OPEN

Introducing a High-Risk HPV DNA Test Into a Public Sector Screening Program in El Salvador

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Objective: In a primary human papillomavirus (HPV) screening program, we compared the 6-month follow-up among colposcopy and noncolposcopybased management strategies for screen-positive women.

Materials and Methods: Women aged 30 to 49 years were screened with HPV DNA tests using both self-collection and provider collection of samples. Women testing positive received either (1) colposcopy management (CM) consisting of colposcopy and management per local guide-lines or (2) screen-and-treat (ST) management using visual inspection with acetic acid to determine cryotherapy eligibility, with eligible women undergoing immediate cryotherapy. One thousand women were recruited in each cohort. Of these, 368 (18.4%) of 2000 women were recruited using a more intensive outreach strategy. Demographics, HPV positivity, and treatment compliance were compared across recruitment and management strategies. **Results:** 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). Women recruited through more intensive outreach were more likely to be HPV positive, lived in urban areas, were more educated, and had higher numbers of lifetime sexual partners and fewer children.

Conclusions: Women in the CM arm were less likely to complete care than women in the ST arm. Targeted outreach to underscreened women successfully identified women with higher prevalence of HPV and possibly higher disease burden.

Key Words: careHPV, human papillomavirus, cervical cancer, screening program, Latin America

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uman papillomavirus (HPV) tests used for cervical cancer screening in higher-resource settings are not accessible to low-resource settings because of cost and lack of infrastructure. An HPV screening test has been developed specifically for lowerresource settings (careHPV Test; QIAGEN, Gaithersburg, MD). Clinical studies have shown that its sensitivity for cervical precancer and cancer approaches that the US Food and Drug Administration–approved Hybrid Capture 2 Test (QIAGEN) on which careHPV was based.^{1,2}

This test has made it feasible to implement HPV screening programs in some lower-resource countries nationwide. However, the most effective strategy for implementation of HPV testing in a public sector program is unknown. High-resource settings generally used colposcopy management (CM) strategies for screenpositive women. However, CM strategies require significant infrastructure and trained personnel, both of which are lacking in the lower-cost settings. Therefore, the World Health Organization (WHO) has endorsed colposcopy referral or immediate treatment after a positive HPV test. A study of an HPV testing program in South Africa showed that providing immediate treatment and eliminating the colposcopy step were more clinically effective and less costly than a CM strategy.³

The Cervical **Cancer Prevention in El Salvador (CAPE)** program was launched in 2011 to identify best practices for incorporating HPV-based screening and management into its national cervical cancer prevention program. The CAPE program is a 3-phase, 30,000-woman demonstration program that assesses the feasibility and cost-effectiveness of a screening and treatment intervention using this HPV test. The CAPE program is administered by the Salvadoran Ministry of Health (MOH) with technical support provided by the nonprofit organization, Basic Health International.

Phase 1 objectives were to the following: (1) screen 2,000 women aged 30 to 49 years living in the Paracentral region of El Salvador; (2) compare HPV-positive women's compliance with 2 management strategies; (3) demonstrate increased participation of underscreened and unscreened women; and (4) determine patient preference for self-sampling or provider sampling.⁴ The results of objectives 1 and 2 are discussed in detail in this article. The results of 3 and 4 are discussed briefly here and in more detail in other publications.^{4,5} The primary objective of this descriptive manuscript is to compare colposcopy and non-CM strategies for HPV-positive women. The secondary objectives included program evaluation, including examination of self-sampling feasibility, reliability of pathology, and assessment of a more intensive recruitment strategy.

MATERIALS AND METHODS

The MOH initiated phase 1 of CAPE at 4 health units (San Pedro Perúlapan, San Rafael Cedros, Apastepeque, and San Sebastián) that provide primary preventive care in the Paracentral region of El Salvador. These health units were selected with the goal of contacting 2,500 women to meet the target of screening 2,000 women, assuming 80% follow-up. According to 2007 national

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census data, 11,046 women aged 30 to 49 were living in these health units' catchment areas. Women were excluded if they lived outside the catchment area, were known to be pregnant, had a hysterectomy, loop electrosurgical excision procedure (LEEP), or cryotherapy, or previously had cervical precancer or cancer. According to government census, the 4 health units served populations similar in age, poverty level, and education.

Community census records were used to identify women aged 30 to 49 years without recent cervical cancer screening. Health promoters contacted women with no record of recent screening and invited them to attend an educational session about HPV testing at their local clinic. The program was internally evaluated by the MOH at periodic intervals. Concerns were raised about the low number of underscreened women who were being recruited. Only 10.7% (167/1565) of women enrolled and screened with HPV testing had either never been screened or not been screened in the past 5 years.

Recruitment was then changed to prioritizing identification of underscreened or unscreened women. Instead of using only community health records, these records were cross-referenced with local health unit Pap records to obtain the women's most current screening histories. This more intensive outreach strategy identified an additional 368 women eligible for screening with HPV testing. Among the 306 women for whom screening records were available, 147 (48%) were unscreened or underscreened. To increase participation, the clinic-based educational session was replaced with individual instruction at home for most women (96%) recruited with intensive outreach. Women were then offered an appointment for screening at a nearby clinic.

All participants provided self-collected and provider-collected specimens. The decision to include self-sampling was made by the MOH to assess the feasibility of using this modality in a larger screening program. However, the MOH decided only to use HPV results from provider-collected samples for clinical management decisions until self-collected sampling was approved.

Women who tested HPV positive on the provider-collected sample were managed with 1 of the following 2 strategies: (1) referral to colposcopy followed by treatment as needed (CM) or (2) screenand-treat (ST) management using visual inspection with acetic acid to determine cryotherapy eligibility, with eligible women undergoing immediate treatment and ineligible women referred for colposcopy (ST). Human papillomavirus–negative women were instructed to rescreen in 5 years.

Follow-up strategies for HPV-positive women varied by health unit. Two health units followed a CM strategy and 2 health units followed an ST strategy. Treatment approaches were not randomized because CAPE was not designed as a research study but rather as a demonstration program. The research study design adhered to principles of implementation science and similar communities were chosen to have different interventions for treatment.

In the ST cohort, HPV-positive women were given a visual inspection with acetic acid examination by a physician-gynecologist at their follow-up visit. In accordance with recent WHO guidelines for treatment in regions where there is insufficient infrastructure for management, all eligible HPV-positive women received immediate cryotherapy even if no lesion was visualized.⁶ Contraindications to treatment included pregnancy, large cervical lesion, suspected cancer, and/or lesion extended into the endocervical canal.⁶ Referrals for colposcopy and further management were provided for women with any contraindications.

For HPV-positive women in the ST cohort eligible for cryotherapy, completion of follow-up was achieved if cryotherapy occurred within 6 months of screening. For women referred for colposcopy (i.e., in the CM cohort or in the ST cohort and not eligible for cryotherapy), follow-up was completed if 1 of 3 following outcomes occurred within 6 months of diagnosis: (1) normal colposcopic impression (no biopsy or endocervical curettage [ECC]); (2) normal biopsy and/or ECC; or (3) treatment based on biopsy or ECC results was completed. Following MOH guidelines, women with cervical intraepithelial neoplasia grade 1 (CIN 1) were treated with cryotherapy. Women with CIN grade 2 or 3 (CIN 2/3) received cryotherapy, LEEP, or a hysterectomy, as determined by the managing physician.

 χ^2 tests, Fisher exact tests, and 2 sample t tests were used to assess associations across recruitment periods and management strategies between demographic variables (age, education attainment, residential area, and number of children), sexual history (age at sexual initiation and number of lifetime sexual partners), time since last screening, HPV positivity, and follow-up compliance. Logistic regression was used to explore relationships between HPV positivity and demographic and screening characteristics, recruitment period, and management strategy. Variables with p values of less than .10 in unadjusted models were entered into the multivariate model using backwards elimination. The κ statistic and McNemar tests were used to compare agreement between provider- and self-collected sampling methods. The significance level was set at .05 and all statistical analyses were conducted using STATA Version 12 software (StataCorp LP, 2011, College Station, TX).

The University of Pittsburgh and the national ethical review board of El Salvador granted institutional review board approval to analyze the data.

RESULTS

Of the women invited to attend an educational session, 1,049 (74.3%) of 1,239 women in the CM cohort and 981 (79.2%) of 1,410 women in the ST cohort attended. Health promoters scheduled a screening appointment within 15 days of the session for the 958 (91.3%) of 1,049 women in the CM cohort and 938 (95.6%) of 981 women in the ST cohort eligible for screening. Fewer women in the CM cohort attended their screening appointment compared with women in the ST cohort (751/958 [78.4%] vs 881/938 [93.9%]; p < .001). Although the subjects were not randomized, the communities where the interventions were done were similar in size and women were similar in terms of important risk factors such as age at first intercourse and number of lifetime partners.

Table 1 presents demographic and screening characteristics of women screened, stratified by management cohort. Women in the CM cohort had less education (p = .003) and were more likely to have been screened within the past 3 years (74.0% vs 54.5%; p < .001) compared with women in the ST cohort. Among women contacted during more intensive outreach, those in the ST cohort had fewer children (p = .04), were less likely to have been screened within the past 3 years (57.2% vs 38.1%; p = .003), and were more likely to have urban residence (87.4% vs 16.9%; p < .001) compared with women in the CM cohort (data not in table).

Table 2 presents results regarding screening outcomes, treatment, and compliance, stratified by management strategy. Human papillomavirus positivity did not differ significantly between CM and ST strategies (9.3% vs 11.9%, respectively; p = .06). In the CM cohort only, 6 (6.5%) of 93 women had a normal colposcopy examination or biopsy; in the ST cohort, colposcopy was only performed if women were not eligible for cryotherapy and all (8/8) had CIN 1 or worse biopsy.

More women in the CM cohort did not attend colposcopy or receive adequate treatment within 6 months of screening compared with women in the ST cohort (23/93 [24.7%] vs 1/119 [1.0%], respectively; p < .001). Therefore, more women in the

	Total		Colposcopy management cohort		Screen and treat cohort		
	n	%	n	%	п	%	р
Total	2000	100.0	1000	50.0	1000	50.0	
Age, mean (median), y	38.4	(38)	38.5	(38)	38	.3 (38)	.61
Highest education							
Elementary/none	1334	67.0	651	65.4	683	68.6	
Middle school	399	20.0	228	22.9	171	17.2	
High school or higher	259	13.0	117	11.7	142	14.3	.003
Missing	8		4		4		
No. children							
0–2	631	31.7	316	31.7	315	31.7	
3–4	843	42.4	407	40.9	436	43.9	
5+	516	25.9	273	27.4	243	24.4	.25
Missing	10		4		6		
Age of first intercourse, y							
<16	363	18.5	191	19.6	172	17.4	
16-19	1009	51.4	494	50.8	515	52.0	
20+	591	30.1	288	29.6	303	30.6	.44
Missing	37		27		10		
Lifetime sexual partners							
1	1088	54.4	559	55.9	529	52.9	
2	517	25.9	240	24.0	277	27.7	
3+	395	19.8	201	20.1	194	19.4	.17
Last screen for cervical can	cer						
3+ y ago or never	659	35.1	249	26.0	410	43.7	
3 y ago	1218	64.9	707	74.0	511	54.5	<.001
Missing	123		44		62		
Residence							
Rural	1854	92.7	958	95.8	896	89.6	
Urban	146	7.3	42	4.2	104	10.4	<.001

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

ST cohort received treatment within 6 months compared with those in the CM cohort (117/119 [98.3%] vs 64/93 [68.8%], respectively; p < .001).

The time in days between screening and treatment was shorter for the ST group than for the CM group during standard recruitment. The mean and median wait time between screening and treatment for CM was 112 and 114 days for CM compared with 26 and 14 days for ST (p < .001).

There was high percentage of women in the CM group given cryotherapy because of the high prevalence of CIN 1 diagnosed by the local pathologist, cryotherapy being the standard treatment in El Salvador for a CIN 1 biopsy result. Women with CIN 1 in the CM cohort, as diagnosed by the local pathologist, received the same treatment as those in the ST cohort after the intervening colposcopy.

During phase 1, 89 women had colposcopy with biopsy. Local pathologists made the initial diagnosis of all specimens, and the treatment course was based on the primary pathologist's diagnosis. Preliminary data indicated an unusually high rate of CIN 1 and an unusually low rate of CIN 2 or worse. An expert gynecologic pathologist conducted quality assurance on 86 biopsy specimens (3 specimens were unavailable for review, see Table 3). The expert pathologist diagnosed fewer cases of CIN 1 than did the local pathologist (6 vs 79; p < .001) and more cases of CIN 2 or more severe (19 vs 7; p < .001).

In the univariate analysis (see Table 4), testing HPV positive was associated with education (reference group, women with elementary education/none; odds ratio [OR], 1.5 for women with high school education or higher; p = .03); recruitment strategy and management cohort (reference group, women in the CM cohort and standard recruitment group; OR, 2.2 for women in the ST cohort and more intensive outreach; p = .005); and number of lifetime sexual partners (reference group, women with 1 lifetime partner; OR, 2.1 for women with 2–3 lifetime partners; p < .001; and OR, 2.6 for women with more than 4 lifetime partners; p < .001).

Overall agreement between self-collected and providercollected HPV samples was 98% with a κ value of 0.75 (p = .4; see Table 5). Among 1,998 samples tested for HPV, 42 (2.1%) tested positive on self-collection and negative on provider collection and 5 (2.6%) tested negative on self-collection and positive on provider collection. Nineteen women with CIN 2 or more severe diagnoses tested positive for HPV on provider collection; of these, 16 (84.2%) tested positive on self-collection.

DISCUSSION

Although both the CM and ST strategies were successful in managing the care of women who tested HPV positive, the ST cohort led to a significantly higher number of women who completed treatment at 6 months (98.3% vs 68.8%). Although it may seem obvious

	Colposcopy management cohort		Screen and treat cohort		
	n	%	n	%	р
Total	1000		1000		
% HPV positive ^a	93	9.3	119 ^b	11.9	.06
Diagnosed without CIN	6	6.5	0	0.0	.005
Normal colposcopy impression	4	4.3	0	0.0	
Normal biopsy	2	2.2	0	0.0	
Treated within 6 mo of screening visit	64	68.8	117	98.3	<.001
Immediate cryotherapy after visual inspection triage	0	0.0	110	92.4	
Cryotherapy for CIN 1 biopsy ^c	48	51.6	7	5.9	
Cryotherapy for CIN 2+ biopsy ^{cf}	8	8.6	0	0.0	
Cryotherapy for CIN 3 biospy ^c	5	5.4			
Hysterectomy for CIN 3 biopsy ^c	3	3.2	0	0.0	
Lost to follow-up	23	24.7	1	0.8	<.001
Did not attend colposcopy within 6 mo ^d	11	11.8	0	0.0	
Did not receive treatment within 6 mo^e	11	11.8	1	0.8	
Inadequately treated	1^f	1.1	0	0.0	
Mean (median) time (days) between:					
Screening specimen collected and results to woman		26.0 (16)		23.2 (14)	.03
Screening results to woman and colposcopy		50.3 (46)		34 (25.5)	.17
Colposcopy and treatment		48.6 (46)		55.7 (52)	.43
Screening and treatment		112.6 (113)		26.1 (14)	<.001

TABLE 2. Screening and Management Outcomes by Management Strategy Cohort and Recruitment Period

CIN indicates cervical intraepithelial neoplasia.

^aClinician-collected sample.

^bOne woman testing HPV positive was found to be without a cervix and was not followed further.

^cWorst histology diagnosis by local and expert pathologist.

^dTwo women did not attend colposcopy because they were pregnant and 1 had a hysterectomy.

^eIn the conservative management cohort, 1 woman was not treated for CIN 1, 1 woman was not treated for CIN 2, and 9 women were treated after 6 months (6 for CIN 1, 2 for CIN 3, and 1 cryotherapy for misdiagnosed adenocarcinoma). In the screen and treat cohort, 1 woman was treated after 6 months (1 for CIN 1).

^fReceived cryotherapy for adenocarcinoma.

that an immediate treatment would yield a greater number of managed cases, the extent of this effect was higher than expected particularly because this was a highly controlled, MOH-driven project.

Although the ST strategy does introduce the risk of overtreatment, the CM strategy poses a risk of undertreatment because of increased likelihood of noncompliance with 1 or more of the multiple visits needed to complete the management protocol. We believe that the benefits of the ST approach far outweigh the risk of overtreatment because the adverse effects of cryotherapy are minimal, particularly in the age group targeted for screening in low- and middle-income countries where cervical cancer rates are extremely high. There is even some evidence that a cryotherapy procedure is protective against future HPV infection and precancer.⁷⁻¹⁰ For this reason, the WHO recommendations for cervical cancer screening in low-resource settings include HPV screening, followed by immediate triage and treatment.¹¹ Furthermore, the CM strategy would likely result in an equal number of cryotherapy treatments as the ST strategy because MOH guidelines dictate cryotherapy for women diagnosed with CIN 1 on biopsy a common finding for women screening HPV positive. In this pilot, 80% of women who completed follow-up in the CM arm had cryotherapy, compared with 100% in the ST cohort.

Outreach and educational sessions were critical factors associated with participation. Although 3 quarters of women contacted during standard recruitment, 2,030 (76.1%) of 2,515 women attended **TABLE 3.** Worst Histopathology Result of Biopsy by Local and Expert Pathologists

Worst diagnosis	Worst dia				
by expert pathologist	Normal	CIN 1	CIN 2	CIN 3	Total
Normal	2	57	1	1	61
CIN 1	0	6	0	0	6
CIN 2	0	8^a	0	0	8
CIN 3	0	5^b	1	3 ^{<i>c</i>}	9
Adenocarcinoma	0	1	1^d	0	2
Missing	1	2	0	0	3
Total	3	79	3	4	89

CIN indicates cervical intraepithelial neoplasia.

^aOne CIN 2 diagnosis was detected by ECC because biopsy result was unsatisfactory. One CIN 2 diagnosis tested HPV negative using the self-collected sample.

 $^b \mathrm{One}\ \mathrm{CIN}\ 3$ diagnosis was detected by ECC because biopsy result was CIN 2.

^cOne CIN 3 case tested HPV negative using the self-collected sample.

 $^d \mbox{One}$ a denocarcinoma case tested HPV negative using the self-collected sample.

	HPV positivity		Unadjusted odds ratio		Adjusted odds ratio		
	Total	%	р	(95% CI)	р	(95% CI)	р
Total	2000	10.6					
Age, y							
30–34 (ref)	642	11.5		1.0			
35–39	505	10.7		0.92 (0.63-1.33)	.66		
40-44	492	10.8		0.93 (0.64-1.35)	.69		
45–49	360	8.3	.15	0.70 (0.45-1.09)	.11		
Management strategy cohort and recruit	ment period						
CM and standard recruitment (ref)	751	8.5		1.0		1.0	
ST and standard recruitment	881	11.2		1.36 (0.99–1.89)	.07	1.32 (0.94-1.84)	.11
CM and intensive outreach	249	11.7		1.41 (1.26-2.25)	.14	1.30 (0.81-2.08)	.27
ST and intensive outreach	119	16.8	.030	2.17 (1.26-3.74)	.005	1.98 (1.14-3.44)	.016
Highest education							
Elementary/none (ref)	1334	10.1		1.0		1.0	
Middle school	399	9.8		0.96 (0.66-1.40)	.84	1.0 (0.68-1.46)	1.0
High school or higher	259	14.7	.08	1.53 (1.04-2.25)	.032	1.47 (0.99–2.17)	.06
Lifetime sexual partners							
1 (ref)	1088	7.1		1.0		1.0	
2–3	517	13.5		2.06 (1.46-2.90)	<.001	2.02 (1.43-2.85)	<.001
>4	395	16.5	<.001	2.59 (1.82-3.68)	<.001	2.55 (1.79-3.63)	<.001
No. children							
0–2	631	11.3		1.0			
3–4	843	10.2		0.90 (0.64-1.25)	.52		
>5	516	10.7	.81	0.94 (0.65-1.37)	.75		
Residency							
Rural	1854	10.4		1.0			
Urban	146	13.0	.33	1.29 (0.78-2.13)	.33		
Last screen for cervical cancer, y				. , ,			
<1	135	12.6		1.0			
1–1.99	553	9.6		0.74 (0.41-1.32)	.30		
2–2.99	530	10.9		0.85 (0.48-1.52)	.59		
>3	659	10.2	.73	0.79 (0.45–1.39)	.41		

TABLE 4. HPV Positivity Given Demographic and Personal Risk Factors

a group educational session and more than 1,632 (86%) of 1,896 women eligible for screening subsequently completed screening.

The outreach strategies of the MOH health promoters were essential to increasing participation at every step of phase 1. Health promoters may have more invested in outcomes, because they are employees of the agency administering CAPE; this motivation likely contributed to almost 90% compliance with colposcopy appointments among women in the CM cohort, higher than the 70% to 80% compliance observed in previous literature. Without the frequent communication and encouragement provided to participants by the health promoters, the number of women who were screened and completed treatment would likely be considerably lower.^{12–16}

We were pleased to find that this project improved the colposcopy referral system in the Paracentral region. Before this program, women had to return to the clinic after receiving an abnormal Pap or HPV positive result to schedule the colposcopy appointment. After phase 1 of CAPE was implemented, the colposcopy appointment was scheduled as soon as women received the abnormal result. Eliminating the additional visit has considerably improved follow-up.

Additional unscreened and underscreened women were successfully identified and treated once health promoters initiated

more intensive outreach by using local health unit Pap records to update screening histories in community census records. Women identified through more intensive outreach had profiles associated with greater risk of HPV and cervical cancer; they were more likely to have 4 or more lifetime sexual partners, and almost half had not been screened in the previous 3 years. It is difficult to draw conclusions about the implications of higher HPV prevalence in

TABLE 5. HPV Positivity by Self- Versus Provider-Collect	ted Sampling
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Provider-collected	Self-collec			
sample	HPV positive	HPV negative	Total	
HPV positive	161	51	212 (11)	
HPV negative ^a	42	1744	1786 (89)	
Total	203 (10)	1795 (90)	1998 (100)	

Data are presented as n or n (%).

Overall agreement = 98%; $\kappa = 0.75$; p = .35.

HPV indicates human papillomavirus.

^aTwo women testing HPV negative by their provider-collected sample did not have a self-sample.

this population because they differ from those identified through standard recruitment. The more intensive outreach strategy of providing individual instruction in women's homes increased participation and encouraged follow-up. The results of more intensive outreach during phase 1 indicate that it will be necessary to employ this recruitment strategy as CAPE expands.

Our study showed that self-sampling was almost as effective as provider sampling at detecting HPV. A separate study conducted in a subset of 518 women found that almost 40% of women preferred self-sampling to provider sampling, and more than 60% of women accepted self-sampling.⁴ Most women with high-grade lesions identified by provider-collected samples were also identified as HPV positive by self-collected samples. Ideally, to ensure optimal sensitivity, all samples would be collected by providers when using careHPV. However, this is not feasible in many lowresource settings. Providing a self-sampling option can greatly increase the number of women screened and treated and may help decrease overall cervical cancer mortality.⁵

One of this program's most important findings is that pathology diagnosis is challenging even in a highly regulated national program. The local pathologist diagnosed only 7 (36.8%) of 19 high-grade lesions identified by the expert pathologist upon secondary review. Even if all women underwent colposcopy, inaccurate pathology diagnosis may limit the effectiveness of a colposcopybased strategy to provide appropriate care, because the success of that approach is dependent on pathology diagnosis. Although the MOH encourages LEEP or hysterectomy for patients with CIN 3, only 3 of 9 patients with CIN 3 received a diagnosis of CIN 2/3 by the local pathologist; the other 6 received cryotherapy (rather than LEEP) for the presumed diagnosis of CIN 1. In addition, the total percentage of women treated in the CM cohort was no different than in the ST cohort because of the overdiagnosis of CIN 1 by the local pathologist. These findings underscore the need to direct more resources toward pathology training to improve pathology diagnosis.

Phase 1 of CAPE was the first government-led implementation of an HPV-based cervical cancer screening program using this HPV test. Cervical Cancer Prevention in El Salvador is a realtime demonstration program that will ultimately screen 30,000 women. The main weakness of this project is that women were not randomized to a management strategy (CM or ST), because CAPE was not designed as a research study. The 2 treatment cohorts, however, were similar enough to conclude that the findings provide valuable insights into how these strategies might perform in a larger context. We found that ST strategy consistent with recent WHO recommendations was successfully and effectively implemented by the Salvadoran MOH.

In conclusion, using the ST management strategy led to a greater likelihood of successful management of HPV-positive women than the CM strategy. The self-sampling strategy was feasible, and active recruitment leads to a higher enrollment of HPV-positive women. There are limitations to local pathology programs and efforts should be made to strengthen these systems because some clinical decisions will be made on the basis of pathologic diagnosis.

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