Implementation of a cervical cancer screening programme using a 3T-Approach in low-and middleincome countries

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SUMMARY

Cervical cancer is one of the main causes of cancer death in women in Cameroon and in low-and middle-income countries (LMICs). Since 2020, and the call for action released by the World Health Organization (WHO) to eliminate cervical cancer, this burden has become an international priority (1). In order to achieve elimination, the WHO has set the "90-70-90 targets": 90% of the target population vaccinated, 70% screened, 90% treated. Thanks to a strong collaboration between Cameroon and the University Hospitals of Geneva for many years, a five-year project (2018-2023) to fight against cervical cancer has been implemented at the Dschang District Hospital (DDH), in the West Region of Cameroon.

The project is based on WHO recommendations and prevention strategies and follows a "screen-triage-treatment" procedure, i.e. targeting women aged between 30 and 49 years for HPV screening, triaging all HPV-positive women and treating them when they present with precancerous lesions, in one day.

This approach is recommended for LMICs such as Cameroon. To date, the implementation of such a prevention project in Cameroon has not been evaluated. In order to make the project sustainable and to replicate it in different areas of Cameroon, an evaluation of the 1) feasibility, 2) safety and 3) acceptability of this approach and its procedures has been conducted since the launch of the project, through close quality control and surveys of the women included in the study.

The results of the evaluation of the implementation of the 3T (test-triage-treat) screening project showed that the recommended practices are adapted to the local context and are embedded in a sustainable approach. Patient safety was not impacted by the various interventions and treatments offered by the project. No serious adverse events (SAE) or events requiring hospitalisation have been noted over the years since the project began.

In general, the 3T-Approach and the interventions carried out during screening, triage and treatment were well accepted by the women, who mostly reported that they would recommend them to others. Based on these results, the 3T project will continue to implement the WHO recommendations for cervical cancer screening in the local context, and will maintain quality control in order to quickly propose strategies for improvement when necessary. An example of a challenge that we have already faced is the COVID-19 pandemic, during which some recruitment strategies had to be promptly readjusted. Through this, and other events during our 4 years of field experience, we have learned that to be successful, a programme like ours needs to be dynamic, provide context-sensitive solutions and follow national and international health recommendations.

In 2022, the project will expand and open new screening facilities at the Bafoussam Regional Hospital. Our prior experience gained from the development of this 3T project will allow us to upscale this feasible, safe and acceptable cervical cancer prevention programme in order to reach other women in need.

RESUME

Le cancer du col utérin (CC) est une des causes principales de décès par cancer chez la femme au Cameroun, et dans les pays à revenu faible et intermédiaire (PRFI). Depuis 2020, et l'appel à action mondial émis par l'Organisation Mondiale de la Santé (OMS), l'élimination du cancer du col est devenue une priorité de santé publique. L'objectif est d'atteindre les cibles « 90-70-90 » éditées par l'OMS d'ici 2030, à savoir 90% de la population cible vaccinée, 70% dépistée, 90% traitée. Grâce à la forte collaboration présente depuis plus de vingt ans entre le Cameroun et les Hôpitaux Universitaires de Genève, un projet quinquennal de lutte contre le cancer du col 2018-2023 a été lancé et implémenté à l'hôpital de District de Dschang, dans la région ouest du Cameroun.

Le projet s'appuie sur les recommandations de prévention et de prise en charge du CC de l'OMS, qui prévoient d'offrir une stratégie « dépistage-triage-traitement ». Dans ce contexte, toutes les femmes âgées entre 30 et 49 ans bénéficient sur une journée d'un test de dépistage du HPV, d'un triage pour les femmes HPV-positives par examen gynécologique et d'un traitement lorsque des lésions précancéreuses sont identifiées. Cette approche est particulièrement recommandée pour les PRFI, dont est issue le Cameroun. A ce jour, l'implémentation d'un tel projet de prévention au Cameroun n'a encore jamais été évaluée. Dans le but de pérenniser le projet et de permettre un passage à l'échelle en proposant le programme dans différentes zones du pays, une évaluation de 1) la faisabilité, 2) la sécurité et 3) l'acceptabilité, de cette approche a été menée depuis le lancement du projet, via un contrôle de qualité rapproché.

Les résultats de l'évaluation de l'implémentation du projet de dépistage selon l'Approche 3T (test-triage-traitement), ont montré que les pratiques recommandées sont adaptées au contexte et s'inscrivent dans une approche pérenne. La sécurité des patientes n'a pas été impactée par les différentes interventions et traitements proposés par le projet. Aucun évènement grave ou évènement nécessitant une hospitalisation n'a été relevé depuis le lancement du projet. Globalement, l'Approche 3T et les interventions menées lors du dépistage, triage et traitement étaient bien acceptées par les femmes, qui les recommanderaient à leur entourage. Sur la base de ces résultats, le projet 3T continuera à mettre en œuvre les recommandations de l'OMS pour le dépistage du CC dans ce contexte local, et maintiendra un contrôle de qualité afin de proposer rapidement des stratégies d'amélioration si nécessaire. Tel qu'expérimenté durant ces quatre années sur le terrain, avec une baisse du recrutement liée à la période de la pandémie du COVID-19, mais également due à d'autres évènements, les stratégies proposées doivent pouvoir être rapidement réajustées. Ceci démontre la nécessité d'avoir un programme dynamique, proposant des interventions adaptées au contexte et aligné aux recommandations sanitaires nationales et internationales.

Une salle de dépistage à l'Hôpital Régional de Bafoussam, verra le jour en 2022. L'ensemble des expériences acquises permettront d'implémenter un programme de prévention du CC faisable, sûr et acceptable pour les femmes.

ACRONYMS AND ABBREVIATIONS

ABCD	A:acetowitheness, B:bleeding, C:coloring, D:diameter
AEs	Adverse Events
CC	Cervical Cancer
CEC	Competent Ethics Committee
CHW	Community Health Workers
CIC	Community Information Channels
CIN	Cervical Intraepithelial Neoplasia
CIN1	Cervical Intraepithelial Neoplasia grade 1
CIN2+	Cervical Intraepithelial Neoplasia of grade 2 or worse
CRF	Case Report Form
DDH	District Dschang Hospital
DNA	Deoxyribonucleic Acid
ECB	Endocervical brushing
FIGO	International Federation of Gynaecology and obstetrics
HCP	Healthcare providers
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
HUG	Hôpitaux Universitaires de Genève
IARC	International Agency for Research on Cancer
LLETS	Large-loop excision of the transformation zone
LMICs	Low-and Middle-Income Countries
PCR	Polymerase Chain Reaction
TA	Thermal Ablation
TZ	Transformation Zone
VAT	Visual Assessment for Treatment
VIA	Visual Inspection with Acetic Acid
VILI	Visual Inspection with Lugol's Iodine
WHO	World Health Organization

1 Introduction

Cervical cancer (CC) is the fourth most common cancer globally, and the second most common cancer in Cameroon with 2'770 cases diagnosed and 1'787 deaths recorded in 2020 (2). More than 85% of cervical cancer cases occur in low- and middle-income countries (3). In Sub-Saharan Africa, CC is the leading cause of cancer death in women, however it is preventable through adequate vaccination and screening. Human papillomavirus (HPV) infection has been shown to be the leading cause of cervical cancer, even though the majority of infected women will never develop cancerous lesions and will clear the virus themselves without treatment (4).

Worldwide, 8 out of 10 women will have been infected at least once with the HPV virus (5). HPV is the most common viral sexually transmitted infection, and is transmitted often unknowingly by skin-to-skin contact of the genital area, or contact with infected mucosal surfaces (6). Condoms provide only limited protection again HPV transmission, due to the fact that they cover only specific areas (7,8). During her sexual life, the same patient may be infected several times by the same HPV genotype, or may acquire different genotypes, as the original immune system response does not appear to fully protect against new infections (9). In Sub-Saharan Africa, the HPV prevalence is 24% with a peak between the ages of 25-34 (10).

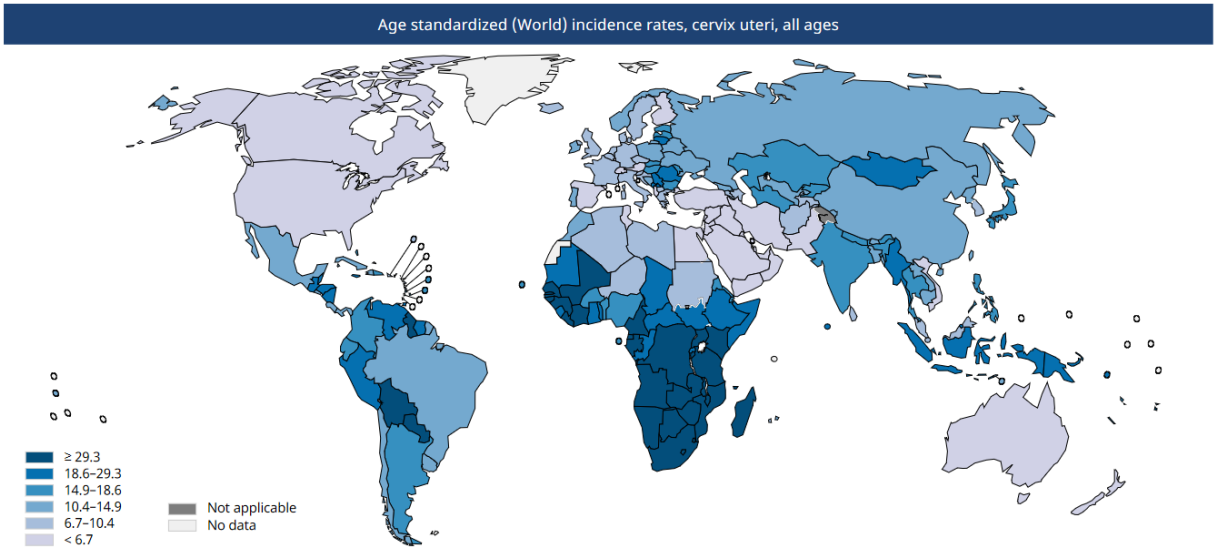


Figure 1: Incidence cervical cancer Worldwide 2020 (Source: IARC, 2021 (11))

More than a hundred genotypes of HPV have been identified, and approximately forty can infect the genital area of both men and women (12). Most HPV is not carcinogenic - only fourteen types are recognised as high-risk (HR) oncogenic HPV strains (13). Among HPV infected women, 1 out of 3 are positive for high risk HPV, which is significant given that 95% of CC are associated with eight HPV HR genotypes (16, 18, 31, 33, 35, 45, 52 and 58) (11). Two of these in particular - 16 and 18 - cause more than 70% of precancerous and cancerous lesions (13). In

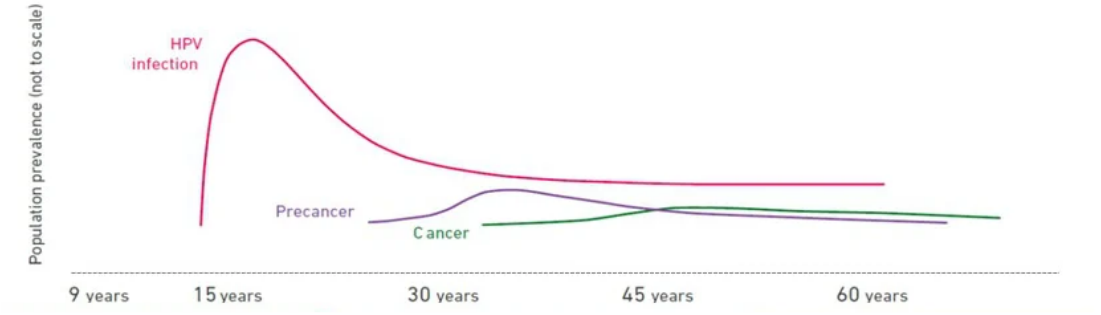
Africa, it is estimated that 3.8% of women infected by HPV have one of these two genotypes (14).

1.1 Comprehensive cervical cancer prevention

The persistence of the infection and the evolution into chronic disease and pre-cancerous lesions is associated with various risk factors such as smoking, being immunocompromised (e.g. People living with HIV), and the presence of coinfection with other sexually transmitted infections (13). However, it usually takes several years for HPV infection to cause the development of pre-cancerous and cancerous lesions. Moreover, almost 80% of women will eliminate their HPV on their own after 12 to 24 months (12,15). This slow progression lends itself to effective prevention through screening and treatment programmes, aiming to avoid the development of cancerous lesions.

The efficacy of these prevention models has been demonstrated for many years now, with the incidence and mortality rate of cervical cancer falling by 70% in industrialised countries since the introduction of screening with the cytological Papanicolaou test in 1940 (16).

For these reasons, the WHO recommends a comprehensive, global approach to cervical cancer prevention and treatment throughout a woman's life (1).



Primary prevention	Secondary prevention	Tertiary prevention
Girls 9-14 years • HPV vaccination	**From 30 years of age for women from the general population and 25 years of age for women living with HIV**	**All women as needed**
Girls and boys should also be offered, as appropriate • Health information and warnings about tobacco use • Sex education tailored to age and culture • Condom promotion and provision for those engaged in sexual activity • Male circumcision	• Screening with a high-performance test equivalent or better than HPV test • Followed by immediate treatment or as quickly as possible after an HPV molecular positive test.	Treatment of invasive cancer at any age • Surgery • Radiotherapy • Chemotherapy • Palliative care

Figure 2 : Life-course approach for cervical cancer prevention and control (source : WHO, 2022 (17))

In 2020, the Director-General of the WHO launched a call to action to eradicate Cervical Cancer. This new global strategy "WHO 90-70-90" according to comprehensive cervical cancer control, established three targets regarding the three prevention axes, which need to be reached by 2030; i) primary prevention: 90 % of girls are fully vaccinated by age of 15; ii) secondary prevention: 70% of women are screened by a high-performance test at least twice in their lifetimes; iii) secondary and tertiary prevention: 90% of women with pre-cancerous or cancerous lesions identified are treated and receive adequate care (18).

Unfortunately, in LMICs such as Cameroon, barriers to these prevention axes are prevalent and still interfere with women's access to care and effective screening (19). The lack of policy, infrastructure, standardised and high quality training, and lack of information and health education of the population limit screening coverage, and for these reasons CC remains largely uncontrolled in LMICs. It is estimated that 20% of eligible women have had a screening test in LMICs versus 60% in high-incomes countries (19). This coverage is lower still in Cameroon where only 4% of women (20) have been screened. Evidently, this is far below the WHO's target (21). Therefore, to overcome the barriers to provision of WHO recommended care, is was necessary to adopt context-sensitive solutions providing a comprehensive cervical cancer screening programme adapted to the local context (18).

1.1.1 Primary prevention – HPV vaccination

The most effective method of primary prevention is introduction of vaccines against HPV. Various vaccines against HPV have been developed, protecting against at least 70% of infections and diseases associated with the virus (17). The vaccine targets the HPV virus and not the precancerous or cancerous lesions themselves. The vaccines cover the HPV viruses that most commonly cause cervical cancer, but do not protect against all strains. Screening is therefore essential to complement this approach. Three vaccines are currently available (22) i) Bivalent-Cervarix ® (GSK) which protects against HPV 16 and 18 ii) Quadrivalent-Gardasil® which protects against HPV 6, 11, 16, 18; iii) Nonavalent-Gardasil®, which is an extension of the quadrivalent-Gardasil which provides protection also against HPV 31, 33, 45, 52, and 58.

These vaccines do not contain active virus, so there is no risk of transmission of HPV to women. They are not equipped to treat a person who already has an HPV infection or HPV-related disease. The target population is girls aged 9-11 years, ideally before first intercourse, but it can be offered beyond this age range. The vaccine may be administered to sexually active young women, however the same protection is not guaranteed (23). It is recommended that boys are also vaccinated before first intercourse given that 3 out of 4 men are infected with HPV in their lifetime. This is important both on a population level as they may become carriers

of the infection, and on an individual level due the possibility of developing cancerous lesions if HPV is not cleared.

However, large-scale vaccination programme implementation and vaccine distribution plans are still several years away in the countries that have the most need (10). In certain less developed regions, 2.7% of the female population aged between 10 to 20 years have been vaccinated (10). Despite a national HPV vaccination programme, only 5% of eligible women had received their final dose of HPV vaccine in Cameroon as of 2020 (14,24). It has been shown that in 78 LMICs, 70% of cervical cancer cases would be prevented if women were vaccinated and screened twice for HPV (19). Consequently, in LMICs, the detection and treatment of precancerous lesions before they evolve into cancer remains the main form of prevention.

1.1.2 Secondary prevention – Screening and treatment of precancerous lesions

Various screening procedures and precancerous treatment have been developed and assessed for their effectiveness in the fight against cervical cancer burden, principally in high-resources countries. In this chapter, the main methods are presented in chronological order.

Cytology
The Papanicolaou (Pap) test or cytology by liquid-based cytology (LCB) has shown to greatly decrease the mortality rate of cervical cancer in countries equipped with resources to provide effective cytological screening (25). This approach involves the identification of abnormal cells collected from the cervix but requires the presence of trained professionals and a laboratory to perform quality preparation and analysis of samples. However, these aspects may be restricting for countries with limited resources, therefore PAP screening is usually not a viable possibility in LMIC contexts (26).

Visual inspection with acetic acid (VIA)
VIA has already been used also for many years as an alternative screening to cytology as it is less resource intensive and can be performed by a variety of health-care workers (physicians, nurses, midwives, technicians) (18). The procedure is easy to perform but it's success is strongly related to the screening performance of the professional and the training received (27). It consists of the application of a 3-5% acetic acid solution on the cervix. The appearance of aceto-white areas touching the squamo-columnar junction helps to define the pathological areas of the cervix if present (27). In general populations VIA has been shown to have an acceptable sensitivity (60–86%) and specificity (64– 94%) similar or better to cervical cytology. VIA is feasible in many low-resource areas where it is difficult to sustain high-quality cytology programmes (18).

Visual inspection with Lugol's iodine (VIL)
Besides VIA, VILI also known as Schiller's test has been used. It is based on the principle that squamous epithelium contains glycogen, whereas precancerous

lesions and invasive cancer contain little or no glycogen. Iodine is glycophilic and is taken up by the squamous epithelium, staining it mahogany brown or black. Precancerous lesions or invasive cancer do not take up iodine and appear as well defined, thick saffron or mustard-yellow coloured areas. However, VIA and VILI are subjective tests as healthcare providers (HCP) interpret what they see on the cervix, leading to possible variations in test interpretation. Overall, evidence shows that using it after HPV testing may decrease slightly overtreatment (18).

HPV-test

A HPV-DNA test detecting high-risk HPV is now recommended as primary cervical cancer screening for early detection and high performance treatment. The screening should start at 30 years among the general population of women , and should be repeated every 5 to 10 years, which is longer than cytological testing which is proposed every 3 years (18). HIV-positive women should start screening earlier from the age of 25, because the prevalence of HPV infection and CC incidence are much higher in this population (17,28). Scientific evidence shows that this test is much more effective than cytology in identifying women at greater risk of developing precancerous cervical lesions (18,29,30). HPV testing provides an objective diagnosis, giving it an advantage over VIA/VILI screening (18).

Additionally, HPV testing permits self-vaginal sample collection - self sampling has been shown to have a similar sensitivity and specificity for the detection of precancerous lesions when compared with samples collected by HCP (3,26,31) – and is considered to be a safe and acceptable screening method by users (32–35). This approach reduces the discomfort and pain of a pelvic examination and increases women's autonomy, so might improve screening coverage (32,36,37) aiming to target the 70% eligible women as recommended by the WHO (18).

The HPV test is a point of-care test (38), therefore it allows women to be treated in a single visit as a screen- and-treat approach which may mitigate loss to follow-up (18).

However, a single HPV test has a disappointing specificity and positive predictive value meaning that a significant number of screen-positive women without cervical pre-cancer or cancer may receive unnecessary follow-up and overtreatment. For this reason, VIA/VILI are proposed as triage strategies after an HPV-positive test, to evaluate and determine the need for treatment or follow-up (1).

Pathological analysis

The most reliable way to diagnose precancerous or cancerous lesions is through histological examination. Cervical biopsy and an endocervical brushing are used as reference standard for monitoring the performance of the screen, triage and treatment approaches. During the histological examination, the physician looks for abnormal tissue in the cervix, which by its presence would indicate a pre-cancerous or cancerous lesion. Abnormalities are classified according to the International Agency of Research on Cancer agency of the World Health Organization (39,40). Tissue biopsies may be classed as follows; cervical intraepithelial neoplasia grade

1 (CIN 1); cervical intraepithelial neoplasia grade 2 (CIN 2) and severe dysplasia (CIN 3/AIS), among lesions with no of invasive cancer.

Precancerous treatment

Since the early 2010s, cryotherapy has been recommended by WHO as a standard treatment for precancerous cervical lesions in a screen and treat approach in LMICs (18). However recent studies have highlighted the logistical difficulties of using cryotherapy, due to the lack of available gas and its high price in the context of these countries (41). An alternative has been proposed, namely another type of ablative treatment, TA. This has been shown to have the same treatment efficacy on precancerous lesions. Henceforth, the WHO also recommends the use of TA in LMICs (18).

Thermal Ablation is provided by applying a probe (WISAP; Medical Technology GmbH, Brunnthal/Hofolding, Germany) which has been electrically heated to 100° Celsius to the cervix for 30 to 60 seconds, leading to destruction of cervical precancerous lesions. If necessary, the application may be repeated multiple times to cover all the suspect areas (42). This process does not require local anaesthesia and can be performed a point-of-care treatment. Furthermore, a range of health care professionals such as nurses and midwives can effectuate it without the presence of a doctor. This latter aspect is fundamental in LMICs, where there is a lack of trained physicians, and subsequent deficits in available care (43,44)

Large Loop Excision of the Transformation Zone (LLETZ) is recommended by WHO as an excisional treatment for women who are not eligible for thermal ablation (cf. Chapter 1.2.6), or when the precancerous lesion is located in the endocervical canal, or if there is a suspicion of an invasive lesion. This surgical intervention allows the treatment of a larger area through the removal of abnormal tissue from the cervix. This approach is provided under local anaesthesia (18), so it allows women to be treated on the same day of their screening. As opposed to TA, LLETZ has to be undertaken by a qualified and trained gynaecologist (17).

The efficacy of TA and LLETZ in treating precancerous lesions has been shown to be equivalent - with more than 65% of women who present with CIN2+ pathology having no further lesions after treatment (45).

1.1.3 Tertiary prevention – Cancerous treatment and palliative cancer care provision

If an invasive cancer is suspected or confirmed by histological diagnosis, women will be referred to tertiary-level institutions for adequate treatment and management.

A workup to assess the extent of disease by the clinical exam will include diagnostic imaging (e.g. ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET)), depending on the availability of equipment. This will further categorise the lesion and determine its extension according to the FIGO's staging system (46,47). The classification is

based on tumour size and the extent of the lesion in the pelvis as well as the presence or absence of metastasis to distant organs (48). In the context of LMICs, diagnostic imaging may not be as widely available as in high-income countries, therefore clinical examination is crucial to determining the strategy of treatment (49).

Once the diagnosis has been established, women will undergo treatment including surgery and/or radiotherapy and/or chemotherapy depending on cervical cancer staging, the patient's comorbidities and the availability of treatment. Surgery is the most common approach for women with cervical cancer diagnosed at an early stage (1). Chemoradiation is generally proposed for more advanced disease. Palliative care is a crucial part of management as in sub-Saharan countries most cancer patients are diagnosed at late stage.

For FIGO stages IA2 – IIA, hysterectomy is the proposed approach and is performed with pelvic lymphadenectomy. Radiotherapy remains an important alternative treatment. Patients who have stage IIB disease or worse are mainly managed by chemotherapy and radiotherapy (50).

Despite WHO recommendations regarding cervical cancer treatment and management, only one-third of low-income countries report having appropriate resources for effective care of cervical cancer in the public sector, compared to over 90% of high-income countries (1).

The WHO and Cameroon have recognised the important role of palliative care for terminal cervical cancer in improving quality of life of people living and their families, which include psychological, physical, social aspects (51). Unfortunately, despite these recommendations, palliative care services for patients with cancer are frequently lacking, because of the lack of awareness and national health policies, and the absence of continuity of care between hospital and community providers (51,52). Efficiency of palliative care has already been studied for terminal HIV/AIDS patients, but little data is available for cervical cancer patients. Cultural beliefs interfere management care, and women explained that their preferred place of care, where to spend the end-of-life is home, surrounded by their family caregivers, traditional healers who can sometimes be trained and supported to provide skilled care (52–54).

1.2 Cervical cancer screening programme

1.2.1 WHO Guidelines for cervical cancer prevention

In this context and with the public health objective to improve women's access to healthcare and to reduce inequalities in access to women's health interventions, the World Health Organization (WHO) recently updated their guidelines for cervical cancer prevention (1). According to the new recommendations, screen, triage and treat methods should be a prioritised approach to optimise cervical cancer control in LMICs (18).

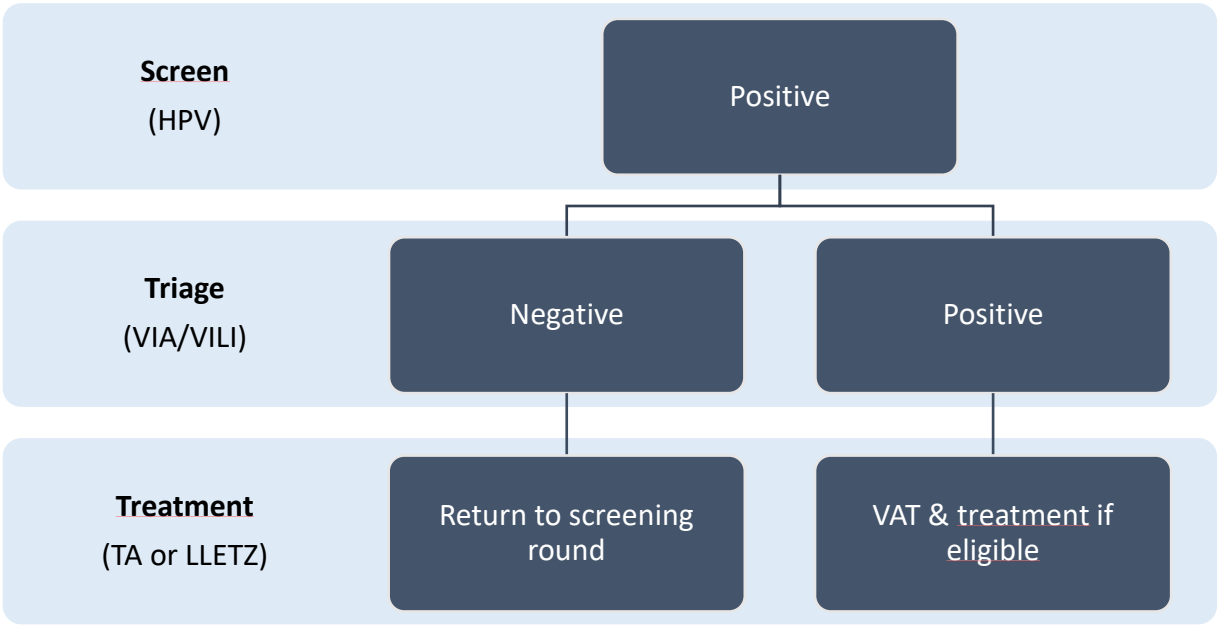


Figure 3: One day: Screen –Triage - Treatment Approach *(HPV: Human Papilloma virus; VIA/VILI: Visual Inspection with Acetic Acid/Visual Inspection with Lugol's Iodine; TA: Thermal Ablation; LLETZ: Large Loop Excision of the Transformation Zone)*

The 3T-Approach programme launched by HUG in 2018, and implemented at the DDH, applies the WHO recommendations by providing to the target population a screen-triage-treatment service in one visit. The goal is to reduce the public health burden of cervical cancer for the women in the area (18).

Before launching the programme, it was necessary to implement the programme in a way that best suited local needs. This involved assessing the material needs and resources available locally, providing the necessary materials for a well-functioning screening, triage and treatment programme, and recruiting and training health care staff in order to build a theoretical and practical training programme.

Also paramount was the need to raise awareness among hospital staff and regional and local health authorities regarding the benefits of implementing a screening programme, whilst also liaising with the leaders of the various Health Areas of the Dschang Health District. These collaborations allow us to work in partnership with relevant bodies to improve access to health care for the local population.

The importance of working with the health system and health authorities and not in parallel has been a pivotal element of our approach, and it represents a sustainable part of the project.

1.2.2 Partnership Cameroon and Geneva University Hospital

Despite well-defined cervical cancer control strategies, obstacles to effective programmes for CC screening remain in LMICs such as poverty, lack of health care infrastructure and low quality of services and trained HCPs. With the availability of

new technologies, researchers are looking for new strategies adapted to the vulnerability of LMICs to sustain comprehensive screening programme implementation.

The relationship between Cameroon and the HUG in the fight against cervical cancer is well established, since the early 2000s (38) and supported by convention. In this context in 2013, a convention was signed between the University of Geneva, the Geneva University Hospital, and the Ministry of Public Health of Cameroon, which the aim to promote primary health care in accordance with the health policies of Cameroon (55), but this collaboration started in the 1970's (56). This cooperation has enabled the training of health professionals in community medicine, local improvement of the medical infrastructure, the establishment of diagnostic and therapeutic guidelines, as well as an integrated financial management system.

Figure 4 Cameroon - Sub-Saharan Africa country (Source: CDC, 2022)

Therefore after 20 years of collaboration to fight cervical cancer in sub-Saharan Africa, the University Hospital of Geneva, the University Hospital of Yaoundé, Cameroon and the University of Dschang, Cameroon, introduced a five-year programme (2018-2023) (PI: Pr Patrick Petignat) with the goal of working towards the WHO cervical cancer recommendations (1,18).

Following this aim, a CC screening unit has been created at the Dschang District Hospital, in West Cameroon, under the supervision of Pr. Kenfack.

Dschang is a semi-rural city located in the West Region of Cameroon (57), with an estimated population of 120'000 inhabitants (58). Dschang District Hospital is a referral centre for the health district covering approximately 300'000 inhabitants.

The health district of Dschang has twenty-two health areas, of which 19 are in rural zones. This health district has hosted cervical cancer screening campaigns conducted by HUG since 2015.

Two years after the launch of the programme, in 2020, a letter of support from the WHO was sent to the University of Geneva and to the "Comité National de Lutte contre Cancer" in Cameroon. In 2022 (the present year) the Geneva University Hospital, the Health District of Dschang, the Ministry of health of Cameroon, the University Hospital of Geneva and the Ecole Polytechnique Fédérale de Lausanne (EPFL), established a consortium. The aim of this collaboration is to contribute to the WHO initiative to eliminate cervical cancer as a public health problem, and bring sustainability to this programme.

1.2.3 Healthcare provider training

Before launching the project, in the aim to contribute to build local capacity, healthcare providers working in the field of cervical cancer prevention were invited to participate in a training programme involving a comprehensive 6-day theoretical and practical training course. The 3-day theoretical courses were composed of 10 training modules using e-learning resources and lectures. Through the modules, the topic of cervical cancer was addressed in a comprehensive manner, starting with an epidemiological overview of the disease, its natural history, the types of prevention available and the diagnosis and treatment of precancerous and cancerous lesions. The screen-triage-treat approach was presented in detail. A focus was also given on how to raise women's awareness of this topic, how to explain the screening process, informing women of their HPV result, and how to provide effective counselling. During this theoretical part the participants were familiarised with conducting counselling interviews through scenario-based role playing.

Subsequently, participants undertook a 3-day advanced practical training, with immediate application of the theory acquired through workshops and simulated practice provided by gynaecologists and midwives specialised in HPV and CC screening (cf. Appendix 5).

At the end of this training programme, participants had to take a practical and theoretical exam to validate their knowledge and to obtain a certificate. Upon graduation, participants in the training programme benefited from two weeks of supervision at HDD. Healthcare providers recruited to be part of the programme 3T, underwent supervision and monitoring (cf. Chapter 1.2.7).

1.2.4 Recruitment strategies

The primary objective of the 3T-Approach was to assess the sensitivity and specificity of the HPV test followed by triage using VIA/VILI to detect CIN2+. In this context, the sample size calculation showed the necessity to include 6000 women in the programme, aged 30-49 years. The target age group was selected based on WHO recommendations (18).

Assuming a prevalence of HPV infection, in Cameroon, of approximately 20% (59), 1200 participants will be HPV-positive. Of the 1200 expected women, 120 will present with a CIN2+ lesion, based on a CIN2+ prevalence of 10% among HPV-

positive women. A loss of follow-up of 20% of patients is estimated for the entire programme, which means that 96 CIN2+ cases can be used for analysis to determine the sensitivity of VIA with an accuracy of +/- 9.8%. Of the expected 1200 HPV-positive women, 864 non-CIN2+ cases will be analysed to determine specificity of VIA with the accuracy of +/- 3.3%.

Various recruitment strategies were adopted at the launch of the programme, in 2018. Communication of the presence of the cervical cancer screening programme at the DDH was transmitted through women's associations, announcements in churches or at community assemblies. The transmission of information between screened women and their peers was also expected. Then, the creation and printing of banners in strategic places in the city and radio announcements were effectuated. Finally, the publication of newsletters was undertaken to raise awareness of the interventions and activities proposed during screening.

Since 2020, recruitment and training of Community health workers (CHW) was implemented in order to reach women living in rural areas who are less covered by the first communication strategies proposed. The CHW is a leader in the community who is trained to raise awareness of the population health issues and who establishes a link with the public health system (e.g.: for vaccination campaigns, screening, etc.).

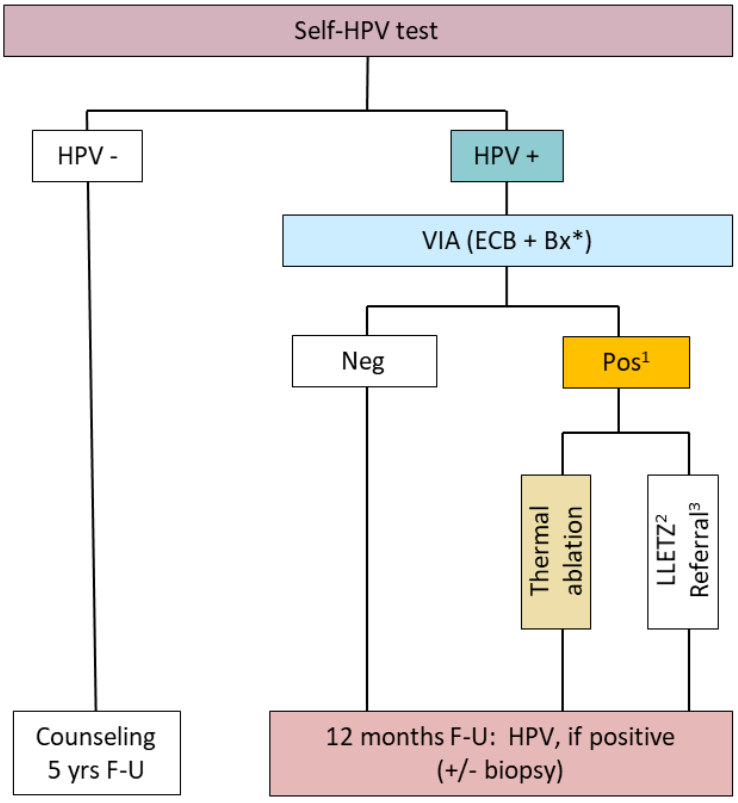
1.2.5 Health education session

The local screening team of three midwives run a one-hour health education session every morning for women who want to be screened. The aim of the session is to raise awareness of HPV transmission, risk factors, risk of unmonitored infection and the importance of the screening procedure to prevent CC. The programme and the 3T screening and treatment and follow up approach is explained to women. After this information session, all target women aged 30-49 years old who meet the eligibility criteria are recruited to the study if they give their informed consent. To demonstrate informed consent, they must have fully understood the procedure, and must have signed the written consent form which is available in French and English. The inclusion criteria are, women aged between 30 and 49 years old, and exclusion criteria are symptoms of cervical cancer, bleeding (menstruation) or obstruction to cervical visualisation, pregnancy and women who have previous history of hysterectomy.

1.2.6 3T-Approach (test–triage–treatment)

The interventions proposed during the same day consultation are adapted from WHO recommendation to fit our local context and are organised as follows; i) screening test by an HPV Self-test (Self-HPV), ii) triage for HPV-positive women by VIA/VILI, iii) treatment by TA or LLETZ if triage results are positive. The final decision to treat the precancerous lesion is established by combining the results of the Self-HPV test and triage. The woman would undergo treatment only if she had positive results for both screen and triage procedures (cf. Figure 5).

In this programme histology provides the gold standard to ensure quality control, and also allows for the identification of women in whom a lesion was not observed during VIA but who in reality had a pre-cancer of the cervix, giving us the opportunity to treat these missed lesions. Histology is not considered mandatory by the WHO in the screen-triage-treat approach, but it is a proposed intervention (18).



*HPV-positive women will undergo endocervical brushing (ECB) and cervical biopsy (Bx); [1]Inspection for eligibility for thermal ablation; [2]If not eligible for thermal ablation; [3]If suspicious for cancer.
HPV: Human papillomavirus; Self-HPV: HPV self-sampling; LLETZ: Large loop excision of the transformation zone; VIA: Visual inspection with acetic acid; F-U: follow-up

Figure 5 Flowchart of the study (courtesy of Pr P. Vassilakos)

Screening

Once included participants were invited to complete a questionnaire in order to collect sociodemographic, reproductive, and health data. Then, women are instructed to perform a Self-HPV HPV DNA vaginal test (FLOQSwabs®; Copan, CA, USA) using a cotton swab for primary cervical cancer screening. The sampling is analysed with a point-of-care assay (GeneXpert® IV; Cepheid, Sunnyvale, CA, USA). This method performs real-time PCR, and detects 14 HR-HPV genotypes (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68). After an hour, the midwives give the women their results individually.

The intake procedure then varies according to the result of the Self-HPV:

- HPV-negative: women require no further procedure and are advised to repeat screening in five years.
- HPV-positive: women will undergo triage to diagnose the presence of a precancerous or cancerous lesion and define the appropriate treatment if necessary

Triage

VIAVILI examination as a triage tool is recommended by the WHO, as it has demonstrated to be effective in helping to avoid unnecessary treatment due to the low specificity of HPV primary screening (60). Therefore, it was decided that VIA/VILI screening should be integrated into this programme.

Immediately after receiving their test results, HPV-positive women are triaged using visual inspection with application of acetic acid (VIA) and Lugol's iodine (VILI) following this sequence:

Pap smear (cytology) > VIA/VILI > Cervical Biopsy (histology) > Endocervical brushing (cytology).

I. Pap smear (Papanicolaou) uses a small brush to remove cells form the cervix with subsequent screening for the presence of cervical cancer or anomalous cells using a microscope.

II. VIA/VILI results were assessed first by using the naked eye and then by smartphone (Samsung Galaxy J5, Seoul, South Korea) through digitalised images of the cervix. Midwives base their assessment on specific criteria, the ABCD criteria(61). The criteria are positive if there is the presence of (A) cervical whitening after application of acetic acid; (B) spontaneous cervical bleeding or bleeding after slightly pressure; (C) colouring after iodine application (to be matched with point A); (D) when the diameter of the acetowhite area exceeds 5mm.

   The VIA test should be considered positive from the outset if criteria AD, or B, or ACD or ABCD are present. All participants with a positive VIA/VILI test will be treated with thermal ablation if eligible or Large Loop Excision of the Transformation Zone (LLETZ).

III. Cervical biopsy is VIA-guided, (i) VIA-positive biopsies are sampled from the lesion(s), or (ii) VIA-negative random biopsy at 6 o'clock on the transitional zone. Biopsy is used as gold standard for pre-cancerous lesion detection.

IV. Endocervical brushing is used to collect the cells at the level of the cervical orifice and the cervical canal where internal lesions are potentially located.

Biological specimens (cytology and biopsy) are transported to Geneva separately. Cervical cells for cytology are preserved and transported in alcohol-based fluid (ThinPrep®, Hologic, USA) and (BD SurepathTM; Becton Dickinson Compagny, Franklin Lakes NJ, USA). Biopsies are transported in vials with formaldehyde

solution. Both are analysed at the Geneva University Medical Center (CMU), at the department of pathology and immunology.

Treatment

Before providing treatment, midwives review all questions about the procedure with women and clarify further the eventual complications and management if required. The follow-up after treatment is also thoroughly discussed.

HPV-positive women who have pre-cancerous lesions identified during VIA/VILI triage undergo treatment by TA or LLETZ according to eligibility criteria (18,38), which are defined by Visual assessment for treatment (VAT). This assessment is used to identify which type of treatment is most appropriate for each woman. The VAT includes a gynaecological examination – either through colposcopy (if possible in the country setting) or through a second VIA.

Two options are offered to women depending on the visibility of the transformation zone (TZ) of the cervix, which is determined through the VAT (62). The TZ is classified into 3 types; Type 1 the TZ is fully visualized and is located on the ectocervical (TZ1); Type 2 the TZ is still fully visible but is partially endocervical (TZ2); type 3 the TZ is no longer fully visible, and extends into the endocervix (TZ3). It is during a second VIA/VILI undertaken to assess the eligibility for treatment that the type of TZ is identified, and the adequate treatment selected (18,62).

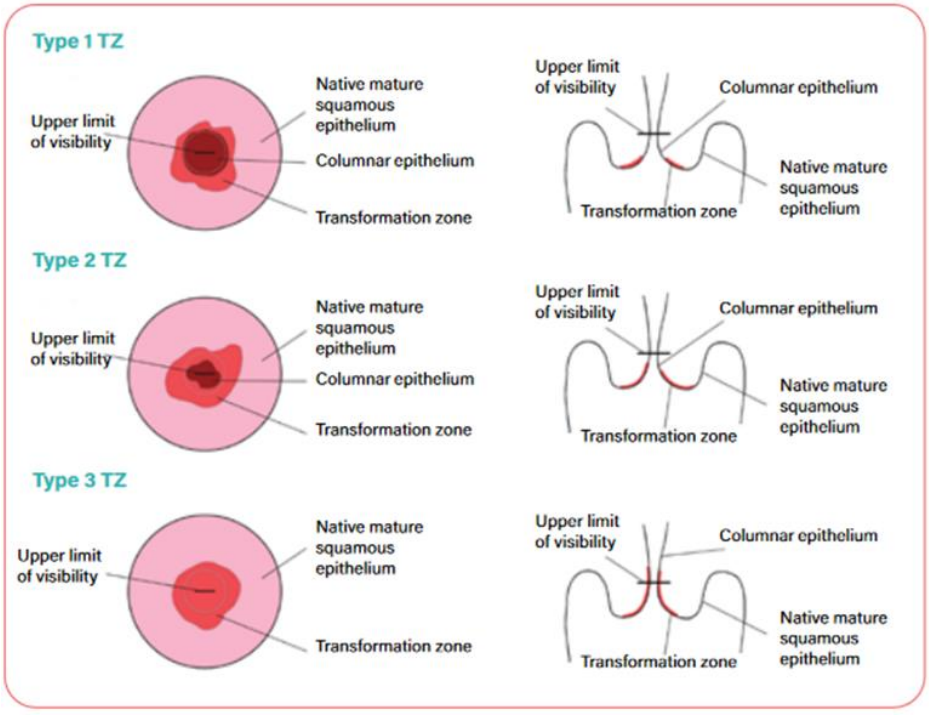


Figure 6: Types of transformation zone (TZ) (source : WHO, 2021 (18))

Women presenting with TZ1, or TZ2 where the lesion is fully visualized using a probe, are eligible for ablative treatment. In this case, midwives proceed directly after a positive VIA/VILI to the treatment. Only women with an identified

precancerous lesion are treated, which allows us to avoid the systematic treatment of all HPV-positive women.

Visit to explain results:
Results of cytological and histological analysis are disclosed and explained to participants by telephone by the midwives. Women who have not been treated at the first visit, but who present with abnormal histological findings, are invited to come back for appropriate treatment.

- HPV-positive women with no pre-cancerous lesions (VIA/VILI-negative) are invited to repeat screening at 12 months.
- HPV-positive women with pre-cancerous lesions (VIA/VILI positive) proceed immediately to treatment

Follow-up visits:
I. At 4-6 weeks, women come back for a post-treatment visit, no HPV screening is done at this time

II. At 6 and 12 months, women come to post-treatment visits. During these visits, they will do a repeat Self-HPV test. After this screening, and independently of the HPV result, they follow the same sequence of the first visit. It means that they will have a Pap smear (cytology) > VIA/VILI > Cervical Biopsy (histology) > Endocervical brushing (cytology). Women with persistent high-grade lesions could be re-treated depending on their clinical situation and their desire for a subsequent pregnancy.

1.2.7 Supervision and monitoring

Daily
During the first two years supervision was provided through a 3-month medical rotation facilitated by a Swiss-trained gynaecologist. This allowed quality control of women's care and ensured compliance with procedures. During their first 6 months of work for the programme, midwives used a logbook to record the interventions that they performed each day in order to have an account of their learning (self-evaluation). The physician countersigned the acts performed by the midwife (cf. Appendix 4).

The data manager monitors the data collection and ensures the validity of the data and its safe storage. He ensures the transcription of the paper case-report form (p-crf) into the SecuTrial software. This software hosts the study database. The data manager and local project manager complete the database developed by the Clinical Research Centre of HUG (CRC) via electronic CRF (e-crf). This practice allows the quality of the data collected to be monitored at all times, as recommended by the WHO (42) .

Weekly
Since May 2020, a Visio conference between the HUG research team and the Dschang local team is organised to exchange updates on current and future

activities, and to provide support to the staff in place. This procedure allows close follow-up of patients and ensures optimal management of patients with severe lesions.

Bi-monthly
At the DDH a local gynaecologist reviews all diagnoses and treatment choices with the clinical local team, through cervical images. If necessary, women are called back for another consultation. Now, and considering the context of the COVID-19 pandemic, the supervision with the gynaecologist is done via telemedicine (cf. Appendix 4)

Monthly
During the first two years, Swiss physicians provide theoretical courses to midwives and evaluate the midwife's consultations (filing out case-report forms, gynaecological exams, counselling) to ensure quality of care and to reinforce practical skills. To monitor the diagnosis, a table containing the diagnostic results of the midwives and those of the gynaecologist was completed in order to assess the agreement of the results and to take prompt action in the case of an over or under diagnosis of precancerous lesions (cf. Appendix 5). In this situation, individual practical training can be provided to the midwife.

During the first two years Swiss physicians were charged with assessing the quality of the delivery of care. To do this they used a questionnaire adapted to Planning Alternative Tomorrows with Hope (PATH) resources on monitoring and evaluation of the CC prevention programme (64). This rigorous data collection contributes to enabling the analysis of the Key Performance Indicators (KPI). Furthermore, the monitoring enables the prompt identification of any potential barriers to the targets predefined by the WHO (cf. Appendix 1) (42).

They also completed a follow-up report on visits to health centres offering the 3T programme, to evaluate medical devices needs. Additionally, they were responsible for assessing the safety of the delivery of care, and for reporting adverse events (cf. Appendix 6). Since 2020 and the COVID-19 pandemic, the local project manager is in charge of the AEs reporting. The data manager has the responsibility of data protection and ensures the privacy, accountability, and accuracy of the data (42). He reports any potential problems to the research team, with the aim of adapting or updating procedures if needed.

Annually
Annual cervical cancer control conferences have been organised in 2018, at the Faculty of Medicine and Pharmaceutical Sciences of Dschang, and at the Hôpital Gynéco-Obstétrique et Pédiatrique de Yaoundé (HGOPY), in 2019. During these conferences the results of the various West African cervical cancer control projects are presented, and the principal investigator and research team chair a supervision workshop with the study site coordinator.

1.3 Thesis objectives

Before expanding the 3T-Approach programme on a wider level, an assessment of the quality and feasibility of the implementation has to be planned and conducted. The overarching aim of such a programme is to promote a comprehensive cervical cancer control and prevention approach, integrated in an existing strategic purchasing system, leading to better women's health.

The assessment of the 3T-Approach implemented in a low-resource setting is the leading aim of this thesis, and will involve an analysis the feasibility, the safety and the acceptability of the interventions proposed.

In this context, nine studies from 2018 to 2022 have been developed and conducted in parallel to the programme in order to evaluate it. All these studies are presented in this thesis, they aimed to:

I. To assess the feasibility of the procedure by monitoring the key performance indicators

II. To assess the acceptability and the safety of the thermal ablation.

III. To assess the acceptability of the procedure of the self-HPV testing and the impact of screening on the level of quality of life, sexual dysfunction and anxiety.

IV. To identify and understand the potential barriers regarding participation to a HPV to cervical cancer screening that affecting decision-making process from women's, healthcare providers' perspectives. To explore also those emerged during the COVID-19 pandemic.

The findings are reported in the following chapter.

The PhD candidate has been involved in the implementation of this cervical cancer screening programme, and in the construction of the project from the beginning in 2018, contributing to develop the protocol and write standard operating procedures (SOP). She participated in meetings with local and international health authorities and decision-makers, and took part in working groups on cervical cancer control in low-resource settings. The candidate was involved in the choice of strategies for the interventions that would be offered to women. She was involved in the fundraising and in the monitoring of the funds received, and in writing operational and financial reports, since 2018 and up to now.

Prior to the launch of the project, the PhD candidate participated in the development of training support and subsequently went on-site to provide training of to healthcare providers prior to the beginning of recruitment. She continues to contribute by providing courses to deliver training to the local teams. She participated in the implementation of quality control of the caregivers' practice and was additionally involved in other screening programmes following the same screening approach, such as working in a project with the French National Research Institute for Sustainable Development (IRD), in Abidjan, in the Ivory Coast.

The PhD candidate was strongly involved in each of the studies presented in this thesis. She developed and conducted as principal investigator four of these ten studies, including one ongoing which will end at the end of the year (cf. Chapter 2.3.2). One article is being written and an abstract has been submitted to the European Congress on Gynaecological Oncology (ESGO) (cf. Appendix 10); the others were already published. She also participated in the supervision of the studies carried out by master's students in medicine and supervised the writing of their articles. The details of her involvement are described, as recommended in the next chapter, following the finding presented by the studies.

2 Findings

2.1 Feasibility of the 3T-Approach

2.1.1 Quality control: Key performance indicators

The method of assessment of the implementation of the programme was defined before the launch of the activities. It is necessary to ensure that the screen, triage and treat programme provides high quality and sufficient care. It is essential that this care is follows procedures and that it works towards pre-established goals. The monitoring of the quality of our 3T-Approach, will show that implementing a cervical cancer screening programme following WHO recommendations (18) is feasible in the context of Cameroon, a lower-middle-income country (65). To demonstrate this, assessment performance indices were selected from a standardised list published by the WHO (42). These Key Performance Indicators (KPI) include monitoring midwife practices and evaluating their diagnostic performance during VIA/VILI, as well as analysis of the rate of follow-up and the rate of treatment provided on the same day of the screening since the launch of the programme. This monitoring allows us to determine if there was gaps with the expected targets, and to propose corrective actions if results were outside the target (cf. Appendix 1).

The results of this study revealed that the approach proposed by this programme works adequately, and the performance of the approach reaches WHO targets. Despite this it is necessary to ensure a periodic assessment of KPIs to assure continuous improvement (cf. Appendix 1). In this study, I was involved in the training of local staff, the launch of the project (ethics committee, fundraising), the development of the data collection support (case-report form), and the supervision of the data collection. Subsequently I aided with the analysis of the data and edited drafts of articles.

2.1.2 Recruitment strategies

In order to maintain an adequate level of programme performance and provide optimal and feasible cervical cancer prevention, it is important to assess and monitor the screening coverage of the target population. Reaching the target population remains a central challenge in LMICs. Women's lack of knowledge on CC, as well as a lack of information available to their relatives and key community members substantially affects the efficiency of a prevention programme (66).

Our recruitment rate is constantly monitored, and one year after launch a significant drop in recruitment was noted. Consequently, it was decided to conduct an analysis of women's recruitment strategies, and compare the first strategy implemented which was the Community Information Channels, to the involvement of Community health workers (CHW). In the socio-demographic questionnaire women were asked through which information channel they had heard about the possibility of being screened at the HDD (banderols, radio, flyers or through

community health workers (CHW). This allowed us to assess the performance of the different recruitment strategies (cf. Appendix 3).

It was highlighted that after the CIC campaign and the intervention of trained CHW among the target population, 50% more women were recruited in rural areas. Considering that in Cameroon about half of the population lives in rural areas, this is significant. Women with higher levels of education were more likely to be recruited through the CIC strategy, while women with lower levels of education or women working as farmers or housewives were recruited through CHWs. This showed the importance of combined strategies to improve screening coverage and reach the WHO recommendations (cf. Appendix 3). In this study, I assumed project administration and contributed to funding acquisition. I participated in the training of study staff, and assumed quality control. I contributed to developing data collection tools, oversaw data collection, interpreted the data, and revised the article.

2.1.3 Feasibility of the 3T-Approach through COVID-19

This retrospective study aimed to analyse the progress and barriers faced by the programme during COVID-19. Like all health systems we were affected greatly by the pandemic. Although, the WHO declared that CC prevention activities should continue to be a priority during the COVID-19 pandemic, cervical cancer screening programmes and follow-up procedures were substantially affected, alongside other preventive health services worldwide. We had to adapt in order to maintain safety for patients and health workers, while continuing to provide quality care. These events had the potential to influence the feasibility of the programme, so it was decided to conduct an analysis on the impact of the pandemic on the screening programme to adapt the programme to the context (cf. Appendix 4).

The main activity from April to September 2020 was ensuring the follow-up of patients who had been treated for pre-cancerous lesions of the cervix. Despite a relaunch of screening activities in July 2020, including major efforts to ensure patient safety, a major drop in the percentage of women screened was recorded in comparison to previous years. This was despite the fact that in this programme the screening test is through self-testing, limiting close contact with healthcare providers. New barriers emerged in the COVID-19 context, and key actions were identified. These included covering the travel cost for women who come to be screened and introducing home-based screening to decrease risk of contamination by COVID-19. In this study, I conduced the literature research, collected local data, analysed data, and drafted and revised the article.

2.2 Safety of the 3T-Approach

2.2.1 Diagnostic agreement

In LMICs such as Cameroon there is an undeniable lack of physicians and trained healthcare providers (HCP). This impacts the quality of the health system and the scope of prevention programmes (48). It was therefore important to work with a

local team of midwives and nurses on this project, thus aligning with the WHO recommendations for task shifting (67). This approach is proposed alongside the guideline of having a CC screening coverage of 90% of the target population, and the treatment of 90% of women diagnosed with a precancerous lesion. The training of HCPs prior to the launch of the project focused on different aspects such as counselling, HPV and its risk factors, HPV modes of transmission and screening, triage and treatment strategies. In order to evaluate the performance of the HCP in making the diagnosis, close monitoring was set up from the beginning to maintain a high level of performance in the care delivered (68).

There was strong agreement between HCPs and supervisors in regards to diagnoses. Healthcare providers' skills were improved through supervision and ongoing training, highlighting the need to continue to monitor practices and conduct regular training to ensure quality and the safety of delivery care for women in the programme. In this study I assumed project administration responsibilities and contributed to funding acquisition. I participated in the training of local staff and launched the project with the ethics committee. I contributed to the conception and the design of the study. I oversaw data collection and performed statistical analysis. I participated by writing sections of the manuscript and contributed to the revision of the article (cf. Appendix 5)

2.2.2 Safety of the thermal ablation

In the screen-triage-treatment approach (18), it is recommended that women are treated immediately if they have a positive triage test. The treatment is therefore carried out on the same day as the screening of the precancerous lesion. This is important as in Sub-Saharan countries the loss to follow-up remains high. The treatment must therefore be able to be carried out in a point-of-care manner, for which the WHO proposes two techniques. In this programme one of these two techniques - thermal ablation - is proposed. Prior studies have shown positive results regarding the use of thermal ablation (70). As the approach is newly introduced in LMICs, it was necessary is this study to monitor potential adverse events. To ensure patient safety, tracking of adverse events related to thermal ablation was implemented. This monitoring took place during and immediately after treatment for two hours, and at 4 to 6 weeks' post-treatment. Treatment-related adverse events (AEs) were collected, and classified according to the Division of AIDS (DAIDS) Severity of Adverse Events (71). Healthcare providers were also asked about their perception of patient comfort.

The analysis of patient safety during the treatment and immediately after demonstrated that no serious events were recorded and the procedure never had to be stopped. Events related to DAIDS Grade I complications (fainting, headaches and nausea) were recorded in less than 4% of cases. Four to six weeks after treatment, the complications that occurred were mostly benign Grade I. No complications requiring hospitalisation or consultation in the medical emergency department were reported. The effectiveness of TA, the demonstrated absence of AEs, and the fact that it is easy to do allowed non-physician providers to carry out

the treatment, which makes TA adapted for LMICs. In this study, I assumed project administration and contributed to funding acquisition. I participated in training local staff and helped to launch the project. I contributed to develop data collection tools, oversaw data collection, conducted analysis and interpreted analysis. I participated in drafting and revising the article (cf. Appendix 6)

2.3 Acceptability of the 3T-Approach

Assessing the acceptability of the 3T-Approach by the participants and health care workers was considered an important step to validate the approach before promoting it to a larger scale. To this end, it was decided to carry out a study on the acceptability of Self-HPV and on the acceptability of thermal ablation.

2.3.1 Self-HPV acceptability

Self-HPV testing contributes as an effective primary screening approach to increase screening coverage, but literature reports that performing a Self-HPV rather than a gynaecological examination by a doctor can be viewed controversially by women. Some women view Self-HPV as representing a poor quality intervention, while conversely others prefer Self-HPV as this avoids a gynaecological examination effectuated by healthcare providers (34). Therefore, it was decided that it would be prudent to assess women's acceptability of the procedure in the cultural context of our screening programme. All women enrolled in the 3T-Approach were invited to complete a questionnaire on the preference and perception around Self-HPV testing during the waiting time before the women received their HPV test result, which took less than one hour (cf. Appendix 7)

In 2021, the majority of the 2229 participants reported a low level of anxiety during the procedure, and generally identified that the source of any anxiety was the fear that they would get a positive HPV result. Self-HPV explanation was easy to understand and easy to perform, and most women reported that they would agree to perform Self-HPV testing again.

However, almost a quarter of the participants reported that they would have preferred to undergo a clinician-test. Implementing a Self-HPV approach in the community may be adapted to the local context, so giving a choice of screening methods to women should be considered for future initiatives to improve screening coverage and make it more acceptable for everyone. In this study, I assumed project administration and contributed to funding acquisition. I trained local staff and participated in launching the project (protocol writing, submission to ethical committee). I developed data collection tools and conducted and interpreted analysis. As first author, I drafted and revised the article (cf. Appendix 7)

2.3.2 Psychological impact of Self-HPV results

The decision to carry out this study came after the launch of the programme, during discussions with the women and the health care team on site in Dschang. We wanted to go further in assessing the impact of screening and test results on

women's quality of life, which encompasses many aspects. We therefore decided to cover three aspects; anxiety, quality of life, and sexual health, which appeared to be the predominant issues in the scientific literature on women's experiences with gynaecological screening. These aspects could be potential barriers to care, and may contribute to a low attendance at screening sites, the effects of which could be low early detection of HPV and loss of women during follow-up if anxiety or fear persists.

This study was due to start in March 2020, but because of the COVID-19 pandemic the launch was postponed to August 2020. A significant delay accumulated in the recruitment procedure, so only partially results are reported below.

Regardless of their Self-HPV result, had a significantly higher mean ASEX score at 6 months than at 1 month (18.4 (4.9) vs. 16.9 (3.9); p = 0.004). This means that they experience more sexual dysfunction (cut off ≤ 18), after the Self-HPV screening. However, the increase in sexual dysfunction between 1 month and 6 months is only visible among HPV-negative women (p=0.002). The mean score of anxiety reported by the women indicates an intermediate level of anxiety which similar to the general population. It did not differ significantly from 1-month and 6-month visits (51.4 (4.1) vs. 51.2 (3.2); p=0.591). There was also no significant difference between the groups of women with a positive or negative HPV test result at 1 month (50.6 (4.5) *vs.* 51.5 (4.0); p= 0.121) or either at 6 months 50.9 (3.4) *vs.* 51.3 (3.2); = 0.335). The results of the 12-months visits will allow us to identify whether women return to a similar level of sexual health and anxiety as before screening. In the literature, after 12 months, the psychological concerns seem to have returned to normal levels, which highlights the importance of long-term follow-up of psychosocial outcomes (72).

2.3.3 Thermal ablation

In the fight against cervical cancer, an effective and safe treatment is required to contribute to reach the third WHO target, 90% of patients with precancerous lesions undergo treatment (18). The 3T-Approach proposes that women are treated on the same day as the screening. This approach reduces loss to follow-up but does not give women time to think about whether or not to accept treatment. Women may also not have time to discuss treatment and ask for advice from their families. It was therefore important for us to assess the acceptability of this method, particularly given that we anticipate a 20% HPV-positivity rate among screened women, a further 50% of whom have VIA/VILI-positive triage tests and thus get offered treatment.

At the end of 2020, around 2230 patients were recruited. Among them, 410 patients were HPV-positive and around 10 percent of these were treated. Nearly 85% received treatment on the same day, as recommended by WHO. The principal reason for not receiving treatment was due to change in management decisions (monitoring, histology). Mostly, women reported low or no anxiety during the treatment, and nearly all women would agree to repeat treatment if necessary and

would recommend it to their relatives. More than 99% of them reported that they were satisfied with TA. In this study, I assumed project administration and contributed to funding acquisition. I participated by training local staff and helped to launch the project (ethics committee). I contributed to developing data collection tools, oversaw data collection, conducted analysis and interpreted analysis. I participated in drafting and revising the article (cf. Appendix 6)

2.3.4 The 3T-Approach among healthcare providers

At the end of 2018, screening recruitment dropped. In order to understand this trend, a qualitative study comprising of healthcare workers in four focus groups took place (16). The study wished to understand the barriers to accessing screening and the acceptability and perception of the single visit approach (cf. Appendix 8).

Maintaining a high recruitment rate and ensuring access to CC screening for rural populations are central aspects of this programme. It was therefore important to assess the potential barriers to accessing this service through the perspective of caregivers. The main findings from the qualitative interviews were that there is a lack of basic knowledge about the problem of cervical cancer among women and men, and a lack of knowledge about the presence of screening programmes like ours. Working with traditional leaders in rural communities and key community figures would be one way to reach the target population, and therefore could be a crucial strategy to reach higher screening coverage. In this study, I contributed to the project administration, the funding acquisition, and the submission to the ethical committee. I contributed to interpreting the analysis, and revised the article.

2.3.5 The 3T-Approach among participants

This study aimed to understand the complex barriers affecting women's decision-making process around whether to participate in a cervical cancer screening programme, and wished to explore the acceptability and perception of Self-HPV testing and the single visit approach. To evaluate this, focus groups were conducted with women and male partners, based on findings obtained from previous interviews with healthcare providers.

Three important barriers were identified that should be targeted by the CC programme to improve recruitment. The lack of health literacy which contributes to a psychological barrier was reported in rural areas where education was lower. Financial constraints, difficult living conditions, poverty and the fact that the screening points may be far away were highlighted as barriers to accessing the screening procedure. Additionally, negative experiences with HCPs in the past sometimes impacted the decision to come for screening. In this study, I contributed to the project administration, the funding acquisition, and the submission to the ethical committee. I contributed to interpretation of analysis, and revised the article (cf. Appendix 9)

3 Discussion

The implementation of this cervical cancer screening programme according to the same day screen - triage - treat approach (18) has been shown to be feasible and adapted to the context of Cameroon - a sub-Saharan lower-middle income country. This approach is also supported by the literature (73,74) .

This 3T-Approach offers comprehensive cervical cancer care as recommended by the WHO and provides procedures that are adapted to the local context (48); Self-HPV point-of-care primary screening tests, triage with VIA/VILI, and treatment of precancerous lesions - in most cases (90%) using thermal ablation. These interventions are effectuated by trained midwives who have received rigorous theoretical and practical training (75). The basic and continuous training offered to local midwives and health care personnel allows the project to be embedded in the established health system, and therefore adheres to WHO recommendations which favour task-shifting. The WHO recommends that midwife care covers 90 per cent of sexual reproductive, maternal, newborn, and adolescent health interventions, including cervical cancer screening (67).

Screening

The results of the literature support that Self-HPV testing for HPV DNA has similar sensitivity and specificity for the detection of precancerous lesions as the tests performed by healthcare providers (33,35,76). Self-HPV and laboratory analysis is easy to use and could contribute to reaching under screened women (77). During the Covid-19 pandemic, this approach has shown to be advantageous by limiting contact between healthcare providers and women, and thus offering safe screening. In the literature, Self-HPV testing also contributes to reaching women who are limited in their movements due to restrictions, and who therefore have more limited access to health services (78).

However, the equipment used to perform the point of care analysis of Self-HPV tests is expensive. The cost of the cartridges and the purchase of the machine - despite a preferential price for LMICs - remains a limiting aspect. Furthermore, the use of Cepheid's recommended content transport medium, PreservCyt, is also a high cost to be taken into account when using the GeneXpert. Validation of other transport products such as NaCl 0.9% would be a step forward in the sustainability of this screening strategy. Interventions by international health authorities should aim to influence the reduction of costs. Despite the aforementioned high price which may limit use in low-resource countries, GeneXpert point-of-care assay is easy-to-use, does not require any special training and allows a result within the hour. Our findings are consistent with other studies which report primary screening with HPV testing is easy to implement (76), facilitates screening in underserved populations in health areas with inadequate physician coverage (30), and can increase the effectiveness of a national cervical cancer screening programme as reported by Zhao et al., in China (79). These various aspects contribute greatly to reducing the risk of loss of women who need to undergo treatment, reduce stigma

for women, and sustain strategies to reach the third target of the WHO, to treat 90 per cent of women with precancerous or cancerous lesions (18,80).

In addition to being feasible and effective, Self-HPV testing has been shown to be well accepted by the women interviewed, who also recommend it to their relatives. However, it should be noted that women with a lower level of education are more likely to be tested by a doctor, often due to a lack of self-confidence regarding effectuation of the test.

A quarter of the women interviewed reported that they would prefer to be tested by a healthcare provider (81). Other authors have also found that women may prefer to undergo clinician testing (32,82). De Pauw et al. showed that more than 40% of the women enrolled in their study would prefer to undergo clinician testing for their next screening (77). From the perspective of sustainability of the project, and with the aim of covering 90% of the target population, consideration should be given to offering the possibility of Self-HPV testing for willing women. Additionally, having the choice of a clinician collecting the sample may help to reach the population who do not wish to perform the Self-HPV test, and those who would not come back for their next screening due to this procedure.

Other barriers to HPV screening have been identified among women, partners, and healthcare providers, such as the lack of knowledge of the population regarding HPV, and the lack of information surrounding the screening programme proposed at the DDH. These elements highlighted the importance of community-based approaches including training those who can facilitate by broadening the transmission of information to cover more women (1).

Reimbursement of patient transport also has been shown to decrease barriers to seeking care. This intervention was not initially foreseen in the programme plans but it had to be integrated in order to improve screening coverage and increase access to care. This has also been related in other studies conducted in Sub-Saharan Africa (83,84).

Triage

Triage by VIA/VILI has shown to be effective with limited overtreatment in this programme. In the context of this study and in other LMICs, VIA/VILI is suitable since it doesn't need specific infrastructure or materials and is low cost (85). The quality control of the care provided, in place since the start of the project as recommended in the implementation of a screening programme (42), showed that the practice was aligned with WHO targets and indicators (86). This is largely due to the fact that performance in diagnosis of the midwives was closely monitored by an experienced physician, allowing rapid and effective corrective action to be taken if needed. The screening and VIA/VILI specific performance indicators (KPIs) were achieved, as demonstrated by the performance of the treatment. However, the sensitivity of VIA/VILI could be increased by combining it with genotyping screening or automated cytology, which are strategies that have shown favourable results in the literature (60). Developing automated cytology through the

application of artificial intelligence and the use of digital image-based machine learning models is currently another branch of work in this programme, and encompasses a collaboration with the EPFL, the University Medical Centre (CMU) of the University of Geneva and the HUG. This too, may assist diagnosis (87).

Treatment

Treatment by TA has been shown to be effective and contextually appropriate when providing support and training to increase midwives' skills. Having trained midwives and enabling them to perform TA autonomously contributes also to the WHO Global initiative for Emergency and Essential Surgical Care (GIEESC). This mandates that high income countries contribute to training and sustaining healthcare providers in LMICs to deliver essential and surgical care services (88).

This practice allows the treatment of women on the same day as screening, as recommended by the WHO, which in turn increases accessibility to necessary care. The advantages of TA are also highlighted in Malawi, where the use of TA enabled 90% of women to be treated on the same day (89). Similar findings have been reported in other low resources settings (70). It is noteworthy that treatment for invasive cervical cancer and palliative care in Cameroon needs improvement, as these services are not adequate for the needs of the population. This programme covers the cost of treatment, but access to care is difficult for patients diagnosed with FIGO stage >II who need chemotherapy and radiotherapy (90). Therefore, it is important to be able to treat women with pre-cancerous lesions effectively and quickly by TA or LEETZ when the disease is in its early stages, in a way that minimises the risk of losing the patients to follow-up (91). Furthermore, TA has been demonstrated to be a safe procedure, as shown by the lack of reported serious adverse events in our study population. Literature predicts that TA may become the new standard treatment for LMICs (45,92).

The treatment of pre-cancerous lesions by TA carried out on the same day as the diagnosis was judged acceptable by the women who were treated, who frequently reported a low pain score. Other positive findings reported include women's satisfaction with TA, and the fact that TA was well received by caregivers. For the health system as a whole TA provides less logistical challenges and is less resource intensive in terms of training when compared with cryotherapy which was previously recommended for LMICs (45,92).

Limits and strengths

The main limitation of this work is its particular geographic focus and therefore the difficulty of extrapolating the findings to other Sub-Saharan African countries. The hospital is a district hospital, it is located in an urban area, and in an area bordering the French-speaking and English-speaking regions where conflicts have been present for several years. The rural population of the remote areas of the Dschang district may also be subject to particular difficulties and dangers when traveling.

Another limitation is related to the women's level of education when filling out the questionnaires, particularly in relation to those covering acceptability of interventions. The women were often assisted if they had difficulty with reading and writing. The answers could therefore be less objective than if the woman had answered alone.

The strength of this work is that the programme evaluated was built step by step on scientifically and clinically proven international recommendations by a team of Cameroonian and Swiss experts in the field of cervical cancer screening with extensive field experience. This partnership and the supervision around it allowed the project to be implemented into existing sexual and reproductive health structures as recommended (1), and thus avoided the creation of a parallel and non-sustainable system. Having good knowledge of the field, the regular missions of the HUG interns and investigators, and the daily contact between the local and Geneva teams (8 people initially, 15 in 2022) allowed the continuous quality control and monitoring of the project, and provided strength to findings.

In general, the COVID-19 pandemic has been a limiting aspect, both in terms of patient recruitment and the provision of care, but from another perspective it has provided an opportunity for improvement. The follow-up and management of the project had to be reviewed and communication exchanges had to be adapted, particularly considering the absence of field missions to Cameroon. The increasing presence of digital health, telemedicine and the reorganisation of meetings has been a strength in our context. Furthermore, the recruitment of new members who contribute to ensure rigorous monitoring and quality control has facilitated the rapid transfer of skills and information between Switzerland and Cameroon.

Perspectives

These results highlight the importance of having a screening programme that follows evidence-based and clinically proven recommendations whilst being dynamic. This means being able to propose different strategies and continuously adapt to local needs in order to be effective and cover a maximum of the target population (93). This was the case for this project during the pandemic where we saw a decrease in new patient recruitment. Quality control is the central aspect that allowed us to react quickly and to set up new actions when facing issues.

Training health care staff to provide counselling and to communicate with patients is an element that should be put in place to improve the quality of care, and this could help to reduce barriers to care. In focus groups we conducted some women revealed that they had experienced disrespectful treatment by healthcare providers in the past when they came to seek care. Other authors have noted the same, and have made the observation linking access to care and quality of care received (94–96). It might be interesting to carry out a large-scale evaluation of patient satisfaction with care, in order to put in place strategies to improve patient-provider-communication, such as including this topic in basic training.

Enhancing health literacy by strengthening community health activities, through recruitment of CHW has been a turning point for the project. This has been paramount in reaching a greater population of women, and has served to increase women's awareness of vital health issues. The importance of this has been reported elsewhere in the literature too (83,97). Establishment of partnerships with key community leaders, civil society and institutions also contributed to increasing screening coverage, by strengthening links between the community, and health system (1). Awareness-raising and health education for the target population are essential to improve women's empowerment in health, and the involvement of community figureheads has proven to be more than worthwhile. These partnerships must be maintained and field monitoring should be done to encourage a high level of participation.

In light of these results and with the aim of developing further a national sustainable screening programme, it was decided to carry out a cost-effectiveness study (cf. Appendix 10). The aim was to determine the cost-effectiveness of two cervical cancer screening strategies (18) starting at various intervals, in Cameroon (98,99). We wished to do this in order to be as aligned as possible with women's needs. Results highlighted that four combinations appeared to be the most cost-effective strategies Self-HPV/VIA at 35-45, and at 30-40-50 years, and Self-HPV every 5 and 10 years between 30 and 60 years old. Cost-effectiveness is related to the frequency of screening, the higher the frequency of screening, the higher the Incremental cost-effectiveness ratio (ICER). These results may support decision-makers in selecting the adequate screening strategies and frequencies according their willingness to pay QALY gained.

Building a national policy-maker group to set up a country wide cervical cancer screening plan in Cameroon is an important step in the fight against cervical cancer. A cohesive and broad taskforce would allow us to ensure that policy is coordinated and practices such as screening procedures are standardised. It would also allow us to train healthcare providers, purchase supplies, raise funding and spread information widely to raise awareness on cervical cancer prevention (100,101). This step would greatly contribute to working towards the WHO targets to eliminate cervical cancer.

In view of these results and the latest WHO recommendations on an integrative approach to cervical cancer control, two components are being developed to strengthen our programme. The first is palliative care, with a first study on the quality and availability of palliative care for women with diagnosed cervical cancer, and to identify ways to improve care by caregivers and to assess the acceptability of this care among women and their communities. The second part of the project will assess the impact of cervical cancer on women and family dynamics. Indeed, cervical cancer often affects young women who have a central role in raising children and maintaining the household.

Conclusion

The 3T-Approach and the strategies implemented in this screening programme - launched in a low-resource country of Sub-Saharan Africa - have met expectations. They have contributed to progression towards the WHO recommendations regarding the prevention and treatment of cervical cancer. Quality control is necessary, and continuous monitoring is required to maintain an effective programme that is adapted to a constantly evolving health, social and economic situation. The long-term goal of eradicating cervical cancer, a public health burden that is preventable and curable must remain central to all stakeholders. Cervical cancer highlights profound social and health care inequities, with nearly 90% of deaths occurring in LMICs. This means that we should act swiftly and decisively to level this imbalance to prevent and alleviate morbidity and mortality that leaves so many suffering unnecessarily. This thesis and the results collected hopes to contribute to advocacy work to be done in conjunction with the health authorities of Cameroon, working towards a nationalisation of the screening programme.

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5 Appendix

Appendix 1

Keys Performance Indicators (KPI) (source: WHO, 2018 (42))

Table 1 Keys Performance Indicators (KPI) to monitor screening and treatment

Indicators	**what it measures**
Screening rate	
Screening rate	Percentage of women within the target age range screened for the first time in a given time period
precancerous lesion post-treatment follow-up	Percentage of women treated for precancerous lesions who return for a 1-year post-treatment follow-up screening test
Screening results and referrals	
Screening Test Positivity Rate	Percentage of screened women aged 30-49 years with a positive result
Triage Examination Percent Positive	Percentage of screen-positive women with a positive triage examination result
Precancerous Lesion Cure Rate	Percentage of women who received a negative screening result at their 1-year post-treatment follow-up
Triage Examination provision	Percentage of screen-positive women who attended the triage visit and received a triage examination
Treatment and referrals	
Precancerous Lesion Treatment	Percentage of screen-positive women with lesions eligible for thermal ablation or LEEP who received that treatment
Treatment rate	Percentage of triage-positive women who have received treatment in 6 months of screening positive
Treatment rate	Percentage of VIA-positive women with lesions eligible for thermal ablation treated during the same visit
Post-treatment Complication	Percentage of women receiving thermal ablation or LEEP who returned with a post-treatment complication
Precancerous lesion post-treatment follow-up	Percentage of women treated for precancerous lesions who returned for a post-treatment follow-up screening test at 1 year
Pre-cancerous lesion cure rate	Percentage of women who received a negative screening test result at their post-treatment follow-up at 1 year
Programme and service delivery	
Community Campaigns	Number of community campaigns (including mass screening campaigns/periodic outreaches) carried out
Confirmed cancer	Percentage of screen positive women diagnosed with cancer

Table 2 : Safety indicators (42)

Indicators	Gold standard
Urgent admission or hospitalization during treatment by thermal ablation	<1%
Severe complications after thermal ablation	<1%
Immediate bleeding after thermal ablation	<5%
Proportion having faintness immediate after thermal ablation	<5%
Mild side effects during thermal ablation (uncomfortable, low pain)	<15%

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Implementing the 3T-approach for cervical cancer screening in Cameroon: Preliminary results on program performance

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Abstract

Option recommended by World Health Organization (WHO) includes human papillomavirus (HPV) primary screening followed by visual inspection with acetic acid (VIA) triage. We implemented a program based on a 3T-approach (Test-Triage and Treat). Our objective was to verify the effectiveness of the program by defining a set of performance indices. A sensitization campaign was performed in Dschang (Cameroon) and women aged 30-49 years were invited to participate for screening based on the 3T-approach. Participants performed HPV self-sampling (Self-HPV), analyzed with the point-of-care Xpert HPV assay followed by VIA/VILI triage and treatment if required. Key performance indicators (KPIs) for screening, diagnosis, treatment and follow-up were defined, and achievable targets were described for which the approach is likely to be running optimally. A total of 840 women with a mean age of 39.4±5.9 years participated. The KPIs included (i) the screening rate (8.4% at 7 months, target =20% at 12 months), (ii) HPV positivity rate (19.8%, expected range 18-25%), (iii) compliance to referral to VIA/VILI and complete test (100%, target >90%), (iv) compliance to referral to thermal ablation (100%, target >90%), (v) VIA/VILI positivity rate (50.6%, expected range 45-55%), (vi) a single visit from diagnostic to treatment (79.8%, target >80%), (vii) compliance to follow-up at 1 month (96.4%, target >80%) and (viii) at 6 months (70.6%, target >80%). Program performance based on the single-visit 3T-approach corresponded to defined targets and preliminary results support adequateness of KPIs for periodic monitoring.

KEYWORDS

cervical cancer, management, prevention, screen-and-treat, sub-Saharan Africa

Juliette Levy and Marie de Preux have contributed equally to this work.

1 | INTRODUCTION

Cervical cancer (CC) is the first cause of women cancer death in sub-Saharan Africa.[1] Every year, this cancer kills 266'000 women and 90% of them are coming from low and medium-incomes countries (LMIC).[2] This inequality is directly linked to the lack of CC prevention, early detection and treatment of precancerous lesions.

In high-income countries having screening programs, there has been a significant decrease in CC incidence and mortality.[3] However, this decline has not occurred in LMIC, mainly because of the absence of prevention programs, lack of infrastructure and trained caregivers. This leads to late management of invasive cancer, for which there is no more curable treatment available. In Cameroon, CC is the second most important cancer in women, with 2356 new cases detected in 2018 and 1546 related deaths.[4] These issues highlight the need for policy makers to focus efforts on improving prevention of CC in the country.

In LMIC, the World Health Organization (WHO) recommends primary human papillomavirus (HPV) screening followed by visual inspection with acetic acid (VIA) for triage of HPV-positive women and treatment if necessary.[4] Screening with HPV testing provides two significant advantages. First, it can be carried out on self-collected vaginal samples (Self-HPV), thus obviating the need of a speculum examination and second, some platforms perform rapid HPV tests allowing for results at the point of care. The combination of these two advantages contributes to propose a screening and treatment approach in a single visit. This strategy increases program effectiveness and makes efficient use of available human and financial resources as well as to reduce loss of follow-up.[5,6] Triage evaluation of HPV-positive women using VIA and VILI can be enhanced by smartphone digital images taken before and after application of acetic acid (D-VIA) and after Lugol's iodine (D-VILI). This innovation is important for settings where the use of colposcope may be economically prohibitive.[7]

We implemented in Cameroon a "single-visit approach," called 3T-approach (Test, Triage and Treat) based on Self-HPV testing, triage with VIA/VILI coupled by digital photographs (D-VIA/D-VILI) and treatment with thermal ablation or Loop Electrosurgical Excision Procedure (LEEP) if needed.[5,8]

The success of a screening program depends on a well-organized patient itinerary as well as a well-trained staff able to clearly explain the process and get women adhesion. To monitor the quality of the program and to ensure that desired outcome are achieved, it is necessary to use a data collection tool to identify problem and plan corrective actions..[9,10]

The aim of this study was to assess quantitatively how a screening program based on the 3T-approach can be evaluated and monitored. For this purpose, over a 7-month pilot phase, we defined a set of key performance indicators (KPIs) including corresponding targets or standards against which performance was assessed.

2 | METHODS

2.1 | Health facility and program description

The 3T-approach was introduced in September 2018, in the District Hospital of Dschang, a rural city located in the West Province of Cameroon, with an estimated population of 220'000 inhabitants. The program, which is scheduled for 5 years, is based on the WHO recommendations to screen women aged 30-49 years at least once in a 5-year period. According to the national census, we estimated that about 10'000 women should be screened in order to obtain an 80% coverage of this targeted population.

Regarding the recruitment, at the beginning of the campaign, women living in town were brought in by word of mouth. Then we used different methods such as talks in community centers, churches and women association's group. We have made radio advertisements and banners. And then we mobilized and trained community health workers to reach out to women living in different rural area to improve women's participation.

The local team organized a one-hour session daily for the women willing to be screened, in order to sensitize participants about CC, HPV and CC prevention. After this information session, all women aged 30-49 years were included in the study after full understanding of the procedure, and an informed consent form, available in French and in English, was signed. Exclusion criteria were pregnancy and previous total hysterectomy. This study was approved by the Ethical Cantonal Board of Geneva, Switzerland and the Cameroonian National Ethics Committee for Human Health Research. It was registered at ClinicalTrials.gov number NCT03757299.

The study procedure was divided in four steps: (a) a case report form (CRF) on socio-demographic data and medical history was completed by a midwife; (b) woman performed a Self-HPV with a flocked swab (Self Collection FLOQSwab™, Copan), and the result was given within 1 hour. During this time, the women completed a questionnaire on the acceptability of Self-HPV; (c) if HPV was negative, women were reassured and advised to repeat the test in 5 years; if HPV was positive, a pelvic examination was completed by the midwife. VIA, D-VILI; (d) if the provider visualized an acetowhite or iodo-negative lesion, the procedure was completed by thermal ablation (WISAP®; Medical Technology GmbH, Brunnthal/Hofolding, Germany) or the patient was referred for LEEP if non eligible. In case of invasive cancer, the woman was led to the gynecologic department to get a full assessment and treatment that was completely covered by the program. All data regarding the gynecological examination and treatment were recorded in the patient's file.

For quality control, cytology and biopsies were performed for all HPV positive women, but results are not reported here. Local staff was trained through an e-learning platform managed by physicians from the University of Geneva and Dschang. One week of theoretical course followed by one week of practical training were required. After two weeks of training, review of normal and abnormal cervical photographs as well as clinical sessions to observe and practice the technique were organized. At the end of the training, a theoretical and practical exam was performed to ensure that all the necessary skills were acquired. Health care providers were certified by the University of Geneva and Dschang. After the implementation of the 3T-approach physicians and consultants continued to provide training to nurses, to verify quality improvement efforts and help manage difficult cases. The files of digital smartphone photographs are used for review and quality improvement.

2.2 | Self-vaginal sampling for HPV testing/ GeneXpert®

Participants performed self-HPV by themselves and those having difficulties were assisted by the health staff. The swab was then plunged into a vial containing 20 ml NaCl 0.9% solution, and then vortexed for 30-45 seconds. One milliliter of the solution was collected with a Pipetman and then transferred into a single-use disposable cartridge that holds PCR reagents of the GeneXpert® machine (GeneXpert®IV. Cepheid, 2015. Sunnyvale, California, USA). The Xpert HPV assay® uses PCR to detect the DNA of 14 high risks HPV. Specifically, it identifies types HPV 16 and HPV 18/45 in two distinct detection channels (channel 1 and 2), and reports 11 other high-risk types (31, 33, 35, 39, 51, 52, 56, 58, 59, 66, and 68) in a pooled result, after detection in three distinct channels.

2.3 | Triage with VIA/VILI

During pelvic examination, VIA and VILI inspection were done to detect precancerous lesions. Only lesions localized into the transformation zone were considered as significant.[11] We applied a cotton-swab soaked with acetic acid on the cervix and waited one minute to evaluate the results. We used "relaxed WHO criteria" meaning that we have considered that any aceto-white lesion including faint whitening were considered as VIA positive.[12] A VILI-positive test was defined as an iodo-negative area corresponding to an aceto-white area.

2.4 | Smartphone (D-VIA/VILI)

We used a Samsung Galaxy® S5 (16 Megapixels) and the application named "Exam".[13,14] First, a native picture was taken, then after VIA and VILI. The ExamApp classified pictures in patient file.[7] Digital imaging of the cervical was used for peer review, quality assurance, continuing medical education and access to expert opinion if needed. Diagnosis and treatment decision were based on a combination of VIA/VILI and D-VIA/VILI interpretation. So, the final diagnosis was made with the combination of the two methods. If we have one negative and one positive, results were considered as positive. Hereafter, VIA/VILI combined with D-VIA/VILI were referred in the document as VIA/VILI.

2.5 | Thermo-ablation

We used a thermocoagulator (WISAP®; Medical Technology GmbH, Brunnthal/Hofolding, Germany), which heats a probe at 100° Celsius. This probe was applied on the precancerous lesion for 60 seconds to eliminate the abnormal zone.[15]

2.6 | Follow-up of positive women at one month and six months

Women who received a treatment (thermal ablation or LEEP) are reconvened one month and six months after the procedure. The control at one month consists of a clinical exam. Then at six month they will have an HPV test, a VIA/VILI inspection and cytology and biopsies. If the cytology or biopsy is positive, they will be reconvened for treatment.

2.7 | Health information system

The sociodemographic and medical data and health outcomes were first collected by midwives on CRF-paper during anamnesis and screening. All data including treatment and follow-up were later registered on SecuTrial® software database by trained doctor. Data are monitored monthly. Screening results and treatment decision of midwives is recorded daily and transcribed on our database, as well as the monthly assessment of their clinical practice.

2.8 | Key performance indicators (KPIs)

Performance threshold have been defined for each KPI with the aim of attain an achievable target or expected range that was developed according to previous studies and local conditions[5,16-18] as well from those issued by the WHO.[19] A total of eight KPIs from screening diagnosis to treatment and follow-up have been developed and include (a) the screening rate of the target population, (b) the percentage of HPV-positive women, (c) the percentage of HPV-positive women

who had VIA/VILI triage, (d) the percentage of VIA/VILI positive, (e) the percentage of VIA/VILI positive women who received treatment, (f) the percentage of women having complete the single-visit 3T-approach, (g) the percentage of treated women having follow-up at 1, and (h) 6 months.

2.9 | Statistical analysis

Quantitative data were entered and analyzed using Stata Statistical Software Release 13 (StataCorp LP, College Station, TX, USA). A descriptive analysis was conducted; categorical variables were summarized with frequencies and percentage, and continuous variables were summarized with means and standard deviations (SD). Women's socio-demographic and medical data were collected, stored, and managed by the SecuTrial online database.

3 | RESULTS

3.1 | Socio-demographics

A total of 840 women participated in the CC screening campaign during the study period (Table 1). Average age of participants was 39.4 ± 5.9 years old. Majority of women (n = 729; 86.7%) were married or in relationship. Most of them (n = 696; 82.9%) had completed high school and had a professional activity (n = 699; 83.2%). The average age of menarche was 14.6 ± 1.8 years old. Mean age of first sexual intercourse was 18.1 ± 2.9 years old and a majority (n = 567, 67.5%) has had between 2 and 5 partners. The socio-demographics are comparable to those obtained in previous studies in Cameroon.[20]

3.2 | HPV prevalence and types

Overall, 166 patients were HPV positive, corresponding to a positivity of 19.8%. The results showed that 3.6% (n = 6) of women were infected by HPV 16, 13.9% (n = 23) by 18/45 and 77.1% (n = 128) by "other" HR HPV. Combined infections were found in 4.1% (n = 9) of women (Table 2). Of the 166 HPV positive patients, 6% (n = 10) were co-infected with HIV and 5.4% (n = 9) were under Antiretroviral therapy (ART). VIA/VILI screening was performed on all 166 patients and 84 (50.0%) were VIA/VILI positive.

3.3 | Screening, triage, and treatment adherence

The process was accepted by all participants and performed according to protocol. The GeneXpert® machine worked as

TABLE 1 Socio-demographic and clinical characteristics of study participants

Variable	N	%
Total	840	
Age (mean ± SD), y	39.4 ± 5.9	
Age groups, y		
30-34	216	25.7
35-39	196	23.3
40-44	230	27.4
>45	198	23.6
Marital status		
Single	68	8.1
Married/ In relationship	729	86.7
Divorced/Widow	43	5.1
Education		
Unschooled/ Primary education	144	17.1
Secondary education/ University	696	82.9
Age at menarche (mean ± SD), y	14.6 ± 1.8	
<13 years	111	13.2
13-15 years	473	56.3
16-20 years	256	30.5
Age of first intercourse (mean ± SD), y	18.1 ± 2.9	
<16 years	104	12.4
16-18 years	441	52.5
>18 years	295	35.1
Number of sexual partners lifetime (mean ± SD)	4.2 ± 3.6	
0-1	105	12.5
2-5	567	67.5
6-9	120	14.3
>10	48	5.7
Overall HPV prevalence	166	19.8
VIA/VILI done	166	19.8
VIA/VILI		
Positive	84	50.6
Negative	82	49.4
Decision to treat		
Final decision to treat	84	50.6
Coinfection HIV-HPV		
HIV positive	10	6.0
HIV treated	9	90.0
Status HIV known[a]	163	98.2
Status HIV unknown	3	1.8

Abbreviations: N, number; SD, standard deviation; y, years; HPV, human papillomavirus; VIA, visual inspection with acid acetic; VILI, visual inspection with Lugol's iodine; HIV, human immunodeficiency virus.

[a]Anamnestic data.

TABLE 2 Types of HPV detected in 166 infected women

Xpert typing	HPV 16 Channel 1	HPV 18/45 Channel 2	11 Other HR HPV 3 Channels[a]
Single HPV detection (N)	6 (3.6%)	23 (13.9%)	128 (77.1%)
Additional HPV detection (N)			
HPV 16	—	2 (1.2%)	2 (1.2%)
HPV 18/45	2 (1.2%)	—	5 (3%)
"Other" HR HPV	2 (1.2%)	5 (3%)	—

Abbreviations: N, number; HPV, human papillomavirus; HR, high risk.

[a]Detection in three separate channels for 11 HR HPVs to generate a pooled result: Channel 3: HPV31, −33, −35, −52, and −58; Channel 4: HPV51 and −59; Channel 5: HPV39, −56, −66, and −68.

expected and delivered the results in 1 hour. In addition, it was possible to repeat the test if it turned out to be uninterpretable due to insufficient sampling or to technical issues so that no women were excluded at this stage of the process due to invalid test results. Pelvic examination with VIA/VILI for HPV positive was well-accepted. Woman that needed a treatment were considered as eligible for treatment (thermal ablation or LEEP), no woman stopped her treatment because of pain or discomfort and all of them have received the therapy (Figure 1).

3.4 | Key performance indicators (KPI)

Over a 7-month period (a) the rate of women screened was 8.4% (840/10 000) (target 20% for 12 months), (b) the HPV positivity was 19.8% (expected range 18%-25%), (c) the number of HPV-positive women who accepted to participate and received VIA/VILI and D-VIA/VILI testing was 100% (target > 90%) and (d) the number of VIA/VILI-positive women who accepted treatment and received the complete therapy (target > 90%. Other KPI registered in the 3T process were (e) the VIA/VILI positivity rate, which reached 50.6% (range 45%-55%), (f) the rate of patient having a 3T process conducted in a single visit, which was 79.8% (target > 80%), (g) follow-up at one month which was 96.4% (target > 80%) and (h) at 6 months which was 70.6% (target > 80%) (Table 3). At 6 months, 58.3% were tested positive for HPV and 25% of them were VIA/VILI positive (patients included in the study who were able to benefit from their visit at 6 months).

TABLE 3 Keys Performance Indicators (KPI) to monitor screening and treatment

Performance Indicator	Target/ range	Status	Results
Screening rate:	2000/year	840/7 months	
i. Target population Dschang ~ 10 000 women, 30-49 years, in a five-year period (screening coverage: 80%)	20%	8.4%	
Diagnostic and Treatment process			
ii. HPV positivity rate	18%-25%	19.8%	
iii. Compliance to referral to VIA/VILI and complete test[a]	>90%	100%	
iv. Compliance to referral to thermal-coagulation and complete treatment	>90%	100%	
v. VIA/VILI positivity rate	45%-55%	50.6%	
vi. Single visit from diagnostic to treatment	>80%	79.8%	
vii. Compliance to follow-up at 1 month	>80%	96.4%	
viii. Compliance to follow-up at 6 months[b]	>80%	70.6%	

[a]Once patient has been included in the study; considered as complete if only if the three sets of photos (native, acetic acid and Lugol) were performed and interpretable.

[b]Patients included in the study who were able to benefit from their visit at 6 months.

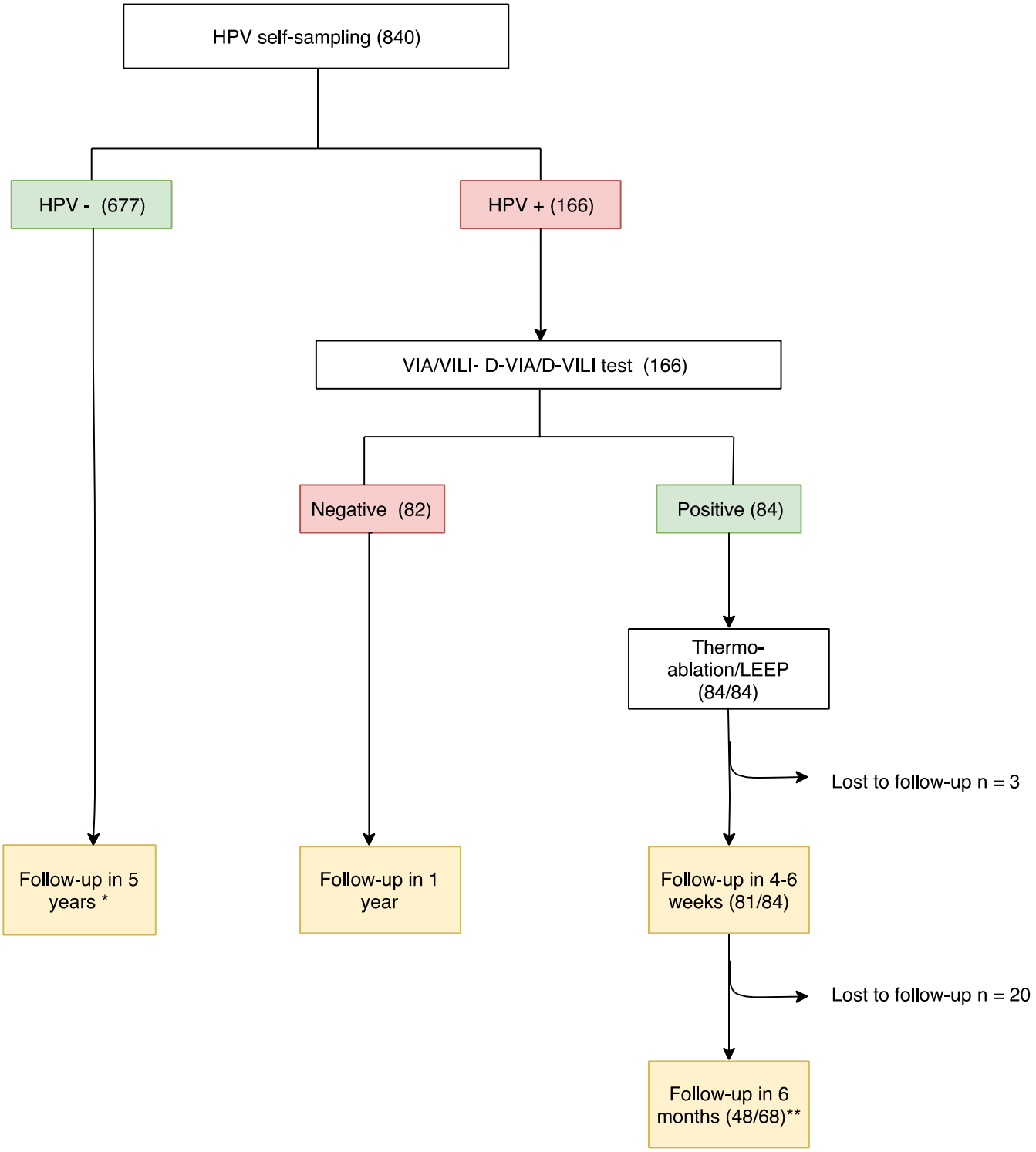

FIGURE 1 Study flowchart and results. Note: (n), number of patients, HPV, human papillomavirus; VIA, visual inspection with acid acetic; VILI, visual inspection with Lugol's iodine; D-VIA/D-VILI, Digital-VIA/Digital-VILI. *If HIV positive, follow-up in 3 years. ** Patients included in the study who were able to benefit from their visit at 6 months

4 | DISCUSSION

We implemented a single-visit 3T-approach, based on Self-HPV for primary screening followed by VIA/VILI triage and treatment with thermal ablation or LEEP if needed. This approach involving HPV test, VIA/VILI and treatment in a single visit needs women's compliance, as well as organizational factors such as adequacy of providers, scheduled service, functionality, and availability of material supply for completing the whole process. Public

health interventions are complex especially in an approach using sequence of tests and treatments, therefore, in order to check the activity and determine if we achieved the desired objective, we introduced a limited number of indicators which are feasible in a primary and secondary level of care with the aim that it should cover the different steps from screening to treatment. It should also be easily understandable and measurable by providers and can be produced periodically.[9,10]

Performance indicators for CC screening and treatment in LMIC are recommended by WHO and the Pan American Health Organization, but to date are still poorly reported in the literature.[9,20] The KPIs evaluated in our study consider different components (ie patient, provider and organizational factors) that should be reached in order to ensure that all steps from screening to treatment are performed and completed appropriately. They were focused on areas that are likely the most important in terms of improving patient outcomes and ensuring the most efficient delivery care.

We found that the rate of patients having a 3T process conducted in a single visit was 79.8% (target > 80%). Associating testing with an immediate offer of triaging and treatment for screen-positive cases is probably the best way to reduce the loss of follow-up.[5] The compliance to VIA/VILI triaging and treatment of positive women was over 90% and might reflect extensive counseling and the opportunity to receive immediate treatment after VIA/VILI. Previous studies have demonstrated that loss of follow-up between test and treatment is a real concern with loss ranging from 5% to 40% reducing program effectiveness.[21-23] Our pilot analysis also demonstrates that the desired screening rate of the target population of Dschang could be achievable. To boost the participation rate, a selection and training of community health workers was planned to provide education on CC and its prevention in the community.

We found a VIA/VILI positivity rate of 50.6% among HPV-positive women, which is higher to what was described in previous studies conducted in population with unknown HPV status,[24-27] ranging between 10% and 35%. This might be due to the IARC criteria considering only dense acetowhite lesion with sharp borders as positive.[3] In our study, in order to maintain the high sensitivity obtained after HPV testing, we consider as positive any acetowhite lesion, localized in the transformation zone including also "faint" or "pale" lesions, which might explain the higher rate of positive cases.[12] Future studies will be necessary to compare overtreatment rates between populations screened primarily by VIA and those screened by a 3T approach.

Our study has some limitations that need to be addressed. First, it was conducted in a single site with a relatively small sample size. Second, data need to be evaluated in a centralized office that serves different health facilities. Finally, it is a preliminary analysis, so results may not be generalized beyond the purpose of the study.

Strength of this study is the high quality of data collection as part of routine care, which allow to evaluate quality of the programs and formulate specific recommendations regarding the 3T-approach.

Using KPIs measures is considered as having an important impact on patient safety, monitoring and quality improvement of a CC screening program.[10] Although, the individual pathway may be different for every woman and achieving or missing a target does not necessarily suggest that women have received a poorer quality of care. Therefore, KPIs should be considered as variables that measure one aspect of the program and determine whether the targets or the standards have been achieved over a period of time. Moreover, KPIs for CC prevention in a LMIC context probably need constant review to ensure appropriateness and applicability.[10]

In conclusion, the performance of the 3T-approach in rural Cameroon can be assessed with a minimum set of key indicators. The analysis demonstrated that the program works adequately whereas it is necessary to define a periodic assessment of KPIs to assure a continuous improvement. This study could help low income countries planning to scale up outcome indicators of interest for their program based on primary HPV testing and treatment in a single visit.

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

MdP and JL led content development and writing of the article. PP and PV provided conceptual input, reviewed and edited article drafts. BK, EFT, and JTF wrote content on Cameroon, described the 3T procedure in Dschang and edited article drafts. RC provided statistical analysis and edited article drafts. JS and CF organized the health information system, provided data, and edited article drafts. The database is available as needed.

DATA AVAILABILITY STATEMENT

The database on which the analysis of the study is based is available if required.

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Appendix 3
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RESEARCH Open Access

Recruitment strategies to promote uptake of cervical cancer screening in the West Region of Cameroon

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Abstract

Objectives: The World Health Organization's (WHO) global strategy for cervical cancer elimination has set the target of 70% of women screened in all countries by 2030. Community sensitization through media is often used, but community health workers' (CHW) involvement may contribute to improving screening coverage. We aimed to assess effectiveness and costs of two cervical cancer screening recruitment strategies conducted in a low-resource setting.

Methods: The study was conducted in the West Region of Cameroon, in the Health District of Dschang, a community of 300,000 inhabitants. From September 2018 to February 2020, we recruited and screened women for cervical cancer in a single-visit prevention campaign at Dschang District Hospital. During the first 9 months, recruitment was only based on Community Information Channels (CIC) (e.g.. street banners). From the tenth month, participation of CHW was added in the community after training for cervical cancer prevention counselling. Population recruitment was compared between the two strategies by assessing the number of recruited women and direct costs (CHW costs included recruitment, teaching, certification, identification badge, flyers, transport, and incentives). The intervention's cost-effectiveness was expressed using an incremental cost-effectiveness ratio (ICER).

Results and discussion: During the period under study, 1940 women were recruited, HPV positive rate was 18.6% ($n=361$) and 39 cases of cervical intraepithelial neoplasia grade 2 or worse (CIN2+) were diagnosed. Among included participants, 69.9% ($n=1356$) of women were recruited through CIC as compared to 30.1% ($n=584$) by CHW. The cost per screened woman and CIN2+ diagnosed was higher in the CHW group. The ICER was 6.45 USD or 16.612021Int'I$ per screened woman recruited by CHW. Recruitment in rural areas increased from 12.1 to 61.4% of all women included between CIC-led and CHW-led interventions. These outcomes highlight the importance of training, preparing, and deploying CHW to screen hard-to-reach women, considering that up to 45% of Cameroon's population lives in rural areas.

Conclusion: CHW offer an important complement to CIC for expanding coverage in a sub-Saharan African region such as the West Region of Cameroon. CHW play a central role in building awareness and motivation for cervical cancer screening in rural settings.

Keywords: Cervical cancer screening, Recruitment strategies, Community health workers, Cost-effectiveness

Background

Nearly 90% of cervical cancer (CC) deaths worldwide occur in low- and middle-income countries, with a mortality rate almost three times higher than in more economically developed countries [1]. Among countries with

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the highest CC burden, 19 of the top 20 are located in sub-Saharan Africa [2]. A key reason for persistent high morbidity and mortality is the lack of sufficient screening coverage [3]. The main challenges for introducing an efficient screening program in sub-Saharan countries are limited resources and health infrastructure, shortage of health care providers, a low level of awareness, and insufficient attention to women's health, especially in rural populations [4, 5]. The result is that the vast majority of women do not have access to screening and treatment.

In response to this growing problem, the World Health Organization (WHO) has launched the 90–70-90 targets for 2030, aiming to eliminate CC [6]. These targets include (i) coverage of 90% of girls vaccinated, (ii) 70% of women screened, and (iii) treatment of 90% of women identified with cervical disease. To reach the second and third WHO targets, it is recommended to use high-performance HPV tests and associate screening with immediate treatment if needed ("screen-and-treat" approach) [7, 8].

The Health District of Dschang (West Region of Cameroon) has about 300,000 inhabitants. The Health District is divided into 22 health areas among which one is urban, 2 semi-urban and 19 rural [9]. In September 2018, we implemented a screening and treatment program in Dschang District Hospital, based on a single-visit approach called 3 T (Test, Triage and Treat). The ongoing program is scheduled over a five-year period (2018–2023) and follows the WHO's recommendations to screen women between the ages 30–49 years at least once every 5 years. According to a national census, we estimated that about 18′000 women should be screened in the Health District of Dschang to reach the 70% coverage rate set by the WHO's "90–70-90 targets" [6]. Therefore, an annual recruitment of 3′600 women was estimated to reach the second WHO target.

A program's performance and its impact on CC prevention highly depends on the screening coverage achieved by reaching the targeted population. This may be enhanced by raising awareness through educational interventions. Outreach strategies to encourage participation in prevention programs may be viewed as low priority activities and may suffer from a lack of resources as they compete with other healthcare issues such as infectious diseases [10, 11]. Several challenges have been raised regarding the optimal recruitment strategies to inform women about screening and motivate them to participate. Screening interventions should also consider geographic conditions and the dispersion of the population living in these areas and be adapted to population needs.

Traditional choices for raising CC awareness in a large population within a short period of time are community information channels (CIC), such as advertising, radio, and television. However, the implication of community health workers' (CHW) living in the community may contribute to improving education and motivation for screening, and therefore increase coverage. The definition of CHW varies according to different cultures and healthcare systems. In Cameroon, they are trusted community members, integrated into the community health system without any formal professional or paraprofessional medical training [12–17]. The purpose of this study was to analyze and compare the recruitment rates and costs of the two different recruitment strategies.

Methods

Setting

The Health District of Dschang is divided into 22 health areas, which we separated into four zones based on accessibility to the district hospital (e.g. distances, roads, weather, and transportation means available). Zone 1 was defined as the most accessible area (urban) and Zone 4 the least accessible (rural).

CIC recruitment

From September 2018 to May 2019, recruitment was entirely based on announcements made and posters hung in women's associations, churches, and integrated health centers (chief nurses of each center were informed of this project). In Dschang District Hospital's waiting room, women were invited to participate in the screening program on a daily basis. Two large street banners were hung on the main tar road at the entrance and exit of Dschang for 1 month. Although the banners were hung in zone 1, this route is an access to district services and to markets where farmers weekly trade. Hence, it is used by inhabitants of all zones. The banners' exposition time was restricted by local authorities as this location was regularly used to announce local events. Local radio announcements were broadcast twice a week for 1 month. The limited duration of broadcasting was due to budget constraints. Radio announcements were made in French which is the official language used in the district. We expected participants to spread information about this campaign to their relatives. The combination of these methods of recruitment is summarized as CIC.

CHW recruitment

From June 2019 to February 2020, a recruitment strategy using CHW was added to the CIC intervention. At district level, district health managers were informed about the campaign and invited to participate by recruiting CHW. Selection was based on volunteer application without any prerequisites. CHW work in their village. They usually have a main job and act as CHW when

called during public health activities. An incentive of 600 CFA (1 USD or 2.62021Int'l$) per woman recruited from June to September 2019 was given, which was then increased to 1000 CFA (1.68 USD or 4.32021Int'l$) since October 2019 to adequately cover cellphone and transportation fees.

In June 2019, 21 CHW attended a half-day informal training. These CHW were based in zone 1. In October 2019, 52 CHW from all health areas (zones 1 to 4) were enrolled in a two-day multi-modal training. Among the trained participants, 5 workers attended both sessions. The second session was based on the "WHO Toolkit for improving CWH Program and Service" [18, 19] and adapted to local barriers by regional caregivers. To differentiate CHW recruitment from CIC, CHW were given invitation vouchers to distribute to each woman they approached. CHW received their financial incentive according to the respective number of vouchers returned by participants attending screening.

Screening process

Recruited participants were expected to be present at the screening unit at 9 am daily, where a one-hour health education session was provided by trained midwives. General information was given on sexually transmitted infections including HPV (its prevention, cancer development and treatment), contraceptive methods, intimate hygiene, and on the study project (inclusion, exclusion criteria, study procedures, planned follow-up). Participants were asked how they heard about the screening program and were encouraged to spread information about the campaign. Questions were addressed during this time. Participants filled a questionnaire on their socio-demographic characteristics and medical history and proceeded to vaginal self-sampling (Self-HPV) for primary screening. Samples were analyzed using the Xpert HPV assay® (GeneXpert®. Cepheid, 2015. Sunnyvale, California, USA). Results were available within 1 h. HPV-negative participants were advised to repeat screening in 5 years. HPV-positive women underwent triage by visual inspection after application of acetic acid (VIA) and Lugol's iodine (VILI), and treatment with thermal ablation or large loop excision of the transitional zone (LLETZ) if required. Biopsy and endocervical curettage were performed on all HPV-positive patients for CC exclusion, quality control and further program evaluation. Further details can be found in previously published articles [20, 21].

Data collection

Before completing their HPV test, participants filled a sociodemographic questionnaire distributed by midwives.

Inclusion

We included for this analysis all women aged 30 to 49 years old living within Dschang's Health District or its surroundings, who underwent an HPV test from September 2018 to February 2020. Exclusion criteria for HPV screening were pregnancy, hysterectomy, and vaginal bleeding. After verification of inclusion and exclusion criteria, volunteers provided informed written consent to participate in the study. To be counted in the CHW recruitment group, women had to present a CHW invitation voucher.

Outcome measures

(i) A comparison of sociodemographic characteristics of women recruited by each method was performed with in-depth analysis for each zone of origin. (ii) The number of participants screened was assessed and costs for the implementation of CHW and CIC interventions compared and (iii) to assess the cost-effectiveness of CHW, the costs and screening recruitment outcomes associated with each intervention were compared to generate an incremental cost-effectiveness ratio (ICER). Costs of recruitment by CHW included workers' recruitment, training supplies, certification, identification badges, vouchers, transportation, meals, accommodation, incentives, per diem, and miscellaneous materials. CIC costs included radio broadcasting, banners, and poster. Both groups included financial aid for women's transportation to the screening center according to hospital accessibility from each health area. To highlight the actual field situation and its margin of error, we decided to compare the real-life cost-effectiveness (actual expenses, including incorrect patient transport financial aid), and the theoretical cost-effectiveness (expected expenses) generated by the CHW intervention to the cost-effectiveness of the CIC intervention. Costs are expressed in USD according to the exchange rate on March 1st, 2020 and, in international dollars to consider purchasing power parity.

Statistical analysis

Quantitative data were stored and analyzed using Stata Statistical Software Release 16 (StataCorp LP, College Station, TX, USA). A descriptive analysis was conducted; categorical variables were summarized with frequencies and percentages, and continuous variables were summarized with means and standard deviations (SD). *P*-values were estimated using Pearson's chi-squared test, Student's t-test, and ANOVA test as appropriate. All analyses were 2-sided and p-values <0.05 were considered statistically significant. Women's socio-demographic and medical data were collected, stored, and managed by the secuTrial® online database. The calculated incremental

cost-effectiveness ratio (ICER) was determined as the additional cost per screened woman by CHW, calculated as the difference between CHW costs and CIC costs divided by the difference of the number of screened women between CHWs and CIC.

Ethical considerations

The study obtained approval from the Cantonal Ethics Board of Geneva, Switzerland (Commission cantonale d'éthique de la recherche [CCER], No. 2017–0110) and the Cameroonian National Ethics Committee for Human Health Research (No. 2018/07/1083/CE/CNERSH/SP).

Results

Population

A total of 1940 women were included during the study period, with an HPV positive rate of 18.6% ($n=361$), and 39 CIN2+ (2.0%) lesions were diagnosed. In the CIC group, 1356 women (69.9%) were recruited and 28 CIN2+ (2.1%) lesions were detected. In the CHW group, 584 women (30.1%) were recruited and 11 CIN2+ (1.8%) lesions identified. Two hundred sixteen participants living outside the health district of Dschang were recruited in the CIC group, and 19 patients in the CHW group. Among the 68 CHW trained, eight did not recruit any participants. The recruitment progress is depicted in Fig. 1 showing reuptake of the recruitment trend when introducing CHW, and a sharp decrease in recruitment in December due to the annual closing of the Dschang Screening Unit for the winter holidays combined with equipment shortage during that period. Figure 2A-B shows the proportion of women recruited by district zone with each method. Using the CIC method, 87.89% of women were recruited in zone 1 ($n=1002$), 7.72% in zone 2 ($n=88$), 2.81% in zone 3 ($n=32$) and 1.58% in zone 4 ($n=18$). With the CHW method, 38.58% of women were recruited in zone 1 ($n=218$); 29.03% in zone 2 ($n=164$); 13.81% in zone 3 ($n=78$); 18.58% in zone 4 ($n=105$).

CIC versus CHW recruitment

As shown in Table 1, the mean age of participants was 40.2 years old (SD ± 5.9). The two groups differed significantly on all socio-demographic variables ($p=<0.001$). However, we did not observe any significant difference between both groups in the proportion of positive HPV test results, HIV self-reported status, and histology among HPV-positive women. Some variables had missing data as a few participants did not answer all questions. Populations recruited by CHW compared to CIC accounted for more divorced and widowed women (11% vs 5.8%) and fewer single women (4.3% vs 8.9%). The predominant education level in the CIC group was secondary (56.0%) and tertiary (23.25%), while in the CHW group, the predominant education level was primary and secondary with 46.9% in each sub-category. Employed and self-employed women were the most represented in the CIC-led intervention at 35.4 and 30.4%, respectively, whereas in the CHW-led recruitment, women were mostly farmers (42.6%) and housewives (25.2%). The unemployment rate in our sample was 0.4%. Women

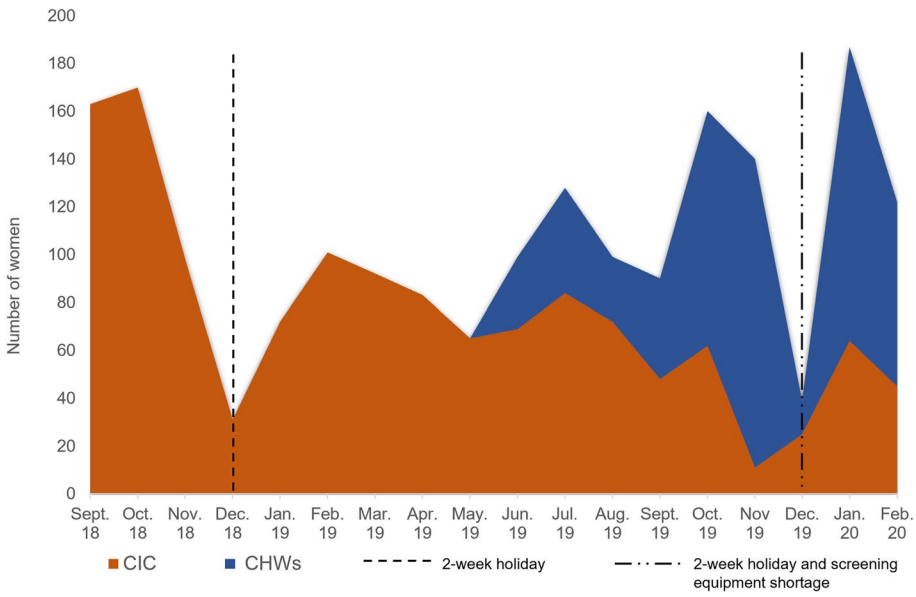

Fig. 1 Recruitment progression from September 2018 to February 2020

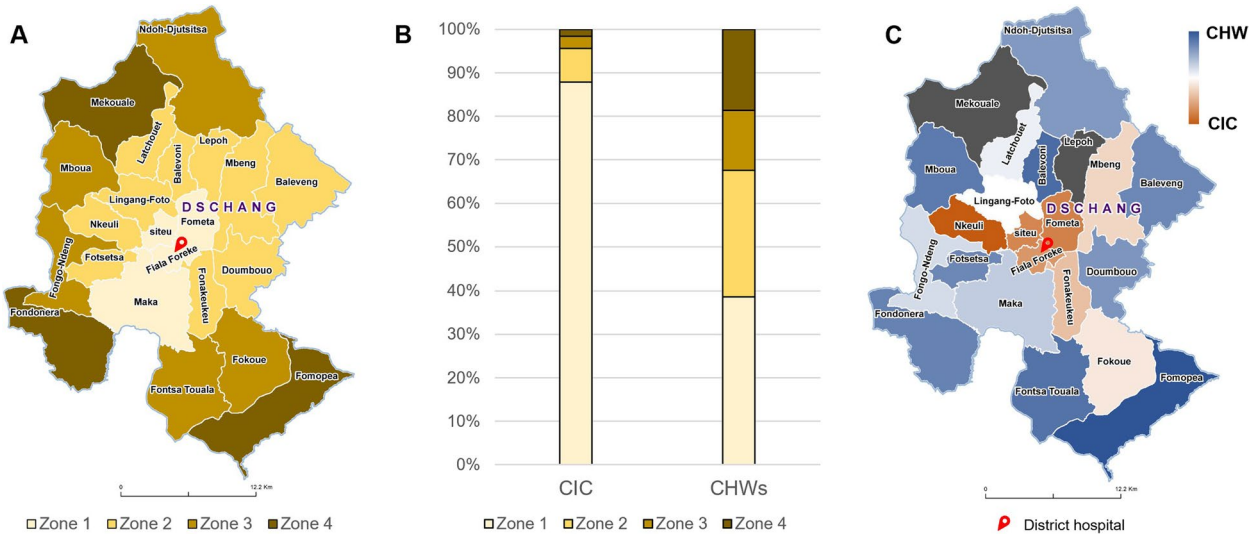

Fig. 2 A-C. **A**. Dschang Health Area separated in 4 zones. Zone 1 being the most accessible areas (urban) and Zone 4 the least accessible areas (rural). **B**. Screening rate per zone according to recruitment method. **C**. Recruitment method predominance. Health areas in dark blue represent a predominance of women recruited by CHW, and orange represents health areas where recruitment was predominantly done through CIC. White color indicates that patients were equally recruited by CIC and CHW. In grey, two health areas were excluded from the analysis (Mekouale and Lepoh) as no CHW participated

recruited by CHW often had more than 4 children (69.2%) compared to CIC-recruited women, among which 48,8% had between 1 and 4 children and 46.2% had more than 4 children. Tobacco consumption was higher among women in the CHW group (4.6% vs 0.5%). Most women (69.8%) did not use any form of contraceptive. Condom usage was reported by 13.9% in the CIC group compared to 3.6% in the CHW group. Intra-uterine devices, hormonal implants, and injections were used as a contraceptive method for 14.7% of participants in the CIC recruitment group and 20.0% of participants in the CHW group. Previous CC screening was reported by 24.3% in the CIC-led intervention and 3.9% in the CHW-led intervention.

Recruitment breakdown by zone

Socio-demographic differences between women recruited by CIC and CHW in the four zones are described in Table 2**.** Participants' mean age varied between urban and rural areas, with women in zone 1 tending to be younger than those in zone 4 ($p < 0.001$). In zone 1, primary education only was attended by 17.4% of women in the CIC group contrasting with 39.5% of women recruited in the CHW group. Furthermore, secondary level and higher was reached by more participants in the CIC group than in the CHW-led intervention except for zone 4, (38.9% in the CIC and 49.5% in the CHW group). Tertiary education was attended by 25.6% in zone 1 recruited by CIC compared to only 7.8% in zone 1 within the CHW group. In the CIC-led intervention, women in zone 1 were more frequently employed (38.1%) and self-employed (33.1%), whereas in zone 2–4, women worked more frequently as farmers (34.1, 34.4 and 50% respectively). In the CHW-led intervention, most participants were self-employed in zone 1 (34.9%), and farmers in zones 2 (49.4%), 3 (92.3%) and 4 (76.2%). We also found that most unemployed women lived in zone 1 and were recruited through CIC. Women coming from zone 1 and recruited through CIC had fewer children than in other zones. Indeed, 49.7% women in zone 1 had between 1 and 4 children and 45.51% had more than 4 children, while in other subgroups, between 62.5 and 80.95% of participants had more than 4 children. Within the CIC-recruited group, most women who used condoms were in zone 1 (15.2%,) and zone 2 (13.6%). Participants who smoked the most were recruited by CHW and live in zone 2 (7.9%) and in zone 3 (12.8%). Variance in previous CC screening was also shown between women living in urban zones compared to those in rural zones and depending on the recruitment method. Among women recruited through CIC, 25.45% of those living in zone 1 had a history of previous CC screening, 15.9% in zone 2, 9.4% in zone 3 and 5.6% in zone 4 ($p = 0.092$). Rates of previous screening were generally lower in women recruited by CHW, where 7.8% of women in zone 1 had a previous CC screening, 1.2% in zone 2, 2.6% in zone 3 and 1.9% in zone 4 ($p = 0.017$).

Table 1 Baseline sociodemographic, reproductive health, and clinical characteristics according to CHW and CIC groups

	CIC, *n* (%)	CHW, *n* (%)	Total, *n* (%)	*P*-value*
Variable				
Participants recruited	1356 (69.9%)	584 (30.1%)	1940 (100%)	
Age (years), mean ± SD	39.4 (±5.9)	41.9 (±5.6)	40.2 (±5.9)	< 0.001
Marital status				< 0.001
Single	121 (8.9%)	25 (4.3%)	146 (7.5%)	
Married/In a relationship	1155 (85.2%)	494 (84.6%)	1649 (85%)	
Divorced/widowed	78 (5.8%)	64 (11.0%)	142 (7.3%)	
Education				< 0.001
Unschooled	5 (0.4%)	9 (1.5%)	14 (0.7%)	
Primary education	275 (20.3%)	274 (46.9%)	549 (28.3%)	
Secondary education	759 (56.0%)	274 (46.9%)	1033 (53.3%)	
Tertiary education	315 (23.2%)	24 (4.1%)	339 (17.5%)	
Employment status				< 0.001
Employed	480 (35.4%)	62 (10.6%)	542 (27.9%)	
Self-employed	412 (30.4%)	121 (20.7%)	533 (27.5%)	
Farmer	130 (10.0%)	249 (42.6%)	379 (19.5%)	
Housewife	274 (20.2%)	147 (25.2%)	421 (21.7%)	
Student	50 (3.7%)	4 (0.7%)	54 (2.8%)	
Unemployed	8 (0.6%)	0	8 (0.4%)	
Age at menarche (years), mean ± SD	14.6 (1.8)	14.9 (1.7)	14.7 (1.8)	< 0.001
Age at first intercourse, mean ± SD	18.0 (2.9)	17.48 (2.4)	17.9 (2.8)	< 0.001
Number of sexual partners, median (IQR)	3 (2–5)	3 (2–4)	3 (2–5)	
Age at first delivery (years), mean ± SD	21.3 (5.8)	19.8 (4.3)	20.9 (5.4)	< 0.001
Parity				< 0.001
Nulliparous	65 (4.8%)	13 (2.2%)	78 (4.0%)	
1–4	662 (48.8%)	166 (28.4%)	828 (42.9%)	
> 4	627 (46.2%)	404 (69.2%)	1031 (53.1%)	
Tabaco consumption				< 0.001
Yes	7 (0.5%)	27 (4.6%)	34 (1.8%)	
None	1347 (99.3%)	555 (95.0%)	1902 (98.0%)	
Contraception				< 0.001
None	924 (68.1%)	430 (73.6%)	1354 (69.8%)	
Condom	189 (13.9%)	21 (3.6%)	210 (10.8%)	
Hormonal pill	23 (1.7%)	8 (1.4%)	31 (1.6%)	
DIU/ implant/ injection	199 (14.7%)	117 (20.0%)	316 (16.3%)	
Other	16 (1.2%)	5 (0.9%)	21 (1.1%)	
Previous cervical cancer screening				< 0.001
None	1025 (75.6%)	560 (95.9%)	1585 (81.7%)	
Yes	329 (24.3%)	23 (3.9%)	352 (18.1%)	
HIV status (self-reported)				0.791
Negative	1327 (97.9%)	574 (98.3%)	1901 (98.0%)	
Positive	27 (2.0%)	9 (1.5%)	36 (1.9%)	
HPV testing results				0.287
Negative	1096 (80.8%)	484 (82.9%)	1580 (81.4%)	
Positive	260 (19.2%)	100 (17.1%)	360 (18.6%)	
HPV-16/18/45	59 (4.4%)	24 (4.1%)	83 (4.3%)	
Other HPV	215(15.9%)	86 (14.7%)	301 (15.5%)	
Histology (% of HPV positive women)				0.437
Normal	179 (68.8%)	62 (62%)	241 (66.9%)	
CIN1	44 (16.9%)	18 (18%)	62 (17.2%)	
CIN2+	28 (10.8%)	11 (11%)	39 (10.8%)	

Abbreviations: *CHW* Community Health Workers, *CIC* Community Information Channels, *SD* Standard Deviation, *IQR* Interquartile range, *HIV* Human immunodeficiency virus, *HPV* Human papillomavirus, *n* number

**p*-values were estimated using chi-squared test, t-test as appropriate

Screening rate

Figure 2C shows recruitment method predominance by health area. We observed a predominance for CHW recruitment in areas distant from the district center.

The cost-effectiveness analysis of recruitment is presented in Table 3.

Cost analysis

A detailed breakdown of CHW training costs for each session is presented in the supplemental table. The June session cost a total of 694.98 USD (cost per trained CHW was 33.09 USD for 21 CHW). The October session's total cost was 1962.88 USD (cost per trained CHW was 37.75 USD for 52CHW). CIC costs include 33.62 USD for four radio broadcasts, 184.92 USD for two street banners, 42.03 USD for a thousand poster. Based on the onsite accounting book, the patients' transport cost was 1411.30 USD without distinction between the two intervention groups. To compare the two groups, the theoretical patients' transport cost is presented on Table 3. This was calculated based on the predefined amount allocated to each participant according to hospital accessibility from each health area and amounted to 1845.87 USD for the CHW-led intervention and 1345.74 USD for the CIC-led intervention. The financial incentives paid to CHW were calculated to be around 1141.57 USD (based on receipts when available, and theoretically calculated for participants with missing receipts). The theoretical cost of CHW incentive, based on the total number of women recruited through CHW was 870.40 USD. The average cost per CIC-recruited woman was 1.18 USD compared to 9.20 USD per CHW-recruited woman. Based on theoretical costs, the ICER was 6.45 USD or 16.612021Int'l$ per screened woman recruited by CHW. The average cost per CIN2+ lesion diagnosed was 57.37 USD in the CIC group compared to 488.56 USD in the CHW group.

Discussion

The global WHO strategy for cervical cancer elimination recommends that each country should meet the 90–70-90 targets by 2030 [6]. Achieving and sustaining the second target (70% of participation rate to screening with a high-performance test) will be one of the most challenging issues for many LMICs. For example, in Cameroon, it was estimated that the cervical cancer screening participation rate in a woman's lifetime is less than 10% [22]. This condition is one of the main reasons for the high cervical cancer incidence and mortality among middle-aged women in the country [8]. Our aim was to explore the effectiveness and costs of two different recruitment strategies in encouraging women to have a screening test.

Media-based information for public education about health-related issues are frequently used in national campaigns in Cameroon [23–25]. However, according to the 2018 Demographic and Health Survey in Cameroon, within the West Region, 38.1% of women were not exposed to any television, radio, or newspapers, 56.5% of women watched television and 22.4% listened to radio at least once a week [22]. This aspect is crucial for any decision making related to information spreading. Considering this data, radio broadcasting in our context may not be the most efficient strategy compared to television-based interventions. However, the latter may be more expensive. Data is still limited about the impact of encouraging behavior changes related to health services, and the resulting cost per person screened.

Efficiency results for screening coverage must consider that CIC and oral communication within the community co-existed with CHW-led interventions during the second period under study. Several women recruited by CHW could have been screened without mentioning the CHW referral, which would lead to their misclassification. Community-spread communication co-existed with the CHW-led intervention and probably also increased recruitment in each group; thus, CHW's impact could be greater than we assumed. At the screening center, warm welcome can lead to a positive experience and favor recruitment.

CHW-led interventions constitute an important step to increase participation in cervical cancer screening programs. They contribute to optimizing the participation as they use their cultural knowledge and ensure that message are delivered in a culturally appropriate fashion according to women's preferences and needs in rural areas where the screening rate is very low, which differ from those of women living closer to the city [14, 26]. As shown in Tables 1 and 2, women recruited by CHW tended to be less educated, had more children, used fewer condoms, and consumed more tobacco. Participant knowledge about cervical cancer in rural areas may not be the same as women living closer to the hospital. Studies have suggested that higher cervical cancer awareness is found among women living in an urban environment due to internet and media access [27]. It has been established that a lack of information and awareness about screening centers' location, the cost of screening, available time, and geographical conditions are the main barriers to CC screening [28–31].

In our study, CIC were used to convey an invitation to get screened. However, in other studies, media used as an educational tool appeared as effective as CHW interventions to raise awareness about the importance of CC screening, although lay health workers were more

Table 2 Baseline sociodemographic, reproductive health, and clinical characteristics according to CHW and CIC groups and Zone subgroups

Variable	CIC (1140/1356), *n* (%)				*P*-Value	CHW (565/584), n (%)				*P*- Value
	Zone 1	Zone 2	Zone 3	Zone 4		Zone 1	Zone 2	Zone 3	Zone 4	
Participants recruited n (%)	1002 (87.9%)	88 (7.7%)	32 (2.8%)	18 (1.6%)		218 (38.6%)	164 (29.0%)	78 (13.8%)	105 (18.6%)	
Age (years), mean ± SD	39.1 (±5.9)	41.4 (±5.6)	41.5 (±5.4)	42.3 (±4.3)	< 0.001	40.9 (±5.7)	43.1 (±5.4)	43 (±5.5)	41.9 (±5.3)	< 0.001
Marital status					< 0.001					0.023
Single	81 (8.1%)	3 (3.4%)	3 (9.4%)	0		15 (6.9%)	6 (3.7%)	2 (2.6%)	0	
Married/In a relationship	870 (86.8%)	76 (86.4%)	25 (78.1%)	13 (72.2%)		189 (86.7%)	133 (81.1%)	65 (83.3%)	91 (86.7%)	
Divorced/widowed	50 (5.0%)	9 (10.2%)	4 (12.5%)	5 (27.8%)		14 (6.4%)	25 (15.2%)	11 (14.1%)	13 (12.4%)	
Education					<0.001					< 0.001
Unschooled	3 (0.3%)	2 (2.3%)	0	0		1 (0.5%)	6 (3.7%)	1 (1.3%)	1 (1.0%)	
Primary education	174 (17.4%)	25 (28.4%)	12 (37.5%)	11 (61.1%)		86 (39.5%)	85 (51.8%)	47 (60.3%)	51 (48.6%)	
Secondary education and higher	824 (82.2%)	61 (69.3%)	20 (62.5%)	7 (38.9%)		131 (60.1%)	72 (43.9%)	30 (38.5%)	52 (49.5%)	
Employment status					<0.001					< 0.001
Employed	382 (38.1%)	16 (18.2%)	8 (25%)	3 (16.7%)		36 (16.5%)	11 (6.7%)	10 (12.8%)	3 (2.9%)	
Self-employed	332 (33.1%)	14 (15.9%)	2 (6.3%)	2 (11.1%)		76 (34.9%)	30 (18.3%)	6 (7.7%)	6 (5.7%)	
Farmer	55 (5.5%)	30 (34.1%)	11 (34.4%)	9 (50%)		33 (15.1%)	81 (49.4%)	50 (92.3%)	80 (76.2%)	
Unemployed, Housewife and student	232 (23.2%)	28 (31.4%)	11 (34.4%)	4 (22.2%)		73 (33.5%)	42 (25.6%)	12 (15.4%)	15 (14.3%)	
Age at menarche (years), mean ± SD	14.6 (1.8)	14.6 (1.8)	15.1 (1.8)	14.7 (1.6)	0.389	15.0 (1.7)	14.7 (1.6)	14.9 (1.7)	14.9 (1.8)	0.583
Age at first intercourse, mean ± SD	18.1 (2.9)	17.3 (1.9)	17.9 (2.8)	16.3 (1.5)	0.004	17.9 (2.5)	17.2 (2.0)	17.4 (2.4)	17.0 (2.5)	0.012
Number of sexual partners, median (IQR)	3 (2–5)	3 (2–5)	3 (2–4)	3 (2.8–4.3)		3 (2–4)	3 (2–4)	2 (1–4)	3 (2–5)	
Age at first delivery (years), mean ± SD	21.5 (5.9)	19.6 (4.2)	20.6 (4.7)	19.7 (2.7)	0.013	19.9 (4.5)	19.59 (3.7)	20.2 (4.1)	19.3 (5.0)	0.777
Parity					0.001					0.001
Nulliparous	47 (4.7%)	3 (3.4%)	1 (3.1%)	0		5 (2.3%)	3 (1.8%)	1 (1.3%)	2 (1.9%)	
1–4	498 (49.7%)	27 (30.7%)	11 (34.4%)	4 (22.2%)		72 (33.0%)	46 (28.1%)	19 (24.4%)	17 (16.2%)	
>4	456 (45.5%)	58 (65.9%)	20 (62.5%)	14 (77.8%)		141 (64.7%)	115 (70.1%)	58 (74.4%)	85 (81.0%)	
Contraception					0.002					0.120
None	659 (65.8%)	61 (69.3%)	28 (87.5%)	14 (77.8%)		160 (73.4%)	131 (79.9%)	57 (73.1%)	66 (62.9%)	
Condom	152 (15.2%)	12 (13.6%)	2 (6.3%)	1 (5.6%)		8 (3.7%)	6 (3.7%)	3 (3.9%)	3 (2.9%)	
Other	190 (19.0%)	15 (17.1%)	2 (6.3%)	3 (16.7%)		50 (22.9%)	26 (15.9%)	18 (23.1%)	34 (32.4%)	
Previous cervical cancer screening					0.092					0.017
None	746 (74.5%)	74 (84.1%)	29 (90.6%)	17 (94.4%)		201 (92.2%)	162 (98.8%)	76 (97.4%)	102 (97.1%)	
Yes	255 (25.5%)	14 (15.9%)	3 (9.4%)	1 (5.6%)		17 (7.8%)	2 (1.2%)	2 (2.6%)	2 (1.9%)	
HIV status (self-reported)					0.004					0.596
Negative	949 (94.7%)	82 (93.2%)	26 (81.3%)	17 (94.4%)		213 (97.7%)	159 (97.0%)	75 (96.2%)	100 (95.2%)	
Positive	39 (3.9%)	5 (5.7%)	3 (9.4%)	0		3 (1.4%)	3 (1.8%)	2 (2.6%)	1 (1.0%)	

Table 2 (continued)

Variable	CIC (1140/1356), *n* (%)				*P*-Value	CHW (565/584), n (%)				*P*- Value
	Zone 1	Zone 2	Zone 3	Zone 4		Zone 1	Zone 2	Zone 3	Zone 4	
HPV testing results					0.091					0.741
Negative	817 (81.54%)	76 (86.36%)	27 (84.38%)	12 (66.67%)		180 (82.57%)	135 (82.32%)	64 (82.05%)	87 (82.86%)	
Positive	185 (18.46%)	12 (13.64%)	5 (15.63%)	6 (33.33%)		38 (17.43%)	29 (17.68%)	14 (17.95%)	18 (17.14%)	

Abbreviations: *CHW* Community Health Workers, *CIC* Community Information Channels, *SD* Standard Deviation, *IQR* Interquartile range, *HIV* Human immunodeficiency virus, *HPV* Human papillomavirus, *n* Number

Table 3 Cost-analysis of recruitment. The incremental cost-effectiveness ratio (ICER) is determined as the additional cost per screened woman calculated as the difference between CHW costs and CIC costs divided by the additional of number of screened women due to CHW

Variable	CIC (USD)	CHW (USD)
Recruited patients (n)	1356	584
Patients' transport reimbursement	1345.74	1845.87
Street Banners ($n=2$)	184.92	N/A
Radiobroadcast ($n=4$)	33.62	N/A
Flyers ($n=1000$)	42.03	N/A
CHW 's training	N/A	2657.86
CHW wages	N/A	870.40
Total costs	1606.31	5374.13 (training included) 2716.27 (training excluded)
Costs per recruited woman		
ACER	1.18	9.20 (training included) 4.65 (training excluded)
Incremental additional cost	N/A	3767.82 (training included) 1109.06 (training excluded)
ICER in USD	N/A	6.45 (training included) 1.90 (training excluded)
ICER in 2021Int'I$*	N/A	16.61 (training included) 4.89 (training excluded)

Abbreviations: *CHW* Community Health Workers, *CIC* Community Information Channels, *ICER* Incremental cost-effectiveness ratios, *ACER* Average cost effectiveness ratio, *n* Number, *N/A* Not applicable

effective to change screening behaviors through encouragement and logistical support [32, 33].

In our study, CIC appeared to be most suitable for women living close to the city center, while CHW improved recruitment coverage in rural areas. CHW not only enhanced recruitment outside urban areas, but they were also able to engage with and invite more women from a different socio-demographic population to be screened, including in zone 1. To avoid a bottleneck effect due to limited capacities at the screening center, one strategy could be to start by using CIC, before gradually implementing CHW intervention. A probable reason for a higher history of previous cervical cancer screening among participants from zone 1 in the CIC group was an increase of awareness and a built trust throughout a previous screening campaign led in Dschang in 2015, in addition to the 20 years of collaboration with our research team in Cameroon [21].

Transportation and childcare have been previously reported as screening barriers [26]. Our screening recruitment heavily depended on rainy seasons as roads were impassible. Moreover, financial transport aid was an essential aspect of our strategy as women living in rural areas had to travel for many hours. The CHW-led intervention helped to decrease these barriers as they recruited hard-to-reach women with multiple children and informed them about the financial subsidies for transportation.

The cost per screened woman and CIN2+ diagnosed was higher in the CHW group. While the media campaign was most efficient in zone 1, the higher recruitment of women in rural areas by CHW highlights the importance of training, preparing, and deploying CHWs to screen hard-to-reach women, especially considering that almost 45% of the Cameroonian population lives in a rural area [34]. Undetected cervical lesions potentially leading to cervical cancer also increase overall costs not only for the healthcare system but can cause direct and indirect costs for affected women and their families, such as cancer management costs, or loss of income due to disease, disability or death.

When possible, CHW selection should be based on abilities and long term motivation, and their work should be adequately compensated to avoid having inactive workers that need to be replaced by newly trained personnel, which would increase the screening cost [13, 35]. Training in October 2019 was more expensive in total than the first session in June 2019; however, the investment was similar if we consider the expense per CHW trained. Improving CHW knowledge is recognized as a key factor to a successful recruitment intervention [16]. This was evidenced during the October session based on a multi-modal training, which was followed by an increase of screened women.

Strategies with multiple visits to get screened, treated, and followed up may decrease screening effectiveness and increase the overall cost of cancer prevention per woman due to loss to follow-up [12, 36]. In our setting, the 3 T strategy led only to a 1.1% loss to follow-up and has the potential to increase program effectiveness as barriers for Cameroonian women include "low health literacy, poverty, lack of resources, and geographical conditions" [20]. However, additional follow-up visits after treatment may increase the need for CHW, as studies have shown that in-person follow-up could be a cost-effective approach to keep women in the screening process [12]. In this study, we only focused on the cost of screening recruitment; however, further studies are needed to assess the full financial and social burden through a cost-benefit analysis of an HPV "screen and treat" program in Dschang. In sub-Saharan Africa, most women dying of cervical cancer are around 50 years old, and DALYs caused by CC were estimated ats 641 years per 100′000 women [21, 37].

The large sample size and heterogeneity of the population regarding social and demographic characteristics are the major strengths of this study. Real-world conditions and thus the amount paid for equipment, supplies, and

labor did not reflect theoretical costs. Health area attribution discordances and village overlap between two health areas/zones could have led to misclassification, as well as inexact cost and recruitment rate estimates, in addition to some miscommunication that led to incorrect patient reimbursement cost. Moreover, measuring the success rate of the CHW-led intervention could have allowed a more detailed analysis of the cost-effectiveness of CHW service. Indeed, the ratio of CHW-approached to screened women is currently unknown. Since recruitment strategies were not led simultaneously, a uniquely CHW-led intervention might have enrolled less participants as some women had already been informed through CIC. Furthermore, as various strategies (e.g. radio broadcasting, street banners) within the CIC intervention were led discontinuously throughout the study period, it is difficult to establish the effectiveness of each individually. Another limitation is that some women recruited by CHW might have eventually attended screening without CHW intervention.

Conclusion

Combining both CIC and CHW approaches according to regional context appeared as the most efficient strategy for increasing recruitment among the target population. CHW play a central role in building awareness and motivation for cervical cancer screening among rural populations. Further studies are needed to explore innovative community-based interventions as effective ways to improve recruitment of the target population.

Abbreviations

WHO: World Health Organization's; HPV: Human papillomavirus; CHW: Community Health Workers; CIC: Community Information Channels; ICER: Incremental Cost-Effectiveness Ratio; CC: Cervical Cancer; SD: Standard Deviation; IQR: Interquartile range; HIV: Human immunodeficiency virus; N: Number.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-022-12951-1.

Additional file 1: Supplemental Table. Detailed breakdown of CHWs training costs for each session.

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Authors' contributions

PP, BK, and PV designed the study protocol, implemented the study. PP, BK, PV, AW, and JS oversaw the data collection and interpreted the data. MP and KB drafted the paper. MP and AW conducted data analysis. AW, JS and ET supported the data collection. KB, BK, ET and JS trained the study staff and assumed quality control. JS assumed project administration and funding acquisition. All authors interpreted the analyses and approved the final manuscript.

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Availability of data and materials

Data are available upon reasonable request. In accordance with the journal's guidelines, we will provide our data for the reproducibility of this study in other centers if such is requested.

Declarations

Ethics approval and consent to participate

The study obtained approval from the Cantonal Ethics Board of Geneva, Switzerland (Commission cantonale d'éthique de la recherche [CCER], No. 2017–0110) and the Cameroonian National Ethics Committee for Human Health Research (No. 2018/07/1083/CE/CNERSH/SP). Protocols are carried out in accordance with relevant guidelines and regulations. All women provided informed written consent to participate in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Publisher's Note

Effects of the COVID-19 pandemic on an urban cervical cancer screening program in West Cameroon

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INTRODUCTION

Cervical cancer is the fourth most common cancer among women worldwide, and in 2020 almost 85% of new cases occurred in low and middle income countries. In Cameroon, 1787 deaths were recorded in 2020, making cervical cancer the second most common cause of cancer deaths among women. Recently, in 2020, the World Health Organization (WHO) launched the 90-70-90 strategy to eliminate cervical cancer (box 1).

In response, the Dschang District Hospital, the Cameroon Ministry of Public Health, and the Geneva University Hospitals launched a community based cervical cancer screening program ('3T-approach': test, triage, and treat) at the Dschang District Hospital in West Cameroon. The program has been presented in this journal previously.

EFFECT OF THE COVID-19 PANDEMIC

Although the WHO considered cervical cancer prevention activities a priority during the COVID-19 pandemic, the Dschang cervical cancer primary screening program and follow-up procedures were substantially affected, as were many preventive health services worldwide. From mid-March until the end of April 2020, the screening unit was closed as it was considered inappropriate to expose women and healthcare providers to the risk of COVID-19. In May 2020, follow-up visits were progressively restarted after implementation of the necessary hygiene measures to control the spread of the virus and ensure the safety of the facilities. Consequently, the number of women screened in 2020 dropped by almost 80% compared with the same period in 2019 (Figure 1). To reduce the risk of exposure between patients and staff, (i) the number of patients attending the clinic was reduced, (ii) physical distancing between patients was implemented, (iii) mask wearing (Figure 2) and (iv) regular hand washing with soap or disinfection with gel was required, as well as (v) careful hygiene regarding equipment and surfaces.

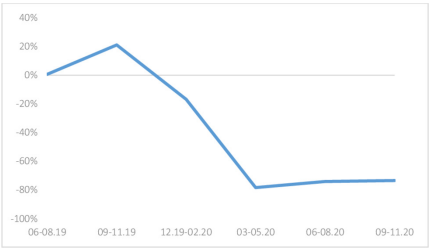

Figure 1 Percentage change in visit 1 from baseline (average of 109 visits/month in 2019) due to the COVID-19 pandemic.

However, as the local health authorities have made substantial efforts in the past few years to launch the cervical cancer program, it was feared that an extended closure of the program might endanger its perennity. Therefore, in July 2020, the cervical cancer screening activities were progressively relaunched. Following the preventative hygienic measures during the COVID-19 pandemic, a major advantage of the program is that human papillomavirus (HPV) based screening can be performed by women themselves (HPV self-sampling). As no pelvic examination is needed, the risk of exposure between patients and providers remains low.

EMERGING BARRIERS TO CERVICAL CANCER SCREENING

However, despite major efforts to ensure patient safety, new barriers to cervical cancer screening emerged during the

Figure 2 Teaching about women's health and cervical cancer by midwifes to patients in the parlor. This space is located outside, allowing social distancing between women and everyone interested in assisting and learning about the benefits of the screening program and women's health, and who can then spread the information to others.

Box 1 Global strategy to eliminate cervical cancer 2020–2030

- 90% vaccination coverage of girls
- 70% screening coverage
- 90% access to treatment for precancerous and cancerous lesions

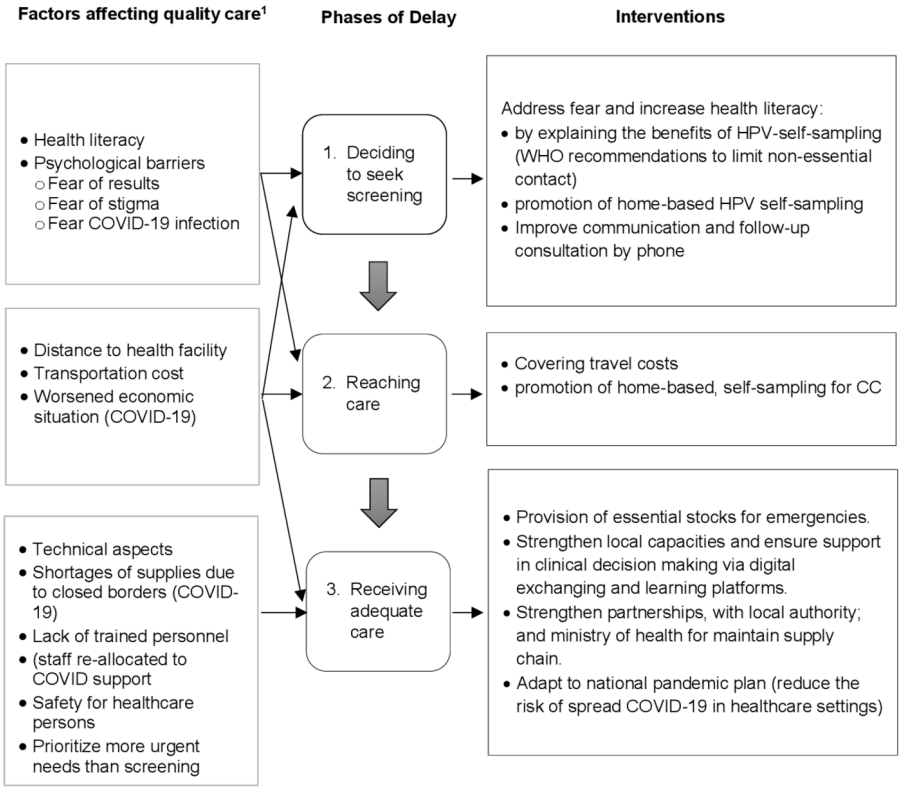

Figure 3 Responses to the three delay model applied to human papillomavirus (HPV) screening (Thaddeus S, Maine D. *Soc Sci Med.* Vol 38. No. 8, pp. 1091-1110, 1994). The decision to seek care, such as screening, is not subject to the same barriers to access to care as it is for follow-up. Follow-up is not impacted by the first delay and is therefore not taken into account in this analysis.

COVID-19 pandemic. The conceptual framework of Thaddeus and Maine's three delay model has been used to describe these barriers and highlight those that newly appeared owing to the COVID-19 pandemic. The model describes factors that delay the process of seeking healthcare according to three critical phases (first delay, family and community factors; second delay, factors related to accessibility; and third delay: services provided at the healthcare facility).

The analysis shows that existing factors affecting women's health seeking behavior remained and new barriers appeared (Figure 3). Importantly, new patient related obstacles emerged, such as less access to health facilities. Also, health system barriers appeared because health services were unavailable owing to closure or stock-outs as supply chains were affected. These findings are in line with recently published studies and highlight the importance of a multisectoral approach to reduce negative effects on women's sexual and reproductive health.

In settings where efficient hygiene measures to avoid COVID-19 transmission can be implemented, cervical cancer screening activities should be maintained and new emerging barriers addressed. For the Dschang cervical cancer program, three important key actions were identified: (1) coverage of transportation costs for women accepting cervical cancer screening at the Dschang District Hospital, (2) improvement of pandemic related health literacy, and (3) introduction of home based HPV self-sampling to reduce the risk of exposure at the hospital or during travel.

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Appendix 5

frontiers in Public Health

ORIGINAL RESEARCH
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Training, Supervision, and Competence Assessment of Cameroonian Health Care Providers Using HPV Self-Sampling, Triage by Visual Inspection, and Treatment by Thermal Ablation in a Single Visit

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Background: Developing human resource capacity and efficient deployment of skilled personnel are essential for cervical cancer screening program implementation in resource-limited countries. Our aim was to provide a context-specific training framework, supervision, and effectiveness evaluation of health care providers in a cervical cancer screening program.

Methods: A 5-year cervical cancer screening program was implemented in Dschang, West Cameroon. Women were invited to perform human papillomavirus self-sampling (Self-HPV), followed by triage using visual inspection with acetic acid (VIA) and thermal ablation if needed. Health care providers were trained in four key learning phases to perform counseling, screening, and treatment process in a single visit. Training included (i) a 3-day basic course, (ii) 3-day advanced practical training, (iii) 2 weeks of supervision, and (iv) bi-monthly supervision by a mentor. The diagnostic performance of health care providers was compared between two time periods, period I (September 2018 to April 2019) and period II (May 2019 to January 2020), for an overall 17-month study period.

Results: Fourteen health care providers were recruited for the training course and 12 of them completed the training objectives. Follow-up and evaluations were conducted for three health care providers working in the screening unit at Dschang District Hospital. During the study period, 1,609 women performed Self-HPV, among which 759 were screened during period I and 850 during period II. HPV positivity was 18.2 and 17.1%, and VIA positivity was 45.7 and 71.0% in period I and II, respectively. VIA sensitivity was 60.0% (95% confidence interval [CI] 26.2–87.8) and 80.8% (95% CI 60.6–93.4) in period I and II, respectively ($p = 0.390$). VIA specificity decreased between period I (57.4, 95% CI 48.1–66.3) and II (30.8, 95% CI 22.6–40.0) ($p < 0.001$). Health care providers

demonstrated substantial agreement with their mentor in their diagnoses during both periods (period I: Cohen's kappa coefficient [k] = 0.73, 95% CI 0.62–0.85, and period II: k = 0.62 0.47–0.76; p = 0.0549).

Discussion: Training, supervision, and a focus on effectiveness in cervical cancer screening are interventions that contribute to improving frontline provider competencies and maintaining a high quality of health care service delivery.

Keywords: cervical cancer screening, resource-limited countries, training, supervision, health care providers, visual inspection with acetic acid, thermal ablation

INTRODUCTION

The burden of cervical cancer remains an important public health concern, especially in low-income countries, where it represents a leading cause of cancer death in women, despite it being a preventable disease (1, 2). In high-income countries, cytology-based programs, vaccination against high-risk human papillomaviruses (HPVs) and more recently, HPV-based screening programs, have led to an important reduction in cervical cancer incidence and mortality (3, 4). In low-income countries, these approaches have been difficult to implement, mainly owing to resource scarcity and for organizational reasons (5, 6).

In response to the problem, the World Health Organization (WHO) has launched a cervical cancer prevention initiative with the aim to eliminate cervical cancer. The WHO has defined a "90-70-90 target," which includes (i) coverage of 90% of girls vaccinated against HPV, (ii) 70% of women screened, and (iii) 90% of women identified with cervical disease receiving treatment (7). To reach the second and third targets, the WHO recommends screening the target population with a high-performance test such as an HPV test, which may be followed by triage and prompt treatment if needed (8, 9). Currently, these procedures are relatively simple, require minimal infrastructure, and can be rapidly scaled-up if they are performed within a well-organized and structured program.

One of the constraints preventing the WHO target being met is the lack of adequately trained and qualified staff and physicians (6). In Cameroon, cervical cancer screening uptake is still very low, with only 4% of women having ever been screened, mostly owing to low awareness in the community and difficulties in accessing screening services within the public health system (6, 10, 11). The WHO has proposed decentralization and "task shifting" from physicians to other health care providers (HCPs) (e.g., midwives or nurses) to scale up cervical cancer prevention in resource-limited settings (6).

One of the first examples of innovative task shifting in the field of cervical cancer prevention was the introduction of HPV self-sampling (Self-HPV), which has been demonstrated to be as accurate as clinician sampling, suggesting that women can effectively replace health care practitioners in this process. A second example is the adoption of screen-and-treat approaches in which the treatment decision is based on a screening test, thereby avoiding colposcopy services and biopsy, which are both important barriers to cervical cancer prevention in low-resource contexts (12, 13). This allows a range of different HCPs such as physicians, nurses, and midwives to perform the screening and treatment procedures. However, to be efficient and impactful, providers should have adequate competencies and quality control of the care delivered is needed; a high level of HCP skills should also be maintained (14, 15). The approach needs to be accompanied by training, mentoring, supervision, and continuous support as well as evaluation of clinical care and patient outcomes (14). Our aim was to implement and evaluate a HCP training and supervision framework to deliver cervical cancer screening in a decentralized geographical area.

MATERIALS AND METHODS

Setting

The screening campaign took place at Dschang District Hospital, West Cameroon between September 5, 2018 and January 10, 2020. This study was embedded in an overall research project called "3T-Approach" (for Test-Triage-and-Treat), which plans to recruit 6,000 women over a 5-year period (2018–2023) (16).

Program for Participants

The program is based on a single-day visit and consists of the following steps: (i) 1 h of community education and counseling on sexual health, HPV infection, cervical cancer prevention, and management in the case of a positive screening result; (ii) Self-HPV analyzed using a point-of-care assay (GeneXpert®); (iii) HPV-negative women are advised to repeat screening in 5 years; HPV-positive women are triaged using visual inspection with application of acetic acid (VIA) and Lugol's iodine (VILI) (hereafter, VIA/VILI assessment is referred to as VIA); naked-eye VIA assessment is followed by systematic digital imaging of the cervix with a smartphone (Samsung Galaxy J5, Seoul, South Korea); (iv) Papanicolaou (PAP) testing, endocervical brushing, and biopsy of VIA-positive areas or random biopsy at 6 o'clock within the transformation zone if VIA is non-pathological are conducted; and (v) treatment is provided with thermal ablation if eligible or referral for additional work-up if not eligible. VIA–positive participants eligible for ablative therapy are treated with a WiSAP thermal coagulator (Wisap® Medical Technology GmbH, Brunnthal/Hofolding, Germany). Follow-up of women treated by thermal ablation or LLETZ is an HPV test at 6 and 12 months followed by

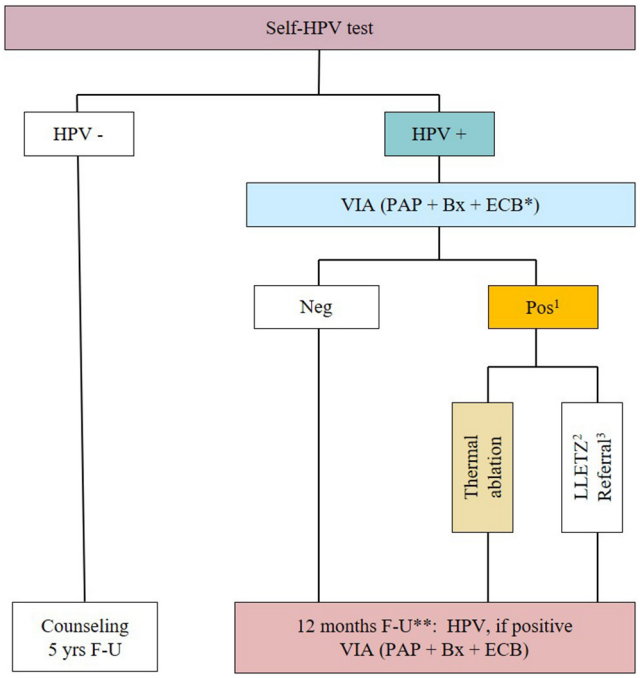

FIGURE 1 | Flowchart of the study. *HPV-positive women will undergo Papanicolaou smear (PAP), cervical biopsy (Bx) and endocervical brushing (ECB); (1) Inspection for eligibility for thermal ablation; (2) If not eligible for thermal ablation; (3) If suspicious for cancer. HPV, Human papillomavirus; Self-HPV, HPV self-sampling; LLETZ, Large loop excision of the transformation zone; VIA, Visual inspection with acetic acid and Lugol's iodine; F-U: follow-up. **Women treated by thermal ablation also had a post-operative consultation at 4 to 6 weeks, and a follow-up at 6 months with Self-HPV, if positive VIA, PAP, Bx, and ECB.

VIA, PAP test, cervical biopsy and ECB (**Figure 1**). VIA assessment of the cervix is done according to the ABCD criteria: (A) an acetowhite area (absent on the native view and visible after acetic acid application); (B) "bleeding on touch"; (C) coloring with VILI, which may aid in confirmation or identification of small acetowhite lesions; (D) diameter >5 mm for acetowhite lesions (about the size of a pencil eraser). The ABCD criteria are positive if ACD or B are present. HCPs are instructed to treat with thermal ablation if the ABCD yield a positive result (17). To avoid endocervical bleeding, endocervical sampling for cytology and endocervical brushing is performed after VIA.

Selection of Trainees

Fourteen HCPs participated in the training sessions. For the study setting, the hospital administration and local authorities participated in selection of the HCPs (nurses and midwives), who agreed that they would remain available to participate in the screening activity for a 5-year period. Nurses and midwives were chosen because they are trusted by women in the community and already have skills in pelvic examination.

FIGURE 2 | Thermal ablation simulation at Dschang district hospital. HCPs become familiar with the equipment and competent at performing thermal ablation through the use of models. Polyvinyl chloride tubes (500 cc water bottle) with a diameter of approximately 5 cm were used to simulate the vaginal canal and potatoes with a diameter of 2–3 cm were used to simulate the cervix. The probe can be placed through the simulated vagina and applied to the simulated cervix. This type of model is widely accessible and useful in achieving clinical competence before performing the procedure on a patient.

Three-Day On-Site Training, Basic Course

Three days were dedicated to learning and training on cancer in general, the cause and risk factors of cervical cancer from HPV disease to the development of cancer, prevention, symptoms of cervical cancer, early detection, treatment of precancerous lesions, and treatment of cancer. After the first session, participants were assessed using a multiple-choice question test covering the content of the 3-day basic course (**Table 1**).

Three-Day On-Site Training, Advanced Course

The second 3-day session was conducted 2 months later and consisted of a refresher in theoretical knowledge and advanced practical training. The trainees conducted simulated gynecologic examinations using a plastic pelvis and learned how to clean the cervix, understand the mechanics and subtleties of cervical photography, and they conducted a simulated thermal ablation procedure using potatoes. The second session was assessed via scenario-based role playing in which participants carried out simulated consultations. Various themes were covered, such as welcoming patients for their screening, counseling, explanation of the screening process, conducting VIA, description of a VIA-positive image, and informing of a precancerous lesion and recommended care (**Table 1** and **Figure 2**).

Two-Week On-Site Supervision

The third part of our training framework took place 2 months later when the screening campaign started and consisted of clinical practice. Didactic training was considered too brief to result in sustained changes in clinical practice; therefore, each

TABLE 1 | Components of frontline provider training using the 3T-approach.

Length	Learning objectives	Themes	Teaching strategy	Evaluation
3 days	Understand development of cervical precancerous and cancerous lesions Be capable of conducting a relevant medical interview Be capable of informing patients before VIA Be capable of obtaining informed consent Be capable of informing patients after VIA Be capable of referring to a specialist	CC prevention: vaccination, screening tests, target population Anatomy of a normal cervix and physiological changes in the cervix during a woman's life Pathogenesis of CC from HPV infection to cancer Screening tests: PAP, VIA, HPV test indications and procedures TA indication, procedure, and side effects Interview with patients: do's and don'ts, informed consent Infection prevention: medical equipment, waste management, hand washing Quality control and key performance indicators	On-site course Role-playing	MCQ test
3 days	Be capable of performing a pelvic exam Be capable of obtaining samples for HPV testing and cervical cytology Adopt good practices in infection prevention Be capable of identifying the transformation zone, of examining the vagina and the cervix with acetic acid and Lugol's iodine, and choosing the site of biopsy Be capable of describing and reporting a cervical exam	VIA: application of acetic acid and Lugol's iodine, smartphone image acquisition, interpretation of normal and pathologic changes Patient information: key points about cervical cancer and plain-language explanation of information How to perform an HPV test, PAP test, biopsy, endocervical brushing, and TA GeneXpert® training and HPV test interpretation Hand washing and device sterilization	On-site course Training using mannequin for pelvic exam and smartphone image acquisition Training for TA	Role play
First 2 weeks of campaign	Observe 5 health education sessions, 10 VIA, 3 TA Perform 5 supervised health education sessions, 10 VIA, 3 TA	3T-Approach	Clinical practice under supervision	On-site feedback
Continuing mentorship	Autonomous practice of educational sessions, patient registration, HPV test, VIA, and TA	3T-Approach	On-site supervisor on request Bimonthly smartphone photo review with a mentor	On-site feedback

VIA, visual inspection with acetic acid; CC, cervical cancer; HPV, human papillomavirus; TA, thermal ablation; 3T-Approach–Test, Triage, and Treat; PAP, Papanicolaou smear; MCQ, multiple-choice question.

provider first observed five patient educational sessions, 10 VIA, and three thermal ablations before supervising a minimum of five patient educational sessions, 10 VIA, and three thermal ablations with simultaneous feedback. A mentor observed HCPs' clinical skills and assessed competencies in counseling, pelvic examination and VIA procedures, smartphone image acquisition, sampling, thermal ablation, follow-up processes, and the quality of data collection.

Activity Monitoring

A personal logbook for each HCP was used as a tool for monitoring midwifery practice. The first part of the logbook included a list of required competencies (general knowledge, clinical skills, administrative and communication skills) and the date on which the skill was acquired. In the second part of the logbook, HCPs recorded their first 100 cervical examinations performed along with the results of VIA; whether a PAP test, biopsy, and ECB was performed; whether the examination was done under supervision or autonomously; and their self-assessment of the full procedure. The last logbook was completed on January 10, 2020. Moreover, providers had to document findings on the appropriate data management forms in the health facility files as well as a case report form.

Bimonthly Mentorship Session

Digital images (native, VIA, and VILI) were reviewed, and the HCP's diagnosis at the time of screening was discussed by the whole team and supervised by a Cameroonian gynecologist trained and experienced in VIA. During the sessions, for each HPV positive case, the digital images were uploaded to a computer. The mentor asked the HCPs to discuss why each case was considered either positive or negative. The mentor then gave their diagnosis based on the digital images. The mentor diagnoses were recorded as well as cases where photos of the cervix were not interpretable. When the mentor thought that a positive case was missed by the HCP, he used his clinical judgment to decide whether to wait for the pathology results or to recall the patient for treatment without waiting for the pathology results.

Statistical Analysis

Cases included in the analyses were the first 100 HPV-positive cases screened by HCPs during the period under study. Two time periods were compared, period I (September 2018 to April 2019) and period II (May 2019 to January 2020) for an overall study period of 17 months. Analyses were performed using Stata Statistical Software: Release 16 (StataCorp LLC, College Station, TX, USA). Categorical variables were analyzed with

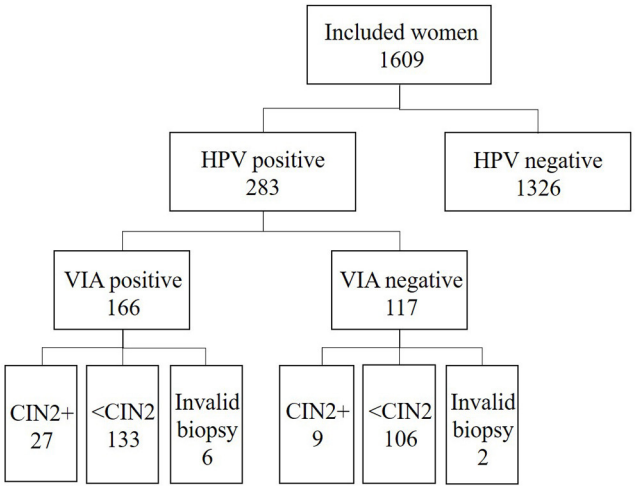

FIGURE 3 | Flowchart of the included population and screening results. HPV, human papillomavirus; VIA, visual inspection with acetic acid; CIN, cervical intraepithelial neoplasia.

Pearson's x^2 or Fisher's test, as appropriate. p-values < 0.05 were considered significant. The sensitivity and specificity of VIA were calculated using the histologic result as reference standard, and p-values for sensitivity and specificity were estimated using the Z-test. The proportion of disagreement (undertreatment and overtreatment) between HCPs and mentor, using the digital VIA (DVIA) diagnosis of the mentor as a reference standard, was compared between period I and II, and p-values were calculated using the Z-test. Cohen's kappa coefficient (k) was used to measure interobserver reliability in VIA/DVIA assessment. The overtreatment rate was assessed using mentor diagnosis as the reference standard in order to replicate a real-life "screen-and-treat" approach without the availability of histological results.

RESULTS

Health Care Providers

A total of 14 HCPs were recruited for the training course; 12 of them fulfilled the training objectives (**Table 1**), which were attendance to at least 80% of the training course and passing the theoretical and practical exams. HCPs participating in the training program were mainly nurses, midwives, and auxiliary nurses, as well as physicians and a laboratory assistant. The median age of participating HCPs was 38.3 years (interquartile range [IQR] 27–46 and the median average work experience was 9 years (IQR 4–16) (data missing for one HCP). Three HCPs with a background in midwifery were retained for the 5-year screening campaign using the 3T-Approach (Test-Triage-Treat) at Dschang District Hospital.

Monitoring Activities

A total of 1,609 women were screened during the study period and the results of 300 consecutive patients with a positive HPV test result (100 patients per HCP) were selected for analysis. After exclusion of non-interpretable cases by VIA (distorted cervix or visual obstruction of the cervix [e.g., large Nabothian cysts, bleeding, or mucus], 283 cases were considered for evaluation. Overall, each HCP performed a similar number of VIA procedures. Small differences in recruitment were owing to holidays, pregnancy in one HCP, and other logistical constraints (**Table 2** and **Figure 3**). No differences in sociodemographic characteristics of the patients examined by the HCPs were noted. We observed an increase of 25.3% in the VIA positivity rate for all HCPs combined between period I and II (45.7, 95% CI 37.2–54.3 vs. 71.0, 95% CI 62.8–78.1, p-value < 0.001) (**Table 3**). During the second period under study, we had a higher VIA positivity

TABLE 2 | Sociodemographic characteristics of HPV-positive participants seen by HCPs.

Variable	HCP 1	HCP 2	HCP 3	*p*-value
Positive HPV test	93	95	95	
Age (y), mean±SD	38.8 (±6.2)	40.3 (±5.8)	39.3 (±6.5)	0.216
• Marital status				0.516
Married/in relationship	70 (75.3%)	74 (77.9%)	78 (82.1%)	
Single/divorced/widowed	23 (24.7%)	21 (22.1%)	17 (17.9%)	
Age at menarche (y), mean ± SD	14.8 (±2.0)	14.5 (±1.9)	14.8 (±1.7)	0.409
Age at first intercourse (y), mean ± SD	18.0 (±2.9)	18.2 (±2.7)	17.6 (±2.5)	0.318
Number of sexual partners, mean ± SD	4.3 (±3.1)	3.8 (±2.9)	4.4 (±3.9)	0.316
• Gravidity				0.626*
Nulligravida	3 (3.2%)	1 (1.1%)	1 (1.1%)	
1–5	48 (51.6%)	42 (44.7%)	48 (51.1%)	
>5	42 (45.2%)	51 (54.3%)	45 (47.9%)	
Age at first delivery (y), mean ± SD	21.2 (±5.9)	21.5 (±4.2)	20.3 (±5.7)	0.208
• Parity				0.866*
Nulliparous	4 (4.3%)	3 (3.2%)	5 (5.3 %)	
1–5	68 (73.1%)	66 (69.5%)	64 (67.4%)	
>5	21 (22.6%)	26 (27.4%)	26 (27.4%)	
• VIA/DVIA				0.914
Positive**	53 (57.0%)	56 (58.9%)	57 (60.0%)	
Negative	40 (43.0%)	39 (41.1%)	38 (40.0%)	
• Cytology				0.736
ASC-H, HSIL, AGC, cancer	10 (10.8%)	9 (9.5%)	7 (7.4%)	
NILM, borderline, LSIL	77 (82.8%)	82 (86.3%)	85 (89.5%)	
Invalid	6 (6.5%)	4 (4.2%)	3 (3.2%)	
• Histology				0.769
CIN2+	12 (12.9%)	12 (12.6%)	12 (12.6%)	
<CIN2	78 (83.9%)	82 (86.3%)	79 (83.2%)	
Invalid	3 (3.2%)	1 (1.1%)	4 (4.2%)	

HCP, health care provider; CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus; HSIL, high squamous intraepithelial lesion; LSIL, low squamous intraepithelial lesion; VIA, visual inspection with acetic acid; DVIA, digital visual inspection with acetic acid; SD, standard deviation; ASC-H, atypical squamous cell evocating high grade lesion; AGC, atypical glandular cells; NILM, negative for intraepithelial lesion or malignancy.

**p-value estimated using Fisher's exact test.*

***Cases with initial suspicion of cancer are included (n = 3).*

TABLE 3 | VIA sensitivity and specificity in screening to detect CIN2+ performed by HCPs.

	Period I (September 2018 to April 2019)				Period II (May 2019 to January 2020)				
	HCP 1	HCP 2	HCP 3	**Overall**	HCP 1	HCP 2	HCP 3	**Overall**	p-value**
HPV positive (*n*)*	44	48	40	**132**	46	46	51	**143**	
CIN2+ (*n*)	3	4	3	**10**	9	8	9	**26**	
VIA/DVIA positivity rate *** (95% CI)	44.7% (30.5–59.8)	43.8% (29.8–58.7)	48.8% (33.6–64.3)	**45.7% (37.2–54.3)**	69.6% (54.1–81.8)	74.5% (59.4–85.6)	69.2% (54.7–80.9)	**71.0% (62.8–78.1)**	**<0.001**
VIA/DVIA sensitivity (95% CI)	33.3% (0.8–90.6)	75.0% (19.4–99.4)	66.7% (9.4–99.2)	**60.0% (26.2–87.8)**	77.8% (40.0–97.2)	100.0% (63.1–100)	66.7% (29.9–92.5)	**80.8% (60.6–93.4)**	**0.390**
VIA/DVIA specificity (95% CI)	56.1% (39.7–71.5)	59.1% (43.2–73.7)	56.8% (39.5–72.9)	**57.4% (48.1–66.3)**	32.4% (18.0–49.8)	31.6% (17.5–48.7)	28.6% (15.7–44.6)	**30.8% (22.6–40.0)**	**<0.001**

HPV, human papillomavirus; VIA, visual inspection with acetic acid; CIN, cervical intraepithelial neoplasia; HCP, health care provider; DVIA, digital visual Inspection with acetic acid; CI, confidence interval.

**With valid biopsy results (n = 275).*

***p-value for overall sensitivity and specificity between periods I and II.*

****Including all 283 patients.*

Bold values indicate overall results (compared to the individual results of the HCPs) which are used to calculate the p-value.

rate (71.0%) than the expected range between 45 and 55% (18). A larger recruitment of patients is needed to assess more precisely the VIA positivity rate. Eight patients had invalid histological results and were excluded in the calculation of sensitivity and specificity. Overall, VIA sensitivity was 60.0% (95% CI 26.2–87.8) in period I and increased to 80.8% (95 CI 60.6–93.4) in period II, but the difference did not reach statistical significance (p = 0.390). VIA specificity decreased between period I (57.4, 95% CI 48.1–66.3) and period II (30.8, 95% CI 22.6–40.0) (p-value < 0.001). Three patients were referred for suspected cervical cancer, among which one was a false positive result, one had cervical intraepithelial neoplasia grade 3, and one was confirmed as having invasive adenocarcinoma on final histological analysis. Two invasive cervical cancers were missed by the screening team upon visual assessment. One was an adenocarcinoma which was essentially endocervical and the other was an early stage, poorly differentiated carcinoma, which was interpreted as negative by the provider, although retrospective analysis of this case based on digital picture assessment has the criteria for a positive VIA. These two cases were used for continuing training of the HCP.

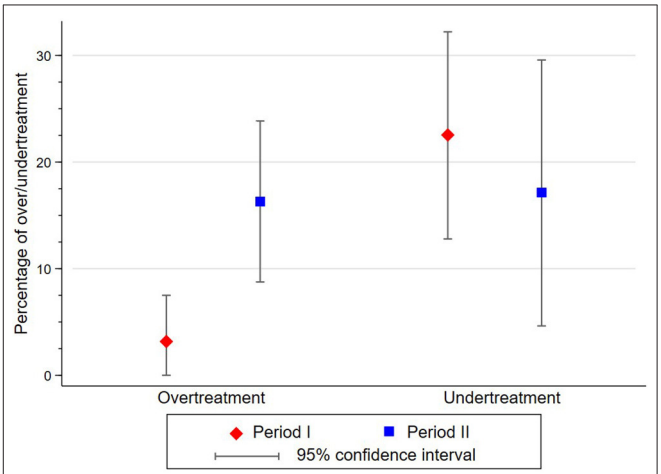

FIGURE 4 | Difference in percentage of cases undertreated and overtreated by HCPs according to mentor diagnosis between period I and period II.

Supervision

Smartphone images were reviewed on a bimonthly basis. Among 283 cases photographed, 267 (94.3%) were discussed (135 in period I and 132 in period II), of which 6 (2.2%) cervical images were considered uninterpretable. Mentor review was not conducted in 16 (5.7%) cases. During period I, the HCP and the mentor agreed in 61 positive and 55 negative cases. During period II, the provider and mentor agreed in 77 positive and 29 negative cases. The proportion of agreement between HCP and mentor was 85.09% during period I and 80.3% during period II (**Table 4**). Cohen's kappa coefficient between HCPs and mentor over period I (k = 0.73, 95% CI 0.62–0-85) and period II (k = 0.62, 95% CI 0.47–0.76) (p = 0.0549) demonstrated substantial agreement. During period I, compared with the mentor diagnosis, treatment was missed by the HCP in 16 patients (22.5% of all patients diagnosed as negative by the HCP; 95% CI 12.8–32.2), and two patients underwent unnecessary thermal ablation (3.2% of all patients diagnosed as positive by the HCP; 95% CI 0.0–7.5). During period II, compared with the mentor diagnosis, treatment was missed by the HCP in six patients (17.1% of all patients diagnosed as negative by the HCP; 95% CI 4.6–29.6; p = 0.697 between period I and II), and 15 patients underwent unnecessary thermal ablation (16.3% of all patients diagnosed as positive by the HCP; 95% CI 8.8–23.9; p = 0.021 between period I and II) (**Figure 4**).

Patients Returning for Treatment

During period I, 15 participants (10.9% of HPV-positive participants) returned for treatment, nine upon request of the mentor and 6 after obtaining pathology results. During period II, 11 women (7.6% of 145 HPV-positive participants) returned for treatment, five on mentor supervision and six based on the pathology results.

TABLE 4 | Interobserver agreement on DVIA evaluation between HCPs and mentor.

	Period I ($n = 135$**; Months 0–8)	Period II ($n = 132$**; Months 9–17)	p-value
DVIA diagnosed by mentor			
Positive	77	83	
Negative	57	44	
Non-interpretable	1	5	
Agreement on positive cases*	61	77	
Agreement on negative cases	55	29	
Cohen's kappa (95% CI)	0.73 (CI 0.62–0.85)	0.62 (0.47–0.76)	0.0549

Cases of initial suspicion of cancer are included (n = 3).
***Cases with missing mentor diagnosis not included.*
HCP, health care provider; CI, confidence interval; DVIA, digital visual inspection with acetic acid.

DISCUSSION

Implementation of cervical cancer screening programs requires development of an effective training method focused on screening and treatment as well as thorough and accurate documentation of procedures using standardized terminology and data collection forms (19). Useful guidance, manuals, and training material for cervical cancer screening program implementation have been published by different agencies, including the Alliance for Cervical Cancer Prevention, International Agency for Research on Cancer, Johns Hopkins Program for International Education in Gynecology and Obstetrics, Pan American Health Organization, Program for Appropriate Technology in Health, and the Union for International Cancer Control. These represent important contributions to informing of evidence-based interventions within low-resource contexts (15). Our training framework was based on recommendations of the above agencies, with an approach based on four key learning steps (i) a 3-day basic course, (ii) a 3-day advanced practical training, (iii) 2-week supervision, and (iv) bimonthly supervision by a mentor. Our aim was to provide insight into how a cervical cancer screening program can function at the local level and how the quality of screening services can be sustained over time.

Our findings showed that with a structured and comprehensive training and supervision framework, HCPs could reach good levels of diagnostic performance based on HPV primary screening followed by VIA assessment, with substantial agreement between provider and mentor, which could be maintained over a 17-month period. Indeed, we observed a trend in favor of increased VIA sensitivity during the second study period, from 60.0 to 80.8% ($p = 0.390$) which did not reach significance, probably because of the small sample size. In contrast, a decrease in specificity and a small decrease in the agreement between HCP and mentor between the two periods were observed. The low specificity was expected in VIA assessment and use of the ABCD criteria in which any whitening after acetic acid application larger than 5 mm is considered positive. HCPs were instructed to consider such cases to be a positive screening result so as to minimize false negative results. In light of the high risk of loss to follow-up and considering the low risk of adverse events associated with thermal ablation, we consider the present approach to be an acceptable strategy for effective control of cervical cancer in this setting.

Over our study period, few patients (1%) were referred for suspicion of cervical cancer. This issue is particularly important in a low-resource setting where referral services are not readily available and the decision to refer is associated with additional exams and consequences for both the women and the health care system.

Within the first 2 weeks, a mentor was on-site to help providers consolidate and gain confidence in the skills obtained during training, after which regular training to maintain quality of care was put in place through a systematic bi-monthly review of cervical pictures with a multidisciplinary board. The success of our mentorship framework is largely based on the use of smartphone photography of the cervix during pelvic examination (20). DVIA has many advantages. First, cervical examination can be discussed immediately in the field with other HCPs, thus providing peer-to-peer learning opportunities, or images can be sent to an expert for real-time advice. Second, images taken during the cervical examination can be reviewed at a later time with colleagues and experts for continuous training, supervision, and quality control. Finally, if a treatment is missed, the patient can be recalled when advised by a specialist without waiting for pathology results.

It is generally difficult to achieve and maintain a well-trained cadre of providers who can consistently perform high-quality care in low-resource settings (21). In this context, supportive supervision can permit identification of gaps to quickly address any issues. To ensure a sustainable approach in a screening program, a quality-assurance system should be in place that is well-integrated among frontline providers and stakeholders, thereby allowing follow-up of the program and diagnostic performance over time (22). To date, there is a paucity of evidence regarding quality assurance and monitoring related to implementation of screening programs in low-income contexts (22). High-quality data, monitoring of these data, as well as documentation of patient-level indicators on a regular basis should be incorporated into on-site practices.

Task shifting to non-physician providers has been implemented and accepted in HIV care delivery to improve access to care and meet the demand for initiating antiretroviral therapy in more patients while maintaining high-quality services (23, 24). This promotes sustainability because non-physician providers are more likely to continue providing services than physicians, who frequently receive new assignments to other health facilities (25). Globally, there is a shortage of 1.1 million sexual, reproductive, maternal, newborn, and adolescent health (SRMNAH) professionals. Trained midwives alone could cover 90% of SRMNAH needs, but they currently only represent 10% of professionals in this field. Through our program, we can contribute to the WHO recommendation to "invest in high-quality education and training of midwives" and in "midwife-led improvements to SRMNAH service delivery" (26).

However, this change needs to be accompanied by regulatory frameworks, supportive supervision, and monitoring (27).

Weaknesses of our study include the limited number of health care workers in the single setting assessed within our training framework, which may not be generalizable to other contexts. Another weakness is that women screened positive for HPV but with a negative VIA (normal-appearing cervix) have a single cervical biopsy at the transitional zone and endocervical brushing. Compared to random 4-quadrant biopsies, our approach may have possibly underestimated the true number of CIN2+.

Strengths of this study are the high quality of data collection as part of routine care and the training model based on histology as a reference standard for HPV-positive cases, enabling the objective measurement of diagnostic performance. Another strength is that the training program was based on recommendations of internationally recognized agencies for cervical cancer screening. The recent international focus on cervical cancer prevention may contribute to raising awareness about cervical cancer as well as increasing the demand for cervical cancer screening and treatment. Therefore, it is important to ensure that adequate training is provided so as to implement strategies that have a positive impact on health care systems and patient outcomes.

In conclusion, our study findings showed that non-physician HCPs can operate a cervical cancer screening program with appropriate training, supervision, and mentorship. Monitoring of clinical activity and patient outcomes are paramount to ensuring the sustainability of screening programs in low-resource settings.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Cantonal Ethics Committee of Geneva, Switzerland (Commission Cantonale d'Ethique de la Recherche, CCER, N°2017-01110) and the Cameroonian National Ethics Committee for Human Health Research (N°2018/07/1083/CE/CNERSH/SP). It was registered on November 28, 2018 at ClinicalTrials.gov with identifier NCT03757299. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

CF, JS, PV, and PP contributed to the conception and design of the study. CF, BK, JS, JF, ET, and PV did the training and mentorship of the health care providers. TM wrote the logbook. CF organized the database and wrote the first draft of the manuscript. CF, JS, and AW performed the statistical analysis. CF, JS, AW and PP wrote sections of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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Acceptability and safety of thermal ablation to prevent cervical cancer in sub-Saharan Africa

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Abstract

Background: The World Health Organization recommends thermal ablation as an alternative to cryotherapy to treat women with precancerous lesions in low-resource settings. However, limited data are available on women's experience and adverse events (AEs) of the procedure in the context of Sub-Saharan Africa. The objective of this study was to evaluate the acceptability and safety of thermal ablation in women screened positive for precancerous cervical lesions.

Methods: Asymptomatic women aged 30–49 years old living in the Dschang Health District were invited to participate in a cervical cancer screening campaign termed "3 T-Approach" (for Test-Triage and Treat). Recruited women were asked to perform HPV self-sampling followed by triage with visual assessment and treatment with thermal ablation if required. After treatment and 4–6 weeks later, interviews were conducted to assess women's experience on anxiety, discomfort, and pain during thermal ablation. AEs were recorded on pre-defined electronic forms 4–6 weeks after treatment to assess the procedure's safety.

Results: Between September 2018 and December 2020, 399 HPV-positive women (18.7% of women screened) were recruited, 236 (59.1%) had a positive visual assessment, 234 were treated by thermal ablation and 198 (84.6%) received therapy in the same visit. Treatment was not considered as painful (score $\leq$ 4/10) by 209 (90.9%) patients while 5 (2.5%) reported high pain (score 8–10/10). During post-treatment interviews 4–6 weeks later, most reported AEs were graded mild or moderate (grade I-II). The most frequent symptoms reported as mild AEs (grade 1–2) were vaginal watery discharge (75.5%), vaginal bloody-stained discharge (21.5%) and malodourous discharge (14.5%). None of the participants experienced serious AEs (grade 3–4) or AEs requiring admission to hospital or emergency consultation. The vast majority of women (99.6%) would agree to repeat the procedure if necessary and (99.6%) would recommend it to friends or family.

Conclusion: Thermal ablation is widely accepted by women and appears as a safe procedure. It may contribute to improving the link between screening and treatment in a single visit and to optimizing cervical cancer control in low-resource settings.

Trial registration: The study was registered on clinicaltrials.gov (NCT03757299) in November 2018 (28/11/2018).

Keywords: Cervical cancer screening, Thermal ablation, Adverse events, Sub-Saharan Africa

Background

Cervical cancer affects over half a million women worldwide every year and is responsible for more than 300′000 deaths per year, although it is a largely preventable disease through screening and treatment of

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precancerous lesions [1]. Cervical cancer disproportionately affects women living in low- and middle-income countries (LMICs), where nearly 90% of new cases are diagnosed [1]. However, lack of infrastructure for satisfactory implementation of vaccination and screening programs, barriers to effective treatments and lack of financial resources are key reasons of the low success of cervical cancer prevention programs in LMICs [2].

To address this gap, the World Health Organization (WHO) emphasized the importance of acting immediately to fight cervical cancer in LMICs through a comprehensive approach including three targets which should be reached by 2030: (i) vaccination of 90% of girls aged 9–14 years, (ii) screening of 70% of women with a high-performance test, and (iii) 90% of women identified with a precancerous or cancerous lesion receiving appropriate treatment and care [3].

Recent development of human papillomavirus (HPV) point-of-care assays suggests that screening women in a single visit with a high-performance test is feasible in LMIC contexts and may contribute to achieving the second target of the WHO global strategy [2]. However, to achieve the third WHO target and have an impact on the burden of disease, women screened positive for cervical precancer need to receive an effective treatment. Further, immediate treatment at the point of care is optimal in order to avoid loss to follow-up, which is of high concern in the Sub-Saharan context.

The WHO has recommended cryotherapy for the treatment of precancerous lesions, and more recently, has issued recommendation regarding the use of thermal ablation (TA) as an alternative to cryotherapy [4]. TA has been used for several decades in the United Kingdom and, in past years, has expanded to many low-resource settings where it seems to be well accepted by health care providers and patients alike [5–8]. While these results are reassuring, generalization to other sub-Saharan populations and regions should not be assumed, due to possible social and cultural differences between various settings, such as the average educational level and the population's relationship with the health system, which may have a strong impact on the acceptability of a medical procedure such as TA.

This innovation overcomes many obstacles of cryotherapy (i.e. reduced running cost and logistical dependency on gas supply) for the treatment of women having a positive screening test [7]. In a previous cohort study conducted in 2015 including more than 1000 participants, we reported that most patients (91%) having a positive screening test were eligible for TA with a treatment success rate at 12 months of more than 70% [9, 10]. TA offers the opportunity to women living in LMICs and having a positive screening test to be treated in a single visit approach [11].

The equipment is small, portable, durable, self-sterilizing and easy to use [5, 6]. While reports about the use of TA in LMICs seems to be encouraging, there is still limited data about the quantification of pain, acceptability of the procedure and rigorous monitoring of adverse event (AEs). The aim of this study was to determine the acceptability of TA by Cameroonian women in a screen-and-treat approach and its safety profile.

Methods

Setting and study design

This study is nested in a larger cervical cancer screening program launched in the Dschang Health District, West Cameroon, as part of a five-year program (2018–2023). The program, termed "3 T-Approach" (for same-day test-triage and treat) combines counselling, primary HPV-based screening, visual triage and treatment of positively triaged women in a single visit. The study protocol has been described previously [12]. Briefly, after being informed about HPV infection and cervical cancer prevention, participants were invited to perform HPV self-sampling (FLOQSwabs®) using a cotton swab which was analyzed by a point-of-care HPV assay (GeneXpert®), followed by triage with visual inspection with acetic acid and Lugol's iodine (VIA/VILI) and TA if VIA/VILI was positive. For quality control, cytology, cervical biopsies and endocervical curettage were performed for all women having a positive HPV test. Women having no lesion on visual assessment had a random biopsy at 6 o'clock at the transitional zone, while biopsies of suspected lesions were sampled when present. Sociodemographic and medical information were registered on paper case report forms and later transcribed in an online electronic database (SecuTrial®).

Visual assessment

VIA and VILI were assessed by naked eye followed by digital imaging (native, after VIA and VILI application) captured with a smartphone (Samsung S5®) [13]. In order to optimize VIA/VILI interpretation, we used "ABCD criteria" considering as positive any cervical whitening after application of acetic acid as well as presence of spontaneous cervical bleeding; decision to treat was based on VIA/VILI assessment [14].

Thermal ablation (TA)

Treatment was performed using a probe (WISAP; Medical Technology GmbH, Brunnthal/Hofolding, Germany) which was heated at 100° Celsius and applied on the cervix for 60 seconds after Lugol's iodine application to delimitate the transitional zone. If necessary, the

application was repeated two or more times in order to cover the entire abnormal area and transformation zone [13]. No local anesthesia was used. Women having a suspicion of cancer or lesion extending into the cervical canal which could not be covered by the probe were excluded, but treated using appropriate methods. Women were advised post-treatment to report any side effects such as abdominal pain and cramps, fever, bleeding, or vaginal discharge at the follow-up visit (4–6 weeks after treatment).

Acceptability

Women were interviewed at the same visit after receiving treatment and 4–6 weeks later, to assess acceptability of the procedure. Respondents were invited to rate answers on a Likert scale of 1 (no acceptability) to 4 (high acceptability) [15]. Self-assessed pain was scored according to the Wong–Baker FACES® scale [16]. This validated scale consists of six different faces with a spectrum of pain intensity from 0 (no pain) to 10 (worst pain). We then formed two subgroups: normal pain (score ≤ 4), and mild pain (score > 4). An overall acceptability score based on participants' answers using five items (anxiety, discomfort, pain, quality of information received and overall satisfaction of treatment) and attributing the same weight to each item between 0 and 10 points (maximum global acceptability of treatment) was calculated [17].

Safety

Presence of adverse events (AEs) related to the treatment during the 30 days (4–6 weeks) after the procedure was recorded on pre-defined electronic forms. AEs were recorded and graded according to the Division of AIDS (DAIDS) Table grading the Severity of Adult Adverse Events version 2.1 [18] and the addendum 1 for the table grading female genital symptoms [18]. AEs not reported in DAIDS tables were reported as follows: Grade 1 – mild, discomfort noticed but no disruption of normal daily activity; Grade 2 – moderate – discomfort sufficient to reduce or affect daily activity; Grade 3 – severe, inability to work or perform normal daily activity; Grade 4 - life threatening, representing an immediate threat to life; and Grade 5 – death. AE severity of grade 3 and higher were considered as serious adverse events (SAEs) [17]. Healthcare providers were also questioned about their perceptions of patients' comfort.

Statistical analyses

Quantitative variables were expressed as means and standard deviations, and qualitative variables were expressed as percentages, unless otherwise stated. Descriptive analyses were carried out to compare women by their socio-demographic characteristics, reproductive

Table 1 Socio-demographic characteristics of participants (HPV-positive women, aged between 30 and 49 years old, treated with thermal ablation)

Variable	Number	Percent
Participants	234	100
Age, y mean ± SD	39.2 (± 6.2)	
Marital status		
Single/divorced/widow	46	19.7
Married/in a relationship	188	80.3
Education ($n = 233$)		
Unschooled/Primary education	73	31.3
Secondary education/University	160	68.7
Employment status		
Housewife	43	18.4
Employee/Independent/Farmer	179	76.5
Other (unemployed, student)	12	5.1
Age at menarche, y mean ± SD	14.7 (± 1.9)	
Number of sexual partners, median (IQR)	3 (2–5)	
1–5	202	86.3
> 5	32	13.7
Age at first intercourse, y mean ± SD	18.1 (± 2.7)	
≤18	152	65
>18	82	35
Gravidity		
Nulligravida	1	0.4
1–5	120	51.3
> 5	113	48.3
Age at first delivery, y mean ± SD	21.2 (± 4.5)	
Parity		
Nulliparous	4	1.7
1–5	159	68.0
>5	71	30.3
Having intercourse in the last 12 months		
Yes	219	93.6
No	15	6.4
Desire for future pregnancy ($n = 232$)		
Yes	103	44.4
No	129	56.6
HIV-positive ($n = 228$)		
Yes	16	7
No	212	93
Smoker		
Yes	7	3
No	227	97
HPV-Positive		
Yes	399	18.7
No	1731	81.3

Abbreviations: *N* number, *SD* standard deviation, *y* years, *HPV* human papillomavirus, *LEEP* loop electrosurgical excision procedure, *G* gravidity, *P* parity

and sexual history, disease status and other aspects. In addition, we used univariate and multivariate logistic regressions to identify socio-demographic factors associated with high scores of reported anxiety, discomfort, pain and overall acceptability. We used a two-sided level of significance of 0.05. Data were analyzed using the Stata Statistical Soft-ware Release 16 (StataCorp LP, College Station, TX, USA).

Results

Population and sociodemographic characteristics

Overall, 2130 women were enrolled in the "3 T-Approach" program between September 2018 and December 2020 and constitute the cohort of the present study. Among them, 399 (18.7%) were HPV-positive, and 234 (58.6%) were VIA/VILI positive and considered for TA (Table 1). Among VIA/VILI positive women, 198 (84.6%) were treated during the same day. Main reasons for treatment delay were the need for a second opinion ($n=19$), technical problems ($n=6$) and other reasons (menstruation, presence of cervical cysts, inability to reach the cervix). Mean age of participants was 39.2 (SD ± 6.2) years old, most of them were married or in a relationship (80.3%), and a majority completed secondary or tertiary education (68.7%). The mean age at first intercourse was 18.1 (± 2.7) years old and the median number of sexual partners was of 3 (IQR 2–5). Almost one third (30.3%) of participants had more than 5 pregnancies; and almost half (44.4%) had a desire for future pregnancy.

Acceptability

Immediately post-treatment, among the 234 women treated by TA, only 30 of them (12.8%) reported to have moderate to high anxiety and 6 of them (2.6%) felt moderate to high discomfort. Most of them (90.8%) expressed low pain scores (≤ 4) according to Wong-Baker faces, although 5 women reported a pain score of 8–10/10. The majority of women felt enough informed (97.3%), and 99.1% felt that the procedure was performed as expected or better than expected and would agree to repeat the treatment if necessary. The mean treatment's satisfaction score was 9.9/10 (SD ± 0.8), and the Global acceptability median score was 9.1/10 (IQR 8.5–9.6) (Table 2).

Acceptability 4–6 weeks post-treatment showed a mean treatment acceptability score of 9.9/10 (SD ± 0.4) ($n=198$), and a mean treatment satisfaction of 10/10 (SD ± 0.3) ($n=195$). Ninety-nine percent ($n=193$) of participants said they would recommend the treatment.

Table 2 Acceptability at T0 (screening day)

Variable	Number	Percent
Treatment's satisfaction[b] (n = 232) (mean ± SD)	9.9 (± 0.8)	
Patient felt enough informed ($n=233$)		
Yes	227	97.4
No	6	2.6
Anxiety ($n=231$)		
No	201	87
Yes	30	13
Pain rating scale[a] ($n=230$) (mean ± SD)	2 (± 2)	
≤ 4	209	90.9
> 4	21	9.1
Procedure performed as expected by the patient ($n=231$)		
Yes	229	99.1
No	2	0.9
Sufficiently informed about side effect of treatment (n = 231)		
Yes	225	97.3
No	6	2.7
Would agree to repeat treatment if necessary ($n=229$)		
Yes	228	99.6
No	1	0.4
Would recommend screening to friends and family (n = 230)		
Yes	229	99.6
No	1	0.4
Global acceptability score[c] (median, IQR)	9.1 (8.5–9.6)	

[a] Pain rating scale according to Wong–Baker Faces (pain felt during the treatment, not during the biopsy) [b] Satisfaction scale 0 = not satisfied at all. 10 = very satisfied
[c] Combined Anxiety, Discomfort, Pain, information received, overall satisfaction of treatment

Table 3 Safety Analysis after treatment at T0 (screening day)

Side effects	Number	Percent
Severity of bleeding [a] (*n* = 234)		
Grade 0	233	99.5
Grade 1	1	0.5
Grade 2–4	0	0
Severity of faintness (n = 233)		
Grade 0	225	96.5
Grade 1	7	3
Grade 2	1	0.5
Grade 3-4	0	0
Severity of hot flush (n = 234)		
Grade 0	230	98.5
Grade 1	4	1.5
Grade 2–4	0	0
Severity of nausea [a] (n = 234)		
Grade 0	233	99.5
Grade 1	1	0.5
Grade 2–4	0	0
Severity of headaches (n = 234)		
Grade 0	232	99.5
Grade 1	1	0.5
Grade 2–4	0	0
Comfortable with the treatment[b] (n = 234)		
Yes	225	97.5
No	6	2.5

Abbreviations: *AE* adverse event, [a] AEs evaluated using the Division of AIDS table for grading the severity of adult and pediatric AEs, [b] Comfort is estimated by midwife

Safety - There were no study withdrawals because of AEs (including pain during the procedure). Immediately after treatment, only few patients reported mild AEs (grade I) such as, faintness (3.4%), headache (3.1%) and nausea (0.4%). From a health care provider perspective, midwives estimated that 81.1% of patients were comfortable during the procedure (Table 3). At 4–6 weeks post-treatment, vaginal watery discharge was the most common AE graded as mild (grade I) reported by 75.8% of women, followed by vaginal bloody-stained discharge (24.2%), and vaginal malodourous discharge (14.7%). The duration of watery discharge was on average 13.1 (± 7.8) days, and 92% of women did not have it anymore after three weeks (Fig. 1). Six (2.5%) patients were prescribed topical antibiotics for infection (AE grade 2), which allowed symptom resolution, among which three (50%) were HIV-positive (Table 4). No SAEs (grade 3–4) were observed immediately after the treatment nor 4–6 weeks post-treatment. None of the participants reported any complications requiring admission to a hospital or a medical emergency room consultation.

Univariate logistic regression showed that education was associated with anxiety, pain and with overall acceptability. Compared to women who were unschooled or with a primary education level, women having a higher education level were more likely to report higher levels of anxiety (OR, 3.35; 95%CI 1.12–9.98), higher levels of pain (OR, 10.22; 95%CI 1.34–77.72), and lower acceptability (OR, 0.22; 95%CI 0.08–0.59). Parity was also associated with anxiety and pain, with women having more than 5 children being less likely to report moderate to high anxiety (OR, 0.22; 95%CI 0.07–0.74), as well as moderate to high pain (OR, 0.16; 95%CI 0.05–0.53), compared to women with fewer children. Older women (aged >40 years old) were less likely to experience pain than younger women (OR, 0.22; 95%CI 0.07–0.67), and had higher odds of

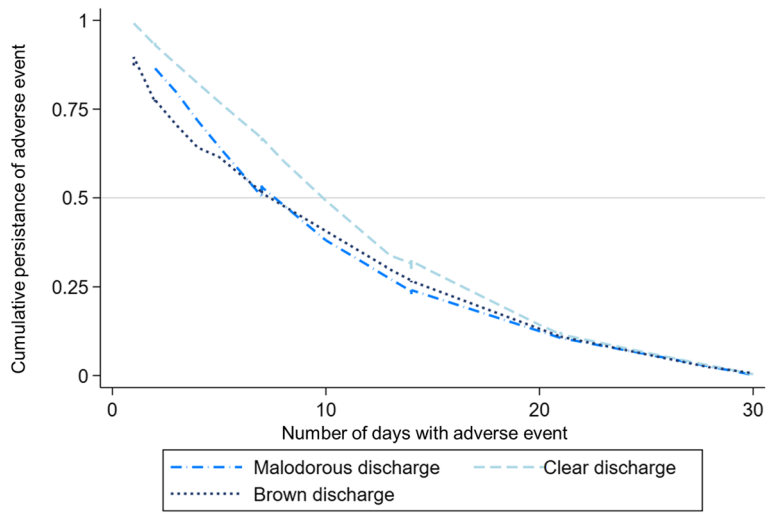

Fig. 1 Cumulative persistence of adverse events over time following thermal ablation

Table 4 Safety analysis after treatment at 4–6 weeks post-treatment

Side effects	Number	Percent
Watery discharge[a] (*n* = 197)		
Grade 0	48	24.5
Grade 1	149	75.5
Grade 2–4	0	0
Days with watery discharge (*n* = 137) (mean ± SD)	13.1 ± 7.8	
Bloody-stained discharge [b] (*n* = 196)		
Grade 0	154	78.5
Grade 1	42	21.5
Grade 2–4	0	0
Days with bleeding (*n* = 34) (mean ± SD)	10.8 ± 8.9	
Malodorous discharge, purulent discharge [b] (n = 197)		
Grade 0	168	85.5
Grade 1	29	14.5
Grade 2–4	0	0
Days of malodorous/purulent discharge (*n* = 25)	10.9 ± 8.3	
Posttreatment bleeding requiring treatment (n = 196)		
Grade 0	195	99.5
Grade 1	1	0.5
Grade 2–4	0	0
Pain when urinating [b] (n = 196)		
Grade 0	192	98
Grade 1	4	2
Grade 2–4	0	0
Days with pain when urinating (n = 3) (mean ± SD)	4.3 ± 2.3	
Infection (n = 197)		
Grade 0	189	97
Grade 1	0	0
Grade 2	6	3
Grade 3–4	0	0
Days with infection treated with antibiotics (n = 6) (mean ± SD)	7.3 ± 4.0	
Emergency consultation n = 196		
Grade 0	196	100
Grade 1–4	0	0

[a] Initially, the patient suffered from watery discharge, but at 4–6 weeks post-treatment she does not anymore. [b] AEs evaluated using the Division of AIDS table for grading the severity of adult and pediatric AEs

overall acceptability (OR, 2.33; 95%CI 1.16–4.54). Finally, the desire for future pregnancy was positively associated with pain (OR, 3.49; 95%CI 1.3–9.35), and negatively associated with acceptability (OR, 0.36; 95%CI 0.18–0.7) as compared to those not wishing a future pregnancy (Table 5). When the variables were included in the multivariate logistic regression model, these results were no longer significant.

Discussion

The main finding of our study is that TA appears to be highly acceptable by women, with a good global acceptability score (including anxiety, discomfort, pain, information received and overall satisfaction) (median 9.1, IQR 8.5–9.6). Almost all patients (98%) were satisfied with the treatment received, would agree to do it again if they had a recurrence of the disease, and would recommend it to a friend or family. The results are in accordance with the study of Mungo et al., conducted in a population of women living with HIV, where the vast majority also reported that they would recommend the treatment to others [9].

Pain intensity and duration as well as pain-related anxiety are factors that may influence and may serve to evaluate the effectiveness of a procedure [19]. Pain perception may differ according to the situation, previous

Table 5 Association of socio-demographic factors with anxiety, pain and overall acceptability of thermal ablation

Sociodemographic variables	Anxiety		Pain		Overall acceptability	
	OR	aOR	OR	aOR	OR	aOR
Age						
30–39	ref	ref	ref	ref	ref	ref
40–49	0.47 (0.21–1.05)	0.7 (0.26–1.84)	**0.22 (0.07–0.67)**	0.74 (0.29–1.9)	**2.3 (1.16–4.54)**	1.31 (0.56–3.06)
Education						
Unschooled/primary education	ref	ref	ref	ref	ref	ref
Secondary / tertiary	**3.35 (1.12–9.98)**	2.2 (0.68–7.16)	**10.22 (1.34–77.72)**	2.39 (0.76–7.57)	**0.22 (0.08–0.59)**	0.37 (0.13–1.06)
Marital status						
Single/divorced/widow	ref	–	ref	–	ref	ref
Married/in a relationship	1.67 (0.55–5.04)	–	2.48 (0.56–11.04)	–	0.34 (0.12–1.01)	0.35 (0.11–1.13)
Employment status						
Housewife	ref	ref	ref	–	ref	ref
Employee/Independent/Farmer	3.39 (0.77–14.93)	2.9 (0.64–13.11)	4.84 (0.63–37.25)	–	0.39 (0.13–1.17)	0.44 (0.14–1.38)
Other (unemployed, student)	6.83 (0.99–47.04)	3.18 (0.41–24.54)	3.64 (0.21–62.93)	–	**0.21 (0.04–1.00)**	0.38 (0.07–2.09)
Number of partners						
1–5	ref	–	ref	–	ref	ref
> 5	1.68 (0.63–4.51)	–	1.07 (0.3–3.87)	–	0.46 (0.2–1.06)	0.45 (0.18–1.14)
Parity						
0–1	ref	ref	ref	ref	ref	ref
2–5	0.43 (0.17–1.12)	-	**0.1 (0.03–0.31)**	-	2.03 (0.85–4.83)	1.42 (0.54–3.76)
> 5	**0.22 (0.07–0.74)**	-	**0.16 (0.05–0.53)**	-	2.48 (0.93–6.65)	1.05 (0.31–3.53)
Desire of pregnancy						
No	ref	ref	ref	ref	ref	ref
Yes	2.05 (0.94–4.49)	1.09 (0.42–2.85)	**3.49 (1.3–9.35)**	1.23 (0.49–3.09)	**0.36 (0.18–0.7)**	0.53 (0.23–1.24)
Number of applications						
1	ref	ref	ref	ref	ref	-
> 1	0.63 (0.2–1.92)	-	2.83 (0.82–9.84)	-	1.39 (0.55–3.53)	-

experience of pain, trust in the health care providers as well as cultural factors. In our report, the procedure was generally well tolerated by participants, with almost 80% of them reporting none to mild pain (0–3/10) and very few of them complaining of severe pain (8–10/10). Univariate regression analysis supported that anxiety was associated with higher levels of education, higher parity and the desire for future pregnancy. However, after adjusting for multiple socio-demographic factors, no significant associations were observed. Perception of pain is important to determine if local anesthesia is required before treatment and which participants may benefit from it. In our multivariate analysis, no factors appeared to be relevant to identify which patients could benefit from anesthesia. A clinical trial conducted in Brazil addressing the question of using anesthesia prior to thermal coagulation in 100 participants, reported a significant reduction in pain [20]. However, other investigators reported essentially mild pain, while severe pain requiring hospitalization (Grade 3 or worse) was exceptional [6, 9, 12, 21, 22].

AEs grade 3 or worse associated with treatment were exceptional, and reported AEs were most of the time of grade 1 or 2 [21]. In a study conducted in Brazil, 52 women were treated without severe adverse events or complications [23]. In a screen-and-treat approach conducted in Malawi and including 381 participants, Campbell et al. reported no serious AEs in association with TA [6]. Mild vaginal discharge was experienced by most patients in our study and support that women should be advised about this symptom in the pretreatment counselling, as well as informed that it disappears after 13 days in 50% and in almost all patients (91%) after 30 days.

From a primary health care provider perspective, TA was considered as easy to perform, safe and interpreted as acceptable according to patients' expectations and wishes. This issue is important as providers may feel more confident when patients are comfortable and satisfied [24]. In our experience, the procedure should ideally be conducted by health care providers that are well trained in pelvic examination in order to avoid any vaginal contact with the probe during the treatment process,

which can be extremely painful and may cause damage to the vaginal wall. Generally, TA is a minor surgical procedure and appears to be a well-tolerated intervention by most of the patients, therefore not supporting the systematic use of local anesthesia.

This study has several limitations. First, it was conducted in a single center in a semi-rural area with few clinicians (three midwives and two part-time gynecologists) administrating screening and treatment procedures. Second, it is difficult to be sure that the anxiety, discomfort, pain and overall acceptability scores reflect only the TA treatment by itself or if women have considered the whole diagnostic and treatment process including the pelvic exam, visual assessment, cervical biopsy, endocervical brushing and TA in their responses. This potential bias has also been reported by other investigators [9, 12].

A major advantage of TA is that it may be performed immediately after visual assessment, without requiring a second pelvic exam, allowing to combine screening and treatment in a single pelvic exam and single-visit approach. This is particularly important considering the difficulty in recalling women for further management, which is a major cause of loss to follow-up and low program impact in LMICs [24] . According to the acceptability by the participants and health care providers as well as the favorable safety profile, we can expect that in the years to come, TA will become the new standard of care for women having a positive screening test in LMIC contexts [25].

Conclusion

In conclusion, these results contribute to the evidence that TA is widely accepted by women, is safe and may become the method of choice to treat cervical precancerous lesions in low-resource settings. TA will contribute to improving feasibility of screening and treatment in a single-visit approach and optimizing programs towards elimination of cervical cancer in LMICs.

Abbreviations

AEs: Adverse events; CC: Cervical Cancer; HIV: Human immunodeficiency virus; HPV: Human papillomavirus; LMICS: Low- and middle-income countries; TA: Thermal Ablation; VIA: Visual inspection with acetic acid; VILI: Visual inspection with Lugol's iodine; WHO: World Health Organization.

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Authors' contributions

PP, BK, and PV designed the study protocol. PP, BK, PV, TM, AW, and JS oversaw the data collection and interpreted the data. TM, JS and PP drafted the paper. TM, JS, and AW conducted data analysis. BK, ET, JS and PV trained the local staff. All authors approved the final manuscript.

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Availability of data and materials

The datasets used during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The study obtained approval from the Cantonal Ethics Board of Geneva, Switzerland (Commission cantonale d'éthique de la recherche [CCER], No. 2017–0110) and the Cameroonian National Ethics Committee for Human Health Research (No. 2018/07/1083/CE/CNERSH/SP). Protocols are carried out in accordance with relevant guidelines and regulations. All women provided informed written consent to participate in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Exploring Factors Associated with Patients Who Prefer Clinician-Sampling to HPV Self-Sampling: A Study Conducted in a Low-Resource Setting

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Abstract: Human papillomavirus (HPV) self-sampling (Self-HPV) is a promising strategy to improve cervical cancer screening coverage in low-income countries. However, issues associated with women who prefer conventional HPV clinical-sampling over HPV self-sampling may affect screening participation. To address this issue, our study assessed factors associated with women's preferences related to Self-HPV. This study was embedded in a large clinical trial recruiting women aged 30–49 years in a primary HPV-based study termed "3T-Approach" (for Test-Triage-Treatment), launched in 2018 at Dschang District Hospital, West Cameroon. Participants were invited to perform a Self-HPV. After the sampling and before receiving the results, participants completed a questionnaire about cervical cancer screening and their preferences and perceptions around Self-HPV. The median age of the 2201 participants was 40.6 (IQR 35–45) years. Most (1693 (76.9%)) preferred HPV self-sampling or had no preference for either method, and 508 (23.1%) preferred clinician-sampling. Factors associated with an increased likelihood of reporting a clinician-sampling preference were tertiary educational level (29.4% CI: 25.6–33.6 vs. 14.4% CI: 12.8–16.1) and being an employee with higher grade professional or managerial occupations (5.5% CI: 3.8–7.9 vs. 2.7% CI: 2.0–3.5). The main reported reason for women preferring clinician-sampling was a lack of "self-expertise". Most women (>99%) would agree to repeat HPV self-sampling and would recommend it to their relatives. HPV self-sampling in the cultural context of central Africa was well accepted by participants, but some participants would prefer to undergo clinician sampling. Health systems should support well-educated women to increase self-confidence in using HPV self-sampling.

Keywords: cervical cancer screening; HPV self-sampling; sub-Saharan Africa; preference

1. Introduction

Cervical cancer (CC) is the second most common cancer in Cameroon, with 2356 cases and 1787 deaths recorded in 2020 [1]. In sub-Saharan Africa, CC is the leading cause of cancer deaths in women, despite being a highly preventable disease [2]. The widespread understanding that almost all cervical cancer cases occur in women who were previously infected with human papillomavirus (HPV) has resulted in the development of HPV tests and primary HPV-based cervical cancer screening. Furthermore, HPV testing is performed

on vaginal smear samples, which has the advantage of allowing collection by patients themselves (Self-HPV).

The World Health Organization (WHO) launched a global initiative in 2020 to eliminate cervical cancer and includes Self-HPV as a part of cervical cancer screening programs [3,4]. Systematic reviews support the finding that Self-HPV has similar sensitivity and specificity for detecting precancerous lesions to samples collected by a physician or nurse [5–7] and is considered a safe and acceptable screening method by users [8–12]. This approach reduces the discomfort and pain that can be associated with pelvic examination, is considered less invasive, allows women more autonomy and privacy, and might facilitate screening participation [8,13,14]. In the context of primary screening, a negative HPV result indicates a very low risk of developing CC within the next decade and a positive result can generally be safely managed by adequately trained health care providers [15].

Self-HPV provides an opportunity to increase screening coverage to 70% of eligible women as recommended by the WHO. However, there are still some uncertainties about the introduction of this method for all women engaged in routine screening campaigns. The main uncertainties reported by participants are the quality of the sample, lack of confidence that they will perform the test correctly, and the reliability of the results [16].

The above results were mostly focused only on the acceptability of self-sampling and were not contextualised to sub-Saharan African countries. For these reasons, our study aimed to evaluate sociodemographic factors associated with preference for conventional HPV clinician-sampling compared with Self-HPV, in order to propose effective screening strategies that are aligned with the WHO's recommendations. Currently the Cameroonian health system supports and follows the WHO's recommendations for cervical cancer screening. There is no effective national screening programme, but early opportunistic screening for cervical cancer by visual inspection with acetic acid and Lugol's iodine (VIA/VILI) is promoted and sporadic campaigns are organized [17].

2. Materials and Methods

2.1. Setting and Study Design

This study was embedded in the research project "Comprehensive Cervical Cancer Prevention and Better Women Health in Medium and Low-Resource Setting" launched in 2018 [15] by the University of Dschang, the Dschang District Hospital, the University of Yaoundé in Cameroon, and the University Hospital of Geneva, Switzerland [18].

2.2. Study Procedures

The research project was based on a "3T-Approach" (for "same-day test, triage and treatment"). After a one-hour health education group session, midwives individually provided detailed information about the study and collected written informed consent. A baseline survey including sociodemographic characteristics and medical history was also conducted. Self-HPV was performed by participants using flocked swabs (FLOQSwabs® Self Collection; Copan, CA, USA). Before performing the self-test, women received instructions and a support guide that provided detailed visual information about the procedure. They were instructed to wash their hands before the procedure; they then performed the test in a dedicated area within the screening room with a midwife available if needed. Instructions directed the women to hold the plastic head of the swab and insert the cotton tip into the vagina until it met resistance. Specimens were analysed by a point-of-care HPV test (GeneXpert®) using the Xpert HPV Assay (Cepheid, Sunnyvale, CA, USA), and results were available after one hour.

Women screened positive underwent visual inspection with acetic acid and Lugol's iodine (VIA/VILI) to detect whether pre-cancerous or cancerous lesions were visible. If the VIA/VILI result was positive, women were treated by thermal ablation or loop electrosurgical excision of the transformation zone (LEETZ) according to predefined eligibility criteria. Quality control was ensured by histological sampling (biopsies and endocervical curettage), which was considered the gold standard.

2.3. Acceptability of and Satisfaction with the HPV Self-Sampling Procedure

After the self-sampling procedure and before receiving the result, women filled in a second survey in their native language. With the assistance of a midwife, the participants reported how they felt during the test, their satisfaction with the procedure, their levels of anxiety and discomfort, their willingness to take the test again, whether they would recommend the test, and where they thought the test should be conducted (at home vs. at a health care centre). Pain experienced during the self-sampling procedure was scored according to the Wong-Baker FACES® scale [19]. This validated scale consists of six different faces with a spectrum of pain intensity from 0 (no hurt) to 10 (hurts worst). We then formed two subgroups: medium pain (score ≤ 4) and strong pain (score > 4). A four-point Likert-type scale was used to evaluate the women's anxiety, discomfort, embarrassment, and level of confidence with scores ranging between 1 (not at all) to 4 (very). Study data were collected with paper Case Report Forms (p-CRF) by trained midwives and later transcribed into an electronic database (SecuTrial®).

2.4. Ethical Considerations

The protocol obtained approval from the Cantonal Ethics Board of Geneva, Switzerland (Commission cantonale d'éthique de la recherche, N °2017-01110) and the National Ethics Committee for Research on Human Health, Cameroun (Comité national d'éthique de la recherche pour la santé humaine, CNERSH, N °2018/07/1083/CE/CNERSH/SP). The study protocol of the overarching 3T Study was registered under ClinicalTrials.gov (number NCT03757299).

2.5. Statistical Analysis

Quantitative variables were expressed as means and standard deviations, and qualitative variables were expressed as percentages unless otherwise stated. Descriptive analyses were conducted to compare baseline sociodemographic and clinical characteristics according to the preference for clinician-sampled versus Self-HPV. Categorical variables were analysed by Pearson's chi-square or Fisher's test when appropriate. In addition, we used univariable and multivariable logistic regression models to identify sociodemographic factors associated with preference for HPV self-sampling. Education, employment status, and parity were used in the multivariable logistic regression model, and were selected based on their *p*-value in the univariable models. We used a two-sided level of significance of 0.05. The analyses were conducted using the software package STATA® 16 (Stata, College Station, TX, USA).

3. Results

3.1. Epidemiological Characteristics

A total of 2201 women were enrolled in the 3T-Approach between September 2018 and January 2021. Median age was 40.6 (IQR 35–45) years. Among participants, 406 (18.4%) were HPV-positive, and 176 (8%) had been previously screened (Table 1). Most (76.9%) preferred HPV self-sampling or had no preference, and 508 (23.1%) preferred clinician-sampling. Demographic characteristics of the participants are shown in Table 1 and stratified by procedure preference (self-sampled or neutral versus (vs.) clinician-sampled). There was a higher proportion of women with a tertiary education level in the clinician-sampling preference group (29.5%) than in the Self-HPV preference or neutral group (14.4%, $p < 0.001$). Similarly, the proportion of women employed with higher grade professional or managerial occupations was higher in the clinician-sampling preference group (5.5% vs. 2.6%, $p = 0.005$). The Self-HPV preference group had a lower proportion of nulligravida than the clinician-sampling preference group (1.9% vs. 3.0%; $p = 0.001$) and a higher proportion of women with more than five pregnancies (56.6% vs. 47.4% $p < 0.001$). There was a higher proportion of women with more than five children in the self-sampling preference group than in the clinician-sampling preference group (35.8%

vs. 26.1%; $p < 0.001$). No difference was found concerning previous HPV sampling by clinicians between the two groups.

Table 1. Baseline sociodemographic and clinical characteristics according to preference for clinician-sampled or self-sampled HPV test.

Variable	Preference for Self-Sampled or Neutral N (%)	Preference for Clinician-Sampled N (%)	*p*-Value
Participants recruited (n = 2201)	1693 (76.9)	508 (23.1)	
HPV testing results (n = 2201)			0.179
Negative	1391(82.2)	404 (79.5)	
Positive	302 (17.8)	104 (20.5)	
Age (y), mean ± SD	39.9 (5.9)	39.1 (6.0)	0.001
Marital status (n = 2198)			0.840
Single/divorced/widowed	257 (15.2)	75 (14.8)	
Married/in relationship	1435 (84.8)	431 (85.2)	
Education (n = 2195)			<0.001
Unschooled/primary education	541 (32.0)	106 (21.0)	
Secondary education	905 (53.6)	251 (49.6)	
Tertiary education	243 (14.4)	149 (29.5)	
Employment status (n = 2198)			0.006
Unpaid worker *	422 (25.0)	126 (24.9)	
Lower grade or intermediate occupation **/self-employed	1224 (72.4)	352 (69.6)	
Higher grade occupation ***	45 (2.6)	28 (5.5)	
Age at first delivery (y), mean ± SD	20.7 (5.1)	21.4 (6.2)	0.006
Age at first intercourse (y) mean ± SD	17.9 (2.7)	18.0 (3.0)	0.354
Pregnancy (n = 2198)			0.001
Nulligravida	32 (1.9)	15 (3)	
1–5	702 (41.5)	251 (49.6)	
>5	958 (56.6)	240 (47.4)	
Parity (n = 2198)			<0.001
Nulliparous	62 (3.7)	26 (5.1)	
1–5	1024 (60.5)	348 (68.8)	
>5	606 (35.8)	132 (26.1)	
Previous HPV screening (n = 2197)			0.405
No	1560 (92.3)	461 (91.1)	
Yes	131 (7.7)	45 (8.9)	
HIV status (self-reported) (n = 2156)			0.535
Negative	1601 (96.4)	480 (94.5)	
Positive	60 (3.6)	15 (5.5)	

Note: N, number; HPV, human papillomavirus; y, years; SD, standard deviation; HIV, Human Immunodeficiency virus, * Unpaid worker (ex: student, housewife), ** Employee with lower grade or intermediate occupation (ex: nurse, technician, and teacher), *** Employee with higher grade professional administrative or managerial occupations (ex: doctor, manager, school director).

3.2. Acceptability of the HPV Self-Sampling Procedure by Sampling Preference

Most women (98.3% in self- and 96.9% in clinician-sampling; $p = 0.053$) reported to be comfortable or very comfortable and confident or very confident (98.9% vs. 99.4%; $p = 0.341$) during the self-sampling procedure. No significant differences were reported. The same observation was made among women who expressed no or low embarrassment (99.3% vs. 98.6%; $p = 0.107$). However, among women who described feeling anxious (1.1% vs. 3.5%; $p < 0.001$), we found that women who preferred clinician-sampling were significantly more anxious (Figure 1). The source of anxiety reported by most participants (86.0% vs. 77.3%) was fear of a positive result, followed by fear of the self-sampling procedure (6.8%) in the clinician-sampled group, and fear of doing the self-test for the first time (4.3%) in the self-test preference group.

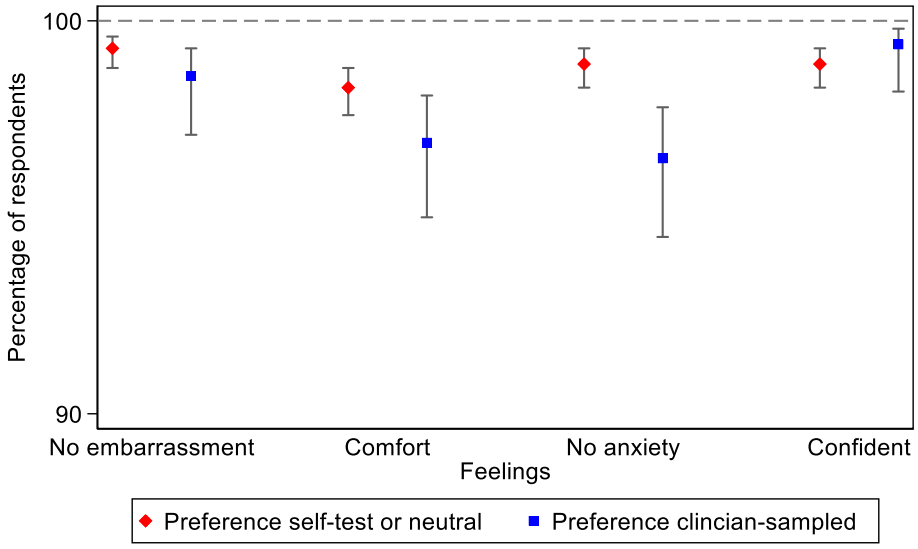

Figure 1. Comparison of women's experiences with Self-HPV (preference for self-test or neutral vs. clinician-sampled).

Few participants reported difficulties in performing the Self-HPV (1.2% vs. 1.6%; $p = 0.488$, in the self-sampled or neutral and clinician-sampled preference groups, respectively). Fewer than 0.05% (1/2201) women reported pain (score >4/10) during Self-HPV across the two groups. Most women in both preference groups were willing to repeat the self-test as a screening test (99.8% vs. 99.2%; $p = 0.035$), and they agreed to perform it at home (98.4% vs. 94.9%; $p < 0.001$). Only one woman in the self-sampled preference group and one in the clinician-sampled preference group reported that they would not recommend the procedure to their relatives. (Table 2).

Table 2. Comparison of feelings about HPV self-sampling between preference groups.

Feelings about Self-Sampling	Preference for Self-Sampled or Neutral N (%)	Preference for Clinician-Sampled N (%)	*p*-Value *
Agree to repeat self-sampling	1687 (99.8)	504 (99.2)	0.035
Agree to perform self-sampling at home	1666 (98.4)	481 (94.9)	<0.001
Difficult to perform self-sampling	20 (1.2)	8 (1.6)	0.488
Would recommend self-sampling			0.573
Yes	1687 (99.9)	507 (99.8)	
No	1 (0.1)	1 (0.2)	

* Fisher's exact test used to account for low cell counts.

Univariate logistic regression showed an association between sociodemographic variables and preference for the clinician-sampled procedure. In particular, education level was significantly higher among women preferring clinician-sampling. Women having attended tertiary education were more than three times more likely to prefer clinician-sampling than women with primary education or no formal education (OR, 3.13; 95% CI 2.34–4.19). Women having attended secondary education were 1.42 times more likely (95% CI 1.10–1.82) to prefer clinician-sampling. These findings show a gradient in the association between level of education and preference for clinician-sampling. Compared with unpaid workers, women employed with higher grade professional or managerial occupations were more likely to prefer clinician-sampling (OR, 2.08; 95% CI 1.25–3.48). However, no difference in preference was observed among women employed with lower grade or intermediate occupation or self-employed women compared with unpaid workers (OR, 0.96; 95% CI 0.76–1.21). Parity was also associated with sampling preference, with women having more

than five children being less likely to prefer clinician-sampling (OR, 0.52; 95% CI 0.32–0.85) compared with nulliparous women.

In the multivariable logistic regression model, parity and employment status were no longer significantly associated with sampling preference. However, the gradient between level of education and preference for clinician-sampling remained, with women with a secondary or tertiary level of education showing a significant preference to undergo clinician-sampling (OR, 1.35; 95% CI 1.05–1.75, and OR, 2.79; 95% CI 2.03–3.82, respectively) (Table 3).

Table 3. Association of sociodemographic factors with preference for clinician-sampled.

Sociodemographic Variables	Clinician-Sampled			
	Unadjusted		Adjusted	
	OR * (95% IC)	*p*-Value	OR (95% IC)	*p*-Value
Education				
Unschooled/primary education	Ref		Ref	
Secondary education	1.42 (1.10–1.82)	0.007	1.35 (1.05–1.75)	0.019
Tertiary education	3.13 (2.34–4.19)	<0.001	2.79 (2.03–3.82)	<0.001
Employment status				
Unpaid worker *	Ref		Ref	
Lower grade or intermediate occupation **/self-employed	0.96 (0.76–1.21)	0.751	0.91 (0.72–1.15)	0.435
Higher grade occupation ***	2.08 (1.25–3.48)	0.005	1.35 (0.79–2.30)	0.272
Parity				
Nulliparous	Ref		Ref	
1–5	0.81 (0.50–1.30)	0.384	1.06 (0.65–1.73)	0.824
>5	0.52 (0.32–0.85)	0.010	0.84 (0.50–1.43)	0.523
Pregnancy				
Nulligravida	Ref			
1–5	0.76 (0.41–1.43)	0.400		
>5	0.53 (0.28–1.00)	0.051		
Marital status				
Married/in relationship	Ref			
Single/divorced/widowed	0.97 (0.74–1.28)	0.840		

Note: OR, odds ratio; CI, confidence interval. * housewife or student; ** Lower grade professional, administrative and managerial occupations and higher grade technician and supervisory occupations, *** Large employers, higher grade professional, administrative and managerial occupations.

3.3. Perceptions Regarding the Sampling Procedure

Most reasons for preferring self-sampling over clinician-sampling were its ease of use (75.2%) and the possibility for increased privacy (16.3%). The top reasons women gave for preferring clinician-sampling over self-sampling were feeling comfortable because of the clinician's greater experience (76.1%) and the higher reliability of the results (19.5%). The possibility to undergo a complete gynaecological exam (2.5%) was a less common reason reported by women, as was the belief that sampling is the role of caregivers (0.8%) (Table 4). Most participants preferred performing self-sampling in a medical centre (96.6%) over home-based screening, because they were afraid of performing the self-test inappropriately (36%) or contaminating it (12%) if performed at home.

Table 4. Reasons for preferring HPV self-sampling or clinician-sampling *.

Reasons for preferring self-sampling (n = 479)	N	(%)
Easy and rapid	360	75.2
Affords privacy	78	16.3
Autonomous	11	2.3
Fear of gynaecological examinations	11	2.3
Reliability of results	7	1.5
Self-confidence	6	1.3
New learning experience	6	1.3
Reasons for preferring clinician-sampling (n = 486)		
Expertise of clinician	370	76.1
Reliability of results	95	19.5
Possibility of inspecting the cervix	12	2.5
Caregiver's role	4	0.8
Difficulty of performing the test	3	0.6
Ease of procedure	2	0.4

* Multiple responses allowed.

4. Discussion

HPV self-sampling may be an effective approach to cervical cancer screening programs, although there are still challenges affecting its implementation. Because low-resource settings are progressively introducing both HPV-based primary screening and Self-HPV sampling [20,21], we sought to explore factors associated with women's preference for sampling performed by health care providers in this context. Our study was conducted in a population where most participants had never undergone screening before (92.0%). Our findings show that most women consider Self-HPV easy to use (97.9%), as previously reported in the literature [22]. More than 99.5% of the women reported that they would agree to do it again, and 97.6% would agree to perform it at home.

Some women (23.1%) preferred sampling performed by clinicians, as was previously reported in other studies [8,23–25]. In Cameroon, an earlier study explored the perceptions and preferences regarding self- versus physician-sampling in a population of women living with HIV and observed that most preferred clinician-sampling [26]. This was found in another study conducted in Britain among Muslim women interviewed in the context of cervical cancer screening [24]. The reasons for preferring clinician-sampling in these studies were concerns about not doing the test correctly and the belief that health providers are more expert (95.6%), which is consistent with our findings. In the literature, women also reported having a low level of self-confidence performing self-sampling properly and providing a good quality sample for analysis [8,16,27–29].

Sociodemographic factors associated with women's preferences show that well-educated women prefer clinician-sampling. Similar findings were reported in Malaysia, where women with a high education level presented a low level of confidence in self-testing [22]. In China, authors investigated the preference for self-testing for streptococcus B infection instead of clinician-sampling, and their findings showed a similar tendency, that women with the highest education level were more likely to prefer clinician-collection [30]. The finding that women with a higher education prefer clinician-sampling may be explained by their increased questioning of their ability to perform the test themselves adequately [22]. Being able to afford going to a hospital to seek care may also influence the preference to have a clinician conduct cervical cancer screening. However, in a different study on vaginal HPV self-sampling, the authors found no association between level of education and preference for procedure type [31]. Cultural beliefs may also influence patients' perception of the self-sampling approach and the idea that health care provider attendance is needed during the procedure [22,29,32]. Qualitative studies could be useful to further explore reasons for clinician- versus self-sampling preferences.

Educational interventions were highlighted as an effective way to improve women's self-confidence and clarify misconceptions [29,33]. Instruction about the validity of the test and how to collect the sample should be simple and should account for the women's cultural and social characteristics [13]. Women who have never used tampons or do not feel comfortable about touching their genital areas perceive this practice as taboo and appear less confident about performing a self-testing procedure [13,16]. Allowing them to observe and manipulate a swab during the educational intervention is one way to reduce their worries [32]. The presence of a healthcare provider during Self-HPV has been reported by some authors to have a positive effect on women. Support is therefore a way of increasing women's confidence and comfort [8,28], but the option to choose clinical-sampled could be a solution for women who are unwilling to undergo Self-HPV, as was proposed in Australia [34]. In our program, an hour of educational and counselling intervention provided to women before performing the Self-HPV probably allows sufficient time to respond to the women's specific fears. Health care providers need to fully understand the Self-HPV screening procedure and should be able to give culturally appropriate messages to participating women [8]. They also need to be prepared to answer any concerns that women may have regarding Self-HPV. This requires rigorous theoretical and practical training of health care providers.

Community health workers and peer-to-peer education also contribute to increasing women's awareness and confidence in Self-HPV by providing them with adequate information [32]. The Cameroonian health system already provides an important value to the community approach to health promotion in the population, as is also the case in other African countries [32]. Political endorsements and health system support are key in this screening process and in health care training [35]. Recommendations on screening and management strategies for cervical cancer elimination from previous research should be applied at a state level, as is the case in Uganda, Rwanda, and Kenya, where these recommendations have been introduced into national guidelines [20,21,36].

The strength of this study lies in the large sample size of women recruited in real-world screening conditions. In addition to the Self-HPV acceptability analysis, we assessed women's preferences regarding the screening procedure. Identifying associations between sociodemographic characteristics and screening preference contributes to providing adapted instructions to women and improving their experiences, thus increasing screening coverage.

There are two main limitations to this study. First, for illiterate women or those who were not comfortable answering independently, the questionnaires were completed with the help of midwives. This could have influenced the women's answers if any women were not comfortable discussing their feelings about intimacy-related topics in the presence of midwives. Second, the women recruited in our study and who took part in our screening program come from a constrained health area and have a higher level of education on average than the general female population in Cameroon [37]. Therefore, our results may not be generalizable to all women in Cameroon.

5. Conclusions

Self-HPV is highly accepted by women and is an effective method of detecting precancerous lesions. Our findings support a self-sampling approach as primary screening method. However, implementation of a community-based Self-HPV approach needs to be appropriate to the local context. Health systems should assist participants with the screening process to increase self-confidence about the accuracy of self-sampling. Given that a minority of participants prefer clinician-based sampling, an approach where women can choose the sampling method should be considered.

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Barriers to cervical cancer prevention in rural Cameroon: a qualitative study on healthcare providers' perspective

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ABSTRACT

Objective Cervical cancer in Cameroon ranks as the second most frequent cancer among women and the leading cause of cancer-related deaths, mainly due to the lack of prevention. Our principal objective was to explore potential barriers to an human papillomavirus (HPV)-based cervical cancer screening from a healthcare provider (HCP) perspective in a low-income context. Second, we aimed to explore the acceptability of a single-visit approach using HPV self-sampling.

Settings The study took place in the District hospital of Dschang, Cameroon.

Participants Focus groups (FGs) involved HCPs working in the area of Dschang and Mbouda.

Primary and secondary outcome measures All FGs were audiorecorded, transcribed and coded independently by two researchers using the ATLAS.ti software. A qualitative methodology was used to capture insights related to the way people perceive their surroundings. Discussion topics focused on perceived barriers, suggestions to improve cervical cancer screening uptake, and acceptability.

Results A total of 16 HCPs were interviewed between July and August 2019. The identified barriers were (1) lack of basic knowledge on cervical cancer among most women and men and (2) lack of awareness of the role and existence of a screening programme to prevent it. Screening for cervical cancer prevention using HPV self-sampling was considered as an acceptable approach for patients according to HCPs. Traditional chiefs were identified as key entry points to raise awareness because they were perceived as essential to reach not only women, but also their male partners.

Conclusions Awareness campaigns about cervical cancer, its prevention and the availability of the screening programmes are crucial. Furthermore, involving male partners, as well as key community leaders or institutions was identified as a key strategy to encourage participation in the cervical cancer screening programme.

Trial registration Ethical Cantonal Board of Geneva, Switzerland (CCER, N°2017-0110 and CER-amendment n°2) and Cameroonian National Ethics Committee for Human Health Research (N°2018/07/1083/CE/CNERSH/SP).

Strengths and limitations of this study

- A strength of this study was its qualitative approach, with the aim to explore cervical cancer screening barriers in Cameroon from the perspective of healthcare providers (HCPs).
- Second, it was conducted on-site with participation of HCPs with different educational backgrounds.
- As focus groups (FGs) were conducted by a Cameroonian anthropologist, interviewer bias was intended to be minimised but cannot be excluded due to his higher education and gender.
- A limitation of the study was the methodology of the FGs which covered a range of topics considered important by the participants, and results might not be applicable to the general population.

INTRODUCTION

According to the WHO, 570 000 cervical cancer cases were diagnosed worldwide and 311 000 deaths were registered in 2018, most of them occurring in low-income and middle-income countries (LMICs).[1] In sub-Saharan Africa, cervical cancer is the second leading cause of cancer among women and the leading cause of deaths.[2] In Cameroon, a total of 2356 new cases were diagnosed in 2018 and 1546 deaths were documented, with cervical cancer being the leading cause of cancer-related deaths among women.[2] Therefore, cervical cancer is a major public health concern in Cameroon.

In high-income countries (HICs) organised screening programmes with high coverage rates have shown a significant reduction in the number of new cases and mortality rates.[3] As a result, there is an important difference in the incidence of and mortality rates from cervical cancer between LMICs and HICs. Thus, prevention strategies are important to reduce the gap in health inequalities between LMICs and HICs.[4]

In 2018, the WHO Director-General called all countries to take action to eliminate cervical cancer worldwide. To reach this goal, every country must achieve the following global targets by 2030[1]: (1) increase vaccination

coverage against human papillomavirus (HPV), (2) increase screening coverage using HPV testing[5] and, (3) offer appropriate management for women with an invasive cervical cancer.

To reach the second goal, HPV-based screening has been suggested that can be performed by women themselves. HPV self-sampling is an innovative approach for cervical cancer prevention, requiring minimal human resources, and sampling kits can be offered anywhere (villages, markets, public squares or homes) increasing reach to vulnerable and underserved populations. Previous studies have demonstrated that, following efficient education and clear instructions, it is a highly acceptable and well-received method for most females eligible for screening and healthcare providers (HCPs).[6]

HPV self-sampling provides a unique opportunity to reduce cervical cancer mortality in women and diminish the inequalities in access to cervical cancer prevention services. Since 2018, a partnership between University Hospitals of Geneva (Switzerland), University Hospital of Yaoundé (Cameroon) and the University of Dschang (Cameroon) introduced a 5-year programme (2018–2023) based on primary self-sampling for HPV screening. This strategy is based on a '1 day visit' termed the 3T-approach (for Testing, Triage and Treatment). Community-based sensitisation campaigns targeted a population of women aged between 30 and 49 years old for cervical cancer screening based on the 3T-approach at the Dschang District Hospital. HPV self-samples were analysed using a point-of-care test (Xpert HPV assay) followed by VIA/VILI triage if HPV positive and treatment if required.[6]

However, approaches to scaling up these interventions in rural settings may differ[7] and its introduction requires preparatory work before implementation. To better reach the target population, cultural, social, societal and financial barriers, as well as other circumstances that may affect the acceptance and uptake of cervical cancer screening, should be identified. Therefore, the first aim of our study was to identify barriers to cervical cancer screening from the HCPs' perspective, as they influence women's prevention behaviour.[8 9] The second aim was to identify facilitators and explore acceptability and perception of a single-visit approach.

METHODS

Study site

The qualitative data were collected between July and August 2019 in the district of Dschang, a city located in the West of Cameroon, 4 hours from Doula and 5 hours from Yaoundé (figure 1). The Dschang city and surrounding areas have an estimated population of approximately 63 838 inhabitants.[10] The present study is part of a large trial termed '3T-approach' implemented with the support of the Ministry of Health in September 2018 for a 5-year period expecting to include 6000 female participants.

Study setting and design

A qualitative methodology using focus groups (FGs) was chosen to capture insights related to the way people perceive and interpret their surroundings.[11 12] A semi-structured questionnaire, inspired by a previous study

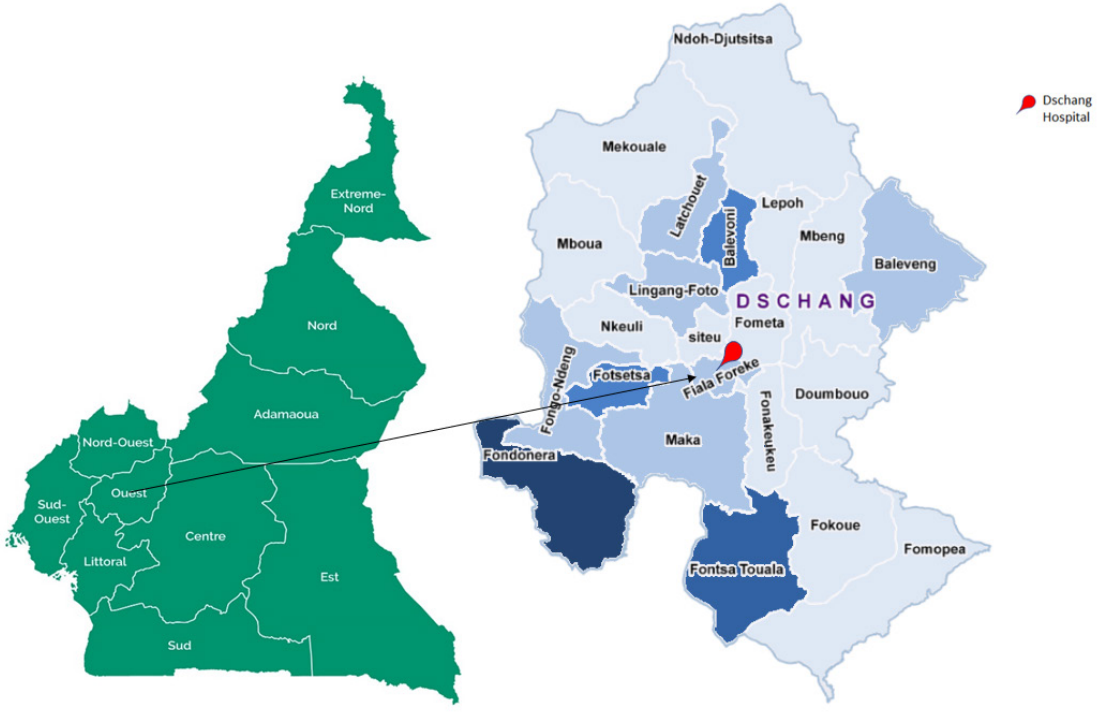

Figure 1 Map of Cameroon and of the districts of health: location of study site.

conducted in Uganda,[12] was used to lead the conversation.[13] Discussion topics focused on (1) perceived barriers, (2) suggestions to improve cervical cancer screening uptake and (3) acceptability of the 3T-approach. The interview guide was pretested and adapted in Geneva prior to the study in Cameroon, addressing factors such as comprehensibility and time. The FGs took place in a private room in the District Hospital of Dschang and were conducted in French, by a Cameroonian anthropologist (NA).

Recruitment and sampling

The study used a systematic, non-probabilistic sampling approach. According to the standards of qualitative methodology, we applied the principle of saturation. HCPs were invited to participate in the small FGs from the District Hospital of Dschang, where the screening programme was based, from the community setting, where cervical cancer screening is promoted, and from the Mbouda District Hospital, which frequently refers women to the screening site. They were either working as medical or as community healthcare workers. An information document and a consent form were distributed prior to the FGs and only those who provided written consent were included in the study.

Patient and public involvement

Only HCPs were involved.

Data analysis

All FGs were recorded, anonymised and fully transcribed. Transcripts were systematically coded with a thematic approach, using ATLAS.ti CAQDAS. Most codes were a priori defined based on the main research questions. Further codes emerged over the coding process itself after initial reading of the transcripts. Codes were aggregated in overarching themes. Main topics and barriers to access screening that were identified in all the FGs were analysed and classified. Coding was conducted by two coresearchers separately and compared afterwards.

Barriers perception

Identified barriers were classified according to the conceptual framework of Thaddeus and Maine of the three-delay model.[7] According to their concept, increasing the availability of services (for instance by building more facilities or expanding health programmes) does not always increase the use of services. Thaddeus and Maine argue that the decision to seek healthcare can be classified into three types of delays: first, the delay in the decision to seek care, including the role of the woman in the decision-making process but also structural factors such as distance from the health facility. Second, the delay to reach adequate care at the health facility mostly due to costs of transportation and poor road conditions. Third, the delay to receive adequate care once at the facility, due to availability of materials or staff. Even though the model was applied originally in the context of maternal mortality, it is adaptable to multiple health situations in order to identify key obstacles and how to address them.

RESULTS

Setting

Between mid-July and mid-August 2019, four FGs with a total of 16 participants (12 women and 4 men) were conducted in the District Hospital of Dschang. The FGs lasted about 60–75 min. All invited HCPs participated in the study. The majority were professionals working in hospitals, but community healthcare workers were also included, as they were doing outreach for the cervical cancer screening programme. Thirteen HCPs were from the Dschang district and three from the Mbouda district, who frequently sent women to Dschang for screening. Participants of two FGs had received specific training on cervical cancer prevention, while the two other FGs were not specialised. Among the female participants 75% had themselves been screened for HPV.

Sociodemographic characteristics of the participants

The 16 participants were all HCPs with an average of 15 years work experience in healthcare. Most of them (44%) were midwives, married (75%) and on average 41 years old (range 28–62 years). Education level was high; more than three quarters had completed at least secondary education and nearly half had obtained a university degree. In one FG (FG with community healthcare workers), the level of education was lower. Further details can be found in table 1.

Barriers to cervical cancer screening

Barriers to cervical cancer screening emerged in different areas and were classified according to the conceptual framework of the three-delay model.[7]

Phase I: delay in the decision to seek screening

According to Thaddeus and Maine, the healthcare seeking process starts with the decision to seek care and various factors will shape the decision of women to get screened. According to this model, barriers most commonly studied in the first delay are distance, cost, quality of care and sociocultural factors.[7] Those barriers also emerged in our study, which revealed the first delay as the most important one.

Costs

The financial cost of receiving care has been extensively studied in the literature.[7] Costs can include transportation costs, but also costs for physicians, facility fees, the cost of medications and other supplies.[14] Previous studies have noted that costs and distance are often closely linked as longer distance to reach a facility results in higher cost.[14] Cost of transportation was indeed frequently mentioned by the HCPs from Mbouda district, from which patients need to travel to the District hHospital of Dschang to get screened.

Table 1 Sociodemographic characteristics of participants

Number of participants	16
Women	12 (75%)
Men	4 (25%)
Age (years)	
Mean	41.7
Range	28–62
Marital status	
Married	12 (75%)
In relationship	0 (0)
Single	4 (25%)
Divorced or widowed	0
Education	
Never attended school	0 (0%)
Finished primary education	2 (12%)
Finished secondary education	6 (38%)
Bachelor's degree or higher	7 (44%)
No answer	1 (6%)
Professional experience	
Mean (in years) range from 2 to 33 years	15.4
Profession	
Nurse	3 (19%)
Midwife	7 (44%)
Community healthcare worker	5 (31%)
Other	1 (6%)

They [the women] will come [to Dschang] because it is free. But when they think there will be no cost for them and finally they do have to pay transport themselves, it might prevent them from going. (Female hospital staff)

Furthermore, opportunity costs were recognised as an important barrier causing a delay to seek care. Professionals noted that getting screened was not a priority for women because of lack of time. Getting to the screening centre, attending the information sessions while waiting for screening services, was mentioned as important time lost for daily duties that still need to be performed.

For those women, they first focus on the daily issues such as farming, or how to get food for their children. They only get free time to get to town on the day of the market and this is when most come to the center. (Male community healthcare worker)

However, besides the financial constraints, several HCPs noticed mistrust and ambivalence regarding the fact that the screening programme is free of charge:

There are two sides with a program free of charge because some people think that when it is free it means that it is something useless. Because when something is be important it cannot be for free. (Female hospital staff)

Distance to the facility

Distance plays an important role as a disincentive to seek care and increases the disparity between people living in rural versus urban areas.[15 16] This barrier influences women's decision process in seeking care, but also the time she needs to reach the facility, therefore also affecting delay of phase II. Several HCPs recognised distance as an important barrier to attending cervical cancer screening, as an HCP explained:

But the problem is that they [the women] are going to say: I do not have transportation means to arrive from so far. I prefer staying at home because of transport. (Female hospital staff).

Illness factors and education

The decision to seek healthcare depends on the patient's recognition of the disease, but also on its perceived severity requiring medical treatment.[7 17] Nearly all HCPs mentioned a profound lack of awareness on cervical cancer and its symptoms among women, which inhibits the recognition of cervical cancer and the perceived need of screening. A female community healthcare worker illustrated:

The issue is that information doesn't come through. They [the women] didn't know what was happening. They did not know that such things existed. (Female community healthcare worker).

Importantly, nearly all FG participants mentioned that the lack of awareness was more prevalent among women living in rural areas, where formal educational levels were lower. The link between lack of knowledge and education has been frequently mentioned in previous studies[15 16] and was confirmed in the current one. One female HCP of the Dschang District Hospital stated:

And for many of them, even when you try to inform them, you realise how important the level of education is. They understand today but they will forget tomorrow. Or maybe they tell you that they understand and they don't truly. (Female HCP)

As a consequence, HCPs mentioned the importance of using appropriate wording that is easy to understand and will not frighten the patients. For example, the wording seropositivity is not appropriate in the area of HPV testing. However, community workers who are influenced by other campaigns, such as HIV testing, have been using it. As the word 'seropositivity' is closely linked to the HIV status, HCPs suggested to use other terms in case of a positive HPV infection.

Seropositive or seronegative is not appropriate. This wording should not be used in our language. (Male community worker)

However, even if women had basic knowledge, two additional factors for not accessing screening were reported. First, misconceptions about symptoms, transmission or

risk factors, but also fear of the severity of the disease. One of the female FG participants illustrated misconceptions around cervical cancer as women did not experience signs or symptoms for cervical cancer:

> *They will tell you : I am not sick ! There is nothing there.* (Female hospital staff).

Second, fear towards results was frequently observed especially by the community health workers who tried to motivate women to attend screening. Some women may give up on being tested because they think a positive result might be a synonym to death.

> *It is fear. Women are afraid of a potentially positive test result, because they wonder how they are going to make it. There is fear. Fear is the barrier. (…)* (Male community health worker)

Perceived quality of care

Perceived quality of care and previous experiences with the healthcare system influences the decision of prospective patients. Important factors highlighted include satisfaction or dissatisfaction with previous treatment or screening, friendliness and communication of hospital staff and experience with administrative procedures.[7 18 19] Even if HCPs noted that most of the women were pleased with the screening and treatment procedures of the cervical cancer programme, HCPs recognised that some patients perceived structural factors (such as waiting times or administrative procedures) as a barrier. One HCP from Dschang noted:

> *And some patients told us that it takes a lot of time. For them it should be a 10 minute thing. But they enter, they stay one hour at the informative causerie (Informative causerie refers to the informative talk that is given to women to give information on cervical cancer prior to screening.) then they register, they do the sampling and they wait for the results! (…). This prevents them from coming.* (Female hospital staff)

Additionally, the study revealed that administrative procedures could be improved in respect to testing results and respect of privacy. As a male HCP explained:

> *There is…there is as well the result. When a group of women arrive and we give them the results, we will tell one of them to wait…when we tell her to wait it will draw attention from the others. If the first ones are gone and this one need to wait it means…it means that there is a problem (…) and because the other women knew (…) As soon as she is back at home there will be some gossip. People will say that she had to stay.* (Male hospital staff)

Lastly, several HCPs admitted that contact with patients could be improved. They recognised the importance of making the patient feel comfortable as well as the need to address the psychological dimensions of screening such as the fear of the outcome.

> *Making the patient feel comfortable is important as well…sometimes we do not manage to welcome patients as we should.* (Female HCP)

Phase II: delay reaching the screening centr

As mentioned previously, the accessibility of services plays a role in influencing the decision to go to the screening centre. Thaddeus and Maine determine the time spent in reaching a facility as an important second delay, which is very common, particularly in rural areas.[7] HCPs participating in the FGs mentioned two important barriers for women to attend the cervical cancer programme. The first one was the financial cost, which has already been illustrated in the first delay. The second equally important barrier was the distribution of facilities. Reaching screening facilities has been linked not only to a lack of transportation, conditions of roads, but also to the distribution of health facilities. The only facility offering cervical cancer screening in Western Cameroon is the District Hospital of Dschang. Therefore, women in rural areas face a double burden in respect to healthcare: costs and difficulty to reach the facility. Additionally, community healthcare workers faced difficulties to reach villages contributing to the lack of knowledge mentioned under the first delay. Therefore, FG participants suggested that motorcycles could be a feasible solution either to educate women and their families about cervical cancer screening or to provide mobile screening facilities.

> *If we had access to a motocycle, …we could go a little further in the villages. Because we musn't forget that sometimes you're ready but you are not able to travel, to travel further…* (Community healthcare worker)

Phase III: receiving adequate and appropriate screening and treatment

The third delay includes factors related to the healthcare at the facility such as shortage of supplies, equipment or trained personnel and competence of the available personnel. None of the HCPs mentioned factors related to shortage of supplies, equipment or staff, but they perceived that referral systems inside the medical community were still inadequate. One female HCP working at the Dschang screening site explained:

> *Honestly doctors here, they are too distant. … I can count maybe only two that have stopped by to see what we are doing here [at the screening facility] since we have started.* (Female HCP)

HCPs perceived a lack of cervical cancer awareness and interest even in the medical community and wondered if doctors had enough knowledge on when and how to refer women.

Furthermore, the study explored HCPs' perception of the single-visit approach using HPV self-sampling testing. Overall, the concept to be tested and treated on the same day was very well regarded by the HCPs. This point was consistent among the various FGs.

There are many advantages because everything is already there. The woman will not need to travel to receive treatment. (Female HCP)

Furthermore, lower loss to follow-up rates due to reduced travel costs was seen as an advantage. However, several HCPs noted that women were sceptical regarding the procedure of the HPV self-sampling. A female HCP stated:

I do not think that they trust themselves [perfoming the test]. They are already worried that they are doing the test themselves. […] Sometimes the HPV self-sampling is done well but they will ask you to do it again to be psychologically reassured. (Female HCP)

Facilitators of cervical cancer screening

As lack of cervical cancer knowledge was perceived by all FG participants as one of the main barriers. FG participants highlighted the need to increase awareness about cervical cancer symptoms, treatment options and prevention strategies by mentioning the available screening programme. As such, churches or 'traditional chiefs' were identified as key actors. While churches already inform attendees about cervical cancer and the possibility of screening, involvement of the 'traditional chiefs (traditional chiefdoms are entities of various size and importance which were former micro precolonial states. They are organised around the emblematic figure of the chief which have a role both political and spiritual. He has a mediator role between world of the livings and of the ancestors.[20] They are physical entities where various meeting are held as they have a political, social and cultural role.)' was seen as crucial to gain access to meetings organised in the 'cheffery'. Furthermore, as the 'traditional chiefs' have enormous influence, their support was seen as very helpful in reducing barriers to cervical cancer screening, but also in involving men in the cervical cancer screening programmes. As most women need their husband's permission for screening, informing men about cervical cancer screening by the 'traditional chiefs' was seen as an important facilitator in encouraging women to attend the screening.

DISCUSSION

The current study is to our knowledge the first conducted in Cameroon aiming to understand women's potential barriers to a cervical cancer screening programme from a qualitative perspective.

Barriers were organised around the three-delay model and most barriers were identified in phase I (delay in the decision to seek screening).[7] Those identified were mainly around the four themes: (1) health literacy, (2) distance to the screening centre, (3) financial constraints and (4) perceived quality of care. The results were concordant with previous international literature. The following discussion concentrates especially on barriers which can be directly addressed by the cervical cancer screening programme. Factors on the macro level, which are dependent on governmental decisions and policies (such as the distribution of healthcare facilities addressing the existing barrier of distance (theme 2)), will not be addressed.

One of the most important barriers identified in our study was health literacy (theme 1). Health literacy has been defined by the WHO as 'the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health'.[21] According to the results of our FGs, the lack of health literacy was noted particularly in rural areas where education was lower and additional barriers due to financial constraints were higher. Kim and Han reported that increasing woman's health literacy might be the first step towards promoting cervical cancer screening programmes.[22]

From a public health perspective, raising awareness through the use of mass media, such as radio and television, can improve uptake.[12 23] However, HCPs in our study mainly highlighted the importance of tailored cervical cancer awareness campaigns that are adapted to the heterogenous levels of education as well as using local languages. Furthermore, involving community healthcare workers, who are familiar with the local conditions, frequent misconceptions and fatalistic concepts in the community, was mentioned as crucial. This is in concordance with Thaddeus and Maine,[7] who reported that women's recognition of illness and their perception of its severity are important influences on their decision to seek care. Promoting tailored educational campaigns respecting different levels of cervical cancer literacy might increase attendance of cervical cancer screening.[22 24]

Traditional chiefs were identified as important entry points to raise cervical cancer awareness, because they were perceived as essential to reach not only women, but also their male partners. Men play a significant role in the healthcare decisions and health-seeking behaviour of women and they are found to lack awareness and basic knowledge with respect to cervical cancer.[25 26] Involving traditional leaders emerged as one of the key facilitators. Leveraging the governance system of chiefs could promote access to cervical cancer prevention services, including rural women who are especially difficult to reach. While few studies have investigated these actors to date, a recent study by Kapambwe and colleagues showed that the influence of traditional chiefs facilitated access to cervical cancer prevention services in rural Zambia.[27]

Financial constraints (theme 3) were another important barrier described by nearly all participants. Costs included opportunistic costs while attending the screening, but also costs for transportation which increased with distance. Distance from a health centre is a major disincentive in the decision to seek care causing disparity between rural and local areas and has been mentioned frequently in the literature.[7] As such, the single-visit approach minimises this barrier by screening and treating precancerous lesions on the same day. HCPs suggested organising mobile screening. Offering early detection services through mobile units has been shown

to be a practical way to increase physical and economic access to screening.[28]

The last barrier influencing women's decision to seek care was the perceived quality of care (theme 4). In contrast to previous studies,[7–12] participants in our FGs mentioned an interesting aspect towards the programme free of charge. While HCPs valued the screening option offered free of charge (intended to decrease barriers), FG participants explained that several patients questioned the quality of the care and the intentions of the cervical cancer screening programme due to the fact that it is offered free. Therefore, HCPs highlighted the importance to disclose more information about the financing of the programme in order to increase its acceptance.

Furthermore, long administrative procedures, structural challenges leading to a lack of confidentiality and insufficient friendliness of HCPs were mentioned as important factors influencing patients' satisfaction, as well as disincentive for peers or family through word of mouth. A study conducted in Malawi showed that patient satisfaction is of utmost importance and was higher when women had an appointment or benefited from shorter waiting time.[29] Furthermore, the importance of appropriate communication skills has been highlighted in a recent review.[30] As a consequence, addressing these identified structural challenges might have a direct benefit to the programme acceptance.

Even if most barriers were mentioned in the first delay, the study revealed that concerns of the HPV self-sampling persist among patients. While the single-visit approach was acknowledged positively, nearly all HCPs mentioned that most women did not trust self-sampling for HPV and preferred physician sampling. Similar concerns have been found in other studies in low-resource settings, but also in HICs, in which women expressed the fear of doing the test wrong, and then getting wrong results.[23 31] A study already conducted in Dschang in 2013[32] showed similar results. Therefore, our study highlights the need not only to educate women about HPV, cervical cancer and its prevention but also to reassure them about the accuracy of HPV self-sampling. The role of HCPs is central to help women build confidence and trust in themselves as well as in the HPV self-sampling. A reinforced trust in HPV self-sampling could be a real asset in maximising geographical coverage of screening as distance was seen as a major barrier.

The study had strengths and limitations. A strength of this study was its qualitative approach with the aim to explore cervical cancer screening barriers in Cameroon from the perspectives of HCPs. Second, it was conducted on-site with participation of HCPs having different educational backgrounds. A limitation of the study was the methodology of FGs which covered a range of topics considered important and chosen by the participants. Therefore results might not be applicable to the general population as another group may have covered others topics. Also, the methodology of the FG design might have prevented some participants from expressing their honest opinion. However, to limit this influence, small FGs with participants from the same educational background were chosen. Moreover, as FGs were conducted by a Cameroonian anthropologist, interviewer bias was intended to be minimised but cannot be excluded due to his higher education and gender. Finally, this study has been based on the HCPs' perspective. We would need to further evaluate our results directly with women eligible for screening. Currently a second qualitative study with patients is being planned, based on current results, in order to resolve this limitation.

CONCLUSION

Understanding barriers associated with underutilisation of cervical cancer screening is key to increasing overall screening uptake. The perspective of HCPs can be leveraged to improve screening programmes as their global view and experience reveal major findings. Although qualitative results cannot be generalised, we believe that our results are confirmed by the national and international literature.[12–19 21 22] Therefore, reducing those barriers may improve cervical cancer screening programmes at the personal and institutional level. Key strategies to address some of the most important barriers identified in our study should focus on improving health literacy (including the empowerment with respect to HPV self-sampling), involving influential community leaders or institutions (such as churches or traditional chiefs) and finally addressing administrative procedures including HCP's communication skills.

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Reproductive Health

RESEARCH

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"Cervical cancer screening: awareness is not enough". Understanding barriers to screening among women in West Cameroon—a qualitative study using focus groups.

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Abstract

Background: Cervical cancer is the second leading cause of cancer-related death among women in sub-Saharan countries, constituting a major public health concern. In Cameroon, cervical cancer ranks as the second most common type of cancer among women and the leading cause of cancer-related deaths, mainly due to the lack of prevention.

Objectives: Our first and main objective was to understand the barriers affecting women's decision-making process regarding participation in a cervical cancer screening program in the Dschang district (West Cameroon). Second, we aimed to explore the acceptability and perception of a single-visit approach (screen and treat).

Methods: A qualitative study using focus groups (FGs) was conducted from February to March 2020. Female participants aged between 30 and 49 years and their male partners were invited to participate. Thematic analysis was used, and barriers were classified according to the three-delay model of Thaddeus and Maine.

Results: In total, six FGs with 43 participants (31 women and 12 men) were conducted. The most important barriers were lack of health literacy, low accessibility of the program (in respect to cost and distance), and disrespectful treatment by healthcare workers.

Conclusions: Our study identified three needs: (1) enhancing health literacy; (2) improving the delivery of cervical cancer screening in rural areas; and (3) providing training for healthcare providers and community healthcare workers to improve patient-provider-communication.

Trial registration Ethical Cantonal Board of Geneva, Switzerland (CCER, N°2017-0110 and CER-amendment n°3) and Cameroonian National Ethics Committee for Human Health Research (N°2018/07/1083/CE/CNERSH/SP). NCT: 03757299

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Plain Language Summary

Cervical cancer is the second leading cause of cancer-related death among women in sub-Saharan countries, constituting a major public health concern. In Cameroon, cervical cancer ranks as the second most common type of cancer among women and is the leading cause of cancer-related deaths, mainly due to the lack of prevention measures, such as cervical cancer screening.

The main aim of the current study was to understand barriers that affect women's decision-making processes regarding participation in a cervical cancer screening program in the Dschang district in West Cameroon.

A qualitative study methodology using focus group discussions was conducted from February to March 2020. Female participants aged between 30 and 49 years and their male partners were invited to participate.

In total, six discussion groups with 43 participants (31 women and 12 men) were conducted. The most important barriers were a lack of health literacy, limited access to the program because of cost and distance, and disrespectful treatment by healthcare workers.

Our results identified three key areas for improvement: first, increasing health literacy; second, providing cervical cancer screening in rural areas; and third, training healthcare providers and community healthcare workers in better patient-provider-communication.

Keywords: Cervical cancer, Prevention, Sub-Saharan Africa, Health literacy, Barriers

Introduction

According to the World Health Organization (WHO), 604,127 cervical cancer (CC) cases were diagnosed worldwide, and 341,831 deaths were registered in 2020, most of them occurring in low- and middle-income countries (LMICs) [1]. In sub-Saharan Africa (SSA), including Cameroon, CC is the second leading cause of cancer among women [1, 2]. A total of 2770 new cases were diagnosed in Cameroon in 2020 and 1787 deaths were documented, rendering CC the leading cause of cancer-related deaths among women [2]. Thus, CC is a major public health concern in Cameroon.

Although organized screening programs with high coverage rates have led to a significant reduction in the number of new cases and mortality rates in high income countries, the incidence and mortality rate of CC remains high in Cameroon, and in many LMICs [3, 4]. In response to this situation, the WHO launched a global strategy to accelerate the elimination of CC in November 2020 during the 73rd World Health Assembly. The WHO's key objectives for 2030 are achieving 90% human papillomavirus (HPV) vaccination coverage for girls, 70% screening coverage and, 90% access to treatment of precancerous and cancerous lesions [5, 6]. Scaling-up or reinforcing these prevention strategies is considered crucial to reduce the gap in health inequalities between high-income and low- and middle-income countries [3].

Aiming to reduce the burden of disease caused by CC in the Dschang district, a 5-year CC screening program was introduced in 2018 at the Dschang District Hospital. However, despite the free provision of clinical services, in the first 6 months the program revealed a 50% lower participation rate than expected [7]. Although previous quantitative studies in SSA have identified a lack of knowledge as an important barrier to CC screening, additional factors may also contribute to the lower participation rate [8–10]. To understand the complex barriers affecting women's decision processes regarding participation in CC screening, a qualitative study was conducted to explore the perspectives of women and their partners in the Dschang district. The secondary objective of the study was to understand the acceptability and perception of the single visit approach.

Methods

Study site

The qualitative data were collected between February and March 2020 in the district of Dschang, located in the west of Cameroon. Dschang city and surrounding areas have an estimated population of approximately 220,000 inhabitants. The study is part of a large trial called the Testing, Triage and Treatment (3T)-Approach, which involves a CC screening program. The 3T-Approach program was implemented in 2018 at the Dschang District Hospital over a 5-year period (2018–2023). This program is a partnership between the University Hospitals of Geneva (Switzerland), University Hospital of Yaoundé (Cameroon), and the University of Dschang (Cameroon) and aims to include 6,000 female participants. The program is supported by the Ministry of Health and is based on a "one day visit" 3T-Approach. The 3T-Approach provides HPV self-sampling, followed by visual assessment for triage of HPV-positive women and treatment by thermal ablation if required, at no cost to participants [4]. HPV self-sampling is one of the three WHO-recommended

methods for CC screening. After individual counselling, each woman receives an HPV self-sampling kit and written information, enabling them to collect their own vaginal sample with a dry swab in a private setting. Following rapid HPV testing (Xpert^{TM} HPV), HPV-negative women are reassured and advised to undertake a next screening 5 years later. HPV-positive women undergo visual inspection with acetic acid and visual inspection with iodine (VIA/VILI) and treatment (if indicated) or follow-up [10]. Further details can be found in a recent publication [10].

The study was approved by the Ethical Cantonal Board of Geneva, Switzerland (CCER, N°2017-0110 and CER-amendment n°3) and the Cameroonian National Ethics Committee for Human Health Research (N°2018/07/1083/CE/CNERSH/SP). NCT: 03757299.

Study setting and design

A qualitative methodology was employed, using focus group (FG) discussions with women eligible for the 3T-Approach (inclusion criteria: 30–49 years of age, compliance with the study protocol) and their male partners. FG participants were recruited from three surrounding districts of the Dschang District Hospital, including an urban area (Fiala-Foreke), a semi-urban district (Siteu) and the district of Fometa, which can be considered rural (Fig. 1).

A qualitative methodology using focus groups (FGs) was chosen as an appropriate approach for capturing insights into the ways people perceive and interpret their surroundings [11, 12]. As men often influence women's decisions about healthcare seeking, positively or negatively, male partners were invited to participate in FGs [13, 14].

Using a semi-structured, pretested interview guide three underlying topics were included to answer the research question: a) knowledge about CC; b) barriers to CC screening; and c) perception and acceptability of the 3T-Approach using HPV-self sampling and providing direct treatment. The FG discussions were conducted either in the home of one of the participants or in a private meeting room provided by the hospitals. As CC is a highly sensitive topic related to sexuality, female health, and gender differences in Cameroon, FGs were conducted in female-only and male-only groups, to allow respondents to communicate freely in group discussions based on shared experiences [12].

Each FG was led by two researchers: one Cameroonian anthropologist (AMD) who facilitated the group discussion in French and one Cameroonian epidemiological student (MEO) who observed group dynamics and body language.

Fig. 1 Map of the district of Dschang, West Cameroon, modified from Ministère de la Santé Publique du Cameroun (https://dhis-minsante-cm.org/portal/)

Recruitment and sampling

We employed non-probability sampling using multiple recruitment strategies. Irrespective of whether they had already attended CC screening, women were invited to participate in the FG by community health workers and personal contacts using a snowball method in three districts. Women living in one of the three districts were eligible to participate in the FGs. At the end of each female FG, women were asked to invite their male partners, male friends, or neighbours to participate in a scheduled FG for men.

In accord with qualitative methodology standards, we applied the principle of theoretical saturation, meaning that no more information related to the main research questions emerged.

Data analysis

All FGs were recorded after having obtained written consent from each participant. FGs were transcribed and coded using content analysis, using Atlas.ti version 6.1 software. After individual coding, both researchers identified the main and sub-topics common to every group, and outlined the knowledge, perceptions and identified

barriers of the women and their partners. Barriers were classified using the conceptual framework of Thaddeus' and Maine's three-delay model [15]. This framework was utilized in a previous study exploring the barriers to CC screening in Dschang district from the perspective of healthcare providers, enabling us to compare findings from both studies [16]. According to this model, the decision to seek healthcare can be classified into three delays. The first delay explores factors influencing a woman's decision-making process, which is affected by her role, the cultural context she is living in, but also the knowledge and the experiences of herself, her family and/or community. The second delay is mainly influenced by factors necessary for reaching the healthcare facility. Such factors include the distance to the facility, road conditions, cost of transportation, and indirect costs, such as being absent from work. The last (third) delay describes factors at the healthcare facility such as the availability of materials or staff. Although the model was originally applied in the context of maternal mortality, it can also be applied to other health situations to identify barriers to screening and assist in the development of appropriate solutions.

Results

In total, six FGs with 43 participants (31 women and 12 men) were conducted in the three districts; four groups consisted of women only, while two groups consisted of men only.

The FG discussions with a mean of seven participants lasted approximately 40 min. Most participants were married, with an average age of 41 years (range 30–56 years). More than two thirds of participants had completed a minimum of secondary high school education. However, clear gender differences in education were apparent: only four women (13%) reported tertiary education attainment, compared with five of 12 (41%) male participants. Gender differences were also found in occupation: only women worked in the household (11 of 11), women were more likely to work as farmers (16% of women compared to 8% of men) and fewer women worked in professions requiring tertiary education (e.g., as teachers) or were currently studying (12% of women vs. 33% of men) (Table 1: Socio-demographic characteristics).

Table 1 Socio-demographic characteristics of FG participants

Variable	N	Percentage (%)
Total	43	100
Gender		
Men	12	28
Women	31	72
Educational level		
Primary school	8	18
Secondary school	26	61
Tertiary education	9	21
Marital status		
Single	4	9
Married/partnership	37	86
Divorced or widowed	2	5
Profession		
Responsible for household	11	25.5
Farmer	6	14
Business	15	35
Other (teacher, student)	11	25.5

Barriers to CC screening

Barriers to CC screening emerged in all FGs, which were then classified according to the conceptual framework of the three-delay model of Thaddeus and Maine [15]. As described above, although the model was originally suggested to explain factors leading to increased maternal mortality, it can be applied to different health situations because it addresses obstacles influencing individuals' decisions about seeking healthcare at different levels (i.e., delays). Therefore, the identified barriers can be linked to the individual level (women and their partners) but also the structural level (health-system directly or indirectly) and inform HCPs and policy experts.

Phase I: delay in decision to seek screening

According to the three-delay model, the healthcare seeking process begins with the decision to seek care. Research has found that various factors will shape women's decision-making process regarding screening for CC. Among the barriers associated with the decision to seek care, sociocultural factors are most commonly reported in the first delay [15]. The following encountered barriers were reported in our study:

1. Psychological barriers

   Among the female participants, experiences, emotions, and behaviours influenced the decision to seek healthcare. Among these women, the *"fear of the result"* was deemed to be important, as cancer is perceived as a fatal disease in Dschang District.

   "Here at home, cancer is a disease that we are afraid of, because in most cases when we [as a family] have already had family members with blood cancer, breast cancer, prostate cancer, who eventually died. So, it's a disease that scares us." (Female P11B)

Participants reported stigma related to fear regarding CC screening results. Women often see themselves as being personally responsible for being diagnosed with CC. A woman from Siteu explained:

"(…) she went to the hospital. When she comes back, you can see that her appearance has changed. She's not the way she used to be, because she knows her result was not good. What makes her ashamed now is that she thinks to herself that you know her result, but you don't." (Female P7A)

Furthermore, because previous studies have reported that male partners play an important role in women's decision-making process, female FG participants were asked about this issue [14]. In contrast to other studies, few women described their spouses as being unsupportive towards them. However, in this situation, relationships were complicated by factors such as substance abuse. A woman from Fiala explained:

"Influence of the husband: People who are drinkers often do not have time for matters concerning children, or anything that will cost them money." (Female P21C)

2. Knowledge-related barriers
   Both female and male participants believed that a lack of knowledge and/or insufficient information about CC screening was one of the most important barriers. Several female and male participants highlighted that most men and women in the community did not know the causes or symptoms of CC. Emphasis was placed on the lack of understanding, particularly regarding knowledge about prevention strategies and treatments for CC at an early stage. A man from Fiala explained:

"…it is a disease that seems new to us. When we were young, we didn't hear about it, but today we are told that there is cancer that attacks the cervix. It bothers us that we do not know where it comes from." (Male P25B)

Phase II: delay reaching the screening centre

Two important barriers emerged from the FGs with both women and men: the financial cost of attending the CC screening program and the time required to reach the healthcare facility where the CC screening program was offered.

Respondents of both genders mentioned direct and indirect costs as important barriers to attending screening. Even if women were aware that the CC screening program was free of charge and perceived this as an important motivational factor, the additional costs of transportation, being absent from work, and having to take care of their children, were still an issue.

The district hospital of Dschang is one of the few facilities that offers CC screening in Western Cameroon. Hence, women, especially those who live in rural areas, face a double burden in respect to healthcare: cost and the difficulty of reaching the facility.

Phase III: receiving adequate and appropriate screening and treatment

The third delay involves factors related to the quality of healthcare at the facility, which can be divided into technical quality and patient experiences. Insufficient technical quality refers to shortages of supplies but also the direct application of clinical services. On the other hand, patients' experiences include non-health needs. In a working paper for the World Health Organization, Gostin et al. defined eight domains of health responsiveness, which included (1) respect for the dignity of persons; (2) autonomy to participate in health-related decisions; (3) confidentiality; (4) prompt attention; (5) adequate quality of care; (6) communication; (7) access to social support networks; and (8) choice of healthcare providers [17].

In our study, FG participants identified in this phase inadequate health communication and disrespectful treatment by HCPs as the two most important barriers to the CC screening program. Participants highlighted that information regarding CC screening needed to be communicated effectively and in a way that could be easily understood by both women and men. Participants in our study also emphasised that healthcare providers (HCPs) need to acknowledge that, besides time and money, the decision to attend screening requires courage, due to the fear of a positive result after screening (see delay 1). Therefore, all women attending screening should be acknowledged by HCPs and treated with respect on the day of their consultation.

In addition, a woman's prior or current experience with an HCP that did not treat her with respect may render her less likely to access the CC screening program and reduce the chances of her returning for a follow-up visit.

"You know others initially traumatize people. For example, the woman [referring to a female HCP] who was recording there, she [….] asks Poupoupou questions (brutally/quickly)! [laughs] [….] She stresses you out by asking the questions quickly. No, that's not the way to do it. She needed to slow down a bit." (Female P13B)

Furthermore, additional negative experiences with HCPs or insufficient information (for example, information regarding the number of days or length of the CC screening) were reported, potentially causing women to actively discourage other women to get screened.

The secondary objective of the study was to understand the acceptability and perception of the single visit approach (3T). While none of the female participants referred to the fact that screening and treatment were offered during the same visit, several women expressed mixed attitudes towards the HPV self-sampling method. While the intention of the HPV self-sampling is to reduce shame and provide more intimacy by enabling women to collect their own vaginal HPV swab, some women perceived it as a way for the program to work more effectively and save HCP's time. Others questioned their ability "to do it right" and would have appreciated clear support from HCPs, as a woman from Fiala explained:

> *"I would still have suggested that they should form a team to help those who do not know how to do it." (Female P41C)*

However, while men understood their partners' concerns, they also perceived the HPV self-sampling method as an adequate way to protect their "wife's nudity". A man from Fometa said:

> *"I choose the method where it is the woman herself who takes it. [Laughs] When she samples it herself, she's not even ashamed since she's doing it alone. But there are women who are even ashamed to examine their sexual parts in private." (Male P26B)*

The results of the FG discussion revealed that barriers to attend CC screening existed in all three delays. The following section will discuss the encountered barriers in the context of the current literature and suggest possible interventions to overcome them.

Discussion

To the best of our knowledge, the current study is one of the few qualitative studies conducted in Cameroon that aims to understand the barriers to attending a CC screening program using the 3T approach, and to suggest possible solutions. Most of the following discussion will focus on encountered barriers at the micro level (HCPs or patients) or meso level (healthcare institutions) that can be addressed by the CC program itself. In this sense, the three most important barriers encountered in all three delays were: (1) knowledge-related barriers (2) difficulties reaching the healthcare centre and (3) disrespectful treatment by healthcare staff. Therefore, the following improvements to the CC program should be made: (1) the advancement of health literacy (at the user and the provider side), (2) the delivery of CC screening and (3) the provision of respectful healthcare.

In the following discussion, we will discuss these principal findings in relation to the findings of previous studies.

- *Enhancing health literacy*

  The identified lack of awareness or insufficient knowledge is associated with a lack of health literacy. Health literacy has been defined by the WHO as "the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health" [18]. As shown in the current study, several participants were not aware of organizational aspects of the CC program (such as days of screening or duration of consultation) which inhibited their ability to "use information" and "maintain good health".

  Lack of health literacy was noted to be greatest in rural areas in which education was lower and additional barriers due to the financial constraints held greater weight. Kim et al. reported that increasing health literacy is the first step in promoting CC screening programs [19]. In this review Kim and colleagues explore the linkage between CC screening behaviours and health literacy. The review indicated that lower participation rates were linked with low knowledge about CC, as well as social determinants beyond health, such as education. Therefore, increasing health literacy in the Cameroonian context entails not only the provision of knowledge about CC symptoms, but also education about CC prevention. Women in our study reported difficulty attending screening for a disease that they did not know about. In addition, respondents were not aware of the importance of prevention and detection of CC at an early stage. This observation is in line with previous studies conducted in Africa, Europe, and Asia, highlighting the need to carry out community education for women and men about the importance of preventive screening, because precancerous lesions are often asymptomatic [20–27]. In addition, in a study conducted by Roux et al. to examine the CC screening program in Dschang, HCPs reported that women's misconceptions about CC symptoms and prevention strategies explained why women did not access CC screening. According to Roux et al., improving health literacy also encompasses addressing fatalistic perceptions and stigma [16]. Because

CC is perceived to be fatal, and sometimes viewed as a punishment, screening can stimulate emotions such as fear and shame. Consequently, it is important to discuss stigma as a barrier to CC screening and prevention [23, 25, 26].

- *Improving delivery of CC screening*
  Nearly all female and male participants mentioned that difficult living conditions act as a barrier, particularly poverty and distance to CC screening facilities. The role of distance is a major barrier in the decision to seek treatment. Previous studies have reported that the disparity between rural and local areas is exacerbated by poverty. [4, 16, 25] Participants identified mobile screening facilities as a practical way to improve physical and economic access to CC screening. A female participant explained:
  "If we come to find you there, we sacrifice ourselves; we close our shops, we know that we are sacrificing ourselves (…). When we were tested for HIV, no one left. They came here, they tested over a hundred people. Whereas if we said we were going to the hospital nobody was going to leave. …" (Female P6A).
  However, even if mobile screening options could address the factors mentioned in the second delay (cost and distance), comprehensive community strategies remain critical for improving women and men's health literacy and supporting women's decision-making processes regarding attending CC screening. Furthermore, participants highlighted the importance of CC awareness campaigns using personal contact, but also mass media, such as radio and television, which previous studies have reported to be used successfully [28, 29].
- *Provision of respectful healthcare*
  Healthcare utilization has been linked to the quality of care patients receive. The current study revealed barriers to CC screening, particularly in respect to communication and respect towards patients. Female participants not only outlined the previously described organizational aspects of the CC screening program, they also reported that disrespectful communication of HCPs negatively influenced their decision to access CC screening. As Larson et al. reported in a recent study in seven African countries, poor provider communication is linked to lower satisfaction, influencing patients' likelihood of returning for a follow-up exam [8]. Improved communication skills could also address concerns about the application of the HPV-self-test, which was highlighted by several women. This possibility is in accord with previous studies reporting that women's concerns about the self-HPV test were present irrespective of their economic situation [30, 31]. Interestingly, a recent study reported a positive correlation between a patient's experience and the level of education of HCPs, as well as the patient's educational level [8]. We propose two possible explanations for this association. First, patients with a higher level of education are more likely to understand what is being said. Second, HCPs may use language based on the educational level of the users, hence increasing the patient's understanding of the consultation with the HCP. Because of the qualitative nature of our study, we were unable to test for this correlation. However, as the education level in the Dschang District/Cameroon is relatively low, it would be useful for future research to explore this association. This applies also to the involvement of community healthcare workers in the CC screening program. Community healthcare workers play an important role in motivating women to attend CC screening. However, as their educational level is often relatively low, training should include communication skills, with a focus on the importance of always treating patients with respect.
  The current qualitative study is among the first to explore barriers to CC screening in the rural area of Dschang. However, several limitations should be acknowledged. First, due to its qualitative methodology, the range of topics considered important by the FG participants does not necessarily reflect their relative importance in the population. Second, the FG methodology might have influenced some participants to give answers that they thought were socially acceptable. Nonetheless, because all FGs were conducted by an experienced anthropologist from Cameroon in a confidential location, we believe that most participants felt comfortable expressing their personal opinions. Finally, although extensive efforts were made to include women and men from different settings (rural vs. urban, with diverse socio-economic characteristics), the sample size was relatively small, and the possibility of selection bias cannot be excluded.

Conclusion

Despite the limitations of our study, the current results corroborate many previous studies and are therefore considered to be generalizable for similar settings. The framework of the three-delay-model of Thaddeus and Maine allowed us to identify barriers to CC screening at the micro- and meso-levels in the Dschang district in all three delays. While barriers in the first two delays, including knowledge- and distance-related barriers, have been reported in previous studies in SSA, our study highlighted the importance of improving the quality of healthcare provided, especially in respect to communication.

Reducing identified barriers may be beneficial at the personal and institutional levels, supporting health system strategies to improve health equity.

Therefore, the following key strategies are suggested: (1) enhancing health literacy by strengthening community health activities; (2) improving the delivery of CC screening activities in rural areas; and (3) providing training for HCPs and community healthcare workers to improve patient-provider-communication.

Abbreviations

FG: Focus group; CC: Cervical cancer; HCP: Healthcare provider; HIV: Human immunodeficiency virus; HPV: Human papillomavirus; LMICs: Low- and middle-income countries; SSA: Sub-Saharan Africa; VIA/VILI: Visual inspection with acetic acid and visual inspection with iodine; WHO: World Health Organization.

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Authors' contributions

MEO supported all phases of the research; she was responsible for the development of the study protocol, recruitment of participants, data collection and data analysis. AMD supported the recruitment of the participants, the process of data collection and data analysis, and wrote the manuscript. PV developed the main idea and provided essential comments on the final manuscript. PP assisted and supervised the conception, writing and revision of the manuscript. NCS helped in all phases of the research and participated in writing the draft and finalizing the manuscript. BK and JS assisted with the design of the study and recruitment of the study participants and provided essential comments on the final manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets (transcripts) generated and analysed during the current study are not publicly available due to the sensitivity of the data. The interview guide or summaries of transcripts, including categories and codes, can be made available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The study is part of a larger trial, which was approved by the Ethical Cantonal Board of Geneva, Switzerland (CCER, N°2017-0110 and CER-amendment n°2) and the Cameroonian National Ethics Committee for Human Health Research (N°2018/07/1083/CE/CNERSH/SP).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Appendix 10

Control/Tracking Number: 2022-RA-566-ESGO
Activity: Abstracts
Current Date/Time: 6/2/2022 2:45:12 AM

Cost-effectiveness of cervical cancer screnning strategies among women in Cameroon

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Abstract:
Introduction/Background: Sub-Saharan Africa has the highest cervical cancer burden worldwide. Before implementing a cervical cancer screening programme, National authorities and decision-makers need to balance the benefits and costs of context-sensitive solutions. Our aim was to assess the cost-effectiveness of two cervical cancer screening strategies in Cameroon: i) HPV self-testing (Self-HPV), and (ii) Self-HPV and triage with Visual Inspection with Acid acetic (VIA) (Self-HPV/VIA) at frequencies twice to seven times between 30 and 60 years, at 5 or 10-year intervals.
Methodology: A lifetime decision-analytic model has been calibrated to Cameroonian women. Costs parameters have been estimated based on real-life screening activities within the 3T-project in Cameroon. Utilities were accounted for in the model. Cost-effectiveness ratios have been assessed for each strategy and screening frequency compared with the absence of strategy.
Results: Four combinations appeared to be the most cost-effective: Self-HPV/VIA at 35-45, and at 30-40-50 years, and Self-HPV every 5 and 10 years between 30 and 60 years old. The incremental cost per QALY gained for Self-HPV/VIA strategies was 403USD (393-413) at 35-45 years, and 690USD (671-708) at 30-40-50 years, 1035USD (1005-1057) for Self-HPV at 30-40-50-60 years, and 1592USD (1553-1620) at 30-35-40-45-50-55-60 years. Cervical cancer mortality was mostly lower with Self-HPV strategies.
Whatever the screening frequency, in both strategies, about 50% of costs were related to Self-HPV testing, while for the Self-HPV/VIA strategy, triage accounted for approximately 1% of costs. At equal frequencies, costs of precancerous treatment were higher in Self-HPV than Self-HPV/VIA strategies, due to high overtreatment rate of CIN1 in the absence of triaging. The costs of cancer treatment were comparable in both strategies.
Conclusion: Cost-effectiveness depends on the type and frequency of screening. These results may support decision-makers in selecting adequate screening strategies and frequencies according to their willingness to pay per QALY gained.