Randomized controlled trial of an implementation science tool to increase cervical cancer screening in Mombasa, Kenya

STUDY PROTOCOL

VERSION 1.0

1st February, 2021
NCT: STUDY00004431

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INVESTIGATORS PI, then alphabetical

McKenna Eastment, MD, MPH
Acting Instructor
University of Washington, Department of Medicine
Email: mceast@uw.edu
Addresses: Box 359909; 325 9th Ave; Seattle, WA USA
Signature:

R. Scott McClelland, MD, MPH
Professor of Medicine, Epidemiology and Global Health
University of Washington
Email: mcclell@uw.edu
Addresses: Box 359909; 325 9th Ave; Seattle, WA USA
Signature:

Walter Jaoko, MBChB, MSc, PhD
Co-Investigator, University of Nairobi
Associate Professor, Department of Medical Microbiology
University of Nairobi
Email: wjaoko@kaviuon.org
Addresses:
Signature:

John Kinuthia, MBChB, MMed, MPH
Co-Investigator, Kenyatta National Hospital
Director of Research, Kenyatta National Hospital
Email: kinuthia@uw.edu
Addresses: Kenyatta National Hospital; PO Box 20723; Nairobi, Kenya
Signature:

Kishorchandra Mandaliya, MBChB, MRCPath
Co-Investigator, Women's Health Project, Mombasa
Affiliate Professor, University of Washington and Director, Pathcare Laboratories Mombasa
Email: kmandaliya@gmail.com
Addresses: Ganjoni Clinic; Mnazi Mmoja Road; Mombasa, Kenya
Signature:

Faiza Nassir, MBChB, MMEd
Co-Investigator, Mombasa County
Obstetrician/Gynecologist
Email: f_nassir@hotmail.com
Addresses:
Signature:

COLLABORATING INSTITUTIONS (PIs institution, then alphabetical)

University of Washington
Kenyatta National Hospital
Mombasa County
University of Nairobi

FUNDING AGENCY

US National Institutes of Health
National Cancer Institute
Grant Title: Randomized controlled trial of an implementation science tool to increase cervical cancer screening in Mombasa, Kenya
Grant Number: 1K08CA228761-01A1
07/06/2018-06/30/2022

A. SUMMARY

Location: Family Planning Clinics in Mombasa County, Kenya

Introduction: Cervical cancer is the most common cancer in women in sub-Saharan Africa, and the majority of cervical cancer mortality occur in low and middle income countries (LMICs). Many of the disparities between high and LMICs are attributed to differences in screening. Kenyan guidelines recommend screening with visual inspection methods followed by treatment of pre-cancerous lesions with cryotherapy and loop electrosurgical excision procedure (LEEP). Implementation of these are poor with only 14% of Kenyan women ever having been screened for cervical cancer as of 2014.

Methods: In Aim 1, we will describe the cervical cancer screening care cascade, from identification of female clients age 21-65 years old, through referral for follow-up of clients with positive or suspicious screens, in family planning (FP) clinics in Mombasa County. Following characterization of this cascade, we will conduct an analysis of correlates of failure to screen for cervical cancer in FP clients seen over a one-year period in Mombasa County. Aim 2 will test whether SAIA increases cervical cancer screening compared to usual procedures in a cluster randomized trial in 20 FP clinics in Mombasa County. Finally, in Aim 3, we will determine the cost and budget impact of using SAIA to increase cervical cancer screening in FP clinics in Mombasa County.

Anticipated Results: The results of this study have the potential to improve cervical cancer screening, and inform policy in the Mombasa DOH for a fiscally responsible evidenced-based approach for cervical cancer screening.

Anticipated Conclusion: The long-term goal is to decrease cervical cancer mortality and improve women's health.

B. ACRONYMS AND ABBREVIATIONS USED

AIDS:	Acquired immune deficiency syndrome
ART:	Antiretroviral therapy
BIA:	Budget Impact Analysis
CFAR:	Center for AIDS Research
CFIR:	Consolidated Framework for Implementation Research
CQI:	Continuous quality improvement
DOH:	Department of Health
DHIS:	District Health Information System
FP:	Family planning
HIV:	Human immunodeficiency virus
HPV:	Human papillomavirus
IDIs:	In-depth interviews
IS:	Implementation science
LEEP:	Loop electrosurgical excision procedure
LMIC:	Low and middle-income countries
MOH:	Ministry of Health
NIH:	National Institutes of Health
PMTCT:	Prevention of mother-to-child transmission
RCT:	Randomized controlled trial
SAIA:	Systems analysis and improvement approach
SSA:	Sub-Saharan Africa
UW:	University of Washington
VIA:	Visual inspection with acetic acid

C. INTRODUCTION

Eighty-seven percent of cervical cancer deaths worldwide occur in low and middle income countries (LMICs) and cervical cancer is the most common cancer in sub-Saharan Africa (SSA) (2-5). The significant disparity between cervical cancer outcomes in the United States and LMICs is largely attributed to differences in screening (6). While approximately 89% of US women receive cervical cancer screening (7), less than 5% of women in LMICs have been screened (5). Barriers to screening in LMICs include challenges with infrastructure to support screening, competing health interests, lack of education, low health literacy, and poverty (3, 8-12).

In addition to the general lack of cervical cancer screening, SSA carries the highest global burden of human immunodeficiency virus (HIV) infection. Women account for 59% of all people living with HIV (13) and cervical cancer incidence is higher in women with HIV (14). With the advent of antiretroviral therapy (ART), women receiving HIV treatment have increased life expectancy approaching that of HIV-negative women (15). However, cervical cancer rates do not significantly decline despite ART and immune reconstitution (16), and invasive cervical cancer incidence remains high even with ART (17). The aging population of HIV-positive women will continue to face a large lifetime risk of cervical cancer (18).

Because of the burden of both cervical cancer and HIV infection in SSA, improving implementation of cervical cancer screening and treatment of pre-cancerous lesions in this region is critical. Existing methods for cervical cancer screening include cytology, human papillomavirus testing (14), and visual inspection methods (19). Pairing screening with treatment of positive screens using cryotherapy or loop electrosurgical excision procedures (LEEP) could prevent progression to cervical cancer (20), and greatly reduce morbidity and mortality in women. To address this implementation gap, simple, scalable, and sustainable interventions are imperative to improve screening and treatment of pre-cancers. The Kenyan Ministry of Health (MOH) guidelines stress the need to strengthen capacity, streamline, and standardize screening, diagnosis, and treatment of cancer (21). To achieve this, our long-term partners in the Mombasa County Department of Health (DOH) are eager to increase rates of cervical cancer screening. We aim to test an implementation science methodology, Systems Analysis and Improvement Approach (SAIA), to address systems barriers to screening and provide quality improvement while relying on existing infrastructure to conduct screening. Rather than directly offering screening, this intervention aims to support systematic improvements in screening processes in facilities throughout the county. We propose a collaborative research project with Mombasa County to achieve the following specific aims:

AIM 1: **To describe the cervical cancer screening care cascade, from identification of female clients age 21-65 years old, through referral for follow-up of clients with positive or suspicious screens, in family planning (FP) clinics in Mombasa County. Following characterization of this cascade, we will conduct an analysis of correlates of failure to screen for cervical cancer in FP clients seen over a one-year period.**

HYP 1: While many FP clinics are capable of providing cervical cancer screening, the majority of clients are not screened appropriately. Failure to screen for cervical cancer will be associated with both patient-level (e.g. age) and clinic-level (e.g. resources available) factors.

AIM 2: **To test whether SAIA increases cervical cancer screening compared to usual procedures in a cluster randomized trial in 20 FP clinics in Mombasa County.**

HYP 2: Family planning clinics randomized to SAIA will have increased rates of cervical cancer screening by modifying bottlenecks in screening processes compared to clinics randomized to usual procedures.

AIM 3: **To determine the cost and budget impact of using SAIA to increase cervical cancer screening in FP clinics in Mombasa County.**

Expected Outcomes and Public Health Impact

As one of the leading causes of cancer mortality in African women, immediate attention to increase rates of cervical cancer screening and treatment of pre-cancers is crucial. This

implementation tool holds potential for addressing gaps in cervical cancer prevention and lowering cancer morbidity and mortality. Use of the reproducible SAIA methodology could provide a template for broader rollout of cervical cancer screening throughout the country and region. Using the Consolidated Framework for Implementation Research (CFIR) to guide the evaluation of this intervention will provide insight about the potential generalizability of the intervention, and improve the likelihood of its successful implementation in diverse settings (22).

D. LITERATURE REVIEW

A.1. As a major contributor to mortality in African women, cervical cancer demands attention. Cervical cancer is the most common cancer in sub-Saharan Africa (SSA) and is potentially preventable with appropriate screening and treatment of pre-cancers (2-5). High HIV prevalence in Africa further increases the risk of cervical cancer in a substantial proportion of women (13, 14), underscoring the need for strengthened screening programs. Potential barriers to cervical cancer screening include challenges with infrastructure to support screening, competing health interests, lack of education, low health literacy, and poverty (3, 8-12). The Kenyan Ministry of Health (MOH) stresses the need to strengthen capacity, streamline, and standardize screening, detection, diagnosis, and treatment of cancers (21). Screening is recommended for women aged 21-65 years. In HIV-negative women, the current guidelines recommend cervical cancer screening using visual inspection with acetic acid (VIA) every 5 years. Screening by VIA in HIV-positive women is recommended every 6 months for the first year, and annually thereafter. Human papillomavirus (HPV) testing and cytology are other screening methods used less frequently in Kenya. At a national level, the MOH has tasked family planning (FP) clinics with implementing cervical cancer screening, and has included specific items to document screening in FP registers (23). In 2014 (this remains the most recent country survey), 44% of women in Mombasa County used contraceptives and 60% of these obtained products from public FP clinics (24), illustrating that FP clinics are a good venue to reach a substantial proportion of women. Our partners in the Mombasa County DOH are eager to collaborate in applying implementation science to improve screening rates in their FP clinics (see C.1.D).

A.2. Cervical cancer screening and treatment of pre-cancers has been studied in low and middle income countries (LMICs), but implementation remains a challenge, and strategies to improve the process are under-studied. While VIA is a cost-effective and validated method in LMICs (25), data on cervical cancer screening in Africa are limited (19, 26). The WHO supports the 'screen and treat' method for cervical cancer screening and treatment of pre-cancerous lesions with cryotherapy and loop electrosurgical excision procedure (LEEP) (20). These services are available in Mombasa County, but linkage to services is challenging. In the most recent survey in 2014, only 14% of women in Kenya had ever been screened for cervical cancer (24). Data on follow-up of positive screens in Africa are sparse, though a single visit screen and treat approach likely results in fewer women lost to follow-up than referral-based linkage to care (27-30). Studies in Malawi and South Africa highlight challenges of linking women with a positive or 'suspected' VIA to appropriate treatment with cryotherapy or LEEP (31, 32). ***In Kenya, research suggests that cryotherapy was the least expensive option and resulted in the highest life expectancy, though VIA was most cost effective if HPV testing took more than 1 visit (33). In a recent study in Kenya, investigators found that of 1180 women surveyed, 16.4% had been screened for cervical cancer (34). Of those women who had never been screened, the majority (67.9%) were aware of the need to screen for cervical cancer. Women with more education and wealth and residing in urban areas were more likely to be screened compared to women with less education and wealth, and residing in more rural settings.*** There is an implementation gap between the evidence for cervical cancer screening efficacy in reducing population rates of cervical cancer and the effective scale-up in many

LMICs (35). We aim to address this gap by testing the effectiveness of a standardized implementation approach to improve this process.

A.3. Utilizing the Systems Analysis and Improvement Approach (SAIA) is a methodology that addresses the current cervical cancer screening and referral system within the existing healthcare framework. Implementation science (IS) research utilizes strategies to adapt, implement, and optimize evidenced-based interventions to improve health outcomes (36). SAIA is based on systems engineering to improve implementation. This tool analyzes the existing care cascade, then maps the work flow process, designs and implements a workflow adaptation, assesses the impact, and repeats this cycle for continued iterative system and process improvement (1). This approach works within the existing health system to address barriers and bottlenecks in the cervical cancer screening cascade (1), without simply performing the screening as an external study team. The SAIA methodology has the benefit of being a generalizable intervention that can be adapted to many different disease models and settings, contributing to the longevity and sustainability of this intervention.

A.4. Budget impact analysis (BIA) of SAIA in collaboration with the DOH aims to improve screening by determining the affordability of this tool. With limited budgets for health care programs in many LMICs, budget impact analyses provide valuable information to guide policy changes that are fiscally responsible and have high potential health impacts. If the budget impact analysis shows a modest impact on the County budget, this argues for further expansion of this tool to other clinics, and potentially to other counties across Kenya.

B. INNOVATION

B.1. First application of SAIA in the field of cervical cancer; one of a few IS approaches applied to cervical cancer. Community engagement (37), education (38, 39), combined cancer screening programs (40), and media interventions (41) have been used in SSA to improve cervical cancer screening. SAIA is an innovative tool for the healthcare setting, and has previously been trialed successfully in other settings for different healthcare indications. This application of SAIA in a randomized controlled trial is an essential step forward for the field of cervical cancer screening and addresses the need for integrating screening into existing healthcare systems (11). Successful completion of this research will demonstrate improved performance at a local level, while providing more generalizable data about the utility of SAIA to guide scale-up nationally and in other countries facing similar challenges with cervical cancer screening.

B.2. A BIA of SAIA has the potential to move the field forward. Understanding the budget impact on the DOH can support broader roll-out of this program in other counties in Kenya and other LMICs facing similar challenges to screening. BIAs move beyond cost-effectiveness to highlight how this approach will affect the budget from the perspective of the payer in the health care system. This BIA is an important and necessary step to scale-up this intervention.

C. APPROACH. C.1.Preliminary Studies

C.1.A. Leader in IS. The UW Department of Global Health is a leader in IS research, including 85 projects in 41 countries, involving 119 faculty (42). Implementation science spans departments and programs including the Health Alliance International, International Training and Education Center for Health, and the Kenya Research and Training Center. Implementation research is also supported by the Center for AIDS Research (CFAR) Implementation Science Scientific Working Group, and an Implementation Science Core is proposed in our 2017 competing renewal (priority score 19). This institutional experience and leadership will benefit the successful completion of this research and Dr. Eastment's training.

C.1.B. Significant experience with SAIA. This research team has significant experience with SAIA, which was originally adapted for healthcare by Dr. Sherr (co-mentor) as an iterative process effective in improving HIV testing and linkage to care in Prevention of Mother-to-Child Transmission of HIV (PMTCT) services in Mozambique, Kenya, and Cote d'Ivoire (PMTCT SAIA Trial) (1, 43). Dr. Sherr is involved in 3 funded ongoing studies adapting SAIA to new disease models, and will provide Dr. Eastment with exceptional mentoring in this field. SAIA has five steps. The first step uses an Excel-based tool to quantify drop-offs, or people who did not progress, in each step of a process (Figure 1). This tool also allows the user to see the downstream effect when improving one step in the cascade, and holding the other steps constant. Step 2 involves process flow mapping with clinic staff to identify modifiable bottlenecks in the process. Step 3 develops and implements a workflow modification to address a bottleneck identified in step 2 (continuous quality improvement [CQI] step). Step 4 assesses impact of the modification and recalculates the cascade analysis in step 1 (CQI step). Step 5 repeats the cycle for CQI. SAIA draws from systems engineering in the Toyota Production Systems and from research in LMICs. Studies in quality improvement in LMICs highlight that CQI processes led to more sustainable, effective, and appropriate interventions (44-46).

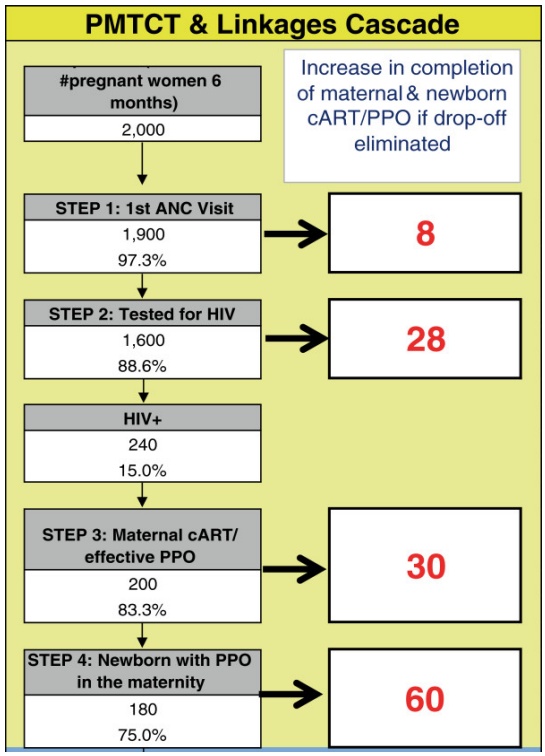

Figure 1. Example of the cascade analysis using SAIA for HIV testing in PMTCT (1).
PMTCT: Preventing mother to child transmission; ANC: antenatal clinic; cART: combination antiretroviral therapy; PPO: prophylaxis

C.1.C. Consolidated Framework for Implementation Research (CFIR) and SAIA: CFIR is an evidenced-based collection of constructs that aim to synthesize multiple implementation theories to explain what works, where it works, and why it works (22). There are five domains in CFIR that describe all aspects of the implementation realm including intervention characteristics, outer setting, inner setting, characteristics of individuals, and process. Each domain includes constructs that are associated with successful implementation (Figure 2). For example, in the PMTCT SAIA trial, five CFIR constructs differed between high and low performing clinics: networks and communication in inner setting, available resources in outer setting, external change agents, executing and reflecting, and evaluating in implementation process (47). Furthermore, qualitative interviews identified flow mapping and CQI as particularly important for process improvement in all study settings (47). We will use CFIR to evaluate the SAIA intervention to improve cervical cancer screening.

Intervention characteristics	Outer Setting	Inner Setting	Characteristics of Individuals	Process
•Intervention source •Evidence strength & quality •Relative advantage •Adaptability •Trialability •Complexity •Design quality & packaging •Cost	•Patient needs & resources •Cosmopolitanism •Peer pressure •External policy & incentives	•Structural characteristics •Networks & communications •Culture •Implementation climate •Readiness for implementation	•Knowledge & beliefs about intervention •Self-efficacy •Individual stage of change •Individual identification with organization •Other personal attributes	•Planning •Engaging •Executing •Reflecting & evaluating

Figure 2. Consolidated framework for implementation research domains and constructs (21).

C.1.D. Adaptations of SAIA methods in ongoing trial, led by Dr. Eastment. Adaptations of SAIA methods are currently being used to address linkage of HIV services in the ongoing trial "*RCT of an implementation science tool to integrate HIV testing into family planning services"* (K24 HD088229-01; PI, McClelland; FP HIV SAIA Trial) with Dr. McClelland (primary mentor) and Dr. Sherr (co-mentor). To meet the national guideline that all women should be tested for HIV when accessing FP services (48), a data entry template for recording of HIV counseling and testing was integrated into the Kenyan FP registers in 2008. Our UW group is addressing this guideline in the FP HIV SAIA trial that compares SAIA to usual procedures to improve HIV testing at FP clinics in Mombasa County. A preliminary performance review of 60 FP clinics in Mombasa County collected data from FP registers and clinic manager interviews. Of 60 clinics, a total of 4389 new FP clients were seen in a 3-month period (mean of 73 new clients per clinic (standard deviation [SD] 81)). Only 23 clinics reported any HIV testing, with a total of 420 new FP clients screened in a 3-month period. Three of these clinics performed the majority of screening (302 screens, 72%). As a Senior Fellow in Infectious Diseases, Dr. Eastment has led the implementation for this project. She prepared the applications for ethical and humans subjects approval in the US and Kenya, developed data collection tools, trained study staff, created the database, launched the study, and coordinated planning, logistics, and dissemination of findings with Mombasa County. This study has provided Dr. Eastment with valuable experience in implementing SAIA, and demonstrates the great potential for additional implementation research in Mombasa.

C.1.E. Preliminary data on cervical cancer screening in Mombasa County from the FP HIV SAIA trial show low screening and incomplete documentation. Dr. Eastment has had discussions with key collaborators in Mombasa County including the Director of Health (see letter), noting that the majority of cervical cancer screening is conducted in either FP clinics or HIV clinics. The County's policy is that screening should be documented in the FP register. Cervical cancer screening is reported to the County for all clinics that receive County FP commodities. These data are compiled into the District Health Information System (DHIS). The quality of different data sources has not been formally evaluated. Preliminary results from the cervical cancer screening review linked to the FP HIV SAIA trial underscore the importance of the project proposed in the present application. The 60 clinics analyzed saw a mean of 204 FP clients per clinic (SD 172) during a 3-month period (a total of 12,236 clients over the three-month period of our data review). Of the 60 clinics, 4 (7%) did not record cervical cancer screening in the FP register, but reported recording it elsewhere. Because we did not review these alternative records in this initial survey, these clinics are excluded from subsequent analyses. Of the 56 remaining clinics, 7 (13%) recorded any cervical cancer screening. Only 120 women (1%) were screened. These preliminary data suggest few FP clinics perform cervical cancer screening, and that most women accessing FP services are probably not being screened for cervical cancer. Of the clinics offering screening, not all are documenting this activity in the FP register. Moving forward, data collected in outside logs could be entered into FP registers or abstracted separately. These preliminary data provide valuable information for this K08 proposal, which will comprehensively document screening practices in Mombasa County using all the available documentation sources. We will explore why screening prevalence and appropriate documentation is so low, and address this implementation gap with clinic-specific interventions using SAIA.

E. METHODOLOGY

1. STUDY AREA

This study will be based at Family Planning clinics in Mombasa County, Kenya. ***In 2016, there were estimated 132 FP clinics in Mombasa County from which we will select our sample. Family planning clinics will be public facilities and private facilities with County-supplied FP products. These FP clinics will be located across Mombasa County in all 6 sub-counties (Changamwee, Jombvuu, Mvita, Likoni, Kisauni, Nyali).***

Included FP clinics may only provide FP care, or may be part of a larger facility with other types of care (e.g. ANC, pediatrics, CCC, etc).

2. STUDY POPULATION

There will be three different groups of subjects in this research proposal:
1. Individual FP clients' data will be abstracted from FP registers. However, there will be no contact with individual FP clients by study staff.
2. Family planning clinics as a unit to be randomized. Study staff will work with clinic staff for both data abstraction and during the intervention if randomized to this arm of the trial. In addition, micro-costing and time-and-motion studies will be conducted in FP clinics for the SAIA budget impact analysis.
3. Family planning clinic managers and staff.

Inclusion Criteria:
Family planning clinics

Sampling plan: A selection of 20 FP clinics will be selected to be randomized to SAIA versus usual procedures. The FP clinics will receive County-supplied FP products, which generally means they are reporting their activities to the County, including cervical cancer screening. Clinics will be spread out throughout the 5 sub-Counties in Mombasa.
Eligibility: All FP clinics that receive County-supplied FP products will be eligible to participate.

FP clinic managers and staff
Sampling plan: A selection of FP clinic managers and staff will be approached to answer questions about their respective FP clinics in a semi-structured interview. To understand the implementation of cervical cancer screening in the CFIR framework, in-depth interviews will also be conducted with a random sampling of FP clinic managers.
Eligibility: Any FP clinic manager that is 18 years and older is eligible to be interviewed. These clinic managers can be male or female.

FP client data abstraction: Family planning client data will be abstracted from included FP clinics for female FP clients who access FP clinics during our data collection windows. We anticipate including all female FP clients.

Exclusion Criteria
Family planning clinics
Any clinic that is expected to be closed during part or all of the SAIA intervention period will be excluded. Any FP clinic that was previously included in the FP HIV SAIA trial will be excluded.
FP clinic managers and staff
No exclusion criteria
FP client data abstraction: No exclusion criteria.

3. STUDY DESIGN
This is a cluster-randomized controlled trial with FP clinics as the unit of randomization.

4. PROCEDURES
C.2.A. **AIM 1: To describe the cervical cancer screening care cascade, from identification of female clients age 21-65 years old, through referral for follow-up of clients with positive or suspicious screens, in FP clinics in Mombasa County. Following characterization of this cascade, we will conduct an analysis of correlates of failure to screen for cervical cancer in FP clients seen over a one-year period.**

Study design: This aim will be accomplished by abstracting data from FP registers and interviewing clinic managers. Given the results of the preliminary data presented in C.1.E, any other logs for cervical cancer screening will also be examined to get the most complete and accurate representation of current screening practices. Brief structured interviews with clinic managers will be conducted to understand screening and referral practices in individual FP clinics. Data from FP registers will be merged with clinic-level data from FP clinic manager structured interviews to explore correlates of screening.

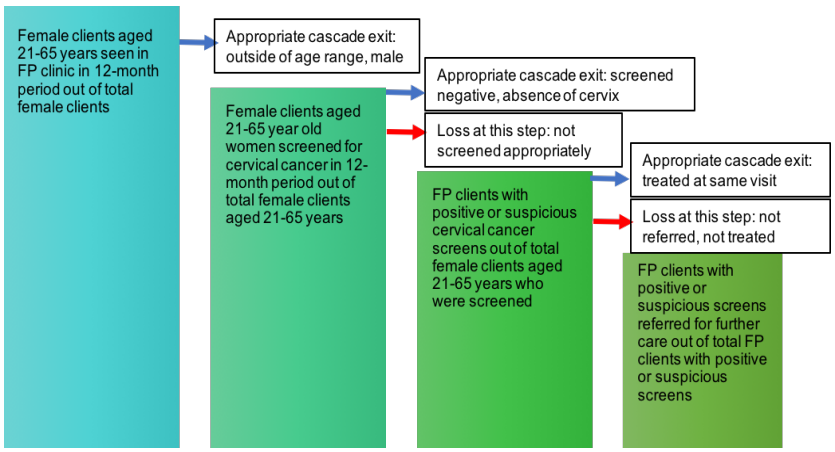

Figure 3. Planned cervical cancer screening care cascade using FP register and other log abstractions

Procedures: *Cervical cancer screening care cascade:* Quantifying the screening care cascade from FP client identification through referrals of positive or suspicious screens will follow a series of steps, illustrated in Figure 4. First, all FP clients 21-65 years of age and recorded at least once during a 3-month period will be identified as a 'cohort' for evaluation over the next 12 months of register data. This step is illustrated taking place retrospectively during the first three months in the figure. Any FP client outside this age range will not be counted as screening is not recommended. The cohort will be followed, using periodic data

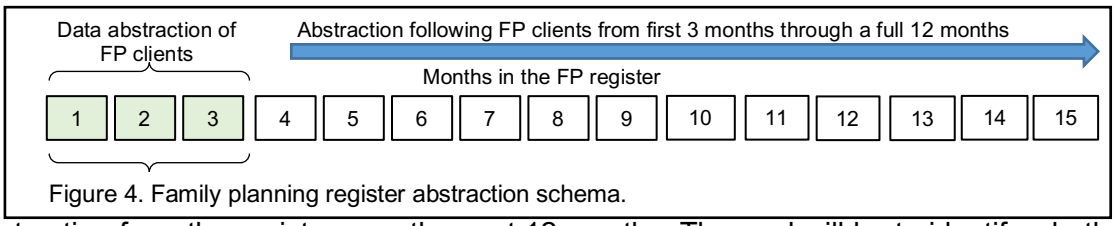

Figure 4. Family planning register abstraction schema.

abstraction from the register over the next 12 months. The goal will be to identify whether or not cervical cancer screening was completed within 12 months. Among women with completed screens, we will also determine how many were positive (lesions meeting criteria for dysplasia, or other positive test) or suspicious, and how many of these women were referred for care. To supplement these data, any clinic-based cervical cancer screening logs will also be examined for the same time-period as the FP register abstraction. To understand if FP register documentation is capturing screening, this cascade will be compared with the County DHIS reports, which provide individual clinic level data. The level of correlation between these two sources for total FP clients and total screens will be calculated. While we anticipate using FP registers in Aim 2, we may modify this approach, based on quality and correlation of DHIS and FP register data.

Correlates of screening: Data will be abstracted from the FP registers for individual level information (e.g. number of HIV-positive clients, number of FP commodities dispensed). Brief in-person structured interviews with clinic managers (e.g. staff to patient ratio, manager experience, commodities/resources available in clinic, size of population served, urban/periurban/rural, public vs. public/private partnership) will collect clinic-level characteristics from all included clinics and together, these sources will be used to explore individual- and clinic-level correlates of screening that are expected to be generalizable to all FP clinics in Mombasa County.

Data management: Data abstracted from FP registers, other clinic logs, and structured interview data from clinic managers will be aggregated in a REDCap database (49).

C.2.B. **AIM 2: To test whether SAIA increases cervical cancer screening compared to usual procedures in a cluster randomized trial in 20 FP clinics in Mombasa County.**

Procedures: *Quantitative data:* Initial information from intervention and control clinics will be obtained from clinic managers. Details about clinic characteristics such as size of the population served and what other services are provided will be collected. Staff characteristics will be collected including the number and type of staff, level of education, and experience of the clinic managers. Cervical cancer screening data will be collected from FP registers including screening method (VIA, visual inspection with Lugol's iodine [VILI], HPV with VILI, HPV alone, Pap smear), clients' HIV status, cervical cancer screening results (positive, negative, suspected), and information on referrals of positive or suspicious screens. These data will be collected at the beginning of the trial during a baseline period before any study procedures are completed, and then periodically every 3 months for all clinics.
Qualitative data: Qualitative IDIs will be conducted with clinic managers to understand cervical cancer screening practices and barriers. Study staff will explain the risks and benefits of participating in the IDIs and the procedures in place to safeguard their opinions. Clinic managers will then be asked to provide written informed consent to participate in an IDI. Types of questions study staff would ask include: "Describe what you know about cervical cancer screening."; "In your clinic, what do you think are barriers to screening more women for cervical cancer?"' "What are some ways that cervical cancer screening could be improved in your clinic?". These IDIs will be completed both prior to the trial and during the trial. Questions in the IDIs will be adapted from readily-available CFIR questions to understand where, when, and why the intervention works (50).

Randomization: Restricted randomization will be used to randomize FP clinics into intervention and control arms based on clinic size and location in Mombasa County(51). If facilities differ dramatically in cervical cancer screening rates at baseline, we will also stratify the randomization according to this factor.

Testing SAIA in intervention clinics: Clinics randomized to the intervention arm will be introduced to the five steps of SAIA by study staff (see C.1.B and C.1.D). The cascade analysis will be performed within the FP clinic to identify drop-offs in cervical cancer screening and referrals, using an Excel-based tool adapted from previous SAIA trials. Flow mapping performed by clinic and study staff will describe the cervical cancer screening process including who the client interacts with, timing of these interactions, any cervical cancer screening performed, and any referrals made. Initial drafts will be reviewed together with clinic and study stuff to ensure adequate and complete representations of processes. Study staff will work with clinic staff to identify bottlenecks in the process and potential solutions to improve flow. Proposed solutions will be implemented, and the process will be examined again to determine the effect of the implemented changes. The cycle will be repeated approximately every 6-8 weeks during the RCT. Data similar to baseline quantitative data, including numbers of FP clients, number of FP clinic visits, and proportion of FP clients who are screened for cervical cancer, will be abstracted to monitor change in screening over the study period.
Control clinics: Clinics randomized to the control arm will continue usual procedures. Periodic evaluation of cervical cancer screening rates will be examined every 3 months using FP register data.

C.2.C: **AIM 3: To determine the cost and budget impact of using SAIA to increase cervical cancer screening in FP clinics in Mombasa County.**

Activity Based Micro-Costing Methods: Costs associated with implementing SAIA will be estimated using micro-costing methods to estimate costs for SAIA start-up, personnel required, transportation to and from study clinics, communication costs, consumable materials, and any overhead costs. These cost data will be abstracted from the study budget, clinic expense reports, published labor costs, and interviews with the staff. Data on costs of the SAIA intervention will be collected at both the beginning of the intervention to estimate start-up costs and during the intervention to estimate on-going implementation costs. Costs will be characterized as fixed costs or variable costs that could change over time. We will not include private identifiable information about interviewees.

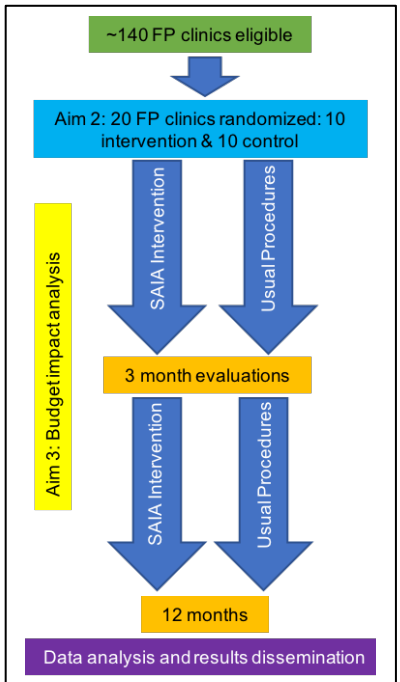

Figure 5. Study Design.

Time-and-Motion Studies: Time-and-motion studies estimate the time involved in each step of SAIA. These will be estimated over a 2-week period at each intervention site. Multiple SAIA visits will be averaged to give the best estimate of time needed for the intervention. Any time that is for research purposes only, like consent processes, will be subtracted from the total time of the intervention. Multiple providers and clients will be observed to provide a good estimate of the time from clinic entry to clinic exit for a cervical cancer screening. We will not collect private identifiable information about individuals that we will be observing and we will not interact with FP clients or clinic staff while we are doing these observations. The micro-costing and time-and-motion studies will be used to calculate the average cost of a new cervical cancer screen.

Budget Impact Analysis: The budget impact analysis will include direct program costs from the perspective of the DOH, that are estimated from the micro-costing methods illustrated above. Both the 'top-down' approach using routine expense reports and the 'bottom-up' approach using micro-costing will be used to refine our analyses. Standard practices for economic evaluations in health (52) and guidelines from the Panel of Cost-Effectiveness in Health and Medicine (53) will be used where possible to produce results that are accurate and generalizable. A standard 3% discounting rate will be used, with sensitivity analyses that use no discounting and 5% rate. Further sensitivity analyses will be conducted to produce best estimates under varying scenarios.

5. SAMPLE SIZE DETERMINATION

Aim 1: In 2016, there were an estimated 140 FP clinics in Mombasa County. We anticipate abstracting data from roughly 75% (N=105) of these FP clinics for this aim. The clinics would be randomly selected from across Mombasa County, stratified by clinic size, including both high-volume and low-volume facilities. This cascade would aim to provide more information from a larger selection of clinics than the preliminary review in C.1.E. For the correlates of screening analysis, we estimate needing a total sample of 1672 FP clients, with 49 (3%) women screened (Table 1). While we saw 1% of clients screened in our preliminary data, we anticipate that a higher proportion of women would be screened if we incorporate other registers being used by clinics. We anticipate being able to reach this number of clients in this study based on data from our preliminary study (with over 12,000 clients seen in 60 clinics in a 3-month period).

Table 1. Sample sizes for failure to screen correlates for individual and clinic-level characteristics.

	Correlate present in women not screened	Correlate present in women screened	Absolute risk difference	Total sample size*
Individual-level characteristics				
HIV-positive	60%	20%	0.4	376
	60%	40%	0.2	**1672**
Younger age	80%	50%	0.3	581
	60%	30%	0.3	717
Clinic-level characteristics				
Facility level 3-4	20%	60%	0.4	325
	40%	60%	0.2	**1672**
High staff:patient ratio	10%	50%	0.4	237
	20%	60%	0.4	325

*This is the sample size required to have 80% power at an alpha 0.05 with varying proportions of women with different characteristics between women not screened and women screened. A ratio of screened to not screened of 1:33 was assumed.

Aim 2: The FP HIV SAIA Trial preliminary results suggest that very little cervical cancer screening is performed or being documented in FP registers. Of these available data, the proportion of FP clients screened was 0.6%. Because this screening prevalence may not be representative, we have used a more liberal estimation of 8% prevalence of screening based on the 2014 DHIS estimates (the most recent resource available). FP clinics had an average of 183 clients in a 3-month period. Most clients follow-up every 3 months so this is a conservative estimate of total clients in a 12-month period. We will assume that following the intervention, 20% of women will be screened for cervical cancer. To calculate a sample size for a cluster RCT, the cluster size variability (κ) must be estimated with literature often citing $\kappa \leq 0.25$ and rarely exceeding 0.5 (54). We have estimated a κ of 0.5 to be conservative, which translates to an intra-class correlation coefficient of approximately 0.05. Cluster size variability of FP clinics was calculated as 0.74 using data in 1.C.E. With an α=0.05, 10 clusters per arm will provide 90% power to detect a risk difference of 12% from the intervention.

6. DATA MANAGEMENT

Aim 1:

Cervical cancer screening care cascade: The care cascade will examine the counts and proportions aggregated from the selected FP clinics as outlined in Figure 3. This cascade will account for appropriate exits from the cascade (e.g. outside screening age range, or screened negative) and losses in the cascade (e.g. not screened, or positive screen not referred for follow-up). Our research group has experience working with this type of complex care cascade in the setting of isoniazid prophylactic therapy for tuberculosis prevention, where there are multiple steps at which individuals can exit appropriately, be lost, or move on to the next step (55). We aim to model a cervical cancer screening care cascade in a similar manner.

Correlates of screening: Cervical cancer screening will be modeled as a binary outcome. Logistic regression will be used to examine correlates of screening including age, HIV status of clients, and specific clinic characteristics (detailed in Procedures). Analyses will be adjusted for any clustering by clinic.

Aim 2: The primary outcome is the proportion of all FP clients aged 21-65 years who were screened for cervical cancer over the total number of eligible clients. These outcomes will be assessed every 3 months in the 12-month study period. We are requesting an extension of the trial for an additional 6 months. Women who are not FP clients who are referred to a clinic solely for screening will be excluded as they could inflate the proportion of women screened. These women will be identified because they did not receive FP products or HIV testing and were only entered in the FP register because of screening. Generalized estimating equations with a binary link, clustered by clinic, will compare proportions screened in intervention versus control clinics longitudinally to account for correlation across time and between clinics. Interviews will be audio-recorded, transcribed, translated, coded for major themes, and analyzed using Dedoose software (56).

7. VARIABLES – DEPENDENT, INDEPENDENT, CONFOUNDERS

Cervical cancer screening care cascade: The care cascade will examine the counts and proportions aggregated from the selected FP clinics. The variables to be abstracted from the FP register includes whether new or return FP client, HIV status, whether cervical cancer screening was conducted, what method of screening was used, what the results were, and if any referrals were made for this screening. This cascade will account for appropriate exits from the cascade (e.g. outside screening age range, or screened negative) and losses in the cascade (e.g. not screened, or positive screen not referred for follow-up).
Correlates of screening: Brief structured interviews with clinic managers as well as FP register data abstraction will collect information on for example, size of the FP clinic, staff, training of staff, age of FP clients, HIV status of clients, availability of FP commodities, level of experience of FP clinic manager, availability of cervical cancer screening commodities, referral practices, and any perceived barriers or facilitators of cervical cancer screening.
Cluster randomized trial: The primary outcome is the proportion of all FP clients aged 21-65 years who were screened for cervical cancer over the total number of eligible clients. These outcomes will be assessed every 3 months in the 12-month study period. We are requesting an additional 6 months for a total RCT study duration of 18 months. In-depth interviews will collect information about implementation of SAIA, barriers and facilitators to screening, and also using consolidated framework for implementation research (CFIR) constructs and domains.
Aim 3: Interviews with clinic managers and clinic observations along with data regarding time and expenses to implement SAIA will be collected. This will include general salary ranges for study staff and clinic staff, commodities needed, time for different clinic procedures, for example.

8. DATA COLLECTION INSTRUMENTS

For Aim 1, we will be abstracting quantitative data from the family planning registers. We will also collect basic information including, for example, clinic location, clinic environment (rural, peri-urban, urban), primary population served, number of women seen per day and number of new women to the clinic, for example.

In-depth interviews (IDIs) for the qualitative component of Aim 2 will be performed by trained study staff. This will follow a topic guide, and we anticipate asking open-ended questions about individual level, facility level and higher-level facilitators and barriers to cervical cancer screening of women presenting for family planning services. Examples of the most sensitive types of questions we would ask include:

- *What patient characteristics informed your decision of whether to offer cervical cancer screening or not?*
- *Describe how time limitations, financial limitations or staff conflicts/concerns affected your decision to offer cervical cancer screening.*

9. QUALITY ASSURANCE PROCEDURES

For quantitative data, data will be manually line-listed where the original images are compared to the soft copy data by a two-person team, with one reading data from the image documented and the other verifying the hard copy to ensure that registry abstraction match the soft-copy database. Incorrect data entries are revised based on re-evaluation of the digital image of the register. If necessary, we will go back to the original register (source document) to look at the data again and clarify response that could not be read clearly in the image. A record of incorrect entries is maintained. Following our data management SOP for the Women's Health Project in Mombasa, we will aim to have a data entry key-in error rate of less than 2 per 1000 entries, and monitor this periodically.

For the in-depth interviews (IDIs), a modified member check will be conducted by presenting the final key findings to a subgroup of clinic administrators and providers to assess completeness, salience, and relevance of our identified themes.

10. MATERIALS – EQUIPMENT AND SUPPLIERS

We anticipate performing in-depth interviews and group activities such as sequential process flow mapping with facility staff and managers either at their facilities (where feasible and desirable) or at our research clinic. Our research clinic is located at Ganjoni Health Center, and has multiple private interview rooms, a boardroom that accommodates 20, and a classroom that accommodates 40. The clinic has a DS-2 Olympus Digital Voice recorder and microphone suitable for both individual and group recording.

We have a central server, LAN, and fifteen computers in Mombasa (3 lab, 12 clinic/office). These are used for data entry, cleaning, analysis, administration, and communications. Two printers are located at the laboratory and three are located at the clinic.

We have 5 offices at Ganjoni clinic, which house the research, clinical, and administrative staff. A fully equipped and furnished boardroom (capacity=20) and classroom (capacity=40) with LAN, internet connection, large screen monitor, white board, blackboard, are available at the clinic for training and teaching activities.

There is one large office available at the laboratory at Coast Hospital, which is on the opposite side of town from Ganjoni Health Center. Depending on the location of activities with FP clinics in different areas, the study team may use the laboratory office for work or meetings when convenient.

We have 2 vehicles in Mombasa for project use, including staff and participant transport, logistical support, and supplies.

11. STUDY STRENGTHS/LIMITATIONS

Aim 1 Limitations:
Family planning register use: There are limitations in using program data from FP registers. These registers can have missing information or illegible entries. Also, some FP clinics may be using prior versions of FP registers that lack key information about cervical cancer screening. However, use of routinely collected register data is a main objective of IS and has

the advantage of scalability as new data sources are not required. This aims to keep programmatic costs low, and increase feasibility and scalability. To address issues with FP registers, any clinic-based logs will supplement data in FP registers.

Poor correlation between FP register data and DHIS reports: After discussions with members of the Mombasa County DOH, cervical cancer screening should be documented in both FP registers and DHIS reports. Results of this comparison will be presented to our County collaborators to find a solution for appropriate documentation. The County may decide to provide further guidance in register documentation to all FP clinics, or the County may decide that it is acceptable to use DHIS reports only for cervical cancer screening documentation. The current state of documentation for screening will guide the outcome assessment in Aim 2 (see C.2.B).

Screening outside FP clinics: The register abstraction process may not capture whether women have been recently screened. These women would appear to need screening and would be counted as a loss in the cascade. According to the DOH, the most common clinics for cervical screening are FP clinics and HIV clinics, but it is unclear where HIV-positive and HIV-negative women are actually accessing screening. The 2014 estimates (the most recent survey) of screening on the coast of Kenya suggest only 8% of women have ever been screened, which is higher than the 3-month screening prevalence of 0.6% in our preliminary data (C.1.E). Given this estimate, the possibility that a woman had been screened recently is expected to be quite low. Consequently, the vast majority of women require screening. Aim 1 will be used to explore how many clinics are performing any screening, the proportion of women screened, and if screening differs by HIV status. We are focusing on FP clinics, as women attending these clinics are generally expected to be sexually active, at risk for HPV infection, and consequently, cervical cancer. Some HIV-positive women could access screening in HIV clinics. We anticipate quantifying the care cascade separately by client HIV status to better illustrate the landscape of screening practices. Future work could also examine cervical cancer screening in HIV clinics.

Aim 2 Limitations:

New versus all FP clients: If prevalence of screening is found to be very low in Aim 1 (as we expect), the RCT will aim to improve screening for both new and existing FP clients. However, if Aim 1 screening prevalence is higher than expected (we anticipate a cut-off of around 20% screening prevalence), then including existing clients may lead to significant misclassification. In this scenario, Aim 2 will focus on new FP clients only. We anticipate having sufficient power for this alternative approach. Preliminary data suggest an average of 60 new FP clients per clinic in a 3-month period (C.1.E), which we would anticipate would continue throughout a 12-month period. Ten clinics per arm in the RCT with only 60 new clients per clinic would provide at least 80% power to detect a 12% difference between intervention and control arms.

Identifying women who should be screened: While it is a goal of IS studies to work within existing systems, the use of routinely collected FP register data to assess the RCT outcome has its challenges. It may be difficult to assess if a woman had been recently screened. This potential limitation may vary in women based on their HIV-status. Because screening for HIV-positive women is recommended annually, HIV-positive women who should be screened may be identified by collecting FP register data over a 12-month period. On the other hand, HIV-positive women may be accessing screening at HIV clinics and not FP clinics. In contrast to HIV-positive women, HIV-negative women should be screened every 5 years. As a result, data abstraction over a 12-month period may incorrectly identify women needing screening when they had recently been screened. The intervention then may appear to be more effective in HIV-positive women only because of the data abstraction period or alternatively, miss screening in HIV-positive women if it is occurring outside of FP clinics. We will use Aim 1 to understand screening practices for HIV-positive and HIV-negative women. We believe it will be reasonable to assume that the majority of women have not been screened recently, should be screened, and then counted in the outcome assessment. If our data in Aim 1 does not

support this assumption, we will adjust our approach depending on what we discover. For example, we may focus on HIV-negative women in the primary analyses as they would be less likely than HIV-positive women to have accessed screening elsewhere, or only include new FP clients as outlined in the first limitation. Alternately, we may find in Aim 1 that HIV-positive women are screened at HIV clinics and not FP clinics. To address differences in screening practices by HIV status, we may stratify results based on HIV status, or exclude HIV-positive women from our primary analysis. The cluster RCT design provides robust power with the same clinic numbers and varying clients in each clinic. Using our conservative estimates of clients per clinic, we will have a sufficient sample size to stratify by HIV status or exclude HIV-positive women from the analysis.

Current screening practices vary between FP clinics: It is possible that randomization would select a disproportionate number of clinics in either intervention or control arms that already perform screening. This may bias results. Aim 1 results will be used to decide whether to stratify randomization based on past screening rates.

SAIA interventions not readily identifiable or feasible: Clinic staff may not identify solutions to address bottlenecks. In discussions with Dr. Sherr (based on his experience with both CQI and the development of SAIA), this can be addressed by highly trained, experienced study staff to guide clinic staff through SAIA. Additionally, other quality improvement tools like root cause analysis and fishbone diagrams can be helpful (57). It is also possible that solutions proposed by staff members may not be feasible. Study staff will help staff to identify solutions that are more feasible in the given context and budget.

Focus on cervical cancer screening: This study will focus on increasing screening and will not address the linkage to treatment for positive screens. While we recognize that referral and treatment are also important, these steps would add complexity to this small study, and we likely would not have sufficient power. In addition, we felt that focusing on screening provided a useful metric for evaluating whether SAIA is potentially effective for addressing cervical cancer prevention. To insure adequate care during the study, we will partner with our Mombasa County collaborators to work programmatically to ensure that women with positive screens are linked to treatment. The extension of SAIA to improve linkage to treatment is a potential aim of a future study.

12. STUDY RESULTS DISSEMINATION PLAN

Results of this study will be published so that the research community and public will have access to it. All publications and presentations of material and data related to this study will include acknowledgement of NIH grant support and a disclaimer following NIH guidelines. In accordance with NIH Public Access Policy, all publications will be submitted to PubMed Central.

Data from this study will be available upon request after publication of the main study manuscripts. A standard approach will be followed for data sharing. Researchers requesting access to data will need to first submit a request in writing describing their qualifications, local IRB approval for the planned analyses, statistical analysis plans, and plans to secure the confidentiality and safety of the data. They will be required to agree, in writing, that they will not share the data with others, will use it only for the research purpose(s) delineated, and will return or destroy the data upon completion. All data will be de-identified. Approval from the Kenyatta National Hospital-University of Nairobi Ethics and Research Committee (KNH-UON ERC) will also be required to have access to any data.

We will not develop any unique research resources, inventions, or patents as a result of this work.

F. PERSONNEL

McKenna Eastment, MD, MPH, principal investigator (PI): Dr. Eastment is an acting instructor in the Department of Medicine at the University of Washington. She has worked previously with her mentor, Dr. McClelland, in leading implementation of his grant in family planning (FP) clinics in Mombasa County. This project is testing an implementation science tool to improve HIV testing in FP clinics. She will provide study oversight and act as the main implementer of the study.

R. Scott McClelland, MD, MPH, mentor to principal investigator: Dr. McClelland is Professor of Medicine, Epidemiology and Global Health at the University of Washington. He is also a Visiting Lecturer, Department of Medical Microbiology, University of Nairobi. Dr. McClelland is the site leader for the Mombasa Cohort, a long-term open cohort study of female sex workers at risk for HIV and STIs. He has studies heterosexual transmission of HIV-1 in Kenya since 1998. Dr. McClelland will serve as the mentor for Dr. Eastment for this study. He will provide mentorship and study oversight.

Walter Jaoko, MBChB, MSc, PhD, Co-investigator, University of Nairobi: Dr. Jaoko is an Associate Professor in the Department of Medical Microbiology at the University of Nairobi. He has been a collaborator in Dr. McClelland's research in Mombasa for over 10 years, and is the UON PI for Mombasa Field Site. Dr. Jaoko is also a Director of the Kenya AIDS Vaccine Initiative. In this project, he will liase with the KNH ERC, will work closely with Dr. Eastment and the site staff in Mombasa to implement the research, and facilitate communication between UON and Mombasa County.

John Kinuthia, Site Principal Investigator, Kenyatta National Hospital Discordant Couples Center: Dr. Kinuthia is a Kenyan Obstetrician and Gynecologist who has worked with investigators at the University of Washington including Dr. McClelland for the past 10 years. For this project, Dr. Kinuthia will contribute to the development, implementation, analysis, and interpretation of the research. Additionally, Dr. Kinuthia will provide content expertise in cervical cancer screening methods.

Kishorchandra Mandaliya, MBChB, Laboratory Director, Mombasa: Dr. Mandaliya is a Pathologist at Pathcare Laboratories in Mombasa, and Director of our Research Laboratory in Mombasa. He has conducted research with Dr. McClelland and the UW group for over 20 years. In this project he will contribute to supervision of staff and trainees. Dr. Mandaliya will also provide content expertise in cervical cancer screening methods.

Faiza Nassir, MBChB, MMed is an Obstetrician and Gynecologist employed by Mombasa County. The County Chief Officer of Health has identified her as the County Representative who will work closely on implementation and diseemination of the study findings. Dr. Nassir has prior experience in revising the family planning register in Mombasa as part of the APHIA II effort to expand HIV testing. She provided input on the development of this grant proposal, and will continue to serve as a co-investigator and advisor during implementation. She will act as a liaison with the County.

G. TIMELINE

Table 2: Timeline for activities during the K08 funding period

		Year 1				Year 2				Year 3				Year 4			
Aims 1, 2, 3	Protocol and instrument development																
	IRB application & In-country ethical approval																
	Staff hiring and training																
	Aim 1 data collection																

	Randomized trial & data collection (Aims 2 & 3)															
	Data analysis															
	Manuscript preparation**															
	Manuscript submission**															

Year 1 is expected to be July 2018-June 2019
Year 2 is expected to be July 2019-June 2020
Year 3 is expected to be July 2020-June 2021
Year 4 is expected to be July 2021-June 2020

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I. ETHICAL CONSIDERATIONS

1. Involvement of Human Subjects

There will be three different groups of subjects in this research proposal:
1. Individual FP clients' data will be abstracted from FP registers. However, there will be no contact with individual FP clients by study staff. We are seeking a waiver of written informed consent for this population.
2. Family planning clinics as a unit to be randomized. Study staff will work with clinic staff for both data abstraction and during the intervention if randomized to this arm of the trial. In addition, micro-costing and time-and-motion studies will be conducted in FP clinics for the SAIA budget impact analysis. We will ask for assent of clinic managers to participate in the randomized trial.
3. Family planning clinic managers and staff. We will verbally consent clinic managers/staff for brief semi-structured interviews. We will seek written informed consent for in-depth interviews with clinic managers/staff.

All the proposed research activities involving human subjects will occur in Mombasa County, Kenya. This is in collaboration with Mombasa County Department of Health, and will provide real-time input and sharing of results. Given the location of this study in Mombasa County, we expect that all participants will be of African descent. The FP clinic staff and managers will be both men and women. All FP clients eligible for cervical cancer screening are expected to be women aged 21-65 years.

This study will be conducted in collaboration with the Mombasa County Department of Health (DOH). Dissemination of results will be implemented in collaboration with representatives from the Mombasa County Department of Health.

2. Research Material Obtained from Participants

Family planning registers: Routinely collected data will be abstracted from FP registers about basic demographics, HIV status, cervical cancer screening and referrals of FP clients.

Family planning clinic managers and staff: Family planning clinic managers and staff will be approached to participate in brief semi-structured interviews and in-depth interviews in clinics chosen for the RCT. Managers will be asked to provide verbal assent for semi structure interviews. Clinic staff participating in IDIs will be asked to sign written informed consent. These interviews will be recorded and detailed field notes will be collected by the interviewer.

Data Management: Abstracted FP register data will be uploaded to a REDCap database. Again, there will be no personal identifiable data collected or uploaded. Interview data will be transcribed and translated. These data will be stored on a password protected encrypted computer. Data that have not been decrypted appear as blank files. Interview recordings will be destroyed five years after completion of the research. Informed consent documents will be stored in a locked cabinet and separate from both recordings and transcripts from interviews.

3. Recruitment of Subjects and Consent Procedures

Recruitment of Subjects:

Individual FP clinics will be approached after the sub-county Ministries of Health are aware of the study. A letter of introduction from the Mombasa County Department of Health will accompany study staff. Clinic managers will assent to the preliminary clinic review and then if selected to be randomized into the study.

Clinic managers and clinic staff will be approached by study staff to discuss participating in in-depth interviews. Study staff will identify clinic managers and staff by visiting the clinic and asking for the clinic 'in-charges'. Staff will ask the clinic managers when would be an appropriate time to answer brief questions for Aim 1 and Aim 3 brief structured interviews. Aim

2 in-depth interviews will be scheduled at a time and place convenient to the clinic members. Individual health workers will be recruited confidentially at a convenient time in their work day. They will be reassured that they are free to decline to participate.

Consent procedures:
Family planning clients: As only FP register data will be used, individual FP clients will not be participating in this study. We will use a unique code number to track women over the year in the FP register for outcome data. Client names and contact information will be covered during image capture and for storage. Personal data will be de-identified upon entry into a database as aggregated data. Digital records will include a unique code without personal identifying information.

Family planning clinics: Using previously successful procedures with FP clinics during the FP HIV SAIA trial, FP clinic managers will be approached. Study staff will explain the study and ask that FP clinic manager provide assent to participate in the study.

Family planning clinic managers and staff: Semi-structured interviews and IDIs with health workers will be conducted in confidential settings either within FP clinics, their associated facilities, or at our research facilities, depending on the space available on-site at the different clinics. Individual health workers will be recruited confidentially at a convenient time in their work day. They will be reassured that they are free to decline to participate. Clinic managers participating in semi-structured interviews will be asked to provide verbal assent as these interviews are anticipated to be brief. Health workers who agree to participate in IDIs will be asked to provide written informed consent. The consent forms will be approved in advance by the Kenyatta National Hospital-University of Nairobi Ethics and Research Committee (KNH-UoN ERC) and the University of Washington Human Subjects Research Committee (UW HSRC). Informed consent procedures will be completed prior to initiating the interview. The consent form will include the possibility of negative consequences regarding employment if staff members are identified as providing negative information about the workplace.

This consent process includes the following procedures:
-Ensure that the consent process is taking place in a private area.
-Use the informed consent checklist as a guide throughout the consent process and enter the time at the beginning of the sheet.
-Give the consent form for the client (FP clinic staff member) to read in their language of choice (English or Kiswahili) and allow enough time for the staff member to read the consent form.
-After the potential participant reads the consent/has it read to her, review the key points.
-Ask the potential participant if they have any questions and discuss any questions or concerns.
-Clarify any misunderstanding and determine eligibility.
-Once eligibility is determined the counselor can proceed with the consent process.
-Sign the informed consent checklist and retain if the staff member enrolls
-The potential participant should sign and date first and must write her/his own name. The person obtaining consent signs last.

Potential participants must demonstrate their understanding of key concepts about the informed consent before signing. Specific questions used to assess understanding may include items such as:

1. Please describe what your role will be in this research study?

2. Is participation in these interviews voluntary?

3. If you do not participate, will this reflect negatively in your work evaluations or job status?

The consent form will include the possibility of negative consequences regarding employment if staff members are identified as providing negative information about the workplace. We will also explain how we plan to keep these data confidential.

4. Risk to Human Subjects
No adverse effects would be expected to result directly from the semi-structured interviews or observation of clinic procedures. However, there is potential for negative consequences regarding employment for staff if they are identified as providing negative information about the workplace. This could take the form of harassment, transfer, lack of promotion, dismissal, etc. Staff in smaller facilities might be particularly at risk for inadvertent disclosure if the content of their interviews identified them as being in a particular position. Several steps will be taken to mitigate this risk, as detailed in the section, “Adequacy of Protection against Risks”.

For patients accessing care through FP clinics, the risks associated with these services will not be different from the risks associated with these interventions in the absence of the research. Data will be abstracted from routinely collected data in FP registers. While this is personal identifiable data in the FP registers, a unique code will be used to track women over time in the register.

5. Adequacy of Protection Against Risks
Family planning clients: For patients accessing care through FP clinics, the risks associated with these services will not be different from the risks associated with these interventions in the absence of the research. Data will be abstracted from routinely collected data in FP registers. While this is personal identifiable data in the FP registers, a unique code will be used to track women over time in the register. Personal names and contact information will be covered and only the unique code will be used. Images captured will have the unique code but no other personal identifying information. Data entered into the database will be aggregated.

FP clinic managers and staff: Brief semi-structured interviews will ask specific questions and record these answers on data collection forms. We do not anticipate that these questions would be sensitive. As more sensitive information is collected for IDIs, these procedures are slightly different. Health worker names will not be recorded in any location except on their informed consent form. Completed informed consent documents will be stored in a locked cabinet within a locked data room at our research facilities in Mombasa. No other personal identifying information will be collected. To further protect facility staff from negative repercussions if they report workplace problems, several additional steps will be taken as needed:

- Staff will be specifically informed of potential risks during the written informed consent process, and will be assured that they may decline to participate
- We will not inform supervisors of staff members decision to participate or decline participation in the interviews
- Data from multiple staff members may be aggregated into a single report for the purposes of discussion, development of best practices, quality improvement steps, etc.
- Participants will be asked, at the end of each interview, if they have concerns about the use of these data within the framework of the protections noted above. If so, these concerns will be taken into account in making decisions about whether/how to utilize these data.
- On the informed consent document, we will provide telephone numbers for contacting both the research team and the ethics committee if an employee feels that they are

being treated unfairly as a result of participation in the research. If such an event occurs, we will work with our partners in the Mombasa County DOH to take steps to correct the problem and add protections against recurrence.

Health worker IDIs will be recorded, and detailed field notes will be collected by the interviewer. Interview data will be stored on a password-protected encrypted computer. Data that have not been decrypted appear as blank files. Interview recordings will be destroyed at the completion of the research.

6. Potential Benefits

Benefits to all Subjects:

The initial cervical cancer screening care cascade will be presented to Mombasa County. This presentation will inform the County of the current screening activities that may highlight areas for continued important. In addition, comparing the FP registers with DHIS report will provide the County with information about the current state of register documentation. If data quality is not consistent and there is not enough correlation between registers and DHIS reports, it might serve as an impetus for further guidance on appropriate documentation to all FP clinics.

All clinics that could be randomized will have a performance evaluation of cervical cancer screening procedures completed. This evaluation alone is useful quality assurance information for the clinic. Clinics could then act independently to make changes to procedures to increase cervical cancer screening.

Benefits to Subjects in the Intervention Arm of the Trial:

Clinics in the intervention arm will have the benefit of in-depth review of procedures and then SAIA interventions that aims to increase cervical cancer screening. This will benefit individual clinic attendees who may be due for screening ***or have never been screened for cervical cancer. Attempts will also be made to make sure that if women are screened by their FP clinics and have an abnormal screen that they are linked with follow-up care.***

The increase in cervical cancer screening and improvement of mechanisms to continue to screen women using SAIA will continue to benefit women and their reproductive health.

7. Importance of knowledge to be gained:

If successful, this research will provide tools that will assist health care workers and managers to understand and improve systems for integrating cervical cancer screening into FP services. The initial cervical cancer care cascade is valuable information for the County to understand the current state of screening and the quality of cervical cancer screening documentation. The SAIA intervention will be conducted in collaboration with local health authorities, and could be scaled up throughout Kenya and in other high burden African countries. Further, the budget impact analysis of SAIA will provide useful information for both the local and national Ministries of Health to use in scaling up cervical cancer screening. The risks to participants are minimal, while the benefits to individual FP clinic clients and the broader population of HIV-positive and HIV-negative women are substantial.

8. Data safety and monitoring plan

The Principle Investigator will take responsibility for data safety and monitoring as part of the oversight of this study. Information collected from FP clients and FP clinic managers will all be de-identified upon storage. Because we will not be enrolling individual participants for the RCT, and individual participant data entered into our dataset will not contain personally identifiable information, we believe this trial does not require a DSMB. This is in conversation with NIH NCI Program Officer. However, if data safety issues arise, these would be reported promptly to both the Kenyatta National Hospital-University of Nairobi Ethics and Research

Committee and the University of Washington Human Subjects Research Committee.

9. Clinical trial registration
This trial has been registered with clinicaltrials.gov

J. BUDGET

Category	Anticipated Amount in USD (Year 1)	Anticipated Amount in USD (Year 2)	Anticipated Amount in USD (Year 3)	Anticipated Amount in USD (Year 4)
Materials and Supplies	$6679.00	$6679.00	$6479.00	$6479.00
Consultant services	$1500.00	$1500.00	$1500.00	$1500.00
Communications	$1000.00	$1000.00	$1000.00	$1000.00
Transportation/travel	***$2000.00***	***$2000.00***	***$2000.00***	***$2000.00***
One computer	$2000.00			
UW-Kenya employees and service fee	$29,821.00	$29,821.00	$29,821.00	$29,821.00
Total costs:	$43,000.00	$41,000.00	$40,800.00	$40,800.00

K. APPENDICES
Informed consent documents
Letter from Dr. Patta
Curriculum vitae attached for principal investigators and co-investigators