

Scale-Up of an Human Papillomavirus Testing Implementation Program in El Salvador

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Objective: The Cervical Cancer Prevention in El Salvador is a demonstration project to introduce a lower-cost human papillomavirus (HPV) DNA test into a public sector project. Started in October 2012, The Cervical Cancer Prevention in El Salvador consists of 3 phases and will ultimately screen 30,000 women. Results of phase 2 of the project are presented. The objective of this project was to compare colposcopy and noncolposcopy management for HPV-positive women.

Material and Methods: In phase 2, a total of 8,050 women, aged 30 to 49 years, were screened; 6,761 provided both self- and provider-collected specimens and 1,289 provided only provider-testing specimens. HPV results from self-collected specimens were not used in clinical management decisions. Women with provider-collected HPV-positive results were treated based on the strategy assigned to their community; the strategy was colposcopy management (CM) or screen-and-treat (ST) management if they were cryotherapy eligible or colposcopy if not eligible. Outcomes were assessed 6 months after screening.

Results: Overall, 489 (12.3%) of 3,963 women receiving CM and 465 (11.4%) of 4,087 women receiving ST tested HPV positive. In the CM cohort, 216 (44.2%) of 489 completed their intervention (203 treated, 11 diagnosed negative, 2 pregnant). In the ST cohort, 411 (88.4%) of 465 completed their intervention (407 treated, 2 diagnosed negative, 1 pregnant). Overall agreement between HPV test results from self-collected and provider-collected specimens was 93.7%, with a kappa of 0.70 (95% CI = 0.63).

Conclusions: Human papillomavirus testing with ST management resulted in an approximately twice completion rate compared with CM management. Agreement between self- and provider-based sampling was good and might be used to extend screening to women in areas that are more difficult to reach.

Key Words: cervical cancer, human papillomavirus, screening and care of human papillomavirus

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Ninety percent of new cases of cervical cancer occur in low-resource settings, but human papillomavirus (HPV) tests used for cervical cancer screening by high-resource settings are often not accessible to low-resource settings because of cost and lack of infrastructure. The careHPV test (Qiagen, Germantown, Md), a low-cost high-risk HPV screening test, was developed specifically for low-resource settings.

Because lower-cost HPV testing is a relatively new tool, the most effective strategy for public sector project implementation is unknown. The World Health Organization (WHO) has endorsed both colposcopy referral and immediate treatment as management strategies after a positive HPV test result. Strategies that employ HPV testing and immediate treatment benefit low-resource settings because they are less costly and more feasible than cytology-based methods and result in a higher proportion of women with cervical precancer receiving appropriate treatment. Several studies have been conducted with careHPV; however, these primarily investigated clinical outcomes. The public-sector implementation program presented in this article was initiated by the government, with the intention of national scale-up.

The Cervical Cancer Prevention in El Salvador (CAPE) program was launched in 2012 to identify best practices for incorporating HPV-based screening into the national cervical cancer prevention project. The CAPE is a 3-phase, 30,000-woman demonstration project that assesses the feasibility and cost-effectiveness of a screening intervention using the low-cost HPV test. The CAPE is conducted by the Salvadoran Ministry of Health (MOH), with technical support provided by the nonprofit organization Basic Health International (BHI). In phase 1 of the project screened 2,000 women. Women testing positive for HPV received 1 of 2 treatment strategies: colposcopy management (CM) consisting of colposcopy and management per local guidelines, or screen-and-treat (ST) management using visual inspection with acetic acid to determine cryotherapy eligibility, with eligible women undergoing immediate cryotherapy and ineligible women undergoing CM. In phase 1, more women in the ST cohort received treatment within 6 months compared with those in the CM cohort (117/119 [98.3%] vs 64/93 [68.8%], $P < .001$). Furthermore, ST was the most cost-effective strategy. During phase 2, a total of 8,000 women were included and the same screening strategies were used. The objective of phase 2 was to scale up the project and compare the CM and ST strategies using a larger sample size. The secondary aims were to assess the feasibility of self-sampling and to perform quality control of the local pathology system.

MATERIALS AND METHODS

Women in the Paracentral region were contacted between October 2013 and July 2014. The 4 health units that participated in phase 1 (San Pedro Perulapán, San Rafael Cedros, Apastepeque, and San Sebastián) were included in phase 2, and 4 health units (Candelaria, Tecoluca, Suchitoto, and Periferica de San Vicente) that provide primary preventive care in the Paracentral region of El Salvador were added. The health units were selected with the goal of contacting 10,000 women to meet the target of screening

8,000 women, assuming 80% follow-up. According to the 2007 national census, there were 21,968 women aged 30 to 49 years (the age range targeted in CAPE) living in these health catchment areas.

Women were excluded if they were known to be pregnant, had a hysterectomy, had any history of loop electrosurgical excision procedure (LEEP) or cryotherapy, or previously had cervical precancer or cancer. According to government census, the 8 health units served populations similar in age, poverty level, and education.

All women were to have both self- and provider sampling with the HPV test. However, because of a power failure that interrupted the refrigeration of the tests and invalid runs caused by human error, a limited number of testing kits were available for self-sampling and these reasons, self-sampling was not available for all women.

Case management was based on HPV results from provider-collected samples only, because self-sampling is not yet a proven method of screening. Women who tested HPV positive were managed by either the CM or ST strategy. Human papillomavirus negative women were instructed to repeat screening in 5 years.

TABLE 1. Demographic and Screening Characteristics of Participants by Management Strategy Cohort and Recruitment Period

	Total		CM cohort		Screen-and-treat cohort		p
	n	Col %	n	Col %	n	Col %	
Total	8,050	100	3,963	100	4,087	100	
Age, mean, median, y			37.8, 37		38.3, 38		<.01
Highest education							
None	1,165	17.2	515	15.4	650	19.0	
Elementary	3,850	56.9	1,955	58.5	1,895	55.4	
Middle school	1,746	25.8	872	29.1	874	25.6	<.01
Missing	1,289		621		668		
No. children							
0-1	993	12.5	565	14.5	428	10.6	
2-3	4,210	53.0	2,050	52.6	2,160	53.4	
4+	2,740	34.5	1,283	32.9	1,457	36.0	<.01
Missing	107		65		42		
Age of first intercourse, y							
<16	1,944	24.4	879	22.3	1,065	26.4	
16-19	3,033	38.1	1,469	37.3	1,564	38.8	
20+	2,988	37.5	1,587	40.3	1,401	34.8	<.01
Missing	85		28		57		
Lifetime sexual partners							
0-1	3,757	46.6	1,901	48.6	1,856	45.4	
2	2,491	30.9	1,195	30.5	1,296	31.7	
3	1,211	15.0	561	14.3	650	15.9	
4+	541	6.8	256	6.5	285	7.0	.03
Missing	50		50		0		
Last screen for cervical cancer							
Never	825	10.4	314	8.0	511	12.8	
>3 y ago	2,270	28.7	1,095	27.9	1,175	29.5	
3 y ago	4,807	60.8	2,514	64.1	2,293	57.6	<.01
Missing	148		40		108		
Residence							
Rural	6,641	82.5	3,172	80.0	3,469	84.9	<.01
Urban	1,409	17.5	791	20.0	618	15.1	
Screening location							
Campaign	6,689	83.1	3,236	81.7	3,453	84.5	
Home	331	4.1	113	2.9	218	5.3	
Health unit	1,030	12.8	614	15.5	416	10.2	<.01

guidelines for regions lacking sufficient infrastructure for period, and management strategy. Variables with of less
 agement, all eligible HPV-positive women received immediate data .10 in unadjusted models were entered into the multivariate
 cryotherapy even if no lesion is visualized. Human papillomavirus model using backward elimination. The sta-
 positive women in the ST cohort were referred to a follow-up tests were used to compare agreement between provider- and
 with a physician gynecologist who performed visual assessments collected sampling methods. The significance level was set
 for treatment (VAT). The purpose of VAT is to assess for control 05, and all statistical analyses were conducted using Stata Ver-
 dications to cryotherapy, which include pregnancy, large cervix 12 (StataCorp LP, 2011, College Station, Tex).
 lesion or lesion that extends into the endocervical canal, the national ethical review board of El Salvador and the
 suspected cancer. Referrals for colposcopy and further management 12 (StataCorp LP, 2011, College Station, Tex).
 ment were provided for women with any contraindications.

In both cohorts, follow-up for HPV-positive women was con-
 sidered completed if treatment occurred within 6 months of screen-
 ing. For women referred for colposcopy (ie, either in the CM cohort
 or in the ST cohort and ineligible for cryotherapy), follow-up was
 completed if 1 of 3 outcomes occurred within 6 months of diagnosis:
 (1) normal colposcopic impression (no biopsy or endocervical
 curettage [ECC] performed), (2) normal biopsy and/or ECC, or
 (3) treatment based on biopsy or ECC results was completed within
 6 months. For women in the ST cohort, follow-up was considered
 completed once they were treated with cryotherapy. The BHI research
 team actively managed the treatment strategies. Five nurses were
 hired specifically to monitor loss to follow-up. If a patient did not
 attend her colposcopy appointment after 6 months, a health
 member contacted a Ministry of Health supervisor.

RESULTS

At total of 8,205 women were contacted and asked to partic-
 ipate in the screening program at the local health center within
 15 days, and 81.1% participated (6,656/8,205). Additional recruit-
 ment strategies were used to achieve the target goal of screening
 8,000 women: (1) providers visited women at home and offered
 home testing with the sample collected by a health promoter (1,312)
 (following Ministry of Health guidelines, women with cervical intraepithelial
 neoplasia grade 1 (CIN 1) were treated with cryotherapy at home health
 centers for other reasons). As a result of these strategies, a total of 8,050
 women were screened. Table 1 presents demographic screening characteristics
 by management cohort. Women in the ST and CM cohorts were
 statistically but not meaningfully different in age, highest education
 level, parity, age at first sexual intercourse, number of lifetime sexual
 partners, time since last screen, screening location, and residence. Women
 in the ST cohort were more likely to have no education than women in
 the CM cohort (515/3,342 [15.4%] vs 650/3,419 [19.0%]; .001). Women in
 the CM cohort were more likely than women in the ST cohort to have been
 screened within the past 3 years (2,514/3,963 [64.1%] vs 2,293/4,087 [57.6%])
 and to have been screened at a health unit (614/3,963 [15.5%] vs 416/4,087
 [10.2%]). Table 2 presents summaries of outcomes within 6 months of
 screening by management cohort (a more detailed description is provided
 in Figures 1A, B). Women in the CM cohort were more

TABLE 2. Compliance by Management Cohort

	CM cohort		Screen-and-treat cohort		
	n	%	n	%	p
Totals					
Approached by health promoters and given appointment	3,556		4,649		
Screened at appointment	3,202	90.0	3,454	74.3	<.001
Screened at home without clinic appointment	114		218		
Screened opportunistically at visit to the health unit	647		415		
Total women screened	3,963		4,087		
Total testing HPV positive among screened	489	12.3	465	11.4	.18
Completed screening project (i.e., HPV negative or HPV-positive with follow-up)					
Completed among screened	3,690	93.1	4,033	98.7	<.001
Completed among HPV-positive women (completion with follow-up)	216	44.2	411	88.4	<.001
Screened HPV positive but failed to complete follow-up					
Did not attend colposcopy within 6 mo	102	20.9			
Did not receive treatment within 6 mo	171	35.0			
Did not get cryotherapy			11	2.4	
Did not get colposcopy/treatment			43	9.2	

^aAn unknown number of women screened opportunistically at the clinic may have been previously approached at their home by a health promoter.
^bTwo HPV+ women in the CM arm and 1 HPV+ woman in the ST arm were pregnant at the time of colposcopy and/or screening and are considered completing colposcopy and/or treatment.
^cAmong 408 women deemed eligible for cryotherapy, and 11 were not treated within 6 months.
^dFifty-six women were deemed ineligible for cryotherapy and referred to colposcopy.

