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Community-integrated self-collected HPV-based cervix screening in a low-resource rural setting: a pragmatic, cluster-randomized trial

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Effective approaches to improve coverage of self-collected human papillomavirus (HPV)-based cervix screening (SCS) as well as attendance at treatment for HPV-positive participants are needed to inform policy on optimal integration of cervical cancer screening programs within existing infrastructure in low-resource settings. ASPIRE Mayuge was a pragmatic cluster-randomized trial in rural Mayuge district, Uganda, comparing the superiority of two recruitment implementation strategies for SCS: Door-to-Door versus Community Health Day. Villages were randomized (unblinded) to a strategy, and participants aged 25–49 years with no previous history of hysterectomy or treatment for cervical cancer or pre-cancer were eligible. Participants completed a survey and participated in SCS. The primary outcome was rate of attendance at treatment after a positive SCS. The trial randomized 31 villages and 2,019 participants included in these analyses (Door-to-Door: 16 clusters, 1,055 participants; Community Health Day: 15 clusters, 964 participants). Among HPV-positive participants, attendance at treatment rates were 75% (Door-to-Door) and 67% (Community Health Day) ($P = 0.049$). Participants in the Community Health Day intervention were less likely to attend treatment compared to Door-to-Door (risk ratio = 0.78, 95% confidence interval: 0.64–0.96). No adverse events were reported. Policymakers in low-resource settings can use these results to guide implementation of SCS programs. ISRCTN registration: 12767014. ClinicalTrials.gov registration: NCT04000503.

In 2018, the World Health Organization (WHO) issued a call to action for the elimination of cervical cancer[1], an almost entirely preventable and treatable disease that causes a substantial global health burden, particularly among women and individuals with a cervix[2] in low- and middle-income countries (LMICs) where 80–90% of cervical cancer death occurs[3,4]. To achieve this objective, the WHO created a Global Strategy to accelerate the elimination of cervical cancer[5], which included goals of having 70% of women screened for cervical cancer twice in their lifetime, 90% of girls fully vaccinated by age 15 years and 90% of women with detected cervical disease treated by 2030. A 2020 modeling study by Canfell et. al.[6] demonstrated that, whereas vaccination alone will have minimal impact on cervical cancer mortality by 2030, scaling up cervix screening programs that achieve screening once or twice in a woman's lifetime and treatment for those with detected cervical disease could avert over 300,000 avoidable deaths globally in this same time period.

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Cervical cancer incidence and mortality rates have declined in most countries that have cervix screening programs[7], yet increases have concurrently been observed in a number of LMICs[7,8]. This appears to be due either to the absence of comprehensive cervical cancer elimination programs[9] or to limited uptake of available programs[10] when such programs exist. Barriers to the implementation of population-wide screening and treatment programs in LMICs may be related to limited availability of screening and treatment resulting from insufficient health systems infrastructure and human resources as well as challenges in engaging with existing infrastructure[11–13]. To achieve the ambitious WHO elimination goals, it is essential to create a body of evidence on how to increase both screening and treatment coverage in highly impacted settings.

Evidence suggests that self-collected human papillomavirus (HPV)-based cervix screening (SCS) is a feasible and cost-effective solution to addressing barriers to screening, especially in low-resourced and rural areas[14–19]. Compared to conventional cytology-based screening, which can be delivered only with a pelvic examination conducted by healthcare practitioners, HPV-based screening programs can offer self-collected screening options to women in their homes or private areas in their communities via community health workers (CHWs)[20]. Active invitation to SCS programs has consistently shown high uptake across diverse populations[17,21–24], and, following the WHO-recommended screen-and-treat approach, HPV-positive women can be referred for visual inspection with acetic acid (VIA) and treatment with cryotherapy or thermal ablation at their nearest health facility[25].

Although improved screening is an essential aspect in the elimination of cervical cancer, the availability of and attendance at treatment is equally as important to the success of any elimination strategy, as pre-cancerous lesions identified through screening must be effectively treated to prevent progression to cancer for screening to offer benefits. Barriers affecting the uptake of screening, such as limited availability of resources, may also affect attendance at treatment for those with positive HPV results. Although many studies have focused on screening uptake[14], data confirming that SCS leads to an increase in treatment after an abnormal screen are more limited. There is a need for studies with a primary objective of attendance at treatment for HPV-positive screeners in priority settings.

Given that SCS programs in LMICs are feasible and acceptable among diverse populations of women[14,16,17,19,24,26], leaders of health systems now need to understand how to best implement this approach to obtain optimal screening and treatment coverage. As it will take decades for the HPV vaccination to realize its full benefits[6], insufficient coverage of screening and treatment remains the greatest short-term barrier to cervical cancer prevention across the world[27]. It is critical to generate evidence that will define best practice of how to improve attendance at treatment situated in existing health systems. This evidence can then be used as a roadmap to facilitate deployment of SCS programs across other similar settings.

Uganda has one of the highest rates of cervical cancer incidence in the world, at 56.2 cases per 100,000 women (https://gco.iarc.fr/). The Advances in Screening and Prevention in Reproductive Cancers (ASPIRE) Mayuge trial[28] investigated the impact of SCS programs embedded into existing health infrastructure on coverage of screening and treatment in a rural population in Uganda with low rates of cervical cancer screening participation[29]. The study team included investigators from the Uganda Cancer Institute (UCI) who selected the Mayuge district as a priority region to conduct the trial. We conducted a pragmatic cluster-randomized trial allowing the intervention to occur at the community level. We used an approach that focused on findings relevant for implementation and assessed screening and treatment strategies that were grounded in the realities of Ugandan health systems, deploying two feasible strategies that differed in the ways in which women were recruited for screening. A pragmatic study design was used to assess the success of the intervention and evaluate the impact of the intervention in the real-world setting of a low-resource community[30].

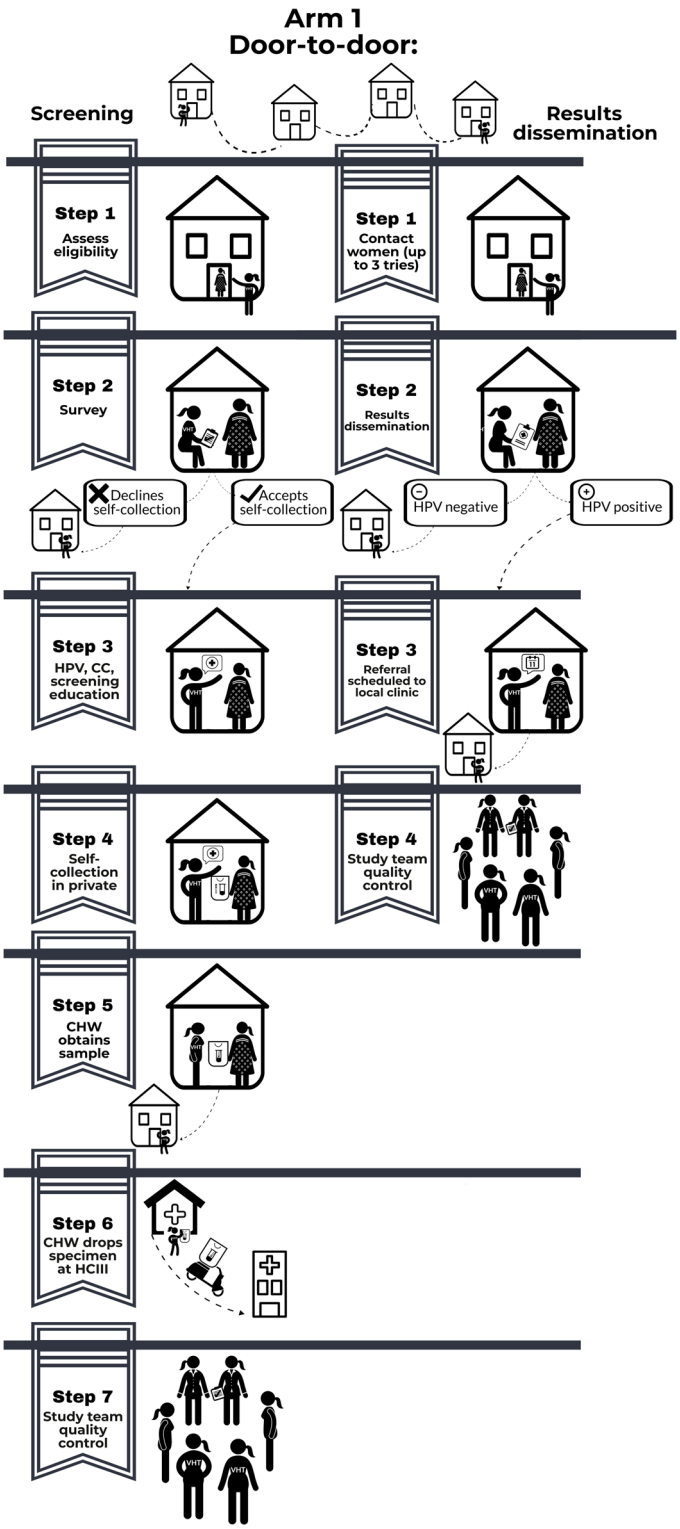

Fig. 1 | Door-to-Door screening and results dissemination study activities. Door-to-Door participants were recruited door-to-door by CHWs. CHWs consented participants, administered a baseline questionnaire and facilitated SCS in a private location in the participant's home. Samples were transported for testing, and, after receiving the results of the test, the CHW returned to the participant's home to discuss the results with the participant and schedule any recommended follow-up for treatment.

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This trial aimed to determine attendance at treatment for HPV-positive participants after SCS and compare those rates across different implementation strategies to inform a roadmap for implementation of SCS programs to decisionmakers across similar settings. We also measured additional outcomes to further inform the decisionmakers who plan to implement cervical cancer screening programs that are integrated into existing health infrastructure in a low-resource setting with a high burden of cervical cancer, such as screening knowledge, uptake and participant experience.

Results

Sixteen villages in the Mayuge district of Uganda were randomized to door-to-door recruitment (Fig. 1: Door-to-Door implementation, $n = 1{,}055$, average cluster size (number of participants) = 66, s.d. = 8.3) between August and December 2019, and 15 villages were randomized to community health day recruitment (Fig. 2: Community Health Day implementation, $n = 964$, average cluster size = 64, s.d. = 14.0) (Fig. 3) between November 2020 and July 2021. One hundred percent of women across both arms who were offered SCS ($n = 2{,}019$) chose to participate. No clusters were excluded, and only a small number of individuals did not receive their results and were considered lost to follow-up (Door-to-Door: $n = 5$, Community Health Day: $n = 4$, from a total of seven clusters) but were included in the intention-to-treat analysis, as they still had the potential to receive screening at the clinic and be identified through clinic records.

Participant characteristics

Table 1 describes participant characteristics by trial arm. Women in Door-to-Door were slightly older than women in Community Health Day (Door-to-Door: 34.6 years, Community Health Day: 33.8 years) (Table 1). Across both arms, over 80% of women were married (Door-to-Door: 83.1%, Community Health Day: 88.3%), and more women were single in Door-to-Door (12.6%) compared to Community Health Day (4.8%). Most women had primary education or less (Door-to-Door: 67.3%, Community Health Day: 66.7%), had between five and six total pregnancies on average (Door-to-Door: 5.8 pregnancies, Community Health Day: 5.4 pregnancies) with the first pregnancy around age 18 years and between four and five living children (Door-to-Door: 4.8 children, Community Health Day: 4.6 children). More women in Door-to-Door visited a health center in the past year (Door-to-Door: 88.4%, Community Health Day: 72.6%), and it took Door-to-Door participants longer on average to walk to the health center (Door-to-Door: 54.7 minutes, Community Health Day: 43.0 minutes). Only around 2% of women had previously screened for cervical cancer across both arms. Despite these differences, some of which were statistically significant, the cohorts appeared to be well matched, and expected differences were adjusted for in multivariable models, as per the analysis plan described in the protocol paper.

HPV screening and attendance at treatments

Primary outcomes. Among those who were HPV positive, 75.3% and 66.7% attended treatment in Door-to-Door and Community Health Day, respectively ($P = 0.049$). The results of our mixed-effect log-binomial regression model are found in Table 2. For each model, the exposure is arm allocation, and the outcome is attendance at treatment in the included population. Models 1–3 include the entire population, whereas model 4 is subset to only HPV-positive participants. Model 1 is unadjusted with cluster as a random intercept. Here, the rate (risk ratio

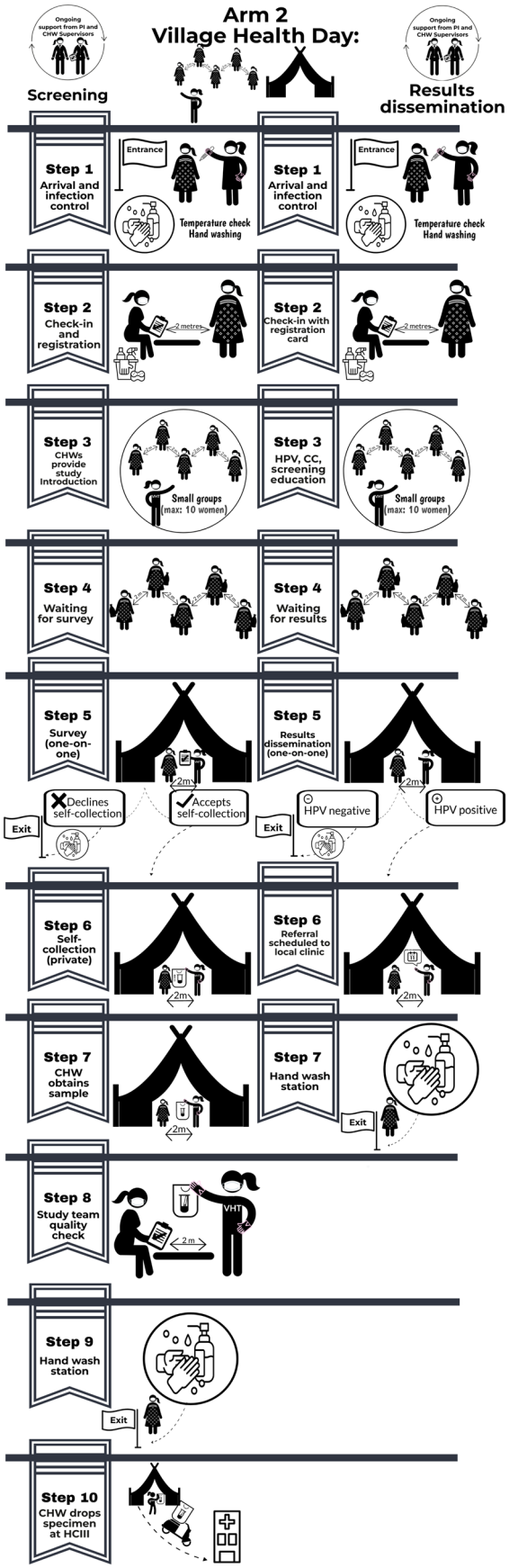

Fig. 2 | Community Health Day mobilization, screening and results dissemination study activities. One week before the start of Community Health Day recruitment, CHWs went door-to-door inviting eligible participants to a cervical cancer screening–focused community health day. On the day of recruitment, women arrived at the community health day where CHWs consented participants, administered a baseline questionnaire and facilitated SCS in a private area in a portable tent that was set up that day. Samples were transported for testing, and, after the results of the test were available, a second community health day was set up where the CHW discussed results with participant and scheduled any recommended follow-up for treatment.

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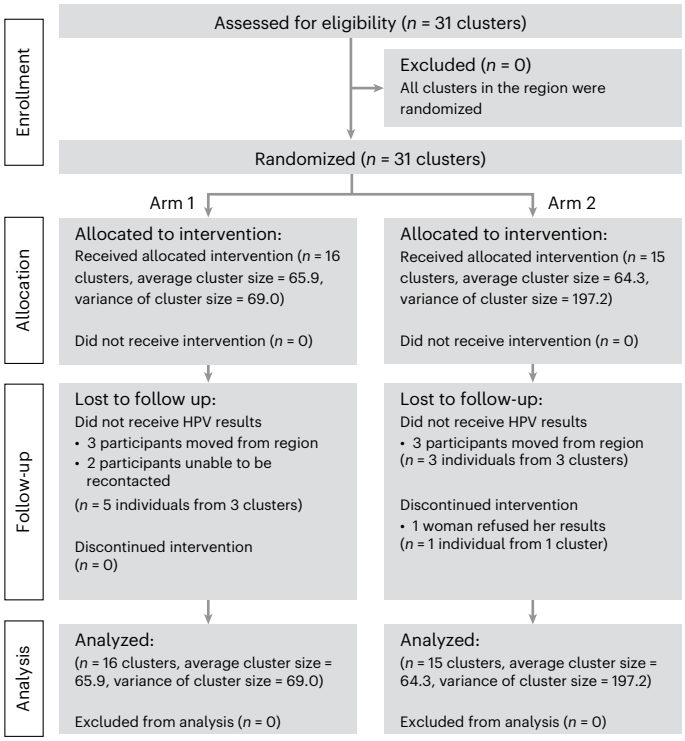

Fig. 3 | CONSORT diagram for cluster-randomized trials. The CONSORT diagram shows that all randomized clusters (that is, villages; $n = 31$) completed the interventions and were included in analyses. Among the 31 included clusters with a total of 2,019 participants (Door-to-Door = 1,055, Community Health Day = 964), a total of nine individuals from seven clusters were lost to follow-up.

(RR)) of attendance at treatment was statistically significantly lower for Community Health Day compared to Door-to-Door (model 1 RR = 0.76, 95% confidence interval (CI): 0.63–0.92). Our main model, model 2, was adjusted for woman's age, education, marital status and if they attended a health center in the past year. Model 1 and model 2 gave similar results (model 2 RR = 0.78, 95% CI: 0.64–0.96). In model 3, we adjusted for cluster HPV positivity rate, which differed across arm, and found slightly different results, with the odds ratio slightly higher than in previous models (model 3 RR = 0.84, 95% CI: 0.69–1.01). We saw similar, although no longer significant, results with model 4, which included only HPV-positive participants (model 4 RR = 0.88, 95% CI: 0.72–1.08). Absolute risk (AR) and risk difference (RD) are also reported in Table 2.

Secondary outcomes. Most HPV-positive women who attended the health center for treatment were able to receive VIA at their appointment (Door-to-Door: 92.4%, Community Health Day: 99.4%) and treatment with thermal ablation, if eligible. Women were unable to receive VIA only when a doctor or materials were unavailable and unable to receive treatment if they were ineligible (and were instead referred to a higher-level clinic).

Door-to-Door had a slightly higher, but not statistically significantly different, HPV positivity rate than Community Health Day (Door-to-Door: 28.1%, Community Health Day: 24.9%, $P = 0.08$) (Table 3). Nearly all women received their HPV test results across both arms (Door-to-Door: 99.5%, Community Health Day: 99.6%). Women who did not receive their results (Door-to-Door: $n = 5$, Community Health Day: $n = 4$) could not be located by CHWs or refused their results.

Among all women who tested positive for HPV, 4.6% were positive for HPV16, 6.3% were positive for HPV18/45, 11.5% were positive for HPV31/33/35/52/58, 5.0% were positive for HPV51/59 and 7.5% were positive for HPV39/56/66/68 (Extended Data Table 1). Age-specific distributions are also provided in Extended Data Table 1.

Knowledge and experience with SCS

Secondary outcomes. At the 6-month post-screening follow-up interaction, 781 participants completed the survey on knowledge and experience (Door-to-Door $n = 406$, Community Health Day $n = 375$) (Extended Data Table 2). The composite knowledge score was slightly higher in Community Health Day (3.86 versus 3.67, $P < 0.001$).

Similarly, over 99% of participants in each arm reported that CHWs spent enough time with them (Door-to-Door: 100%, Community Health Day: 99.5%), explained things in a way that was easy to understand (Door-to-Door: 99.2%, Community Health Day: 99.4%), gave them the opportunity to ask questions or raise concerns about the recommended treatment (Door-to-Door: 99.5%, Community Health Day: 99.5%) and involved them as much as they wanted in decisions about care and treatment (Door-to-Door: 99.7%, Community Health Day: 99.7%). All except for one participant said that the overall quality of the consultation with CHWs was good or very good; however, more participants in Community Health Day rated the CHWs as very good (50% versus 21%).

Healthcare-seeking behavior during the Coronavirus Disease 2019 pandemic

The Community Health Day arm was conducted during the Coronavirus Disease 2019 (COVID-19) pandemic, and study activities were modified from the original protocol to comply with the Uganda government's pandemic regulations. As healthcare-seeking behaviors are known to have changed during the height of the pandemic, a follow-up survey was added to the study to assess if the pandemic may have confounded the results of the main outcome (attendance at treatment after a positive HPV test).

Of the 375 women from Community Health Day selected to complete the follow-up survey, 288 (77%) reported needing healthcare of any kind at some point during the COVID-19 pandemic (Extended Data Table 3). Of those, 279 (97%) attended healthcare services, and 268 (96%) received the care they needed; those who did not receive the care they needed reported that services were unavailable or wait times were too long. Overall, 74.9% ($n = 209$) found it more difficult to receive services during the pandemic than before.

Safety and adverse events

Per the protocol, no midpoint evaluation was conducted, and a data monitoring committee was not established as no major safety concerns were expected. Weekly meetings were held with the study team and CHWs to collect information on adverse events. No harms or unintended effects were reported throughout the duration of the trial.

Discussion

In this pragmatic cluster-randomized trial, we used an approach focused on intervention implementation to demonstrate the feasibility of integrating SCS programs into existing health systems in low-resource settings with a high burden of cervical cancer. This trial provides evidence on how to improve coverage of cervical cancer screening and treatment attendance using SCS programs, particularly in rural, low-resource settings. As both coverage of screening and subsequent attendance at treatment when the screening result is positive are the important factors in our immediate ability to eliminate cervical cancer, the primary outcome of each implementation strategy was measured by the proportion of HPV-positive women who attended treatment.

We found that both implementation strategies for SCS (Door-to-Door and Community Health Day), embedded within a region's existing health system and infrastructure (health staff and treatment clinics), were feasible and showed high uptake of screening and treatment attendance in a community where prior screening participation was almost non-existent. Active invitation to screening by CHWs was feasibly integrated into CHW existing activities. Women

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Table 1 | Baseline characteristics by arm

	Door-to-Door (*n*=1,055)		Community Health Day (*n*=964)		*P* value
	n	%	*n*	%	
Socio-demographics					
Age (years), mean (s.d.)	34.6	7.5	33.8	7.7	0.02[a]
Marital status					
Married	875	83.10	849	88.25	<0.001[b]
Separated/divorced	23	2.18	55	5.72	
Single	133	12.63	46	4.78	
Widowed	22	2.09	12	1.25	
NA	2		2		
Education					
None	132	12.52	130	13.49	0.02[b]
Primary (P1 to P7)	578	54.84	513	53.22	
O level (S1 to S4)	281	26.66	281	29.15	
A level (S5 to S6)	10	0.95	16	1.66	
Tertiary education/university	53	5.03	24	2.49	
NA	1		0		
Total pregnancies, mean (s.d.)	5.76	3.12	5.43	2.97	0.01[a]
Mother age (years) at first birth, mean (s.d.)	18.16	3.14	17.96	3.08	0.15[a]
Living children, mean (s.d.)	4.79	2.51	4.59	2.5	0.08[a]
Visited a health center in the past 12 months					
Yes	931	88.41	700	72.61	<0.001[b]
No	122	11.59	264	27.39	
Don't know	2		0		
Travel time from home to nearest HCIII facility (minutes), mean (s.d.)	54.66	45.36	42.96	34.84	<0.001[a]
Previously screened for cervical cancer	21	1.99	23	2.39	0.65[a]

[a]*t*-test. [b]Chi-square test.

who were allocated to the Door-to-Door arm were more likely to attend treatment than those in the Community Health Day arm, even though they reported longer walking time to the health center.

Before enrollment, approximately 5% of women had received cervical cancer screening in Mayuge district of Uganda[29], although the Uganda Ministry of Health has worked to make VIA-based cervical cancer screening available at health centers for all eligible women[31]. SCS with thermal ablation treatment programs, such as those implemented in this study, would help mitigate some common barriers to care seen in low-resource settings such as Uganda (for example, lack of medical personnel and supplies). SCS would reduce the number of providers needed, as only those who screened positive would need to see a provider. Among study participants, 100% chose to participate in SCS, and 72% of those who were HPV positive attended treatment. These results align with previous work in Latin America showing that women prefer to screen in private, non-clinic versus public locations[21] and that offering at-home SCS could increase screening uptake four-fold compared to referral to a health clinic for screening[32].

Attendance at treatment was higher in Door-to-Door than Community Health Day, likely due to a variety of factors associated with the Door-to-Door implementation strategy. In Door-to-Door, CHWs provided more individualized behavior change techniques (BCTs) during recruitment and results dissemination than was possible during group information sessions at community health days. BCTs tailored to the individual are typically more effective than general health information[33]. Furthermore, CHWs in Door-to-Door educated both the participant and her family on cervical cancer screening if they were in the home during recruitment, whereas, in Community Health Day, only the participant was invited to attend the community health day (due to COVID-19 risk mitigation strategies) and received the education. Familial support is a known predictor in treatment attendance across a range of health issues[34–36]. Although women in Community Health Day screened and received their results in a private tent during community health days, women in Door-to-Door may have felt more comfortable asking additional questions in the security of their own home. Community health day activities occurred during the pandemic, a global event that reduced visits to health centers across the world[37], and, although we cannot rule out an impact of the pandemic on our results relating to attendance at treatment, our survey on the impact of the pandemic on healthcare-seeking behavior found that over 96% of Community Health Day participants reported being able to access needed healthcare throughout the pandemic. This suggests that the pandemic did not deter healthcare-seeking behavior, such as attendance at treatment after a positive HPV result, among Community Health Day participants.

Although slightly lower than Door-to-Door, Community Health Day also had high rates of treatment attendance, and potential benefits of the community health day approach include broader community reach and the ability to bundle with other health services. The community health day was planned to include information sessions for women who were ineligible for the study and male partners of participants. However, due to COVID-19 distancing measures, only participants were

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Table 2 | Results from mixed-effects log-binomial regression models estimating the RR, AR and RD of VIA attendance between study arms

	M1	*n*=2,019			M2	*n*=2,012			M3	*n*=2,019			M4	*n*=536		
Predictors	RR[a] (95% CI)	AR[b] (95% CI)	RD[c] (95% CI)	*P*[d]	RR (95% CI)	AR (95% CI)	RD (95% CI)	*P*[d]	RR (95% CI)	AR (95% CI)	RD (95% CI)	*P*[d]	RR (95% CI)	AR (95% CI)	RD (95% CI)	*P*[d]
Intercept	0.29 (0.22–0.38)			**<0.001**	0.29 (0.15–0.57)			<0.001	0.11 (0.06–0.20)			<0.001	0.85 (0.63–1.15)			0.30
Door-to-Door	REF	0.22 (0.20–0.25)	REF		REF	0.30 (0.23–0.39)	REF		REF	0.21 (0.18–0.24)	REF		REF	0.75 (0.66–0.86)	REF	
Community Health Day	0.76 (0.63–0.92)	0.17 (0.15–0.20)	−0.05 (−0.09 to 0.02)	**0.005**	0.78 (0.64–0.96)	0.24 (0.18–0.30)	−0.05 (−0.09 to 0.009)	0.02	0.84 (0.69–1.01)	0.18 (0.15–0.20)	−0.03 (−0.07 to 0.003)	0.07	0.88 (0.72–1.08)	0.67 (0.57–0.78)	−0.09 (−0.23 to 0.06)	0.24
Age					0.99 (0.98–1.01)			0.42								
Education																
Primary					0.96 (0.72–1.28)			0.78								
O level					1.06 (0.77–1.44)			0.73								
A level					1.61 (0.86–3.01)			0.14								
Tertiary/ university					1.23 (0.77–1.95)			0.39								
Health visit (yes)					1.07 (0.84–1.36)			0.57								
Marital status																
Separated/ divorced					1.29 (0.84–2.00)			0.25								
Single					1.4 (1.08–1.81)			0.01								
Widowed					1.64 (0.96–2.81)			0.07								
Cluster HPV positivity rate									1.03	1.01–1.05		<0.001				
ICC	0.004				0.005								0.110			

[a]RR, risk ratio. [b]AR, absolute risk. [c]RD, risk difference. [d]Wald test. Model 1: unadjusted with cluster as random intercept. Model 2: adjusted for age, education, health visit in last year and marital status with cluster as random intercept. Model 3: adjusted for cluster HPV positivity rate with cluster as random intercept. Model 4: subset to HPV-positive participants.

able to attend. Furthermore, an adjunct study on sexually transmitted infection (STI) testing was planned for the community health days; however, the pandemic also prevented this from occurring. This method of bundling information and integrating health services may work well with HIV care and other preventive and reproductive health services[38]. Although studies show preference for home-based screening[21,32], there is evidence that some women may be less comfortable depending on who is present in their household during the screen[17]. The option to screen at a community health day could alleviate this discomfort. The Community Health Day model also required half the number of CHWs needed in the Door-to-Door model, which is a consideration in many settings where there are limited resources.

This study provides insights on different models for SCS using an implementation-focused approach that is grounded in the realities of the local health system. Our implementation-focused approach is a strength, allowing for evidence on SCS to be readily integrated into health systems. Although other studies have assessed the acceptability and feasibility of SCS, few have attempted to directly study attendance at treatment after different approaches to provide this type of care. This study demonstrated the feasibility of implementation of two ideal screening models embedded in existing systems to increase both screening and treatment coverage. The randomization of villages attempted to reduce confounding factors that may affect the association between the intervention and the outcome. CHWs were used to conduct the study, ensuring community trust in study activities. This study was designed and conducted using pre-existing infrastructure and personnel, including the GeneXpert IV System for HPV testing, thermal ablation for treatment and local CHWs, nurses and laboratory technicians, so that successful models for screening could continue after the conclusion of the trial. Our pragmatic approach facilitates the scalability and sustainability of an intervention that maximizes limited health system resources.

Table 3 | Screening and treatment attendance results by arm

	Door-to-Door (*n*=1,055)		Community Health Day (*n*=964)		*P* value
	n	%	*n*	%	
HPV result					0.08[a]
Positive	296	28.06	240	24.90	
Negative	747	70.81	723	75.00	
Invalid	12	1.14	1	0.10	
Received HPV result					0.43[b]
Yes	1,050	99.53	960	99.59	
No	5	0.47	4	0.41	
Attended treatment (total population)	233	22.09	162	16.80	0.003[a]
Received VIA (total population)	215	92.27	161	99.38	0.003[a]
VIA result (total population)					0.05[b]
Positive	30	14.00	38	23.60	
Negative	173	80.47	110	68.32	
Indeterminate	8	3.72	8	5.00	
Suspect cervical cancer	4	1.86	5	3.11	
Attended treatment (HPV-positive subpopulation), *n*=536	223	75.34	160	66.67	0.049[a]
Received VIA (HPV-positive subpopulation)	206	92.38	159	99.38	0.003[a]
VIA result (HPV-positive subpopulation)					0.06[b]
Positive	29	14.08	38	23.90	
Negative	165	80.10	108	67.92	
Indeterminate	8	3.88	8	5.03	
Suspect cervical cancer	4	1.94	5	3.14	

[a]Chi-square test. [b]Fisher's exact test.

However, the limitations of this study must also be considered. Although all Door-to-Door study activities were completed before the start of the pandemic, Community Health Day activities occurred during the pandemic. Worldwide, healthcare visits declined throughout the pandemic owing to both provider and patient concerns with disease transmission[37]. Thus, the impact of the pandemic may have been an unmeasured confounding factor in our analyses. However, both interventions led to significant uptake in attendance at treatment, and data showed that women still had access to health services throughout the pandemic. Furthermore, all collected data were manually entered into a database, creating the possibility of data entry errors. However, quality control measures and audit procedures were in place, and random data checks occurred during data cleaning to minimize these errors.

Previous work has shown that simple referral by CHWs to SCS at a clinic increases screening uptake[39] but perhaps at a lower rate than seen with door-to-door recruitment models[16,21]. Both arms in our study used active invitation to screening, increasing uptake significantly from the baseline screening rate in Uganda. Ease of access to SCS and results of HPV testing certainly played a role in the uptake of treatment attendance in this study. Cervical cancer screening education provided by CHWs likely also contributed to the high treatment attendance rates seen in both arms. Many studies have shown that increased health literacy is associated with increased cancer screening adherence[40,41] and attendance at treatment[42]. We found that, after participation in the trial, women had high levels of understanding of cervical cancer screening and reported positive experiences with SCS in the trial.

The consecutive nature of the trial, with Community Health Day activities occurring after the conclusion of Door-to-Door, indicated that these implementation strategies may require capacity building as follows. Although only 92% of women who attended treatment were able to receive a VIA in Door-to-Door (due to lack of available resources and personnel when they attended their appointment), by Community Health Day, 99% of attending participants received VIA, suggesting that, with better understanding of resource needs, clinics were able to prepare for the substantial uptake of attendance at treatment after participation in the trial. Both strategies appear to benefit cervical cancer screening programs in an under-resourced setting, and these results can be used to inform the national scale-up of cervical cancer screening in Uganda and other LMICs. Furthermore, these data can inform the WHO on the factors that influence the success of alternative implementation strategies for HPV self-collection.

As treatment experience might be a barrier to attendance, we have investigated and published findings on the acceptability and side effects of thermal ablation treatment to better understand if this type of treatment is suitable among the study population[43]. Additionally, given that both approaches led to high treatment attendance, we next plan to assess economic costing of the strategies to guide future implementation. However, because nearly a quarter of women with positive results did not attend treatment, we also plan to investigate additional implementation strategies, including SCS integrated into existing primary health clinics and strategies involving digital health in an attempt to identify barriers that were not addressed by the interventions presented in this trial, to improve attendance at treatment and to compare participant preferences of implementation strategies. These future studies will provide further insight into the strengths and limitations of different implementation strategies.

The results from this trial show a slightly improved treatment attendance with Door-to-Door compared to Community Health Day strategies. Future analyses will investigate if the Community Health Day strategy requires fewer personnel and effectively allows for the bundling of health services, allowing for those who are planning the implementation of SCS programs to consider this tradeoff while still feeling confident that either approach will have strong impact relative to baseline. The 2020 modeling study by Canfell et al.[6] found that, if the WHO cervical cancer elimination goals can be met, more than 62 million women's lives will be saved over the next century. The trial provides evidence on the impact of two promising and feasible strategies for SCS, both of which obtain a high coverage rate of coverage for screening and treatment. This evidence can provide an important contribution to the policies as countries strive to achieve the goal of cervical cancer elimination.

Online content

Any methods, additional references, Nature Portfolio reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41591-023-02288-6.

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Methods

ASPIRE Mayuge[28] was a pragmatic, sequential, two-arm, cluster-randomized trial that recruited participants from 31 villages (clusters) in the Mayuge district of eastern Uganda between August 2019 and December 2019 (Door-to-Door) and November 2020 to July 2021 (Community Health Day). The trial was built upon previous research findings on the acceptability of SCS and was designed to guide intervention implementation of the screening into real-world practice in an LMIC setting[44]. The study was embedded within the existing health system infrastructure in Uganda with the goal of demonstrating feasibility of screening models integrated into existing health infrastructure and providing a roadmap for decisionmakers in other similar settings interested in SCS.

Villages were selected around health centers that were equidistant to the referring health center. The degree of rurality of the area[45] is representative of many sub-Saharan regions and LMICs that have similar challenges and realities regarding cervix screening. The cluster design of the trial was to allow for the intervention to occur at the community (village) level.

The study protocol can be found in ref. 28.

Study design and setting

The Door-to-Door arm recruited participants from 16 villages, and the Community Health Day arm recruited participants from 15 villages. Villages were randomly assigned to study arm to create relatively similar populations. Study interventions were guided by UCI investigators, who considered existing infrastructure and screening recommendations from the Uganda Ministry of Health. A total of 61 CHWs, known locally as village health teams (VHTs) (approximately two CHWs from each village), were recruited from existing VHTs and trained using the WHO's CHW training guidelines for cervical cancer screening[46]. The study population included women living in participating villages and meeting the following eligibility criteria: (1) no previous history of hysterectomy or treatment for cervical cancer or pre-cancer and (2) between the ages of 25 years and 49 years. Eligible women were invited by a CHW member to participate in the study and were administered a baseline demographic and health survey and offered home or meeting-based community-integrated SCS (based on village trial arm designation) and verbal education on cervical cancer and screening that was developed from a WHO program specifically tailored for populations in sub-Saharan Africa[46]. Approximately 6 months after recruitment, a random subset of participants was recontacted to complete a follow-up survey on cervical cancer screening knowledge and trial experience.

Randomization, sample size calculations and masking

Participating villages were randomized to arm by sub-district stratification using 1:1 allocation using STATA[47]. Power calculations were estimated using R statistical software[48] across a range of interclass correlation coefficients (ICCs) and potential effect sizes (as minimal prior accurate screening and treatment data exist in this region), assuming 15 clusters per study arm with an average size of 70 women per cluster. A baseline rate of 20% attendance at treatment was assumed for the 'control arm' (Community Health Day), based on previous findings from our study team among populations in urban areas of Uganda, which found treatment attendance rates of approximately 40% (ref. 16). As this was a rural area, the team assumed a rate of half that found in urban areas. CHWs recruited eligible women by starting in an assigned random location and circling around the houses in each village until the sample size was met. The study was powered to detect a 20–30% absolute difference in treatment attendance rate between arms. Power calculations for the follow-up survey resulted in a target to randomly select 25 participants per cluster. Additional details can be found in the study protocol[28].

The trial was designed with sequential recruitment of arms: door-to-door activities occurred before the start of community health day recruitment to prevent contamination between arms due to community mobilization efforts for the community health day. The study team was concerned that the community messaging involved in recruitment for the Community Health Day arm would cascade into Door-to-Door-randomized villages in uncontrollable ways if both arms were conducted concurrently. For example, messaging to recruit Community Health Day participants to attend community health days would have likely spilled over to women in Door-to-Door villages, who might have attended the community health days, causing participation rates in the Door-to-Door intervention to decrease. To mitigate the potential information spillover, a sequential approach was used, and CHWs were selected from the villages they lived in and recruited participants only from their respective villages. In addition, Door-to-Door recruited participants in a private manner in the home, and Community Health Day, which involved community messaging, occurred after the closure of Door-to-Door.

Due to the spatial and temporal nature of intervention arms, blinding of study staff, data collectors or participants was not feasible.

Door-to-Door SCS

CHWs recruited Door-to-Door participants by going door-to-door to potential participants' homes. Those eligible and who consented to participation were administered a baseline survey assessing demographics, health history and knowledge of cervical cancer and screening. After survey completion, they were provided with educational material on HPV, cervical cancer and screening. Available family members also received information on cervical cancer screening. Participants were then offered SCS and, for those who consented, instructions for how to self-collect. Women collected the sample in a private location in their home. Although samples could remain unrefrigerated for up to 7 days, usually at the end of each day CHWs dropped specimens off at a local health clinic, where they were kept until they were transported by motorbike to the laboratory for testing every few days (Fig. 2). The results of the HPV tests were available and returned to participants within 2 weeks after the sample was collected. CHWs went door-to-door to deliver results to each participant and provided counseling and scheduled a treatment appointment at the nearest health clinic for HPV-positive individuals (Fig. 2). Up to three attempts were made to contact women over a 2-week period at different times and days of the week before a woman was considered lost to follow-up. All study activities were completed before the start of the COVID-19 pandemic (follow-up survey data collection concluded in December 2019).

Community Health Day SCS

CHWs recruited Community Health Day participants during an organized community health day that was modeled after pre-existing community health days commonly held in the villages. One week before the study community health day, CHWs mobilized their communities to attend the event by going door-to-door to invite women and working with community leaders to disseminate the information to their community. Women received a ticket to attend, along with COVID-19 resources, including masks and government-approved information pamphlets about restrictions and how to stay safe.

At the community health day, there were mandatory temperature checks and handwashing. All participants and staff were required to wear masks. CHWs introduced the study to groups of ten attendees at a time. Portable tents were set up on the day of the meeting allowing for participants to complete the baseline survey and cervical cancer screening in a private setting (Fig. 3). At the end of the day, all specimens were transported to a laboratory for testing. A second community health day was held within 2 weeks after the first to return results following the same mobilization strategy used for recruitment. During this second day, a nurse provided cervical cancer screening education in small groups, and CHWs provided one-on-one results and counseling

in a private portable tent and scheduled treatment appointments for HPV-positive women (Fig. 3).

Across both arms, CHW-led theory-based BCT[49] intervention activities were used to support sustained uptake of screening behaviors, including education on benefits and risks of cervical cancer screening, instructions on how to self-collect, the opportunity to try SCS and timely dissemination of screening results with treatment scheduling for those who were HPV positive[49]. Six months after recruitment, a random subset of participants in each arm was recontacted by study team members and completed a questionnaire assessing their knowledge of HPV and cervical cancer screening as well as their experiences with SCS. CHWs were not used during the follow-up survey because survey questions asked about the quality of the CHWs throughout recruitment.

Laboratory analyses and treatment appointments

Existing laboratory staff and facilities, as well as nurses from local health centers in Mayuge, tested all samples and provided treatment, respectively. Given the implementation-focused approach of the trial, testing protocols were determined to allow the program to be embedded in the Ugandan infrastructure. The Uganda Ministry of Health advised the use of GeneXpert for HPV testing, as it is a scalable option given its existing use and availability for tuberculosis and HIV testing in Uganda. Before recruitment start, laboratory staff were trained on the use of GeneXpert IV for HPV sample analysis. Established nurses from three designated health centers, which already provided cervical cancer screening and treatment, were given refresher training on cervical cancer screening, VIA, thermal ablation treatment and quality monitoring.

The GeneXpert IV System genotyped for HPV16, HPV18/45, HPV31/33/35/52/58, HPV51/59 and/or HPV39/56/66/68. Samples with invalid results were re-run once. Participants who were positive for one or more HPV genotype were considered HPV positive.

Both arms followed the recommendations of the Uganda Ministry of Health regarding pathway to care after screening. The Uganda Ministry of Health advised the study team that future cervix screening programs would occur at health center level III (HCIII) facilities, so HPV-positive women were referred to these centers. In accordance with the Uganda Ministry of Health's cervical cancer screening screen-and-treat approach, HPV-positive women received treatment where a nurse performed both VIA and thermal ablation. Thermal ablation was performed using a Cure Medical thermal coagulator with a 19-mm probe. Adhering to UCI protocols, participants with suspicious lesions were referred to UCI for biopsy and loop electrosurgical excision procedure (LEEP) or cancer treatment, if necessary.

Trial outcomes

The primary endpoint was attendance at treatment after a positive self-collected HPV screen. Secondary outcomes included baseline HPV prevalence, uptake of SCS, cervical cancer knowledge measured approximately 6 months after recruitment into the trial and patient-reported experience measures for SCS. Each outcome was measured for each arm.

Variable creation and outcomes

The baseline survey included items assessing demographics categorized as follows: age (years), marital status (married, separated/divorced, single, widowed) and education (none, primary, O level (early secondary), A level (late secondary), tertiary education/university). It assessed health history, including total pregnancies, mother's age at first birth, number of living children, health center visit in the past year, walking time to the nearest health center (minutes) and prior cervix screening. The healthcare-seeking behavior during COVID-19 survey included questions about need and ability to access healthcare for a variety of reasons during the pandemic.

Participation in cervical cancer screening, HPV results and if the participant received her result were recorded on an internal spreadsheet. Attendance at treatment after a positive HPV test was identified through clinic records reviewed by research assistants approximately 6 months after the final woman was recruited. Research assistants recorded if a participant had attended her treatment appointment, if she had received VIA and thermal ablation and the results of her VIA.

Four true/false knowledge questions were included in the 6-month follow-up survey: 'Early detection of CC is helpful', 'CC is curable when detected early', 'There is a vaccine against CC' and 'CC is preventable'. A composite score was created by coding each correct answer as 1 and each incorrect answer as 0 and summing the four questions. An additional five questions were asked about the participant's experience with the CHW during screening: did the CHW spend enough time with them, did the CHW explain things in a way that was easy to understand, did the CHW give them the opportunity to ask questions or raise concerns about the recommended treatment, did the CHW involve them as much as they wanted in decisions about care and treatment and what was the overall quality of the consultation with the CHW. All five questions were asked on a four-point rating scale.

Statistical analyses

Descriptive statistics of demographic and health history characteristics, as well as primary (attendance at treatment) and secondary (HPV prevalence, knowledge, and experience) outcomes, were summarized for each arm.

There was concern that screening uptake might differ substantially by implementation strategy, which would in turn impact the primary outcome: attendance at treatment. To account for the potential impact of this difference in screening uptake on the outcome rate, per the protocol paper[28], using an intention-to-treat approach, the primary outcome was defined as treatment attendance at a designated health center *among all screened participants*. As opposed to defining the outcome as treatment attendance among only HPV-positive participants, by defining the primary outcome to include all screened participants, we avoid misinterpreting the potential scenario where, in one arm, few women participated in screening, but among those who participated in screening, the treatment attendance rate was high. Instead, with the intention-to-treat definition, the outcome rate in the potential scenario described would remain relatively low in the total screened population compared to in the subset who tested positive for HPV. By including all screened participants in the denominator, our findings account for both screening participation and treatment attendance, both of which are necessary for an effective screening intervention.

Upon implementation of the trial, there was identical screening uptake in each arm. However, likely due to chance, the HPV positivity rate differed by arm. Thus, because treatment was directly recommended only to those who screened positive, additional models were run where the primary outcome was defined as treatment attendance *among only HPV-positive women*.

The protocol-defined primary outcome was first estimated using an unadjusted mixed-effect log-binomial regression model with cluster as a random intercept to estimate the RR, AR and RD (model 1). As expected, due to the small number of clusters, differences were identified in demographic and health history characteristics across the arms. Thus, as described in the protocol, next we estimated a model using predefined confounders (age, number of living children and education as a proxy for socioeconomic status) and additional confounders that were unbalanced across arms (health visit in the past year and marital status). Walking time to the nearest health center was also somewhat unbalanced, but this variable was not included in the adjusted models as the quality of the data was low because of issues with unreliability due to self-reporting. This model did not converge, likely due to collinearity between age and number of living children, so number of living children was removed from the model, and the resulting model

converged (model 2). Model 2 was considered our main model, per the protocol paper. We additionally constructed a model that adjusted for cluster-level HPV positivity rate, which differed slightly across arms (model 3). Finally, we estimated a crude model using the subset of HPV-positive women as the denominator (model 4).

We also summarized data from the healthcare-seeking behavior survey that was given to Community Health Day participants. As Community Health Day study activities were conducted during the COVID-19 pandemic, whereas Door-to-Door was conducted before the pandemic began, we wanted to investigate whether Community Health Day participants were potentially less likely to attend their recommended treatment appointment than Door-to-Door due to reduced healthcare-seeking behaviors related to the pandemic.

Results were analyzed in R statistical software[48].

Protocol deviations

Community Health Day activities began after the start of the COVID-19 pandemic and were modified from the protocol[28] to comply with the Uganda government's COVID-19 regulations and to ensure participants' safety. All protocol changes were determined based on consultation with the community advisory group and the research team and were approved by all ethics boards. Before the start of Community Health Day recruitment, Uganda had implemented policy restrictions to reduce the transmission of COVID-19, including requiring all health visits to include education around transmission prevention measures and limiting group meetings to ten people[50,51].

Due to restrictions on gathering sizes during the pandemic, only 15 of the 30 CHWs (one per village) selected for Community Health Day were used during mobilization and recruitment, and women were pre-screened for eligibility to limit the size of the event. Although the original protocol planned for family members to be invited with participants to the community health days to receive education about cervical cancer screening, pandemic-related restrictions required reduced numbers of attendees at gatherings, and only participants were invited to attend. An adjunct study on STI testing was planned for the community health days; however, the pandemic also prevented this from occurring. The subset of Community Health Day participants who were contacted 6 months after recruitment was additionally surveyed about their healthcare-seeking behavior during the COVID-19 pandemic to gain insight into how the pandemic may have affected treatment attendance at this time.

Safety and adverse events

Per the protocol, no midpoint evaluation was conducted, and a data monitoring committee was not established as no major safety concerns were expected. Weekly meetings were held with the study team and CHWs to collect information on adverse events.

Inclusion and ethics statement

This project was designed through a longstanding partnership among the University of British Columbia, Makerere University and UCI, initiated by the Department of Obstetrics and Gynecology at Makerere University, which has led to many collaborations, including multiple SCS acceptability and feasibility studies[16–19,52]. The Mayuge district was selected as a study site by UCI, which has a clinical infrastructure established in this community. Intervention models were determined by Ugandan investigators and Mayuge village leaders, who advised that recruitment through door-to-door and community health days were feasible, long-term options for health system interventions.

In keeping our focus on providing implementation-centered results, Ugandan study team members led the intervention design, selection of the study locations and implementation and evaluation of the intervention. All team members collaborated on data ownership, intellectual property and authorship of publications related to the work. Key questions were identified by UCI to ensure relevant, deployable and sustainable interventions for their health system. Roles and responsibilities were agreed upon among collaborators ahead of the research, including having both a Ugandan and a Canadian researcher as a co-principal investigators as well as working with Ugandan study coordinators, CHWs and medical providers to implement the trial.

As the data collected for this trial involved results of a test for cancer caused by an STI, procedures were put into place to ensure the safety and well-being of participants. Women who test positive for an STI may face intimate partner violence[53] and community stigmatization[54], so protection of their data was critical. Participants received information on the test and the meaning of the test results during screening. Test results were kept in a spreadsheet located in a password-protected folder on a secure network. CHWs were trained before returning results to participants to give appropriate messaging about the meaning of a result as well as next steps, and nurses were on hand to answer additional participant questions.

Previous work from this region (both from our team[16,17,19,52,55] and other Ugandan researchers[29]) was used to guide the design of this study as well as connect our findings to similar research and has been taken into account in the citations for this manuscript.

Ethics approval

Ethics approval was obtained from the University of British Columbia/Women's Health Centre of British Columbia Research Ethics Board (UBC C&W REB H17–03332), UCI (UCIREC REF-08–2018) and the Uganda National Council for Science and Technology (UNCST HS 2517). All study participants provided written informed consent. Those who were unable to provide written signatures provided a stamped fingerprint, as approved by both ethics boards.

Reporting Summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

Data access for the ASPIRE Mayuge trial, restricted to non-identifying data owing to privacy concerns, can be requested only for scientific purposes from the corresponding or senior authors, who will handle all requests. Either data will be shared through an institutional data sharing agreement or arrangements will be made for analyses to be conducted remotely without the necessity for data transfer.
The study protocol can be found in ref. 28.

Code availability

The underlying code for the results detailed in this manuscript can be requested for scientific purposes only from the corresponding or senior authors, who will handle all requests. If the request is deemed scientifically appropriate, code will be shared through a secure file transfer process.

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Author contributions

A.G. (formal analysis, writing—original draft, writing—review and editing); B.A.P. (data curation, investigation, writing—review and editing); J.T. (formal analysis, visualization, writing—original draft, writing—review and editing); A.A. (formal analysis, writing—review and editing); J.J. (conceptualization, writing—review and editing); S.M.F. (conceptualization, writing—review and editing); N.M. (project administration, writing—review and editing); R.N. (project administration, writing—review and editing); PN (project administration, writing—review and editing); J.O. (conceptualization, writing—review and editing); H.P. (methodology, writing—review and editing); A.R. (methodology, writing—review and editing); P.N.S. (conceptualization, writing—review and editing); J.S. (conceptualization, methodology, writing—review and editing); L.W.S. (conceptualization, writing—review and editing); D.V.N. (conceptualization, writing—review and editing); C.N. (conceptualization, project administration, writing—review and editing); and G.O. (conceptualization, funding acquisition, writing—review and editing).

Competing interests

The authors declare no competing interests.

Additional information

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Extended Data Table 1 | HPV genotypes positivity rates (*n*=2,006)[a]

	Total	*n*=2,006	25–29	*n*=694	30–34	*n*=393	35–39	*n*=349	40–44	*n*=258	45–49	*n*=312
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
HPV16	92	4.59	48	6.92	10	2.54	17	4.87	10	3.88	7	2.24
HPV18/45	127	6.33	47	6.77	32	8.14	25	7.16	12	4.65	11	3.53
HPV31/33/35/52/58	230	11.47	100	14.41	41	10.43	37	10.60	23	8.91	29	9.29
HPV51/59	100	4.99	51	7.35	18	4.58	14	4.01	3	1.16	14	4.49
HPV39/56/66/68	151	7.53	65	9.37	34	8.65	19	5.44	8	3.10	25	8.01

[a] Study sample *n*=2,019; 13 samples gave invalid results after two rounds of processing.

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Extended Data Table 2 | Endline cervical cancer knowledge and trial experience by trial arm

	Door-to-Door		Community Health Day		*P*
	n=	406	*n*=	375	
	n	%	*n*	%	
Early detection of CC is helpful	386	95.1	375	100.0	<0.001[a]
CC is curable when detected early	385	94.8	374	99.7	<0.001[a]
There is a vaccine against CC	332	81.8	341	90.9	0.001[a]
CC is preventable	387	95.3	357	95.2	0.34[a]
Knowledge score, mean (s.d.)	3.67	0.65	3.86	0.42	<0.001[a]
Did the CHW spend enough time with you?					<0.001[b]
Yes, definitely	402	99.0	311	82.9	
Yes, basically	4	1.0	62	16.5	
No, not really	0	0.0	2	0.5	
No, definitely not	0	0.0	0	0.0	
Did the CHW explain things in a way that was easy to understand?					<0.001[b]
Yes, definitely	394	97.0	263	70.1	
Yes, basically	9	2.2	110	29.3	
No, not really	2	0.5	2	0.5	
No, definitely not	0	0.0	0	0.0	
Don't know	1	0.2	0	0.0	
Did this CHW give you an opportunity to ask questions or raise concerns about recommended treatment?					<0.001[b]
Yes, definitely	388	95.6	279	74.4	
Yes, basically	16	3.9	94	25.1	
No, not really	2	0.5	2	0.5	
No, definitely not	0	0.0	0	0.0	
Did this CHW involve you as much as you wanted to be in decisions about your care and treatment?					<0.001[b]
Yes, definitely	396	97.5	293	78.1	
Yes, basically	9	2.2	81	21.6	
No, not really	1	0.2	1	0.3	
No, definitely not	0	0.0	0	0.0	
Overall, how would you rate the quality of this consultation with the CHW?					<0.001[b]
Very good	86	21.2	186	49.6	
Good	319	78.6	189	50.4	
Bad	0	0.0	0	0.0	
Not sure	1	0.2	0	0.0	

[a] *t*-test [b] Chi-square test

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Extended Data Table 3 | Healthcare-seeking behavior during the COVID-19 pandemic (Community Health Day; *n*=375)

	n	%
Since the beginning of the COVID-19 pandemic (March 2020), have you wanted or needed to get healthcare for any reason?	288	76.8
Since the beginning of the COVID-19 pandemic (March 2020), did you attend healthcare services for any reason?	279	96.9
What was your reason for attending healthcare services?[a]		
Child health concern	143	51.3
Family planning	33	11.8
Other reproductive health concern	38	13.6
ANC	25	9.0
Diabetes	6	2.2
Hypertension	29	10.4
Acute injury or accident	7	2.5
HIV/ARV	27	9.7
Malaria (flu, fever)	225	80.6
Tuberculosis	3	1.1
Other	1	0.4
Where did you go for healthcare services?[a]		
Hospital	162	58.1
Health center/clinic	171	61.3
Pharmacist/drug dispenser	69	24.7
CHW	23	8.2
Traditional healer	1	0.4
Compared to before the COVID-19 pandemic, did you find that attending healthcare services during the pandemic is:		
More difficult	209	74.9
Less difficult	62	22.2
No difference	8	2.9
Did you receive the care that you needed?	268	96.1
Why did you not receive the care you needed?[a]		
Services not available	10	90.9
Long wait times/left before receiving care	5	45.5

[a] Participants could select more than one response.

nature portfolio

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Software and code

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Data collection	No software used (paper collection), data stored in Excel spreadsheet version 2201
Data analysis	Stata version 15.1, R Statistical Software version 4.1.3; Code Availability Statement: The underlying code for the results detailed in this manuscript can be requested for scientific purposes only from the corresponding or senior authors, who will handle all requests. If request is deemed scientifically appropriate, code will be shared through a secure file transfer process.

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Data access for the ASPIRE Mayuge trial, restricted to nonidentifying data owing to privacy concerns, can be requested for scientific purposes only from the

corresponding or senior authors, who will handle all requests. Data will either be shared through an institutional data sharing agreement, or arrangements will be made for analyses to be conducted remotely without the necessity for data transfer.

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	The term "women and individuals with a cervix" is used to discuss cervical cancer in the Introduction. Upon consultation with Ugandan collaborators, we learned that it would not be culturally appropriate to ask about sex and gender for this trial. All participants included in this trial were women with cervices.
Population characteristics	Participants were 25-49 years old with no prior cervix treatment from rural Uganda. Approximately 2% had been previously screened for cervical cancer.
Recruitment	Participants were randomly recruited from 31 villages in the Mayuge district of Uganda either through door-to-door recruitment or at a community health day.
Ethics oversight	Ethics approval was obtained from the University of British Columbia/Women's Health Centre of British Columbia Research Ethics Board (UBC C&W REB #H17–0333), the Uganda Cancer Institute (UCIREC REF-08-2018), and the Uganda National Council for Science and Technology (UNCST #HS 2517). All study participants provided written informed consent. Those who were unable to provide written signatures provided a stamped fingerprint, as approved by both ethics boards.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

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Behavioural & social sciences study design

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Study description	ASPIRE Mayuge was a pragmatic cluster-randomized trial in rural Uganda comparing two implementation strategies for self-collection HPV-based cervix screening: door-to-door (Arm 1) versus community health day (Arm 2).
Research sample	The research sample is a representative group of women of cervical cancer screening age (25-49) with no prior cervix treatment from the rural Mayuge District of Uganda, a community with low rates of screening.
Sampling strategy	Participating villages were randomized to arm by sub-district stratification using 1:1 allocation using STATA (30). Power calculations were estimated using R statistical software (31) across a range of interclass correlation coefficients (ICCs) and effect sizes, assuming 15 clusters per study arm with an average size of 70 women per cluster. Eligible women were approached randomly in each village until the sample size was met. The study was powered to detect a 20-30% absolute difference in follow-up attendance rate between arms. The baseline attendance rate for follow-up was assumed to be 20% of the entire population.
Data collection	Data was collected on paper surveys by community health workers and then entered into an Excel database. Lab results were entered directly from the GeneXpert machine into an Excel database. Researchers were not blinded to the intervention arm.
Timing	All study activities occurred between August 2019 to December 2019 (Arm 1) and November 2020 to July 2021 (Arm 2).
Data exclusions	No data were excluded.
Non-participation	There were a small number of individuals who did not receive their results and were considered lost to follow-up (Arm 1: n = 5, Arm 2: n = 4), but were included in the intention to treat analysis, as they still had the potential to receive screening at the clinic and be identified through clinic records.
Randomization	Participating villages were randomized to arm by sub-district stratification.

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Clinical data

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Clinical trial registration	ISRCTN, ISRCTN12767014. Registered 14 May 2019, https://doi.org/10.1186/ISRCTN12767014; clinicaltrials.gov, NCT04000503; Registered 27 June 2019, https://clinicaltrials.gov/ct2/show/NCT04000503
Study protocol	Nakisige C, Trawin J, Mitchell-Foster S, Payne BA, Rawat A, Mithani N, et al. Integrated cervical cancer screening in Mayuge District Uganda (ASPIRE Mayuge): a pragmatic sequential cluster randomized trial protocol. BMC Public Health. 2020;20(142).
Data collection	Advances in Screening and Prevention in Reproductive Cancers (ASPIRE) Mayuge (26) was a pragmatic, two-arm, cluster-randomized trial that recruited participants from 31 villages (clusters) in the Mayuge district of Eastern Uganda between August 2019 to December 2019 (Arm 1) and November 2020 to July 2021 (Arm 2). Arm 1 participants were recruited in their homes while Arm 2 participants were recruited at a community health day. Both arms completed a survey and were offered self-collection HPV-based cervix screening.
Outcomes	The primary endpoint was attendance at a scheduled treatment follow-up appointment after receiving a positive HPV test. Secondary outcomes included baseline HPV prevalence, cervical cancer knowledge measured approximately six months after recruitment into the trial, and patient-reported experience measures for self-collected cervix screening. Each outcome was measured by arm and is reported here.