TITLE: Systems Analysis and Improvement Approach to Optimize the Hypertension Diagnosis and Care Cascade for HIV-infected Individuals (SAIA-HTN)

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STUDY OBJECTIVE: The overall goal of this application is to evaluate a model for systematic assessment and improvement of HTN diagnosis and management services for people living with HIV (PLHIV) in Mozambique.

STUDY DESIGN: Over the five-year project, we will conduct a parallel cluster randomized trial to evaluate the effectiveness of SAIA-HTN. We will use qualitative methods (focus group discussions and in-depth interviews with health workers) to identify drivers of SAIA-HTN's implementation success and collect data to determine the intervention's costs and cost effectiveness on HTN and HIV performance measures.

BACKGROUND: Undiagnosed and untreated hypertension (HTN) is one of the largest drivers of cardiovascular disease (CVD), which contributes to one third of deaths globally (and disproportionately affects low and middle income countries (LMICs)). A systematic review across sub-Saharan Africa (sSA) reported HTN prevalence between 14.7-69.9% (median prevalence 29%). In Mozambique (a low-income country with >13% adult HIV prevalence), HTN prevalence among adults increased sharply from 2005 to 2015, now affecting nearly 40% of adults. Yet just 14.5% are aware of their HTN status (the lowest in sSA); among these, only 50.1% are in treatment, less than half of whom have controlled HTN. As a result of this leaky cascade, only 3% of the adult population with HTN in Mozambique have their condition controlled.

Across sSA, evidence-based, clinical guidelines to screen and manage HTN exist; however, country-level application is low and uneven due to lack of service readiness, uneven health worker motivation, lack of accountability for health worker performance, and poor integration of HTN screening and management with chronic care services. In Mozambique – like many countries with high HIV burden – the HIV treatment platform was the first broadly implemented chronic care service. With large numbers of patients on anti-retroviral treatment (850,000 in Mozambique), it presents a unique opportunity to standardize and scale HTN screening and management. The HTN care cascade steps – blood pressure screening, diagnosis, linkage to care, treatment initiation, ongoing blood pressure monitoring, and adherence to anti-hypertensive medications – are complex and critical for improving health outcomes. Low-cost, systems level interventions are effective and efficient approaches to improve linked cascade services, and may be effective for routinizing HTN diagnosis and management within existing outpatient services; addressing both individual- and systems-level barriers; improving flow through the HTN cascade; and ultimately improve patient-level outcomes.

EXPERIENCE AND PRELIMINARY WORK: The *Systems Analysis and Improvement Approach (SAIA)* is designed to optimize cascade performance, is feasible for frontline healthcare workers and managers and is applicable to optimize the HTN testing and treatment cascade for people living with HIV (PLHIV) across multiple contexts. SAIA is an evidence-based strategy which is flexible to local context and supports frontline facility staff to gain a comprehensive view of their complex delivery system, identify and prioritize areas to improve, and iteratively test modifications to increase system outputs and patient outcomes. Health workers in the original cluster randomized trial that tested the intervention to improve prevention of mother-to-child HIV transmission (PMTCT) services noted that SAIA stimulated communication, consensus decision-making, and accountability across multiple service points in their facility (e.g. patient care, pharmacy, laboratory services); was accessible by relying on routinely collected data to guide decision-making in a real-world service delivery environment; and resulted in significant improvements in service delivery outcomes. We have successfully piloted SAIA for the HTN cascade for PLHIV, and as HTN screening and management is mainstreamed into chronic care services in sSA (including in Mozambique), demonstrating SAIA-HTN potential effectiveness as an adaptable, scalable model for broad implementation.

We have been conducting formative research since February 2018 to design and pilot SAIA-HTN for PLHIV. Four focus group discussions (FGDs) were held with frontline health workers and regional

clinical experts, and 24 in-depth interviews (IDIs) with key informants (frontline health workers and managers), to assess feasibility and refine the SAIA-HTN strategy. Critical HTN cascade steps were identified, and the HTN Cascade Analysis Tool (HCAT) developed. Data sources were mapped, and a registry to populate the HCAT and capture relevant study outcomes from outpatient registries and patient charts was developed. Clinical pathways and tasks were described in outpatient and emergency services, where both HIV and HTN screening and care is provided by both mid- and higher-level providers at the health center level, with complicated cases referred to reference hospitals. Mid-level providers may initiate HTN medications under supervision of a higher-level provider, while both mid- and higher-level providers may prescribe anti-retrovirals. SAIA-HTN was piloted in one facility and after twelve weeks of implementation, HTN screening improved 4-fold. In FGDs and IDIs, frontline health workers and managers were enthusiastic about SAIA-HTN and found the focus on HTN relevant and timely. Through other research in the study area (R01HD075057, R01MH113435, and R01HD092449), we have translated and adapted the CFIR tools for the local setting, and trained study personnel on their application. Stakeholder meetings have also been held with national, provincial and district authorities to seek consensus on the SAIA-HTN and trial design, including study location.

PARTICIPANTS: Health Facility Managers, District Health supervisors and leading cardiovascular and HIV Clinical Experts (medical doctors or nurses) at the sub-national level (provincial, district) will participate in in-depth individual interviews. A small number of providers will also be recruited to complete a recall survey on the amount of time they spend dedicated to hypertension care which will inform the costing analysis. There will be no direct contact with patients, as the SAIA-HTN intervention only involves periodic engagement with health workers. Regularly collected, de-identified clinical outcomes related to controlled hypertension and process outcomes related to blood pressure screening, anti-hypertension medication initiation and maintenance in care will be obtained as part of the study.

There are two groups of human subjects involved in this project. The first group are patients ≥18 years old accessing services at the 16 facilities, eight of which will be implementing the Systems Analysis and Improvement Approach (hereafter referred to as patient subjects). Over the course of the study, we expect that the number of patient subjects attending HIV care and linked hypertension screening, care and treatment services will number in the thousands. Using de-identified, routine health system records, we will be measuring outcomes that reflect more consistent implementation of Ministry of Health norms (including blood pressure screening, treatment initiation and maintenance in care for hypertension as well as monitoring controlled hypertension). We expect the sample to be approximately half male and half female, given that HIV services are typically gender-balanced in the study setting.

The second group of human subjects involved in this study are Frontline Health Workers and Health Facility Managers working in outpatient and HIV services, and District Health Supervisors and Clinical Experts who will support dissemination of the study intervention. We expect Frontline Health Workers, Health Facility Managers, District Health Supervisors and Clinical Experts to be approximately half male and half female, aged 18-65 years. These participants will be recruited and asked to consent to participate in FGDs, individual interviews, or an end-of-day recall survey to estimate time spent on hypertension-related tasks. Participants recruited are free to decline to enroll or to decline to continue participation with no adverse consequences to their employment.

INCLUSION CRITERIA: (A1) Frontline Health Workers / Health Facility Managers currently working in outpatient and HIV services at one of the study clinics in Manica and Sofala provinces, Mozambique; (A2) District Health Supervisors currently employed in a study district in Manica and Sofala provinces, Mozambique regularly engaged in service provision or management of HIV-infected and/or hypertensive populations; and (A3) Clinical Experts currently working in Mozambique in the clinical delivery of HIV and/or hypertension care and treatment *or* (B1) PLHIV ≥18 years old who also access HIV care and treatment services via outpatient services in study clinics.

EXCLUSION CRITERIA: (A1) not currently working as a Frontline Health Worker/Health Facility Manager at a participating study facility or (A2) not currently working as a District Health Supervisor in a participating district or (A3) not currently working in Mozambique in the clinical delivery of HIV and/or hypertension care and treatment or (B1) HIV-negative or of unknown status or <18 years old or age not recorded, or or pregnant or postpartum.

NUMBER OF SUBJECTS:

Group name/description	Maximum desired number of individuals (or other subject unit, such as families) who will complete the research **For clinical trials: provide numbers for your site and for the study-wide total number*
Frontline Health Workers (FGD)	224
Frontline Health Workers (ORIC)	70
Health Facility Managers (IDI)	48
Health Facility Managers (ORIC)	12
District Health Supervisors (IDI)	24
Provincial Health Experts	4
Frontline Health Workers (Costing)	30

RESEARCH SETTING: The SAIA study includes 16 public sector facilities, 8 of which will receive the SAIA intervention in outpatient, emergency and related (pharmacy, etc) services where HIV care and treatment is currently mainstreamed into primary healthcare services in Manica and Sofala provinces in Mozambique. Manica and Sofala provinces (population ~4 million, HIV prevalence 15.3% and 15.5%, respectively) were selected because of the deep relationship between investigators and health authorities, and absence of structural interventions for HTN diagnosis and management (both within HIV care and general outpatient services).

LOCAL CONTEXT: In the study area (central Mozambique), over 98% of formal health services are offered through the public sector, and primary care utilization is high, supporting spread and likelihood of population-level impact for a supply-side intervention delivered through the HIV treatment platform.

RECRUITING AND SCREENING: This research study will include: 1) review of routinely reported Ministry of Health facility-level data, abstraction of registry data, and abstraction from patient clinical records from 16 public sector facilities, 2) twice over the life of the study, individual interviews with leading cardiovascular and HIV Clinical Experts (medical doctors and/or nurses) in each study province to review study materials, preliminary results, evaluation of findings and dissemination plans (28 participants), 3) two rounds of focus group discussions (FGDs) with Frontline Health Workers in eight intervention facilities (with 7-14 participants each) and one additional FGD with high and low performing health facility staff (by province) after the maintenance phase (17 FGDs total), 4) two rounds of 24 semi-structured in-depth interviews with Health Facility Managers (2-3 health facility managers per study facility) in each of the eight intervention facilities (48 interviews in total), 5) two rounds of 12 semi-structured in-depth interviews with District Health Supervisors (24 interviews total), 6) in-depth interviews with 2 provincial leads for HIV and NCDs will be conducted at mid-point and endline, 7)

repeated observation of facility-level characteristics in 16 public sector facilities (including staffing levels, clinic volume, physical space and services offered, wait/consult times, commodity availability, and stock outages for hypertension-related medicines and supplies), and 8) completion of an end-of-day recall survey for approximately 30 frontline health workers (conducted twice in 2 sites with approximately 15 participants each). All recruitment will be carried out by SAIA-HTN study team members.

Group interviews, focus group discussions and in-depth interviews will be audio taped. Participants who do not consent to be audiotaped in group interviews and focus group discussions will not participate in these activities, however participants in in-depth interviews who do not consent to audio taping will still be able to participate. The interviewer in those cases will take notes during the interview.

The human subjects who will be consented to be involved in this project are 1) Frontline Health Workers at the eight intervention study facilities, 2) Health Facility Managers at the eight intervention study facilities, 3) District Health Supervisors in the 6 study districts, and 4) provincial health supervisors / Clinical experts in HIV and NCDs, 5and 6) frontline health workers engaged in hypertension care participating in end-of-day recall survey of time spent dedicated to SAIA-HTN related care.

All Frontline Health Workers and Health Facility Managers at study facilities will be invited to participate in the SAIA-HTN intervention by study nurses. In addition, District Health Supervisors and Clinical Experts in HIV or non-communicable diseases will also be screened and recruited into the trial by study nurses. Note, as previously mentioned we will <u>not</u> directly enroll any patients seeking health services as participants in this study but will abstract medical records and registries of all adult PLHIV (≥18 years) who access HIV care and treatment services via outpatient.

Over the course of the study, we expect that the number of adult PLHIV patients attending outpatient and HIV services and receiving hypertension screening, treatment and ongoing monitoring services will number in the thousands. Using available records at the health facility-level, we will be measuring outcomes that reflect more consistent implementation of Ministry of Health norms (including hypertension screening, initial diagnosis, anti-hypertensive medication initiation, and adherence as measured by antihypertensive medication pharmacy pick up, as well as HIV viral load suppression).

RECRUITMENT MATERIALS: In each study facility, an introduction to the study will take place. One to two hour meetings will take place daily over four days, whereby the study aims and procedures will be introduced, followed by an introduction to the SAIA-HTN tools, namely cascade analysis, process mapping and continuous quality improvement. This approach has been tested and across the multiple SAIA-related studies and adapted and piloted for SAIA-HTN in the previous study. A recruitment script and a consent form has been developed for the study and are uploaded. The consenting process occurs on the first day after a brief introduction to the study aims. For the costing time and motion and out of pocket spending surveys the consent documents for those surveys include information that will be used for recruitment.

NON-MONETARY COMPENSATION: A basic snack (crackers and fruit juice) will be provided to health workers during monthly visits. Likewise at FGD/IDIs/group interviews snacks will be provided.

CONSENT FOR RECRUTING AND SCREENING: All Frontline Health Workers and Health Facility Managers at study facilities will be invited to participate in the SAIA-HTN intervention. In addition, District Health Supervisors and Clinical Experts in HIV or non-communicable diseases will also be recruited into the study. Written consent will be obtained from all participants engaged in service readiness questionnaires, focus group discussions, in-depth interviews and group interviews.

PROCEDURES: The overall goal of this application is to evaluate a model for systematic assessment and improvement of HTN diagnosis and management services for HIV-infected individuals in Mozambique. Over the five-year project, UW faculty and colleagues will conduct a parallel cluster randomized trial to

evaluate SAIA-HTN effectiveness on HTN cascade optimization (Aim 1); identify its drivers of implementation success (Aim 2); and determine costs and cost effectiveness on HTN and HIV performance measures (Aim 3). The SAIA-HTN trial was conducted in eight intervention and eight control health clinics, between 2019 and 2023 and over three phases: (1) a 3-month preparatory phase, which included the baseline period from July to September 2020, (2) a 24-month intensive implementation phase in which implementation was supported by the research team, and (3) a 12-month sustainment phase where research team support is removed in Manica and Sofala provinces in central Mozambique. District Health Supervisors, supported by study nurses, will deliver the intervention during the intensive phase, followed by a one-year sustainment phase led by the District Health Supervisors without additional study personnel support. In all 16 health clinics, government health workers provided hypertension care to clients accessing HIV services. Clinician training included a refresher on Mozambique Ministry of Health guidelines on clinical management of hypertension and the use of hypertension treatment job-aids. Both clinicians and data clerks received phone credit vouchers as incentives for the additional work of data collection for the purpose of the study. Sphygmomanometers were allocated to every consultation room where clinicians provided outpatient/HIV services to allow for similar opportunity for hypertension screening in all sites. From July 2020, all 16 sites began to use study data collection tools to collect patient level hypertension care data at every ambulatory care visit, for both new and returning clients. The frequency and schedule of ambulatory consultations was not uniform across clients.

In eight health clinics assigned to the intervention arm, SAIA-HTN implementation started in October 2020. SAIA is composed of four components – (1) the Hypertension Cascade Analysis Tool – HCAT, (2) Process Mapping, (3) Continuous Quality Improvement – CQI, all of which are operationalized during (4) monthly SAIA meetings. The HCAT uses health facility aggregate patient data to assess the flow of patients through the care cascade, indicate where in the cascade major drop-offs occur, and indicate at which step improvements may result in more patients achieving controlled hypertension. Process mapping consists of a health worker joint assessment of patient paths through hypertension services within the health facility to identify inefficiencies and inconsistencies that may be addressed for improvement. The CQI consists of Plan, Do, Study, Act monthly cycles, in which implementers define a problem based on findings of the hypertension care cascade assessment and process mapping, define and implement solutions to address the defined problem, and iteratively assess the effect of the solutions implemented by reassessing the performance of the hypertension care cascade, reviewing the process map, and sharing anecdotal experiences together. Depending on the perceived feasibility and effectiveness of the solutions implemented during the month, implementers decide if solutions are to be abandoned, adapted for further testing, or adopted as a practice that is to be continued.

The mixed-methods evaluation will evaluate the impact of SAIA-HTN on clinical (controlled HTN, HIV viral load suppressed) as well as process (BP screened, HTN diagnosis, HTN medications prescribed, HTN medications picked up) outcomes. The consolidated framework for implementation research (CFIR) will be used to guide data collection and interpretation related to implementation, to assess fidelity to intervention protocol, describe intervention adaptations when integrated into routine management systems, and identify organizational-level determinants of successful SAIA-HTN implementation. Based on trial results, we will model out the costs and potential benefits on HTN control given different scale-up scenarios within Mozambique. The trial will culminate in a dissemination package, summarizing trial results and providing implementation and cost guidance to support national SAIA-HTN scale-up.

Costing and economic evaluation sub-study: In addition to the interviews/FGDs described above, we will conduct a sub-study to conduct a costing and economic analysis of SAIA-HTN. Study team members will conduct a brief recall survey at the end of the day with all healthcare providers directly engaged with HTN services to record the amount of time spent on HTN-specific tasks throughout the day. This survey will take approximately 10-15 minutes to complete.

The costing activities described above will be done twice. Subjects will be selected from both control and intervention sites to compare differences in time and costs. In this way we can similarly evaluate differences in time/costs between intervention/control. Frontline health workers participating in the costing study do not require audio taping. Surveys will be administered by study team members who will enter information and survey responses on a paper-based or electronic study tool that will be used to support the data analysis.

COMMUNICATION WITH SUBJECTS DURING STUDY: We will have no direct or indirect interaction with patients attending services that are the target for improvement via the study intervention. For Frontline Health Workers, Health Facility Managers, District Health Supervisors and Clinical Experts engaged in qualitative data collection activities, we will not have any contact after the qualitative data collection procedures are finalized.

LINKS TO SUPPORTING DOCUMENTS:
CFIR description available at www.cfirguide.org/constructs

OUTCOME DEFINITION: The study has two primary endpoints. The first is a process outcome and measures the activation of the hypertension care cascade – the proportion of ambulatory care consults for PLHIV at which blood pressure was screened. The second is a patient level clinical outcome – the proportion of clients eligible for hypertensive medication who attain blood pressure control. Hypertension medication eligibility was guided by a simplified risk stratification tool, but ultimately established by clinicians. This tool describes eligibility as an additive risk score of at least 3 according to the following parameters: 1) score of three for PLHIV previously on or presently initiating hypertensive medication and/or with blood pressure of at least 160/100 mmHg; score of two for blood pressure between 140/90 mmHg and 160/100 mmHg, score 1 for the presence of any number of non-modifiable risk factors (such as previous Myocardial Infarction, Coronary Vascular Disease and Diabetes Mellitus); and score of 0.33 for any number of modifiable risk factor (such as smoking, overweight, and sedentarism). Controlled hypertension is defined as blood pressure reading of ≤140/90 mmHg in clients with verified hypertension. Between these two endpoints, we also assess the proportion of patients that successfully progress from being screened, to treatment eligible, to receiving a prescription, to accessing the prescribed medication and to attaining blood pressure control.

SAMPLE SIZE AND RANDOMIZATION: Sample size estimation was based on the anticipated absolute difference in the proportion of ambulatory care consults at which hypertension is screened during the last three months of using the SAIA-HTN implementation strategy. Hypertension screening was selected because it is the first step of the hypertension care cascade and its routine use in outpatient visits is recommended by existing guidelines. In the pilot study leading up to this trial, the proportion of ambulatory care consults at which hypertension was screened at the beginning of the pilot was less than 10%, and a 31% increase was observed at the end of the pilot. Assuming an $\alpha = 0.05$ and 1000 HIV care outpatient visits over each 3-month period, we estimated that eight intervention and eight control clusters would be sufficient to have 80% power to detect an absolute difference in the outcome of between 15 and 29%, depending on plausible values of the effect size in the control sites (i.e. 10 to 20% of care consults at which hypertension screening was done) and intra-cluster correlation between 5 and 15%. To select the eight intervention and control clusters, 29 eligible health facilities across the two provinces were stratified by province (Manica or Sofala) and by type (urban or peri-urban) and 1:1 randomized to either intervention or control arm within each stratum, so that two urban and two peri-urban health facilities were allocated for each arm, in each province. Adult (>18 y/o) clients were automatically assigned to either intervention or control arms in dependence of the respective cluster where they access ambulatory care consults.

ANALYSIS APPROACH:

Descriptive analysis

We described health facility characteristics at baseline and the study participant population both during baseline, and at the time of recruitment for each study phase, in terms of sex, age and hypertension care outcomes status. For the primary process outcome, we describe the number and proportion of outpatient consultations at which blood pressure was screened in each study phase. To describe the hypertension care cascade, we ascertain the proportion of patients who, within the phase they are recruited, are ever screened and diagnosed as eligible for hypertensive treatment, ever receive a prescription and pick-up the medication prescribed, and who present controlled blood pressure control in the last two ambulatory consultations (if same outcome observed in both visits) or in most consultations. Ambulatory consultations beyond the phase of recruitment are censored.

Inferential analysis

To assess the effect of SAIA-HTN, we ascertained clinical outcomes in all ambulatory care visits within each phase (observations attributed to the phase in which consultations took place), and estimated the population level risk of the outcomes using Generalized Estimation Equations (GEE) and Log-binomial or Poisson regressions, assuming an exchangeable correlation structure to account for clustering at the level of health clinic, and adjusted for study phase and for whether patients were newly recruited or retained from a prior study phase (**Model 1**).

Model 1: $log(E[yij])=\beta_0+\beta_1 \cdot x_{ij}+ \beta_2 .phase_{ij} + \beta_2 .recruitment_{ij} + u_{ij}$