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Nationwide cervical precancer screening in Ghana: concurrent HPV DNA testing and visual inspection under an expanded hub-and-spoke model

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Cervical cancer continues to disproportionately burden women in sub-Saharan Africa, and is the commonest gynecological cancer in Ghana. The Cervical Cancer Prevention and Training Centre (CCPTC), Battor, Ghana spearheaded the Ghana arm of the mPharma 10,000 Women Initiative (mTTWI) between September 2021 and October 2022. The aim of this study was to examine the outcomes of nationwide concurrent screening using high-risk human papillomavirus (hr-HPV) DNA testing and visual inspection methods, as well as factors associated with the screening outcomes. We conducted a descriptive retrospective cross-sectional study to estimate the prevalence of hr-HPV infection (nationally and regionally) and cervical lesions among women screened by graduates of our training center in their own settings (spokes) with remote supervision and mentoring by CCPTC trainers (hub). We modeled factors associated with hr-HPV infection using nominal logistic regression. Among 5217 women screened (mean age, 40.1 years), the overall prevalence of hr-HPV infection and cervical lesions were 29.1% (95% confidence interval [CI] 27.9–30.3) and 3.7% (95% CI 3.2–4.2), respectively. The prevalence distribution varied widely among regions, with the highest recorded in the Oti Region (32.8%) and the lowest recorded in the Upper West (20.7%) and North-East (20.7%) regions. The most frequently detected HPV genotype was *other* hr-HPV type(s) only (non-HPV16, non-HPV18) (23.5%; 95% CI 22.3–24.7), followed by HPV16 only (1.5%; 95% CI 1.2–1.8), and mixed infection with HPV18 + other hr-HPV type(s) (1.2%; 95% CI 0.9–1.5). Factors found to be significantly associated with hr-HPV infection among women screened included age < 35 years, having a relationship status apart from married/cohabitation, nulliparity, and HIV positivity. Drawing from our implementation of this model within the mTTWI, we posit that while Ghana prepares for organized screening, coordinating opportunistic screening could enable a phased expansion of cervical precancer screening with the help of international and local partners. This approach, combined with concurrent testing (hr-HPV DNA testing and visual inspection), holds promise for mitigating loss to follow-up among women requiring additional evaluation and lesion management.

Keywords Human papillomavirus infection, Cervical cancer, Hub-and-spoke model, Opportunistic screening, Visual inspection with acetic acid, Mobile colposcopy

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Despite global advancements in screening and diagnostic tools, cervical cancer continues to disproportionately burden women in sub-Saharan Africa[1–3]. In Ghana, the Global Cancer Observatory estimated that cervical cancer constituted 19.2% of all newly diagnosed cancer cases and 10.1% of cancer-associated deaths in 2022[4]. This large disease burden is driven in part by the absence of a national cervical precancer screening program[5,6], with screening remaining mainly opportunistic[7] and more available to women who are able to access higher-level facilities in larger towns[8]. The latter issue of accessibility is in turn perpetuated by the fact that most non-physician health workers, who mostly attend to the healthcare needs of women in smaller communities lack the requisite training to equip them to educate patients on cervical cancer, perform screening, and administer lesion management where necessary.

To equip health workers with the knowledge and skill to educate, screen, and treat cervical precancer, the Cervical Cancer Prevention and Training Centre (CCPTC), Battor, has implemented a modular training system that has trained a steady stream of health workers who have set up cervical cancer screening units in their community-based health facilities/centers (spokes). Again, the CCPTC has implemented innovative approaches to address the prevailing sporadic nature of cervical screening and promote early disease detection using existing health systems[9]. First, during 2018–2019, in collaboration with the North Tongu District Health Directorate and the Catholic Hospital, Battor, the CCPTC piloted a hub-and-spoke model of cervical precancer screening[8]. Under this model, the CCPTC (hub) provided training to nurses from six surrounding health centers and community health planning and services (CHPS) compounds (spokes), enabling them to begin cervical screening with HPV DNA testing and visual inspection with acetic acid (VIA) upon completing training. The spokes mostly used VIA, but had the option of taking cervical samples which had to be transported to the hub for HPV DNA testing. As a hub, the CCPTC was equipped with various screening methods, including visual inspection with VIA and Enhanced Visual Assessment (EVA) mobile colposcopy; cytology (Pap) testing; as well as HPV DNA testing with the *care*HPV, AmpFire, and GeneXpert platforms. After successfully introducing a fourth HPV DNA testing platform (the MA-6000 system) in 2021, the CCPTC documented its evaluation of concurrent HPV DNA testing and visual inspection methods as an alternative to the 'screen-and-treat' approach recommended by the World Health Organization (WHO)[10]. Prior to introducing this concurrent approach, standalone HPV DNA testing was the *status quo*. In November 2017, to facilitate the training of health workers taking part in its two-module program[11], VIA was performed routinely without extra cost to women screened at the CCPTC; however, women had to pay out-of-pocket to undergo EVA colposcopy or HPV DNA testing. This allowed us to compare various combinations of concurrent testing approaches with standalone HPV DNA testing in a routine real-world clinical setting. One important finding of our study was a high rate of 30.5% loss to follow-up among women in the standalone screening group who tested high-risk HPV (hr-HPV) positive, despite efforts to reach all screen-positive women for follow-up EVA colposcopy[10]. In addition, considering existing poor socioeconomic conditions, the additional cost of transportation when women visit health facilities multiple times, and the fact that many people in Ghana do not have reliable physical addresses, we posited that concurrent testing would better mitigate the high anticipated loss to follow-up associated with successfully implementing a nationwide 'screen-and-treat' model.

The CCPTC has engaged in partnerships with various local and international entities. One notable collaborator is mPharma, a technology-driven company committed to enhancing access to quality and affordable healthcare for African women. mPharma rolled out its 10,000 Women Initiative (mTTWI) in September 2021, with the aim of providing complimentary cervical precancer screening, specifically hr-HPV DNA testing (with MA-6000), to 10,000 women in Nigeria and Ghana who lack the means to undergo such tests[12,13]. In Ghana, the CCPTC took charge of the initiative, extending screening services across all sixteen regions through graduates of its training program. These graduates conducted screenings using brushes to collect cervical samples for hr-HPV DNA testing and performed VIA simultaneously during the same visit. The Ghana segment of the mTTWI extended the spokes of our previously documented hub-and-spoke model to all regions in Ghana and concluded in October 2022. Following program implementation, we conducted this study to examine the outcomes of nationwide concurrent screening using hr-HPV DNA testing and visual inspection methods, as well as factors associated with the screening outcomes.

Methods

Study design

Among women screened by alumni of the CCPTC under the Ghanaian arm of the mTTWI carried out between September 2021 and October 2022 with long-distance supervision by trainers at the CCPTC, we conducted this descriptive retrospective cross-sectional study to estimate the prevalence of hr-HPV infection (on a national and regional scale) and cervical lesions. We further modeled factors associated with hr-HPV infection as a screening outcome.

Health worker training, remote supervision, and recruitment

Graduates of the CCPTC who conducted screening for women in their respective settings under the mTTWI had at least completed the first training module. In all, 106 graduates practicing in all 16 regions of Ghana took part in the screening, among whom 12 had completed Module 2. The components of each module of the training program have been detailed elsewhere[9,11]. In brief, Module 1 teaches and equips health workers with the theoretical and practical knowledge (such as VIA and correct cervical sampling techniques) needed for the setup and administration of units for cervical precancer screening. Module 2 largely focuses on getting more

experience in colposcopy (especially being able to pick up cases suspicious of early invasive disease) and the treatment of cervical precancers using thermal coagulation and cryotherapy.

Upon completing the program, each participant had to devise plans for establishing a screening center in their respective practice area, such as health posts and CHPS compounds. This equipped them with the necessary skills for basic cervical precancer screening, performing VIA, and handling the administrative aspects of setting up screening facilities. The graduates were also capable of conducting cervical screening using HPV DNA testing and VIA at their institutions. Remote support from CCPTC trainers aided them in establishing these centers and assisted in following up with screen-positives and referring them to appropriate hubs. Following their training, all health workers agreed to join a WhatsApp group, where they received updates such as new information from the WHO regarding HPV vaccination, screening guidelines, and the treatment of precancerous cervical lesions through ablation.

The WhatsApp platform was also used as an avenue for ongoing/updated training on the latest guidelines and best practices in VIA and HPV DNA testing; regular case reviews and feedback sessions were also conducted by CCPTC trainers to ensure quality and consistency in screening practices. Graduates could also share their experiences with CCPTC trainers, seek a second opinion, and connect with other alumni and healthcare professionals, including specialists, for referrals. Graduates referred women with treatable precancerous cervical lesions to colleagues trained in Module 2 or to other institutions capable of treating such lesions. Suspicious cases of cervical cancer were referred to medical facilities with physicians who could perform biopsies for histopathology and provide further treatment.

Sample size

No a priori sample size calculation was performed in this study, primarily because screening in each setting was conducted as part of service provision, and not in a research context. The final sample size was thus a convenience sample that included all women with complete screening outcome data collected by CCPTC graduates in their respective settings and outreaches under the mTTWI during the study period.

Data collection and transmission

After providing relevant screening details and obtaining verbal consent, data were collected by graduates using a structured questionnaire developed by the CCPTC. The filled questionnaires were subsequently sent to the CCPTC and inputted into REDCap version 11.0.3 (Vanderbilt University, Nashville, Tennessee, USA)[14] and securely stored within databases hosted at the CCPTC. Before conducting any analyses, the data underwent several steps, including querying, extraction, and conversion into an Excel spreadsheet (Microsoft Corporation, Redmond, WA, USA). To ensure accuracy, manual crosschecking was carried out. Participant privacy and anonymity were upheld by data deidentification using a three-step process that involved removing all direct identifiers (such as names, addresses, and telephone numbers), assigning unique codes, and storing identifiable information separately. Access to identifiable information was restricted to authorized personnel only.

Study variables and outcomes

We gathered information about sociodemographic factors such as age, education level, marital status, number of births, occupation, income level, place of residence, National Health Insurance Scheme (NHIS) coverage, religion, and number of lifetime pregnancies. In addition, data regarding self-reported risk factors were collected, which included information about current and past use of contraceptives, whether the women had ever smoked or were currently smoking, and their HIV status. The screening outcomes of interest were a positive hr-HPV DNA test result or the presence of cervical lesions as observed on visual inspection procedures like VIA or EVA mobile colposcopy.

Cervical specimen collection, VIA, and EVA mobile colposcopy

During the screening session at each spoke, all women underwent thorough counseling on the benefits of cervical screening, as well as the potential risks and outcomes involved. Subsequently, they were positioned in the dorsal lithotomy position, and a speculum was inserted to expose the cervix, allowing for the collection of cervical samples using a disposable cytobrush or Bioline sterile swab stick (Bioline Diagnostics LLP, New Delhi, India) for HPV DNA testing. Sampling involved gently inserting the cytobrush/cotton tip into the cervical os and rotating through 360° to collect endocervical cells. Liquid-based samples were prepared by rinsing the brush head into 5 ml of ThinPrep/PreservCyt solution, whereas dry brushes and cotton swab samples were placed in a plain specimen collection tube and sealed. Samples were submitted to the central laboratory within 7 days. When this was not possible, the samples were kept in a freezer at – 16 °C or in a refrigerator at 0 to 4 °C in the institutions the samples were taken and submitted within two weeks. Prior to testing, all dry brush and cotton swab samples were stored in a freezer at – 16 °C, while liquid-based samples were stored in an air-conditioned room with temperatures in the range of 16–20 °C.

After sample collection, visual inspection was conducted using either VIA or mobile colposcopy with the EVA system 3.0 to detect cervical abnormalities. In most cases, VIA was employed, involving the examination of the cervix under proper lighting for abnormal changes following the application of 5% acetic acid, with a waiting period of 120 s. VIA results were classified as *positive* if acetowhite lesions were observed at the transformation zone (TZ), or *negative* otherwise. Observations from EVA mobile colposcopy were recorded using the 2011 International Federation for Cervical Pathology and Colposcopy (IFCPC) terminology, which includes features such as adequacy, TZ type, and the presence of major/minor changes. Health workers who performed the screening could share their colposcopic images with their trainers at the CCPTC for second opinions/discussions on the next steps of management. Where VIA was performed and they needed discussions, the health workers

who did the screening could take anonymized images with mobile phones to discuss with their trainers at the CCPTC just as they had been taught during their training.

Definitions of TZ types

TZ types seen at VIA or EVA colposcopy were classified according to the 2011 criteria of the IFCPC[15], viz:

Type 1 The entire circumference of the squamocolumnar junction (SCJ) is visible; fully ectocervical.
Type 2 The entire circumference of the SCJ is visible; partly or fully endocervical.
Type 3 The entire circumference of the SCJ is not visible; partly or fully endocervical.

Laboratory processing of cervical specimens and MA-6000 PCR assay

Upon arrival at the central laboratory of the CCPTC, the cervical samples collected as previously described were processed and tested using HPV 13 + 2 DNA diagnostic kits (S3057E; Sansure Biotech Inc., Hunan, China) on an MA-6000 real-time PCR device (Sansure Biotech Inc.). Testing was conducted following the manufacturer's instructions[16], as described elsewhere[17]. Samples were tested individually or in batches of up to 94, including positive and negative controls, with results obtained within two hours. The MA-6000 platform was utilized in its semi-quantitative module to detect HPV genotypes 16 and 18 separately, and to collectively identify *other* high-risk HPV types (HPV31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, and 68). While the platform could operate in full-genotype mode, this was not chosen due to cost and throughput considerations[18] for the participants screened under the mTTWI.

General strategy for treatment and follow-up of screen-positives

The approach used for treatment and follow-up has been elaborated elsewhere[10,19]. Typically, the standard protocol involved waiting for the results of the HPV DNA test, which usually took about a month, before initiating treatment, even if a lesion was detected during VIA or mobile colposcopy (screen/see, triage, and treat). However, in certain cases, after discussion with the women, treatment was administered immediately on-site using thermal coagulation, even before receiving the HPV results (screen/see and treat). Generally, women who tested hr-HPV negative and had normal visual inspection findings were advised to undergo rescreening in five years. Women who tested hr-HPV negative but showed minor changes on visual inspection, which were most likely CIN I lesions were mostly offered conservative management, which involved rescreening using visual inspection in 6 months to 1 year, primarily because these lesions may resolve spontaneously. Those who tested hr-HPV negative but had major cervical lesions detected during visual inspection were given the choice of immediate on-site treatment with thermal coagulation if they met specific criteria. Those with major cervical lesions that did not meet the criteria for ablation were offered the option of undergoing a loop electrosurgical excision procedure (LEEP). While some funding was provided by the mTTWI for thermal ablation and LEEP, it was inadequate to cover the cost of biopsying all lesions before treatment. Due to financial constraints, many women in this category preferred a 'diagnostic LEEP,' which served both diagnostic and therapeutic purposes and was covered by the mTTWI, reducing the expenses associated with multiple facility visits and fees for histopathology. Women who tested positive for hr-HPV but showed no abnormalities on visual inspection were advised to undergo HPV DNA testing again after one year. They were also given the choice of retesting at other nearby facilities or at the spoke where they initially underwent screening.

Statistical methods

Descriptive statistics are used to summarize the data of all relevant variables. Categorical variables are summarized using frequencies and percentages. Continuous variables with symmetric distributions, such as age, are summarized as means and standard deviations (SDs), while count or continuous variables with skewed distributions such as parity are summarized as medians and interquartile ranges (IQRs). The overall prevalence of hr-HPV and cervical lesions are presented as proportions with their 95% Clopper–Pearson confidence intervals (CIs). We further disaggregated the hr-HPV prevalence by region, hr-HPV genotype, as well as single-*vs*. mixed-genotype infections. We then explored the relationship between hr-HPV positivity and selected sociodemographic and clinical characteristics of interest using the chi-squared test. The directionality and strength of the associations between hr-HPV infection and the selected sociodemographic or clinical variables were further examined using univariate and multivariable binary logistic regression analyses. Due to the small number of missing values among the variables assessed, missing data were handled via listwise deletion. Two multivariable models were fitted, one with adjustment for all variables assessed in the univariate analyses and a second model fitted using the backward stepwise elimination procedure with an arbitrary probability threshold of 0.25. Likelihood ratio tests were used to compare the fit and performance of the nested models. Effect sizes from the logistic regression analyses are reported as odds ratios (ORs) and adjusted ORs (aORs) with their 95% CIs. The statistical analyses were performed using Stata version 14.2 (StataCorp LLC, College Station, TX, USA). All null hypotheses were rejected at a two-tailed alpha level of 0.05.

Results

Participant recruitment and selection

A flowchart of participant selection, screening, and outcomes is shown in Fig. 1. During program implementation, 5,559 women presented for cervical screening using hr-HPV DNA testing and visual inspection (VIA *or* mobile colposcopy). The HPV DNA test results of 72 women returned 'invalid', 3 women had duplicate samples, 218 women underwent standalone HPV DNA testing, and 14 women had forms presented without cervical samples for HPV DNA testing despite having undergone VIA. Fifteen (15) women had missing samples or unsubmitted samples, 11 had samples submitted without forms, 2 had undergone total abdominal hysterectomies, and 7 had

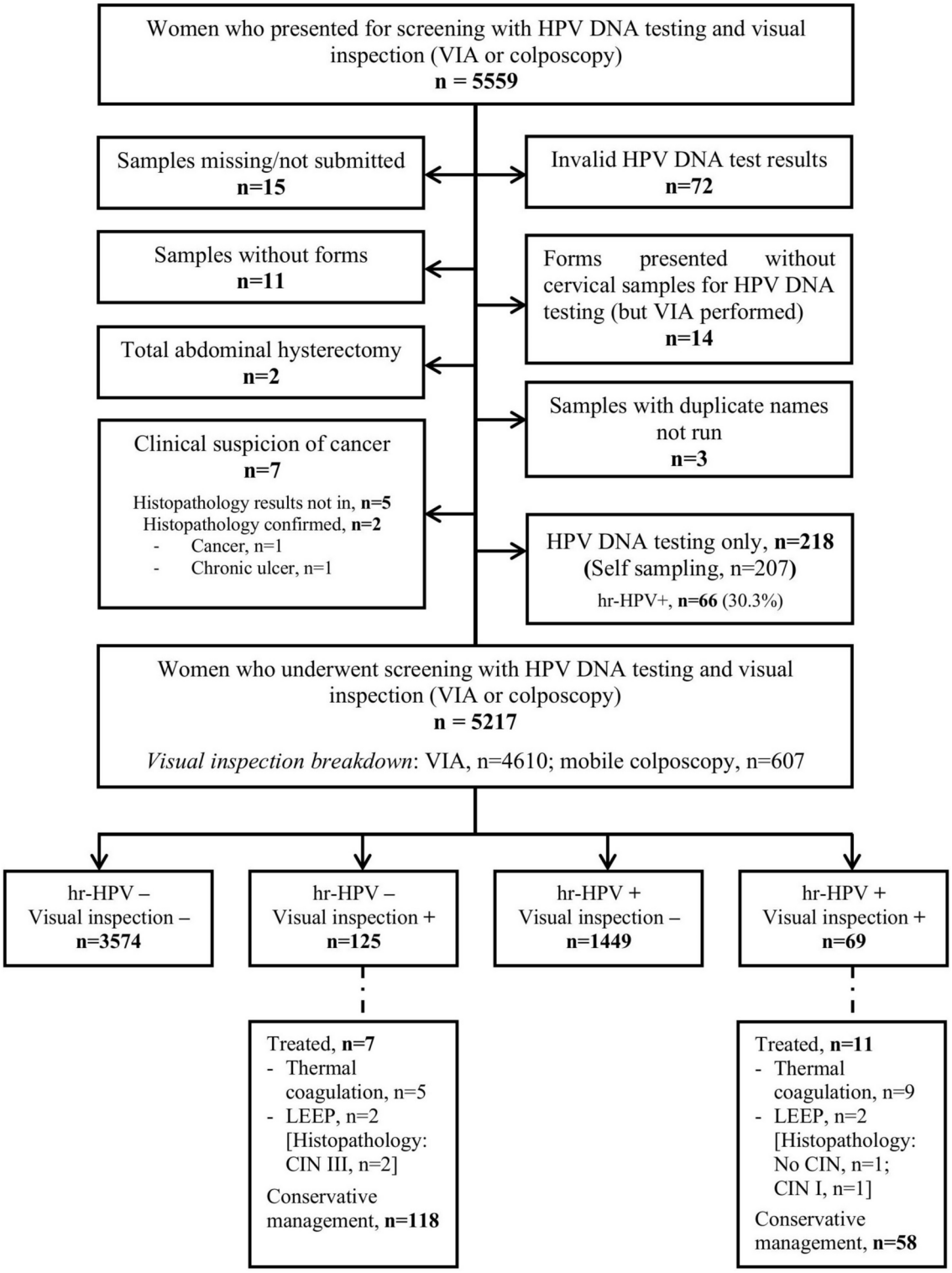

Fig. 1. Flowchart for nationwide cervical precancer screening performed under the mPharma 10,000 Women Initiative by graduates of the CCPTC, and screening outcomes and treatment of screen positives. hr-HPV, high-risk human papillomavirus; VIA, visual inspection with acetic acid; LEEP, loop electrosurgical excision procedure; CIN, cervical squamous intraepithelial neoplasia.

clinical suspicion of cancer on VIA. After excluding these women, 5217 women who underwent screening with HPV DNA testing and VIA (n = 4610) *or* EVA mobile colposcopy (n = 607) were included in the final analysis.

Sociodemographic and clinical characteristics of the women

The sociodemographic and clinical characteristics of the women screened are summarized in Table 1. The mean age at screening was 40.1 (SD, 12.7) years. The median parity was 2 (IQR, 0–4), and a majority of women were

Sociodemographic and clinical details	Estimate
Age, mean (SD)	40.1 (12.7)
Age group, n (%)	
<25	365 (7.0)
25–34	1751 (33.6)
35–44	1424 (27.3)
45–54	861 (16.5)
≥55	814 (15.6)
Missing	2 (0.0)
Marital status, n (%)	
Single	1090 (20.9)
Has a steady partner	344 (6.6)
Married/cohabiting	3102 (59.5)
Divorced	269 (5.2)
Widowed	409 (7.8)
Missing	3 (0.1)
Number of children, median (IQR)	2 (0–4)
Number of children, categorical; n (%)	
0	1380 (26.5)
1–2	1579 (30.3)
3–4	1400 (26.8)
≥5	856 (16.4)
Missing	2 (0.0)
Highest education level, n (%)	
No formal education	603 (11.6)
Elementary education	628 (12.0)
Secondary education	2112 (40.5)
Tertiary education	1674 (32.1)
Vocational/technical/other	170 (3.3)
Missing	30 (0.6)
Religious faith, n (%)	
Christian	4645 (89.0)
Islam	476 (9.1)
African traditional religion	79 (1.5)
Other	17 (0.3)
History of contraceptive use, n (%)	2250 (43.1)
Prior (pre)cancer screening, n (%)	447 (8.6)
National Health Insurance Scheme coverage, n (%)	4024 (77.1)
Ever smoked, n (%)	17 (0.3)
HIV status, n (%)	
Positive	364 (7.0)
Negative	2783 (53.3)
Unknown/missing	2070 (39.7)
Hypertension, n (%)	732 (14.0)
Diabetes, n (%)	315 (6.1)
Asthma, n (%)	92 (1.8)

Table 1. Sociodemographic and clinical characteristics of 5217 women screened using HPV DNA testing and visual inspection under the mTTWI. HPV, human papillomavirus; HIV, human immunodeficiency virus; SD, standard deviation; CI, confidence interval; IQR, interquartile range; CCPTC, Cervical Cancer Prevention and Training Centre; mTTWI, mPharma 10,000 Women Initiative.

married or cohabitating (n = 3102, 59.5). The women were predominantly Christians (n = 4645, 89.0%) and most had a minimum of secondary or vocational education (75.9%). A large majority (n = 4024, 77.1%) relied partly or entirely on the NHIS to cover their medical bills. Three hundred and sixty-four women (7.0%) reported that they were HIV-positive, while the remaining 93.0% reported a negative or unknown HIV status. The rate of prior/current contraceptive use was 43.1% and a small minority (n = 17, 0.3%) of women had ever smoked. In terms of medical history, the most commonly reported condition was hypertension (n = 732, 14.0%), followed by diabetes mellitus (n = 315, 6.1%), and asthma (n = 92, 1.8%). Four hundred and forty-seven (8.6%) had received prior cervical screening.

Participant triaging, outcomes of cervical screening, and treatment of screen-positives

At screening, 3574 women (68.5%) tested negative on both HPV DNA testing and visual inspection while 1449 (27.8%) tested hr-HPV positive but showed no cervical lesions on visual inspection (Fig. 1). Similarly, 125 women (2.4%) showed clinically significant lesions on visual inspection despite testing negative for hr-HPV; among these, 118 (2.3%) were managed conservatively whereas 7 (0.1%) underwent treatment (n = 5 via thermal coagulation and n = 2 via LEEP). Sixty-nine women (1.3%) tested positive for hr-HPV infection and simultaneously showed clinically significant lesions on visual inspection; of these, 58 (1.1%) were managed conservatively whereas 11 (0.2%) underwent treatment (n = 9 by way of thermal coagulation and n = 2 via LEEP).

Overall, the hr-HPV infection rate among the women was 29.1% (95% CI 27.9–30.3). Considering single- *vs*. mixed-genotype HPV infections, the most frequently detected HPV genotype was *other* hr-HPV type(s) only (indistinguishable) (23.5%; 95% CI 22.3–24.7), followed by HPV16 only (1.5%; 95% CI 1.2–1.8), and mixed infection with HPV18 + *other* hr-HPV type(s) (1.2%; 95% CI 0.9–1.5). The least frequently detected HPV genotype combination was mixed infection with HPV16 + HPV18 (0.2%; 95% CI 0.1–0.3) (Table 2).

Exploratory analysis of factors associated with hr-HPV infection

The results of chi-squared analyses of factors associated with hr-HPV infection among the women are shown in Table 3. Variables that showed statistically significant associations with hr-HPV infection were age group (p-value < 0.001), marital status (p-value < 0.001), number of children (p-value < 0.001), religious faith (p-

Gross screening characteristic	Estimate
Abnormal vulval inspection findings, n (%)	35 (0.7)
Missing	3 (0.1)
Abnormal vaginal inspection findings, n (%)	37 (0.7)
Missing	7 (0.1)
Cervical inspection findings, n (%)	
Normal	5135 (98.4)
Abnormal	72 (1.4)
Missing	9 (0.2)
TZ type[a] on visual inspection (VIA or colposcopy)	
1	364 (7.0)
2	1055 (20.2)
3	3715 (71.2)
Missing	83 (1.6)
Screening outcome (prevalence estimates)	
Overall hr-HPV positive, % (95% CI)	29.1 (27.9–30.3)
Single *vs*. mixed hr-HPV infections, % (95% CI)	
HPV16 only	1.5 (1.2–1.8)
HPV18 only	0.9 (0.6–1.1)
Other hr-HPV type(s) only	23.5 (22.3–24.7)
HPV16 + HPV18	0.2 (0.1–0.3)
HPV16 + *other* hr-HPV type(s)	1.1 (0.8–1.4)
HPV18 + *other* hr-HPV type(s)	1.2 (0.9–1.5)
Overall visual inspection 'positive', % (95% CI)	3.7 (3.2–4.2)
VIA 'positive', % (95% CI)*	3.2 (2.7–3.7)

Table 2. Screening characteristics and outcomes of 5217 women screened using HPV DNA testing and visual inspection under the mTTWI. hr-HPV, high-risk human papillomavirus; TZ, transformation zone; VIA, visual inspection with acetic acid; CI, confidence interval; CCPTC, Cervical Cancer Prevention and Training Centre; mTTWI, mPharma 10,000 Women Initiative. [a]Transformation zone types. TZ1: The entire circumference of the squamocolumnar junction is visible; fully ectocervical. TZ2: The entire circumference of the squamocolumnar junction is visible; partly or fully endocervical. TZ3: The entire circumference of the squamocolumnar junction is not visible; partly or fully endocervical. *Denominator: n = 4610 women who were screened using VIA.

Characteristic	hr-HPV positive, n (%)	*p*-value
Age group, years		
< 25	162 (44.4)	< 0.001*
25–34	538 (30.7)	
35–44	358 (25.1)	
45–54	212 (24.6)	
≥ 55	247 (30.3)	
Missing	1 (50.0)	
Marital status		
Single	413 (37.9)	< 0.001*
Has a steady partner	129 (37.5)	
Married/cohabiting	746 (24.1)	
Divorced	91 (33.8)	
Widowed	139 (34.0)	
Missing	0 (0.0)	
Number of children		
0	490 (35.5)	< 0.001*
1–2	433 (27.4)	
3–4	360 (25.7)	
≥ 5	235 (27.5)	
Highest education		
No formal education	188 (31.2)	0.199
Elementary education	194 (30.9)	
Secondary education	613 (29.0)	
Tertiary education	476 (28.4)	
Vocational/technical/other	37 (21.8)	
Missing	10 (33.3)	
Religious faith		
Christian	1351 (29.1)	0.001*
Islam	127 (26.7)	
African traditional religion	28 (35.4)	
Other	12 (70.6)	
History of contraceptive use		
Yes	625 (27.8)	0.151
No	893 (30.1)	
Missing	0 (0.0)	
Prior pre(cancer) screening		
Yes	124 (27.7)	0.652
No	1393 (29.2)	
Missing	1 (50.0)	
National Health Insurance Scheme coverage		
Yes	1161 (28.9)	0.474
No	357 (29.9)	
Smoker		
Yes	6 (35.3)	0.842
No	1511 (29.1)	
Missing	1 (33.3)	
HIV status		
Positive	181 (49.7)	< 0.001*
Negative	747 (26.8)	
Unknown/missing	590 (28.5)	
Hypertension		
Yes	198 (27.1)	0.188
No	1320 (29.4)	
Diabetes mellitus		
Yes	74 (23.5)	0.024*
No	1444 (29.5)	
Continued		

Characteristic	hr-HPV positive, n (%)	*p*-value
Asthma		
Yes	22 (23.9)	0.269
No	1496 (29.2)	

Table 3. Associations between hr-HPV positivity and sociodemographic/clinical characteristics among women screened using HPV DNA testing and VIA under the mTTWI. HPV, human papillomavirus; HIV, human immunodeficiency virus; hr-HPV, high-risk human papillomavirus; VIA, visual inspection with acetic acid; CCPTC, Cervical Cancer Prevention and Training Centre; mTTWI, mPharma 10,000 women initiative. *Statistically significant.

value = 0.001), HIV status (p-value < 0.001), and diabetes mellitus (p-value = 0.024). Other variables of interest such as education level, history of contraceptive use, prior precancer screening, dependence on the NHIS, prior/current smoking, hypertension, and asthma did not show statistically significant associations with hr-HPV infection.

Logistic regression analysis of factors associated with hr-HPV positivity

In the logistic regression analysis, the univariate relationships mostly remained after adjusting for other important predictors of hr-HPV infection (Table 4). For example, compared to women aged 35–44 years, women younger than 25 years (aOR = 1.93; 95% CI 1.48–2.53; p-value < 0.001) and those aged 24–34 years (aOR = 1.27; 95% CI 1.07–1.51; p-value = 0.006) were more likely to test positive for hr-HPV infection after controlling for all other studied factors in the final model. Also, compared to married/cohabitating women, women with other marital statuses were more likely to test hr-HPV positive, with aORs ranging from 1.38 (95% CI 1.08–1.77; p-value = 0.011) for widows and 1.54 (95% CI 1.29–1.84; p-value < 0.001) for single women. Again, compared to multiparous women with 3–4 children, nulliparous women were more likely to test hr-HPV positive (aOR = 1.24; 95% CI 1.01–1.53; p-value = 0.037) after adjusting for other variables. Women of other religious faiths were approximately five times more likely to test hr-HPV positive (aOR = 5.20; 95% CI 1.79–15.11; p-value = 0.002) compared to Christian women. HIV-positive women were close to three times more likely to test hr-HPV positive (aOR = 2.73; 95% CI 2.15–3.47; p-value < 0.001) than HIV-negative women. Other variables of interest, such as the highest level of education, diabetes, hypertension, and prior/current smoking were not independently associated with hr-HPV positivity in the final adjusted model (Table 4).

Discussion

Our study had two main aims: to assess the prevalence of hr-HPV infection (nationally and regionally) and of cervical lesions among women opportunistically screened by graduates of the CCPTC in their own practice settings with remote supervision by trainers, and to examine the factors associated with hr-HPV positivity among the women. For each woman, concurrent testing by way of hr-HPV DNA testing and a visual inspection method was employed. The prevalence of hr-HPV infection found among women screened under the mTTWI (29.1%) was higher than that reported by the WHO for women in the general population of West Africa (21.3%)[20,21]. The national rate recorded was also higher than the prevalence of 17.9% (95% CI 16.7–19.0) recorded in a prior study of women also screened using the concurrent approach in place at the CCPTC[10]. The prevalence distribution varied widely among regions (Fig. 2), with the highest recorded in the Oti Region (32.8%; 95% CI 26.1–39.5) and the lowest recorded in the Upper West Region (20.7%; 95% CI 14.2–27.2) and North-East Region (20.7%; 95% CI 12.4–29.0). Overall, the Oti, Volta, Greater Accra, Central, Eastern, and Savannah Regions exceeded the national prevalence; however, there was no statistically significant difference in prevalence across regions (chi-squared p-value = 0.081). In trying to understand the difference in prevalence across regions, while the age distribution across regions was found to differ significantly (ANOVA p-value < 0.001), the prevalence did not significantly differ across regions with and without adjustment for age. Factors found to be significantly associated with hr-HPV infection among women screened under the mTTWI included age < 35 years, having a relationship status other than married/cohabiting, nulliparity, and HIV positivity.

In order to target socioeconomically disadvantaged women, to whom our model was tailored, it is necessary to incorporate cervical screening in basic health services through primary care[22]. Despite being opportunistic in nature, the collaboration between the CCPTC and mPharma should give hope that it is possible to achieve coordinated large-scale screening in Ghana through primary healthcare workers. While participant recruitment was left to the discretion of the CCPTC graduates, age-eligible women attending their health posts for minor conditions, follow-up visits, or unrelated concerns (through outreaches), as well as accompanying family members were counseled and motivated to get screened. As the CCPTC continues to develop and provide training, scale-up, and implementation would require additional investments to develop the requisite infrastructure for screening and ablative therapy in the spokes. There is enough evidence that screening for cervical precancer opportunistically is limited in achieving population coverage[23], which in turn depends on knowledge, nearness to screening services, and frequency of screening[24]. In addition, opportunistic screening would miss women who seldom take part in outreach programs or visit health centers[25,26], many of whom may have a higher risk of cervical cancer[27]. While these all point to a need to move from opportunistic to organized screening, in reality, until Ghana achieves the resources to implement an invitation-based screening approach, we must continue to rely on and refine opportunistic models of the nature described here, despite

Characteristic	Univariate analyses		Full multivariable model		Final multivariable model	
	OR (95% Cl)	*p*-value	aOR (95% CI)	*p*-value	aOR (95% CI)	*p*-value
Age group, years						
< 25	2.38 (1.87–3.02)	< 0.001*	1.95 (1.49–2.56)	< 0.001*	1.93 (1.48–2.53)	< 0.001*
25–34	1.32 (1.13–1.55)	0.001*	1.27 (1.07–1.52)	0.006*	1.27 (1.07–1.51)	0.006*
35–44 (Ref.)	1.00	–	1.00	–	1.00	–
45–54	0.97 (0.80–1.18)	0.782	0.92 (0.74–1.13)	0.419	0.92 (0.75–1.13)	0.408
≥ 55	1.30 (1.07–1.57)	0.008*	1.18 (0.93–1.50)	0.169	1.16 (0.93–1.45)	0.180
Marital status						
Single	1.93 (1.66–2.23)	< 0.001*	1.54 (1.29–1.84)	< 0.001*	1.54 (1.29–1.84)	< 0.001*
Has a steady partner	1.89 (1.50–2.39)	< 0.001*	1.42 (1.10–1.83)	0.007*	1.43 (1.11–1.84)	0.006*
Married/cohabiting (Ref.)	1.00	–	1.00	–	1.00	–
Divorced	1.61 (1.24–2.11)	< 0.001*	1.45 (1.09–1.92)	< 0.010*	1.44 (1.09–1.91)	0.011*
Widowed	1.63 (1.30–2.03)	< 0.001*	1.37 (1.06–1.76)	0.014*	1.38 (1.08–1.77)	0.011*
Number of children, n (%)						
0	1.59 (1.35–1.87)	< 0.001*	1.23 (1.00–1.51)	0.055	1.24 (1.01–1.53)	0.037*
1–2	1.09 (0.93–1.28)	0.292	1.00 (0.84–1.20)	0.959	1.01 (0.85–1.21)	0.889
3–4	1.00	–	1.00	–	1.00	–
5 or more	1.09 (0.90–1.32)	0.363	1.00 (0.81–1.23)	0.977	1.00 (0.81–1.23)	0.984
Highest education						
No formal education	1.14 (0.93–1.40)	0.204	1.26 (0.99–1.61)	0.065	1.23 (1.00–1.61)	0.054
Elementary education	1.13 (0.92–1.37)	0.248	1.17 (0.93–1.47)	0.183	1.16 (0.93–1.46)	0.186
Secondary education	1.03 (0.89–1.19)	0.691	1.10 (0.94–1.30)	0.222	1.10 (0.94–1.29)	0.228
Vocational/technical/other	0.70 (0.48–1.02)	0.066	0.78 (0.52–1.17)	0.237	0.79 (0.53–1.18)	0.251
Tertiary education (Ref.)	1.00	–	1.00	–	1.00	–
Religious faith						
Christian (Ref.)	1.00	–	1.00	–	1.00	–
Islam	0.89 (0.72–1.10)	0.270	0.87 (0.69–1.09)	0.229	0.87 (0.69–1.10)	0.117
African traditional religion	1.34 (0.84–2.13)	0.219	1.33 (0.81–2.17)	0.262	1.34 (0.82–2.20)	0.238
Other	5.85 (2.06–16.64)	0.001*	5.32 (1.82–15.50)	0.002*	5.20 (1.79–15.11)	0.002*
History of contraceptive use						
Yes	0.89 (0.79–1.01)	0.067	0.96 (0.84–1.09)	0.505	–	–
No (Ref.)	1.00	–	1.00	–	–	–
Screened for cervical precancer/cancer before						
Yes	0.93 (0.75–1.15)	0.512	1.02 (0.81–1.28)	0.872	–	–
No (Ref.)	1.00	–	1.00	–	–	–
National Health Insurance Scheme coverage						
Yes	0.95 (0.82–1.09)	0.386	1.00 (0.86–1.15)	0.961	–	–
No (Ref.)	1.00	–	1.00	–	–	–
Smoker						
Yes	1.33 (0.49–3.60)	0.574	0.76 (0.26–2.20)	0.614	–	–
No (Ref.)	1.00	–	1.00	–	–	–
HIV status						
Positive	2.70 (2.16–3.37)	< 0.001*	2.71 (2.13–3.44)	< 0.001*	2.73 (2.15–3.47)	< 0.001*
Negative (Ref.)	1.00	–	1.00	–	1.00	–
Unknown/missing	1.09 (0.96–1.23)	0.200	1.07 (0.94–1.23)	0.315	1.08 (0.94–1.23)	0.281
Hypertension, n (%)						
Yes	0.89 (0.75–1.06)	0.188	1.03 (0.84–1.28)	0.720	–	–
No (Ref.)	1.00	–	1.00	–	–	–
Diabetes, n (%)						
Continued						

Characteristic	Univariate analyses		Full multivariable model		Final multivariable model	
	OR (95% Cl)	*p*-value	aOR (95% CI)	*p*-value	aOR (95% CI)	*p*-value
Yes	0.74 (0.56–0.96)	0.024*	0.84 (0.62–1.14)	0.265	–	–
No (Ref.)	1.00	–	1.00	–	–	–
Asthma, n (%)						
Yes	0.76 (0.47–1.24)	0.271	0.74 (0.45–1.22)	0.243	–	–
No (Ref.)	1.00	–	1.00	–	–	–

Table 4. Exploratory logistic regression analyses of selected sociodemographic and clinical characteristics associated with hr-HPV infection among women screened using HPV DNA testing and VIA under the mTTWI. hr-HPV, high-risk human papillomavirus; HIV, human immunodeficiency virus; CI, confidence interval; OR, odds ratio; aOR, adjusted odds ratio; Ref., reference category; CCPTC, Cervical Cancer Prevention and Training Centre; mTTWI, mPharma 10,000 Women Initiative. *Statistically significant.

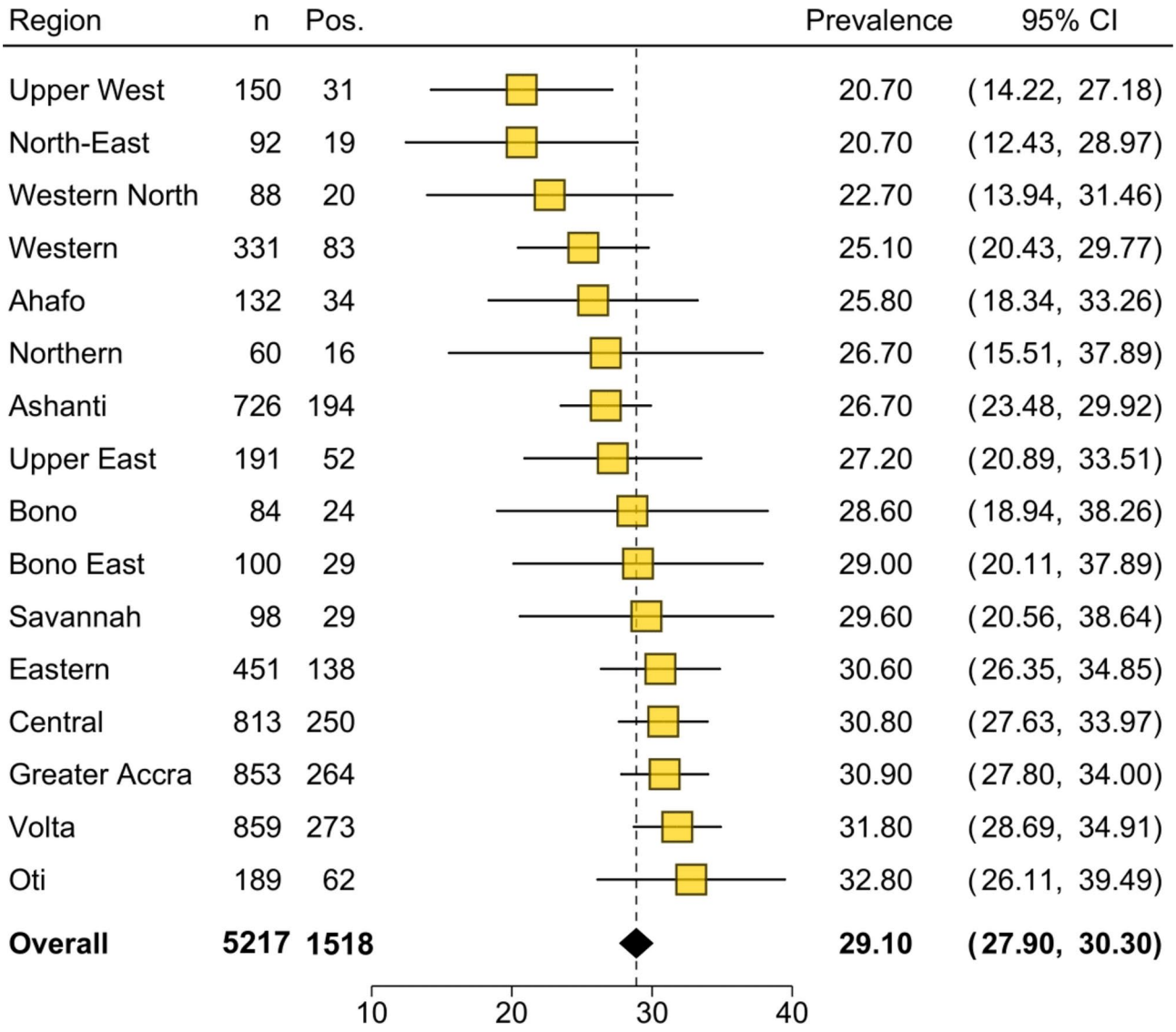

Fig. 2. Forest plot showing the distribution of the prevalence of hr-HPV infection stratified by region among women screened under the mPharma 10,000 Women Initiative by graduates of the CCPTC. n, number of women screened; CI, confidence interval.

their shortcomings. We however demonstrate the feasibility of establishing a national screening program that relies on health centers and community-based health workers.

Apart from funding under the mTTWI, the most important factor in successful model implementation was the effort and enthusiasm of the CCPTC graduates in providing counseling to eligible women to screen. Supportive remote supervision also enabled fidelity with the screening protocol, as shown by the low percentage of invalid HPV test results (which could indicate poor sampling technique or specimen handling) and women screened below the age of 25 years. Another encouraging observation was that women counseled to undergo ablation generally complied, even if this meant returning to the clinic at a later date or going to another center. Our concurrent testing approach also had the two-pronged benefit of combining the advantages associated with using both subjective (VIA/EVA mobile colposcopy) and objective (hr-HPV DNA testing) methods, thereby improving their diagnostic yields in a single visit. On the other hand, there were logistic challenges with transporting cervical samples from all over the country to the CCPTC as a single hub for testing. While this was driven largely by funding considerations (since mPharma provided funding for MA-6000 testing), there was a glaring lack of nearby facilities with the technology to carry out HPV DNA testing as well. Thus, our expanded hub-and-spoke model could be further enhanced by adding extra hubs equipped with the technology and human resources to carry out HPV DNA testing. This would either require strategic vertical investments from government and non-governmental organizations alike, or co-opting existing PCR platforms for HPV DNA testing, thereby freeing the CCPTC to focus on its mandate of training health workers and informing/shaping the development of policy.

The number of trained health workers by the CCPTC continues to increase. It is not clear the maximum capacity a center like the CCPTC can mentor routinely. In future, the use of artificial intelligence to guide health workers in screening and follow up of screen positives may take some pressure off centers like the CCPTC. Also, the availability of point-of-care molecular tests for cervical screening will make it unnecessary to transfer samples over long distances across a country to a central point for testing, and make it possible to get results onsite so that decision making is much faster, even in a single visit.

Strengths and limitations

To the best of our knowledge, this is the first large-scale study to document nationwide cervical precancer screening in Ghana using multiple cadres of trained health workers with the backing of trainers at a training center who provided remote mentoring and supervision during program implementation. Consequently, we could not design a more robust study as there was no pre-implementation period to compare our findings with. For many of the spokes, this was the first time primary cervical screening was being introduced with hr-HPV DNA testing and visual inspection methods. Our expanded hub-and-spoke approach was groundbreaking for several reasons. Firstly, it allowed trained health workers to conduct screening and treatment in their own settings, maintaining their responsibility to the women without unnecessary referrals, which could lead to women being lost along the care continuum. Secondly, our approach utilized commonly available mobile phones and internet services in Ghana, offering graduates near-immediate virtual assistance for lesion identification, management, and case referral.

Despite these strengths, our study and approach do have their limitations. Firstly, there are concerns regarding the primary mode of transmitting and storing patient images through WhatsApp, which lacks established compliance standards[28–30], necessitating evaluation for patient confidentiality. Furthermore, while implemented within the existing opportunistic screening context in Ghana, we could not explore the long-term sustainability of this intervention as it would require additional resources and partnerships for training and equipment provision outside the research scope. Also, the hr-HPV prevalence of 29.1% identified cannot be extrapolated to the entire country since screening was still carried out opportunistically even in the context of funding under the mTTWI program, and preference was given to women who would not typically afford HPV DNA testing. Previous studies of HPV distribution in cervical cancer have shown a wide range of genotypes with varying prevalence for non-HPV16/18 infections[5,31]. While cost constraints limited our ability to perform full HPV genotyping for the women, further stratifying non-HPV16/18 infections, which had the highest combined prevalence, could have enabled targeted follow-up and management strategies. In addition, understanding the specific genotypes present could inform future vaccination and screening efforts, potentially leading to more effective preventive and control measures. Similarly, given that women of relatively poor socioeconomic circumstances were selected for screening, the regional estimates may not be representative of the true prevalence for women in the general population and the comparisons across regions may not be reliable. Last, while we aimed for standardization with regard to sample collection and transportation to the central laboratory, local adaptations in the sampling process and transportation times could have influenced the regional outcomes.

Conclusion

Despite its limitations, using an expanded hub-and-spoke model with remote supervision of graduates of the CCPTC training program enabled nationwide screening of socioeconomically disadvantaged women in an opportunistic context with funding under the mTTWI. Drawing from our implementation of this model within the mTTWI framework, we posit that while Ghana prepares for organized screening, leveraging this model could enable a phased expansion of cervical precancer screening with the help of international and local partners. While there is an urgent need to quickly establish a national (organized) screening program, this approach, combined with concurrent testing, holds promise for mitigating loss to follow-up among women requiring additional evaluation and lesion management after screening.

Data availability

The data supporting the conclusions of this article will be made available, upon reasonable request from the corresponding author.

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Author contributions

Study conceptualization: JA, KE, ET, CMW, BHA, EA-B, ENK, IG, SK, and JEA. Trainee mentoring, screening, and data collection: ET, CMW, ES, and KE. HPV DNA testing: SK, IG, ENK, and EA-B. Data curation: JEA, SD, NOME, ET, CMW, SK, ES, HMAF, and KE. Formal analysis: JEA, SD, NOME, ET, CMW, SK, ES, HMAF, and KE. Project administration: KE and JA. Data validation: KE, ET, and JEA. Writing–original draft: NOME, JEA, ET, KE, SK, and PKA. Writing–review and editing: KE, JA, ET, CMW, JEA, EA-B, ENK, SK, IG, HMAF, SD, ES, BHA, NOME, and PKA. All the authors read and approved the manuscript in its current form.

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Declarations

Competing interests

The authors declare that the research was conducted in the absence of any financial and non-financial relationships that could be construed as a potential conflict of interest.

Ethical approval

This study complied with the Declaration of Helsinki (1964) and its later amendments. Verbal informed consent was sought from the women before administering the questionnaire, collecting cervical samples, and additional screening procedures. The consent procedure was approved by the Ethical Review Committee of the Catholic Hospital, Battor (approval no. CHB-ERC 0120/06/22), which also permitted the researchers to publish the study findings retrospectively.

Additional information

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