

ESTHER Switzerland Partnership Project Grant - Final report July 2019

Promoting comprehensive cervical cancer prevention and better women health in Cameroon



Figure 1 Health education courses at Dschang district Hospital, November 2018

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SUMMARY

PROPOSAL SUMMARY	3
ABBREVIATIONS	4
EXECUTIVE SUMMARY	5
PROJECT PROGRESS	8
PATNERSHIP DEVELOPMENT	11
1. GOALS and OBJECTIVES	13
2. IMPACT	20
3. MONITORING AND SUPERVISION OF ACTIVITIES.....	22
4. SUSTAINABILITY	24
5. RISKS AND MITIGATION	26
6. PROJECT MANAGEMENT	27

The ESTHER Switzerland programme (<https://www.esther-switzerland.ch>)is implemented by the Institute of Social and Preventive Medicine (ISPM) of the University of Bern, on behalf of the Swiss Agency for Development and Cooperation SDC).

PROPOSAL SUMMARY

Project Title	Promoting comprehensive cervical cancer prevention and better women health in Cameroon
Country	Cameroon
Goal	Determine the performance of HPV test followed by VIA/VILI to detect precancerous lesions of the cervix in a screen-and-treat strategy in sub-Saharan Africa.
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Requested grant (CHF) (max. CHF 100'000.--)	100'000 CHF
Project Timeframe	October 2017 – June 2019

ABBREVIATIONS

CA	Competent Authorities
CC	Cervical cancer
EC	Ethics Committee
CIN	Cervical Intra Epithelial Neoplasia
CIN1	Cervical Intra Epithelial Neoplasia grade 1
CIN2+	Cervical Intra Epithelial Neoplasia grade 2 or above
EPFL	Ecole Polytechnique Fédérale de Lausanne
FIGO	International Federation of Gynecology and Obstetrics
GCP	Good Clinical Practice
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
HUG	Hôpitaux Universitaires de Genève
ICF	Informed Consent Form
NGO	Non governmental organization
SE	Serious Event
SOP	standard operating procedures
STD	Sexually transmitted diseases
VIA	Visual Inspection with Acetic Acid
VILI	Visual inspection with Lugol's iodine
WHO	World Health Organization

EXECUTIVE SUMMARY

CONTEXT

Cameroon, a country with 22'179'707 inhabitants, faces the double burden of communicable and non-communicable diseases (the latter accounts for 31% of deaths). Life expectancy at birth is 57.3 years. HIV prevalence is 4.3%. The Dschang and Mfou health district hospitals serve as referral facilities for 250'000 and 83'977 inhabitants respectively. The study will take place in these two regions. Cervical cancer incidence is rising from 24/100'000 cases in 2008 to 30/100'000 cases in 2012, and it accounts for 24% of female cancers. There is no CC prevention (screening, vaccination) program and curative actions are ineffective. Key facts on the health system with respect to CC are:

1. Service delivery: lack of comprehensiveness and low quality of services. There is only one underequipped and overloaded radiotherapy unit serving the whole country and neighboring countries. There are only two medical oncology units in the country.
2. Health workforce: two key indicators: 1 physician/11'335 inhabitants and 1 nurse/3'157 inhabitants. There are only 4 oncologists and 20 anatomopathologists in the country. With this study, we hope to contribute to health staff training, including nurses, to teach them how to identify cervical pre-cancer lesions and to perform respective treatment.
3. Information: There is no strong central health information system but rather several subsystems (some run by international partners) that are neither comprehensive nor coordinated. National statistics on CC are obtained by extrapolation / there is no national cancer registry. Policy decisions based on routinely collected information are difficult to make. With this study, we hope to allow the two Cameroonian hospitals included to keep registries of patients' data by using an electronic database conceived especially for CC screening and we hope that this can be further expanded to other district hospitals.
4. Medical products, vaccines and technology: the expanded program of immunization does not provide HPV vaccines. The national system for essential drug supply does not provide anticancer drugs. There is a low quality and quantity of equipment, with only one outdated radiotherapy unit, that has frequent breakdowns. With this study, we hope to better understand the best available technologies present in the country. We will also be providing both hospitals with a gynecological consultation room, including a gynecological chair. Both hospitals will be fully equipped with cervical sampling methods and a GeneXpert machine for rapid Human papillomavirus testing (these machines are already in place and fully operational from a previous CC screening campaign). Cepheid provides easily available technical support and guarantee. Laboratory staff has already been trained to use the GeneXpert machine in a previous CC screening campaign in 2015 in the District Hospital of Dschang and a refresh course will be provided if needed.
5. Financing: 70% of health care costs are supported by households through direct payments. The cost of HPV vaccines is strongly prohibitive. The high treatment costs of late stage CC are beyond the reach of most Cameroonians.
6. Leadership/governance: is characterized by weak community involvement, generalized corruption, policy uncertainty and weak monitoring and evaluation. A national cancer control committee has been set up, but has not enough funding to implement a comprehensive nationwide cancer screening



program. There is no strong political commitment for cancer control. With this study we hope to shed more light on the high burden of CC, to inform the population of the need for this screening and raise awareness among the ministry of health.

PARTNERSHIP

This project was developed thanks to the collaboration of The Ministry of Health (www.minsante.gov.cm) in Cameroon, the Dschang district Hospital (DDH), and the Geneva University Hospitals (HUG) (www.hug-ge.ch). HUG and the Ministry of health collaborate for the training of health staff and research. This relationship is in place for more than 20 years now, and links have been strengthened throughout the years.

Ministry of Health is a governmental department in charge of health in Cameroon. At its peripheral level, hospitals serve as referral facilities for health districts. The Mfou and Dschang district hospitals will host the study (no websites).

The Dschang district Hospital (DDH): referral hospital for 250'000 people, staffed with 10 physicians (3 specialists) and 160 beds, one Gynecologist-Obstetrician and 2'000 deliveries annually.

The Geneva University Hospitals (HUG) Group was created in 1995 via a merger of the Geneva public sector hospitals. As the first Swiss university hospital it is dedicated to care, research and teaching. Its excellence dates back hundreds of years with several internationally recognized areas of expertise. It comprises 11'148 (1'784 physicians) collaborators and is dedicated to global health within the framework of WHO and 70 cooperation agreements with 30 countries.

The first CC screening campaign took place in Bafang in 1997. Since then, multiple healthcare workers have been trained in Cameroon, as well as in Switzerland, and some are now heads of medical units in Cameroon, allowing continuous education and training of new generations. The HUG and DDH collaborate in research and control of CC in rural sub-Saharan Africa. This started in 2014, when the DDH and the University of Dschang co-hosted the 4th international workshop on cervical cancer co-organized with the HUG and the Yaoundé University Teaching Hospital. This was followed by a free of charge screening campaign of 1'012 women, who made up a cohort for a research on CC screening (doi: 10.1002/cam4.1089; doi: 10.1186/s12905-016-0355-x).

The follow up of that cohort is ongoing and future steps include: the opening of a unit of CC and STI prevention and the implementation of the current project.

PROJECT OBJECTIVES

Cervical cancer (CC) is largely preventable but still accounts for 24% of female cancers in Cameroon and is the first cause of cancer-related deaths due to the lack of screening and vaccination programs. WHO recommends three screening methods: cytology, HPV test and visual inspection with acetic acid (VIA). Cytology (effective in developed countries) is clearly not adapted for Cameroon, due to structural weaknesses of the health system (low resources not covering the high material costs and lack of trained pathologists for result interpretation). The WHO screen-and-treat strategy based on HPV test followed by VIA (test-triage-treatment) was difficult to apply in poor countries because of expensive laboratory-

based HPV tests. With the recent marketing of cheap and rapid on-site HPV tests this strategy appears to be the most promising.

Advantages for the Swiss partner:

- As a member of the WHO steering committee on CC control, the HUG will implement their commitment for global partnership for health: development of human resources and control of non-communicable diseases in resource-poor countries.

Advantages for Cameroonian partners:

- Workforce and Medical technology: training of on-site staff with a very recent technology (HPV GeneXpert®)
- Information: implementing the latest WHO recommendations
- Governance: strengthening international cooperation

CC control is a priority of the WHO 2014 – 2020 agenda for control of non-communicable diseases. The Cameroonian 2016-2027 Health Sector Strategy emphasizes the commitment for effective international partnership to strengthen the building blocks of its health system in view of controlling non-communicable diseases.

For the reasons mentioned above, in 2017, the Geneva University Hospitals and the Dschang district Hospital, with financial support from ESTHER, continue their partnership to carry out this subproject at Dschang district Hospital as part of the five-year program aimed at promoting comprehensive cervical cancer prevention and better women health in Cameroon.

The overall goal of this subproject is to determine a context-relevant strategy for CC screening in Cameroon (sub-Saharan Africa), by investigating the performance of emerging CC screening and triage techniques among women aged 30-49 years and to evaluate the feasibility of different approaches for implementation of organized HPV-based screening programs.

The specific objects of this partnership were:

1. To estimate the proportion of high risk HPV positive women referred to VIA/VILI examination in a population of 6'000 Cameroonian women aged 30 to 49 years old.
2. To evaluate the feasibility of implementing organized HPV-based CC screening program within the health systems participating in the study.
3. To evaluate the feasibility of implementing a HPV-rapid test in a screen and treat strategy already used in Cameroon, but at a larger scale.
4. To determine the performance characteristics (sensitivity, specificity, positivity and negative predictive values) of VIA/VILI as triage test for HPV-positive women to detect cervical pre-cancer in a screen-and-treat approach in real life Cameroonian context, using histologically confirmed cervical intraepithelial neoplasia grade 2 or more severe lesion (CIN2+) as gold standard.
5. Create a database of digital cervical images (native, VIA and VILI) for training health personnel on visual methods of CC screening (teaching material).
6. Create an electronic database with contact information, sociodemographic information, cervical pre-cancer and cancer registries, including information on follow-up for the 6'000 included women.

7. Reducing the burden of cervical cancer by treating all precancerous lesions detected during the study in the selected area.

PROJECT PROGRESS:

The project implementation finally commenced in September 2018 and ended with one month extension, in July 2019. The project managed to implement a sustainable screening room, increase Cameroonian women's knowledge of sexual and reproductive health, train nursing staff and thus offer adapted and qualitative care, and detect and treat women with precancerous and cancerous lesions. Today the authorities are more aware of the need to work towards the prevention of cervical cancer, which allows us to continue on with our five-year program under good conditions.

We were delayed due to setbacks in project planning. In fact, validation of our request to the Cameroonian ethics committee has taken longer than expected and delayed us in starting the project. We had indeed received a favorable response from the Ethics Commission (EC) in November 2017, subject to modification. This has been done, but in the meantime the file has been lost, which resulted in a delay of 4 months. We had to resubmit it and received authorization from the EC to begin the study in September 2018. This experience made us wonder about the next steps and the submission of amendments. It seems that having a reference person who is in charge of the ethical clearance of IRD projects is essential for the future, so we aim to start such collaboration.

This delay has also impacted the clinical practice of our healthcare providers, because they were not able to start practicing immediately. Thankfully this allowed us to reinforce the training of our service providers concerning theoretical aspects and administrative activities, such as filling out CRFs, raising women's awareness and recognizing pathological cervical changes. As a result, they have become more autonomous and have increased their skills.

It should also be noted that women's attendance at screening was lower than we had planned. We have found some reasonable explanations and developed solutions to remedy them.

External causes:

1. **Cause:** The project began at the peak of the rainy season, which had the following consequences: firstly, frequent power failure, secondly, difficulty to spread the information about the screening campaign to women in rural areas, and thirdly, lack of access to care.

Solutions:

1. We looked for Cameroonian engineers who could develop and install a voltage regulator and backup battery to carry out the examinations despite power outages. At the beginning of April 2019, during the international congress of the fight against the CC, we had the opportunity to get in contact with an engineer's team from Yaoundé, specialized in this type of devices. After a preliminary assessment of the field in mid-April, the team returned in mid-June to install a tailor-made system. Working with local people has been very beneficial because they have a good knowledge of local issues and can therefore easily adapt to the needs of the field.

From now on, we no longer suffer from power cuts and we can now work despite the lack of electricity. This device allows us not only to prevent the waste of cartridges that became unusable when the power stopped, but also to preserve the GeneXpert machines, which suffered from the voltage variation. With this device in place, we also avoid having to send the women home and call them back the next day. These difficulties allow us to analyze the feasibility of setting up a one-day screening consultation with care.

2. Cause: Decrease in the number of people attending screening consultations

Solutions:

1. In order to compensate for the population's lack of attendance at the screening room, the local project manager and his wife went to various events organized by the villages and in the churches, to pass on the information. After this first intervention we noted an increase in the number of women coming to the consultation. We therefore continued to transmit information through communication campaigns among women in the city of Dschang and in the countryside. Also since the beginning of the year, women from different associations were contacted, radio messages were broadcasted and banners were put up in public places to give visibility to the screening program.
2. After a further decrease in attendance, we implemented a new strategy, proposed by the Chief Medical Officer of the Reproductive Health Department. During the month of May, we implemented a one-day training course for community workers. We will soon offer 4 more training sessions. These community workers are responsible for raising awareness among women in the town of Dschang and providing them with all the information about the screening room and the need for testing. Thereafter, a second training course for rural mobilizing agents will be organized. These agents will go to rural areas to inform and raise awareness among remote women with limited access to care. A few days after the training we saw women arrive who had been informed by community workers of the organized screening. The agents give women tickets with their names on them, this way we can find out which agent gave them the information. This method is used frequently in the region and works well. The need to collaborate with local staff and follow their strategies is again highlighted.

2. Cause: Batch of cartridges required for the HPV examination was non usable by our laboratory staff.

Solutions: We had to put in place strategies to overcome this cartridge problem and for that we had to collaborate with the company's technicians, and specialists in HPV testing. During a period of 3 weeks we lost 45% of the tests performed, without obtaining any results, due to cartridge problems. This forced us to repeat the tests twice and even three times before obtaining any results. Today, thanks to this collaboration, we have found a solution to carry out the tests without losing the cartridges. We are still in discussion about the refund of lost cartridges and wasted sampling equipment.

- 3. Cause:** Conflict between the government and an armed separatist movement in the English-speaking area of Cameroon since the beginning of 2018 and political elections occurring in October 2018. This has resulted in an increase in the insecurity of our Swiss and Cameroonian employees and the screening consultations were stopped for 3 weeks

Solutions: These conflicts required the Swiss doctor and a medical student to travel to Yaoundé at the request of the Swiss ambassador. We have implemented a security protocol for residents and students. We have a dedicated driver for the project, who takes care of the transport between Douala and Dschang for all people arriving from Switzerland.

Doctors and students are housed and fed at the family home of the chief reproductive health physician (principal investigator). They are accompanied to the hospital every morning by car and cannot walk unaccompanied outside the city of Dschang. After the election in October 2018 the conflicts calmed down, and it was safe to proceed with the screening project, with our Swiss and Cameroonian team on the spot. Since then, consultation happened normally and we never had any problems regarding security.

- 4. Causes:** The screening project in Mfou hospital could not start because of the renewal of the Mandate of Manager of the Mfou Hospital Centre, by our respondent for the Mfou site. In fact, we had no guarantee concerning his successor, so we preferred to remove the project from this site. The renunciation of the mandate is a consequence of the withdrawal of funds from the Canton of Jura.

Solutions: After the renunciation of the program in Mfou, we made analyzed different hospitals where we could implement the second screening room. We have received many offers from hospitals in Cameroon to host the project. Finally, for logistical and collaboration reasons, we decided to launch this project in Bafoussam. The Bafoussam Regional Hospital is located in the same region as Dschang, 45 minutes by car. This proximity allows for easy quality control, exchange of healthcare staff and training covering both sites.

Our contact person at the Bafoussam hospital is Dr. J. Foguem, an internal doctor who did part of his training at the University Hospitals of Geneva and who has been back in Cameroon for 3 years. He is familiar with the screening project and its challenges, because he already worked on this research project from 2015 to 2016.

In this new site, we also have the support of the IRD, which is also conducting a clinical research project on HPV in a female HIV-infected population. Setting up this partnership consolidates and pools the activities related to this project.

Internal causes:

1. In order to provide quality care, we initially limited the screening attendance to 8 women per day. Indeed, all health care providers are newly trained in the 3T program. To enable them to establish their expertise, we have therefore limited the capacity of reception. We are currently working with the IRD to file an ethical clearance for the Bafoussam site.

PATNERSHIP DEVELOPMENT

Dschang district Hospital

This project was able to highlight the strong collaboration with the Dschang district Hospital. The four Swiss interns and three masters' students who went to Dschang were given excellent support by the Cameroonian partners. The training of health care providers that we conducted on site in May and July 2018 went well thanks to the commitment of our local partners. On this occasion we had the opportunity to train 15 healthcare providers, eight are working in the Dschang District Hospital. Since then, further training of the caregivers has continued, and is now extended to community workers.

Since the project implementation, we have been having frequent exchanges by email or phone call with the local partners (project manager, midwives, and biologist). This allows us to be updated on the evolution of the screening attendance, the screening process, the treatment decision and the logistical needs. We benefit from good team cohesion and everyone contributes to the smooth running of the project.

Health and political authorities and University of Geneva

We have been collaborating with Cameroon for 20 years now (Vassilakos and al., Swiss Rev Med May 2019) and we benefit from an agreement between the Ministry of Public Health of Cameroon, the Faculty of Medicine of the University of Yaoundé, and the University Hospitals of Geneva, in the field of training, research, care, and hospital-university exchanges. The first agreement was published in 1980, the last one dates from 2013.

In this context, during the last international congress to fight cervical cancer in Cameroon, Professor Petignat was able to meet the Swiss Ambassador of Cameroon, with whom he was able to discuss the project and future activities. This year, the International Congress against Cancer celebrated its 10th anniversary. This longevity is due to the close partnership between the University Hospitals of Geneva, the Ministry of Public Health.

We participated as members and organizer at this 10th International Congress on Cervical Cancer Control in Sub-Saharan Africa, in March 2019 in Yaoundé. Last year the congress was hosted by the University of Dschang. This time we had the opportunity to present the first results of the project and the training we implemented. We also had the opportunity to discuss the perspectives of the national public health strategy regarding cervical cancer.

The results of the project have generated great interest from cervical cancer specialists and many regional hospitals are interested in following our approach. Therefore we decided to develop a guideline describing the key steps in setting up a screening room in a low resource setting. It explains how a standard screening consultation is carried out, in terms of procedures, the necessary nursing staff, the equipment to be purchased and the budget. We are in the process of finalizing this paper that we will publish shortly. This document can be used as a basis for any hospital or NGO wishing to initiate HPV screening counselling.

On May 23rd, we had the honor of organizing, on the sidelines of the World Health Assembly, an event to celebrate the 20 years of collaboration between the HUG, the University of Geneva and the Ministry

of Public Health in Cameroon. On this occasion, the new Minister of Public Health in Cameroon attended our presentations, as well as His Excellency, the Ambassador of Cameroon in Bern, Switzerland, as well as 100 other participants. During this event, 15 master's theses from our screening project of CC in Cameroon were presented and this long-term collaboration was illustrated.

OCEAC / CIESPAC

During the congress, we also met the President of CIESPAC, Pierre Marie Tebeu and his colleagues from the OCEAC. Pierre Marie Tebeu was one of the first to collaborate with the cervical cancer control project in Cameroon. He did his gynecology residency in Geneva and continues to advocate for the fight against cervical cancer. He honored us with his presence during the 20 years of collaboration. The CIESPAC informed us that they are integrating our 3T approach to screening into their curriculum for Masters in Health. So we are working with them to elaborate the best strategy to develop this training.

Research Institute for Development IRD

We are collaborating with the IRD and particularly the AIMA-CC project on the training of health care providers. We provided training on HPV screening and the 3T approach in Abidjan, Cote d'Ivoire earlier this year. 18 agents were trained during this session and graduated. We provide them with support and expertise in anatomopathology and onco-gynecology. We are also working with the IRD to set up the project for a new screening room in Bafoussam.

CIRES

We are pleased to collaborate with CIRES, another organization that benefits from the ESTHER Switzerland fund. We discuss the procedures and protocols for implementing the HPV screening strategy in Cameroon. We also support each other in the transport of medical equipment, as well as in the development of technical equipment such as a voltage regulator and battery to carry out the examinations despite power outages. We have regular exchanges on the progress of the project and on the needs related to screening, as was the case during the 10th International Congress.

EPFL

Since 3 years, we have a collaboration in the field of artificial intelligence (AI) with the EPFL, Lausanne. The aim is to create an algorithm capable to detect cervical pre-cancer with device adapter to low-resource context. Health care workers will be able with smartphone or similar device to visualize the cervix and determine the presence or absence of cervical precancer. Until now, we have essentially provided training material for the computer to develop a detection algorithm.

1. GOALS and OBJECTIVES		
Goal ,	To determine a context-relevant strategy for CC screening in Cameroon (sub-Saharan Africa), by investigating the performance of emerging CC screening and triage techniques among women aged 30-49 years and to evaluate the feasibility of different approaches for implementation of organized HPV-based screening programs	
Specific goal 1	To estimate the proportion of high risk HPV positive women referred to VIA/VILI examination in a population of 6'000 Cameroonian women aged 30 to 49 years old.	
Achievements	Activities 1.1 Achieved	<p>1.11 Communities in the study areas must receive information of the screening</p> <ul style="list-style-type: none"> - We conducted few awareness sessions with women's associations and with women in rural areas. We disseminated information through the radio, and the local television and we have installed banners in public areas. These campaigns have shown positive results with an increase in the frequency of visits of the screening room, but must be renewed frequently. - We have published two newsletters for the population to inform them about HPV but also about the progress of the screening project. - We worked with the hospital's caregivers to make banners and posters about the screening, which also worked well. - Last month we set up training for community workers to get as close as possible to the women with limited access to care and information. <p>This training shows good results with an increase in screening attendance noted. This awareness model is local and has already proven its worth, which is why we have decided to use it for our project.</p>
	Activities 1.2 Not achieved	<p>1.12 Recruit women at risk to develop cervical cancer</p> <ul style="list-style-type: none"> - 980 women were screened, 185 were HPV positive from 1st of September 2018 to the 19th of June 2019. These women meet the inclusion and exclusion criteria, understand study procedures and accept to participate in it by signing an informed consent form. - The communication and recruitment activities mentioned above have been effective, but due to the delay in launching the project and the decision to ensure the quality of care by welcoming the first few months less than 10 women per day, we have not been able to reach the estimated number of women.
	Activities 1.3 Achieved	<p>1.13 Optimally test women at risk to develop cervical cancer</p> <ul style="list-style-type: none"> - Performance of self-collection for HPV test and analysis using the Xpert HPV assay, which offers simultaneous detection of 14 HR-HPV genotypes (HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68).

		<ul style="list-style-type: none"> - The use of the self-test was optimal and no adverse events were reported. The women performed the sampling in an appropriate manner, allowing for a correct GenXpert analysis. The satisfaction rate of women using this method of sampling is high. - The difficulties we encountered were all related to the GeneXpert machine (Cepheid). We had difficulty maintaining a stable voltage and finding a battery that could replace the power during the outages. Today, thanks to the collaboration with Cameroonian engineers, we were able to set up a generator to better protect the machines and take over the power supply during power outages. <p>We also had difficulty transporting the Cepheid cartridges and then recovering them from customs. We are currently working on a new agreement between the Cameroonian Ministry of Public Health and the University of Geneva, to avoid such problems in the near future.</p>
Specific goal 2	To evaluate the feasibility of implementing organized HPV-based CC screening program within the health systems participating in the study. To evaluate the feasibility of implementing an HPV-rapid test in a screen and treat strategy already used in Cameroon, but at a larger scale.	
	Activities 2.1 Achieved	<p>2.11 Securing funds and clearances were the starting point of implementing our project</p> <ul style="list-style-type: none"> - We have obtained private funds that allow us to carry out our project for almost another year. - We received the administrative clearance from the Cameroon Ethics Committee. Following the difficulties encountered during the first submission and the loss of our file, we contacted someone from the Ministry of Health who accompanied us in tabling the amendments. Our active collaboration with the IRD will allow us in the future to exploit their contact within the ethics committee in order to avoid seeing the same mistakes repeated. - We received the administrative clearance from the Geneva Ethics Committee and then we submitted and received validation of our amendment at Geneva EC in November 2018.
	Activities 2.2 Achieved	<p>2.12 Train our study staff to enable them to conduct study tasks</p> <ul style="list-style-type: none"> - Health care providers working in the field of cervical cancer prevention were invited to participate in a comprehensive 6-day theoretical and practical training course at the Dschang District Hospital, Cameroon and at CHU de Yopougon, Ivory Coast, following the request of the IRD. - At the end of the training, participants had to take a practical and theoretical exam to validate their knowledge. - Training modules are based on e-learning lecture with practical training provided by gynecologists and midwives specialized in HPV and CC screening.

		<ul style="list-style-type: none"> - Results: A total of 32 participants have completed the training modules, 15 in Cameroon and 17 in Ivory Coast and 30 have successfully passed the exam. - Satisfaction rate was 9/10. - Currently, the Centre Inter-Etats d'Enseignement Supérieur en Santé Publique d'Afrique Centrale (CIESPAC) will integrate our module in their Master of Science curriculum. - The continuous training is provided by on-site resident doctors from HUG, who are present in Dschang since September 2018. The self-assessment and the quality control (monitoring of the caregivers' performance indicators) have shown conclusive results.
	<p>Activities 2.3 Achieved</p>	<p>2.13 All HPV positive women will go through gynecological examination comprising VIA/VILI examination, cytology and biopsy</p> <ul style="list-style-type: none"> - Women who tested HPV positive were all able to benefit from the planned management, i.e. a gynecological examination with VIA/VILI and DVIA/DVILI. Women with gynecological infections were treated before screening. - The equipment for the gynecological examination, for the samples, as well as all the consumables necessary for the operation of the screening room are available. Some products are shipped from Switzerland. - Gynecological examinations are carried out under the supervision of a resident doctor of the HUG. - No woman decided to redraw from the study before the examination, once the consent was signed. - The samples are prepared and analyzed in Geneva by our laboratory technician, who is trained in this practice.
	<p>Activities 2.4 Achieved</p>	<p>2.14 Publication of results to ensure impact on policy choices in Cameroon and sub-Saharan Africa</p> <ul style="list-style-type: none"> - We presented our first results regarding the training at: <ul style="list-style-type: none"> o The GRSSGO congress in Montreux, Switzerland, in November 2018 o The 10th International Congress for Cervical Cancer Control in Sub-Saharan Africa in Yaoundé, in March 2019 o The SSGO congress, in St-Gallen, in June 2019 where we received the first humanitarian award - Three studies are in press and 5 others are in progress. - One master thesis is already done.
Specific goal 3	<p>To determine the performance characteristics (sensitivity, specificity, positive and negative predictive values) of VIA/VILI and cytology as triage tests for HPV-positive women in order to detect cervical pre-cancer lesions in a screen-and-treat approach in real life Cameroonian context. We are using histological confirmed cervical intraepithelial neoplasia grade 2 or more severe lesion (CIN2+) as gold standard.</p>	

	<p>Activities 3.1 In process</p>	<p>3.1.1 VIA/VILI performance in detecting pre-cancer lesions</p> <ul style="list-style-type: none"> - Out of the 1000 patients screened so far, 191 were HR HPV positive, which corresponds to the estimated 20 percent. Out of the 191, the histology and cytology confirmed so far 6 CIN 2+ (1 cancer and 5 CIN3) lesions, which were treated appropriately by LEEP conization or total hysterectomy. Out of these 6 cases, 4 were correctly identified with VIA/VILI and treated beforehand with thermoablation. Thus, so far we have a detection rate of 66.6% of CIN 2+ lesions with VIA/VILI. Histological examination of the samples is still ongoing. The performance of VIA /VILI will be evaluated as soon as the histological results are available.
<p>Specific goal 4</p>	<p>Create a database of cervical images (native, VIA and VILI) for training health personnel on visual methods of CC screening (teaching material).</p>	
	<p>Activities 4.1 Not Achieved</p>	<p>4.1.1 Develop a Smartphone application</p> <ul style="list-style-type: none"> - In collaboration with the EPFL in Switzerland, we developed an application that allows us to photograph the cervix with the objective to develop an artificial intelligence model that would indicate to caregivers where precancerous lesions are and where to perform treatment if necessary. - The project to develop this application is ongoing with EPFL and still requires photos to improve sensitivity and specificity. - All photos of VIA/VILI taken during gynecological examinations in HPV positive women are recorded on a hard disk, where they are anonymized. When the Swiss doctors return to Geneva, they bring us back these photos, which are then securely stored on a disk at the HUG and therefore destroyed from the external hard disk. They are then analyzed by colposcopy specialists, who mark on the photos the areas with precancerous lesions before being transmitted to Professor Thiran's team at EPFL; - This application allows us to use the Smartphone as a colposcope and to zoom in on the picture for better analysis. - Doctors and midwives reevaluate the photos bi-monthly, with a consulting gynecologists from Yaoundé.
	<p>Activities 4.2 Achieved</p>	<p>4.2.1 Train midwives to use the Smartphone during the gynecological examination</p> <ul style="list-style-type: none"> - Midwives were trained by doctors to photograph the cervix during the exam and analyze pictures to make a treatment decision. - We had to make adjustments for the tripod so that caregivers can use it to take pictures - We also had to implement a new way of observing and describing the cervical lesions. Caregivers should first examine the cervix with the naked eye, then document the lesions seen, then take pictures with the smartphone, observe the pictures and record their impressions. This two-step method allows us to document and observe the differences between lesions seen with the naked

		eye versus what is observed with the smartphone, with the possibility of zooming in.
	Activities 4.3 Achieved	<p>4.3.1 Control of the quality of the pictures</p> <ul style="list-style-type: none"> - The photos are reviewed locally bimonthly by a consulting gynecologist from Yaoundé, to ensure their quality. - Then they are analyzed at the HUG in Geneva by a team of colposcopy specialists. - Photos taken since September 2018 are all usable and of good quality. They made it possible to catch up on suspicious cases, identified during the bimonthly consultations with a specialist gynecologist based in Yaoundé. This allowed to convoke the patients to catch up on biopsies or treatment of lesions, which first were not identified correctly.
Specific goal 5	Create an electronic database with contact information, socio-demographic information, cervical pre-cancer and cancer registries, including information on follow-up for the 6'000 included women.	
	Activities 5.1 Achieved	<p>5.11 Create a data base</p> <ul style="list-style-type: none"> - First we developed paper crf from previous studies conducted by our research group and then adopted them based on current literature. - Once this work was completed, we collaborated with the Clinical Research Centre of the HUG to develop a database based on the Secutrial software. - A first crf assessment was conducted in Geneva to ensure that the questions were understood by people outside the field of HPV prevention. This evaluation proved to be conclusive. Then, when the project was launched in Dschang, adjustments were made to our crf after being confronted with the reality on the ground.
	Activities 5.2 Achieved	<p>5.12 Data recording on the e-CRF</p> <ul style="list-style-type: none"> - On-site residents are the only ones allowed to complete the e-crf on the software Secutrial® of the HUG, Clinical Research Center. - This allows them to check directly if data are missing in the paper crf filled out by the caregivers. - At the HUG, we have access to the data and we can regularly carry out checks on the filling in of the data and inform doctors when there are errors. - HUG doctors have been trained in the use of the safety software to ensure its optimal use. Doctors already on mission are a support to new doctors during the first fillings.
Specific goal 6	Assure the quality of the study	
	Activities 6.1 Achieved	<p>6.1.1 Train healthcare staff members</p> <ul style="list-style-type: none"> - Healthcare staff members received 6-days of theoretical and practical training by the HUG team.

		<ul style="list-style-type: none"> - Once a month, the Swiss doctors give a theoretical course to midwives. - Midwives record in their logbook the procedures performed during the day so that they have a record of their learning (self-assessment)
	<p>Activities 6.2 Achieved</p>	<p>6.2.1 Coordination of the study</p> <ul style="list-style-type: none"> - The study is coordinated by the HUG research team, which includes research assistants, doctors, professors and medical students. At the site, the local principal Investigator is responsible for all study activities, scientific coordination, regulatory aspects and supervision of day-to-day operations. - Members of the HUG research team are present to locally coordinate activities, supervise the screening room and give training. - Compliance with local regulations and specific requirements are the responsibility of the local PI.
	<p>Activities 6.3 Achieved</p>	<p>6.3.1 Supervisions</p> <ul style="list-style-type: none"> - The resident evaluates every month one consultation per midwife, to ensure quality of care. This is based on a system for monitoring the actions of healthcare providers (based on KPI performance indicators). This assessment makes it possible to quickly fill in gaps in care providers by ensuring continuous training and quality control. - Additional verifications of SOPs are implemented by the HUG research team at the site to comply with local regulations and institutional standards. - Cf. monitoring.
	<p>Activities 6.4 Achieved</p>	<p>6.4.1 Laboratory</p> <ul style="list-style-type: none"> - HPV tests are analyzed on site, by our qualified laboratory technician. - Cytology and histology are transported to Switzerland, where they are prepared and analyzed. The laboratory in Yaoundé, where the samples were originally to be analyzed, is still under renovation and therefore not ready to receive them. We have so far worked with a private laboratory but we are setting up a project with the HUG laboratory so that they can take over. This partnership would allow the two services to collaborate also on research projects and possible publications. - The transport of this equipment is currently subject to a Material Transfer Agreement, (MTA) that we have established between the Yaoundé Gynaeco-Obstetrics and Pediatric Hospital and the Geneva University Hospitals. A quality control of samples is implemented to ensure the quality of the results. - Clinical and laboratory procedures are documented and controlled.
Specific goal 7	Treating 120 CIN2+ lesions among the 1'200 estimated HPV-positive women, among the 40'000, 30-49 year old women in the study area	

	<p>Activities 7.1 In process</p>	<ul style="list-style-type: none"> - Only 1000 women were screened so far, 191 were HPV positive. Among them, almost 50% were VIA/VILI positive, so 99 were treated. - Among the women screened and treated, we had 6 CIN2+ lesions confirmed by histology, including one cervical cancer, and furthermore 9 CIN1 lesions. CIN2+ prevalence is 7.7% - For the reasons mentioned at the beginning of the report, we were delayed in launching the project and then had to focus on training the midwives, thus limiting the frequency of visits at the consultation room to 10 patients per day. - We estimated the number of patients to be screened according to the screening campaign scheme we had conducted in the past, which lasted one month and was conducted only by Swiss and Cameroonian doctors. This proved to be a mistake since the scheme no longer applies in this five-year program, which is intended to be sustainable. This first year serves as a pilot study and allows us to review our expectations regarding the amount of screening participants and to focus more on the long term.
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2. IMPACT

1. CC prevention is a major objective for both WHO and public-health policy - makers in sub-Saharan Africa (SSA), but effective evidence-based strategies are still to be adopted and implemented. Our project's aim is to work on this WHO-recommended screen-and-treat 3T (Test (HPV) – Triage (VIA/VILI) -Treatment (Thermocoagulation)) strategy. The first results of the feasibility of the 3T approach were presented at the international congress to fight cervical cancer in sub-Saharan Africa, in Yaoundé in March 2019 and disseminated to health professionals working in this field of public health. The latest international and national recommendations were transmitted to the participants and workshops were organized. We were also able to launch a partnership with the CIESPAC that will take over this training by integrating it into its master training course.

- This annual workshop plays an active role in maintaining active cooperation between Cameroon and Switzerland and in ensuring the sustainability of the cervical cancer screening project over the years.

2. The project has contributed to the Sustainable Development Goal (SDG-3). Indeed, thanks to the training of community workers, who relayed awareness in areas with limited access to information, women were made aware of the importance of screening, and subsequently benefiting from HPV testing and appropriate management. They also, raise awareness among women in the city of Dschang of the importance of cervical cancer screening and contribute to their empowerment.

The costs of the screening and treatment are all at the expense of the project, as well as the hysterectomies that had to be performed in advanced cases of the lesion. This project, in addition to what was planned, made it possible to detect and treat gynecological infections free of charge among the women who came for consultations. This has improved their quality of life and also raised their awareness of sexually transmitted diseases and sexual health.

The purchase of the GeneXpert machine, which analyses HPV tests, the thermo-ablation machine for the treatment of precancerous lesions and the renovation of the screening room will enable the target population of women to benefit in the long term from adequate care. It is an investment for the people of Dschang and allows women to no longer have to go to a regional hospital or the capital to get this type of care. This would help reducing health inequalities within the country (SDG-10) and empower women toward health seeking behavior (SDG-5).

3. Our project addresses the SDG-17 by promoting partnership for sustainable development. The WHO and the Geneva University Hospitals (HUG) have a Memorandum of Understanding (since 2013) as part of a broader framework of the Country Cooperation Strategy (CCS). This WHO-HUG partnership include increasing the knowledge basis on feasible CC screening and screen-and-treat strategies in low and middle income countries. It will catalyze translation of cancer research into policies (WHO-IARC) and support WHO member states in national cancer control planning. Under the SDG-4, our project provided continuous training for non-academic health

personnel in the domain of CC prevention and foster research activities of local academic stakeholders in five disciplines (obstetrics-gynecology, pathology, public health, laboratory technicians and nurses).

4. Our project, which aims to assess on a large scale basis the performance of this recent WHO-recommended screen-and-treat strategy (Test (HPV) – Triage (VIA/VILI) -Treatment (Thermo coagulation)), has allowed us also to :
 - a. Screen 1000 women in nine months. Among these women, 191 were tested positive for HPV. Among the HPV-positive women, almost 50% had a positive VIA/VILI test. 99 received an appropriate treatment. We have identified on laboratory results, nine low-grade precancerous lesions, and five high-grade precancerous lesions with a significant risk of developing into cancerous lesions, and two cancers. So we can say that since the beginning of the project we have detected 14 precancerous lesions that might have developed into cervical cancer.
 - b. Train health workers in evidence-based practices for cervical cancer prevention, screening and management. These health workers were working in the area of Dschang but also at Mbouda hospital and in a health center in Akonolinga. This transfer of knowledge in the various health centers between participants and their colleagues allows the dissemination of information, and thus the prevention of cervical cancer. The information therefore goes further than Dschang Hospital. So we can say that this training was done at different levels :
 - At local level for health care providers in Dschang District Hospital.
 - At national level with the dissemination of information by trained officers.
 - c. Perform an ongoing training for health care providers working in the screening room.
 - d. Train community workers who relayed awareness in areas with limited access to information.
 - e. Raise awareness among women in the city of Dschang of the importance of cervical cancer screening and to contribute to their empowerment.
 - f. Send four Geneva doctors to participate at a humanitarian mission.
 - g. Conduct 2 master's theses and eight quantitative and qualitative studies simultaneously.
 - h. Recruit 3 midwives and a laboratory technician dedicated to screening who are now specialists and who have become more autonomous.

3. MONITORING AND SUPERVISION OF ACTIVITIES.

We have set up a monitoring plan that is progressing as planned:

Every day:

- We have organized a 3-months medical rotation for volunteer Swiss-trained gynecologists to go to the Dschang District Hospital to supervise our health workers, 3 midwives and a laboratory technician, who work in the screening room. This rotation allows us to guarantee a quality control of the care of women and of the procedures.
- Midwives record in their logbook the procedures performed during the day so that they have a record of their learning progress (self-assessment).
- The maternity manager is also available if the midwives have questions or doubts about the diagnosis and procedures. He is the one who performs the conizations.

Twice a month:

- In order to offer quality training, a Cameroonian gynecologist makes the trip to Dschang to review with the midwives the cases they saw during her absence. Thanks to the photos of the cervix that were taken during the gynecological examination, the doctor reviews all the cases and indicates whether the patient has been treated correctly. If not so, women are called back for further consultation and treatment.

Once a month, later on quarterly, review workshops under the supervision of Prof. Bruno Kenfack

- Swiss doctors give a theoretical course to midwives, and evaluate one consultation per midwife to ensure quality of care. They also look at the confidential midwives' records table to see which ones make the most misdiagnosis in order to strengthen practical skills. This assessment makes it possible to quickly fill in gaps in care providers if necessary. Using a roadmap of the study protocol they assess
 - o Filling out of the crf
 - o Conduction of the gynecological examination and diagnosis
 - o Counseling
- The Swiss doctors also have the role of evaluating the screening room and reporting any problems potentially encountered (ex: stock shortage)
 - o Reporting of adverse events
 - o The needs in terms of material (laboratory and medical devices) and workforce
- The data manager monitors the collected data and ensures the validity of the data
 - o The storage of data

More specifically, the checklist was designed as follows for each of the respective tasks:

1. Number of women recruited/day;
2. Number of cartridges for HPV tests used and number of successfully completed tests;
3. Number of VIA/VILI performed successfully
4. Number and type of each adverse event
5. Number of study investigators available and number of materials needed, in proportion to the number of women to be recruited, in particular:
 - o Laboratory tubes, pipettes

- HPV testing cartridge
- Storage mediums (formol, NaCl)
- Acetic acid, Lugol's iodine
- Gloves

A large part of the equipment is purchased locally in Dschang but some tests and specific equipment are currently being sent by air-transport to Cameroon, which can cause delays in deliveries if they are not sufficiently anticipated. It is also important to be aware of customs fees, which can vary greatly between two deliveries and which are to be considered in a budget.

Annual supervision workshop (march 2019) :

- Once a year Pr. Patrick Petignat and Dr. Pierre Vassilakos went to the supervision workshop with the coordinator of the Dschang site, Dr. Bruno Kenfack. They review the cases and the evaluations.
- They assess the problems identified during quarterly reviews with the work team. All project members have been working together to identify a solution for these problems. This worked out well and made it possible to adjust certain practices to meet the needs of the team and the study.

4. SUSTAINABILITY

Continuation of the partnership:

Dschang District Hospital

- The screening room has now become a part of the routine of care providers working in it as well as the rest of the hospital. We have trained the staff in order to screen women optimally. We have not been confronted with serious complications or undesirable pupils. Continuous training is necessary, which is why we will continue to send the resident doctors of the HUG on missions to Cameroon.
- The purchase of the GeneXpert machine, which analyses HPV tests, the thermo-ablation machine for the treatment of precancerous lesions and the renovation of the screening room will enable the target population of women to benefit in the long term from adequate care. It is an investment for the people of Dschang and allows women to no longer have to go to a regional hospital or the capital to get this type of care.
- We brought with the project all the procedures for prevention, screening, diagnosis, as well as treatment and follow-up. These were implemented and adopted by the Dschang team. Today, women will continue to benefit from quality care.

Health and political authorities and University of Geneva

- The 10th international congress against cervical cancer in sub-Saharan Africa, in Yaoundé, plays an active role in maintaining the cooperation between Cameroon and Switzerland and in ensuring the sustainability of the cervical cancer screening project over the years.
- The presence of Cameroon's Minister of Public Health and Cameroon's Ambassador to Switzerland at the celebration of 20 years of collaboration strengthened the partnership ties between our institution and the local authorities. We brought in two Cameroonians who are very involved in the project to present the partnership of the last 20 years.
- We would also like to set up an agreement with the University of Dschang and the HUG and the University of Geneva to provide the best possible framework for knowledge sharing.

OCEAC / CIESPAC

- The collaboration with the CIESPAC, Pierre Marie Tebeu and his colleagues from the OCEAC is strong and we are working to move forward together in the transition to the 3T approach in the country. We also worked on the best strategy to develop the curriculum for the Master in Health course.

Research Institute for Development IRD

- We are collaborating with the IRD and particularly the AIMA-CC project, at the implementation of the new screening room in Bafoussam.

CIRES

- The partnership with CIRES is very active and will continue for the rest of the program. We collaborate on many different aspects. We provide them with expertise and experience in the field of cervical cancer screening and they support us in the logistical and human resources aspects. CIRES/ASCRES is responsible for paying the allowances of our health workers on site, through their recognized local association, in exchange we work with them on procedures

and train their health personnel. We also perform quality control on some of their laboratory samples.

HUG – Laboratory

- The laboratory is now in charge of preparing and analyzing our cytological and histological samples, which they will continue also in the future. This collaboration also involves the more research-oriented part of the project with joint publication projects.

EPFL

- Our collaboration with EPFL focuses on the development of an application using artificial intelligence to help caregivers diagnose pre-cancerous and cancerous lesions and support them in making treatment decisions. For this reason, we have been collaborating for several years with Professor Thiran's team. We are still in the training phase of the software, and we provide pictures of cervixes with lesions for this purpose. The partnership will continue with EPFL, as well as with other institutions interested in joining this project.

Project perspectives:

- The CC screening project continues, the five-year program , which it is part of, plans to continue until 2023 and screen 6'000 women, 20% of whom will have a positive HPV result and will undergo triage and will be treated if necessary. The partnership with the Cameroonian Ministry of Public Health, the University of Geneva, the University of Dschang, the District Hospital of Dschang and the HUG will continue in order to carry out this mission.
- We aim to set up a vaccination project with the health authorities.
- To send annually three doctors and a master's student for a humanitarian mission tour.
- To open soon a second screening room at Bafoussam Provincial hospital, under the same scheme of the 3T approach in order to reach a wider area in the West Cameroon.
- To edit the training manual, which was elaborated by a group of experts during 2018. This manual is for trainers and participants in cervical cancer control training in sub-Saharan Africa. We would like to print it and soon distribute it to training centers in Central Africa.
- To Publish an article about “how to set up an HPV screening room in a developing country” to guide those interested in promoting the fight against cervical cancer
- To publish several studies that are in progress, including two master's theses and a doctorate in life sciences.

5. RISKS AND MITIGATION				
Risk	Probability, that the risks occurs (low / medium / high)	Impact, if the risks occurs (low / medium / high)	Mitigation measure	Results
Peri-electoral and Socio-political instability in 2018	Medium	Medium	<ul style="list-style-type: none"> - Choice of (semi-) rural areas (usually less concerned than cities) - Choice of coordinators with a long and deep experience of public administration in the study areas - Study period ranging beyond 2018 (start before and end after 2018) 	<ul style="list-style-type: none"> - The election impacted the recruitment part. In fact, we had a lower screening attendance than expected. - We had to send 2 doctors to Yaoundé during this period to assure their security. - They came back to Dschang after the election, since then we didn't notice any complications.
Insufficient Funding	Medium	High	-Diversification of funding sources	<ul style="list-style-type: none"> - New funds: Solidarity international, GRSSGO, the Committee on Humanitarian Affairs and private funds

6. PROJECT MANAGEMENT

1. Initiation

- The study starts with a delay of several months and only in one site, at the District hospital of Dschang.
- We are looking forward to starting at the Bafoussam Provincial Hospital, that's why we started buying the screening equipment and trained the health care staff.

2. Implementation/execution

- Ethical clearance from Geneva has been obtained in august 2017. But Since the beginning of the study, mainly due to the delay in the start of the study, we had to make an Amendment to the Geneva Ethics Committee. The amendment was accepted in December 2018. The Ethical clearance in Cameroon, as explained before, took us time and delayed us in the beginning of the study. We obtained Ethical clearance in September 2018.
- After a delay in launching the project, our project is progressing well. Attendance at the screening room is monitored and the means put in place to increase it seem to be working. In addition, caregivers have made their mark and screening has become a routine.
- Continuous training, quality control and monitoring enable us to be as close as possible to the needs of the screening room.
- The presence of HUG doctors on site is necessary to support the nursing staff in their autonomy.

3. Monitoring and controlling

- Doctors with experience in Cameroon are in charge of routine monitoring and evaluation of activities.
- Annual reviews are held with all the stakeholders.
- The internal study supervisor is the Professor Bruno Kenfack.

4. Funding management

- New funds: Solidarity international, GRSSGO, the Committee on Humanitarian Affairs of HUG and private funds.
- Our budget is under the supervision of Professor Patrick Petignat.