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Adolescent transition to adult care for HIV-infected adolescents in Kenya (ATTACH): study protocol for a hybrid effectiveness-implementation cluster randomised trial

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ABSTRACT

Introduction Successfully transitioning adolescents to adult HIV care is critical for optimising outcomes. Disclosure of HIV status, a prerequisite to transition, remains suboptimal in sub-Saharan Africa. Few interventions have addressed both disclosure and transition. An adolescent transition package (ATP) that combines disclosure and transition tools could support transition and improve outcomes.

Methods and analysis In this hybrid type 1 effectiveness-implementation cluster randomised controlled trial, 10 HIV clinics with an estimated ≥100 adolescents and young adults age 10–24 living with HIV (ALWHIV) in Kenya will be randomised to implement the ATP and compared with 10 clinics receiving standard of care. The ATP includes provider tools to assist disclosure and transition. Healthcare providers at intervention clinics will receive training on ATP use and support to adapt it through continuous quality improvement cycles over the initial 6 months of the study, with continued implementation for 1 year. The primary outcome is transition readiness among ALWHIV ages 15–24 years, assessed 6 monthly using a 22-item readiness score. Secondary outcomes including retention and viral suppression among ALWHIV at the end of the intervention period (month 18), implementation outcomes (acceptability, feasibility, fidelity, coverage and penetration) and programme costs complement effectiveness outcomes. The primary analysis will be intent to treat, using mixed-effects linear regression models to compare transition readiness scores (overall and by domain (HIV literacy, self-management, communication, support)) over time in control and intervention sites with adjustment for multiple testing, accounting for clustering by clinic and repeated assessments. We will estimate the coefficients and 95% CIs with a two- sided α=0.05.

Ethics and dissemination The study was approved by the University of Washington Institutional Review Board and the Kenyatta National Hospital Ethics and Research Committee. Study results will be shared with participating facilities, county and national policy-makers.

Strengths and limitations of this study

- The hybrid effectiveness implementation design will enable assessment of the intervention's effects on clinical outcomes while simultaneously understanding factors that influence effective implementation.
- The pragmatic trial design, and adaptive framework, enhances the external validity of study findings and allows for implementation in a more 'real-world' setting, with health workers collectively deciding how to integrate the intervention into their existing work streams.
- Inclusion of HIV clinics in multiple counties improves generalisability, and allows testing of the intervention in different HIV prevalence settings.
- There will be differences in intervention implementation by clinic; data collection will include tracking intervention adaptations made in each clinic.

Trials registration number NCT03574129; Pre-results.

INTRODUCTION

Transition from paediatric/adolescent to adult HIV care is an area of emerging importance.[1–3] Increasing survival of perinatally infected children due to advances in HIV treatment, coupled with high HIV incidence among adolescents, has resulted in a growing population of adolescents living with HIV (ALWHIV).[4] ALWHIV face psychosocial and mental health challenges and need support to gain independent illness management skills.[5–7] ALWHIV have poorer treatment outcomes than adults and younger children, including viral suppression, adherence to medication and higher mortality.[8–12] While high mortality may be related to complications

from perinatal HIV,[13–15] lack of motivation to remain in care also contributes to poor health outcomes.[16 17]

Effective transition to independent care requires timely disclosure of HIV status. Disclosure (telling a child they have HIV) rates among adolescents range from 0% to 62%,[18] and disclosure is often initiated late (8.7–15 years vs the recommended 6–12 years).[19–23] Caregivers may be reluctant to begin the disclosure process because of concerns about developmental readiness, fear of blame and stigmatisation.[24] Healthcare workers (HCWs) find it difficult to begin disclosure discussions with caregivers and children, lack skills and tools to effectively disclose, and are often overburdened by high patient volumes.[25] Following disclosure, adolescents are expected to develop knowledge and skills to navigate adult services and manage their health independently. Tools and HCW training to guide the transition process are lacking, particularly in sub-Saharan Africa (SSA).[2 26]

The Namibia HIV Disclosure Intervention, a clinical intervention that included a cartoon book developed with input from front-line HCWs, was associated with improved HCW, caregiver, and adolescent confidence in disclosure, improved adolescent HIV knowledge, medication adherence and viral suppression.[27] Outside SSA, tools to support transition to adult care are available and associated with successful transition to adult care, confidence in adult services and adherence to care.[28–30] The 'Got Transition' tool is a US-based transition framework that supports a structured transition process.[31] The tool has six core elements, including transition policy development, tracking progress, readiness assessments, planning for adult care, transfer to adult services and transfer completion. The United States Agency for International Development (USAID) has also developed tools that incorporate some of these elements.[32 33] However, these tools are not currently used in programme settings and transition practices are heterogeneous.[34] The Kenya National HIV guidelines provide a framework for transition, with job aids to support assessment of transition milestones, but tools to track individual progress and outcomes are lacking.[35]

Combining disclosure and transition interventions may offer clinics a holistic framework to support successful adolescent care. Our study team partnered with stakeholders working with ALWHIV in Kenya to adapt and combine the Namibia HIV Disclosure Intervention and currently available transition tools into an adolescent transition package (ATP) for use in HIV programme settings. This study will test the effectiveness of the ATP to improve readiness to transfer to adult services or independent care among ALWHIV in Kenya and simultaneously study implementation outcomes. This paper describes the study protocol, design and analytical considerations.

METHODS AND ANALYSIS

Study design

The adolescent transition to adult care for HIV infected adolescents (ATTACH) study aims to determine the effectiveness of an ATP using a hybrid type 1 effectiveness-implementation cluster randomised controlled trial (RCT) design in 20 HIV clinics in Kenya. A hybrid type 1 approach allows testing an intervention's effects on clinical outcomes while simultaneously understanding factors that influence effective implementation[36] (figure 1). A cluster RCT design was chosen as the intervention will be implemented at the clinic level. The ATP will be administered in 10 randomly selected intervention sites. Standard-of-care practices for disclosure and transition, consistent with Kenyan national guidelines and clinical care policies, will continue in the 10 control sites.[34 37] Standard of care practices include age-based disclosure and transition assessments, including job aids to remind clinicians to explore disclosure and transition topics at clinic visits.

Study sites and population

Prior to the RCT, 102 clinics in 26 counties in Kenya participated in a clinic survey and electronic medical records (EMR) abstraction to evaluate disclosure and transition services available, correlates of successful transition and inform ATP tool development. The survey results have been reported previously and were incorporated in ATP development meetings.[34] Clinics were randomly selected from ~300 HIV clinics in Kenya that used EMR systems in 2016 and had ≥300 total (including adults, adolescents and children) active patients (estimated at least 30 adolescents) enrolled in HIV care.

Twenty RCT sites were selected from 32 HIV clinics that had an estimated ≥100 adolescents and young adults (AYA) age 10–24 years and were in the four counties participating in the pretrial surveys with the highest number of ALWHIV (Homa Bay, Nairobi, Kajiado and Nakuru counties) (figure 2). Specific clinic adolescent volumes were obtained from national viral load registers and data abstractions from EMR records in individual clinics. Where clinics had fewer than 100 ALWHIV, they were replaced with other clinics in the county that did not participate in the pre-trial surveys. For Homa Bay County, of the initial 15 clinics that met selection criteria; one clinic was excluded because the clinic size (1700 enrolled adolescents) was much higher than the other clinics and would likely have undue influence on the results, and another 8 with the lowest number of ALWHIV were excluded. In Nairobi and Kajiado, three new clinics were included due to low numbers of ALWHIV or logistical concerns due to the presence of other transition related studies (figure 2). The final list of sites is available in online supplemental material appendix 1.

Randomisation and blinding

Clinics were randomised using computer generated random numbers to either intervention or control status, using restricted randomisation. Restriction was performed to balance clinics by county and estimated number of ALWHIV (<200, 201–400, 401–500 and >500). Randomisation was performed at the University of Washington by a biostatistician with access only to the clinic characteristics of interest. After randomisation, the list

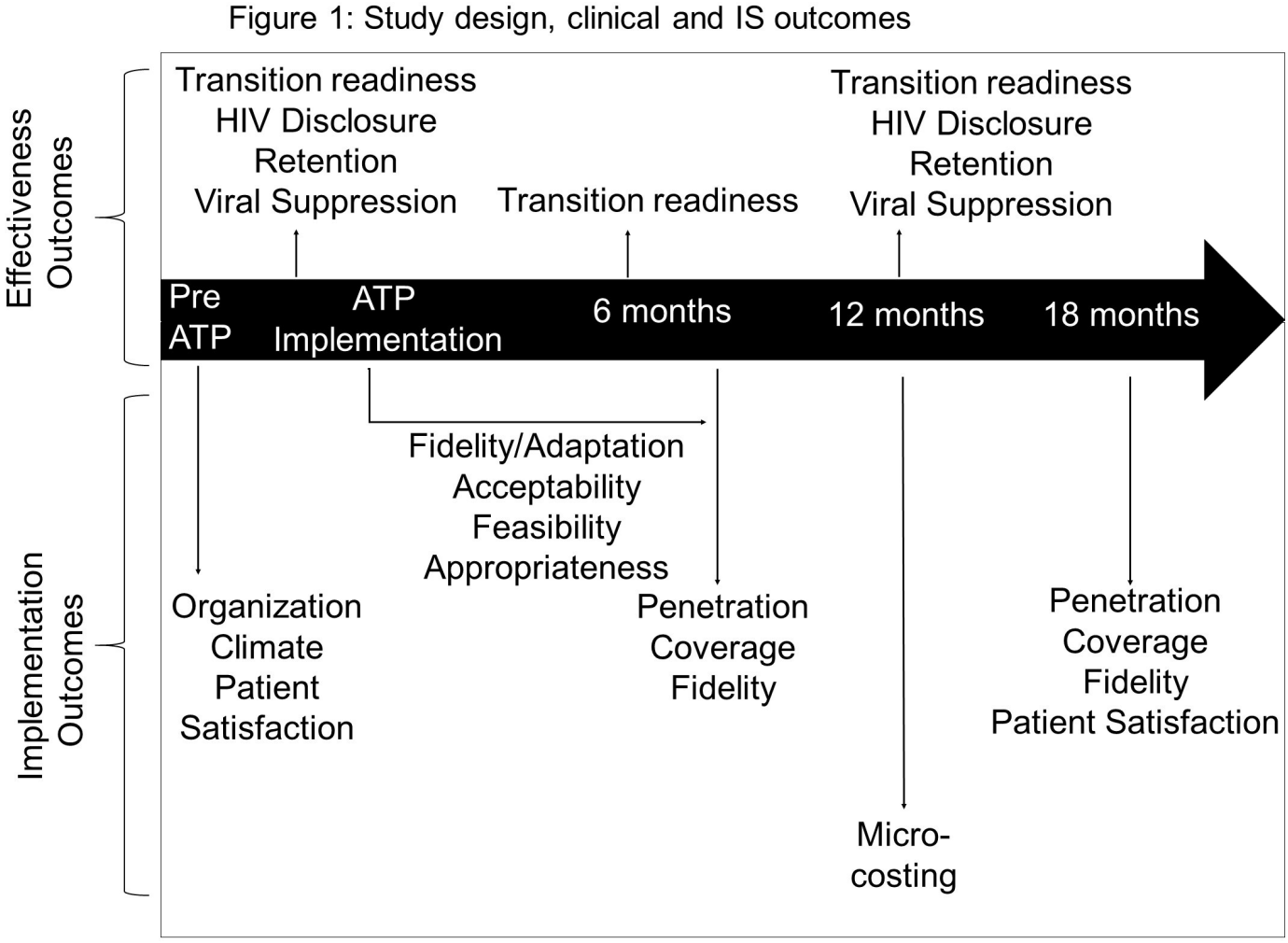

Figure 1 Study time line and time point for assessment of effectiveness and implementation outcomes. Prior to trial implementation, data on organisation climate, patient satisfaction and baseline effectiveness outcomes are collected. In the first 6 months of the trial implementation outcomes are continuously evaluated. Effectiveness outcomes are measured 1 year after ATP implementation. Implementation outcomes are measured at 1 year (microcosting) and at the end of ATP implementation. ATP, adolescent transition package;

of clinics with their allocation arm was sent to the study team. The intervention is administered at the clinic-level, therefore, it is not possible to blind participating clinics or study team members.

ATP intervention

The ATP will include two evidence-based interventions.

The validated Namibia HIV Disclosure Intervention[38] consists of a disclosure intervention comic book 'Why I take my medicine', HCW training material, a disclosure readiness assessment, and a disclosure tracking tool (to be used with ALWHIV over 10 years of age) (cover page and select pages presented in online supplemental material appendix 2 (full material available on request: email beimak@uw.edu)). The disclosure intervention progresses from incomplete to complete disclosure using a narrative about soldiers fighting the battle of infection as the rationale for taking medicine.

The transition intervention is an adapted transition toolkit consisting of a systematic transition guide 'Taking Charge', tracking tool to monitor individual progress and a readiness assessment tool (transition guide cover page and select pages presented in online supplemental material appendix 3 (full material available on request: email beimak@uw.edu)). The transition intervention will be administered to all ALWHIV ages ≥15 years who know their HIV status. The transition toolkit was informed by existing tools, including the US-based 'Got Transition' tool, USAID tools and qualitative work with HCWs, policymakers, adolescents and caregivers[31–33] and supported by evidence that structured transition programmes improve transition outcomes.[30] For this study, core elements of transition were contextually and culturally adapted to develop the 'Taking Charge' transition intervention at an adolescent stakeholder's workshop in Kenya.[3]

The ATP will be implemented during regularly scheduled clinic visits with periodic assessments as described in table 1 (adapted Standard Protocol Items Recommendations for Interventional Trials checklist) and has

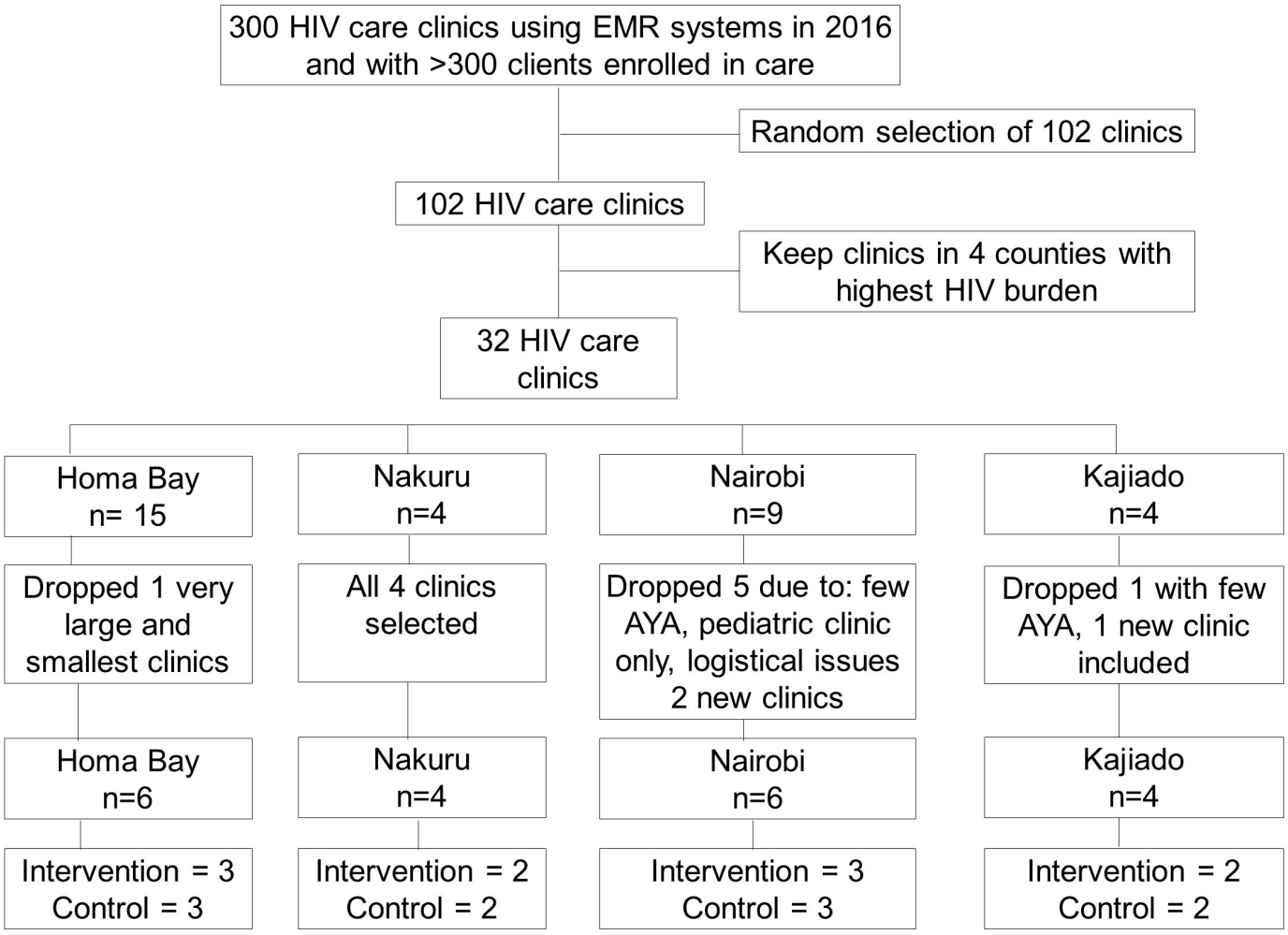

Figure 2 Site selection criteria and reasons for inclusion and exclusion. From 300 clinics using EMR systems and that had >300 enrolled clients in 2016, we randomly selected 102 clinics, then 32 clinics in 4 counties with the highest HIV burden. Clinics found to have few AYA, logistically difficult to conduct the study due to ongoing studies were replaced to a final list of twenty clinics, ten intervention and 10 control sites across four counties. AYA, adolescents and young adults; EMR, electronic medical records.

been translated to two local languages (Swahili and Luo). HCWs working in the HIV clinic including doctors, clinical officers, nurses, counsellors, social workers and peer leaders who are involved in adolescent care will participate in intervention delivery.

Standard-of-care practices

We have previously described varying transition and disclosure practices by clinic, with majority of clinics adopting specific adolescent clinic days and varying ages of transition to adult care,[34] and no differentiation of adolescents with perinatally or behaviourally acquired HIV. Typically for disclosure, caregivers give permission for disclosure processes to begin. For transition, national guidelines recommend an age-based transition approach focusing on HIV disclosure and basic HIV literacy among adolescents age 10–12, and importance of medication adherence and participation in support groups (age 13–19).[37]

Participants

All ALWHIV aged 10–24 years attending the selected clinics will be eligible to participate in the study. The intervention will be offered based on disclosure status and age. ALWHIV who have not attained full disclosure will be offered the disclosure intervention, while those age 15 years and above will be offered the transition intervention. This is because the intervention period (12–18 months) is not long enough to observe adolescents passing from disclosure (early adolescence: 10–13 years) to transition preparation (middle adolescence: 13–17 years) to effective transition (late adolescence/young adulthood: 18–24 years).

Study procedures

Permission will be sought from county and clinic administrators for clinic participation. Separate study training will be conducted for intervention and control sites. HCWs from intervention clinics will be trained on the intervention procedures and supported to implement

Table 1 Adapted Standard Protocol Items Recommendations for Interventional Trials

Timepoint (months)	Enrolment	Allocation	Post-allocation						
	−1	0		t1*		t2*			
	Pre-study	Baseline	3	6	9	12	15	18	Close-out
Enrolment									
Eligibility screening	X								
Allocation	X								
Informed consent		X							
Intervention									
Intervention arm									
Control arm									
Assessments									
Transition readiness		X		X		X			
Viral load data pulls		X		X		X			X
EMR data pulls		X		X		X			X
HCW surveys†		X	X	X					X
Qualitative interviews									X
Disclosure outcomes		X	X	X	X	X	X	X	
Time and motion surveys						X			

*Time points for assessing primary outcome.
†Bimonthly for the first 6 months.
EMR, electronic medical records; HCWs, healthcare workers.

the ATP by the study team. During the first 6 months of the trial, clinics will participate in twice-monthly continuous quality improvement (CQI) meetings that use modified plan-do-study-act cycles for ATP adaptation at each clinic. CQI meetings are used to review key performance indicators at a clinic level (eg, number of trained HCWs providing the intervention, number of adolescents exposed to the intervention) to identify opportunities to optimise intervention delivery. Attendees of CQI meetings will complete surveys to assess implementation challenges, successes and outcomes. Control sites will be trained on study related data collection.

All ALWHIV age 10–19 will be assessed by clinic staff to determine disclosure status. Caregivers and adolescents in intervention sites who have not reached full disclosure will be offered the disclosure intervention and will be followed up until they reach full disclosure or end of study period. Those in control sites will be offered standard of care disclosure procedures and similarly followed up. All disclosure tools and outcomes will be administered and assessed by clinic staff. The study team will support retention by phone calls in all sites to remind ALWHIV to attend clinic visits if not already part of regular care. Caregivers of ALWHIV will review disclosure material and will give consent to allow disclosure procedures with the adolescent. Disclosure status will be assessed at every visit and caregiver disclosure readiness information reviewed every 6 months.

ALWHIV age 15–24 who have reached full disclosure will be recruited to participate in the transition intervention by clinic staff during their scheduled clinic visits. Prior to exposure to the transition intervention, informed consent will be obtained by study staff from individual ALWHIV for study staff administered transition readiness assessments conducted at baseline, 6 and 12 months. Since ALWHIV age 15 and above frequently come to clinic alone, the study has obtained approval for waiver of parental consent for those under 18 years (the legal age of consent in Kenya). All other intervention materials (the systematic transition guide 'Taking Charge' and transition guide tracking tool) will be implemented by clinic staff. Enrolled ALWHIV in intervention sites will be individually monitored for progress through the chapters in the transition guide.

Retention and viral suppression will be determined through medical record abstraction. Data quality checks will be routinely conducted to ensure EMR records match viral load data. Study staff will collect data on transfers to adult clinic or clinic days (specific day of the week dedicated to adolescent care) and monitor post-transfer retention.

HCWs will participate in quantitative and qualitative data collection. At baseline, HCWs will complete an organisational readiness for implementation change[39 40] assessment before intervention implementation to quantify attitudes and beliefs that may impact later-stage

implementation outcomes. At 6 and 18 months after beginning of ATP implementation, HCWs will be invited to participate in focus group discussions (FGDs) and complete quantitative surveys to identify factors influencing effective implementation. We will evaluate determinants of later-stage implementation outcomes including intervention coverage, penetration, and fidelity. HCW FGDs and survey questions will be guided by the Consolidated Framework for Implementation Research (CFIR).[41] At the end of the intervention period, a subset of adolescents, caregivers and HCWs from clinics will participate in anonymous post-trial surveys, and post-trial in-depth interviews (IDIs) and FGDs to measure satisfaction and implementation outcomes. Adolescents and caregivers participating in surveys will be randomly selected, while HCW surveys will include all available HCWs from study clinics. IDIs will use stratified purposive sampling to recruit adolescents with varied modes of HIV transmission (perinatal or behavioural), age, and transition status (transitioned or not). FGDs will be conducted with HCWs from intervention sites, and additional IDIs will be conducted with a subset of HCWs from low and high performing intervention sites. For costing and cost-effectiveness analyses, HCWs will be interviewed and observed to assess the average time needed to complete the ATP intervention. Time in motion observations will be conducted and variability in clinic flow assessed to inform efficiency assumptions. Up to 200 HCW (20 per intervention clinic) working in ALWHIV clinics and who are willing to participate will complete implementation surveys.

Primary outcome

The primary outcome will be assessed using a 22-item scale that measures adolescent readiness to transition to adult care. The scale has questions measuring attainment of knowledge and skills to navigate adult care systems. The scale is divided into four domains: HIV literacy (maximum score 5), self-management (maximum score 9), communication (maximum score 5) and support (maximum score 3). Scores across all domains will be summed to get a total readiness score (maximum score 22, minimum 0). A higher score indicates the more prepared an ALWHIV is to transition to adult care. Individual scores for each domain will also be assessed as separate primary outcomes (table 2).

Secondary clinical outcomes

Secondary outcomes will be retention and viral suppression in 10–24 year olds (defined as proportion of 10–24 year olds completing one or more visits within 6 months of their last visit and viral load of less than 1000 copies per ml after at least 6 months of antiretroviral therapy (ART), respectively) at the end of the intervention period (month 18).

Exploratory outcomes will be proportion of adolescents in intervention and control sites with full disclosure by age 10–12, 13–15 and 16–19 years, time to full disclosure and post-transition retention (defined as completing an adult clinic visit day after transfer to adult services and at least one other visit within 6 months of the first adult visit (total of 2 visits)) (table 2).

Secondary implementation outcomes

Implementation outcomes include intervention acceptability, feasibility, appropriateness, penetration, coverage, intervention fidelity, programme costs and cost-effectiveness (outcome definitions and measurement approach in table 2). HCWs will complete surveys during clinic CQI meetings to determine the association between intervention adaptations and implementation outcomes. These surveys use validated measures of perceived appropriateness, acceptability, feasibility and fidelity of the ATP adaptations.[42 43] We anticipate that adaptations made during quality improvement cycles will be associated with improved acceptability, coverage and appropriateness of the intervention, and improved feasibility and fidelity of intervention implementation. Adaptations will be evaluated over time at each clinic and summarised over the 6-month adaptation period to determine the number and types of changes tested. Adaptations will be described using a standardised classification system based on the Framework for Reporting Adaptations and Modifications-Enhanced (FRAME) framework to determine the content and nature of the modification, as well as who will be making the modifications and the level of delivery impacted by the modification.[44 45]

Cost outcomes

We will estimate the economic cost of providing the ATP intervention per ALWHIV. We will conduct a microcosting study in intervention and control clinics from a payer perspective.[46] Costs (2019 US dollars) will be collected from expense reports, staff and expert interviews, and divided into: personnel, equipment, supplies, buildings and overhead, and start-up. In-country time and motion observations will be conducted by a trained research assistant using cost menus in Excel. Research time (eg, administering informed consent) and other research costs will be removed from programmatic costs. We will conduct semistructured interviews with staff to assess daily responsibilities associated with the ATP intervention. Time and motion surveys and staff interviews will be used to inform productivity assumptions (average number of ALWHIV provided the intervention per day). Capital costs and start-up costs (eg, staff hiring/training) will be annualised assuming 5-year useful life and discounted annually at 3%. We will assume 5% supply wastage. We will conduct sensitivity analyses to assess the impact of uncertain parameters on the cost of providing the intervention.

Cost-effectiveness outcomes

We will parameterise a model with cost and effectiveness data from the ATTACH trial and project HIV infections, HIV-related deaths and disability-adjusted life-years averted associated with scaling up the ATP. Trial outcomes

Table 2 Summary of primary and secondary outcomes

Primary outcome	Indicator	Time points	Source
Transition readiness	22 item score (maximum score 22, minimum 0)	Enrolment, 6 monthly	Transition readiness surveys
Transition readiness by domain	HIV literacy (maximum 5) Self-management (maximum 9) Communication (maximum 5) Support score (maximum 3)	Enrolment, 6 monthly	Transition readiness surveys
Secondary outcomes			
Viral suppression	% of ALWHIV on antiretroviral therapy (ART) for >6 mo and with viral load of <1000 copies/mL	Study end	Viral load database
Retention	% of ALWHIV completing visits within 6 months of last visit	Study end	Clinic EMR
Exploratory outcomes			
Proportion with full disclosure (overallandby age group)	% of ALWHIV with full disclosure	Study end	Disclosure checklists
Time to full disclosure	Months from enrolment to full disclosure	Longitudinal	Disclosure checklists
Post-transition retention	Return for adult clinic visits	Longitudinal	Transition log
Implementation outcomes			
Acceptability[42]	Validated acceptability measure (acceptability of intervention measure)	Enrolment, bimonthly, study end	HCW surveys
Appropriateness[42]	Validated appropriateness measure (intervention appropriateness measure)	Enrolment, bimonthly, study end	HCW Surveys
Feasibility[42]	Validated feasibility measure (feasibility of intervention measure)	Enrolment, bimonthly, study end	HCW Surveys
Adaptability/fidelity[45]	FRAME to measure context and content of adaptations and core elements	Enrolment, bimonthly, study end	HCW Surveys, FGDs and IDIs
Penetration[55]	% HCWs implementing the intervention out of trained HCWs	Bimonthly, study end	HCW Surveys, FGDs and IDIs
Coverage[55]	% of adolescents attending clinic exposed to the intervention	Bimonthly, study end	Clinic records and study tracking tools

ALWHIV, adolescents living with HIV; EMR, electronic medical records; FGDs, focus group discussions; FRAME, Framework for Reporting Adaptations and Modifications-Enhanced; HCWs, healthcare workers; IDIs, in-depth interviews.

to be used in the model include proportion of ALWHIV are retained and virally suppressed after 6 months in adult care by gender and mode of transmission. We will use a previously published compartmental mathematical model of HIV transmission and progression parameterised to epidemiological data from Kenya and focusing on the AYA population.[47] Individuals in the model are stratified by sex, 5-year age group (0–59 years), sexual activity (low, medium and high), circumcision status, and ART status. HIV natural history is modelled through six stages of viral load and six stages of CD4 count. Susceptible individuals can acquire HIV and transition to acute infection, characterised by short duration and high probability of HIV transmission. Individuals then progress through CD4 and viral load stages and can initiate and drop out of ART. The model tracks costs and health outcomes over time allowing for the estimation of the incremental cost effectiveness ratio of implementing the ATP intervention compared with standard of care.[48]

Data management

Data for outcomes will be collected from study tools introduced to the clinics as part of the ATP intervention. Disclosure and transition tracking tools will be completed by HCWs in intervention and control sites, manually abstracted and entered into Research Electronic Data Capture (REDCap). REDCap is a secure, web-based electronic data capture tool, hosted at the University of Washington, that supports research data collection, provides an intuitive interface for validated data entry, audit trails for tracking data manipulation, and automated export procedures for seamless data downloads to common statistical packages.[49] A 10% data check for consistency between REDCap and paper forms will be conducted for all forms in each site. Retention and viral suppression data will be obtained from clinic EMR systems and the Kenya National Viral load database respectively. Study staff have been trained in data protection; link logs linking participant to study data will be accessible only to study staff.

Sample size calculation

With 20 clinics, 10 intervention and 10 control, and an average cluster size of 50 ALWHIV, we will have ≥80% power to detect mean transition readiness score differences of >1.0, assuming a two-sided test, alpha=0.05 and an SD of 3 (table 3).

Table 3 Power and sample size calculations for the primary outcome

Mean difference in transition readiness score	SD	No of clusters per arm
0.5	1	4
0.5	2	15
1.0	2	4
1.0	**3**	**9**
1.5	3	4
1.5	4	7
2.0	5	6
2.0	6	9

Alpha=0.05, two-sided test, 80% power, average cluster size 50.

Statistical methods and analysis

The primary analysis will be intent to treat, assuming ALWHIV in the intervention arm will be exposed to the ATP intervention. Baseline clinic and adolescent characteristics will be summarised by arm and presented using descriptive statistics.

Primary outcomes will be estimated using mixed effects linear regression models to compare transition readiness scores (overall and by domain (HIV literacy self-management, communication and support)) over time in control and intervention sites with adjustment for multiple testing (Benjamini-Hochberg method). These models will account for clustering at the clinic level and repeated transition assessments. We will estimate the coefficients and 95% CIs with a two-sided α=0.05.

For secondary outcomes, retention/suppression in intervention and control sites will be compared using generalised estimating equations with a log link (adjusting for baseline retention/viral suppression). Proportions of adolescents with full disclosure by age 10–12, 13–15 and 16–19 in the study arms at 12 months post enrolment will be compared using generalised linear models) with a log link and random effect for site.

Survey data on implementation determinants and adaptations will be summarised as Likert data and evaluated using basic descriptive statistics including frequencies (variability), median values (central tendency), Kendall τ (associations) and χ^2 tests. Interrupted time series analysis will be used to evaluate whether the adaptation process improved implementation outcomes. Adaptations made to the intervention over time will be compared with planned implementation procedures to evaluate fidelity and categorised using the FRAME framework. Determinants of implementation will be evaluated using FGDs and IDIs with HCWS that are guided by the CFIR. Qualitative analysis will focus on identifying and understanding key factors facilitating or impeding ATP coverage, penetration and implementation fidelity in intervention clinics. Qualitative analysis of IDIs with adolescents and caregivers will focus on understanding personal experiences with transition and satisfaction with intervention materials. IDIs and FGDs will be analysed using a combination of directed and conventional content analysis,[50] and thematic network analysis.[51] Analysis will employ a modified version of the constant comparison approach and will use within and between case analysis methods[52] to compare experiences between clinics and individuals. All data will be coded in ATLAS.ti by at least two members of the research team, using codebooks that are developed inductively using open and in vivo coding strategies and deductively based on literature reviews, IDI/FGD guides and the team's previous research experience. All data will

be summarised to align with the Consolidated Criteria for Reporting Qualitative Research.[53]

We will use mathematical modelling to estimate the incremental cost-effectiveness of adding the ATP intervention to adolescent HIV care. We will calculate ICER as the ratio of the difference in costs divided by the difference in effects for the intervention compared with standard-of-care scenario over a 20-year horizon. Consistent with guidelines, we will discount costs and health benefits at 3% annually, and consider ICERs below Kenya's per capita GDP to be cost-effective. We will perform extensive sensitivity analyses to identify influential assumptions.

Exploratory stratified analysis by mode of HIV infection (perinatally or behaviourally acquired HIV defined by maternal HIV status and or age at ART initiation (age 10 and 12))[4 13] will be conducted for primary, secondary and cost outcomes.

All coauthors will have access to the final study dataset.

ETHICS AND DISSEMINATION

This study is approved by the Kenyatta National Hospital/University of Nairobi Ethics Review Committee (KNH ERC) (P248/05/2017, approval date: 2 October 2018, Ethics committee contact: Professor Guantai, KNH ERC P.O. Box 20 723–00202, Nairobi, Kenya) and the University of Washington Human Subjects Institutional Review Board (UWHSD) (STUDY00001756, approval date: 1 June 2018 Contact Kristen Wittmann, Tel+12062212093, email: kmw89@uw.edu). All protocol modifications will be approved by regulatory bodies prior to implementation. Adverse events or unintended events resulting from the study intervention will be reported to the Kenyatta National Hospital ethics and review committee within 72 hours of notification of the event.

Written informed consent will be obtained from all participants. Consent forms are available in three common languages (English, Swahili and Luo). A sample consent form is provided in online supplemental material.

At the end of the study, results will be presented to all participating sites, community advisory board and national HIV care partners. This study will comply with the NIH Public Access Policy, to ensure public access to the published results of NIH funded research. A deidentified participant-level dataset, statistical code and codebook will be deposited in a widely accessible repository based on available best practices and hosted at the NIH data repository or other repository.

DISCUSSION

Increasing evidence of poor HIV treatment outcomes among ALWHIV demonstrate a need to develop, optimise and evaluate interventions to improve clinical care for ALWHIV. This study fills an important gap in evaluating an intervention to improve transition services in SSA.[26] The proposed disclosure tool is a comic book that was developed and validated in a low-resource setting, and could be appropriate for other similar settings in SSA. The transition tool was developed and adapted to be culturally and contextually relevant to Kenya through collaboration with key stakeholders including the Ministry of Health, HIV care implementing partners, HCWs caring for both adolescents and adults, and adolescent representatives. Inclusion of a wide range of stakeholders during intervention development, including the Ministry of Health, provides potential for more widespread use of the intervention if found effective. As a result, this study could contribute indicators for monitoring successful adolescent HIV transitions, an important component of the third 95 of the 95-95-95 UNAIDS targets for global HIV.

A major strength of the RCT presented here is the inclusion of an adaptive framework, where HIV clinics are supported to make minor planned adjustments to implementation to ensure effective delivery and interventional fit within each health facility. This pragmatic design allows for the ATP to be implemented in a more 'real-world' setting, with HIV clinic staff collectively deciding how to integrate the ATP into their existing work streams. This approach enhances the external validity of study findings by providing evidence regarding what adaptations are needed to effectively deliver the ATP, and in what environments.

Successful implementation of the ATP requires attention to partnership development because it relies on routine HCWs to implement the intervention. Partnerships with the Ministry of Health, county governments, as well as early engagement of adolescents and HCWs in intervention development, is critical to obtain buy-in and ensure feasibility for the intervention. Our established partnerships prior to and during intervention development will facilitate access to clinics, and provide insight on current and future policies on adolescent HIV. Within clinics, the study team will support successful intervention implementation by meeting consistently with front-line implementing HCWs and supporting modified CQI meetings to review challenges and successes, and make minor adaptations to ensure optimal implementation.

We have engaged a Community Advisory Board consisting of a diverse group of stakeholders including ALWHIV, representatives of youth and adolescents, parents of ALWHIV, religious leaders, community health workers and HCWs that meets regularly to discuss adolescent health and ongoing studies.

An external advisory panel (EAP) comprised of individuals who are not part of the study team will act in an advisory capacity to the sponsor and study team and will monitor recruitment, enrolment and potential social harms of the intervention. The EAP will meet soon after trial start and yearly thereafter.

Details on the EAP charter can be found at this link: http://depts.washington.edu/gwach/wp-content/uploads/2012/10/ATTACH-EAP-Charter-Agreement-10-23-19.pdf

Cost-effectiveness analysis will provide useful data for policy makers making decisions to effectively allocate

resources for HIV programmes. Our approach will largely use existing resources at the clinics, and is designed to be utilised during regular clinic visits.

Strengths and limitations

The study takes an implementation science approach, using available clinic staff and systems making it feasible to operationalise with currently available resources. Selection of sites with EMR systems, small number of clinics included (20) and inability to have proportional geographic representation may limit the generalisability of our results. However, our approach captures clinics with large numbers of ALWHIV as well as counties with high burden of HIV in Kenya. The national adult HIV prevalence is estimated at 4.9%; selected counties have varying prevalence: 19.6% in Homa Bay, 3.8% in Nairobi, 4.6% in Kajiado and 3.0% in Nakuru.[54] The intervention will be implemented by clinic staff within regular clinic schedules and may therefore differ by clinics. To understand these differences we will collect data on changes and adaptations made in each of the clinics. The transition readiness assessment tool was developed by the study team and is not validated; however, the tool was developed with input from a wide range of stakeholders and other validated tools are lacking. Lastly, while some of the implementation outcomes are validated in the USA, it is unclear if they perform well in a different cultural setting.

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