., consumables, delivery services, packaging, assays) represented 56·1% and 24·7% of the total annual cost of the program, respectively (Figure 2). The financial cost (as implemented) was 171,307·48 USD (63·1%) and the rest was opportunity cost, the majority of which was the Hope Ladies' time. The program administrators' time dedicated to meeting with health providers in local health clinics to sensitize and advocate for HPV testing and appropriate follow-up of the tested women attributed 14·2% (10,806·38 USD) of the fixed personnel costs.

From the interviews with program administrators about daily program activities, we estimated that 62 Hope Ladies collectively dedicated 33,765 hours to the program during the study period. The minutes of activity and transit is available in the supplementary material. As an employee working 1·0 FTE (including holidays and leave), each Hope Lady would have worked for an equivalent of four months. The total opportunity cost of the Hope Ladies' labour was 76,045·58 USD (1,226·54 USD per person) and consisted of 75·8% of all

	Output	Unit cost*
Unit cost per Hope Lady recruited and trained	62	$147·51
Unit cost per HPV kit distributed and tested	4,882	$45·39
Unit cost per HPV-positive women identified	586	$378·14
Unit cost per women follow up	4,882	$55·64
Unit cost per HPV-positive women linked to care	365	$744·18

***Table 2*: Program output and unit cost per activity.**
* All values represented in 2018 USD.

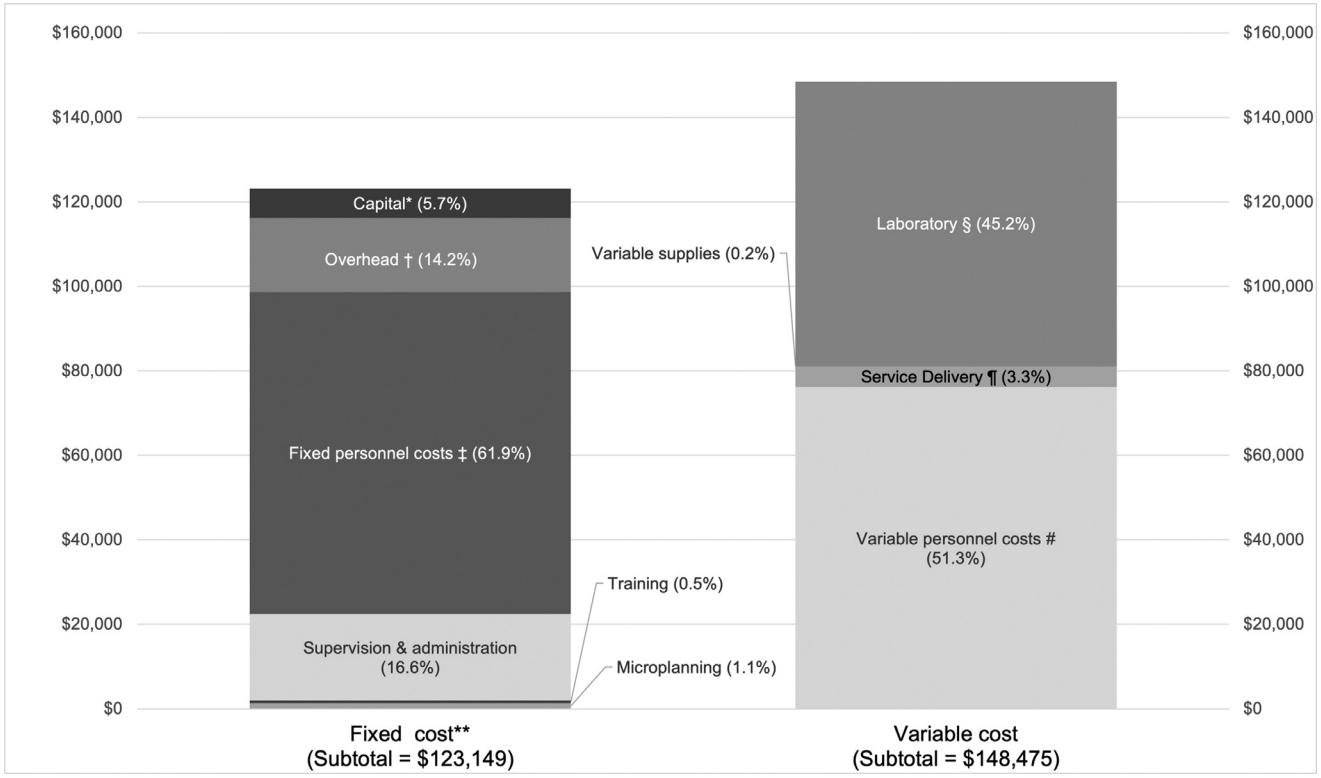

Figure 2. Cost breakdown by input categories.

* Capital: careHPV® equipment.

** Proportions represent the percentage of the input in respective categories, either "Fixed" or "Variable".

† Overhead: buildings and utilities.

‡ Fixed personnel costs: includes administrators' salary and Hope Ladies' opportunity costs associated with supervision & administration, microplanning & training, lab personnel.

§ Laboratory: consumables, delivery services, packaging, assays.

¶ Service delivery: activities related to HPV self-sampling kit distribution and testing and results follow-up.

Variable personnel costs: includes administrators' salary and Hope Ladies' opportunity costs associated with HPV kit distribution & follow-up visit.

opportunity costs incurred by the program. On average, each Hope Lady sold ~79 kits and earned about 120·00 USD over the study period, which is 10.6% of what they would have earned with a job that paid the minimum wage of 282·67 USD (930 PEN) per month for four months.

Our sensitivity analysis showed a direct relationship between varied parameters (i.e., cost per kit and screening coverage) and the total program cost, which ranged from 168,678 USD to 1,082,157 USD. Between the two parameters, the magnitude of variability introduced by cost per kit was higher than screening coverage. Holding the screening coverage constant at 4·1% (Figure 3, light grey bars), the total program cost increased by 61% when varying the cost per kit from 5 to 26 USD (price at the time of analysis), whereas the program cost increased by 147% when the screening coverage was held constant at 20·3%. In contrast, when the cost per kit was at 5 USD, varying the screening coverage from 4·1% (program output at the time of analysis) to 20·3% only increased the total program cost by 107% (168,678 USD to 349,857 USD), whereas the program cost increased by 218% when the non-cumulative variable cost per kit at 26·09 USD.

Discussion

We estimated the total and unit costs of a community-based HPV self-sampling and testing program within social entrepreneurship in Ventanilla, Callao region, Peru, from the program perspective. We assumed that the program itself was the sole provider and conducted a micro-costing study to estimate the costs associated with recruitment and training of Hope Ladies, HPV self-sampling kit distribution and testing and follow-up with screened women. We also estimated the average monetary incentives the Hope Ladies received and the time they contributed toward the program activities and compared it with what they would have earned with a job that paid the Peruvian minimum wage.

Many barriers to Pap tests have been documented in Peru, the only screening test studied nationwide.[34] The barriers include environmental factors,[10,35] fear of gynaecological exams, shortage of laboratories and cytopathologists,[10] as well as insurance status.[36] Those who have been screened are often lost to follow-up and/or cannot access the necessary treatment due to prohibitive cost or geography.[11] The reported screening coverage in Peru varies widely based on the region, study period, and how the coverage was defined.[37] For example, based on data from 2005-2008, Barrionuevo-Rosas et al. found that 72·4% of the women in Callao aged 30 to 49 reported having a Pap smear in the last five years.[36]

While the screening rates in coastal, urban regions tend to be higher than in the highlands, rainforest, or rural areas,[38] women are still subjected to socio-demographic inequities.[34] Education has been identified as a significant determinant of screening coverage among younger women living in urban areas (ages 18-29),[38] and among Pap test-eligible women (ages 30-59) in Peru.[34] Among the 98 women who were surveyed after participating in our 2015 pilot, 85 (86·7%) had secondary education or less.[15] In Ventanilla, Mi Perú, and Pachacútec, where the Hope Project operates, about 30% live in poverty, and one hospital and 13 community clinics serve the population of about 500,000.[39] In Callao where these areas are located, only ten colposcopy instruments were found in public health clinics in 2017, along with one cryotherapy and loop electrosurgical excision procedure instruments to treat precancerous lesions for the entire region.[40]

HPV self-sampling has demonstrated great potential to overcome these barriers in LMICs.[41] A four-year demonstration project in Nicaragua, Guatemala, and Honduras showed high acceptability towards HPV self-sampling among nearly a quarter-million women and feasibility of screening.[42] A large proportion (55·8% in Nicaragua and 30·0% in Guatemala) of women were screened for the first time, and the number of women screened increased substantially upon extending the option to self-sample in Honduras. In Peru, high levels of satisfaction with HPV self-sampling have been documented in the Loreto province and our 2015 pilot, where 74·2% of the users reported feeling at least satisfied with the program and 68·0% preferred the self-sampling to clinician-sampling.[15,43]

In a systematic review on cost-effectiveness studies of HPV self-sampling, Malone et al. found that only five of the 16 studies included in their analysis were from LMICs, despite bearing the majority of the global burden of cervical cancer.[23] The drivers of cost-effectiveness in LMICs varied, including screening attendance,[44] the cost of HPV self-sampling materials and testing,[45] and higher sensitivity to detect precancerous lesions.[31] While further information is needed to demonstrate the cost-effectiveness of HPV self-sampling in Peru compared to other screening methods such as the Pap test, our analysis confirms that both the cost per kit and screening coverage would be important drivers of cost-effectiveness.

Our study also shows that women from the community can play an important role in improving screening uptake among other women, especially in socioeconomically disadvantaged areas where the screening coverage is already low. The 62 Hope Ladies in the current program were instrumental in raising awareness about cervical cancer, educating their peers about HPV self-sampling and how to perform it, and widely distributing 4,882 kits over one year. In a meta-analysis, women were 2·37 times (95% CI: 1·12-5·03) more likely to participate in cervical cancer screening when health workers offered HPV self-sampling door-to-door than under standard of care conditions.[14] Another meta-analysis showed that self-sampling increased screening coverage

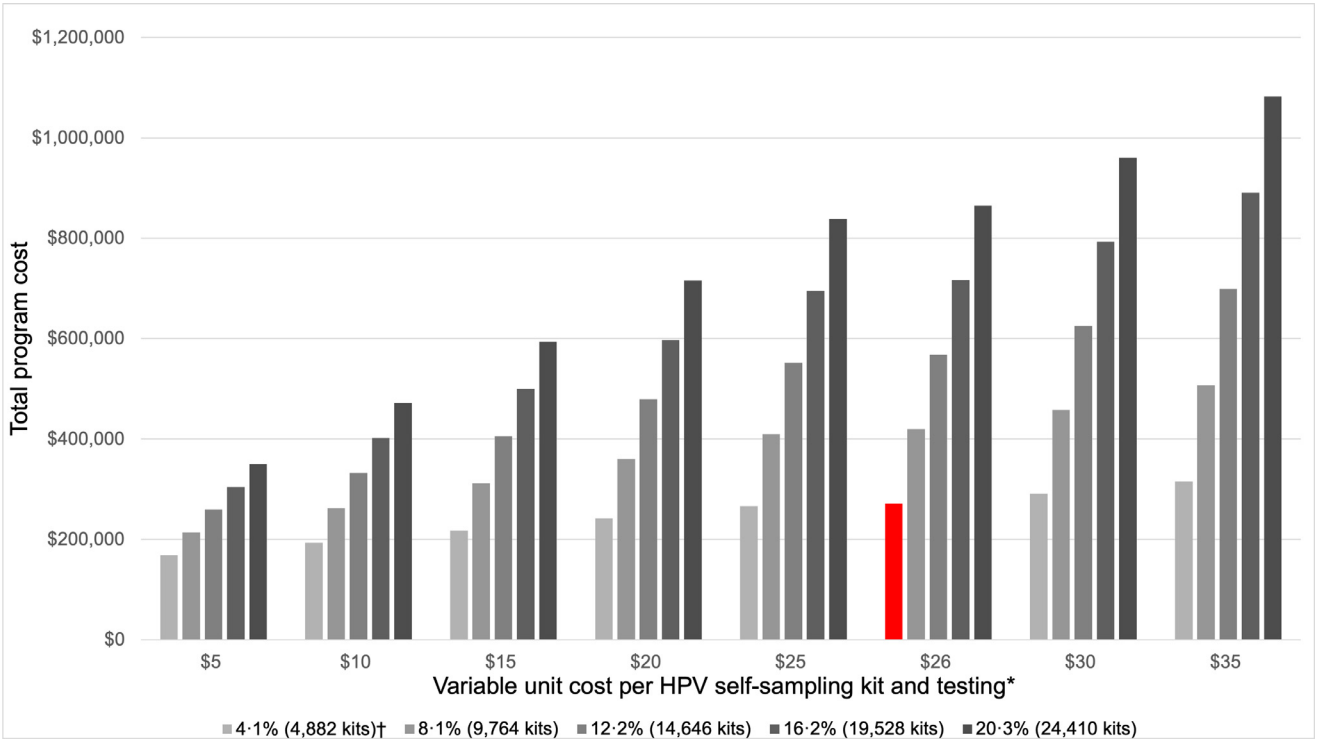

Figure 3. Two-way sensitivity analysis adjusting HPV self-sampling price per kit and screening coverage.

*The total cost of the program based on the current variable unit cost per HPV self-sampling kit and testing (26.09 USD) and coverage (4.1%) is reflected in red.

† The coverage is calculated based on the number of eligible women (n=120,523) in Callao, Mí Peru, and Ventanilla ages 30-49 reported in the 2017 Demographic Census Survey.[33]

among never- or under-screened populations.[46] In this study, the door-to-door outreach method achieved pooled participation of 94·2% in the self-sampling arms compared to 53·3% in the control arms with practitioner-sampled Pap tests, HPV tests, or VIA.

The Hope Ladies' ability to minimize loss to follow-up among HPV-positive women could impact the cost-effectiveness of HPV self-sampling against Pap tests. As of August 2020, the proportion of HPV-positive women successfully seen in their public health clinics was 62·3% in our study, comparable to 58·8-84·7% in the demonstration project in Nicaragua, Honduras, and Guatemala.[42] More women are expected to follow up once the clinics open again after the pandemic. The administrators reported that the Hope Ladies spend a significant amount of time supporting some of the screened-positive women who are reluctant to follow up for care due to long queues and fear, and sometimes accompany the women to the local public health clinics for peer support. The administrators also described the challenges of educating the providers in the local clinics about HPV testing because it is not yet widely available in the public health system in Peru. In addition to sending the test result to the screened women's phones via text messages, there is an online platform where they can access their test results at any time, although not all participants have access to the internet or computers. The Hope Project began printing and delivering individual test results shortly after the kit sales because the local health clinics were demanding to have a paper result to offer care to the HPV-positive women. Costs associated with such activities can be saved if HPV testing is widely endorsed by the public health system itself.

The Hope Ladies each contributed around four months of labour, which was captured via estimation of the opportunity cost of time in our analysis. While the discussion around volunteer versus paid work is an important topic for determining the feasibility and effectiveness of interventions as well as the value of time for CHWs, a formal assessment of the incentive scheme was out of scope for this micro-costing study. The incentive per kit (5 PEN [~1·50 USD]) was not intended to fully compensate the Hope Ladies for their time; rather, was suggested by the community women (who eventually became Hope Ladies) at the conception of the Hope Project when it was unclear how many hours they would dedicate to the program. The time commitments from the Hope Ladies were greater than anticipated at the program conception, as some of the activities (e.g., accompanying HPV-positive women to follow-up visits) were developed ad hoc voluntarily by the Hope Ladies. Although it is common to use minimum wage as a proxy of the value of volunteers' time, the rates vary widely across countries and settings (e.g., urban vs. rural).[47] In transitioning economies such as Peru where 73% of the workforce remain in the informal sector,[48] most workers do not enjoy the benefits stipulated by the local labour legislation such as social security and paid holidays.[49]

Furthermore, while valuing the Hope Ladies' time is a useful proxy for personnel cost during programmatic scale-up, it may not be a good predictor of performance that can be achieved with a formal, salaried position. For example, if the Hope Project model were to be integrated into the public health system without maintaining the incentivized payment structure, the motivation to sell the self-sampling kits among the Hope Ladies may dissipate, which might hinder the screening coverage. On the other hand, it is also possible that the Hope Ladies could sell more kits or guide more HPV-positive women to follow-up care in a salaried position for a similar amount of labour if their time would be protected instead of utilizing their spare time between tasks at home or work. A study in rural Kenya found that personnel costs of notifying the participants of the results in home-based HPV testing were three times higher than that of community health campaigns because of logistical challenges.[50] Our findings also suggest the potential to save costs by streamlining the process linking HPV-positive women with care and treatment. Further studies will be needed to determine the components of the Hope Project that should be scaled up and their impact on the cost-effectiveness of the program.

Our study has several limitations. First, all our costing data came from the Hope Project, which is the sole provider of its services, and our data may be subjected to self-reporting and recall bias. This may limit the generalizability of our findings to other settings, especially when integrating the program components into a public health system. The COVID-19 pandemic imposed several challenges in conducting our study. We were unable to perform a time-and-motion study with independent observers. Using an alternate approach, we extrapolated the amount of time dedicated by the Hope Ladies from interviews with the program administrators conducted online instead of direct observation. We did not interview the Hope Ladies directly because they have limited technological resources and it was not feasible to interview some of them virtually. Additionally, our scope did not include costs incurred in the public health clinics as they were closed. Lastly, our findings vary from the preliminary results that were published as an abstract,[51] because the current analysis includes a longer observational period (16 months instead of 12 months).

Despite the challenges, we found valuable information pertinent for the scale-up and sustainability of this model, especially in Peru. We captured the time and cost associated with the efforts of the Hope Ladies, including transportation. We also learned that the sales trend might vary by season. According to the administrators, the Hope Ladies reported that they were able to sell more self-sampling kits during the months that their children were attending schools (March-June, and

August-November). Indeed, we observed a drop in kit sales in July and another sharp decline in December (supplementary material). We also captured the variations in opportunity costs related to travel during the warmer months, as the administrators observed that the Hope Ladies spent more of their money and time on travel to conduct outreach. Since the Hope Ladies sell self-sampling kits in dense neighbourhoods where they live, this variation was unanticipated, which may have more significant cost implications in regions with less accessible geographical terrains and extreme climates. Furthermore, our findings identified specific points in the screening pathway to maximize efficiency (e.g., the process of care linkage) and challenges associated with making these improvements, as well as providing a foundation to determine essential components for scale-up and their impact on the cost-effectiveness of the program.

In conclusion, our findings indicate that implementation of a community-based HPV self-sampling has competitive prices, which increases its likelihood to be feasible in Peru. Further economic evaluation is needed to quantify the incremental benefits of HPV self-sampling compared to more established options such as Pap tests. These findings can inform costing inputs for a model of HPV infection and cervical cancer for LMICs, which can then be used as the basis for economic evaluations, such as cost-effectiveness analysis, or to model the scaling of the intervention.

Contributors

MBS: Conceptualization, Formal analysis, Investigation, Funding acquisition, Visualization, Writing - original draft, Writing - review and editing; PJG: Conceptualization, Supervision, Writing - review and editing, Resources; JLF: Data curation, Project administration, Resources; EMS: Conceptualization, Investigation, Methodology, Writing - review and editing; KA: Writing - review and editing, Supervision; SJI: Writing - review and editing, Supervision; RVB: Conceptualization, Methodology, Writing - review and editing, Supervision; SG: Conceptualization, Writing - review and editing, Supervision.

Data Sharing Statement

The data supporting the findings of this study, which does not contain any identifiable data, as well as the spreadsheet that contains the tables, figures, and the analysis are available in the supplementary materials.

Declaration of Interest

The authors declare no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.lana.2021.100160.

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