Enhancing HIV assisted contact tracing in Malawi through blended learning: an implementation science study

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PROTOCOL SUMMARY

Research question/Objective

This study seeks to understand whether a "blended learning" implementation approach is an implementable, effective, and cost-effective modality for building health worker capacity for voluntary assisted contact tracing.

Rationale

Voluntary assisted contact tracing (ACT) is an evidence-based approach that efficiently identifies persons in need of HIV treatment and prevention. Malawi, like many countries in sub-Saharan Africa, has adopted ACT policies to support its "95-95-95" targets for HIV testing, treatment, and viral suppression. However, Malawi's ACT implementation has been poor due to deficits in health worker capacity and clinical coordination. Our team has developed a theory-based health worker training and continuous quality improvement process that addresses these barriers through a "blended learning" platform that combines digital and face-to-face modalities. This training package was field-tested in Malawi with promising preliminary results. In this proposal, the training package will be refined and rigorously evaluated. This is a two-arm pragmatic cluster randomized controlled trial (RCT) to compare the blended learning enhanced implementation package to the standard implementation package. This study aims to determine whether the enhanced blended learning package: enhances implementation outcomes (Aim 1), increases HIV service uptake (Aim 2), and is cost-effective (Aim 3).

Methods

Study design

This is a 2-arm pragmatic cluster RCT comparing an enhanced blended learning implementation package to a standard implementation package. The study will be conducted at Tingathe-supported health facilities in Machinga and Balaka, Malawi. Thirty-three clusters will be randomized in a 2:1 ratio to the standard versus enhanced packages. All clusters will receive the standard of care. Additionally, enhanced clusters will receive an enhanced blended learning training and enhanced facility support. Three sets of primary outcomes will be compared between the standard and enhanced arm: implementation outcomes, service uptake outcomes, and cost-effectiveness outcomes. The standard of care sites will receive the enhanced implementation package after the primary observation period ends. Long-term outcomes will be examined at all clusters. Prior to the trial, the enhanced implementation package and all study tools will be pilot tested for feasibility and acceptability.

Population

Study activities will take place in 33 clusters. At each cluster, two study populations will be enrolled and evaluated separately: health workers and patients. To be eligible for participation, **health workers** must be: (a) >=18 years old, (b) working full-time at one of the health facilities included in the study, and (c) involved in Malawi's HIV program. **Patients** must be: (a) >=15 years old and (b) an index, contact or parent/guardian of an index or contact. Persons that do not meet these criteria will be excluded. We aim to enroll at least 2 health workers per cluster for a minimum of 66 health workers in the study. We will enroll up to 800 patients (600 indexes and 200 contacts) over the study period.

Procedures and implementation interventions

Standard implementation

All facilities participating in the study will receive standard ACT implementation strategies. In Malawi, the standard ACT implementation strategies consist of 1) a brief ACT training, and 2) routine facility support. The brief training is centralized and conducted in-person. It is primarily didactic and provides an overview of ACT procedures and counseling approaches. Tingathe (or other partners) provide routine supervision to all facilities for all supported activities. Routine supervision consists of examining facility performance data, and providing feedback on the overall program. None of these procedures will be altered by the study.

Enhanced implementation

In addition to receiving the standard implementation strategies described above, the facilities randomized to the enhanced implementation arm will 1) receive the blended learning training and 2) participate in enhanced continuous quality improvement (CQI) processes. The blended learning training is designed for decentralized delivery. The content of the blended learning training builds on the themes described in the standard training, but includes more role modeling, practice and feedback. Furthermore, health workers involved in ACT will participate in ongoing CQI to examine their facility's ACT performance, identify gaps, and implement actionable solutions.

Participant recruitment

Within each participating cluster, we will recruit health workers involved in ACT activities, along with a subset of patients. Recruitment of health workers from included clusters will occur primarily at the beginning of the study, but will remain open over the study period. All health workers at a given cluster who are involved in ACT will be invited to participate, and a member of the study team will engage potential participants in a conversation about the purpose, nature, and duration of the study.

Recruitment of patients (indexes and contacts) is expected to occur at each facility. The study team will approach potential indexes and contacts about participation. If interested, potential participants will be offered the opportunity to provide informed consent, and those who consent will be enrolled.

Data collection, management, and analysis

Data collection

Health workers will be involved in: 1) a series of three health worker surveys 2), implementation adoption records, 3) simulated fidelity assessments for indexes and contacts, 4) authentic fidelity assessments for indexes and contacts, 5) in depth interviews and/or focus group discussions, and 6) time and motion assessments. All participating health workers will be assigned a unique study identification (ID) number.

Enrolled patients (indexes and contacts) will take part in the following procedures: 1) recorded counseling session, 2) index and contact exit interviews, and 3) clinic record abstraction. All participants will be assigned a unique ID number, which will be used instead of personal identifiers to identify the patient in all data collected.

We will also collect de-identified routine data from participating facilities. These records reflect routine programmatic data collected by the Malawi Ministry of Health or Tingathe. Data will be abstracted retrospectively. These records will include a) facility-level HIV testing registers, b) contact registers and c) index registers. Data from these sources will be used to inform our assessment of service uptake outcomes.

Management

Paper-based records will be stored in locked filing cabinets in locked rooms. Electronic data will either be collected using an encrypted electronic device or entered into a password-protected database by a trained data entry clerk. Electronic data will be stored on secure, password-protected servers.

Analysis

For **Aim 1**, we will compare health worker fidelity to ACT counseling procedures between the enhanced and standard implementation arms. We have >99% power to detect a difference in fidelity outcomes between arms.

For **Aim 2**, we will compare HIV service uptake outcomes between the enhanced and standard implementation arms. Outcomes will include indexes who participate in ACT, contacts elicited, HIV self-test kits distributed, contacts tested, and contacts identified as HIV positive. We have $\geq$80-85% power to detect a difference in each of the outcomes of interest between randomization arms.

For **Aim 3**, we will compare the cost-related outcomes between the enhanced and standard implementation arms through cost-effectiveness analyses.

Risks/benefits to subjects

Risks: Risks are minimal for health workers and patients. For individuals participating in this study, there is a potential risk of breach of confidentiality as well as a risk of discomfort related to participation. Breach of confidentiality may occur if unique identifiers in datasets are linked back to personal identifiers. This is highly unlikely and measures will be taken to ensure that this does not occur. There is also a risk of discomfort with participation, but this is expected to be rare and minor.

Benefits: Health workers may gain new knowledge and skills that make them better ACT providers or enhance their counseling skills. They may also enjoy the different study activities, such as discussing the ACT program in focus groups or interviews. Individual patients may enjoy exit interviews. This research is designed to create generalizable knowledge and enhance HIV programs in Malawi.

Costs/compensation

Health workers will receive the local equivalent of US$10 as compensation for study visits. Patients will receive the local equivalent of US$10 as compensation for their participation.

Confidentiality assurances

Measures will be taken to minimize the risks of breached confidentiality and participant discomfort. All study-related activities will occur in private locations. To protect participants against risks associated with sensitive topics, they will be reminded that their answers to study questions will be kept confidential and that this information will not be shared with anyone. They will be allowed to refuse to answer certain questions.

Clusters and participants will all be given unique ID numbers and all data will not contain any personal identifiers. Electronic data will either be collected using an encrypted device or entered into a password-protected database by a trained data entry clerk. Electronic data will be stored on secure, password-protected servers. All paper-based data, such as signed consent forms, will be stored in locked filing cabinets in locked rooms. Data will be stored following the termination of study completion and then destroyed.

No subjects will be identified in any report or publication about this study. In some cases, information in this research study could be reviewed by representatives of the University of North Carolina, research sponsors, or Malawi government agencies for purposes such as quality control or safety. We may present de-identified data for open access publications.

Conflict of interest

There are no conflicts of interest.

Collaborative agreements

We will also seek approval from University of North Carolina at Chapel Hill Institutional Review Board (IRB).

Intended use of results

The results of the study will be presented at international and local scientific meetings and published in scientific journals. The results will also be submitted to the NHSRC. The information collected in this study may lead to scale up of this implementation package in Malawi and beyond.

PROTOCOL

Title

Enhancing HIV assisted contact tracing in Malawi through blended learning: an implementation science study

Abstract

Voluntary assisted contact tracing (ACT) is an evidence-based approach that efficiently identifies persons in need of HIV treatment and prevention. Malawi, like many countries in sub-Saharan Africa, has adopted ACT policies to support its "95-95-95" targets for HIV testing, treatment, and viral suppression. However, Malawi's ACT implementation has been poor due to deficits in health worker capacity and clinical coordination. Through preliminary work, our team has developed a theory-based health worker training and continuous quality improvement process that addresses these barriers using a "blended learning" platform that combines digital and face-to-face modalities. This training package was field-tested in Malawi with promising preliminary results. In this proposal, the package will be rigorously evaluated in Malawi for implementation, service uptake, and cost-effectiveness outcomes. This is a two-arm pragmatic cluster randomized implementation trial (n=33 clusters) to compare the enhanced implementation package to standard package. There are three objectives: determine whether the intervention enhances ACT implementation (Aim 1), determine whether the intervention increases HIV service uptake (Aim 2), and determine whether the intervention is cost-effective (Aim 3). The findings will offer important insights and innovations into how to bridge the gap between ACT research and practice, a critical step towards achieving the 95-95-95 targets.

Background and justification

Despite progress towards the UNAIDS "95-95-95" targets (95% of HIV-positive persons tested, 95% of tested persons on treatment, and 95% of treated persons virally suppressed), a large gap remains in achieving the first 95% target.[1] In sub-Saharan Africa, 81% of HIV-positive persons know their HIV status, leaving 4.9 million persons undiagnosed.[1] Index-based interventions, in which HIV-positive "indexes" recruit their "contacts" (sexual partners and children) for HIV testing, efficiently identify HIV-positive persons in need of HIV treatment and HIV-negative persons in need of HIV prevention.[2] In a randomized trial in Malawi, our team found that an assisted index-based approach, in which lay health workers traced contacts, led to 22% more contacts tested than a passive approach, which relied on patient recruitment.[3] The assisted approach also led to more HIV-positive contacts linked to HIV treatment, more HIV-negative contacts using condoms, and improved index retention in HIV care.[3, 4] In 2016, based on these and other compelling findings,[5-8] the World Health Organization (WHO) issued guidelines strongly recommending voluntary Assisted Contact Tracing (ACT) and the President's Emergency Plan for AIDS Relief (PEPFAR) has vigorously promoted ACT.[9, 10] Many countries, including Malawi, have begun national ACT implementation.[10, 11] However, ACT outcomes in routine programs have been worse than those in trials.[11] In our initial ACT trial in Malawi, 74% of contacts received HIV testing compared to 13% in Malawi's national program.[12] Rigorous implementation science is needed to optimize ACT in routine programs.

Through formative work guided by the Consolidated Framework on Implementation Research,[13] our team identified deficits in health worker counseling capacity and clinical coordination as the key determinants of poor ACT implementation in Malawi. At the health worker level, the need for ongoing ACT capacity-building was identified as critical. To address this, we developed an enhanced skill-building training guided by the theory of expertise[14] and social cognitive theory[15] which included: a) explanations of ACT skills; b) observations of modeled ACT skills, c) practice through ACT role-plays, and d) structured feedback. At the facility level, the need for greater coordination between health workers was identified as a key deficit. To address this deficit, we adapted a problem-solving process guided by continuous quality improvement principles.[16] When this enhanced implementation package (training and problem-solving) was implemented with 500 health workers in 36 facilities, the number of sexual contacts elicited, tested, and identified as HIV-positive all doubled.[17]

In spite of these encouraging findings, we sought an alternative delivery modality to improve the scalability and sustainability of the enhanced implementation package. Digital packaging with a blended learning approach was a promising delivery modality. Blended learning is promoted by the WHO for health worker in-service training in low- and middle-income countries (LMIC).[18] These modalities blend the best features of electronic learning (e.g. quality, consistency, and convenience) with the best features of face-to-face learning (i.e. group engagement, interactivity, and feedback). Blended approaches are typically more effective than either face-to-face or digital modalities alone for improving health worker knowledge and skills.[19-21] In spite of these favorable characteristics, blended learning has never been rigorously evaluated for a full range of implementation, service uptake, and cost-effectiveness outcomes in a LMIC setting.[18] Guided by principles of human-centered design thinking,[22-24] we adapted our ACT implementation strategies into a tablet-guided blended learning package for facility-level use. When pilot-tested in six Malawian health facilities, we observed substantial increases in both health worker fidelity to ACT counseling procedures and the mean number of contacts tested. In "Enhancing HIV assisted contact tracing in Malawi through blended learning: an implementation science study," we will assess this blended learning package using the RE-AIM framework.[25]

Literature review

Although 81% of HIV-positive persons in sub-Saharan Africa (SSA) are now aware of their HIV status, 4.9 million persons remain undiagnosed and half a million HIV-exposed infants do not receive timely early infant diagnosis each year.[1, 26-28] Furthermore, a large share of HIV-negative adults remain unaware of being in HIV-discordant relationships, and less likely to use effective HIV prevention strategies.[29, 30] Index-based approaches, in which HIV-positive "indexes" recruit their "contacts" (sexual partners and children) for HIV testing, efficiently identify other HIV-positive persons in need of HIV treatment and HIV-negative persons in need of HIV prevention.[2] Index-based approaches have higher diagnostic yields than any other testing approach[2, 11] and hold promise for achieving the global target of 95% of HIV-positive persons tested for HIV.[31]

Voluntary assisted contact tracing: "Assisted" index-based approaches, in which health workers support indexes with contact recruitment, are more effective at identifying contacts tested than "passive" approaches, which rely on patient recruitment.[3] Assisted approaches also lead to more HIV-positive contacts linked to HIV treatment, more HIV-negative contacts using condoms, and improved index retention in HIV care.[3, 4] In 2016, based on these and other compelling findings,[5-8] the World Health Organization (WHO) issued guidelines recommending the implementation of voluntary Assisted Contact Tracing (ACT) and the President's Emergency Plan for AIDS Relief (PEPFAR) has vigorously promoted ACT.[9, 10] Many countries, including Malawi, have adopted ACT policies and intensified ACT implementation.[10, 11, 32] However in most settings, routine ACT outcomes have been inferior to ACT trial outcomes. For example, in our Malawi-based ACT trial, 74% of sexual contacts received HIV testing and 72% were HIV-positive.[3] Thus, it took two indexes to find one new HIV-positive contact. In contrast, in Malawi's national ACT program, 13% of contacts received HIV testing[12] and 17% were HIV-positive, thus requiring 45 indexes to find one new HIV-positive contact.

Barriers and facilitators to ACT implementation in Malawi: To characterize the barriers and facilitators to implementation in the Malawian context, our research team used the Consolidated Framework on Implementation Research (CFIR).[13, 33-35] The CFIR is a determinants framework comprised of five domains (intervention characteristics, individual characteristics, outer and inner organizational settings, and processes) and 39 constructs within these domains that interact with one another.[13] With respect to intervention characteristics, complexity of ACT implementation was identified as a formidable barrier due to sensitivities around discussing sexual behavior with indexes, multiple potential contacts for each index, multiple tracing options for each contact, challenges with obtaining correct locator information for sexual contacts, and concerns around index safety. This level of complexity, along with the minimal pre-service training of lay health workers delivering ACT,[36] exposed a set of individual characteristics: low competence and self-efficacy among both health workers and supervisors. For example, health workers expressed discomfort eliciting sexual partners and helping indexes decide which tracing method to select. Supervisors suggested that modeling these counseling behaviors would enhance skills, but were uncomfortable doing it themselves. In the outer setting, diverse patient needs of both indexes and contacts were not being met, as counseling was conducted generically in a non-client-centered manner. Networks and communication were identified as challenges in the inner setting: health workers in many parts of a single health facility (e.g., antenatal care, pediatrics, ART) interacted with potential indexes and contacts, but responsibilities were not clearly delineated and coordination between health workers was minimal. To address these challenges, several processes were proposed: training that consisted of engaging strategies (role modeling) and planning strategies (practice and feedback) to address perceived intervention complexity, low health worker competence and self-efficacy, and patient needs. To address network and communication challenges, group problem-solving approaches that incorporated reflection and evaluation were suggested.

Lessons from other ACT programs in SSA: The facilitators we identified using the CFIR closely mirrored findings from successful ACT programs in SSA.[37] In 2017-2018, contacts form Kenya and Mozambique accounted for 51% of the 1.7 million contacts tested across eighteen SSA PEPFAR countries, even though these countries only accounted for 14% of the population. Similarly, several Cameroonian districts scaled and sustained ACT before the WHO guidelines were published.[38, 39] In an analysis of ACT implementation in these countries, the intensive ongoing nature of health worker capacity-building was essential.[37] Although the implementation contexts differed, capacity-building processes were similar. Initial face-to-face trainings imparted ACT

counseling skills through skill-based learning and practice role-plays. Ongoing on-the-job mentorship and refresher trainings reinforced and enhanced these skills, consistent with regional capacity-building best practices.[40-42] Routine monitoring and evaluation of implementation allowed for identification of challenges and improvements.

Developing an enhanced ACT implementation strategy: From these findings, we arrived at two sets of implementation strategies: 1) enhanced health worker training to improve ACT competence and 2) group problem-solving grounded in continuous quality improvement principles to facilitate ACT coordination. This set of strategies aligns with a seminal review showing the combination of training and group problem-solving consistently and meaningfully improves health worker practices in low and middle income countries (LMIC).[43] Our specific training and problem-solving approaches were guided by theory and evidence:

Training is the most common implementation strategy in LMICs, but is often conducted with suboptimal pedagogical practices and without any ongoing reinforcement.[43] We developed a training guided by the theory of expertise,[14] an educational theory which considers deliberate practice and a core set of activities (learning, observing, practicing, and receiving feedback) as essential for mastery.[44-46] Applying this theory to ACT, we developed a set of training activities consisting of: a) explaining ACT counseling skills (learning), b) modeling ACT counseling skills through vignettes (observing), c) practicing counseling skills through role-plays (practice), and d) providing suggestions on improvement (feedback). This approach is supported by social cognitive theory, which posits that learning occurs in a social context with reciprocal interactions between the person, environment, and behavior.[15] Observation of modeled ACT vignettes facilitates social learning; practice solidifies behavioral skills and enhances self-efficacy; and feedback refines and reinforces behavioral skills. These activities have enhanced counseling skills across a range of behavioral interventions, including those related to HIV treatment, prevention, and psychosocial support.[20, 47-50] Group problem-solving draws on concepts from continuous quality improvement (CQI), a set of formal and systematic processes to identify and address health systems challenges.[51, 52] Similar processes have led to improvements in a range of outcomes in several SSA contexts, including with lay cadres. [53-58]

Using blended learning to promote scalability and sustainability: We evaluated the strategies outlined above in Mangochi, Malawi and demonstrated improved service uptake.[17] While these strategies were effective, scaling and sustaining them posed a challenge. We hypothesized that delivering these effective strategies using a digital platform would make them more scalable and sustainable.[59, 60] In recent years, digital learning has proliferated in the health sector, including in LMIC contexts, due to many enticing features: 1) learning is not time- or place-dependent; 2) learning does not require an on-site instructor; 3) pace and degree of difficulty can be tailored to each learner; 4) progress and aptitude can be easily monitored; 5) high quality content can be delivered consistently; and 6) infrastructure needs are minimal.[19, 21, 61-66] For in-service training in LMIC contexts, these features are appealing. Digital learning can be delivered at the health facility, eliminating travel and lodging expenses associated with centralized face-to-face trainings. Individual sessions can be delivered asynchronously so all staff are not absent from the clinic simultaneously, minimizing understaffing. New staff can acquire necessary skills right away, rather than waiting for a scheduled training. Health workers can further receive high quality instruction without relying on a highly skilled trainer.[67, 68] The WHO has promoted the incorporation of digital modalities for training health workers in LMICs, but suggests complementing, rather than replacing, face-to-face learning.[18, 69] These "blended learning" approaches combine the best features of digital learning (i.e. quality, consistency, convenience) with the best features of face-to-face learning (i.e. interactivity, group engagement).[64-66] They are typically more effective than either electronic or face-to-face learning alone for acquiring new knowledge and skills,[19, 20] and are promising modalities for improving health worker counseling and communication.[70-73]

Delivering ACT training through blended learning modalities:
To facilitate meaningful and sustainable blended learning programs, technological, human, and cost features must be taken into consideration. We used human-centered design thinking to guide the adaptation of our effective ACT implementation strategies into a blended learning delivery platform.[22, 23] Human-centered design thinking is

an approach that integrates the possibilities of technology, the preferences of people, and the requirements for business viability.[24] Applied to rural Malawian health facilities, we identified important technological challenges, including limited internet connectivity, limited computer literacy, and non-universal personal mobile devices.[74, 75] These considerations led us to develop tablet-based content that did not require continuous internet connectivity for functionality. We provided the tablets. To address desirability for Malawian health workers, we developed content that was primarily audio- or video-based to ensure ease of use for this low literacy audience.[21] All content was delivered with Malawian cultural and linguistic considerations in mind. Content was divided into modules and sub-modules to enable learning to occur in brief segments when workload permits. Finally, with respect to business aspects, we selected tablets, which are less costly than laptops. We opted for simple visuals and basic editing to limit the budget. For blended learning packages to be cost-effective, it is important to minimize up-front development costs, maximize the number of users, or, preferably, do both simultaneously.[76-78] The final blended learning product was pilot-tested with promising preliminary results. The next step is to rigorously evaluate the blended learning ACT package at scale for a broader range of outcomes.

Overarching objective and specific aims/study objectives

The overarching objective is to determine whether an enhanced "blended learning" approach is an implementable, effective, and cost-effective modality for building health worker capacity for voluntary assisted contact tracing. This study has three specific aims:

Aim/Objective 1: To compare the standard and enhanced arms for ACT implementation outcomes. Health worker fidelity to ACT counseling procedures will be assessed through audio-recorded encounters between health workers and indexes and between health workers and contacts.

Aim/Objective 2: To assess the impact of the enhanced versus standard arms on ACT service uptake, including HIV-positive indexes identified, contacts elicited, self-test kits distributed, contacts tested, and HIV-positive contacts identified.

Aim/Objective 3: To evaluate the cost-effectiveness of the enhanced versus standard arms. Using a hybrid decision tree/Markov model and prospectively collected cost data, we will estimate cost-effectiveness

Study design and outcomes

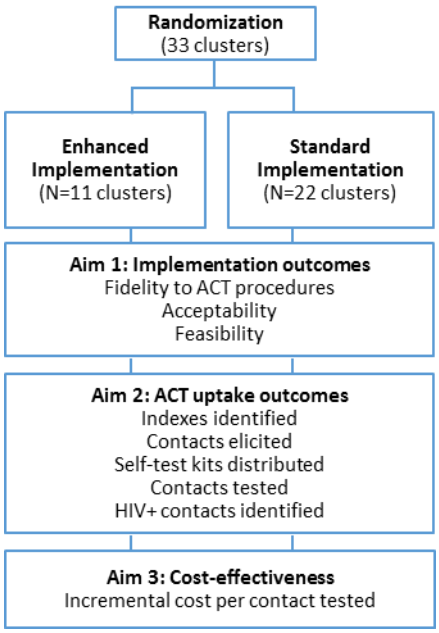


Figure 1.Study design and aims

This is a 2-arm pragmatic cluster RCT comparing an enhanced blended learning implementation package to a standard implementation package. The study will be conducted at 34 Tingathe-supported health facilities in Machinga and Balaka, Malawi. Thirty-two of these facility will be considered unique clusters and 2 facilities will be combined to create a 33rd cluster. These 33 clusters will be randomized in a 2:1 ratio to the standard versus enhanced arms. All 33 clusters will receive the standard of care. Additionally, 11 of these clusters will receive an enhanced blended learning training (quarter 0) and enhanced facility support throughout quarters 1-4. Three sets of outcomes will be compared between the standard and enhanced arm over one year: implementation outcomes, service uptake outcomes, and cost-effectiveness outcomes.

For **Aim 1**, the primary outcome is health worker fidelity to ACT counseling procedures.

For **Aim 2**, the ACT cascade will be examined: indexes identified, contacts elicited, HIV self-test kits distributed, contacts tested, and contacts identified as HIV-positive.

For **Aim 3**, we will compare the cost effectiveness between the enhanced and standard implementation arms through cost-effectiveness analyses.

The 22 standard of care sites will receive the enhanced implementation package after the initial cluster RCT period ends. All 33 sites will remain under observation for one additional year. Long-term outcomes will be examined at all 33 clusters through quarter 8 to examine delayed implementation and durability (Figure 2). The main study period will compare all outcomes in A versus B. Additionally, we will examine service uptake outcomes in (A+C+E) compared to (B+D).

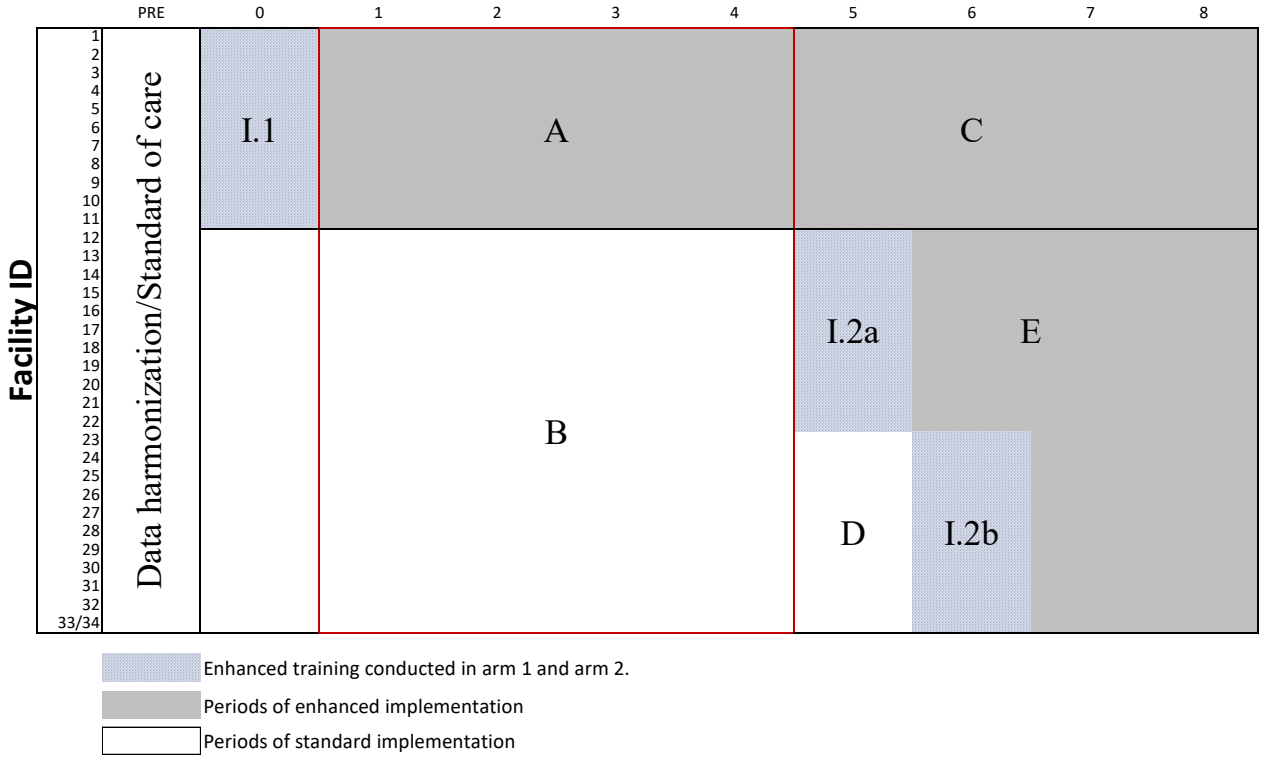


Figure 2. Study schedule

Prior to implementation of the main trial, the blended learning package and all of the study tools will be pilot tested. The purpose of the pilot test is to examine feasibility and acceptability and refine the tools and implementation package for the trial.

Randomization

Machinga and Balaka Districts contain 34 facilities. Two small comparable facilities will be combined to create a total of 33 clusters (a number divisible by 3) to achieve 2:1 randomization. The clusters will be classified into strata of sizes 3, 6, or 9 based on key cluster-level characteristics, including district, facility type (hospital, health center, dispensary), and baseline performance (number of indexes identified) to help ensure balance of facility characteristics between the arms. Within each stratum, clusters will be randomly assigned in a 2:1 ratio to the standard or enhanced arms for the cluster RCT period (quarters 1-4). The facilities and their staff will not be blinded to study arm. However, on certain measures, such as audio-recorded fidelity assessments, coders will be blinded to randomization arm. The randomization schedule will be created by an independent statistician using a random number generator in SAS or comparable program.

Evidence based practice

In implementation science, an important first step is clear identification of the evidence-based practice, which in this case is ACT. In the Malawian context, ACT is a voluntary service which consists of offering support to HIV-positive clients to recruit sexual partners and family members for HIV testing. ACT is simple in theory, but complex in practice. Indexes may be adults or children, newly diagnosed or already on treatment. Adult contacts may be

spouses or casual partners, in heterosexual or same-sex partnerships. For each contact, indexes may select one of four contact recruitment options: 1) passive referral, in which the index invites partners or provides them with a self-test kit; 2) provider referral, in which a health worker recruits contacts; 3) contract referral in which a health worker recruits a contact if passive referral has been unsuccessful, and 4) dual referral in which a health worker supports disclosure to a contact, often in the context of couples HIV counseling and testing.[9] Within a given facility, there are typically multiple possible entry-points for identifying indexes, including antenatal care, outpatient departments, labor and delivery wards, pediatrics, and HIV care clinics. The diversity of indexes and contacts (often with sensitive family and sexual dynamics) and the range of recruitment options give rise to a complex set of counseling tasks for health workers. Similarly, the multiple entry points for indexes and contacts pose coordination challenges throughout the facility.

Implementation strategies

Standard implementation

All facilities participating in the study will receive standard ACT implementation strategies. In Malawi, the standard ACT implementation strategies consist of 1) an introductory, brief ACT training, and 2) routine monthly supervisory activities by an implementing partner like Tingathe. The training is centralized and conducted in-person. It occurs one time, is primarily didactic, and provides an overview of ACT procedures and counseling approaches. Tingathe provides routine monthly supervision to all facilities for all of its supported activities, including HIV testing, ART provision, and viral load monitoring, in addition to ACT. In this standard implementation condition, the study will not alter anything.

Enhanced implementation

In addition to receiving the standard implementation strategies described above, the 11 clusters randomly assigned to the enhanced implementation arm will 1) receive the blended learning training and 2) participate in continuous quality improvement (CQI) processes. Unlike the standard training, the blended learning training is designed for decentralized delivery at the facility level. The content of the blended learning package builds on the themes described in the standard training. The training contains modules with individual asynchronous learning sessions and a synchronous interactive small-group session. The individual learning sessions contains descriptions of ACT skills, vignettes modeling these skills, and embedded comprehension questions. The small-group learning session contains practice role-plays, individual feedback, and facilitated group discussions. All training activities are documented in the tablet. To complement the training, all health workers involved in ACT will participate in ongoing problem solving examine their facility's ACT performance, identify gaps, and work towards actionable solutions. These activities will be guided by and documented in the tablet.

Study Setting

The study will be conducted in Malawi, a country in Southeastern Africa with 19 million people. Malawi has a 10.6% adult HIV prevalence and 1.1 million people living with HIV.[79] Malawi has a mature HIV program that is approaching the 95-95-95 targets. In the first Malawi Population-based HIV Impact Assessment (MPHIA), an estimated 77% of HIV-positive adults were aware of their HIV status, 91% of these adults were on treatment, and 91% of those on treatment were virally suppressed.[79]

The study will be conducted in 34 health facilities that are supported by the Tingathe Program, the organization that will lead study implementation. The Tingathe Program is one of the three largest PEPFAR implementing partners in Malawi. Tingathe was initiated by Baylor College of Medicine Children's Foundation-Malawi in partnership with the Malawi Ministry of Health (MOH). Tingathe takes a family-focused approach to the HIV epidemic by supporting the provision of high-quality, comprehensive HIV services. Tingathe has over 10 years of experience implementing HIV testing, care, and treatment programs in Malawi and currently provides support to Malawi's HIV care and treatment program with more than 1,000 staff in 130 MOH facilities.

Malawi has a dire human resource shortage with fewer than 2 physicians, 0.02 psychiatrists, and 0.01 psychologists per 100,000 people, some of the lowest global rates.[80, 81] To address its formidable HIV burden with limited human

resources, Malawi has task-shifted many HIV-related activities, especially counseling tasks, to lay cadres. In 2015, to respond to gaps in HIV testing, Malawi introduced a cadre of HIV diagnostic assistants to improve coverage of early infant diagnosis, viral load testing, and rapid HIV antibody testing.[36] HIV diagnostic assistants are lay persons with secondary education and four weeks of pre-service training. In its first year, nearly 1200 HIV diagnostic assistants were deployed to 450 facilities, resulting in improved diagnostic indicators.[36] PEPFAR implementing partners, including Tingathe, have been integral in supervising this cadre. Tingathe also supervises community health workers who are responsible for a range of HIV-related tasks, including community tracing. HIV diagnostic assistants and community health workers conduct most ACT implementation.[82] HIV diagnostic assistants typically diagnose HIV-positive indexes and support contact elicitation and selection of ACT options and community health workers typically conduct tracing.

Populations, Eligibility Criteria, and Sample Sizes

At each facility, two study populations will be enrolled: health workers and patients (indexes and contacts). Within each participating facility, we will recruit health workers, along with a subset of indexes and contacts (patients). Sample sizes were determined by conducting empirical power simulations using data from all 34 Tingathe-supported facilities in Machinga and Balaka from 2019-2020. See power calculations in analytic sections.

Health workers will be eligible for study participation if they are: (a) 18 years of age or older, (b) working full-time at one of the health facilities included in the study, and (c) staff in Malawi's Assisted Contact Tracing program. Persons who do not meet these criteria will be excluded. We will aim to enroll at least 2 health workers per cluster for a minimum of 66 health workers in the study, though we may enroll up to 400 health workers. In addition, in the pilot test, up to 20 health care workers will be enrolled. Persons will be excluded for conditions that in the opinion of the study investigator would compromise the ability of the participant to provide informed consent, undergo study procedures safely, or would prevent proper conduct of the study.

Recruitment of health workers from included facilities will occur primarily at the beginning of the study, but will remain open to health workers who become eligible at any point in the two-year period. This may include health workers at the same facility who rotate into new roles or health workers from other facilities who transfer in. All health workers at a given facility who are involved in ACT will be invited to participate in the study, and a member of the study team will engage potential participants in a brief conversation about the purpose, nature, and duration of the study.

Patients will be eligible for study participation if they are: (a) 15 years of age or older; (b) a potential index, contact, or the parent/guardian of a pediatric index or contact. Persons who do not meet these criteria will be excluded. We will enroll up to 600 indexes and 200 contacts over the study period. Persons will also be excluded for conditions that in the opinion of the study investigator would compromise the ability of the participant to provide informed consent (e.g. not understanding Chichewa), undergo study procedures safely, or would prevent proper conduct of the study. In the pilot test, an additional 30 patients may be enrolled.

Recruitment of patients (indexes and contacts) is expected to occur at each facility during the study period. The study team will be assigned to spend time at each facility and will approach potential indexes and contacts about participation in the study. Study team members will be trained in effective communication techniques and will engage the potential participants in brief conversations about the purpose, nature, and duration of the study. If interested, potential participants will be offered the opportunity to provide informed consent, and those who consent will be enrolled.

Procedures

	Pre	Q0	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
Facility survey (FS)		X								
SOC training	X									
Data harmonization		X								
Randomization		X								
Enhanced training Adoption/adherence (AD)		11 clusters					11 clusters	11 clusters		
SOC implementation			X	X	X	X	X	X	X	X
Enhanced implementation			11 Clusters	11 clusters	11 clusters	11 clusters	22 clusters	33 clusters	33 clusters	33 clusters
Service uptake			X	X	X	X	X	X	X	X
HCW consent	X									
HCW surveys	X		X			X				
Simulated fidelity		X	X							
Authentic fidelity			X	X	X	X				
Exit interviews			X	X	X	X				
Time and motion			X	X	X	X				
Focus groups/in-depth interviews	~8 clusters		~8 clusters			~8 clusters				

Facilities will participate in the following procedures**:**

Pre-trial

- All sites will have standard of care training

Quarter 0

- A facility survey will be conducted
- Data harmonization will occur to ensure all facilities are collecting the same data in the same way.
- All facilities will be randomized to one of the two study arms
- 11 sites randomized to the enhanced arm will receive enhanced blended learning training package

Quarters 1-4

- All ACT procedures will be conducted and service uptake data will be collected
- All clusters will receive standard of care implementation
- 11 clusters will receive enhanced implementation

Quarters 5-8

- All ACT procedures will be conducted and service uptake data will be collected
- 11 clusters randomized to the standard arm will receive enhanced package (Q5)
- 11 clusters randomized to the standard arm will receive enhanced package (Q6)

Health care workers (e.g. HDAs, CHWs, etc.) will participate in the following procedures:

Pre-trial

- At the time of recruitment, health workers will be offered the opportunity to provide informed consent. Those who provide informed consent will complete the remaining study procedures.
- All participating health workers will be assigned a unique study ID number.
- They will fill out HCW survey 1
- Some will be purposively invited to participate in IDIs and/or FGDs

Quarter 1

- HCW Survey 2

- Simulated fidelity assessments
- Some will be purposively invited to participate in IDIs/FGDs
- Health workers may be selected for authentic fidelity assessments throughout the study period. In these assessments, their interactions with indexes and contacts will be recorded.
- Health workers will be observed for time-motion assessments for the costing component.

Quarters 2-4

- HCW Survey 3
- Health workers may be selected for fidelity assessments throughout the study period. In these assessments, their interactions with indexes and contacts will be recorded.
- Health workers will be observed for time-motion assessments for the costing component.
- Some will be purposively invited to participate in IDIs/FGDs in ~quarter 4

Patients (indexes and contacts) will participate in the following study activities (Quarters 1-4):

- At the time of recruitment, patients will be offered the opportunity to provide informed consent. Those who provide informed consent will complete the remaining procedures.
- All participating patients will be assigned a unique study ID number. This ID will be used, rather than personal identifiers.
- Patients will have their ACT counseling session audio-recorded for the fidelity assessment. The purpose of the audio-recorded session is to evaluate the quality and thoroughness with which the counselor conducts the session.
- Patients will then complete an exit interview. The goal of the exit interview is to learn about acceptability and the patient's experience of their session. This exit interview will contain basic demographic questions and questions about the encounter. It will also contain questions to inform the costing components of the study.
- Record abstraction will be conducted to learn about the impact of the study on their care-seeking.

Procedures in the context of COVID-19

Over the course of the study period, we will continue or suspend study procedures in accordance with guidance from the sponsor, NHSRC, UNC IRB, WHO, and the Government of Malawi in response to the evolving COVID-19 situation. We will be flexible with procedures to maximize the safety of study staff and participants and ensure scientific integrity.

Where necessary and appropriate, we will conduct in-person procedures using precautions intended to safeguard the study staff and participants. These precautions may include: having study staff wear personal protective equipment (PPE) when interacting with attending participants; screening study staff and participants for COVID-19 using temperature and a symptom questionnaire. Additionally, we will be flexible on the timing, location, and modality of study activities. We may go to the community to conduct procedures if this is deemed safer than clinic-based activities, use electronic platforms like video-conferencing or voice calls as needed, and conduct certain activities at earlier or later times if needed. Social distancing will be practiced. This applies to both programmatic activities (e.g. implementation) and research activities (e.g. assessments).

Data collection

All data will be collected by trained research assistants with certifications in human subject protections and good clinical practices. Electronic data will either be collected on an encrypted device or entered into a password-protected database by a trained data entry clerk on an encrypted computer. Electronic data will be stored on secure, password-protected servers. Paper-based data will be stored in locked filing cabinets in locked rooms.

Data sources

The following data sources will be used to collect study outcomes. All forms may undergo modification in content or timing of administration following pilot testing:

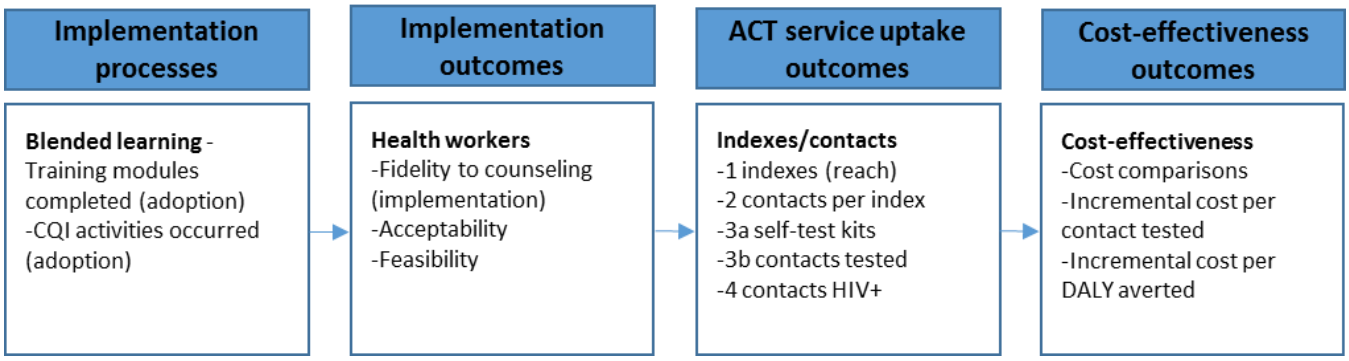
- **Facility survey:** This tool will capture facility characteristics, including staffing, space, and ACT practices, as well as available modes of communication and transportation.
- **HCW surveys:** This tool will capture key characteristics of health care workers enrolled in the study, including: demographics, technological literacy and attitudes, professional and training history, time spent on ACT, attitudes towards PLHIV; and knowledge, attitudes, and practices surrounding ACT.
- **Blended learning monitoring records:** These data and meta-data, generated from blended learning modules, will monitor blended learning adoption. These data will only be available in the enhanced arm and will monitor blended learning adoption.
- **Authentic fidelity assessments/simulated fidelity assessments:** These assessments will be completed by the study team to document fidelity to ACT counseling between health workers and indexes/contacts based on audio-recordings with clients (authentic) or actors (simulated).
- **Patient exit interviews:** These will be collected by the study team to document index and contact acceptability, as well as intentions, anticipated stigma, and perceived health worker respect.
- **Focus group discussion and in-depth-interview transcripts:** These will be collected by the study team to understand health worker acceptability and feasibility, as well as attitudes towards PLHIV.
- **HIV testing registers:** These are facility-level documents with all persons tested, as well as age, gender, and HIV status. This data source will contribute to the total number of potential indexes.
- **Index registers:** These are routine program documents that contain a list of all persons offered ACT services. They include index information. This will contribute to service uptake outcomes.
- **Contact registers:** These are routine program documents that contain a list of all persons offered ACT services. They include a list of contacts, whether testing occurred, and HIV status. This will contribute to service uptake outcomes.
- **Time and motion survey:** These will be collected by the study team to document the amount of time health workers spend on ACT activities.

Data elements

Data element	Description	Population and Frequency	Approximate Timing	Source
Implementation and cost outcomes				
Enhanced arm Adoption/adherence (AD)	Completion of all modules and CQI activities. (Fidelity to the implementation intervention)	All enrolled health care workers in enhanced arm (N=11 facilities x ~2+ HCWs/facility=~22+ *This will be examined in the SOC arms when enhanced implementation strategy is rolled out.	1— Q.0 2a—Q.5* 2b—Q.6*	Module completion data (SurveyCTO)
Facility survey (FS)	Staffing, services, tracing modalities, volume, characteristics.	All clusters (N=33 x 2-6 times)	Q.0, 4	facility survey (SurveyCTO)
Simulated fidelity assessments (SFA)	-Observe HCW conducting simulated index and/or contact encounter	Health care workers (N=33 clusters x ~2+ HCWs/facility=66+)	Q.0-1	Fidelity assessment tool (paper to SurveyCTO)
Health care worker (provider) survey	-Demographics, cadre, technology literacy, knowledge, attitudes, practices, aptitudes, past training, time spent on ACT activities	All enrolled health care workers (N=33 clusters x ~2+ HCWs/cluster=66+)	PRE Q.1 Q.4	Provider survey (SurveyCTO)
Focus group discussions (FGDs)/In depth interviews (IDIs)	-Learn about HCW feasibility and acceptability Compare SOC to ENH and PRE/Q1/Q4	Health care workers (N=8 groups x 3 times~=24 FGDs) (N=3 IDIx x 8 facilities x 3 times~=72 IDIs)	PRE Q.1 Q.4	Semi-structured guides (audio recording) (Survey CTO to document participants and timing)
Fidelity Assessments (FA)	-Observe HCW conducting true index and/or contact encounters	Health care workers, indexes, contacts ((N= 33 cluster x minimum of 2 indexes/cluster=66-600) (N= 33 cluster x minimum of 2 contacts/cluster=66-200)	Q.1-4	Fidelity assessment tool (audio recording to paper to SurveyCTO)
Index exit interviews Contact exit interviews (XIs)	-Examine index acceptability -Examine contact acceptability	Indexes and contacts: (N= 33 cluster x minimum of 2 indexes/cluster=66-600) (N= 33 cluster x minimum of 2 contacts/cluster=66-200)	Q.1-4	Index exit interview (SurveyCTO)
Time and motion assessment (TM)	-Assess the effort to which HCWs work on each activity	Health care workers N=(~2-3/cluster x 33 facilities=66-100 days of observation)	Q.1-4	Time and motion survey (paper to SurveyCTO)
Effectiveness outcomes (EF)				
Total potential indexes	#ART patients who were supposed to be assessed per quarter plus the #new HIV+ patients per quarter	N=33 clusters x 8 quarters=264	Q.1-8	ART and HTS registers HTS registers (register to SurveyCTO)
# indexes, #contacts elicited, # STKs distributed	Number of indexes captured, contacts elicited and STKs distributed	N=33 clusters x 8 quarters=264	Q.1-8	Index and contact registers
# contacts tested # HIV+ contacts	Number of contacts returned and the proportion HIV+	N=33 clusters x 8 quarters=264	Q.1-8	Index and contact registers

Evaluation framework

Consistent with implementation science best practices,[13, 37, 38] we have used an evaluation framework, RE-AIM, to guide analysis. [93, 94] The five RE-AIM constructs—Reach, Effectiveness, Adoption, Implementation, and Maintenance—align with our research questions. Reach, persons receiving the intervention, will be measured by the rate of potential indexes who are offered ACT. Effectiveness, the ability of an intervention to impact outcomes, will be measured by a range of service uptake outcomes. In addition, positive and negative aspects of index and contact experiences will be measured through exit interviews. Adoption will be measured by the proportion of the enhanced implementation package completed per site. Implementation will be assessed through fidelity assessments, measuring how well health workers adhere to counseling protocols. Maintenance, the degree to which a program becomes part of routine organizational practice, will be examined through the consistency in the other outcomes (effectiveness and implementation) over time. In addition, we expect to explore how the five RE-AIM domains relate to one another (Figure 8).[83, 84] We hypothesize that adoption of blended learning activities will lead to better implementation and reach which, in turn, will lead to greater ACT effectiveness, and ultimately maintenance (sustainability) over time.



Aim 1 Analytic methods and power calculations (implementation outcomes)

In Aim 1, we will compare the implementation outcomes of the enhanced and standard arms. The primary hypothesis is that fidelity to counseling procedures will be better in the enhanced arm than the standard arm.

Primary outcome of interest (fidelity): The primary implementation outcome of interest is health worker fidelity to ACT counseling procedures. This was selected as the primary implementation outcome because the enhanced training directly targets this outcome. Fidelity will be assessed using a 15-item scale assessing the quality, completeness, and adherence to ACT procedures with raw scores ranging from 0-30 (and recalculated as 0 to 100 percentage points).

At each of the 33 clusters, at least 2 ACT encounters between health workers and indexes at least 2 ACT encounters between health workers and contacts will be audio-recorded. A minimum of 132 observations total are needed for both indexes and contacts (4/per cluster), but up to 200 contact encounters and 600 index encounters may be conducted. For indexes, attempts will be made to achieve balance between recruitment from the ART and HTS settings. For contacts, attempts will be made to achieve balance between the clinic and community settings.

Each audio-recording will be scored by two research officers blinded to the study arm and the two scores will be averaged. This tool has been field-tested.

Analyses: Generalized estimating equations (GEE) to account for potential correlation at the cluster level will be implemented to compare health worker fidelity scores between the enhanced and standard arms. Models with identity links and normal distributions will be used to compare means between the two arms. A working correlation structure will account for the correlated nature of observations from the same cluster. Models will contain a term for randomization arm. To assess fidelity maintenance over time, we will implement models with an interaction

term between time and randomization arm. To assess differences by setting (indexes: ART vs. HTS; contacts: clinic vs. community), we will implement an interaction term between randomization arm and setting. Indexes and contacts will be analyzed separately. Data from the authentic and simulated fidelity assessments (below) may be combined.

Statistical power and sample size: Sample size calculations are based on data collected during our pilot assessment of provider fidelity. The pilot fidelity score standard deviation, after rescaling to percentage points, was 20.5%. With 132 fidelity assessments from 33 clusters and assuming SD=20.5% and a working correlation estimate of 0.3 or smaller, we will have >99% statistical power to detect a 30 percentage point difference between means (90 versus 60) between the enhanced and standard arms. Even with smaller differences between arms of 15 percentage points (75 versus 60), we have >81% statistical power to detect a difference. Although only 132 authentic fidelity assessments are needed to achieve >80% power, up to 200 authentic fidelity assessments (contact clients) and 600 (index clients) per cluster may be collected to examine trends within sub-groups. Power was calculated by inverting the closed-form sample size equation from section 4.1 of Liu & Liang (1997), where the average cluster size was used in place of n for a reasonable power approximation.

Additional (tertiary/exploratory) implementation outcomes: Exploratory implementation outcomes of interest include simulated fidelity assessments, facility adoption of and adherence to the implementation strategies, health worker feasibility and acceptability, and patient acceptability.

- **Health care worker knowledge, attitudes, practices:** These constructs will be assessed through the health worker survey.
- **Simulated fidelity assessments:** These will be analyzed similarly to the authentic fidelity assessments described above. However, rather than conducting these with real patients and contacts, they will be conducted with actors simulating indexes and contacts. Each enrolled health care workers may participate in staged fidelity assessments with indexes and contacts.
- **Facility adoption/adherence:** This will be assessed as the degree to which all blended learning activities took place in the enhanced arm, including modules viewed, practice sessions completed, feedback provided, and continuous quality improvement conducted. Each participating health worker will receive an adoption score. The facility score will be the mean of the health worker scores. We will analyze whether this adoption/adherence score is associated with fidelity and ACT service uptake outcomes among sites in the enhanced arm. This will allow for a detailed understanding of the relationship between the amount and nature of blended learning activities, as well as continuous quality improvement activities associated with outcomes of interest.
- **Health worker feasibility and acceptability:** This captures the extent to which health workers find the implementation strategy and ACT intervention to be desirable and viable. This will be assessed through a series of three longitudinal focus group discussions (FGDs) and/or in-depth interviews with health workers in approximately 8 facilities ensuring balance between district and study arm. The purpose is to understand experiences with implementation barriers and facilitators. FGDs will be conducted immediately after randomization to learn about pre-study implementation, in quarter 1 to learn about early implementation, and in quarter 4 to learn about implementation maintenance. Each FGD will be conducted with a subset of 2-10 health workers from each facility. Data will be analyzed using thematic content analysis consisting of: 1) reading for content and writing memos, 2) coding, 3) data consolidation to identify key sub-themes, 4) data display, and 5) interpretation.
- **Patient acceptability:** Index and contact acceptability using adapted validated scales of perceived health worker respect and anticipated stigma. This will be the same target population as the authentic fidelity assessments. We will explore the relationships between health worker fidelity and patient acceptability, as well as the relationship between patient acceptability and ACT service uptake outcomes.

Aim 2 Analytic methods and power calculations (HIV service uptake outcomes)

In Aim 2, we will compare the HIV service uptake outcomes between the enhanced and standard arms. The overarching hypothesis is that the enhanced package will lead to a range of improved HIV service uptake outcomes.

Outcomes of interest: Five ACT service uptake outcomes will be measured from index and contact registers on a quarterly basis. Each of these outcomes will be measured as a count per cluster per calendar quarter (three-month period). We will use facility-level data because the facility (i.e. cluster) is the primary unit of randomization. With 33 clusters under observation for four quarters, the facility-level dataset for the primary analyses will contain 132 observations (33 clusters * 4 quarters), 44 observations in the enhanced arm and 88 observations in the standard arm. The full two-year analyses will contain 264 observations (33 clusters * 8 quarters). The following measures will be calculated on a quarterly basis:

- **Total potential indexes:** This is the total number of ART and HTS patients that should be screened for and potentially offered ACT.
- **1: Indexes who participate in ACT:** The number of indexes in the index register.
- **2: Number of contacts elicited:** The number of contacts listed by the participating indexes. Are they put into the index register here?
- **3a: Number of self-test kits distributed:** The number of HIV self-test kits given to indexes for secondary distribution. Often, this is used as a method for testing contacts, rather than presenting to the clinic.
- **3b: Number of contacts tested:** The number of contacts with a recorded HIV test result. These tests are typically performed by a health care worker.
- **4: Number of contacts diagnosed HIV-positive:** The number of contacts in the contact register with an HIV-positive test result.

Analyses: Data from quarters 1 through 4 (the cluster RCT design) will be analyzed using a negative binomial mixed-effects model accounting for quarterly repeated measures within each cluster. Models will use a log link, contain terms for randomization arm, and the natural-log transformed number of potential indexes will be incorporated as an offset term. Key baseline variables of interest, such as district, will be adjusted for. Rate ratios and 95% confidence intervals will be used to estimate the effect sizes and quantify the precision of effect estimates for the main analyses which will compare the enhanced versus standard arms for rates of each service uptake outcome per the total number of potential indexes (5 main endpoints denoted above). Secondary endpoints will take the same approach and use a negative binomial mixed effects model as well. Several secondary endpoints are proportion measures; for those endpoints effect size will be measured using a risk ratio and corresponding 95% confidence interval comparing the enhanced versus standard arms.To assess maintenance, interaction terms between quarters and randomization arm will be included to assess whether effects remain constant, intensify, or diminish over time during quarters 1 through 6.

Statistical power assumption, models, and estimates: Sample size calculations were guided by data from the 33 proposed clusters in the two districts from 2019-2020. In these two districts (Machinga and Balaka), Tingathe supports 34 MOH facilities with implementation of the national HIV program and supervises approximately 150 community health workers and 100 HIV diagnostic assistants. Two nearby facilities in Balaka will be combined for analysis such that the 34 facilities are handled as 33 clusters.

Across these 33 clusters, 4600 persons are diagnosed with HIV each year and another 49,000 are already taking ART. From this, we estimated 35 new HIV-positive diagnoses per cluster per quarter and 372 ART patients per cluster per quarter or approximately 407 total potential indexes per facility per quarter. On average, of these 407 total potential indexes, there were approximately 86 indexes identified (0.21), 97 contacts elicited (0.24), 12 self-test kits distributed (0.03), 25 contacts tested (0.06), and 3 contacts diagnosed as HIV-positive (0.007). These values informed our assumptions for the standard arm.

Power for primary analyses:
Standard power formulas were not equipped for this cluster RCT design due to contingencies in the count outcomes with differing cluster sizes, repeated measures and within-facility correlated data. Thus, for power calculations in Aim 2, we applied these parameters to a simulation study of these facilities in SAS v9.4.[87, 88] The number of total potential indexes per facility per quarter was accounted for as a statistical offset term.[89] The number of total potential

indexes per facility per quarter was generated from a Poisson distribution with a cluster-specific mean. Count values per cluster per quarter for each of 5 outcomes were generated from a negative binomial distribution with the random intercept variance, over-dispersion parameter, and arm-specific rates specified using a generalized linear mixed effects model with a log link. The Poisson facility-specific means, random intercept variances negative binomial over-dispersion parameters, and mean values for the standard arm were estimated from background data. To compute power, the simulated study data were analyzed using a negative binomial mixed-effects model accounting for repeated measures within a cluster. Statistical power was computed using simulation studies of 10,000 cluster RCT datasets. Based on these assumptions, and a significance level α=0.05, we have **80-85% statistical power to detect a difference between the arms for each of the outcomes of interest**.

	Assumed values for empirical power calculations:							
TPI denominators	**Endpoint Rates**		**Effect size**	**Expected counts**		**Nuisance parameters**		**Statistical Power**
Key measures:	**Enhanced**	**Standard**	**RR**	**Enhanced**	**Standard**	**RIV**	**Scale**	
0. Total potential indexes	n/a	n/a	1	407	407			n/a
1. Total indexes	0.3100	0.2113	1.47	126	86	0.0981	0.0854	85%
2. Contacts Elicited	0.3700	0.2383	1.55	151	97	0.1268	0.1880	81%
3a. Self-test kits distributed	0.0650	0.0295	2.20	26	12	0.0001	1.9077	82%
3b. Contacts Tested	0.1247	0.0614	2.03	51	25	0.3340	0.2847	85%
4. HIV+ Contacts Diagnosed	0.0155	0.0074	2.10	6	3	0.3334	0.3039	82%
RR=rate ratio								
RIV = random intercept variance; estimated variance of the random intercept for cluster j								
Scale parameter for the negative binomial mixed-effects model summarizes over-dispersion								
Standard arm counts calculated by averaging background data from Oct 2019-April 2020 and Sep–Nov 2020								
Nominal type I error rate of α=0.05 is used throughout, with no adjustment for multiple endpoints								

Additional service uptake analyses from the trial (tertiary outcomes)

In addition to the primary analyses described above, rather than using total potential indexes as the statistical offset value, an indicator from the previous step of the cascade will be used. Power calculations were conducted for these secondary endpoints as well. The empirical power approach for rate ratios was described for the primary analysis. For proportion endpoints, a logistic mixed-effects model was used to simulate proportion values between [0, 1], and empirical power to detect a given risk ratio was calculated from a log-binomial mixed-effects model analysis.

		Assumed values for empirical power calculations:							
Cascade Denominators	**Type**	**Endpoint Rates**		**Effect size**	**Expected counts**		**Nuisance parameters**		**Statistical Power**
Key measures:		**Enhanced**	**Standard**	**RR**	**Enhanced**	**Standard**	**RIV**	**Scale**	
0. Total potential indexes (TPI)		n/a	n/a	1	407	407			n/a
1. Total indexes (TI)	R	0.3100 per TPI	0.2113 per TPI	1.47	126	86	0.0981	0.0854	85%
2. Contacts Elicited (CE)	R	1.4200 per TI	1.1279 per TI	1.26	179	97	0.0274	0.0658	83%
3a. Self-test kits distributed	P	0.2250 per CE	0.1237 per CE	1.82	40	12	0.4260	n/a	83%
3b. Contacts Tested	P	0.4400 per CE	0.2577 per CE	1.71	79	25	0.5770	n/a	82%
4. HIV+ Contacts Diagnosed	P	0.0770 per TI	0.0349 per TI	2.21	14	3	0.5681	n/a	81%
R = Rate; P = Proportion; RR = rate ratio for rates or risk ratio for proportions;									
RIV = random intercept variance (i.e., estimated variance of the random intercept for each cluster)									
Scale nuisance parameter for the negative binomial mixed-effects model summarizes over-dispersion for rate endpoints									
Standard arm counts are per cluster per quarter and calculated by averaging background data from Oct 2019-April 2020 and Sep-Nov 2020									
Nominal type I error rate of α=0.05 is used throughout, with no adjustment for multiple endpoints									

Temporal trend analyses

In addition to analyzing the primary cluster RCT data described above, we will explore temporal trends. Based on Figure 2, we will examine all of the indicators described above, comparing the periods preceding enhanced implementation (B+D) to the periods following enhanced implementation (A+C+E). Period A will also be compared to period C. In these analyses, the analytic procedures described for the primary and secondary analyses will be followed. These models will have terms for the primary exposure of interest and time.

Aim 3 Analytic methods (Cost-effectiveness)

In Aim 3, we will explore the budget impact and cost-effectiveness of the enhanced and standard approaches. Our modeling will allow us to examine the inherent tradeoffs of the high upfront and ongoing expenditures of the enhanced package with the anticipated future health benefits, such as earlier linkage to care and averted illness that are known to be realized with more effective contact tracing and testing. All analytic decisions will be guided by best practices in implementation economics, a rapidly evolving field.

Cost measurement: We will embed an empirical costing study in our trial. Costs will be collected in two ways: micro-costing and time-motion logs (self-reported and directly observed). Micro-costing will be used to quantify resources associated with the development and implementation of the entire enhanced package. This includes costs of blended learning development, tablets, HIV tests and supplies, travel and telecommunications for tracing, and training expenses. Cost data will be available through contractual information with developers, receipts, and MOH supply chain partners. We will also extract data from project expenditure and management records, including purchase logs and human resources records (e.g. health worker rota), where appropriate. Time-motion assessments in both arms will record staff time and effort on ACT tasks, allowing us to reliably apportion effort expended on ACT activities. This includes health worker and facilitator time spent with the blended learning package and time spent counseling indexes, tracing contacts, and supporting contacts with HIV prevention or treatment services. Data for time-motion logs will be collected by observing staff in each cluster approximately two times. Our research team has conducted these assessments previously. They will be conducted in line with the STAMP checklist (Suggested Time and Motion Procedures).[90-92] Additionally, on the provider survey, health care workers will report estimated time spent on these activities.

We will record this information in structured spreadsheets that document each resource, category, quantity, and unit cost. This comprehensive costing will follow international conventions for costing (i.e. including items for staff, equipment, consumables, and any overhead that are not common to both arms); discounting future costs; and reporting based on accepted practices[93] and guidelines from the Panel on Cost-Effectiveness in Health and Medicine.[94] We will not include any costs related to study-specific activities (e.g. data collection).

We will first conduct a budget impact analysis, comparing total costs associated with the development and implementation of the enhanced implementation strategy to the standard strategy to provide affordability information.[95-97] This will be conducted from the perspective of the health-system, evaluating programmatic costs at a per facility basis. We will initially examine only facilities under observation, but ultimately extrapolate the model to 750 sites that make up Malawi's national HIV program.[98] Due to up-front costs of developing the capacity-building blended learning tool, as the scale and duration of implementation increases and expands, we expect that the cost per facility will decrease.

Cost effectiveness modeling: We will conduct cost-effectiveness analysis, modeling incremental cost effectiveness ratios (ICERs) per contact tested and per HIV-positive patient diagnosed. We may also examine incremental cost per HIV infection averted and per disability adjusted life year (DALY) averted comparing the enhanced to the standard approach. We will construct a hybrid decision-tree/Markov model to reflect the relevant programmatic components and clinical outcomes based on ACT implementation as described above and a literature review of key parameters. This model will first be limited to the trial population, estimating approximately 50,000 total potential index patients in these 33 clusters over one year, and then expanded to the national program—estimating approximately 800,000 potential annual indexes over one, three, and five years. Imbedded Markov models will

account for the health-state trajectories of HIV-positive and HIV-negative contacts, as well as pediatric and adult contacts. All transition probabilities will be informed by mean observed ACT indicators in the trial (base case) with distribution of upper and lower extremes informed by the highest and lowest performing sites. One-way sensitivity will be conducted with all model parameters individually. Probabilistic uncertainty will be conducted using Latin Hypercube Sampling, varying all parameters simultaneously. Analyses will be performed using Excel and the Excel-based add-on, DecisionTree or comparable software.

Additional exploratory analyses of interest

In addition to the three aims described above, a range of exploratory questions and tertiary analyses may be explored relating different indicators to one another. Some examples include:

- Which health worker, patient, and facility characteristics are associated with selection of each type of contact tracing method?
- Which health worker and facility characteristics are associated with improved fidelity?
- Which facility characteristics are associated with adoption and adherence to the implementation intervention?
- Is adoption of and adherence to the implementation intervention associated with improved service uptake?
- Is health worker fidelity associated with patient acceptability?

Ethical and human subjects considerations

Institutional Review Board oversight and informed consent

Approval for the study will be sought from UNC's IRB and Malawi's National Health Sciences Research Committee. These two bodies will provide oversight for the study. This protocol and the informed consent documents and any subsequent modifications will be reviewed and approved by both bodies. All procedures conform to US and Malawian ethical standards regarding research involving human subjects.

Written informed consent will be obtained on paper or electronically. All study participants will sign an informed consent prior to enrollment in an appropriate language (English or Chichewa). The consent form will describe the purpose of the study, the procedures to be followed, the contact information of the local study contact investigator, and the risks and benefits of participation in accordance with all applicable regulations.

Literate participants will document their provision of informed consent by signing their informed consent form. Non-literate participants will be asked to document their informed consent by marking their informed consent form (e.g., with an X, thumbprint, or other mark) in the presence of a literate third-party, impartial witness. Any other local IRB/ethics committee requirements for obtaining informed consent from non-literate persons also will be followed.

Participants will be provided with copies of their informed consent forms if they are willing to receive them and believe they will not lead to difficulties if found by partners or other persons. It will be stressed with each potential participant that participation in this study is completely voluntary. Potential participants will be told that if they choose not to participate, there will be no penalty; they can continue to participate in other research studies or programs at the site and there will be no changes in the services they may receive at the clinic where they were contacted about this study. The consent will also inform participants that they have the right to refuse or withdraw from participation at any time.

The investigators have experience obtaining informed consent for trials in Malawi and thus the informed consent process has been designed to maximize understanding of potential risks.

Potential risks to subjects

There are two types of potential risks that may occur during this study: breach of confidentiality as well as a risk of discomfort related to participation.

Breach of confidentiality may occur if unique identifiers in datasets are linked back to personal identifiers. This is highly unlikely and measures will be taken to ensure that this does not occur. Discomfort with participation is also expected to be rare and minor. Health workers may feel uncomfortable about participating and may not enjoy having their performance and counseling skills assessed, or discussing experiences in a group of colleagues and peers. Indexes and contacts may feel uncomfortable having sensitive discussions with health workers recorded, as they may be of a sensitive nature. Similarly, they may feel uncomfortable answering questions on a survey about personal information, especially about sexual or care-seeking behaviors. Should a social harm or adverse event occur as a result of study participation, this will be documented, and appropriate referrals for medical, legal, or psychosocial support will be made.

Adequacy of protection against risks

Health workers and patients will be recruited at the facility. Eligible persons will be recruited by trained research staff fluent in their native language to initiate the consent process. Research staff will go over the entire informed consent with the eligible persons and describe: the purpose of the study, the detailed procedures to be followed, the risks and benefits of participation, the duration of participation, and the steps taken to protect the participant. The eligible person will be given the opportunity to ask questions. No coercion will be placed on persons to enroll in the study. It will be explained that declining consent will not have any impact on the care they receive. Trained research staff will be trained to discuss the pros and cons of participation with all prospective participants. The consent will also inform persons that they can withdraw at any time should they change their mind. Written informed consent will be obtained from each participant and participants will be provided with a copy of their informed consent forms. Study staff will document the informed consent process. The entire consent process will be conducted in accordance with the relevant US-based institutional review board, as well as the National Health Sciences Research Committee, the local regulatory body.

To minimize the risk of breach in confidentiality, all study-related activities will occur in private locations. All health worker and patient-level datasets will contain a unique ID number and will not contain any personal identifiers. All logs connecting participants to their unique ID will be maintained separately from all data and securely stored in double-locked filing cabinets in a central office, rather than at the facility level. Individual-level data will be collected and transmitted using encrypted technologies and saved on secure password-protected servers. All audio-recorded data will be processed, coded, and verified in a timely manner. As audio-recorded data is processed, the original audio-files will be destroyed.

To protect participants against risks associated with sensitive topics, they will be reminded that the answers to their questions will be kept confidential and that this information will not be shared with anyone. If patients or health workers anticipate discomfort, they can decline consent, as participation is voluntary. If any patients or health workers experience discomfort with any aspect of participation, they can terminate their participation early and withdraw from the study. Alternatively, they can continue participation, but decline a particular activity.

Potential benefits to subjects

Health workers may gain new knowledge and skills that make them better ACT providers or enhance their counseling skills more generally. Those in the enhanced arm may enjoy participating in blended learning activities. Those in the standard arm will have access to blended learning after the end of the main trial and knowing this may be appealing. Those in both arms may enjoy discussing the ACT program with their colleagues in focus group discussions. For individual patients, they may enjoy exit interviews and reflecting on their experience in ACT. Finally, this research is designed to create generalizable knowledge and enhance ACT programs in Malawi and beyond. Some patients and health workers may experience benefits from believing that their participation may contribute to improved service delivery.

Costs/compensation

Health workers will receive the local equivalent of US$10 as compensation for study visits. Patients will receive the local equivalent of US$10 as compensation for their participation.

Importance of the knowledge to be gained

There is considerable potential for the proposed research to generate findings of importance. Specifically, the activities proposed are designed to enable the delivery of high-quality ACT training to scale across Malawi. This has implications not only for Malawi but also for other countries with high HIV prevalence. Results will be disseminated nationally, regionally, and internationally.

Reportable events

All serious adverse events associated with the procedures will be appropriately reported to the UNC IRB and the Malawi NHSRC according to their reporting procedures. Field staff in Malawi will be trained to complete descriptions of adverse events that will then be sent electronically to both the PI and the co-PI. Thus, adverse events will be monitored at three levels; by the Principal Investigators, by the UNC IRB and by the NHSRC. Of course, efforts will be taken to minimize the potential for adverse events. Intervention and research staff training will stress ensuring confidentiality and avoidance of negative events, and quality assurance/quality control (QA/QC) will be performed regularly to ensure adherence to proper counseling techniques. Two types of reports will be made involving the conduct of the study. Adverse Events Reports will be made using standard forms available from the relevant IRBs for adverse events associated with the study procedures or subject participation. Serious medical adverse events are unlikely. Incident Reports will also be made of any incidents involving the conduct of the trial (e.g., enrolling a participant who did not meet eligibility criteria, etc.) These reports will be made in the form of a letter or memo to the Chairs of the relevant IRBs signed by either the PI or a co-PI. All reporting form study staff to the PI, site PI, or co-PI should be made in real-time whenever possible (i.e. when the participant is still present). However, if this is not possible, a written report must be made within 24 hours.

Copies of adverse event reports will be stored at UNC and in the study offices at Tingathe. Adverse events or incident reporting in this trial has been considered in the context of several important characteristics of the study. First, this is a minimal-risk study as defined in federal regulations: “the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.”

In addition, we will provide contact information for participants, information on how to contact the local research staff to report such events as breaches of confidentiality, HIV-related disruption of families, acts of discrimination, and physical harm. We will ask participants to return to the research site or otherwise contact research staff in order to make such reports as well as receive referrals to mitigate potential harm. This will not include identifying information about the study or references to HIV or HIV testing, so that the cards will not have the potential to jeopardize the confidentiality of participants.

Dissemination of results

The results of the study will be presented at international and local scientific meetings and published in scientific journals. The results will also be submitted to the NHSRC. The information collected in this study may lead to larger cluster randomized trials that will allow further evaluation of the impact of blended learning modalities for training health workers in voluntary assisted contact tracing.

Work plan and Timeline

The timeline below depicts planning, implementation, data collection, data analysis, manuscript preparation, and stakeholder engagement during the full research period.

The study is divided into three phases (preparation, implementation, and analysis/dissemination) that occur over a three-year period (Table 1). The first six months of the study reflect a planning phase. Trial implementation and analysis will occur over the next 2-year period. The final six months of the study will be dedicated to analysis and dissemination and providing technical assistance to support scale-up.

Timeline

Activity	**Year 1**				**Year 2**				**Year 3**			
Calendar Quarter	1	2	3	4	1	2	3	4	1	2	3	4
Finalize intervention for enhanced arm	x	x										
Site selection	x											
Site/community sensitization	x	x										
Data training harmonization		x										
Randomization		x										
Standard training (both arms)		x										
Enhanced implementation activities (enhanced arm, n=11 sites)			x	x	x	x	x	x	x	x	x	
Standard implementation activities (standard arm, n=22 sites)				x	x	x	x	x	x	x	x	
Delayed implementation of enhanced activities (standard arm, n=22 sites)							x	x				
Technical assistance to support scale up												x
Data collection			x	x	x	x	x	x	x	x		
Adoption			x	x	x	x	x	x	x	x		
Fidelity assessments			x	x	x	x	x	x	x	x		
ACT data abstraction from registers			x	x	x	x	x	x	x	x		
Feasibility/acceptability			x		x				x			
Time and motion			x		x				x			
Annual facility surveys			x				x					
Analysis							x	x			x	x
Manuscript development			x					x	x			x
Local/international presentations			x			x						x

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