USAID
FROM THE AMERICAN PEOPLE

PEER is implemented by

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

Partnerships for Enhanced Engagement in Research (PEER): Expanding Cervical Cancer Screening and Preventive Therapy through Introducing New Technologies and Integrating with Voluntary Family Planning

Request for Applications

Date Issued: November 1, 2018
Closing Date: December 11, 2018 at 5:00 PM EST

I. PROGRAM INFORMATION 2
II. TIMELINE AND APPLICATION 4
III. AVAILABLE FUNDING SUPPORT 6
IV. ELIGIBILITY 6
V. PURPOSE, OBJECTIVES, AND RESEARCH PRIORITIES 8
VI. OUTLINE OF REQUESTED CONCEPTS 12
SUB-SECTION 1: Institutional Capability, Partnerships, and Management Plan 12
SUB-SECTION 2: Implementation Research 13
SUB-SECTION 3: Service Delivery of CCS&PT Integrated with Voluntary Family Planning 15
SUB-SECTION 4: Capacity Building 16
SUB-SECTION 5: Monitoring and Evaluation 16
VII. DRAFT BUDGET FORM AND JUSTIFICATION 17
VIII. KEY PERSONNEL 19
IX. LETTERS OF SUPPORT 19
X. SUBMISSION INSTRUCTIONS 19
XI. REVIEW CRITERIA 20
Appendix I: Country Information 21

I. PROGRAM INFORMATION

Background

Every year approximately 283,439 women die from cervical cancer, with over 90% of those deaths occurring in low-and middle-income countries (LMICs).[1] Nearly all cervical cancers are preventable through vaccination against human papillomavirus (HPV), the virus that causes nearly all cervical cancers, or by screening for and treatment of precancerous lesions among women already infected with HPV. While deaths from cervical cancer have declined dramatically in high-income and some middle-income countries, cervical cancer mortality has continued to increase in developing countries. At current trajectories, cervical cancer is projected to cause an estimated 443,000 deaths globally in 2030.[2] To reduce the incidence and mortality of cervical cancer in developing countries, the U.S. Agency for International Development (USAID) seeks to generate evidence that will inform national and global efforts to scale-up effective and efficient screening and treatment programs. To meet this goal, and in furthering its commitment to increasing women's access to quality voluntary family planning and women's health care, USAID is seeking innovative approaches to increasing cervical cancer screening and preventive therapy (CCS&PT) through introduction of new technologies and integration with voluntary family planning programs.

Through the Partnerships for Enhanced Engagement in Research (PEER), USAID will partner with the U.S. National Academies of Sciences, Engineering, and Medicine (hereafter referred to as the National Academies) and other key U.S. Government agencies to facilitate the introduction and scale-up of innovative CCS&PT approaches that can be implemented in conjunction with voluntary family planning activities, with a focus on generating evidence that will inform sustainable scale-up of cervical cancer control programs in LMICs. A primary focus of this partnership will be to leverage longstanding investments in voluntary family planning programs, as well as other efforts to address cervical cancer, and to build capacity in partner countries to sustainably address the burden of cervical cancer.

PEER is a USAID-sponsored program implemented by the National Academies. Since its inception in 2011, PEER has supported more than 300 research projects on multiple topics led by developing country investigators in USAID priority countries. The umbrella program is designed to support research capacity building and partnerships between developing country investigators and U.S. researchers. In addition, nine science agencies from the U.S. federal government currently participate in PEER, including the U.S. National Institutes of Health within the U.S. Department of Health and Human Services (HHS/NIH), which serves as a founding partner. More information can be found online at the PEER program website.

Geographic Scope

USAID has designated funding to the PEER program to support work in Malawi and Mozambique, two countries with some of the highest cervical cancer burden and mortality in the world. These efforts will focus on testing and identifying efficient and scalable implementation models of CCS&PT interventions within voluntary family planning programs in ways that optimize the uptake and health impact of both services. More information on these two countries can be found in Appendix I: Country Information.

Program

Funds will support work in Malawi and Mozambique to identify efficient and scalable implementation models of integrating CCS&PT interventions within voluntary family planning programs. For the

purposes of this solicitation, CCS&PT includes screening for and ablation of cervical pre-cancerous lesions, or, when required, enabling adequate referrals to services for evaluation of high-grade or potentially cancerous lesions. Funds can also support other non-ablative procedures (i.e., loop electrical excision procedure) at referral sites to remove precancerous lesions. Additional information on activities that may/ may not be funded under this award can be found below. Integration will be defined as clients having same-visit access to both quality voluntary family planning information and services and CCS&PT services, provided by one provider or multiple providers working as a team.

All applicants are required to include a strong monitoring and evaluation component that will effectively capture the impact of integrating these services on access and uptake of CCS&PT, as well as on quality counseling and uptake of voluntary family planning. It is expected that part of this effort will include supporting the testing and introduction of new technologies that increase the quality and efficiency of CCS&PT programs. Given the need to test and evaluate approaches and technologies at significant scale, it is expected that most of the funding under the program will be used to support implementation of integrated CCS&PT services at a large number of sites in Malawi and Mozambique, although a substantial amount will be allocated toward research studies embedded within the implementation. Site selection should be determined through consultations to identify country and program needs but should also consider inclusion of sites where access to care for large numbers of women can be increased by capacity building. With regard to new technologies, particular interest will be given to testing innovative approaches that increase access and availability of HPV-DNA testing, technologies that increase efficiencies in triage, and more portable, affordable technologies for ablation of precancerous lesions.

In its partnership with the National Academies, USAID will advance global engagement through the provision of funds to the National Academies to support partnerships between U.S. Government-supported researchers, local partners, and other partners with significant experience and capacity in service delivery of voluntary family planning and CCS&PT in Mozambique, Malawi, and/or other low-income countries in sub-Saharan Africa. These partnerships will implement promising high-quality research projects related to the integration of CCS&PT within existing voluntary family planning programs in Malawi and Mozambique. The activities proposed under these awards will support capacity building, as appropriate, across both static and mobile outreach service delivery platforms. The activities will also be implemented within country-level guidelines, policies, plans, and strategies and can be used to inform other country and donor-led investments in the scale-up of efficient CCS&PT, both nationally and globally. To ensure results inform national-level decision-making, partners should also regularly meet with, and incorporate guidance from, Ministries of Health and other relevant national and global-level policymaking and normative bodies.

To ensure efficient implementation, academic or research institutions funded through this announcement will be required to partner with one or more additional implementing organizations (U.S., international, or local) that have collectively demonstrated strong experience in delivering both voluntary family planning and CCS&PT interventions in LMICs in sub-Saharan Africa, ideally in diverse regions of Malawi or Mozambique, though experience in other contexts that share similar characteristics would also be applicable. U.S. institutions, as well as any non-local non-governmental organizations (NGOs), that receive funding through this announcement will be expected to invest in building the institutional capacity of local organizations. This includes building capacity to implement programs, conduct high-quality research, analyze data, and apply the findings to improve programs.

In their applications, prospective partners will be expected to demonstrate how requested funding from PEER is complemented by non-U.S. Government funding for cervical cancer prevention (including screening and vaccination) and treatment in that country. Applicants should also seek to leverage and build upon existing programmatic and research investments by HHS/NIH, USAID, the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), and other U.S. Government agencies.

It is estimated that a maximum of U.S. $5,100,000 of funding will be allocated for each country. While this is a best estimate, the competitive procurement process will likely elicit multiple proposals, and ultimately, funding decisions will be based upon several factors, including proposals' quality and feasibility, the strength of the relationship between local and US scientists, the capacity of the partner organizations and countries to implement activities, and how well proposed activities respond to the technical and programmatic scope of the program and meet the partner country needs. More information on how proposals will be evaluated can be found in Section XI: Review Criteria.

II. TIMELINE AND APPLICATION

The timeline of this PEER award spans four phases as outlined in the table below:

	Date	**Action**
Phase I Competition and Partner Selection	November 1, 2018	National Academies releases Partnership RFA for full and open competition among potential partners.
	December 11, 2018	Partnership proposals from U.S. institutions are due to National Academies via online submission platform.
	December 12, 2018 – January 31, 2019	National Academies convenes independent technical merit review of proposals and partners are selected.
	February 2019	Negotiations lead to finalization of the terms of the grants between National Academies and new awardees.
Phase II Start-up	March 2019	National Academies organizes a kick-off forum for the Principal Investigators (PIs) and key team members from the funded projects, to be held in Malawi and Mozambique with the participation of USAID and HHS/NIH representatives. At this meeting both U.S. and country partners will be asked to begin finalizing a joint work plan and budget for the program.

	March-May 2019	Multi-stakeholder engagement to inform research activities. Research protocols are finalized and approved.
	March-May 2019	Visits of National Academies staff and experts to local partners to assess, address, and support priority steps and activities as needed related to organizational capacity building, such as strengthening financial management. U.S research institutions also work during this time to further assess the local partners' research capacity and other areas like IT systems and data sharing platforms and develop plans for strengthening those aspects.
	March-May 2019	Initial support for programmatic implementation can begin as indicated (e.g., training of staff, lab strengthening, and procurement of needed commodities by the U.S. or local institutional partners).
Phase III Implementation and Research	June-August 2019	Research studies commence following protocol finalization with activities such as training of research staff completed during this period.
	September 2019-March 2021	Research studies continue with support for program implementation and administrative compliance continuing throughout the entire period. Site visits as needed by the National Academies' program manager and USAID staff will be scheduled.
Phase IV Analysis, Dissemination, and Close-out	March 2021-September 2021	Data cleaning, analysis, and dissemination. Technical assistance and other support provided to incorporate findings into national policy and global recommendations as applicable. National Academies will convene a final forum in Africa for the PIs, key team members, USAID and HHS/NIH representatives, and important local or regional stakeholders to facilitate the sharing of findings and recommendations by the participants.

In addition to the above, and as the program proceeds, biannual meetings will be coordinated by the National Academies and held in Malawi and/or Mozambique in coordination with the partner country governments to allow for a regular review of annual work plans and project updates to key stakeholders. These meetings may bring together all partners, or a selected group of country-based or international partners, as determined in consultation with USAID and the U.S. National Cancer Institute (NCI) to share findings, discuss common problems, coordinate work plans, and receive training on communications and outreach skills. To enhance collaboration and networking, these fora may be

coordinated or combined with other working meetings supported by other key stakeholders, such as the World Health Organization (WHO), International Atomic Energy Agency, or UNITAID.

III. AVAILABLE FUNDING SUPPORT

For CCS&PT activities, USAID anticipates a total of U.S. $10,200,000 for subawards from the National Academies under the PEER Program. Of this total, a maximum of U.S. $5,100,000 is intended for subawards to be made for work in Malawi and U.S. $5,100,000 for subawards in Mozambique.

Applications should be submitted as a joint application between one U.S. institution and one local partner that plan to work together, with each presenting its own budget and the total amount of the two budgets combined not to exceed $5,100,000. For the proposal that receives funding, both the U.S. and local partner will receive a prime subaward from the National Academies. At least 70% of the total budget of the two prime partners combined should be allocated to strengthening implementation of CCS&PT integrated within voluntary family planning, and the introduction of new technologies for CCS&PT. Up to 30% of the budget can include costs specific to conducting, analyzing, and disseminating the embedded implementation research, including engaging stakeholders throughout the research-to-use process and ensuring findings are incorporated into policies and programs in real-time. Dissemination plans for activities in Mozambique should include plans to prepare and disseminate materials in both English and Portuguese. Budgets should delineate the costs that are specific to implementation and those that are specific to research. More information on allowable and unallowable costs can be found in Section VII: Budget Form and Justification. Final budgets for Malawian, Mozambican, and U.S. partners will be developed as part of a work-planning process to commence in the first half of calendar year 2019. The National Academies, in consultation with USAID and NCI, will approve the final budget for all subawardees. Allocation of funds to all recipients is contingent upon meeting required standards to receive and properly manage U.S. Government funds.

A cost share of 10% will be required of U.S. institutions applying as prime subawardees. This can be in the form of in-kind and/or financial contributions. Some examples of possible cost share might include provision of equipment, space, or staff time; private sector donations of technologies to support the project; or reduction of overhead costs.

IV. ELIGIBILITY

Only local academic institutions and/or other local NGOs with demonstrated expertise in health-related research and U.S institutions that are the prime recipients of HHS/NIH funding (either academic institutions or NGOs) for research are eligible to submit an application to be prime subawardees of the National Academies. When appropriate, U.S. NGOs applying as a prime partner are encouraged to include U.S. academic institutions as partners that can assist in building capacity and stronger technical collaborations with partner country academic institutions. To apply as a prime subawardee, a U.S. institution must have a current history of working in Mozambique and/or Malawi or demonstrate a substantial understanding of implementing CCS&PT and voluntary family planning programming in the region and demonstrate a partnership capable of rapid implementation in the partner country. As noted above, this application must be submitted as a joint application between the local partner and U.S. partner with separate budgets included for each. Both the U.S. institution and the local institution will

be prime subawardees of the National Academies. The joint application should present a coherent description of how the activities in each application will complement one another. Local organizations that do not have expertise in implementation research or U.S or other international organizations that do not receive HHS/NIH funding for research can be part of the application as sub-partners of the prime subawardees, but cannot be prime subawardees.

The local partner that is a prime subawardee of the National Academies will play a key role in designing, conducting, and analyzing results from implementation research, as well as in helping with real-time translation of results into policy and programs within the country. The U.S. institution that is a prime subawardee will collaborate with the local partner on the research components, including specific activities designed to strengthen the local institution's research capacity. To ensure efficient implementation, the U.S institution and/or potentially the local partner (if it has a strong track record of managing large implementation projects), will be expected to make subawards to one or more additional implementing organizations that have demonstrated capacity to support integrated family planning and CCS&PT in low-income countries in sub-Saharan Africa, preferably in diverse regions of Malawi or Mozambique. Details of available funding support for these awards are outlined in Section III: Available Funding Support.

As noted earlier, while a substantial proportion of the funding should support implementation research, the majority of funding should be utilized to improve service delivery, including through supporting implementation and scale-up of innovative or improved technologies and approaches. With regard to support for implementation, forming consortia of partners with complementary expertise is encouraged. Such consortia would include one or more NGOs with proven expertise in implementation of new technologies for CCS&PT, local NGOs that support government health facilities, and other implementers that support health facilities operated by the private sector, such as networks of facilities operated by faith- and/or community-based organizations. Opportunities to engage with the for-profit, private sector in a consortium could be explored, including with manufacturers of relevant CCS&PT products or technologies as well as with commercial outlets to reach patients, such as local drug shops or private clinics.

Protecting Life in Global Health Assistance *(Formerly known as the Mexico City Policy)*

On January 23, 2017, a Presidential Memorandum was issued reinstating the 2001 Presidential Memorandum on the Mexico City Policy for USAID family planning assistance and directing the Secretary of State to implement a plan to extend the requirements of the Mexico City Policy to "global health assistance furnished by all Departments or Agencies." USAID began implementing the policy, now known as the Protecting Life in Global Health Assistance policy on May 15, 2017, for grants and cooperative agreements that provide global health assistance. The policy requires foreign NGOs to agree, as a condition of receiving global health assistance, that they will not perform or actively promote abortion as a method of family planning and will not provide financial support to any other foreign NGO that conducts such activities. To implement the Protecting Life in Global Health Assistance Policy, USAID issued a new standard provision on May 15, 2017, which is publicly available here: https://www.usaid.gov/sites/default/files/documents/1868/303maa.pdf. This provision must be included in all new USAID awards that include global health assistance.

V. PURPOSE, OBJECTIVES, AND RESEARCH PRIORITIES

Purpose

The purpose of the PEER-supported CCS&PT activities is to strengthen capacity in Malawi and Mozambique to more efficiently and effectively implement CCS&PT interventions at scale that are effectively integrated and linked with voluntary family planning programs. The activities will generate evidence that will inform efforts to introduce and scale-up CCS&PT interventions nationally and in other LMICs.

Objectives

The CCS&PT program has two interrelated objectives, which are described below:

1. To accelerate the scale up of more efficient implementation models of integrating CCS&PT with voluntary family planning programs that optimize the uptake and health impact of both.

Other organizations have previously supported and implemented activities integrating CCS&PT with voluntary family planning, while measuring the potential of integration to increase the health impact of both services. For example, The Bill and Melinda Gates Foundation (BMGF) supported integration of quality CCS&PT into voluntary family planning programs. This initiative, which was called the Cervical Cancer Screening and Preventive Therapy Initiative, worked in Uganda, Nigeria, Tanzania, and Kenya, generating preliminary evidence to indicate that the integration of CCS&PT with voluntary family planning programs could increase uptake of both health care services. In addition to this work, other organizations have implemented pilot projects around integration of cervical cancer with family planning; however, gaps remain in the evidence.

Therefore, it is expected that all potential funding recipients clearly establish how proposed activities can leverage the existing evidence base, as well as establish innovative approaches to fill evidence gaps. Examples of evidence generated might include: (1) quantifying demand for and uptake of CCS&PT and voluntary family planning offered in tandem vs. separately; (2) determining the cost per client of adding CCS&PT to voluntary family planning programming; (3) documenting additional voluntary family planning acceptors disaggregated by method; (4) estimating increased client load per provider; (5) documenting the number of women coming in for voluntary family planning and accepting CCS&PT; and (6) determining whether or not integration efforts could increase provider/client experience, quality, and satisfaction. It is expected that projects implemented under PEER Program awards will build on this existing evidence and establish a clear learning agenda that will define common challenges of integrating these services, while documenting innovative solutions to overcoming those challenges. Other potential indicators can be found in sub-Section 5 of Section VI: Outline of Requested Partner Program Concepts/ Descriptions.

2. To accelerate the introduction and scale-up of new technologies that will increase the health impact and efficiency of CCS&PT programs

Examples of these technologies include:

HPV-DNA Testing

The past few decades have seen a dramatic decline in cervical cancer deaths in higher-income countries. This can be attributed initially, in part, to increased availability of Pap smears, which enable precancerous lesions to be detected and treated before they spread. To overcome concerns with

infrastructure and cost, screening in developing countries is most commonly done by visual inspection of the cervix with acetic acid (VIA). VIA is not only cheaper and easier to implement than Pap smears, but also allows women to receive immediate treatment after a positive screen, which can help avoid treatment delays and loss to follow-up. Cervical cancer screening and treatment of precancerous lesions has been described by the WHO as a "best buy."[3] However, there are considerable concerns with VIA that make it a less-preferred method of screening moving into the future. As VIA has been implemented outside of clinical trial settings, a high inter-provider variability has become apparent, leading to low sensitivity in many cases. Moreover, even in clinical trial settings, VIA only prevents a minority of deaths from cervical cancer. New and emerging technologies like HPV-DNA testing have the potential to increase the quality of cervical cancer screening services.

HPV-DNA testing is more sensitive and specific than VIA and Pap tests,[4] can be provided by a lower cadre of health worker, requires less training, and has the potential for sample self-collection, which is less invasive and could decrease stigma and other barriers that keep women from screening.[5] Furthermore, self-collection of HPV-DNA test samples can potentially be integrated into mobile outreach and community health worker programs. This approach could increase the reach of cervical cancer prevention services while providing avenues to increase efficiencies, and decrease the loss to follow-up seen with technologies that are not as conducive to single-visit "screen and treat." While activities performed under this program should work closely with partner governments to implement programs that can best inform national-level implementation plans and policies (which given cost constraints, may include a focus on VIA), partners will be encouraged to consider innovative pilot programs to decrease costs and increase access to new technologies like HPV-DNA testing. Where national guidelines or policies do not exist, partners will be expected to work with Ministries of Health to ensure appropriate development of guidelines and resource packages for the introduction of new technologies. As mentioned above, activities might include feasibility studies around integration into mobile or static clinics, but could also include innovative approaches towards leveraging equipment that may already be available in LMIC settings, such as platforms used for HIV viral load testing and/or tuberculosis testing; using iterative user research methodologies like human-centered design to understand patient values and preferences that hinder/drive uptake of different types of HPV-DNA tests; or employing market shaping interventions that aim to reduce long-term demand and supply imbalances.

New Ablation Technologies

While providing quality screening for precancerous lesions is a critical step for decreasing cervical cancer incidence and mortality, access to early and cost-effective treatment of pre-cancerous lesions including ablation is of equal importance. Recently, innovative new approaches to the ablation of precancerous lesions have been developed and introduced. For example, thermocoagulation has been shown to be effective and in many cases, simpler to implement than traditional cryotherapy interventions. Recently, with the help of the Global Fund, Malawi has procured 300 portable thermocoagulation devices. Additionally, new portable technologies, including portable gas-less cryotherapy devices as well as enhanced ethanol ablation, may be able to overcome the challenges with existing ablation technologies, like the need for large medical-grade gas tanks. As is the case with the introduction of screening technologies, implementing partners should work with countries to ensure protocols used in these programs are in line with national guidelines and policies for ablation of precancerous lesions in partner countries. Where national guidelines or policies do not exist, partners will be expected to work with Ministries of Health to ensure appropriate development of clinical guidelines and resource packages for the introduction of new technologies. There is a clear value in increasing women's access to existing high-quality commodities, including through the strengthening of country supply chains and service

delivery points in an effort to lay a foundation for the introduction of new technologies that will overcome barriers to making a significant global impact on cervical cancer incidence and mortality. Therefore, applicants are encouraged to consider innovative approaches towards the integration of new, proven technologies into country-level programs, including coordinated strategic planning in partnership with manufacturers, health care providers, policymakers, and market shaping interventions.

New Visualization Approaches/Technologies that Improve the Accuracy of Visual Assessment of the Cervix for Precancerous Lesions

Imaging plays a central role across the comprehensive cancer care spectrum from screening, to early detection and diagnosis, through treatment and follow-up. The ability to non- or minimally-invasively visualize anatomy and physiology empowers healthcare teams in providing optimal care to patients. It reduces unnecessary treatment and further testing, especially in already overburdened medical systems. Particularly relevant to cancer care, optical imaging tools are safe, fast, and versatile: useful for repeated procedures to evaluate disease progression and monitor treatment. Rapid, point-of care (POC) imaging, coupled with image-analysis software and proper training programs, can change the landscape of cancer staging and diagnosis in settings where a lack of pathology services has created a bottleneck in clinical work-flows or can enhance capacity for traditional pathology services, offer new avenues for digital telepathology, or task-shift roles to primary care providers to improve the early detection of cancer.

Colposcopy, an examination of the cervix performed using a magnifying device called a colposcope, allows providers to identify abnormal cervical cells for biopsy and further evaluation. Traditional colposcopy requires a trained provider; adequate equipment (including a functioning colposcope), space, and time for a pelvic exam. Innovative approaches to colposcopy in resource-limited settings, however, have the potential to redefine these requirements. In particular, low-cost, portable approaches to performing colposcopy at the point-of-need have been developed that allow for image capture and analysis while simplifying workflow. By reducing the training level required for use, these tools allow for task-shifting models that empower community-level providers to enhance early detection of cervical abnormalities at the point-of-need.

Low-cost, portable optical microscopy may also allow for high-quality, real-time imaging at the cellular level *in vivo.* Real-time evaluation, diagnosis, and staging of cervical neoplasia can assist providers in determining the necessity of immediate cryotherapy, improving the efficiency of both mobile and in-clinic see-and-treat approaches and ultimately reducing over-treatment.

An integrative approach using a first-line self-sampled molecular test that provides a high level of reassurance when negative, such as POC HPV-DNA testing, followed by triage, employing these emerging imaging strategies, could achieve high program efficiency. It would rule out disease risk in the majority of women and reduce the need for gynecologic examinations. HPV-DNA tests that are faster and less expensive than current options would be welcomed.

mHealth/eHealth Strategies

The enormous potential for mobile technology to transform health care has led to the rapid development of new health-related phone applications and device attachments. The potential of mHealth is especially relevant to LMICs, where cell phone ownership is rising rapidly, but access to health care and providers is often limited. mHealth strategies may be employed to support early detection, facilitate accurate diagnosis and effective treatment planning; support reliable

communications between all members of the care team, including the patient, during treatment; and offer an unbroken system of support during follow-up, survivorship, and at end-of-life.

In particular, mHealth can be used to enhance screen-and-treat program efficiency through behavioral interventions focused on patient follow-up, referral, or abandonment of care, improving patient education, and by creating a communication safety net for cancer survivors that will allow them to thrive after treatment, while adhering to the evolving guidance of a proactive survivorship care plan.

mHealth tools can also be used in conjunction with a screening program to translate data from the visit into e-Health records and cancer surveillance systems.

Liquid cytology[6]

In higher-income countries evidence suggests that liquid cytology may have advantages over conventional cytology. Similar to HPV-DNA testing, this may result in an increase in overall cost–effectiveness for the process, even though the test itself is more expensive. The advantages of liquid-based cytology are that it produces a uniform layer of cells and removes cellular and other debris. Liquid cytology has the potential to offer improved sensitivity and specificity as well as increased laboratory efficiency. However, its implementation requires health professional and technician training, as well as the provision, storage and transport of media, new equipment, and ongoing quality assurance review. Evidence suggests, however, that health professionals and technicians learn the needed new skills rapidly and reliably.

Implementing or expanding cervical cytology screening on a subset of patients is important to assure the quality of screening and increase program efficiency by reducing under-treatment or over-treatment (see Section VI, Subsection 3 below for further details). Private sector engagement as well as innovative ways to leverage existing resources could help expand the use of liquid cytology.

Research Priorities

The PEER activities will utilize implementation research to generate evidence that can be applied to programs in real-time. This will be done by providing support to build capacity of country partners to expand implementation of CCS&PT integrated with voluntary family planning while at the same time embedding research within this implementation.

Research activities should generate evidence that is relevant to the following two broad questions:

1. How can CCS&PT and voluntary family planning be integrated and linked with one another in different types of service delivery settings to increase the health impact of both services, as measured by increased numbers of precancerous lesions ablated and increased availability of voluntary family planning counseling, uptake, and client satisfaction?
2. How can new technologies for cervical cancer screening be most effectively utilized within programs in low-income countries to increase the impact of CCS&PT, while also potentially decreasing the burden on health systems and health providers in terms of the overall resources required (as measured by the fully-loaded costs of screening, including time spent by providers for screening and reduction of client costs)?

As they seek to increase uptake of cervical cancer screening by women age 30 and older in voluntary family planning programs, the projects should also seek to identify efficient approaches to leverage these efforts to also improve screening among women who are beyond their childbearing years. (Please see Section VI, Subsection 2 for further discussion of this important issue.)

A key priority of the CCS&PT program will be to generate evidence with a potential to be used to inform global and national guidelines and policies. In May of 2018, the WHO Director General made a call to eliminate cervical cancer as a public health threat. In the months since, WHO has convened a number of technical expert group meetings and is working to galvanize a global group of stakeholders towards elimination. While significant advancement in reducing incidence and mortality can be achieved in the near-term, it's clear that the horizon for global elimination is much longer. Achievement of these goals will require sustained investments in HPV vaccination, identification and ablation of precancerous lesions, identification of and linkage to care for invasive cervical cancer, and palliative care. As WHO and other international stakeholders work to increase attention and focus on elimination of cervical cancer, it is important for governments and global donors to provide support that not only will catalyze global investment, but also lead to increased efficiencies among programs. With USAID's long history in implementing voluntary family planning and reproductive health programs, and NCI's expertise in cutting-edge cervical cancer interventions, the PEER partnership represents an excellent opportunity to leverage each organization's comparative advantage to generate evidence that can support partner countries and the global community to implement innovative and cost-effective programs.

VI. OUTLINE OF REQUESTED CONCEPTS

The program description of the joint application submitted by the U.S. partner and the local partner should not exceed 25 pages in Times New Roman 12-point font, single-spaced with 1-inch margins. However, applicants may include additional information in Appendices (e.g., Key Personnel CVs, letters of support, detailed budgetary information, etc.).

SUB-SECTION 1: Institutional Capability, Partnerships, and Management Plan

In this section, please describe the background that the two prime partners bring to the proposed project, including expertise in support for implementation of voluntary family planning provision, CCS&PT interventions, and the integration of the two, as well as expertise in implementation research and research capacity building. Please clearly outline the roles of the two prime subawardees, one U.S. and one local, as well as the roles of any subawardees included in your partnership. Please include relevant expertise in other key areas such as biostatistics, laboratory, health policy, supply chain and program management in low-income countries, highlighting relevant experience in Malawi and/or Mozambique.

Proposed projects should seek to add value by augmenting existing efforts in country, helping to fill critical gaps in evidence and availability, and assisting country partners to build their own capacity to overcome bottlenecks to impact and scale. Therefore, the proposals should clearly outline how the proposed activities would leverage, complement, and link to other investments related to CCS&PT currently being made, or anticipated, in Malawi and Mozambique. This includes investments from the country governments and partners such as the HHS/NIH, PEPFAR,

Global Fund for AIDS, Tuberculosis, and Malaria, International Atomic Energy Agency, UNITAID, as well as from the private-sector investments, including from private philanthropic foundations/ organizations. Though funding cannot be provided under this RFA for invasive cervical cancer treatment or palliative care, partners are highly encouraged to find other resources to support invasive cervical cancer treatment and palliative care, and leveraging of such support will be included in the evaluation criteria (see Section XII below).

Proposals should demonstrate an understanding of the overall landscape of cervical cancer prevention, treatment, research, and care activities in the country, spanning from HPV vaccination to screening and treatment of precancerous lesions to treatment of invasive cancer and palliative care, including providing specific information as it is available about what other funding is being invested in these areas. A table that clearly summarizes this information is recommended.

Proposals should include a management plan which articulates the processes by which the various partners involved will manage the activities, as well as the structure that the partners will use to coordinate different elements of the projects and ensure accountability.

SUB-SECTION 2: Implementation Research

In this section, please describe how the proposed implementation research activities will be conducted and justify the reasons for the approaches used. As part of this, it is essential that applicants outline a clear theory of change to guide the implementation research activities they propose, and the overall set of activities in which the research is embedded.

Research activities under the project should use a mix of quantitative and qualitative methods to generate practical data that can be applied to program implementation, with an emphasis on relevance to programs within the partner country. Proposals should focus on research designs and questions that are feasible, appropriate, and adequately powered to test a small number of clear hypotheses that fall within the broad objectives listed in Section V above.

Applications should outline a clear process by which the projects will conduct ongoing multi-stakeholder engagement according to best practices to refine research questions and activities. This will help ensure research is locally-owned and that the findings are disseminated and translated in real-time into national plans, policies, and programs throughout the course of the research. Dissemination should take into consideration language requirements relevant to both local and global populations, at minimum English and Portuguese (for Mozambique). Proposals should clearly explain which stakeholders will be engaged, how and when they will be engaged, and what support will be provided for translating research findings into use over the course of the projects. Please also see this link as a reference that outlines some best practices for multi-stakeholder engagement for implementation research in LMIC.

Research activities should be consistent with the "research-to-use" approach outlined in USAID's Global Health Research and Development Strategy 2017-2021, which outlines USAID's global health R&D goals across product development, introduction, and scale up; implementation science; and research capacity building. Implementation research should seek to understand both which approaches work, and which approaches do not work in different contexts including clinical and community-based settings in rural and urban areas. Proposals should also include

clear utilization plans. If applicable to local context, mobile and static service-delivery approaches should both be evaluated. The research-to-use effort should also identify and disseminate key lessons for programs, promising innovations, and useful practices and tools for them to adopt. While the focus of the implementation research should be on identifying how best to implement interventions in different settings, the process should also gather information about processes that may be effective for building capacity of health systems for CCS&PT.

Applicants should clearly define proposals for two types of implementation research:

1. **Implementation research embedded within programs to evaluate and improve approaches to integrating and linking CCS&PT with voluntary family planning programs.** Implementation research should assess the impact of different approaches on both CCS&PT and voluntary family planning outcomes and seek to identify solutions that work in specific settings to improve uptake and impact of both types of health services. The primary focus of these activities should be on service-delivery approaches at the primary care level implemented through clinical and community-based platforms. Activities should also include efforts to raise demand and awareness of CCS&PT and address social norms that are barriers to women accessing cervical cancer prevention. However, applicants are also encouraged to include activities to explore how improvements in referral networks might improve outcomes for women with cervical precancerous lesions and cancer. They are also encouraged to assess how improvements in health workforce, equipment, and supply chain capacity might increase the uptake of both CCS&PT and voluntary family planning. A secondary focus of these activities could expand to include older women, for example by studying how increasing the acceptability of cervical cancer screening in younger women accessing voluntary family planning could be leveraged to increase screening for older women. This would address the concern that over-reliance on voluntary family planning services for screening may result in disparities in cervical cancer mortality between younger and older women. In the former case, women screened under those services may assume that there is no need to continue screening after they finish childbearing and/or enter menopause. As a result, no screening mechanisms are put in place for older women, who have the highest rates of invasive cancer.[7]
2. **Implementation research to utilize improved technologies and pathologic confirmation for cervical cancer screening and preventive therapy sustainably and at scale.** This should include exploring innovative ways to deploy these technologies to decrease burdens on women's health providers, health systems, and supply chains while increasing the health impact of screening, testing, and triage. One high priority is to test the feasibility and cost-effectiveness of different approaches to implementing HPV-DNA testing, including evaluating self-collection of HPV-DNA test samples through delivery channels like static clinics, mobile outreach, community health workers, or drug shops. As technologies receive global endorsement, additional studies could determine the feasibility and affordability of coupling HPV-DNA testing with more portable ablation devices. If indicated by country needs and interest, support could also be provided to assess low-cost ways to improve accuracy of visual assessment of the cervix, such as approaches that utilize mHealth and artificial intelligence, and/or to improve diagnostic pathology services and laboratory medicine at higher levels of the health system. Pathology and lab medicine systems are a key component of accurate diagnosis and treatment. Applications should include a quality assurance plan addressing test turnaround time, test report availability, and tissue diagnosis of procedural specimens to inform patient selection and procedure effectiveness.

SUB-SECTION 3: Service Delivery of CCS&PT Integrated with Voluntary Family Planning

Applications should provide plans to support activities that will build partner countries' capacity to (1) integrate CCS&PT with voluntary family planning programs and (2) introduce new technologies that can make CCS&PT more efficient and effective. In accordance with global guidelines, programs should focus on CCS&PT in population of women 30 year and older, unless there is a clear reason to provide services to women under the age of 30 (i.e., testing positive for HIV). Given the importance of having a strong platform in place as soon as possible to evaluate the best approaches to integration and introduction of new technologies, the projects are encouraged, as needed, to begin to provide support for staff training and new technology and supplies procurement prior to the official start of research activities, but not prior to confirmation of the award.

This may include assisting partner countries in strengthening their capacity to implement CCS&PT through support for the following areas, depending on country needs: (1) training and supervision (including working alongside partner countries to harmonize policies and guidelines for integrated service delivery and the development of new training materials/ guidance for providers of integrated services); (2) quality improvement approaches to increase implementation fidelity and referrals of patients with cancer to specialized sites; (3) strengthening systems for monitoring and evaluation (including cancer registries if indicated); (4) improving supply chains for cervical cancer prevention commodities including support as needed for demand forecasting, market shaping, and in-country logistics; and (5) integrating social and behavior change activities into existing platforms to increase demand for voluntary family planning and CCS&PT.

Also of importance are activities to assist countries in strengthening their capacity to evaluate, introduce, and scale-up improved technologies for CCS&PT. These technologies might include HPV-DNA testing, improved diagnostic capabilities, and more affordable, more portable technologies for ablation of cervical precancerous lesions. Examples of these activities could include the following, depending on country needs: (1) providing and building capacity to provide training, mentorship, and supervision of health providers and technicians in the new technologies; (2) strengthening laboratory and health system capacity to roll-out HPV-DNA tests and cervical cancer diagnostic technology that is suitable to the country context; (3) developing clinical and other guidelines, standard operating procedures, and training materials for screening and treatment, HPV-DNA testing, diagnosis, referrals, or new ablation technology; (4) quality assurance or validation; (5) coordinating delivery of HPV-DNA tests and other needed commodities for CCS&PT; (6) expediting in-country registration of new technologies, in collaboration with medicines regulatory authorities and other stakeholders like WHO; (7) utilizing market shaping opportunities to increase the efficiency of markets for improved product availability and affordability of new technologies on a faster timeframe; and (8) strengthening monitoring and evaluation, including strengthening outreach and follow up, systems to report and respond to possible adverse events from cryotherapy or thermocoagulation.

Additional service delivery requirements for inclusion of cytology and histopathology
Cervical cancer prevention, diagnosis, and treatment programs frequently include components related to cytology, pathology, and laboratory medicine services. While it is unclear whether the future of exfoliative cervical cytology (Pap tests) is limited, especially given improvements in technology such as liquid-based cytology, histopathology remains the standard of diagnosis of precancerous lesions targeted by screening. Maintaining high-quality cervical histopathology is often challenging in the context of developing countries, but strengthening of these services will

in the short- and long-term lead to better quality and patient outcomes. When designing and validating screening and treatment methods, it is essential to (1) compare screening methods to accurate endpoints of "precancer," which is then (2) treated appropriately with an excisional or ablative therapy and (3) followed up. Once a screening method is validated, an option might be for "see and treat" strategies to not include histopathology, if acceptable to local authorities. However, where appropriate and within national-level guidelines and policies, regional or national histopathology services should be established and strengthened, teaming with international experts, in a few centers within the country. This would permit local evaluation of new screening technologies against a truth standard, leading to continuation of those screening services without routine need for expert histopathology.

For projects funded under this RFA, if consistent with partner country policies, plans, and guidelines, periodic checks of screening and immediate treatment against a histopathology standard must be introduced as quality assurance, even when histopathology is not performed as part of the routine screening practice. This is essential to avoid both over-treatment and under-treatment. For example, in some previous program assessments, the lack of premalignant pathology on LEEP specimens was an indicator of over-diagnosis in a VIA program. On the other hand, under-diagnosis can lead to invasive cancer being inappropriately treated with ablation. Incomplete treatment can also occur for other reasons, such as inadequate depth of treatment with both cryotherapy and thermal coagulation. If consistent with partner country policies, guidelines, and plans, to help mitigate the risks of over-treatment and under-treatment, projects must include a planned interval follow up for all women treated and a quality assessment program that includes pre-procedure biopsy on a subset of patients. This planned interval follow-up will not guide individual patient decision-making at the time of treatment. Instead, it will provide validation of screening, feedback on case selection at the program level, and assessment of the appropriateness of treatment. If (1) a high percentage of high-grade precancerous lesions or invasive cancers are identified in the treatment population; (2) a high percentage of women in the treatment population have negative pathology; (3) women return with invasive disease; or (4) there is a high loss to follow up rate, this will serve as a safety signal indicating the need to modify screening, change case selection criteria, reconsider treatment algorithms or strengthen follow up and outreach.

SUB-SECTION 4: Capacity Building

In this section please describe activities to support individuals as well as institutional capacity of local partners that are not otherwise described in the sections above. In this regard, we are looking for U.S. partnership proposals that go beyond traditional training and exchange models to truly build human and institutional capacity. For additional reference, we encourage applicants to review the USAID Human and Institutional Capacity Handbook. Please describe special resources/expertise that can be leveraged from the applying U.S. institution to support proposed capacity building activities.

SUB-SECTION 5: Monitoring and Evaluation

Proposals should outline their overall framework or approach for monitoring and evaluation and describe how partners will work together to collect, analyze, and utilize data to track program progress. This should include activities related to data quality assurance. The focus should be on working within and strengthening national monitoring and evaluation systems, and activities should strengthen ability of providers and policy makers to analyze and use data for decision-

making. Activities should avoid contributing to the development of parallel data systems, though it is understood that research activities may require the use of short-term approaches to collect indicators that are not available within the existing national systems. Proposals are encouraged to include elements to build capacity for providers to utilize data to change how their facilities operate.

Proposals should define specific, measurable, realistic outcomes, and indicators that will enable the projects to determine whether there is a change in:

- Number of cervical cancer screenings completed;
- Number of cases where histopathologic quality assessment indicated discrepant results between screening and pathology;
- Number of precancerous lesions ablated (compared with previously-existing protocols);
- Improved quality of pathologic services as measured by acceptable sensitivity and specificity for detection of cervical dysplasia, and increased inter-observer reproducibility;
- Number of women who follow up, and are contacted for follow up, after screening and treatment;
- Number of women diagnosed with high-grade precancerous or cancerous lesions;
- Number of women accepting CCS&PT and voluntary family planning;
- Uptake of voluntary family planning by method;
- Changes to facility-level contraceptive method mix (if any);
- Quality of counseling or service delivery (ex. measurement of facility wait times);
- Cost per user of voluntary family planning and CCS&PT services delivered, including by method of voluntary family planning adopted;
- Provider/client satisfaction; and
- Other priority outcomes/indicators as appropriate to the project or partner country.

VII. DRAFT BUDGET FORM AND JUSTIFICATION

Using the budget form provided, each of the two prime partners involved in the submission of a joint application should submit its own itemized draft budget in U.S. dollars. The sum of the two budgets cannot be greater than the U.S. dollar amount described for activities outlined in Section III. These itemized budgets can be submitted separately from one another or together depending on the partners' preference. However, it is recommended, though not required, that the two partners submit a summary joint budget that displays how the proposed expenditures of the U.S. partner and Malawi or Mozambique partner budgets are complementary. Unless otherwise agreed upon, all project activities must be completed by September 30, 2021. Equipment and other direct costs may be supported by either the U.S. partner budget or the Malawi/Mozambique partner budget as needed. Final budgets for partners will be developed as part of a work-planning process in the Q1/2 of the 2019 calendar year. The National Academies, in consultation with USAID, will approve the final budget for all subawardees.

The draft budget table should list estimated annual costs by year. The following budget requests are <u>not allowed</u>:

- Costs for the construction of new buildings or the repair, renovation, or refurbishment of existing buildings;

- Contingency costs; and
- Customs duties, as normally awards supported with USAID funds are exempt from duties in countries receiving U.S. assistance. If the items to be bought will not be exempt from such duties, funds to pay these charges must come from other non-PEER sources.

Draft budget request justification: In addition to the budget request form, provide an explanation and justification for support requested in the following categories:

1. **Labor:** Applicants requesting salary coverage in their project budgets must include a list of positions to be supported, an explanation of their roles, and the percentage of their time that would be devoted to the project. For salaries of U.S. faculty members, it is expected that their home institution would participate in cost sharing. Please make sure to document the cost sharing amounts in the budget form under "Other Contributions."

2. **Equipment:** Proposals for the purchase of equipment required for *research*, *training, and service delivery* are allowed. Costs for new technologies related to HPV testing and the ablation of precancerous cervical lesions, including machines and ablation devices can be a substantial part of the budget (up to 25%) if this is needed for implementation (costs of associated reagents should be included in the materials and supplies line of the Other Direct Costs section of the budget). Cost of instruments for histopathologic sampling; sample media; sample transport; and costs of training and lab upfitting for cytology and/or histopathology testing may also be included, but should not exceed more than 5% of the budget, though partners could include additional pathology-related costs as part of cost share. Where possible, projects should leverage existing durable equipment and infrastructure. Requests for new durable equipment (items with an individual cost of U.S. $5,000 or more) should be justified in terms of importance to successful implementation of the proposed program. Please also include plans for maintenance of the equipment during and beyond the project period.

3. **Travel Costs:** Provide the number, duration, location, and purpose for any project-related trips for which funds are requested, along with the titles or positions of the travelers. International air travel must be by U.S. air carriers to the maximum extent such service is available as required under the Fly America Act,(http://www.gsa.gov/portal/content/103191), so applicants should estimate their air travel budgets accordingly. First class or business class travel is not permitted**.**

4. **Other Direct Costs:** Explain any costs for materials and supplies (including smaller pieces of equipment costing less than U.S. $5,000), Internet or telephone services, publications costs, the organization of workshops or conferences, computer services, non-travel training costs, subawards, or other direct costs that have been included in this section of the budget form.

5. **Indirect Costs:** If requested, indirect costs (costs supporting overall institutional operations and management) should be kept to a minimum and must be fully explained and justified in the budget justification section of the full proposal, with details provided on what specific institutional infrastructure elements or support services are covered. If your institution has an official Negotiated Indirect Costs Rate Agreement (NICRA) with a U.S. federal agency, that rate can be used, and documentation of that NICRA will need to be uploaded in the application.

6. **Cost share:** As applicable, please describe what costs the applicant will share.

VIII. KEY PERSONNEL

Please attach CVs for all members of the leadership team who will be involved in managing and providing technical direction and oversight for the proposed activities at the applicant's institution. Project Coordinator positions are strongly encouraged. Each CV should be no more than three pages in length.

IX. LETTERS OF SUPPORT

Please attach a separate letter of support from an official at the primary U.S. partner institution, the primary African partner institution, and the implementing partner organization who is legally authorized to make commitments on the institution's behalf. These letters must be signed and written on official institutional letterhead and must include the following elements:

- Confirmation that the institution supports the participation of its staff in the proposed project and would be willing to receive and administer any grant funds awarded;
- A brief description of the institution's structures and practices for project management and financial oversight; and
- A brief description of resources that the institution would be making available (if any) to facilitate the project, whether in cash or in kind, for example, by paying the salary of any staff members involved for the time they work on the program, providing substitute instructors to cover their other duties so they are free to work on the program, or providing laboratory or office space, access to equipment, or office support staff.

Additional letters of support for the proposed program are encouraged but not required.

X. SUBMISSION INSTRUCTIONS

Proposals must be submitted through the PEER online system by **5:00 PM U.S. Eastern Standard Time on December 11, 2018.** The U.S. and Malawian or Mozambican partners involved in each project should work together to prepare one complete joint proposal, which may be submitted by either side to the PEER online site.

Applicants should **not** reach out to USAID or HHS/NIH directly during the RFA process, as this would be in violation of USAID's procurement rules. Applicants should direct all questions or comments on the PEER/Building Capacity for Cervical Cancer Screening and Treatment of Precancerous Lesions through Innovative Approaches program or RFA to the U.S. National Academies (peer@nas.edu).

Applicants are kindly requested to send an e-mail stating their intent to apply to peer@nas.edu, with the subject line "Intent to Apply: PEER Cervical Cancer," by November 27, 2018.

Webinars: Please note that there will be upcoming informational webinars. Please check back soon for dates and times.

XI. REVIEW CRITERIA

Partnership proposals will be evaluated by an external review panel convened by the National Academies in consultation with USAID. Programs developed under this program should be effective, scalable, and designed for evidence generation and utilization primarily in Malawi and Mozambique, though generating evidence to inform global decision making is considered a plus. The proposed programs should be in line with USAID's and Global Health's strategic interests. The proposed programs should also prioritize implementation within the national-level guidelines and policies for the partner country. The following criteria also will be used to determine eligibility for consideration:

Factor 1: Technical Merit

- Degree to which proposed activities contribute to Section V: Purpose, Objectives, and Research Priorities. Of particular importance will be the potential impact of the activities in Malawi and Mozambique in terms of improving voluntary family planning outcomes and increasing the numbers of precancerous lesions that would be expected to be treated effectively over the course of the project. The potential long-term health impact and sustainability resulting from capacity building efforts will also be considered.
- Degree to which the proposed activities reflect the priorities and approaches described in sub-sections 2-5 of Section VI: Outline of Requested Concepts.
- Degree to which technical proposals are likely to generate high-quality evidence and support utilization of this evidence to inform country-level and global decision-making for CCS&PT and voluntary family planning programs.
- Clear commitment and capability to disseminate findings at a national and international level, including the generation of materials and dissemination plans in languages relevant to the partner countries (i.e., English and Portuguese for Mozambique activities).

Factor 2: Organizational Capability and Personnel

- Degree to which the proposed organizational capabilities and partnerships respond to what is described in sub-section 1 of Section VI: Outline of Requested Concepts.
- Expertise of key personnel, including demonstration of key personnel with significant experience working in Malawi or Mozambique, including in voluntary family planning and cervical cancer service delivery.
- Team composition should include experience with voluntary family planning, cervical cancer screening and treatment, implementation science research (including in the technical areas mentioned above), experience referring patients to appropriate care, monitoring and evaluation, and other key technical experience that demonstrates an organizational capacity to meet the needs outlined in this RFA and the goals outlined in proposed activities.

Factor 3: Co-investment, Partnership, and Leverage

- Intent and likely ability to co-invest a substantial amount of their own financial, human, or other resources, and/or ability to leverage a substantial amount of non-U.S. Government resources from other partners. This includes non-PEER resources and expertise leveraged from the U.S. medical schools and/or universities.
- As noted above, this program will be unable to provide funds for the treatment of invasive cancer or palliative care. Applicants should demonstrate organizational capability to coordinate with global partners providing these services and ensure a strong referral system is in place to link women to appropriate care. It is especially important that linkages to care are done in a manner consistent with national guidelines and policies of the partner country.

- Applicants should provide a detailed description of established or potential partnerships that leverage existing or planned investments, or technical assistance, that increases the likelihood of successful program implementation, including potential for data generated to influence national, multilateral, or global decision making and policy guidance.

Factor 4: Budget

- Appropriateness of draft budget for carrying out proposed activities.

Appendix I: Country Information

Malawi Background Information

At 2.7 percent, Malawi has one of the highest rates of population growth in the world, creating substantial demands on the health system. Malawi's population has grown rapidly from almost 3.6 million in 1960 to around 17 million in 2017 with about 85 percent of the population residing in rural areas.[8] Almost half (46.4 percent) of this population is below the age of 15 years and owing to an estimated growth rate of 3.2 percent per annum in 2015, Malawi's total population is expected to reach 26.1 million by 2030 .[9] The government of Malawi recognizes rapid population growth as one of its principal development challenges and has prioritized voluntary family planning.

Malawi has made great strides in improving health outcomes over the past decade. While still high, the maternal mortality ratio (MMR) declined from 984 per 100,000 live births in 2004 to 439 per 100,000 live births in 2016, while the infant mortality rate (IMR) decreased from 104 deaths per 1,000 live births in the year 2000 to 42 per 1,000 live births in 2016. The neonatal mortality rate has gone down from 42 deaths per 1,000 live births in the year 2000 to 27 deaths per 1,000 live births in 2016. The child mortality rate has decreased from 95 deaths per 1,000 live births in the year 2000 to 23 deaths per 1,000 live births in 2016, while the under-five mortality rate has gone down from 189 deaths per 1,000 live births in the year 2000 to 64 deaths per 1,000 live births in 2016.

Despite this progress in reducing mortality, weaknesses in the health system could stall or reverse progress. Significant health system bottlenecks limit service coverage and provision of quality health care. These bottlenecks include a critical shortage of key health systems inputs (human resources, medicines and medical supplies, and poor/inadequate infrastructure). An acute shortage of critical health workers is a major constraint to the achievement of all health objectives. Only 52% of established posts are filled (Annual Joint Health sector Report 2017/18).

The epidemiological profile of Malawi is characterized by a high prevalence of communicable diseases like HIV/AIDS, malaria and tuberculosis, high incidence of maternal and child health problems; an increasing burden of non-communicable diseases and resurgence of neglected tropical diseases. Approximately 1.1 million people are living with HIV in Malawi. Sixty-four percent of them are women. Cervical cancer is the most common and leading cause of cancer deaths among women in Malawi. Cervical cancer represents 40% of all cancers among females and Malawi has the highest age standardized incidence rate (ASR) in the world at 75.9 per 100,000 population. It is estimated that 3,684 women develop cervical cancer and 2,314 die from the disease annually.[10] HPV prevalence is also high at 33.6%.[11] High-grade pre-cancerous lesions and cervical cancer are also very common among Malawian women.[12] It is expected that the number of cervical cancer cases and deaths will continue to increase if

preventive and treatment efforts are not scaled up to reach more of the infected women. Given that cervical cancer affects women who are still in the economically productive age group, the morbidity and mortality of women with this disease has serious implications on the wellbeing of families and the nation's development as a whole.

In response to this high burden, the Ministry of Health established a Cervical Cancer Control Program (CECAP), which started the screen and treat program beginning in 2004 with support from USAID partners using voluntary family planning as a point of entry. The vision was to gradually scale- up nationally. However, due to resource constraints the scale-up effort did not progress as envisioned. As a result, screening and treatment services are mainly limited to high volume sites and some MOH partners are providing screening through their outreach services to family planning clients over 30 years of age. Even in sites and outreach services where screening and treatment services should be available, the interventions are not routinely available due to factors including shortage of personnel, space, equipment and supplies. One key constraint has been the unavailability of gas required for cryotherapy. The country is strongly advocating shifting focus to thermocoagulation. Between 2013 and 2015, with support from GAVI and other partners, Malawi successfully implemented an HPV vaccination demonstration program in two districts: Zomba City (urban) and Rumphi (rural). The demonstration project achieved nearly 90% coverage through school-based vaccination sessions for a single-age cohort of 10-year-old girls, both in and out of school. Beginning 2019 MOH and partners will start rolling out the vaccine nationally, but due to inadequate funding, the vaccination effort will be limited to a 9-year-old age cohort only.

The National Cervical Cancer Control Strategy is currently being revised to cover the period 2016-2020, to incorporate new developments and emerging issues such as the availability of the HPV vaccine as a preventive measure and promote the integration of cervical cancer screening into HIV care, in addition to the existing efforts at cervical cancer prevention and control. Recently, PEPFAR Malawi received $5.4 million to support cervical cancer screening and treatment of pre-cancerous lesions among Women Living with HIV/AIDS (WLHIV) at high volume antiretroviral treatment clinics at district hospitals and other high HIV burden facilities. PEPFAR's cervical cancer activities will be implemented in 39 high burden health facilities spread across 22 districts with an intention to scale-up over time. With this funding, PEPFAR will support revision of guidelines, national level coordination, and technical assistance, and the provision of equipment and supplies, training, hiring of staff. Using Global Fund resources, the Ministry of Health recently procured 300 portable thermocoagulators and other equipment to scale-up cervical cancer screening and treatment. This equipment is already in-country and distribution to sites is in progress.

Challenges for the CECAP include weak national coordination, inadequate funding, inadequate trained providers, inadequate monitoring and evaluation tools, and failure to maintain unbroken supply chain for consumables, poor referral system and inadequate community mobilization. Diagnosis and management of advanced cancer cases also remains a major challenge.

Mozambique Background Information

In Mozambique, cervical cancer comprises 32% of new cancers diagnosed in women—the leading cause of cancer and cancer-related deaths among women. While efforts are underway to strengthen cancer diagnosis and treatment in Mozambique, progress continues to be constrained by a lack of resources, including a limited number of healthcare providers trained and equipped to diagnose and treat pre-invasive cervical disease, and a lack of public education to increase awareness and demand for services.

Women living with HIV are four to five times more likely to develop invasive cervical cancer, are more vulnerable to persistent HPV infections, and can develop pre-cancerous lesions faster. Recognizing this, in 2018, the President's Emergency Plan for AIDS Relief (PEPFAR), the George W. Bush Institute, and the Joint United Nations Programme on HIV/AIDS (UNAIDS) announced the Partnership to End AIDS and Cervical Cancer among HIV-positive women in Africa. As a focus country for this partnership, Mozambique is currently receiving PEPFAR funds to strengthen health system capacity to screen and treat pre-invasive cervical lesions. PEPFAR funding is supporting efforts to prevent progression to cervical cancer and mortality among HIV-positive women by integrating cervical cancer screening for HIV-positive women into routine HIV treatment services. In order to reduce loss to follow-up, those efforts undertake a "screen-and-treat" approach to management of precancerous lesions to maximize opportunities for immediate cryotherapy treatment (for eligible women) without need of diagnostic pathology confirmation.

---

[1] Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2016. Geneva, World Health Organization; 2018.
[2] http://www.who.int/healthinfo/global_burden_disease/projections/en/
[3] http://www.who.int/nmh/publications/best_buys_summary.pdf
[4] https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0013711
[5] https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0013711
[6] http://www.who.int/cancer/media/en/cancer_cervical_37321.pdf
[7] http://www.who.int/cancer/media/en/cancer_cervical_37321.pdf
[8] https://dhsprogram.com/pubs/pdf/fr247/fr247.pdf; and
http://www.nsomalawi.mw/images/stories/data_on_line/demography/mdhs2015_16/MDHS%202015-16%20Final%20Report.pdf
[9]http://www.nsomalawi.mw/images/stories/data_on_line/demography/census_2008/Main%20Report/ThematicReports/Population%20Projections%20Malawi.pdf
[10] https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-017-4526-y
[11] http://www.hpvcentre.net/statistics/reports/MWI.pdf and
Bruni L, Barrionuevo-Rosas L, Albero G, Serrano B, Mena M, Gómez D, Muñoz J, Bosch FX, de Sanjosé S. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in Malawi. Summary Report 27 July 2017. [Date Accessed]
[12] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4870149/