Co-produced Community Action for Cervical Cancer Screening Uptake (Act4CC): a randomized controlled trial in rural areas of the West Region of Cameroon

An ancillary study to the GENOVA study – HPV Screening with Triage by HPV Genotyping versus Visual Inspection with Acetic Acid: A Randomized Controlled Trial (CCER N° AO_2021-0006)

Research legislation:	Law No. 2022/008 of 27 April 2022 relating to medical research involving human subjects in Cameroon
Type of Research Project:	Research project involving human subjects
Risk Categorization:	No greater than minimal risk
Principal investigator:	**Prof. Patrick Petignat** Division of Gynecology, Geneva University Hospitals Boulevard de la Cluse 30, 1205 Genève Phone: +41 22 372 4300 E-mail: patrick.petignat@hcuge.ch

PROTOCOL SIGNATURE FORM

Study Title	*Co-produced Community Action for Cervical Cancer Screening Uptake (Act4CC): a randomized controlled trial in rural areas of the West Region of Cameroon*

The sponsor-principal investigator, the co-principal investigator (at the local site) and the co-investigator/project leader have approved the protocol version **1.2 (dated 20 April 2023)**, and confirm hereby to conduct the project according to the protocol, the Cameroonian legal requirements (1), the current version of the World Medical Association Declaration of Helsinki (2) and the principles and procedures for integrity in scientific research involving human beings.

Sponsor-Principal Investigator:

Prof. Patrick Petignat
Head of Gynecology Division, Geneva University Hospitals
Boulevard de la Cluse 30, 1205 Geneva, Switzerland
Phone: +41 22 372 4300 / E-mail: patrick.petignat@hcuge.ch

Date: 20/04/2023 _____ Signature: _____

Co-Principal investigator at local center/site:

Prof. Bruno Kenfack
Head of Gynecology and Obstetrics Department, Annex Regional Hospital of Dschang
Dschang, Cameroon
Phone: +237 33 45 12 06 / E-mail: brunokenfack@gmail.com

Date: 20/04/2023 _____ Signature: _____

Co-investigator / project leader:

Dr Ania Wisniak
PhD Candidate at the Institute of Global Health, Faculty of Medicine, University of Geneva
Geneva, Switzerland
Phone: +41 78 908 86 65 / E-mail: ania.wisniak@hcuge.ch

Date: 20/04/2023 _____ Signature: _____

Other co-investigators / project collaborators:

Virginie Yakam
Annex Regional Hospital of Dschang (Cameroon)
yakamvirginieflore@gmail.com

Prof. Cicely Marston
London School of Hygiene and Tropical Medicine (United Kingdom)
cicely.marston@lshtm.ac.uk

Prof. Nicole Schmidt
Catholic University of Applied Sciences Munich (Germany)
Nicole.Schmidt@ksh-m.de

Prof. Gregory Edie Halle-Ekane
University of Buea (Cameroon)
halle-ekane.edie@ubuea.cm

TABLE OF CONTENTS

GLOSSARY OF ABBREVATIONS

BASEC	*Business Administration System for Ethical Committees*
BRH	*Bafoussam Regional Hospital*
CBPAR	*Community-based participatory action research*
CCA	*Community co-produced action*
CDMS	*Clinical Database Management System*
CHW	*Community health worker*
CRF	*Case report form*
DSI	*Direction of Informatics Systems*
FGD	*Focus group discussion*
FOPH	*Federal Office of Public Health*
HAL	*Health area leader*
HIV	*Human immunodeficiency virus*
HPV	*Human papillomavirus*
HUG	*Geneva University Hospitals*
IHC	*Integrated health center*
LMIC	*Low- and middle-income country*
RCT	*Randomized controlled trial*
UIC	*Unit of Clinical Investigations*
VIA	*Visual inspection after application of acetic acid*
WHO	*World Health Organization*

1 STUDY SYNOPSIS

1.1 Synopsis in English

Sponsor-Principal Investigator	Prof. Patrick Petignat Head of Gynecology Division, Geneva University Hospitals Boulevard de la Cluse 30, 1205 Geneva, Switzerland Email : Patrick.Petignat@hcuge.ch Tel : +41 22 372 4300
Study Title	Co-produced Community Action for Cervical Cancer Screening Uptake (Act4CC): a randomized controlled trial in rural areas of the West Region of Cameroon *An ancillary study to the GENOVA study – HPV Screening with Triage by HPV Genotyping versus Visual Inspection with Acetic Acid: A Randomized Controlled Trial (CCER N° AO_2021-0006)*
Short Title / Study ID	Act4CC (Study ID to be determined)
Protocol Version and Date	Version 1.2 (dated 20/04/2023)
Study Registration	Clinicaltrials.gov – *not yet registered*
Investigators	**Co-principal investigator at local study site:** Prof. Bruno Kenfack Dschang Annex Regional Hospital Dschang, Cameroon Email: brunokenfack@gmail.com Tel: +237 33 45 12 06 **Project leader:** Dr Ania Wisniak Geneva University Hospitals, Division of Gynecology 1205 Geneva, Switzerland Email: ania.wisniak@hcuge.ch Tel: +41 22 372 4270 **Other co-investigators / project collaborators:** Virginie Yakam Dschang Annex Regional Hospital (Cameroon) Prof. Cicely Marston London School of Hygiene and Tropical Medicine (United Kingdom) Prof. Nicole Schmidt Catholic University of Applied Sciences Munich (Germany) Prof. Gregory Edie Halle-Ekane University of Buea (Cameroon)
Study Center(s)	**Bafoussam Regional Hospital** Marche B, Bafoussam West Cameroon
Study Category and Rationale	No greater than minimal risk: the planned measures for sampling biological material and collecting personal data entail only minimal risks and burdens
Background and Rationale	Cervical cancer is the fourth most frequent cancer worldwide, causing over 300'000 deaths yearly. The global burden of this disease, however, is unequally distributed, with over 90% of cervical cancer deaths occurring in low- and middle-income countries (LMICs). In Sub-Saharan Africa, the incidence of cervical cancer cases has continued to rise in past decades and it is now the first cause of cancer death among women. Global inequalities in the burden of cervical cancer can mainly be attributed to the high vaccination rate against human papillomavirus (HPV) and the extensive screening of HPV

	infection and/or precancerous lesions in high-income countries. In contrast, uptake of these preventive measures has been insufficient in many LMICs. In the face of these large regional disparities despite the preventable nature of cervical cancer, the World Health Organization (WHO) launched a global initiative in 2020 for the worldwide elimination of cervical cancer as a public health issue. To achieve this, the following targets were established to be met by 2030: i) vaccination of 90% of girls against HPV, ii) screening of 70% of women with a high-performance test, and iii) treatment of 90% of women diagnosed with precancerous lesions. The reasons for insufficient screening coverage in LMICs are multifactorial. Some of the main obstacles identified are a lack of trained personnel and adequate infrastructures, cultural and social barriers, financial constraints, and loss to follow-up. Previous experience of our research team at the Annex Regional Hospital of Dschang, in the West Region of Cameroon, has shown that even with an efficient screening strategy in place (using a single-visit "test-triage-treat" strategy), adequate population coverage remains a challenge. To address the lack of screening uptake, the WHO recommends the development of context-specific and culturally appropriate screening strategies, by integrating and engaging local stakeholders, health care providers and communities in the program design and implementation process. Community-engaged approaches ensure that barriers to screening are well understood and addressed, leading to the development of screening programs which are acceptable and accessible to the local population. Community-based participatory action research (CBPAR) aims to engage local stakeholders and those affected by a particular problem in a collaborative decision-making research process, from study design and preparation to implementation and dissemination of results, combining research with action for social change. This enables the development of projects that are well adapted to the local context and integrated within the health care system, and potentially enhances program sustainability. In the field of cervical cancer prevention, several research teams have successfully used community-based research to increase the population's awareness of cervical cancer and screening uptake. Assessing the effectiveness of a cervical cancer screening strategy based on community co-produced action in rural Cameroon has the potential to improve uptake of screening services in a sustainable way, and thus contribute to eliminating cervical cancer as a public health problem.
Study Intervention	Community mobilization for co-produced action (hereafter referred to as "community co-produced action") with the aim to develop and implement one or more community-based strategies to increase uptake of HPV-based cervical cancer screening (including primary HPV screening, triage of HPV-positive patients and treatment of patients triaged positive) in the health district of Mifi, West Region of Cameroon.
Control Intervention	Recruitment of women for cervical cancer screening coordinated centrally at district level (from the district capital Bafoussam) following procedures previously established within a cervical cancer screening program in the health district of Dschang since 2018. This standard procedure includes the training of 2 community health workers (CHWs) by health area to raise awareness around cervical cancer, who recruit women by going door-to-door or through community meetings in their respective health areas.
Research Questions	<u>Primary research question (RQ):</u> **RQ1**. Does community co-produced action (CCA) increase uptake of cervical cancer screening (including primary screening, triage, treatment and follow-up when necessary) in rural Cameroon compared to a traditional hospital-based recruitment strategy for screening? <u>Secondary research questions:</u> **RQ2**. What are the determinants of access to cervical cancer screening in rural areas of the West Region of Cameroon? *(formative research)* **RQ3**. How do affected communities and stakeholders perceive cervical cancer screening strategies developed through CCA compared to a traditional hospital-based strategy? *(process evaluation)* **RQ4**. How is CCA implemented in selected communities and how is the co-production process perceived by participating stakeholders? *(process evaluation)* **RQ5**. What is the cost-effectiveness of an intervention using CCA to provide access to screening services in a rural population in Cameroon? *(economic evaluation)*
Objective(s)	**RQ1 Objectives** Primary objective:

	1.1. To determine whether a recruitment process for HPV-based cervical cancer screening developed using CCA allows better population coverage than the traditional hospital-based approach at district level, in rural areas of the West Region of Cameroon. Secondary objectives: 1.2. To assess the effectiveness of CCA for primary HPV screening uptake compared to a traditional recruitment strategy; 1.3. To assess the effectiveness of CCA for compliance to the complete screening procedure (including triage, treatment and follow-up) among women who test HPV positive upon primary screening; 1.4. To determine whether the effectiveness of CCA for cervical cancer screening uptake differs according to women's socio-demographic characteristics. **RQ2 Objectives** 2.1. To determine the attitudes, practices and knowledge related to cervical cancer prevention among community members, local stakeholders and health care providers in rural health areas of the West Region of Cameroon; 2.2. To identify potential barriers and facilitators of cervical cancer screening in rural Cameroon; 2.3. To assess whether health literacy among eligible women acts as a facilitator of cervical cancer screening in Cameroon. **RQ3 Objectives** 3.1. To explore the acceptability of recruitment and screening strategies by users (patients) and healthcare providers in both study arms, including the satisfaction with and perceived appropriateness of the strategies. 3.2. To evaluate the feasibility in the context of rural Cameroon of the recruitment and screening strategies developed using CCA, including linkage to triage and treatment. **RQ4 Objectives** 4.1. To evaluate whether the CCA intervention was implemented as planned; 4.2. To determine the challenges and enablers of successful CCA implementation; 4.3. To assess acceptability of the CCA process by participating community members and stakeholders; 4.4. To identify any unintended consequences of the CCA process within communities selected for the intervention. **RQ5 Objectives** 5.1. To determine the cost-effectiveness of CCA (including facilitation of workshops, implementation planning, etc.) for screening and treatment of precancerous cervical disease in the West Region of Cameroon.
Study Design	The use of community co-produced action to increase cervical cancer screening coverage in the health district of Mifi, West Region of Cameroon, will be evaluated using a mixed-methods approach: **1. Formative research** Qualitative (focus group discussions, in-depth interviews) and quantitative (surveys) methods will be used to assess the determinants of access to cervical cancer screening in rural communities of the region. **2. Single-center open-label cluster-randomized controlled trial (RCT)** Fourteen rural health areas of the health district will be randomized into two study arms. Cervical cancer screening coverage will be compared between the health areas allocated to the intervention arm (community co-produced action) and the control arm (standard hospital-based recruitment and screening strategy already in place in the health district). **3. Process evaluation** Qualitative research (focus group discussions and in-depth interviews) will be led with relevant local stakeholders to assess the acceptability and feasibility of recruitment and screening strategies used in both study arms, as well as acceptability of the CCA process and whether CCA was implemented as planned within the community. **4. Economic evaluation** A cost-effectiveness analysis will be conducted to evaluate the incremental cost-effectiveness ratios of individual strategies implemented and of the CCA process overall.

	Throughout all phases of the study, principles of community-based participatory action research (CBPAR) will be integrated in the project design, such as forming a partnership with the community, assessing community strengths and dynamics in the formative research phase, co-designing health interventions, and interpreting and disseminating research findings in a culturally appropriate format and in a way that is relevant for the community and promotes sustainable action. Community members will also be integrated in the partnership as "co-researchers" during phases of implementation planning, designing methods for data collection and monitoring of research activities.
Outcomes	Outcomes are not described for objectives assessed through qualitative methods (RQ2, RQ3 and RQ4). **RQ1 Outcomes** Primary outcome: Coverage rate of screening (Self-HPV +/- triage for HPV-positive women) among the eligible population in both study arms within 12 months. Secondary outcomes: - Rate of primary screening (self-HPV) among the eligible population in both study arms within 12 months; - Proportion of women with positive primary screening who proceed to completing triage and treatment in both study arms; - Proportion of HPV-positive women who attend the follow-up visit at 12 months after primary screening in both study arms; - Distribution of socio-demographic characteristics among screened women in both study arms; **RQ2 Outcomes** - Level of health literacy (general and specific to cervical cancer) among women eligible for cervical cancer screening - Association of health literacy with cervical cancer screening uptake and HPV infection; **RQ5 Outcomes** - Cost of the CCA intervention per woman screened, cost per case of precancerous cervical disease (CIN2+) and cervical cancer detected, and cost per woman treated for CIN2+ and for cervical cancer; - Incremental cost-effectiveness ratio (ICER) of CCA compared to traditional hospital-based recruitment and screening methods for the following outcomes: number of women screened, number of CIN2+ detected, number of cervical cancers detected, number of women treated for CIN2+ and number of women treated for cervical cancer.
Inclusion- / Exclusion Criteria	**Formative research, community co-produced action and process evaluation** Relevant stakeholders in the rural health areas, which may include women of the community with or without their partners, local health care providers, community health workers, community leaders (including traditional and religious), representatives of the health district and local researchers. **Cluster-RCT** - Inclusion criteria: women aged 30-49 years old (25-49 years old if HIV-positive) residing in one of the 14 rural health areas of Mifi health district, who are able to understand the risks and benefits of their participation in the study and have provided written or oral consent (depending on their level of literacy). - Exclusion criteria: known cervical cancer or symptoms compatible with cervical cancer, previous hysterectomy, terminal disease other than cervical cancer, cervical cancer screening test in the last 5 years (3 years if HIV-positive), pregnancy at the time of screening.
Number of Participants with Rationale	**1. Formative research** We plan to conduct in-depth interviews with ~5 participants and focus group discussions with a total of ~60-90 participants; we aim to enroll ~40 women eligible for screening (all women participating in FGDs) in the health literacy survey. **2. Single-center open-label cluster-randomized controlled trial (RCT)** We expect to enroll approximately 800 women in the cluster-RCT (~530 in the intervention arm and 270 in the control arm). Within Mifi district's rural population, we estimate there to be approximately 15,200 women between 30-49 years old (10% of the total population) who would

	be eligible for the cervical cancer screening program. According to the WHO's 90-70-90 targets for cervical cancer elimination, 70% of women in this age group should be screened at least twice in a lifetime, at an interval of 10 years. In other words, we would expect 7% of women in this age group to complete screening each year. To detect a 3.5% difference between both research arms based on our previous experience in Dschang Health District (3.5% with traditional vs 7% with CCA-based recruitment) with 95% significance and 80% power, 632 women would be needed in each study arm (1264 in total). Accounting for a degree of intracluster correlation, the calculated sample size should be multiplied by the design effect (DE = 1 + ICC*(cluster size - 1)). Assuming an intracluster correlation coefficient (ICC) of 0.01 and clusters of approximately 1086 women aged 30-49 years (15,200 divided by 14 health areas), we obtain a DE of 12. The final sample size is therefore 12*1264 = 15,168 women. Thus, the total rural population of women aged 30-49 years of approximately 15,200 in the district should be enough to detect a 3.5% difference in screening rate between both study arms (total expected participation of 532 (7% of 7600) and 266 (3.5% of 7600) women in the intervention and control arms respectively, over one year). **3. Process evaluation** We plan to conduct in-depth interviews with 7 health area leaders and FGDs with a total of ~50-70 participants.
Study procedures	**Formative research** Formative research will be carried out only in the health areas randomized in the intervention arm of the cluster-RCT and will include the following steps: 1. **Identification of relevant stakeholders** for cervical cancer screening at health-area level in the selected rural health areas. 2. **Assessment of determinants of access to cervical cancer screening** in selected communities: a mixed-method approach including in-depth interviews, FGDs and a quantitative survey will be used. Interviews and FGDs will focus on objectives 2.1 and 2.2 (attitudes, practices and knowledge related to cervical cancer prevention, and potential barriers and facilitators of screening), while the survey will address objective 2.3. (health literacy assessment among women eligible for screening). **Community co-produced action** 1. **Participatory and community-based development of context-specific strategies to increase uptake of cervical cancer screening** at rural health-area level: these may include recruitment and/or primary screening (HPV testing) strategies, as well as potential strategies to facilitate linkage to triage and treatment. Using participatory methods and building on existing resources within the community, participants of each health area will reach a consensus on an adapted recruitment and/or screening strategy to be implemented within their community. This strategy can be shared across all health areas of the intervention arm or adapted to account for local specificities of each health area, as needed. 2. **Implementation of developed strategies** in health areas of the intervention arm: the exact study procedures of this step will depend on the results of the participatory workshops and will therefore be described in more detail at that point of the study. 3. **Interpretation and dissemination of study results** within communities and to relevant stakeholders: a community dissemination group made of local stakeholders (including community members) will be created in order to take ownership of the overall study results (including formative research, cluster-RCT and process evaluation) and effectively share knowledge within the community. **Cluster-randomized controlled study** The 14 rural health areas of the Mifi district will be cluster-randomized between two study arms. Randomization will be stratified according to health area population size and distance to the reference district hospital. The cluster-RCT will aim to compare population coverage for cervical cancer screening between two study arms over a period of 12 months: 1) **Intervention arm: CCA-based recruitment and screening strategy.** After appropriate training, designated health area leaders (HALs) will be responsible for carrying out recruitment of eligible women and facilitating HPV-based screening at rural health area level, in accordance with the strategy agreed upon for their respective health areas during CCA. 2) **Control arm: hospital-based recruitment and screening**. Recruitment of participants from all rural health areas in the control arm will be carried out centrally by a project manager at the Bafoussam Regional Hospital (BRH), in the capital of the

	Mifi district. The recruitment strategy in the control arm will follow procedures carried out until now in a previous screening program (the *3T study*) in the neighboring health district of Dschang. Primary screening by HPV self-sampling will be carried out at the BRH, followed by same-day triage of HPV-positive women and treatment when necessary. In both study arms, women diagnosed HPV positive will be invited for triage and if needed treatment at the BRH, where a cervical cancer screening program will be launched in March 2023. HPV-negative women will be advised to repeat screening after five years (3 years for women living with HIV). The screening program at the BRH is part of the GENOVA study, a randomized controlled trial comparing triage of HPV-positive women by VIA with triage by HPV genotyping (treatment of women with selected high-risk genotypes only). All HPV-positive participants will be advised to repeat screening after 12 months. Screening and treatment procedures will be provided free of charge to study participants. Participants' socio-demographic, medical and clinical data collected within the GENOVA study will be used in the analysis of outcomes of the ancillary study presented in this protocol. **Process evaluation** 1) **Assessment of feasibility and acceptability of implemented strategies** compared to the standard hospital-based cervical cancer screening strategy: FGDs will be conducted with health care providers, screened patients and eligible unscreened women, 6 months after initial implementation of the strategies across populations of both study arms. 2) **Assessment of the acceptability and implementation of the CCA process:** at the end of the RCT, in-depth interviews and FGDs will be conducted with community members, local stakeholders and the 7 HALs in health areas of the intervention arm, and study records and field notes will be reviewed to assess the implementation process of CCA. **Economic Evaluation** Total cost of the CCA intervention and incremental cost-effectiveness ratio (ICER) of CCA compared to traditional hospital-based recruitment and screening methods will be calculated for the following outcomes: number of women screened, number of CIN2+ detected, number of cervical cancers detected, number of women treated for CIN2+ and number of women treated for cervical cancer.
Statistical Considerations	The null hypothesis will be considered as both study arms having the same proportion of eligible women undergoing a complete screening procedure (defined as primary HPV testing and triage (by VIA or genotyping) for HPV-positive participants, and HPV testing only for HPV-negative participants). P-values will be calculated accordingly using the chi-square test for comparison of proportions, after adjusting for the clustering effect. Secondary outcomes including the proportion of eligible women completing primary screening within 12 months, the proportion of HPV-positive women who complete triage and treatment, and the proportion of HPV-positive women who return for follow-up after 12 months, will also be assessed using the chi-square test with two-sided p-values. Distribution of socio-demographic, behavioral and medical characteristics in both study arms will be expressed as proportions, means with standard deviations or medians as appropriate, and p-values will be calculated using chi-squared statistic test, t-test and/or Wilcoxon and Mann-Whitney tests as appropriate. The significance level will be two-sided with $\alpha = 0.05$.
Study Duration and Schedule	First participant in for formative research: 04/2023 First participant in for CC screening (RCT): 01/2024 Last participant in for screening (RCT): 12/2024 Last participant in for process evaluation: 03/2025
Data privacy	Project data will be handled with uttermost discretion and is only accessible to authorized personnel who require the data to fulfil their duties within the scope of the research project. On the CRFs and other project specific documents, participants are only identified by a unique participant number. Coded data will be used. A contact sheet linking each participant's identity and contact information with their participant number will be stored at the local research site in a locked cabinet. Only the local sponsor-principal investigator and designated local research assistants will have access to those documents.
Risk / Benefit Assessment	The study will be carried out in a setting where there is no structured screening program to date, with the aim of improving access to screening in disadvantaged rural areas. The study participants will benefit from a free screening for cervical cancer, and when necessary, will be treated. Local doctors, in accordance with the recommendations of the International Federation

	of Gynecology and Obstetrics (FIGO) and the WHO, will manage women with cervical dysplasia or cancer. Using community-based participatory research methods increases the likelihood of developing context-sensitive solutions to the lack of access to screening services which are sustainable, acceptable to local communities, and well integrated in the current health care system. One possible risk is the unauthorized data access or unwanted identification of project participants. However, all necessary caution will be undertaken to limit this risk by attributing unique identifiers to all participants and using only these identifiers on study documents and databases. An additional risk may be adverse events from treatment by thermal ablation, such as bleeding or infection. However, the risk of such events is low with thermal ablation which has been assessed as safe and acceptable for women. This risk will additionally be minimized by offering extensive training and supervision of health care providers involved in the study. Any side effects of the screening and/or treatment procedure will be managed free of charge in the reference hospital according to international standard of care. Finally, the participatory process in itself comes with risks to community members taking part in the intervention, such as stigma, opposition or rejection by their community. We will attempt to mitigate these risks by working with local researchers and health care providers who will provide regular reports on challenges encountered on the field to the project management team, so that appropriate measures can be taken in response.
Ethical considerations	This project is within the focus of the WHO to develop a global strategy towards eliminating cervical cancer as a public health problem. As part of a Swiss-Cameroonian collaboration of over 20 years, our research team benefits from the support of the Cameroonian Ministry of Health and the Ministry of Women's Empowerment and the Family. Our experience in the implementation of a cervical cancer screening program in Dschang and our previous collaboration with local stakeholders at health district level, will facilitate the launch of the new screening program in Bafoussam as well as the organization of this ancillary study. Our community-centered approach with the inclusion of a diverse range of local stakeholders will inform district, regional and national Cameroonian health officials on priorities for secondary cervical cancer prevention and will strengthen the capacity to implement a locally adequate cervical cancer screening program in the district. Participation in the study will take place on a voluntary basis. Study participants will be dispensed of screening costs and offered financial compensation for their travel costs to the screening center. At all study phases, participants will be provided a participant information sheet and a consent form describing the study and providing sufficient information to make an informed decision about their participation in the study. Participants will be offered the opportunity to ask questions before providing consent. Those needing more time to consider their participation will have the opportunity to come back at another date for screening.
GCP Statement	This study will be conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH-GCP, as well as Cameroonian legal and regulatory requirements.

1.2. Synopsis en français

Sponsor-Investigateur principal	Prof. Patrick Petignat Chef du service de gynécologie, Hôpitaux Universitaires de Genève Boulevard de la Cluse 30, 1205 Geneva, Switzerland Email : Patrick.Petignat@hcuge.ch Tel : +41 22 372 4300
Titre de l'étude	Action coproduite en communauté pour la participation au dépistage du cancer du col de l'utérus (Act4CC) : un essai contrôlé randomisé dans les zones rurales de la région de l'Ouest du Cameroun. *Une étude ancillaire à l'étude GENOVA – Dépistage HPV avec triage par génotypage HPV versus inspection visuelle après application d'acide acétique : un essai contrôlé randomisé (CCER N° AO_2021-0006)*
Titre court / ID d'étude	Act4CC (ID d'étude à déterminer)

Version et date du protocole	Version 1.2 (datée du 20/04/2023)
Enregistrement de l'étude	Clinicaltrials.gov – *pas encore enregistrée*
Investigateurs/ Investigatrices	**Investigateur principal au site local :** Prof. Bruno Kenfack Hôpital Régional Annexe de Dschang Dschang, Cameroun Email: brunokenfack@gmail.com Tel: +237 33 45 12 06 **Chargée de projet :** Dr Ania Wisniak Hôpitaux Universitaires de Genève, Service de gynécologie 1205 Genève, Suisse Email: ania.wisniak@hcuge.ch Tel: +41 22 372 4270 **Autres co-investigateurs/investigatrices :** Virginie Yakam Hôpital Régional Annexe de Dschang (Cameroun) Prof. Cicely Marston London School of Hygiene and Tropical Medicine (Royaume Uni) Prof. Nicole Schmidt Université catholique des sciences appliquées de Munich (Allemagne) Prof. Gregory Edie Halle-Ekane Université de Buea (Cameroun)
Centre d'étude	**Hôpital Régional de Bafoussam** Marché B, Bafoussam Ouest Cameroun
Catégorie de risque d'étude	Risque minimal : les mesures prévues pour l'échantillonnage de matériel biologique et la collecte de données personnelles n'impliquent que des risques minimaux.
Contexte et justification	Le cancer du col de l'utérus est le quatrième cancer le plus fréquent dans le monde, causant plus de 300'000 décès par an. La charge mondiale de cette maladie est toutefois inégalement répartie, plus de 90% des décès par cancer du col de l'utérus survenant dans les pays à revenu faible ou intermédiaire (PRFM). En Afrique subsaharienne, l'incidence des cas de cancer du col de l'utérus n'a cessé d'augmenter au cours des dernières décennies et il s'agit désormais de la première cause de décès par cancer chez les femmes. Les inégalités mondiales dans la charge du cancer du col de l'utérus peuvent être principalement attribuées au taux élevé de vaccination contre le virus du papillome humain (HPV) et au dépistage étendu de l'infection par HPV et/ou des lésions précancéreuses dans les pays à revenu élevé. En revanche, l'adoption de ces mesures préventives est insuffisante dans de nombreux PRFM. Face à ces grandes disparités régionales et malgré le caractère évitable du cancer du col de l'utérus, l'Organisation mondiale de la santé (OMS) a lancé en 2020 une initiative mondiale visant à éliminer le cancer du col de l'utérus en tant que problème de santé publique. Pour y parvenir, les objectifs suivants ont été fixés et devront être atteints d'ici 2030 : i) vaccination de 90 % des jeunes filles contre le HPV, ii) dépistage de 70 % des femmes avec un test performant, et iii) traitement de 90 % des femmes diagnostiquées avec des lésions précancéreuses. Les raisons de la couverture insuffisante du dépistage dans les PRFM sont multifactorielles. Parmi les principaux obstacles identifiés figurent le manque de personnel qualifié et d'infrastructures adéquates, les barrières culturelles et sociales, les contraintes financières et les pertes de suivi. L'expérience antérieure de notre équipe de recherche à l'Hôpital Régional Annexe de Dschang (HRAD), dans la région de l'Ouest du Cameroun, a montré que même

	avec une stratégie de dépistage efficace en place (utilisant une stratégie de "test-triage-traitement" à visite unique), une couverture adéquate de la population reste un défi. Pour remédier au manque de recours au dépistage, l'OMS recommande de développer des stratégies de dépistage adaptées au contexte et à la culture, en intégrant et en faisant participer les parties prenantes locales, les prestataires de soins de santé et les communautés au processus de conception et de mise en œuvre du programme. Les approches faisant appel à la participation de la communauté garantissent que les obstacles au dépistage sont bien compris et pris en compte, ce qui conduit à l'élaboration de programmes de dépistage acceptables et accessibles pour la population locale. La recherche d'action participative communautaire vise à faire participer les parties prenantes locales et les personnes concernées par un problème donné à un processus de recherche décisionnel collaboratif, depuis la conception et la préparation de l'étude jusqu'à la mise en œuvre et la diffusion des résultats, en associant la recherche à l'action pour le changement social. Cela permet de développer des projets bien adaptés au contexte local et intégrés au système de soins de santé, et d'améliorer potentiellement la durabilité des programmes. Dans le domaine de la prévention du cancer du col de l'utérus, plusieurs équipes de recherche ont utilisé avec succès la recherche communautaire pour accroître la sensibilisation de la population au cancer du col de l'utérus et le recours au dépistage. L'évaluation de l'efficacité d'une stratégie de dépistage du cancer du col de l'utérus basée sur l'action communautaire en co-production dans les zones rurales du Cameroun a le potentiel d'améliorer l'adoption des services de dépistage de manière durable, et de contribuer ainsi à l'élimination du cancer du col de l'utérus en tant que problème de santé publique.
Intervention de l'étude	Mobilisation communautaire pour la co-production d'action (ci-après dénommée "action coproduite en communauté") dans le but de développer et de mettre en œuvre une ou plusieurs stratégies communautaires visant à augmenter la participation au dépistage du cancer du col de l'utérus basé sur le HPV (y compris le dépistage primaire du HPV, le triage des patientes positives au HPV et le traitement des patientes triées positives) dans le district de santé de Mifi, dans la Région Ouest du Cameroun.
Intervention contrôle	Recrutement des femmes pour le dépistage du cancer du col de l'utérus coordonné de manière centralisée au niveau du district (depuis la capitale de district, Bafoussam) selon des procédures préalablement établies au sein d'un programme de dépistage du cancer du col de l'utérus dans le district de santé de Dschang depuis 2018. Cette procédure standard comprend la formation de 2 agents de santé communautaire (ASC) par aire de santé pour la sensibilisation autour du cancer du col de l'utérus, qui recrutent les femmes en faisant du porte-à-porte ou en organisant des réunions communautaires dans leurs aires de santé respectives.
Questions de recherche	<u>Question de recherche primaire (RQ) :</u> **RQ1**. L'action coproduite en communauté (ACC) augmente-t-elle la participation au dépistage du cancer du col de l'utérus (y compris le dépistage primaire, le triage, le traitement et le suivi si nécessaire) dans les zones rurales du Cameroun, par rapport à une stratégie traditionnelle de recrutement hospitalier pour le dépistage ? <u>Questions de recherche secondaires :</u> **RQ2**. Quels sont les déterminants de l'accès au dépistage du cancer du col de l'utérus dans les zones rurales de la Région Ouest du Cameroun ? *(recherche formative)* **RQ3**. Comment les communautés affectées et les parties prenantes perçoivent-elles les stratégies de dépistage du cancer du col de l'utérus développées par l'ACC par rapport à une approche traditionnelle hospitalière ? *(évaluation du processus)* **RQ4**. Comment l'ACC est-elle mise en œuvre dans les communautés sélectionnées et comment le processus de co-production est-il perçu par les parties prenantes participantes ? *(évaluation du processus)* **RQ5**. Quel est le rapport coût-efficacité d'une intervention utilisant l'ACC pour permettre l'accès aux services de dépistage dans une population rurale du Cameroun ? *(évaluation économique)*
Objectifs	**Objectifs RQ1** Objectif primaire: 1.1. Déterminer si un processus de recrutement pour le dépistage du cancer du col de l'utérus basé sur le HPV, développé à l'aide de l'ACC, permet une meilleure couverture de la population que l'approche traditionnelle hospitalière pour le recrutement, dans les zones rurales de la Région Ouest du Cameroun.

	Objectifs secondaires : 1.2. Évaluer l'efficacité de l'ACC pour la prise en charge du dépistage primaire du HPV par rapport à une stratégie de recrutement traditionnelle ; 1.3. Évaluer l'efficacité de l'ACC sur la conformité à la procédure complète de dépistage (y compris le triage, le traitement et le suivi) chez les femmes dont le test HPV est positif lors du dépistage primaire ; 1.4. Déterminer si l'efficacité de l'ACC sur la participation au dépistage du cancer du col de l'utérus diffère selon les caractéristiques socio-démographiques des femmes. **Objectifs RQ2** 2.1. Déterminer les attitudes, les pratiques et les connaissances liées à la prévention du cancer du col de l'utérus parmi les membres de la communauté, les acteurs locaux et les prestataires de soins de santé dans les zones de santé rurales de la Région Ouest du Cameroun ; 2.2. Identifier les obstacles et les facilitateurs potentiels du dépistage du cancer du col de l'utérus dans les zones rurales du Cameroun ; 2.3. Évaluer si la littératie en matière de santé chez les femmes éligibles agit comme un facilitateur du dépistage du cancer du col de l'utérus au Cameroun. **Objectifs RQ3** 3.1. Explorer l'acceptabilité des stratégies de recrutement et de dépistage par les utilisatrices (patientes) et les prestataires de soins de santé dans les deux bras de l'étude, y compris la satisfaction et la perception de la pertinence des stratégies. 3.2. Évaluer la faisabilité, dans le contexte du Cameroun rural, des stratégies de recrutement et de dépistage élaborées à l'aide de l'ACC, y compris le lien avec le triage et le traitement. **Objectifs RQ4** 4.1. Évaluer si l'intervention de l'ACC a été mise en œuvre comme prévu ; 4.2. Déterminer les obstacles et les facteurs favorables à une mise en œuvre réussie de l'ACC ; 4.3. Évaluer l'acceptabilité du processus d'ACC par les membres de la communauté et les parties prenantes ; 4.4. Identifier toutes les conséquences involontaires du processus d'ACC dans les communautés sélectionnées pour l'intervention. **Objectifs RQ5** 5.1. Déterminer le rapport coût-efficacité de l'ACC (y compris la facilitation des ateliers, la planification de la mise en œuvre, etc.) pour le dépistage et le traitement des maladies cervicales précancéreuses dans la Région Ouest du Cameroun.
Design d'étude	L'utilisation de l'ACC pour augmenter la couverture du dépistage du cancer du col de l'utérus dans le district sanitaire de Mifi, dans la Région Ouest du Cameroun, sera évaluée en utilisant une approche méthodologique mixte : **1. Recherche formative** Des méthodes qualitatives (discussions de groupe dirigées, entretiens individuels) et quantitatives (questionnaire) seront utilisées pour évaluer les déterminants de l'accès au dépistage du cancer du col de l'utérus dans les communautés rurales de la région. **2. Essai contrôlé randomisé en grappes ouvert et monocentrique (RCT)** Quatorze aires de santé rurales du district de santé seront randomisées en deux bras d'étude. La couverture du dépistage du cancer du col de l'utérus sera comparée entre les aires de santé allouées au bras d'intervention (action coproduite en communauté) et au bras de contrôle (stratégie standard de recrutement et de dépistage hospitaliers déjà en place dans le district de santé). **3. Évaluation du processus** Une recherche qualitative (discussions de groupe dirigées et entretiens individuels) sera menée avec les parties prenantes locales concernées afin d'évaluer l'acceptabilité et la faisabilité des stratégies de recrutement et dépistage utilisées dans les deux bras de l'étude, ainsi que l'acceptabilité du processus de l'ACC et si ce dernier a été mis en œuvre comme prévu au sein de la communauté. **4. Évaluation économique** Une analyse coût-efficacité sera menée pour évaluer les rapports coût-efficacité différentiels des stratégies individuelles mises en œuvre et du processus de l'ACC dans son ensemble.

	Durant toutes les phases de l'étude, les principes de la recherche d'action participative basée sur la communauté (RAPC) seront intégrés dans la conception du projet, tels que la formation d'un partenariat avec la communauté, la prise en compte des forces et dynamiques de la communauté dans la phase de recherche formative, la co-conception des interventions sanitaires, et l'interprétation et la diffusion des résultats de la recherche dans un format culturellement approprié et d'une manière qui soit pertinente pour la communauté et favorise une action durable. Les membres de la communauté seront également intégrés au partenariat en tant que "co-chercheurs" pendant les phases de planification de la mise en œuvre, de conception des méthodes de collecte des données et de suivi des activités de recherche.
Issues	Les issues ne sont pas décrites pour les objectifs évalués par des méthodes qualitatives (RQ2, RQ3 et RQ4). **Issues pour la RQ1** Issue primaire : Taux de couverture du dépistage (HPV +/- triage pour les femmes HPV-positives) parmi la population éligible dans les deux bras de l'étude sur 12 mois. Issues secondaires : - Taux de dépistage primaire (HPV) parmi la population éligible dans les deux bras de l'étude sur 12 mois ; - Proportion de femmes avec un dépistage primaire positif qui passent au triage et au traitement dans les deux bras de l'étude ; - Proportion de femmes HPV-positives qui se présentent à la visite de suivi 12 mois après le dépistage primaire dans les deux bras de l'étude ; - Distribution des caractéristiques socio-démographiques parmi les femmes dépistées dans les deux bras de l'étude ; **Issues pour la RQ2** - Niveau de littératie en matière de santé (« health literacy », générale et spécifique au cancer du col de l'utérus) chez les femmes éligibles au dépistage du cancer du col de l'utérus. - Association de la littératie en matière de santé avec le recours au dépistage du cancer du col de l'utérus et l'infection par le HPV ; **Issues pour la RQ5** - Coût de l'intervention de l'ACC par femme dépistée, coût par cas de maladie précancéreuse du col de l'utérus (CIN2+) et de cancer du col de l'utérus détecté, et coût par femme traitée pour une CIN2+ et pour un cancer du col de l'utérus ; - Rapport coût-efficacité différentiel de l'ACC par rapport aux méthodes traditionnelles de recrutement et de dépistage pour les issues suivantes : nombre de femmes dépistées, nombre de CIN2+ détectées, nombre de cancers du col de l'utérus détectés, nombre de femmes traitées pour une CIN2+ et nombre de femmes traitées pour un cancer du col de l'utérus.
Critères d'inclusion / d'exclusion	**Recherche formative, action coproduite en communauté et évaluation du processus** Les parties prenantes concernées dans les aires de santé rurales, pouvant inclure les femmes de la communauté avec ou sans leurs partenaires, les prestataires de soins de santé locaux, les agents de santé communautaires, les leaders communautaires (y compris les autorités traditionnelles et religieuses), les représentants du district de santé et les chercheurs locaux. **Essai randomisé contrôlé en grappe** - Critères d'inclusion : femmes âgées de 30 à 49 ans (25 à 49 ans si elles sont VIH-positives) résidant dans l'une des 14 aires de santé rurales du district de santé de Mifi, capables de comprendre les risques et les avantages de leur participation à l'étude et ayant donné leur consentement écrit ou oral (en fonction de leur niveau d'alphabétisation). - Critères d'exclusion : cancer du col de l'utérus connu ou symptômes compatibles avec un cancer du col de l'utérus, hystérectomie antérieure, maladie terminale autre que le cancer du col de l'utérus, test de dépistage du cancer du col de l'utérus au cours des 5 dernières années (3 ans si VIH-positive), grossesse au moment du dépistage.
Nombre de participant.es avec justification	**1. Recherche formative** Nous prévoyons de mener des entretiens individuels avec ~5 participant.es et des discussions de groupe dirigées avec un total de ~60-90 participant.es ; nous visons à recruter ~40 femmes

	éligibles pour le dépistage (toutes les femmes participant aux discussions de groupe) pour le questionnaire sur la littératie en matière de santé. **2. Essai contrôlé randomisé en grappes** Nous comptons recruter environ 800 femmes dans l'ECR en grappe (~530 dans le groupe d'intervention et 270 dans le groupe de contrôle). Au sein de la population rurale du district de Mifi, nous estimons qu'il y a environ 15'200 femmes âgées de 30 à 49 ans (10% de la population totale) qui seraient éligibles pour le programme de dépistage du cancer du col de l'utérus. Selon les objectifs 90-70-90 de l'OMS pour l'élimination du cancer du col de l'utérus, 70% des femmes de ce groupe d'âge devraient être dépistées au moins deux fois dans leur vie, à un intervalle de 10 ans. En d'autres termes, on s'attendrait à ce que 7 % des femmes de ce groupe d'âge effectuent un dépistage complet chaque année. Pour détecter une différence de 3,5 % entre les deux bras de recherche sur la base de notre expérience précédente dans le district de santé de Dschang (3,5 % avec le recrutement traditionnel contre 7 % avec le recrutement basé sur l'ACC) avec 95 % de confiance et une puissance de 80 %, 632 femmes seraient nécessaires dans chaque bras de l'étude (1264 au total). En tenant compte d'un degré de corrélation intra-groupe, la taille de l'échantillon calculée doit être multipliée par l'effet de design (DE = 1 + ICC*(taille du groupe - 1)). En supposant un coefficient de corrélation intra-clusters (ICC) de 0,01 et des grappes d'environ 1086 femmes âgées de 30 à 49 ans (15'200 divisées par 14 aires de santé), nous obtenons un DE de 12. La taille finale de l'échantillon est donc de 12*1264 = 15'168 femmes. Ainsi, la population rurale totale des femmes âgées de 30 à 49 ans d'environ 15'200 personnes dans le district devrait être suffisante pour détecter une différence de 3,5% dans le taux de dépistage entre les deux bras de l'étude (participation totale attendue de 532 (7% de 7600) et 266 (3,5% de 7600) femmes dans les bras d'intervention et de contrôle respectivement, sur une année). **3. Évaluation du processus** Nous prévoyons de mener des entretiens individuels avec 7 responsables d'aires de santé et des discussions de groupe dirigées avec un total de ~50-70 participant.es.
Procédures d'étude	**Recherche formative** La recherche formative sera menée uniquement dans les aires de santé randomisées dans le bras d'intervention de l'essai randomisé et comprendra les étapes suivantes : 1. **Identification des parties prenantes pertinentes** pour le dépistage du cancer du col de l'utérus dans les aires de santé rurales sélectionnées. 2. **Évaluation des déterminants de l'accès au dépistage du cancer du col de l'utérus** dans les communautés sélectionnées : une méthodologie mixte comprenant des entretiens individuels, des discussions de groupe dirigées et un questionnaire quantitatif sera utilisée. Les entretiens et les discussions de groupe se concentreront sur les objectifs 2.1 et 2.2 (attitudes, pratiques et connaissances liées à la prévention du cancer du col de l'utérus, et obstacles et facilitateurs potentiels du dépistage), tandis que le questionnaire portera sur l'objectif 2.3 (évaluation de la littératie en matière de santé chez les femmes éligibles au dépistage). **Action coproduite en communauté** 1. **Développement participatif et communautaire de stratégies spécifiques au contexte** pour augmenter la prise en charge du dépistage du cancer du col de l'utérus au niveau de l'aire de santé rurale : celles-ci peuvent inclure des stratégies de recrutement et/ou de dépistage primaire (test HPV), ainsi que des stratégies potentielles pour faciliter le lien avec le triage et le traitement. En utilisant des méthodes participatives et en s'appuyant sur les ressources existantes au sein de la communauté, les participant.es de chaque aire de santé parviendront ensuite à un consensus sur une stratégie adaptée de recrutement et/ou de dépistage à mettre en œuvre au sein de leur communauté. Cette stratégie pourra être partagée par toutes les aires de santé du groupe d'intervention ou adaptée pour tenir compte des spécificités locales de chaque aire de santé, selon les besoins. 2. **Mise en œuvre des stratégies développées** dans les aires de santé du bras d'intervention : les procédures exactes de cette étape dépendront des résultats des ateliers participatifs et seront donc décrites plus en détail à ce stade de l'étude. 3. **Interprétation et diffusion des résultats de l'étude** au sein des communautés et aux parties prenantes concernées : un groupe de diffusion communautaire composé de parties prenantes locales (y compris des membres de la communauté) sera créé afin de s'approprier l'ensemble des résultats de l'étude (y compris la recherche

	formative, l'étude randomisée contrôlée et l'évaluation du processus) et de partager efficacement les connaissances au sein de la communauté. **Étude contrôlée randomisée en grappes** Les 14 aires de santé rurales du district de Mifi seront randomisées en grappes entre deux bras d'étude. La randomisation sera stratifiée en fonction de la taille de la population de l'aire de santé et de la distance à l'hôpital de district de référence. L'essai randomisé visera à comparer la couverture de la population pour le dépistage du cancer du col de l'utérus entre les deux bras d'étude sur une période de 12 mois : 1) **Bras d'intervention : Stratégie de recrutement et de dépistage basée sur l'ACC**. Après une formation appropriée, les responsables des zones de santé seront chargés de recruter les femmes éligibles et de faciliter le dépistage du HPV au niveau des aires de santé rurales, conformément à la stratégie convenue pour leur aire de santé respective pendant l'ACC. 2) **Bras de contrôle : recrutement et dépistage traditionnel basé à l'hôpital**. Le recrutement des participantes de toutes les aires de santé rurales dans le bras de contrôle sera effectué de manière centralisée par un chef de projet à l'hôpital régional de Bafoussam (HRB), dans la capitale du district de Mifi. La stratégie de recrutement dans le bras de contrôle suivra les procédures appliquées jusqu'à présent dans un précédent programme de dépistage (l'étude 3T) dans le district de santé voisin de Dschang. Le dépistage primaire par auto-prélèvement du HPV sera effectué à l'HRB, suivi d'un triage le jour même des femmes positives au HPV et d'un traitement si nécessaire. Dans les deux bras de l'étude, les femmes diagnostiquées HPV positives seront invitées à un triage et, si nécessaire, à un traitement à l'HRB, où un programme de dépistage du cancer du col de l'utérus sera lancé en mars 2023. Les femmes HPV négatives seront invitées à répéter le dépistage après cinq ans (trois ans pour les femmes vivant avec le VIH). Le programme de dépistage à l'HRB fait partie de l'étude GENOVA, un essai contrôlé randomisé comparant le triage des femmes HPV-positives par VIA avec le triage par génotypage HPV (traitement des femmes avec des génotypes à haut risque uniquement). Il sera conseillé à toutes les participantes HPV-positives de répéter le dépistage après 12 mois. Les procédures de dépistage et de traitement seront fournies gratuitement aux participantes de l'étude. Les données sociodémographiques, médicales et cliniques des participantes recueillies dans le cadre de l'étude GENOVA seront utilisées dans l'analyse des résultats de l'étude auxiliaire présentée dans ce protocole. **Évaluation des processus** 1. **Évaluation de la faisabilité et de l'acceptabilité des stratégies mises en œuvre** par rapport à la stratégie standard de dépistage du cancer du col de l'utérus en milieu hospitalier : des discussions de groupe dirigées seront menées avec les prestataires de soins de santé, les patientes dépistées et les femmes éligibles non dépistées, 6 mois après la mise en œuvre initiale des stratégies dans les populations des deux bras de l'étude. 2. **Évaluation de l'acceptabilité et de la mise en œuvre du processus de l'ACC** : à la fin de l'essai randomisé, des entretiens individuels et des discussions de groupe seront menés avec des membres de la communauté, des parties prenantes locales et les 7 responsables des aires de santé dans les aires du bras d'intervention. Les dossiers d'étude et les notes de terrain seront examinés pour évaluer le processus de mise en œuvre de l'ACC. **Évaluation économique** Le coût total de l'intervention de l'ACC et le rapport coût-efficacité différentiel de l'ACC par rapport aux méthodes traditionnelles de recrutement et de dépistage en milieu hospitalier seront calculés pour les résultats suivants : nombre de femmes dépistées, nombre de CIN2+ détectées, nombre de cancers du col détectés, nombre de femmes traitées pour des CIN2+ et nombre de femmes traitées pour un cancer du col.
Considérations statistiques	L'hypothèse nulle sera considérée comme le fait que les deux bras d'étude présentent la même proportion de femmes éligibles se soumettant à une procédure de dépistage complète (définie comme le test HPV primaire et le triage (par VIA ou génotypage) pour les participantes HPV-positives, et le test HPV seul pour les participantes HPV-négatives). Les valeurs P seront calculées en utilisant le test du chi-carré pour la comparaison des proportions, après ajustement de l'effet de regroupement. Les résultats secondaires, y compris la proportion de femmes éligibles qui terminent le dépistage primaire dans les 12 mois, la proportion de femmes HPV-positives qui terminent le triage et le traitement, et la proportion de femmes HPV-positives qui reviennent pour un suivi après 12 mois, seront également évalués en utilisant le test du

	chi-carré avec des valeurs p bilatérales. La distribution des caractéristiques sociodémographiques, comportementales et médicales dans les deux bras de l'étude sera exprimée en proportions, moyennes avec écarts types ou médianes selon le cas, et les valeurs p seront calculées à l'aide du test statistique du chi carré, du test t et/ou des tests de Wilcoxon et de Mann-Whitney selon le cas. Le niveau de significativité sera bilatéral avec $\alpha = 0,05$.
Durée et calendrier de l'étude	Premier participant entrant pour la recherche formative : 04/2023 Première participante entrante pour le dépistage (essai randomisé) : 01/2024 Dernière participante sortante pour le dépistage (essai randomisé) : 12/2024 Dernier participant sortant pour l'évaluation du processsus : 03/2025
Protection des données	Les données du projet seront traitées avec la plus grande discrétion et ne seront accessibles qu'au personnel autorisé qui a besoin de ces données pour remplir ses fonctions dans le cadre du projet de recherche. Sur les formulaires d'étude et autres documents spécifiques au projet, les participant.es ne seront identifié.es que par un numéro de participant.e unique. Des données codées seront utilisées. Une fiche de contact reliant l'identité et les coordonnées de chaque participant.e à son numéro de participant.e sera conservée sur le site de recherche local dans une armoire fermée à clé. Seuls le sponsor local - investigateur principal et les assistant.es de recherche désigné.es auront accès à ces documents.
Evaluation risque / bénéfice	L'étude sera menée dans une région où il n'existe pas à ce jour de programme de dépistage structuré, dans le but d'améliorer l'accès au dépistage dans les zones rurales défavorisées. Les participantes à l'étude bénéficieront d'un dépistage gratuit du cancer du col de l'utérus et, si nécessaire, seront traitées. Les médecins locaux, conformément aux recommandations de la Fédération internationale de gynécologie et d'obstétrique (FIGO) et de l'OMS, prendront en charge les femmes présentant une dysplasie ou un cancer du col de l'utérus. L'utilisation de méthodes de recherche participatives basées sur la communauté augmente la probabilité de développer des solutions contextuelles au manque d'accès aux services de dépistage qui soient durables, acceptables pour les communautés locales et bien intégrées dans le système de soins de santé actuel. Un risque possible est l'accès non autorisé aux données ou l'identification non souhaitée des participant.es au projet. Toutes les précautions nécessaires seront prises pour limiter ce risque en attribuant des identifiants uniques à tous les participant.es et en utilisant uniquement ces identifiants dans les documents et bases de données de l'étude. Les effets indésirables du traitement par thermoablation, tels que les saignements ou les infections, peuvent constituer un risque supplémentaire. Cependant, le risque de tels événements est faible avec la thermoablation qui a été évaluée comme sûre et acceptable pour les femmes. Ce risque sera en outre minimisé par une formation et une supervision approfondies des prestataires de soins de santé participant à l'étude. Tout effet secondaire de la procédure de dépistage et/ou de traitement sera pris en charge gratuitement dans l'hôpital de référence, conformément aux normes internationales de soins. Enfin, le processus participatif en lui-même comporte des risques pour les membres de la communauté prenant part à l'intervention, tels que la stigmatisation, l'opposition ou le rejet par leur communauté. Nous tenterons d'atténuer ces risques en travaillant avec des chercheurs et prestataires de soins de la région qui fourniront des rapports réguliers sur les défis rencontrés sur le terrain à l'équipe de gestion du projet, afin que des mesures appropriées puissent être prises en réponse.
Considérations éthiques	Ce projet s'inscrit dans le cadre de l'élaboration par l'OMS d'une stratégie mondiale visant à éliminer le cancer du col de l'utérus en tant que problème de santé publique. Dans le cadre d'une collaboration helvético-camerounaise de plus de 20 ans, notre équipe de recherche bénéficie du soutien du ministère camerounais de la santé publique et du ministère de la promotion de la femme et de la famille. Notre expérience dans la mise en place d'un programme de dépistage du cancer du col de l'utérus à Dschang et notre collaboration antérieure avec des acteurs locaux au niveau du district de santé, faciliteront le lancement du nouveau programme de dépistage à Bafoussam ainsi que l'organisation de cette étude ancillaire. Notre approche centrée sur la communauté avec l'inclusion d'un éventail diversifié de parties prenantes locales informera les responsables de la santé du district, de la région et du pays sur les priorités de la prévention secondaire du cancer du col de l'utérus et renforcera la capacité à mettre en œuvre un programme de dépistage du cancer du col de l'utérus adéquat dans le district. La participation à l'étude se fera sur une base volontaire. Les participantes à l'étude seront dispensées des frais de dépistage et se verront offrir une compensation financière pour leurs

	frais de déplacement vers le centre de dépistage. À toutes les phases de l'étude, les participant.es recevront une fiche d'information et un formulaire de consentement décrivant l'étude et fournissant des informations suffisantes pour prendre une décision éclairée quant à leur participation à l'étude. Les participant.es auront la possibilité de poser des questions relatives à l'étude avant de donner leur consentement. Celles qui ont besoin de plus de temps pour réfléchir à leur participation à l'étude auront la possibilité de revenir à une autre date.
Déclaration BPC	Cette étude sera conduite en accord avec le protocole, la version actuelle de la Déclaration d' Helsinki, l'ICH-GCP, ainsi que les exigences légales et régulatoires camerounaises.

2 BACKGROUND AND PROJECT RATIONALE

Cervical cancer is the fourth most frequent cancer worldwide, causing over 300'000 deaths yearly.(3) The global burden of this disease, however, is unequally distributed, with over 90% of cervical cancer deaths occurring in low- and middle-income countries (LMICs).(3) In Sub-Saharan Africa, the incidence of cervical cancer cases has continued to rise in past decades and it is now the first cause of cancer death among women.(4,5)

Global inequalities in the burden of cervical cancer can mainly be attributed to the high vaccination rate against human papillomavirus (HPV) (causing nearly all cervical cancers) and the extensive screening of HPV infection and/or precancerous lesions in high-income countries.(6,7) In contrast, uptake of these preventive measures has been insufficient in many LMICs. The lowest prevalence rate of cervical cancer screening worldwide has been reported in Sub-Saharan Africa, ranging between 0.9 and 50.8% of the population screened at country-level.(3) In Cameroon, a demographic survey in 2018 reported that only 4% of women of reproductive age had been screened for cervical cancer at least once in their lifetime.(8)

In the face of these large regional disparities despite the preventable nature of cervical cancer, the World Health Organization (WHO) launched a global initiative in 2020 for the worldwide elimination of cervical cancer as a public health issue.(9) To achieve this, the following targets were established to be met by 2030: i) vaccination of 90% of girls against HPV, ii) screening of 70% of women with a high-performance test, and iii) treatment of 90% of women diagnosed with precancerous lesions.

The reasons for insufficient screening coverage in LMICs are multifactorial. Some of the main obstacles identified are a lack of trained personnel and adequate infrastructures, cultural and social barriers, financial constraints, and loss to follow-up.(10,11) In recent years, innovative strategies have allowed to mitigate some of these barriers. For instance, highly sensitive point-of-care HPV tests and treatment modalities adapted to low-resource settings have allowed to implement same-day testing, triage and treatment, therefore reducing loss to follow-up. Other strategies such as vaginal self-sampling and task-shifting of screening and treatment procedures to non-medical health care providers were implemented to reduce barriers to screening. However, even where screening programs do exist, reaching the target population often remains a challenge in low-income regions. Previous experience of our research team at the Annex Regional Hospital of Dschang, in the West Region of Cameroon, has shown that even with an efficient screening strategy in place (using a single-visit "test-triage-treat" strategy), adequate population coverage remains a challenge.(12)

To address the lack of screening uptake, the WHO recommends the development of context-specific and culturally appropriate screening strategies, by integrating and engaging local stakeholders, health care providers and communities in the program design and implementation process.(9,13) Community-engaged approaches ensure that barriers to screening are well understood and addressed, leading to the development of screening programs which are acceptable and accessible to the local population.(9,14) Moreover, integrating cervical cancer screening into primary health care services, such as family planning or HIV clinics, is seen as an effective way to sustainably improve screening uptake.(9,15)

Community-based participatory action research (CBPAR) aims to engage local stakeholders and those affected by a particular problem in a collaborative decision-making research process, from study design and preparation to implementation and dissemination of results, combining research

with action for social change.(16,17) This enables the development of projects that are well adapted to the local context and integrated within the health care system, and potentially enhances program sustainability.(14,16,18) Studies conducted in a variety of settings have demonstrated that the use of CBPAR and similar participatory approaches improved the population's health and wellbeing, decreased barriers to implementation and built organizational capacity within the community.(19–21) In the field of cervical cancer prevention, several research teams have successfully used community-based research to increase the population's awareness of cervical cancer and screening uptake.(22–24) In sub-Saharan Africa, methods identified as most effective included community-based self-sampling, the integration of cervical cancer screening with other health care services,(25) and engaging local networks such as community health workers, religious organizations, traditional leaders and educational institutions to increase awareness of cervical cancer.(23,25)

Furthermore, community-engaged research frequently involves decentralizing health programs to increase accessibility, as offering services closer to the community instead of at district- or regional hospital-level only may reduce time-related and financial barriers to screening. In a study conducted in Ghana, 95% of women who were invited for cervical cancer screening at a location within the community attended screening, while only 39 to 47% of women invited to the hospital came for screening.(26) In the North-Western region of Cameroon, a community-based cervical cancer screening strategy was deemed feasible and effective in hard-to-reach communities; however the effectiveness of such an approach compared to hospital-based screening was not determined.(27) Assessing the effectiveness of a cervical cancer screening strategy based on community co-produced action in rural Cameroon has the potential to improve uptake of screening services in a sustainable way, and thus contribute to eliminating cervical cancer as a public health problem.

This research project entails no greater than minimal risk, as the planned measures for sampling biological material and collecting personal data entail only minimal risks and burdens. It is an ancillary study to the GENOVA study (HPV Screening with Triage by HPV Genotyping versus Visual Inspection with Acetic Acid: A Randomized Controlled Trial), which has already been approved by ethics committees of Geneva, Switzerland (CCER N° AO_2021-0006), and Cameroon (N°2022/09/1487/CE/CNERSH/SP).

3 PROJECT OBJECTIVES AND DESIGN

3.1 Study intervention

The study intervention will consist in community mobilization for co-produced action (hereafter referred to as "community co-produced action") with the aim to develop and implement one or more community-based strategies to increase uptake of HPV-based cervical cancer screening (including primary HPV screening, triage of HPV-positive patients and treatment of patients triaged positive) in the health district of Mifi, West Region of Cameroon (see Figure 1). Possible strategies co-developed may include collaboration with community health workers (CHWs) or local associations (e.g. women's groups), awareness campaigns at health area level, development of culturally appropriate health education materials, integration of primary HPV screening at local integrated health centers (IHCs), organization of group transportation to the district screening center, etc.

3.2 Research questions

Primary research question (RQ):

RQ1. Does community co-produced action (CCA) increase uptake of cervical cancer screening (including primary screening, triage, treatment and follow-up when necessary) in rural Cameroon compared to a traditional hospital-based recruitment strategy for screening?

Secondary research questions:

RQ2. What are the determinants of access to cervical cancer screening in rural areas of the West Region of Cameroon? *(formative research)*

RQ3. How do affected communities and stakeholders perceive cervical cancer screening strategies developed through CCA compared to a traditional hospital-based strategy? *(process evaluation)*

RQ4. How is CCA implemented in selected communities and how is the co-production process perceived by participating stakeholders? *(process evaluation)*

RQ5. What is the cost-effectiveness of an intervention using CCA to provide access to screening services in a rural population in Cameroon? *(economic evaluation)*

3.2 Research hypothesis

We hypothesize that recruitment strategies for HPV-based cervical cancer screening developed through CCA will improve uptake of screening services in rural communities of the West Region of Cameroon compared to traditional hospital-based screening.

3.3 Primary and secondary objectives

RQ1 Objectives

Primary objective:

1.1. To determine whether a recruitment process for HPV-based cervical cancer screening developed using CCA allows better population coverage than the traditional hospital-based approach at district level, in rural areas of the West Region of Cameroon.

Secondary objectives:

1.2. To assess the effectiveness of CCA for primary HPV screening uptake compared to a traditional recruitment strategy;

1.3. To assess the effectiveness of CCA for compliance to the complete screening procedure (including triage, treatment and follow-up) among women who test HPV positive upon primary screening;

1.4. To determine whether the effectiveness of CCA for cervical cancer screening uptake differs according to women's socio-demographic characteristics.

RQ2 Objectives

2.1. To determine the attitudes, practices and knowledge related to cervical cancer prevention among community members, local stakeholders and health care providers in rural health areas of the West Region of Cameroon;

2.2. To identify potential barriers and facilitators of cervical cancer screening in rural Cameroon;

2.3. To assess whether health literacy among eligible women acts as a facilitator of cervical cancer screening in Cameroon.

RQ3 Objectives

3.1. To explore the acceptability of recruitment and screening strategies by users (patients) and healthcare providers in both study arms, including the satisfaction with and perceived appropriateness of the strategies.

3.2. To evaluate the feasibility in the context of rural Cameroon of the recruitment and screening strategies developed using CCA, including linkage to triage and treatment.

RQ4 Objectives

4.1. To evaluate whether the CCA intervention was implemented as planned;

4.2. To determine the challenges and enablers of successful CCA implementation;

4.3. To assess acceptability of the CCA process by participating community members and stakeholders;

4.4. To identify any unintended consequences of the CCA process within communities selected for the intervention.

RQ5 Objectives

5.1. To determine the cost-effectiveness of CCA (including facilitation of workshops, implementation planning, etc.) for screening and treatment of precancerous cervical disease in the West Region of Cameroon.

3.4 Study design

The use of community co-produced action to increase cervical cancer screening coverage in the health district of Mifi, West Region of Cameroon, will be evaluated using a mixed-methods approach (see Figure 1):

1. **Formative research**

   Qualitative (focus group discussions, in-depth interviews) and quantitative (surveys) methods will be used to assess the determinants of access to cervical cancer screening in rural communities of the region.

2. **Single-center open-label cluster-randomized controlled trial (RCT)**

   Fourteen rural health areas of the health district will be randomized into two study arms (**Figure 1**, right panel). Cervical cancer screening coverage will be compared between the health areas allocated to the intervention arm (community co-produced action) and the control arm (standard hospital-based recruitment and screening strategy already in place in the health district, detailed in “recruitment for cluster-RCT” in section 4.2).

3. **Process evaluation**

   Qualitative research (focus group discussions and in-depth interviews) will be led with relevant local stakeholders to assess the acceptability and feasibility of recruitment and screening strategies used in both study arms, as well as acceptability of the CCA process and whether CCA was implemented as planned within the community.

4. **Economic evaluation**

   A cost-effectiveness analysis will be conducted to evaluate the incremental cost-effectiveness ratios of individual strategies implemented and of the CCA process overall.

Throughout all phases of the study, principles of community-based participatory action research (CBPAR) will be integrated in the project design, such as forming a partnership with the community, assessing community strengths and dynamics in the formative research phase, co-designing health interventions, and interpreting and disseminating research findings in a culturally appropriate format and in a way that is relevant for the community and promotes sustainable action (18). Community members will also be integrated in the partnership as “co-researchers” during phases of implementation planning, designing methods for data collection and monitoring of research activities. We will follow an approach similar to that previously used by Manandhar et al. **(28)** to evaluate the effect of a participatory intervention with women’s groups on birth outcomes in Nepal. Recommendations of the WHO guideline on community mobilization through facilitated participatory learning and action cycles with women’s groups for maternal and newborn health **(29)** have also been taken into consideration in the development of this protocol.

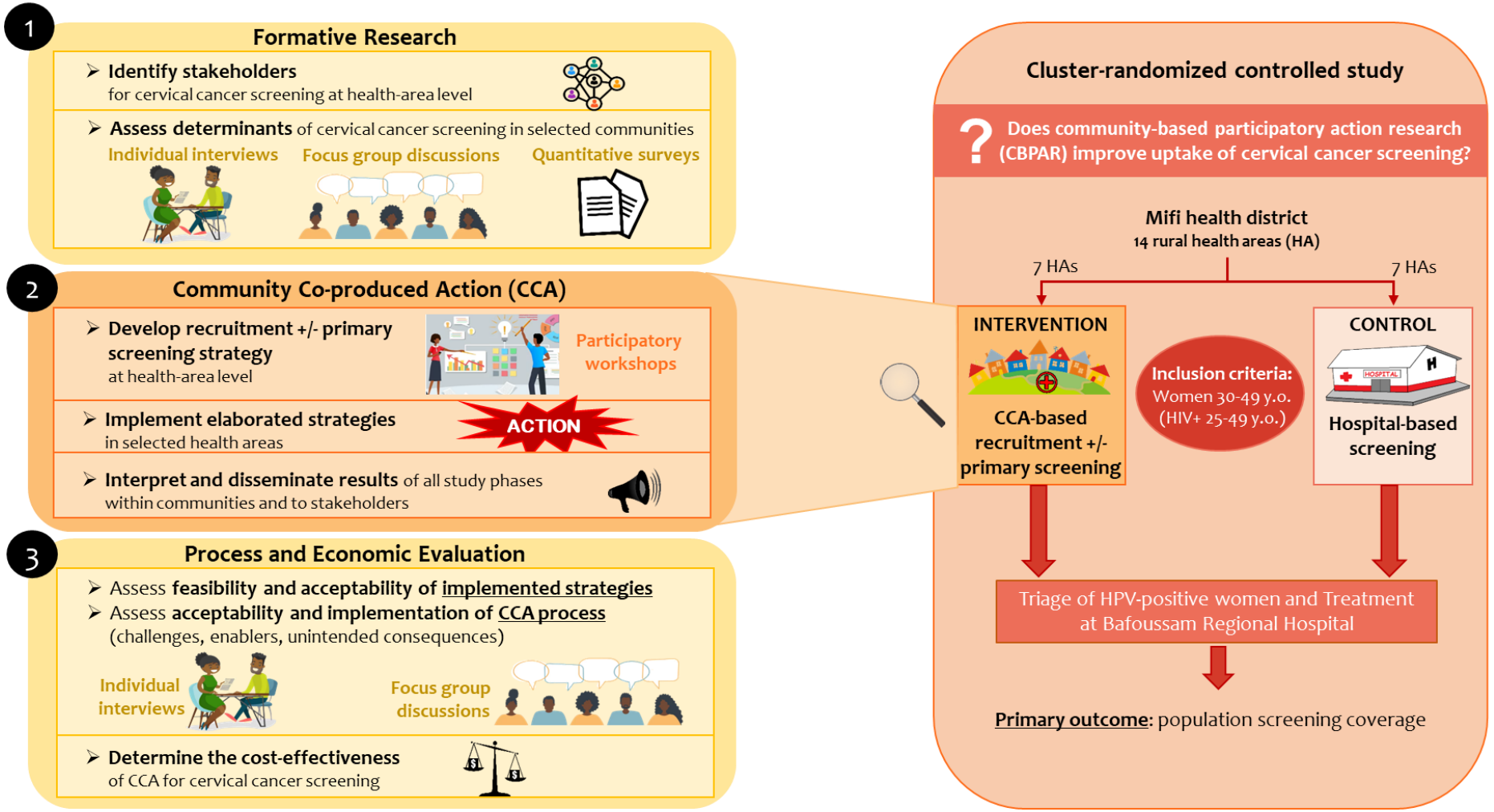

Figure 1 - Study design

3.5 Primary and secondary outcomes

Outcomes are not described for objectives assessed through qualitative methods (RQ2, RQ3 and RQ4).

RQ1 Outcomes

Primary outcome: Coverage rate of screening (Self-HPV +/- triage for HPV-positive women) among the eligible population in both study arms within 12 months.

Secondary outcomes:

- Rate of primary screening (self-HPV) among the eligible population in both study arms within 12 months;
- Proportion of women with positive primary screening who proceed to completing triage and treatment in both study arms;
- Proportion of HPV-positive women who attend the follow-up visit at 12 months after primary screening in both study arms;
- Distribution of socio-demographic characteristics among screened women in both study arms;

RQ2 Outcomes

- Level of health literacy (general and specific to cervical cancer) among women eligible for cervical cancer screening
- Association of health literacy with cervical cancer screening uptake and HPV infection;

RQ5 Outcomes

- Cost of the CCA intervention per woman screened, cost per case of precancerous cervical disease (CIN2+) and cervical cancer detected, and cost per woman treated for CIN2+ and for cervical cancer;
- Incremental cost-effectiveness ratio (ICER) of CCA compared to traditional hospital-based recruitment and screening methods for the following outcomes: number of women screened, number of CIN2+ detected, number of cervical cancers detected, number of women treated for CIN2+ and number of women treated for cervical cancer.

4 PROJECT POPULATION AND STUDY PROCEDURES

4.1 Project population, inclusion and exclusion criteria

Formative research, community co-produced action and process evaluation

Relevant stakeholders in the rural health areas, which may include women of the community with or without their partners, local health care providers, community health workers, community leaders (including traditional and religious), representatives of the health district and local researchers.

Cluster-RCT (RQ1)

- Inclusion criteria: women aged 30-49 years old (25-49 years old if HIV-positive) residing in one of the 14 rural health areas of Mifi health district, who are able to understand the risks and benefits of their participation in the study and have provided written or oral consent (depending on their level of literacy).
- Exclusion criteria: known cervical cancer or symptoms compatible with cervical cancer, previous hysterectomy, terminal disease other than cervical cancer, cervical cancer screening test in the last 5 years (3 years if HIV-positive), pregnancy at the time of screening.

The age groups of 30-49 years for HIV-negative women and 25-49 years for HIV-positive women were selected according to the WHO's recommendation to prioritize cervical cancer screening in these age groups, particularly in settings with limited resources, as they are at higher risk of cervical cancer. (30) The minimal screening intervals of 3 to 5 years depending on HIV status were also selected based on these recommendations. HIV-positive women in particular are at increased risk for persistent HPV infection and potentially faster progression to precancerous/cancerous disease. (31)
We chose to exclude women with known cervical cancer or symptoms of cervical cancer from the trial, as this study aims to assess screening strategies, not diagnostic or therapeutic modalities. Pregnant women will be excluded temporarily to avoid potential complications of the pregnancy and will be advised to come back for screening at three months postpartum. Finally, women with terminal disease other than cervical cancer will be excluded from the study as the benefit of cervical screening would probably be minimal given the slow progression of this cancer.

4.2 Recruitment, screening and informed consent procedure

Setting

The health system in Cameroon is organized in a three-level pyramidal form: the peripheral level corresponding to the health district, the intermediate or regional level, and the national or central level (see **Table 1**).

Table 1. Organization of the Cameroonian health system at central, intermediate and peripheral levels.

Level	Administrative	Care	Community involvement
Central	Central structures Ministry of health	General hospitals University hospitals Central hospitals	Administrative board Management committees
Intermediate	Regional delegations	Regional hospitals	Regional funds for health promotion
Periphery	Health districts Health areas Villages	District hospitals Integrated health centers	District health committees Health committees Village delegates

Cameroon does not have a national screening program for cervical cancer. A national strategic plan for the control of cervical cancer was drafted in 2016. However it has not been implemented to date (32). Currently, cervical cancer screening is mostly available in some public hospitals of larger cities where cytopathologists and gynaecologists are present. A few private initiatives, such as the Cameroon Baptist Convention Health Services and the Presbyterian Church in Cameroon Health Services, offer routine screening and treatment of precancerous lesions of the cervix in a few cities throughout the country, while other initiatives organize sporadic screening campaigns. No national guidelines exist for cervical cancer prevention, but VIA/VILI is suggested as a screening strategy in the National Strategic Plan for Prevention and Cancer Control (32). This strategic plan further recommends implementation of a cervical cancer screening strategy in collaboration with other existing health services, such as maternal and child health and family planning units.

This study will take place in the rural health areas of Mifi district, in the West Region of Cameroon, where no organized cervical cancer screening program exists presently. Mifi district is divided in 20 health areas, among which 6 are urban (with a population of approximately 328,000) and 14 are rural (population of approximately 152,000) (see **Table 2**). Each health area is in charge of ensuring access to essential health services for their population, under the coordination of the health district. Most rural health areas in the Mifi district have at least one integrated health center

(IHC), headed by a certified nurse and serving the primary health care needs of the local community (14 IHCs overall in the rural health areas).

Table 2. Characteristics of the 20 health areas of Mifi District, West Region of Cameroon

Health area	**Rural/urban**	**Number of villages**	**Estimated population**	**Estimated number of women aged 30-49**	**Types of health centers available***
Badiembou	Rural	8	16830	1683	1 IHC 8 HCs
Bapi	Rural	19	5386	539	3 IHCs 1 HC
Batoukop	Rural	10	10612	1061	1 IHC 1 HC
Baye	Rural	11	3344	334	1 IHC
Djeleng	Urban	15	77557	7756	9 HCs 1 maternity
Djietcha	Rural	10	9851	985	1 IHC 1 HC
Djunang	Rural	6	5367	537	2 HCs
Famla	Urban	12	39897	3990	1 district hospital 7 HCs
Famtchouet Baleng	Rural	6	5937	594	1 IHC 1 HC
Kamkop	Urban	9	34655	3466	6 HCs 2 emergency centers
Keuleu	Rural	6	5555	556	1 IHC 2 HCs
King Place	Urban	15	74360	7436	2 IHCs 1 community hospital 7 HCs
Kongso Bamougoum	Rural	16	9461	946	1 DMC 1 HC
Kouogouo	Rural	10	27910	2791	4 HCs
Lafe Baleng	Urban	9	38828	3883	1 DMC 7 HCs
Tchada	Rural	8	5690	569	3 IHCs
Tocket	Rural	5	15284	1528	2 HCs
Tyo	Urban	11	62422	6242	Regional hospital 1 DMC >10 HCs
Wouong	Rural	5	6539	654	2 HCs
Yagou	Rural	9	24140	2414	2 IHCs 5 HCs
Total	**14 rural** **6 urban**	**200**	**479625**	**47963**	

*Excluding specialized health centers if not related to women's health/reproductive health care.
Abbreviations: IHC = integrated health center / DMC / district medical center / HC = other health centers

Recruitment for formative research, CCA and process evaluation

The formative research phase, CCA process to establish a context-appropriate strategy for cervical cancer screening, and process evaluation, will be led in collaboration with IHCs in the health areas randomized in the intervention arm of the study. When no IHC exists in a health area, district medical centers (available in 2 of the 14 rural health areas) or other non-integrated health centers will be considered as local reference centers for the health area. A health care provider from the reference center of each health area will be designated on a voluntary basis to help in the coordination of the CCA process (hereafter referred to as "health area leader" or HAL).

With the help of the designated HALs and of local researchers accustomed to the Cameroonian health system, further stakeholders of cervical cancer prevention in selected health areas will be identified and invited to take part in the research process. Recruitment of participants for focus group discussions (FGD) and in-depth interviews in the formative research phase and process evaluation, and participatory workshops for CCA, will be facilitated by the designated HALs by using both purposive and snowball sampling methods. Participants of FGDs or interviewees from the formative research phase may also be invited to take part in ulterior participatory workshops. During the formative research phase, consent will be asked from all focus group/interview participants to share the anonymized research findings with the community during the community-based participatory workshops. All participants of the CCA process, focus group discussions and in-depth interviews will be financially compensated for their time and potential transportation costs. The seven designated HALs will receive additional remuneration for the full duration of their involvement in the research project.

Recruitment for cluster-RCT

Once the developed strategies in health areas of the intervention arm are implemented, their effectiveness on cervical cancer screening uptake among women aged 30-49 years (25-49 if HIV-positive) in rural health areas of Mifi Health District will be assessed through a cluster-RCT. In the intervention arm, the recruitment methods of participants for cervical cancer screening will therefore depend on the strategies established as part of the CCA process.

In the control arm, recruitment of study participants will be coordinated centrally at district level (from the district capital Bafoussam) following procedures previously established within a cervical cancer screening program in the health district of Dschang since 2018. This standard procedure includes the training of 2 CHWs by health area to raise awareness around cervical cancer. After an initial theoretical and practical training in cervical cancer prevention, CHWs recruit women by going door-to-door or through community meetings in their respective health areas. Through a system of nominal invitation vouchers distributed to eligible women, CHWs receive a financial incentive for each woman that shows up for cervical cancer screening. Twice a year, CHWs of all health areas are invited to a feedback session to discuss difficulties encountered on the field and propose solutions to face any identified challenges. Of note, such collaboration with CHWs may also be implemented in health areas of the intervention arm if considered appropriate by the participants involved in the CCA process, in addition to any other recruitment strategies established.

Women attending screening in Bafoussam will be enrolled in the associated clinical trial (GENOVA - CCER N° AO_2021-0006) after providing written or oral consent depending on their level of literacy. Women who refuse to provide consent to participate in the GENOVA study will be referred to a gynecologist to receive screening outside of the study. Based on our previous experience with a cervical cancer screening trial in the neighboring health district of Dschang, we expect this to occur rarely (considering the lack of organized screening in the health district of Mifi and the gratuity of screening and treatment within our study).

For all study phases, participants (including screened women and stakeholders taking part in the formative research, CCA process, and process evaluation) will be required to provide written informed consent before enrolment in the study. Participants will be provided sufficient time to

consider their participation in the study and will have the opportunity to ask questions before being enrolled. Selected research participants from the CCA phase will be invited to contribute to the dissemination of results at the community and district level at the end of the study.

4.3 Study procedures

Formative research (RQ2)

Formative research will be carried out only in the health areas randomized in the intervention arm of the cluster-RCT (see below) and will include the following steps:

1. **Identification of relevant stakeholders** for cervical cancer screening at health-area level in the selected rural health areas: these may include women of the community with or without their partners, local health care providers, community health workers, community leaders (including traditional and religious), representatives of the health district and local researchers.
2. **Assessment of determinants of access to cervical cancer screening** in selected communities: a mixed-method approach including in-depth interviews, FGDs and a quantitative survey will be used, led by a Cameroonian anthropologist with experience in cervical cancer screening. Interviews and FGDs will focus on objectives 2.1 and 2.2 (attitudes, practices and knowledge related to cervical cancer prevention, and potential barriers and facilitators of screening), while the survey will address objective 2.3. (health literacy assessment among women eligible for screening).
    a. In-depth interviews will be held with the following participants:
        i. Head of Mifi district health office
        ii. Religious leaders (~2)
        iii. Traditional leaders (village chiefs, ~2)
    b. FGDs will target the following population groups:
        i. Women from selected rural health areas eligible for screening (2-4 groups of ~6-10 participants);
        ii. Men of selected communities, including partners of women eligible for screening and men from the general population (~6-10 participants);
        iii. Women > 50 years old non-eligible for screening (~6-10 participants);
        iv. Health care providers from selected rural health areas (~6-10 participants);
        v. Community health workers from selected health areas (2 groups of 6-10 participants, separated by gender).
    c. A quantitative survey developed based on previously published literature and adapted to the local context will assess health literacy related to cervical cancer among eligible women for screening. We define health literacy as “the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health care decisions” (33).

Community co-produced action (RQ1)

1. **Participatory and community-based development of context-specific strategies to increase uptake of cervical cancer screening** at rural health-area level: these may include recruitment and/or primary screening (HPV testing) strategies, as well as potential strategies to facilitate linkage to triage and treatment. To achieve this, participatory workshops will be led by a Cameroonian anthropologist experienced in cervical cancer screening with local stakeholders from all seven health areas randomized in the intervention arm. During these workshops, an introductory presentation by research team members and local health care providers will be given on essential theoretical and

practical aspects of cervical cancer screening, and results of the previous qualitative assessment of local determinants of access to cervical cancer screening will be presented and discussed to inform the screening strategy development process. Using participatory methods (e.g. social mapping, participatory observational surveys, narratives, problem-trees, resource maps, etc.) and building on existing resources within the community, participants of each health area will then reach a consensus on an adapted recruitment and/or screening strategy to be implemented within their community. This strategy can be shared across all health areas of the intervention arm or adapted to account for local specificities of each health area, as needed.

2. **Implementation of developed strategies** in health areas of the intervention arm: the exact study procedures of this step will depend on the results of the participatory workshops and will therefore be described in more detail at that point of the study.

3. **Interpretation and dissemination of study results** within communities and to relevant stakeholders: aiming a collaborative production of knowledge and actions with affected community members through all study phases, results of the overall study process (including formative research, cluster-RCT and process evaluation) will be co-interpreted and disseminated within communities using culturally adapted communication means. A community dissemination group made of local stakeholders (including community members) will be created in order to take ownership of the study results and effectively share knowledge within the community. Members of this group will receive a financial compensation for the time spent planning result dissemination.

Cluster-randomized controlled study (RQ1)

The 14 rural health areas of the Mifi district will be cluster-randomized between two study arms. Randomization will be stratified according to health area population size and distance to the reference district hospital. Cluster-randomization at the health area level aims to limit contamination between study arms during the recruitment process.

The cluster-RCT will aim to compare population coverage for cervical cancer screening between two study arms over a period of 12 months (see Figure 1):

3) **Intervention arm: CCA-based recruitment and screening strategy.** After appropriate training, designated health area leaders will be responsible for carrying out recruitment of eligible women and facilitating HPV-based screening at rural health area level, in accordance with the strategy agreed upon for their respective health areas during CCA. All material and tools for recruitment (posters, leaflets, etc.) and vaginal self-sampling (swabs, patient information leaflets) will be made available by the research team if necessary. Regardless of the recruitment strategy implemented and whether primary HPV screening will take place locally at health-area level or centrally at district level, women diagnosed HPV positive will be invited for triage and if needed treatment at the Bafoussam Regional Hospital (BRH), in the capital of the Mifi district. HPV-negative women will be advised to repeat screening after five years (3 years for women living with HIV).
4) **Control arm: hospital-based recruitment and screening**. Recruitment of participants from all rural health areas in the control arm will be carried out centrally by a project manager at the BRH. The recruitment strategy in the control arm will follow procedures carried out until now in a previous screening program (the *3T study*) in the neighboring health district of Dschang, in which our research team has been involved (see detailed description in section *4.2 – Recruitment for cluster-RCT*). Primary screening by HPV self-sampling will be carried out at the BRH, followed by same-day triage of HPV-positive women and treatment when necessary. As in the intervention arm, HPV-negative women will be advised to repeat screening after five years (3 years for women living with HIV).

In March 2023, a cervical cancer screening program will be launched at the BRH based on primary HPV testing, triage by visual inspection after application of acetic acid (VIA) or extended genotyping, and same-day treatment by thermal ablation for eligible women or referral for more extensive treatment as needed. This screening program is part of the GENOVA study, a randomized controlled trial comparing triage of HPV-positive women by VIA with triage by HPV genotyping (treatment of women with selected high-risk genotypes only). All HPV-positive participants will be advised to repeat screening after 12 months. Screening and treatment procedures will be provided free of charge to study participants and women traveling to the BRH from rural areas of both study arms will be given financial compensation for transportation fees. The GENOVA study has received a favorable opinion by the cantonal research ethics committee of Geneva (CCER N° AO_2021-0006) and has been approved by the Cameroonian national ethics committee for research on human health (CNERSH, N°2022/09/1487/CE/CNERSH/SP). Participants of both study arms of the present study (Act4CC) will receive sufficient oral and written information on the study procedures, as well as benefits and risks involved with their participation, and will be asked to provide written consent prior to enrolment in the study. Participants' socio-demographic, medical and clinical data collected within the GENOVA study (including screening and triage results, and treatment of precancerous lesions) will be used in the analysis of outcomes of the ancillary study presented in this protocol.

Process evaluation (RQ3-4)

1) **Assessment of feasibility and acceptability of implemented strategies (RQ3)** compared to the standard hospital-based cervical cancer screening strategy: FGDs will be conducted by an experienced Cameroonian anthropologist 6 months after initial implementation of the strategies across populations of both study arms.
    a. FGDs will be conducted with health care providers involved in the cervical cancer screening process at both health-area level (intervention arm, ~7 participants) and at hospital-level (Bafoussam Regional Hospital, ~4 participants).
    b. FGDs with screened patients and unscreened women eligible for screening will be conducted in health areas of both study arms. Focus groups will be homogenous within control and intervention arms, as to not influence perceptions of the screening experience (2-3 FGDs in each study arm, including ~6-10 participants each).
2) **Assessment of the acceptability and implementation of the CCA process (RQ4):** at the end of the RCT, in-depth interviews and FGDs will be conducted by a Cameroonian anthropologist in health areas of the intervention arm, and study records and field notes will be reviewed to assess the implementation process of CCA.
    a. Review of study records and field notes will assess how many health areas of the intervention arm participated in CCA, and whether the number/format of meetings, activities and participating community members corresponded to what was originally planned with HALs;
    b. FGDs will include community members and local stakeholders having participated in CCA (~3 focus groups of ~6-10 participants) and in-depth interviews will be conducted with all 7 HALs to evaluate their perception and acceptability of the process, identify challenges and enablers of successful CCA, as well as any unintended consequences of the CCA process.

Economic Evaluation (RQ5)

Total cost of the CCA intervention and incremental cost-effectiveness ratio (ICER) of CCA compared to traditional hospital-based recruitment and screening methods will be calculated for the following outcomes: number of women screened, number of CIN2+ detected, number of cervical cancers detected, number of women treated for CIN2+ and number of women treated for cervical cancer.

Costs will include salaries and financial compensations of all local staff and participating community members/stakeholders, room rental, transportation fees, equipment and office fees, food and beverages, and all costs associated to recruitment/screening strategies either developed as part of CCA or corresponding to traditional hospital-based methods.

For study phases using qualitative research (RQ2-4), semi-structured interview guides and FGD topic guides will be developed by a multidisciplinary team composed of physicians, public health specialists and anthropologists and pretested on fellow members of the research team or health care providers working in cervical cancer screening programs at hospital-level. Provisional interview and focus group topic guides may be adapted after pretesting with local research team members and if additional feedback or ideas emerge during qualitative data collection.

All interviews and FGDs will be audio-recorded (using a recorder or smartphone), and later transcribed and coded by designated researchers using a qualitative data coding software such as ATLAS.ti or NVivo.

4.4 Study timeline

Study phase	2023				2024				2025		
	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Aug
Formative research & CCA											
Submit protocol for ethical approval											
Study preparation: interview/ FGD guides, questionnaires, workshops											
Stakeholder identification											
Conduction of interviews/FGDs											
Data transcription and analysis											
Participatory workshops											
Presentation and publication of results											
Cluster RCT											
Study preparation (equipment, documents…)											
Finalize study design based on PAR results											
Training of study personnel											
Conduction of the RCT											
Data analysis											
Presentation and publication of results											
Process evaluation											
Assessment of feasibility & acceptability											
preparation of interview/FGD guides, participant selection											
Conduction of interviews/FGDs											

Data transcription and analysis																									
Assessment of the CCA process																									
preparation of interviews/FGD guides, participant selection																									
Conduction of interviews/FGDs																									
Review of study records/field notes																									
Data transcription and analysis																									
Presentation and publication of results																									
Economic evaluation																									
Data collection (review of costs)																									
Cost-effectiveness analysis																									
Presentation and publication of results																									

4.5 Withdrawal and discontinuation

The participants can choose to withdraw from the study at any moment during its course. We will explain to them that all medical and biological data obtained up until then will be used for the purposes of the study. The data obtained up to this point in the study will be anonymized by attributing a unique codified identification to each participant. The full name of the participant will appear only on the consent form; all other study documents, in paper or electronic form, will contain only the participant unique identifier.

5 STATISTICS AND METHODOLOGY

5.1. Statistical analysis plan

The null hypothesis will be considered as both study arms having the same proportion of eligible women undergoing a complete screening procedure (defined as primary HPV testing and triage (by VIA or genotyping) for HPV-positive participants, and HPV testing only for HPV-negative participants). P-values will be calculated accordingly using the chi-square test for comparison of proportions, after adjusting for the clustering effect. Secondary outcomes including the proportion of eligible women completing primary screening within 12 months, the proportion of HPV-positive women who complete triage and treatment, and the proportion of HPV-positive women who return for follow-up after 12 months, will also be assessed using the chi-square test with two-sided p-values. Distribution of socio-demographic, behavioral and medical characteristics in both study arms will be expressed as proportions, means with standard deviations or medians as appropriate, and p-values will be calculated using chi-squared statistic test, t-test and/or Wilcoxon and Mann-Whitney tests as appropriate. The significance level will be two-sided with $\alpha = 0.05$. Analyses will be conducted using Stata Statistical software Release 16 (StataCorp LP, College Station, TX) or R statistical software.

5.2. Calculation of sample size

According to national estimates, women aged between 30 and 49 years represent approximately 10% of the Cameroonian population.(26) Within Mifi district's rural population of 152,000, this represents 15,200 women between 30-49 years old who would be eligible for the cervical cancer screening program. According to the WHO's 90-70-90 targets for cervical cancer elimination, 70% of women in this age group should be screened at least twice in a lifetime, at an interval of 10

years.(7) In other words, we would expect 7% of women in this age group to complete screening each year. In our previous experience in cervical cancer screening in the Health District of Dschang (West Region of Cameroon), only half of this target population (approximately 3.5%) has been screened each year with traditional recruitment methods.

To detect a 3.5% difference between both research arms (3.5% with traditional vs 7% with CCA-based recruitment) with 95% significance and 80% power, 632 women would be needed in each study arm (1264 in total) (calculated using the online statistical software OpenEpi, version 3, www.OpenEpi.com). However, as randomization is done in clusters, a certain degree of intracluster correlation is expected within health areas, and the calculated sample size should therefore be multiplied by the design effect (DE = 1 + ICC*(cluster size - 1)). Assuming an intracluster correlation coefficient (ICC) of 0.01 (27) and clusters of approximately 1086 women aged 30-49 years (15,200 divided by 14 health areas), we obtain a DE of 12. The final sample size is therefore 12*1264 = 15,168 women. Thus, the total rural population of women aged 30-49 years of approximately 15,200 in the district should be enough to detect a 3.5% difference in screening rate between both study arms (total expected participation of 532 (7% of 7600) and 266 (3.5% of 7600) women in the intervention and control arms respectively, over one year).

5.3. Handling of missing data

Missing data will be reported as such. Drop-outs at any stage of the study after enrolment will be considered in the analysis of any secondary outcomes which may be assessed up to the time of withdrawal (e.g. proportion completing primary screening, triage, treatment).

5.5. Qualitative methodology

The French transcripts will be analyzed using qualitative content analysis supported by the software Atlas.ti. A mixed deductive and inductive approach will be used to develop coding categories. Prior to the initial coding, deductive categories will be defined based on the theoretical, scientific evidence and summarized in a coding agenda consisting of definitions, examples and coding rules for each deductive category.
Based on this, a sample of the interviews will be coded by one or multiple members of the research team. In a step-by-step analysis consisting of individual deductive coding, revising categories and the coding agenda, researchers will determine the main topics and sub-topics common to every interview, and identify inductively, emerging codes.

6 REGULATORY ASPECTS AND SAFETY

6.1 Local regulations / Declaration of Helsinki

This research project will be conducted in accordance with the protocol, the Declaration of Helsinki (2), the principles of Good Clinical Practice, the Cameroonian Law (1) and regulatory authority´s requirements as applicable.

6.2 Notification of safety and protective measures

If, during the research project, circumstances arise which could jeopardise the safety or health of the participants or lead to a disproportionate relationship between the risks and burdens and the benefits, all the measures required to ensure protection are to be taken without delay.
The project leader and the Sponsor are promptly notified (within 24 hours) if immediate safety and protective measures have to be taken during the conduct of the research project. The Swiss Ethics Committee will be notified via BASEC and the Cameroonian national Ethics Committee via postal mail of these measures and of the circumstances necessitating them within 7 days.

6.3 Serious events

If a serious event occurs, the research project will be interrupted and the Ethics Committees notified on the circumstances via BASEC (Switzerland) or postal mail (Cameroon) within 7 days.

6.4 Amendments

Substantial changes to the project set-up, the protocol and relevant project documents will be submitted to the Ethics Committees for approval before implementation. Exceptions are measures that have to be taken immediately in order to protect the participants.

6.5 End of project

Upon project completion or discontinuation, the Ethics Committees are notified within 90 days. All biological materials and health-related data are anonymized upon termination of data analysis.

6.6 Insurance

In the event of project-related damage or injuries, the Sponsor will be liable, except for damages that are only slight and temporary; and for which the extent of the damage is no greater than would be expected in the current state of scientific knowledge.

7 FURTHER ASPECTS

7.1 Overall ethical considerations

The demand for programs to combat cervical cancer in low-resource settings is strong and within the focus of the WHO to develop a global strategy towards eliminating cervical cancer as a public health problem. As part of a Swiss-Cameroonian collaboration of over 20 years, our research team benefits from the support of the Cameroonian Ministry of Health and the Ministry of Women's Empowerment and the Family. Our experience in the implementation of a cervical cancer screening program in Dschang and our previous collaboration with local stakeholders at health district level, will facilitate the launch of the new screening program in Bafoussam as well as the organization of this ancillary study (including the CCA approach). Lessons that we have learned from our previous experience, combined with results of recent researches have put our group in an excellent position to identify innovative strategies to increase access to screening in disadvantaged population groups and therefore reduce morbidity and mortality of cervical cancer in low-income countries. The developed recruitment and screening procedures will be thoroughly evaluated and, if successful, will have the potential to be replicated in other rural regions of Cameroon to create a sustainable health delivery system. Our community-centered approach with the inclusion of a diverse range of local stakeholders will inform district, regional and national Cameroonian health officials on priorities for secondary cervical cancer prevention and will strengthen the capacity to implement a locally adequate cervical cancer screening program in the district. At a larger scale, it may catalyze development and implementation of relevant policies, strategies and plans for cervical cancer prevention in other LMICs.

Participation in the study will take place on a voluntary basis. Study participants will be dispensed of screening costs and offered financial compensation for their travel costs to the screening center. At all phases of the study, participants will be provided a participant information sheet and a consent form describing the study and providing sufficient information to make an informed decision about their participation in the study. Participants will be offered the opportunity to ask questions relative to the study before providing consent. Those needing more time to consider their participation in the study will have the opportunity to come back at another date for screening.

7.2 Risk-Benefit Assessment

The study participants will benefit from a free screening for cervical cancer, and when necessary, will be treated immediately with thermal ablation. The study will be carried out in a setting where there is no structured screening program to date, with the aim of improving access to screening in disadvantaged rural areas. As such, this study contributes to mitigating health inequalities and improving women's health in Cameroon following WHO-recommended guidelines for cervical cancer screening. The screening and treatment procedures planned within the study are highly accepted and well tolerated by women. Local doctors, in accordance with the recommendations of the International Federation of Gynecology and Obstetrics (FIGO) and the WHO, will manage women with cervical dysplasia or cancer.

Through the participatory approach chosen for our study, we aim to conduct research *with* rather than *for* the affected communities in rural Cameroon, considering members of the community as research partners instead of research subjects. Using community-based participatory research methods increases the likelihood of developing context-sensitive solutions to the lack of access to screening services which are sustainable, acceptable to local communities, and well integrated in the current health care system.

One possible risk is the unauthorized data access or unwanted identification of project participants. However, all necessary caution will be undertaken to limit this risk by attributing unique identifiers to all participants and using only these identifiers on study documents and databases. An additional risk may be adverse events from treatment by thermal ablation, such as bleeding or infection. However, the risk of such events is low with thermal ablation which has been assessed as safe and acceptable for women, and is one of the WHO-recommended treatment modalities for cervical precancerous lesions.(34) This risk will additionally be minimized by offering extensive training and supervision of health care providers involved in the study. Any side effects of the screening and/or treatment procedure will be managed free of charge in the reference hospital according to international standard of care. Finally, the participatory process in itself comes with risks to community members taking part in the intervention, such as stigma, opposition or rejection by their community. We will attempt to mitigate these risks by working with local researchers and health care providers who will provide regular reports on challenges encountered on the field to the project management team, so that appropriate measures can be taken in response.

8 QUALITY CONTROL AND DATA PROTECTION

8.1 Quality measures

To minimize risk of missing data, collected data will be recorded both on paper (p-CRF) and electronic Case Report Forms (e-CRF). P-CRFs will be filled in on site by trained study personnel and later transcribed electronically by designated study investigators. The eCRF will ensure high data quality control by applying logical and managerial controls over data capture in order to ensure consistency, completeness and coherence of data. An elaborated electronic process to comment, query and claim correction actions on data via reviewing will reinforce data quality throughout the study conduct and termination.

All study personnel, including social scientists, gynaecologists, midwives, laboratory technicians and research assistants, will be trained on all important study-related aspects.

Supervision of the trial will be ensured by the main investigators at the local site and the principal investigator and project leader in Switzerland through regular on-line meetings (minimum 1x/month) with the study personnel and on-site quality visits at least 1x/year.

For quality assurance, the sponsor, the Ethics Committee or an independent trial monitor may visit the research site. Direct access to the source data and all study related files is granted on such occasions. All involved parties keep the participant data strictly confidential.

8.2 Data recording and source data

Quantitative data will be collected by health care providers and research assistants through structured surveys and will cover the following areas/topics:

- Inclusion criteria and consent
- Demographics
- Socio-economic characteristics
- Gynecological and obstetrical history
- Medical history
- Acceptability of the screening procedure (including recruitment)
- Health literacy

All research subjects will be pseudonymised. Quantitative survey data that are collected for each research subject will constitute the subject CRF (Case Reports Form).

In addition, qualitative data from semi-structured individual interviews, focus group discussions and participatory workshops will also be collected in audio-recorded format (wav or MP3 format) and typed transcripts (.docx format) of the recordings. Digital photographs (JPEG files) and video recordings (.wmv format) may also be taken during participatory workshops with the consent of all individuals appearing in them. Transcripts (textual data) of the audio and/or video recordings will be produced in the original language and English translations (when necessary) will also be created.

Daily, each investigator will transfer the qualitative data (i.e. audio recordings, video recordings, photographs) from the recording instruments to their professional password-secured laptop locally in Cameroon. In addition, data will be transferred to a designated research assistant at Geneva University Hospitals (HUG) using SWITCH, a secure swiss cloud-based storage service, daily or as soon as a reliable internet connection and sufficient bandwidth are available on site. To limit the risk of data loss in Cameroon prior to the data transfer to the HUG, the laptop used for the study will be stored in a locked cabinet or room whenever not in use by one of the research assistants. The data received via SWITCH will be saved daily (or as soon as possible) on the HUG secure servers by a designated research assistant in order to be protected by backup plans in place at the HUG (see below).

Quantitative data obtained from surveys will be physically stored in an Oracle ver.11g. RDBMS (Relational Database Management System) using the dedicated CDMS software (Clinical Database Management System) secuTrial®. This CDMS is a central Web-based system consolidating all CRF related data, whether the project is mono or multi centric. The investigation team will enter the data interactively in the CDMS by means of its interactive graphical interface. Transfer of quantitative data from paper CRFs to electronic CRFs on secuTrial® may be done directly on-site in Cameroon if there is a reliable internet connection or by designated research assistants in the HUG after a secure data transfer via SWITCH. Data will be edited and viewed by the investigation personnel based on the role of each participant. Validation/review will be performed in parallel by appropriate people designated by the sponsor (monitors, sponsor, coordinators, data managers, etc.).

All modifications to the eCRF during the study conduct will be tracked and dealt with consequently (version numbering). Data will be electronically and systematically revalidated after each major change, and corrections/completeness applied whenever necessary.

On HUG premises, all data are physically stored in dedicated data centers. The physical hardware consists of enterprise-grade servers, networking, and storage solutions from tier 1 vendors and trustworthy and stable GNU/GPL solutions. HUG infrastructure is under the responsibility of DSI (*Direction des Systèmes d'Information* at HUG). All exploitation, monitoring and backup operations are performed by DSI, in accordance with the Unit of Clinical Investigations (UIC) policies. All systems and applications are continuously monitored. Appropriate measures are automatically taken whenever an alert is issued.

Backup operations are performed by the DSI service at HUG, in accordance with UIC policies. Frequent backups are performed using the best enterprise backup solutions at HUG, and are

physically stored in a fire-proof safe. The backup strategy comprises an optimised hourly, daily, monthly and yearly retention plan.

All system logins, interventions, modifications and form status changes will be thoroughly recorded in an Audit Trail log system. Deviations to the protocol will be also tracked and resolution status indicated.

8.3 Confidentiality and coding

Project data

Project data will be handled with uttermost discretion and is only accessible to authorized personnel who require the data to fulfil their duties within the scope of the research project. On the CRFs and other project specific documents, participants are only identified by a unique participant number. Coded data will be used. A contact sheet linking each participant's identity and contact information with their participant number will be stored at the local research site in a locked cabinet. Only the local principal investigator and designated local research assistants will have access to those documents. The information on the contact sheets will be transcribed on an excel file which will be shared securely via SWITCH to the project leader in Switzerland, in order to safely back the data electronically. This file will be password-protected and accessible on Geneva University Hospital (HUG) servers only to the project leader and principal investigator.

Physical access to the data centers at HUG is logged and limited to authorized personnel only (principal investigator and authorized research assistants). On a regular basis, vulnerability testing is performed to reduce potential exposure.

Remote access to servers is limited to authorized personnel. Connections to servers are encrypted using SSH. System logs are stored in a dedicated centralized system for audit purposes. The internal HUG network is protected by multiple firewalls, proxy, reverse-proxy and anti-virus solutions. Web servers operate under SSL (HTTPS) certifications, ensuring Web connections are encrypted and secure.

At the CDMS level, only people part of the investigation team, the sponsor team, the affiliated reviewers or auditors, as well as inspection authorities are given access to data.

Personal accounts are granted individually for each person. Identification is made by a personnel ID and a password. Failure to provide the correct password after a limited number of attempts automatically deactivates the faulty account (protection against non-authorized attacks).

Only institutional e-mail addresses will be accepted for any communication of sensitive data regarding account creation and management.

Pen-Tests (simulation of malware attacks) are regularly performed, and measures taken whenever necessary.

Biological material

Biological material in this project is not identified by participant name but by a unique participant number. Biological material is appropriately stored in a restricted area locked by key only accessible to authorized personnel. Biological material is stored at room temperature. All biological material transferred from Cameroon to Switzerland (HUG, Gynecology division, Boulevard de la Cluse 30, 1205 Geneva) for analysis is listed on an excel file containing the participant identifier, date of sampling and the nature of samples shipped. Biological material is only sent abroad in the scope of the research project, if the participant involved has given her consent to do so upon having been sufficiently informed.

8.4 Retention and destruction of project data and biological material

At the end of the project, the entire database will be archived in a reusable format. Archives encompass all raw data, meta-data, transformed data, transformation operations, deviations, version history, and audit trails. Redeployment of the entire database is therefore possible whenever needed.

The comprehensive archive will remain propriety of the sponsor and will be preserved during a minimum period of 10 years. The UIC will also ensure an electronic copy of the archive will be stored within the DSI infrastructure for a theoretical infinite period of time.

All biological material will be destroyed by the laboratory conducting analyses after the analysis has been completed and its result recorded and transmitted to the project investigators, and at the latest at the end of the study.

9 FUNDING / PUBLICATION / DECLARATION OF INTEREST

Funding has been requested to the Doc.CH grant of the Swiss National Science Foundation and will be applied for at the HUG Commission des Affaires Humanitaires for a duration of three years.

Priority will be given to open-access scientific peer-reviewed journals for publication of results. Descriptive statistics and data analysis will be made available through our publications for third party review or reuse. The anonymized quantitative data will be shared on Yareta, the data repository of the University of Geneva, under a CC BY license. The dataset will also be identified with a DOI.

The project investigators declare no conflict of interest with the present study.

10 INFORMATION LETTER

Informations destinées aux membres de la communauté du district de santé de la Mifi

Concerne l'étude: « Action coproduite en communauté pour la participation au dépistage du cancer du col de l'utérus (Act4CC) : un essai contrôlé randomisé dans les zones rurales de la région de l'Ouest du Cameroun ».

Cette étude est organisée par l'Hôpital Régional Annexe de Dschang, l'Hôpital Régional de Bafoussam et les Hôpitaux Universitaires de Genève, Suisse.

Madame, Monsieur, nous vous invitons à participer à une recherche (étude).

Contexte et justification de l'étude

Le col de l'utérus donne souvent naissance à des cancers. Par un prélèvement vaginal, on peut détecter ces cancers très tôt, puis les enlever avant qu'ils ne causent des dégâts. Ce dépistage est recommandé par l'Organisation Mondiale de la Santé et le Ministère de la Santé Publique du Cameroun à travers son Comité National de Lutte Contre le Cancer. Une procédure de dépistage de ce type a été mise en place au sein de l'Hôpital Régional de Bafoussam.

Toutefois, l'expérience de notre équipe de recherche dans la Région Ouest du Cameroun nous a montré que de nombreuses femmes camerounaises en zone rurale n'ont pas ou peu accès à ces services de dépistage. Dans un souci d'égalité des chances et dans le but de toucher un maximum de femmes, nous avons décidé de faire appel aux membres des communautés directement affectées par cette inégalité d'accès aux soins, dont vous faites partie. Le co-développement d'actions de promotion de la santé par les membres de communautés directement affectées par une problématique, en collaboration avec des expert·es du domaine (soignant·es et scientifiques), peut mener à des solutions innovantes, acceptables pour la population et plus adaptées au contexte local. Le but de notre projet est

donc de faire appel aux connaissances, compétences et ressources existantes des communautés rurales du district de santé de la Mifi pour développer et mettre en place des stratégies communautaires pour améliorer l'accès au dépistage du cancer du col de l'utérus pour les femmes âgées entre 30 et 49 ans (25 et 49 ans pour les femmes vivant avec le VIH). Pour cela, plusieurs phases d'étude seront menées, qui sont détaillées ci-dessous. Vous pouvez être invité.e à participer à l'une ou plusieurs de ces phases d'étude, selon votre rôle dans la communauté et les besoins de l'étude.

Description détaillée de l'étude

1) Phase de recherche formative

Dans le but de comprendre les déterminants de l'accès au dépistage du cancer du col dans les zones rurales du district de santé de la Mifi, nous allons évaluer les aspects suivants :

- les attitudes, les pratiques et les connaissances liées à la prévention du cancer du col de l'utérus parmi les membres de la communauté, les acteurs locaux et les prestataires de soins de santé;
- les obstacles et les facilitateurs potentiels du dépistage du cancer du col de l'utérus dans les zones rurales du district ;
- l'influence des connaissances en matière de santé et du système de santé (général et en lien avec le cancer du col de l'utérus) sur l'accès au dépistage.

Population cible : vous pouvez être invité.e à participer à cette phase de l'étude si vous êtes :

- acteur/actrice du système de santé du district
- personnel soignant local
- une autorité traditionnelle ou religieuse locale
- une femme éligible pour le dépistage (voir critères d'éligibilité ci-dessous)
- une femme d'une des communautés sélectionnées de plus de 50 ans
- un homme d'une des communautés sélectionnées (partenaire ou non d'une femme éligible au dépistage)
- un.e agent.e de santé communautaire exerçant une activité dans une des communautés sélectionnées

Forme de la participation : vous pourrez être invité.e à prendre part à la recherche sous l'une de ces deux formes :

- **entretien individuel** approfondi d'une durée de 45-60 minutes
- **discussion dirigée de groupe** (environ 6-10 participant.es par groupe) d'une durée d'1h-1h30

Dans les deux cas, les entretiens et discussions seront menées par une anthropologue (spécialiste des sciences humaines et sociales) camerounaise expérimentée dans le dépistage du cancer du col de l'utérus dans la région.

Les femmes éligibles pour le dépistage sont également invitées à participer à un **questionnaire** anonyme sur l'état de leurs connaissances en matière de santé et d'accès aux soins d'une durée d'environ 30 minutes. Le but de ce questionnaire sera d'évaluer si ce niveau de connaissances a un impact sur l'accès au dépistage et, le cas échéant, quelles mesures d'éducation de la population pourraient être utiles pour améliorer l'accès au dépistage pour les femmes en zone rurale au Cameroun.

2) Action co-produite en communauté

Le but de cette phase du projet est de développer et planifier une stratégie d'action communautaire pour améliorer l'accès au dépistage aux femmes éligibles de la communauté. Pour cela, des **ateliers participatifs** seront menés avec des membres de la communauté et parties prenantes locales intéressé.es à la thématique de la prévention du cancer du col de l'utérus et plus généralement la santé de la femme en zone rurale au Cameroun.

Population cible : Les participants à ces ateliers (appelés ci-après « participants-chercheurs » peuvent être : les femmes de la communauté (éligibles ou non au dépistage) avec ou sans leurs partenaires, les prestataires de soins de santé locaux, les agents de santé communautaires, les leaders communautaires (y compris les autorités traditionnelles et religieuses), les représentants du district de santé, les chercheurs locaux et toute autre personne proche de la communauté souhaitant participer au processus de co-production.

Déroulement des ateliers : Pour le développement de stratégies localement adaptées, les participant.es seront guidées par des membres du projet de recherche expérimentés en santé publique et sciences sociales, avec une expérience préalable dans la prévention du cancer du col de l'utérus. Des informations sur le cancer du col et sa prévention seront partagées en début des ateliers participatifs afin d'aider les participants-chercheurs à développer des stratégies adaptées. Les résultats de la première phase de recherche formative (voir point 1 ci-dessus) pourront également être partagés si jugés utiles pour l'élaboration de stratégies de recrutement de femmes pour le dépistage.

Les stratégies développées en communauté sont totalement libres pour autant qu'elles respectent les standards éthiques reconnus au niveau local et international (ceux-ci seront détaillés lors des ateliers participatifs). A titre illustratif, elles peuvent inclure la collaboration avec des agents de santé communautaires ou des associations locales (par exemple de femmes), des campagnes de sensibilisation dans les aires de santé, le développement de matériel éducatif adapté à la culture locale, l'intégration du dépistage dans les centres de santé locaux, l'organisation de transport en groupe au centre de dépistage, etc.

Cette phase de co-production en communauté sera documentée par une prise de notes, ainsi qu'éventuellement des photos et enregistrements vidéos, si le consentement est obtenu de toute personne figurant sur ces derniers. Cette documentation pourra ensuite être utilisée pour la diffusion des résultats de ce processus participatif à des fins scientifiques ou au sein de la communauté.

Au total, **4 ateliers participatifs d'une demi-journée** chacun auront lieu dans un local identifié comme adéquat dans votre aire de santé respective, et seront répartis sur un mois selon un horaire à convenir. La participation aux 4 ateliers n'est pas obligatoire mais fortement recommandée afin de garder une cohésion de groupe et un fil conducteur dans les décisions prises. A la fin de ces 4 ateliers, il est attendu que le groupe d'action de chaque aire de santé inclue dans le projet ait convenu d'une stratégie qu'il souhaite adopter et mettre en place au niveau de son aire de santé. L'efficacité, l'acceptabilité et la faisabilité des stratégies développées sera ensuite évaluée dans des phases subséquentes du projet de recherche.

3) Evaluation des stratégies de dépistage communautaires

Dans le but d'apprécier la perception par les membres de la communauté des stratégies de dépistage implémentées, les aspects suivants seront évalués :

- Leur acceptabilité par les femmes éligibles pour le dépistage et les prestataires de soins;
- La faisabilité des stratégies implémentées dans le contexte des aires de santé rurales du district, y compris la prise en charge des femmes avec un test de dépistage positif (nécessitant d'autres examens ou traitements).

Population cible :

- Prestataires de soins du district de santé de la Mifi
- Femmes ayant participé au dépistage
- Femmes éligibles n'ayant pas fait de dépistage

Les participant.es ci-dessus peuvent être issues d'aires de santé inclues dans le projet de recherche participatif (ayant participé à la phase 2 « action co-produite en communauté ») tout comme d'autres aires de santé du district de santé, afin de comparer les stratégies de recrutement et dépistage développées par un processus participatif avec les stratégies traditionnelles (basée sur un dépistage hospitalier).

Forme de la participation : vous serez invitée à participer à une **discussion dirigée de groupe** (environ 4-10 participant.es par groupe) d'une durée d'1h-1h30. Les discussions seront menées par une anthropologue (spécialiste des sciences humaines et sociales) camerounaise expérimentée dans le dépistage du cancer du col de l'utérus dans la région.

4) Evaluation du processus participatif « d'action co-produite en communauté »

Dans le but d'évaluer l'utilisation d'un processus participatif pour le co-développement d'actions communautaires pour la promotion de la santé en zone rurale au Cameroun, les aspects suivants seront investigués :

- La perception des membres de la communauté ayant participé aux ateliers participatifs du processus de co-production en communauté, ainsi que leur acceptation de ce type de projet ;
- Les obstacles et facilitateurs d'un processus participatif de co-production en communauté ;
- Les conséquences inattendues du processus participatif sur les participants-chercheurs et la communauté en général.

Population cible : membres de la communauté et parties prenantes locales ayant participé aux ateliers participatifs (phase 2 ci-dessus).

Forme de la participation : vous pourrez être invité.e à prendre part à la recherche sous l'une de ces deux formes :

- **entretien individuel** approfondi d'une durée de 45-60 minutes
- **discussion dirigée de groupe** (environ 6-10 participant.es par groupe) d'une durée d'1h-1h30

Dans les deux cas, les entretiens et discussions seront menées par une anthropologue (spécialiste des sciences humaines et sociales) camerounaise expérimentée dans le dépistage du cancer du col de l'utérus dans la région.

<u>Gestion des données</u>

Les entretiens et discussions groupées de toutes les phases du projet (hormis les ateliers participatifs) seront enregistrés puis retranscrits et étudiés. La retranscription des

enregistrements sera menée de manière confidentielle et d'éventuelles citations dans le cadre de l'étude seront anonymisées (c'est-à-dire que votre nom ne sera pas publié ni divulgué en dehors de l'équipe investigatrice de l'étude). Les résultats de cette enquête seront publiés sous différents formats à des fins scientifiques et pour le développement de programmes de santé dans la communauté. Les enregistrements seront conservés en lieu sûr (et accessibles seulement par du personnel autorisé) au minimum 10 ans après la fin de cette étude.

Retrait de l'étude

Vous pouvez à tout moment vous retirer de l'étude si vous le souhaitez ou quitter les entretiens/discussions de groupe/ateliers sans en donner de raison, sans que cela n'affecte votre activité professionnelle ou votre éventuelle participation à un dépistage du cancer du col de l'utérus.

Rémunération

La participation à la présente étude repose sur une base volontaire. Votre participation n'est pas rémunérée, mais des frais de dédommagement pour le transport au lieu d'entretien et le temps consacré à votre participation vous seront offerts. En même temps, elle n'implique pas de frais supplémentaire de votre part. Aucun but lucratif n'est poursuivi.

Réparation des dommages subis

Cette étude n'implique aucun risque pour votre santé. Le processus participatif en lui-même comporte des risques pour les membres de la communauté prenant part au projet, tels que la stigmatisation, l'opposition ou le rejet par la communauté. Ces risques sont atténués par la collaboration avec des chercheurs/chercheuses et prestataires de soins de la région accoutumé.es à la culture locale, qui fourniront des rapports réguliers sur les défis rencontrés sur le terrain à l'équipe de gestion du projet, afin que des mesures appropriées puissent être prises si nécessaire.

Financement de l'étude

L'étude est intégralement financée par des fonds privés (à préciser dès l'obtention de fonds).

Interlocuteurs

En cas de doute, de crainte ou de besoin pendant ou après l'étude, vous pouvez vous adresser à tout moment à l'un des interlocuteurs suivants :

Prof. Bruno Kenfack
(investigateur principal local)
Chef du dép. de gynécologie et obstétrique
Hôpital Régional Annexe de Dschang
Tél: +237 33 45 12 06
Email: brunokenfack@gmail.com

Prof. Patrick Petignat (promoteur)
Chef du service de gynécologie
Hôpitaux Universitaires de Genève (Suisse)
Tél. +41 (0)22 372 44 32
Email : Patrick.Petignat@hcuge.ch

Adresse du Comité National d'Ethique de la Recherche en Santé Humaine du Cameroun

Ministère de la Santé Publique
Division de la Recherche Opérationnelle en Santé

Comité National d'Ethique de la Recherche pour la Santé Humaine
Secrétariat Technique Tél : (+237) 222 76 21 14
Email : cnethique_minsante@yahoo.fr

11 CONSENT FORM

Déclaration de consentement

Veuillez lire attentivement ce formulaire.
N'hésitez pas à poser des questions lorsque vous ne comprenez pas quelque chose ou que vous souhaitez avoir des précisions.

Titre de l'étude : « Action coproduite en communauté pour la participation au dépistage du cancer du col de l'utérus (Act4CC) : un essai contrôlé randomisé dans les zones rurales de la région de l'Ouest du Cameroun »

Investigateur principal local : Prof. Bruno Kenfack, Hôpital Régional Annexe de Dschang, Tel : (+237) 33 45 12 06, Email : brunokenfack@gmail.com
Institution responsable (promoteur) : Prof. Patrick Petignat, Chef du Service de Gynécologie des Hôpitaux Universitaires de Genève (Suisse). Boulevard de la Cluse 30, CH-1205 Genève.

Lieu de réalisation de l'étude : District de santé de la Mifi

Participant(e) (nom et prénom en majuscules) :

Date de naissance :_____/_____/_____
Par la présente,

- Je déclare avoir été informé·e, par le/la responsable de l'étude soussigné·e, oralement et par écrit, des objectifs et du déroulement de l'étude ainsi que des effets présumés, des avantages, des inconvénients possibles et des risques éventuels.
- J'ai reçu des réponses satisfaisantes aux questions que j'ai posées en relation avec ma participation à l'étude.
- Je conserve la feuille d'information datée du 24.01.2023 et reçois une copie de ma déclaration de consentement écrit. J'accepte le contenu de la feuille d'information qui m'a été remise sur l'étude précitée.
- Je prends part à cette étude de façon volontaire. Je peux, à tout moment et sans avoir à me justifier, révoquer mon consentement à participer à l'étude.
- J'ai eu suffisamment de temps pour prendre ma décision.
- J'accepte que les spécialistes compétents du mandataire de l'étude, des autorités et de la Commission d'éthique compétente pour cette étude puissent consulter les transcriptions des enregistrements à condition toutefois que la confidentialité de ces données soit strictement assurée.
- Le cas échéant, je consens à l'utilisation de photos/enregistrements vidéos prises durant les ateliers participatifs auxquels je prendrai part, à des fins de publication des résultats de l'étude destinées à un public à la fois scientifique et communautaire. *[Veuillez tracer la phrase précédente si vous ne consentez pas à ce point]*
- Mon consentement ne décharge pas les investigateurs de leurs responsabilités, je conserve tous mes droits garantis par la loi.

- En signant le présent formulaire, je donne mon consentement pour la participation aux phases d'étude suivantes (veuillez cocher les phases d'étude qui vous concernent) :
    - ☐ Phase 1 : recherche formative
    - ☐ Phase 2 : action co-produite en communauté (ateliers participatifs)
    - ☐ Phase 3 : évaluation des stratégies de dépistage communautaires
    - ☐ Phase 4 : évaluation du processus participatif

▪ Lieu et date : ▪ Signature du/de la participant·e :	▪ Lieu et date : ▪ Signature de l'investigateur/investigatrice :

12 REFERENCES

1. Republic of Cameroon. Law relating to medical research involving human subjects in Cameroon. 2022/008 Apr 27, 2022.

2. World Medical Association. Declaration of Helsinki - ethical principles for medical research involving human subjects. 2013 Oct.

3. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209–49.

4. Jedy-Agba E, Joko WY, Liu B, Buziba NG, Borok M, Korir A, et al. Trends in cervical cancer incidence in sub-Saharan Africa. Br J Cancer. 2020;123(1):148–54.

5. GLOBOCAN 2020. Global Cancer Observatory. International Agency for Research on Cancer. [Internet]. [cited 2021 Nov 16]. Available from: https://gco.iarc.fr/

6. Falcaro M, Castañon A, Ndlela B, Checchi M, Soldan K, Lopez-Bernal J, et al. The effects of the national HPV vaccination programme in England, UK, on cervical cancer and grade 3 cervical intraepithelial neoplasia incidence: a register-based observational study. The Lancet. 2021 Dec 4;398(10316):2084–92.

7. Landy R, Pesola F, Castañón A, Sasieni P. Impact of cervical screening on cervical cancer mortality: estimation using stage-specific results from a nested case-control study. Br J Cancer. 2016 Oct 25;

8. Okyere J, Duodu PA, Aduse-Poku L, Agbadi P, Nutor JJ. Cervical cancer screening prevalence and its correlates in Cameroon: secondary data analysis of the 2018 demographic and health surveys. BMC Public Health. 2021 Jun 5;21(1):1071.

9. World Health Organization. Global strategy to accelerate the elimination of cervical cancer as a public health problem. Geneva: World Health Organization; 2020 p. ISBN 978-92-4-001410-7.

10. Lim JNW, Ojo AA. Barriers to utilisation of cervical cancer screening in Sub Sahara Africa: a systematic review. Eur J Cancer Care (Engl). 2017 Jan;26(1).

11. Mutyaba T, Mirembe F, Sandin S, Weiderpass E. Male partner involvement in reducing loss to follow-up after cervical cancer screening in Uganda. Int J Gynecol Obstet. 2009;107(2):103–6.

12. Pham MA, Benkortbi K, Kenfack B, Tincho Foguem E, Sormani J, Wisniak A, et al. Recruitment strategies to promote uptake of cervical cancer screening in the West Region of Cameroon. BMC Public Health. 2022 Mar 19;22(1):548.

13. World Health Organization. Introducing and scaling up testing for human papillomavirus as part of a comprehensive programme for prevention and control of cervical cancer. Geneva, Switzerland: WHO; 2020 Nov.

14. Rodriguez NM. Participatory innovation for human papillomavirus screening to accelerate the elimination of cervical cancer. Lancet Glob Health. 2021;9(5):e582–3.

15. Fitzpatrick MB, El-Khatib Z, Katzenstein D, Pinsky BA, Chirenje ZM, McCarty K. Community-based self-collected human papillomavirus screening in rural Zimbabwe. BMC Public Health. 2019 May 29;19(Suppl 1):603.

16. Wallerstein N, Duran B. Community-Based Participatory Research Contributions to Intervention Research: The Intersection of Science and Practice to Improve Health Equity. Am J Public Health. 2010 Apr;100(Suppl 1):S40–6.

17. Wilson E. Community-Based Participatory Action Research. In: Liamputtong P, editor. Handbook of Research Methods in Health Social Sciences [Internet]. Singapore: Springer; 2019 [cited 2022 Nov 30]. p. 285–98. Available from: https://doi.org/10.1007/978-981-10-5251-4_87

18. Simonds VW, Wallerstein N, Duran B, Villegas M. Community-based participatory research: its role in future cancer research and public health practice. Prev Chronic Dis. 2013 May 16;10:E78.

19. Salimi Y, Shahandeh K, Malekafzali H, Loori N, Kheiltash A, Jamshidi E, et al. Is Community-based Participatory Research (CBPR) Useful? A Systematic Review on Papers in a Decade. Int J Prev Med. 2012 Jun;3(6):386–93.

20. Barbee L, Kobetz E, Menard J, Cook N, Blanco J, Barton B, et al. Assessing the acceptability of self-sampling for HPV among Haitian immigrant women: CBPR in action. Cancer Causes Control CCC. 2010 Mar;21(3):421–31.

21. Accoe K, Marchal B, Gnokane Y, Abdellahi D, Bossyns P, Criel B. Action research and health system strengthening: the case of the health sector support programme in Mauritania, West Africa. Health Res Policy Syst. 2020 Feb 19;18(1).

22. Shah SK, Nakagawa M, Lieblong BJ. Examining aspects of successful community-based programs promoting cancer screening uptake to reduce cancer health disparity: A systematic review. Prev Med. 2020;141:106242.

23. Habila MA, Kimaru LJ, Mantina N, Valencia DY, McClelland DJ, Musa J, et al. Community-Engaged Approaches to Cervical Cancer Prevention and Control in Sub-Saharan Africa: A Scoping Review. Front Glob Womens Health. 2021;2:697607.

24. Nguyen TT, McPhee SJ, Bui-Tong N, Luong TN, Ha-Iaconis T, Nguyen T, et al. Community-based participatory research increases cervical cancer screening among Vietnamese-Americans. J Health Care Poor Underserved. 2006 May;17(2 Suppl):31–54.

25. Lott BE, Trejo MJ, Baum C, McClelland DJ, Adsul P, Madhivanan P, et al. Interventions to increase uptake of cervical screening in sub-Saharan Africa: a scoping review using the integrated behavioral model. BMC Public Health. 2020 May 11;20(1):654.

26. Awua AK, Wiredu EK, Afari EA, Tijani AS, Djanmah G, Adanu RMK. A tailored within-community specimen collection strategy increased uptake of cervical cancer screening in a cross-sectional study in Ghana. BMC Public Health. 2017 01;18(1):80.

27. Fokom Domgue J, Futuh B, Ngalla C, Kakute P, Manjuh F, Manga S, et al. Feasibility of a community-based cervical cancer screening with "test and treat" strategy using self-sample for an HPV test: Experience from rural Cameroon, Africa. Int J Cancer. 2020 01;147(1):128–38.

28. Manandhar DS, Osrin D, Shrestha BP, Mesko N, Morrison J, Tumbahangphe KM, et al. Effect of a participatory intervention with women's groups on birth outcomes in Nepal: cluster-randomised controlled trial. The Lancet. 2004 Sep 11;364(9438):970–9.

29. World Health Organization. WHO recommendation on community mobilization through facilitated participatory learning and action cycles with women's groups for maternal and newborn health. Geneva, Switzerland; 2014.

30. World Health Organization. New WHO recommendations on screening and treatment to prevent cervical cancer among women living with HIV - Policy brief. Geneva, Switzerland; 2021. Report No.: ISBN 978-92-4-003096-1.

31. Castle PE, Einstein MH, Sahasrabuddhe VV. Cervical cancer prevention and control in women living with human immunodeficiency virus. CA Cancer J Clin. 2021;71(6):505–26.

32. Ministry of Public Health, Republic of Cameroon. National Strategic Plan for Prevention and Cancer Control 2020-2024 [Internet]. 2020. Available from: https://www.iccp-portal.org/system/files/plans/FINAL%20COPY%20OF%20PSNPLCa%20ENGLISH.pdf

33. Ratzan S, Parker R. Introduction. In: Selden C, Zorn M, Ratzan S, Parker R, editors. Health Literacy. Bethesda, Maryland: National Institutes of Health. National Library of Medicine; 2000. (Current bibliographies in medicine).

34. WHO guidelines for the use of thermal ablation for cervical pre-cancer lesions [Internet]. [cited 2021 Jan 24]. Available from: https://www.who.int/publications-detail-redirect/guidelines-use-of-thermal-ablation-for-cervical-pre-cancer-lesions