Research Protocol

Analysis of Existing Medical Record Data to Evaluate Coverage, Uptake, Benefits, and Costs of Differentiated Models of Service Delivery for HIV Treatment in Africa

Short title: Gathering Records to Evaluate Antiretroviral Treatment (GREAT)

- Malawi Country Protocol -

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CONTENTS

1. SUMMARY

To achieve global goals for the treatment of HIV, most high-prevalence countries are experimenting with and scaling up differentiated service delivery models (DSD). A handful of efforts have been formally described and evaluated in the literature; many others are being implemented formally or informally under routine care, without a research or evaluation goal. For most countries, however, we have little evidence on the big picture—the proportion of clinics offering alternative models, eligibility criteria and the proportion of patients considered eligible, the number of patients actually participating, health outcomes such as viral suppression, empirical resource utilization compared to traditional care, variations among the models, duration of patient participation, fidelity to model guidelines, effects on clinic efficiency, and sustainability without external donor support.

AMBIT a set of data synthesis, data collection, and data analysis activities aimed at generating information for near- and long-term decision making and creating an approach and platform for ongoing evaluation of differentiated models of HIV treatment delivery in the future. The project will collect and analyze a wide range of existing data sets pertinent to DSD. This protocol is for an analysis of existing medical record data collected by the Ministry of Health (MOH), implementing partners, and other completed, ongoing, or new evaluations, trials, and observational studies. Outcomes to be reported include coverage/uptake of DSD, patients' outcomes, and distribution of each model. **There will be no study interaction with individual patients, providers, caregivers, or others for this analysis.**

2. INVESTIGATORS

This evaluation will be conducted by investigators from Boston University in the U.S., Wits University in South Africa, and a local partner in Malawi. Individual investigators are:

Boston University, United States

Principal investigator
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Assistant Research Professor, Boston University School of Public Health

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Local Partner, Malawi

Discussions are currently underway with potential local partners in Malawi. Prior to starting data collection, the name of the local partner organization and the principal investigator will be submitted to the institutional review boards.

3. BACKGROUND, RATIONALE, AND OBJECTIVE

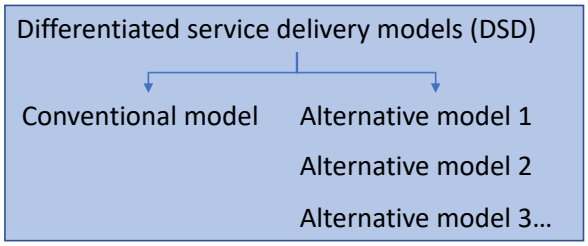
a. Background

To achieve global goals for the treatment of HIV, most high-prevalence countries are experimenting with and scaling up differentiated service delivery models (DSD). To date most of these efforts have focused on "stable" antiretroviral therapy (ART) patients, who have passed the period of high mortality and loss-to-follow-up immediately after initiating ART. Stable patients are believed to require fewer provider resources (e.g. clinical consultations) and are able to benefit from community-based service delivery that is closer to home[1] and from less intensive clinic visits. A handful of efforts have been formally described and evaluated in the literature[2–6]; many others are being implemented formally or informally under routine care, without a research or evaluation goal. While there is currently no reliable count of how many ART patients are participating in alternative service delivery approaches, it is likely that nearly every major HIV treatment partner supported by PEPFAR and the Global Fund have introduced one or more alternative models of care into the programs they support.

At present, some studies have reported outcomes for specific models of care and/or compared one model to another, and several large studies are currently underway to evaluate individual models. For most countries, though, we have little evidence on overall impact. We cannot currently estimate basic aggregate descriptive measures such as the proportion of clinics offering alternative models, the proportion of patients considered eligible or the number of patients actually participating. Nor do we know eligibility criteria for each model in each country, empirical resource utilization compared to traditional care, or core outcomes such as viral suppression. We have almost no data on variations among the models, duration of patient participation, fidelity to model guidelines, effects on clinic efficiency, and sustainability without external donor support. Many efforts are underway to improve use of alternative models, but their focus is on implementation rather than high-level evaluation or analysis of the phenomenon as a whole.

For purposes of this protocol, we will refer to any approach to service delivery that is tailored to some aspect of patient needs as a "differentiated service delivery model," or DSD. The original model of clinic-

based ART provision for all patients will be called the "conventional" model and will be considered a single model of care. All other models of care will collective be called "alternative" models. A health system that optimizes the provision of approaches will offer one or more alternative models of care for all ART patient populations, stratified on the basis of criteria ranging from setting (e.g. rural v urban) to risk factors (MSM v young women), patient characteristics (age, sex, condition), to clinic capacity. In this taxonomy, the conventional model of care may serve a specific group of patients—those who require additional services—and it is thus a differentiated model in itself.



In Malawi, the Ministry of Health (MOH) and its implementing partners are currently supporting the scale-up of several alternative models of care ART patients who are stable on ART. These include amongst others, multi month dispensing, fast track refills, nurse led community ART and adolescent centric treatment groups. While some specific DSD models have been or are being evaluated[7-10], there has not yet been an assessment of the reach or impact of DSD at national scale.

b. Rationale

In the published literature and conference presentations, calls for funding proposals, and MOH documents, DSD are assumed to generate a wide range of potential benefits. These include better access to and outcomes of treatment, increased clinic capacity and lower costs for providers, lower costs for patients, and better quality and greater satisfaction for both providers and patients. Despite a high level of confidence on the part of DSD advocates, ministries of health, funders, and implementing partners that at least some of these benefits must materialize, there is in fact very little evidence to support these assumptions. Published research to date has suggested modest or minimal improvement in health outcomes and small reductions (if any) in per-patient provider costs. We note that there is little room for short-term improvement in health outcomes, as most patients enrolled in alternative models to date have been virally suppressed at entry, but DSD may certainly affect long-term retention in care. We also expect only modest potential for per-patient out-of-pocket cost reductions, due in part to the large share of costs attributable to medications[11-13]. We have found no published evidence that moving HIV patients into alternative models increases the quality or quantity of services that clinics provide to conventional-model patients or patients with non-HIV conditions.

Fortunately, in the past half-decade, substantial groundwork has been laid for standardizing methods for evaluating the performance of DSD at the patient level. We are thus at a point in time at which many alternative models are already being implemented and some evaluated, and an initial set of evaluation indicators has been published[14]. With some micro-data in hand, but little "macro" evidence of overall scale, impact, costs, and benefits, this is therefore an apt time to launch a big picture analysis of DSD, to help guide ministries of health, donor agencies, and others to make better decisions about what to scale up, where, and for whom.

c. Objective

The objective of this study is to analyze existing data sets with data relevant to differentiated service delivery for HIV treatment in Zambia, Malawi, and South Africa. **This protocol is solely for the analysis of existing data; the study contains no interaction with patients, providers, or other individuals.**

The specific aims of the study are to assess the current extent of DSD implementation and uptake under current guidelines and to evaluate outcomes, costs, and benefits of DSDs.

The AMBIT project has three focus countries, South Africa, Zambia, and Malawi. This protocol is specifically for data collected in Malawi. Protocols specific to Zambia and South Africa will be submitted separately to the appropriate governmental and institutional review boards.

4. OVERVIEW OF STUDY DESIGN

To achieve the study aims, we will analyze pre-existing data sets that contain information relevant to DSD at national and sub-national levels. All adult patients seeking care for HIV in the country during the study period will be eligible to be included in the study through use of their clinical record data. There will be no direct interaction with study subjects. Data will be collected from existing patient records, including clinic files, registers, and databases. We will find, access, and then synthesize existing data from as many sources as we can identify.

Prior to starting data collection for this evaluation, we will develop descriptions of the available data sources and the models of care reflected in the data sets. We will then collect primary data from the Ministry of Health, treatment support partners, researchers, and funders, as described below. Finally, we will analyze individual and pooled data sets to generate as much information as possible about the uptake, utilization, outcomes, benefits, and costs of different models of care.

5. STUDY SITES AND POPULATION

a. Study Sites

The evaluation will be conducted nationally in Malawi. Data collected may pertain to the entire national cohort of ART patients (e.g. Baobab Health NART) or to specific smaller cohorts developed by implementing partners, other researchers, and clinics themselves.

b. Inclusion Criteria

This study aims to measure coverage and outcomes of DSD across Malawi. For this reason, we will include in our study all adults who are accessing care for HIV anywhere in the country. The inclusion criteria are shown below.

Inclusion criteria

- ≥ 15 years old
- Patients accessing care for HIV within the data collection period (January 1, 2014 to February 28, 2021)
- In any HIV transmission risk group (general adults and adolescents, high transmission risk populations)

Exclusion criteria

- None

Children younger than 15 are excluded from this study for two reasons. First, they are typically treated in pediatric HIV programs that have different drug regimens, visit schedules, and models of care than do adults. Second, the vast majority of DSD implementation in the focus countries to date has involved only adult and adolescent patients, not children [15].

6. DATA SOURCES AND MANAGEMENT

a. Data Sources

The MOH and its partners will implement the DSD strategies addressed in this study. This protocol is solely for an evaluation of the coverage and outcomes of the interventions. The study team will have no involvement in providing services nor any interaction with patients. The evaluation will instead rely solely on existing, retrospective national-, facility-, and patient-level records.

Routine data sources to be accessed for this study include:

- Baobab Health National ART (NART) System
- Baobab Health Laboratory Information Management Systems (LIMS)
- Other MOH electronic and paper patient records and registers which capture relevant information related to the care and treatment of patients in any model of ART care and treatment. NART does not currently fully capture model of service delivery, for example, so access to paper files at clinics may be required to build the study database.
- Existing, de-identified data sets from trial, cohort, and observational studies, in collaboration with implementers, technical support partners, and research organizations.

The Ministry of Health will be asked to assure and facilitate access to Baobab Health's NART, LIMS and other routinely collected sources of electronic data.

Data will be collected for all patients in each data set who accessed care for HIV on or after January 1, 2014. The focus countries began large-scale implementation of DSD in 2015 or 2016. Starting in 2014

will thus allow us a pre-intervention period for comparison. Data collection will continue throughout the study period, which ends on February 28, 2021.

b. Data Fields to be Collected

Below (Table 1) we summarize the existing data required for the evaluation. A detailed list of data fields follows this summary.

Table 1. Data sought for evaluation of DSD

Themes	Potential availability and source(s)
Proportion of current ART patients meeting definition of stable; distribution of reasons for not meeting definition	Data from electronic medical records, existing M&E reports, IeDEA and PEPFAR partners, cohorts under observation, facilities participating in others' studies
Geographic distribution and description of differentiated models in use	Reports from existing implementers and technical support partners and MOH
Number (proportion) of patients in each model at time of data collection; patient-months enrolled in each model in previous 12-month period	Data from existing implementers and technical support partners, with quality assessment through primary data collection at a sample of sites
Location, duration, and frequency of dispensing for ARVs and other ART-related medications (e.g. INH)	Electronic medical record data; pharmacy data
Number of facility and non-facility visits per patient per year, by model of care and purpose of visit (e.g. clinical consultation, medication pickup)	Electronic medical record data
Number and outcomes of viral load tests, CD4 counts, and other ART-related laboratory assays per patient per year, by model of care	Electronic medical record data

The specific data fields available and required for different patient types will vary slightly (e.g. viral loads will not be available for patients newly initiating treatment). In general, however, we will collect a common set of variables for all patients. The specific fields are listed below:

Demographic information

- Electronic medical record system number (e.g. Baobab Health NART record number)*
- Clinic file, register, and card numbers (assigned by the clinic)*
- National ID number*
- Name*
- Date of birth*
- Weight and height or BMI
- Sex
- Age in years
- Marital status if recorded
- Employment status if recorded
- Education level if recorded

- Smoking and alcohol use if recorded

*Identifiers like name and date of birth are required to link electronic and paper-based records pertaining to individual patients. Many clinics use name or initials and date of birth to create a clinic record number. For example, numbers and dates of clinic visits can typically be extracted from Baobab Health, but the specific model of care used by an individual patient may require linking Baobab Health records to data manually transcribed from paper clinic records.

Clinical information

- Date of positive HIV test (if available)
- Dates of all clinic visits (including pre-ART and after ART initiation)
- Primary purpose of all clinic visits (e.g. HIV test, CD4 count, counselling, ARV dispensing, ART monitoring, etc.)
- Dates of next scheduled clinic visits (dates patients are expected to return to clinic)
- Date treatment eligibility determined, if reported
- Date and result of CD4 count indicating treatment eligibility (baseline)
- WHO stage and clinical conditions
- Date and result of TB symptom screen
- Date, type, and result of TB test
- Date TB treatment initiated, if relevant
- Date ART initiated (first dose of medications dispensed)
- First-line regimen prescribed
- Any changes to first line regimens and dates of changes
- Dates, quantity (duration), and type for all medication collections
- Dates and results of all viral load tests
- Dates and results of all other laboratory investigations

DSD information

- Model(s) of care enrolled in and duration of enrollment
- Eligibility criteria and dates for alternative model of care
- Dates of participation in DSD activities (e.g. adherence club attendance, CCMDD pickups, multi-month dispensing, etc.)
- Other resources used for ART and recorded in the data source

In addition, we will collect aggregate, clinic- or DSD-level information about resources utilized, providers accessed, volumes served, etc. **This will not be human subjects research.** We will obtain this information from descriptions included in papers and reports, and, where necessary, surveys conducted by the study team.

c. Data Entry and Storage

The data sets that will be analyzed in this study will be shared with the study team by the Ministry of Health, implementing partners, or other researchers/evaluators. For all patient data extracted from paper files and registers, we anticipate entering all data onto electronic case report forms on tablets on site, so that paper forms do not need to be removed from the study clinics. Once patient information is captured on the tablet, the information will be immediately sent to a highly secure cloud server and wiped from the tablet. Once the databases are received by the study team, the data will be downloaded onto secure, protected drives at the HE^{2}RO office in South Africa and at Boston University, with access limited to relevant study staff. Details on data transfer and drive security are provided under Subject Confidentiality below.

Each subject in a data set will immediately be assigned an anonymous patient ID number. For each subject, a national ID number, electronic clinic record number, date of birth, and name will be collected to allow linking of fields extracted from multiple data sources (registers, records, lab reports, etc.). An electronic linking file will link this information to the patient ID number. The linking file will be kept until all data collection is complete, the data set has been closed, and all data has been linked. Once the linking is complete, the linking file will be destroyed. All data collection files will be coded using patient ID numbers and not contain subject identifiers. We note that some data sets, such as those from completed trials, will be closed (no further updates expected) when we receive them, and these data can be de-linked soon after receipt. Other data sets, like longitudinal electronic medical record data, will not be closed until the study is completed.

Study databases will be managed at the HE^{2}RO Johannesburg office by the study team. On a regular basis, the data will be converted to SAS, STATA, or SPSS for cleaning and data analysis. All data management and analytic databases will be password-protected with access restricted to the members of the study team. All linking files will be destroyed once the analytic data sets are cleaned and closed. De-identified analytic datasets will be provided to the study collaborators to allow participation in analysis.

7. DATA ANALYSIS

a. Sample Size

In order to measure national coverage of DSD, we will access data for up to the entire national ART cohort. In Malawi, the estimated number of individuals on ART is currently 740,000 [16]. This is expected to increase to ≥ 90% of the entire HIV-infected population by the time the study ends. We therefore expect to collect and analyze data for up to 1,000,000 individuals, the estimated HIV-positive population in Malawi [16]. As noted above, all data will be drawn from records that exist at the time of data collection; the study will have no interaction with study subjects.

b. Outcomes

To estimate uptake, benefits, and costs of DSD, we will aim to report the following results, stratified by model care and/or other patient or clinic/model characteristics:

1. Percentage of current ART patients eligible for any alternative model, under current guidelines
2. Demographic, economic, and clinical characteristics of patients in each model, as data allow.
3. Patient-months enrolled in any DSD and in each model
4. Frequency of transfer between models of care, including back to the conventional model
5. Location, duration, and frequency of ARV dispensing
6. Number of clinical visits/patient/year
7. Quantities of resources used/patient/year
8. Geographic distribution of patients enrolled in each DSD
9. Retention on ART, measured at 6-month intervals
10. Proportion virally suppressed (< 400 copies/ml[3])
11. Other outcomes relevant to DSD that can be estimated from available data

Note: as this is not a clinical trial, we have not designated primary and secondary outcomes. We will report as many of the above outcomes as data allow.

c. Analysis

To evaluate the broad, national- or system-wide implications of differentiated models of ART delivery in the context of health systems in sub-Saharan Africa, we will conduct the following analyses.

Outcomes 1-4 above entail description of the models of care and the patients enrolled in them. For these outcomes, we will begin by categorizing patients in the sample as to whether they are eligible for and receiving one of the models of care and report the proportion in each group. We will then describe the demographic, economic, and clinical characteristics of patients stratified by model of care (age, gender, time on ART, baseline CD4, and others) using means or medians as appropriate for continuous variables and proportions for categorical variables. We will further quantify the number of patient-months enrolled in any DSD model and in each specific model and the frequency of transfer between models of care, including back to the conventional model. We will look for differences in the models of care, number of patient-months enrolled, and frequency of transfer by demographic, economic, and clinical characteristics using stratified analyses and report risk differences and corresponding 95% confidence intervals. As the analysis is meant to be descriptive we will not conduct regression analyses as our primary analyses.

Outcomes 5-6 describe characteristics of the models of care that are being implemented. Separately from this protocol, we will review governmental and implementing partner SOPs, reports, and manuscripts in order to describe features of the models of care including location, duration, frequency

of ARV dispensing, and the number of clinical visits per patient per year (all non-human subjects research). We will report these using means or medians as appropriate for continuous variables and proportions for categorical variables. We will then compare the expected features to patient data and report the proportion of agreement to determine whether the models of care are being implemented as per SOP. We will present these as proportions with corresponding 95% confidence intervals.

Outcome 7 measures the quantities of resources used per patient per year. For this outcome, we will estimate the quantities of resources used per patient per year enrolled in DSD. We will start with bottom-up costing of the resources utilized per patient served in the clinics as recorded in the data. The quantity of each resource used by each enrolled patient will be estimated and then multiplied by the unit cost for that resource. Unit costs will be calculated from clinic invoices, MOH price lists, government salary scales, and other sources of actual costs incurred. We will use a top-down approach to estimate shared costs (e.g. clinic management) where necessary. These will be reported as means and medians, with standard deviations/IQRs.

Outcome 8 measures the geographic distribution of patients enrolled in each DSD. For this outcome we will calculate the percentage of people enrolled in a differentiated model of ART delivery at the facility level, defined as the number of patients enrolled in differentiated service delivery divided by the number of patients currently accessing ART at a site. This will be estimated through either routine patient-level indicators available from national data sources, or aggregate facility-level information from service delivery partners. We will use heat maps to geographically map the level of DSD model coverage by most granular level of information available (province, district, etc.).

Outcomes 9-11 measure health outcomes by model of care. For these outcomes, we will begin with descriptive analyses of the characteristics of the population stratified by model of care. For each outcome described above, we will conduct a crude analysis comparing the proportion of subjects with the outcome by model of care. Next, we will conduct an analysis for each outcome accounting only for clustering using generalized estimating equations (GEE) with an unstructured correlation matrix and clustering by treatment site. In all cases the outcomes are dichotomous and therefore we will calculate risk differences comparing the intervention to the comparison arms using a linear link function and a binomial distribution. Next, should any imbalances between models of care be detected, we will adjust for those covariates in our GEE model. Finally, we will look for differences in the effects of the models of care by important baseline characteristics (e.g. size of the treatment population, rural vs. urban, province, etc.) using stratified analyses.

d. Dissemination of Findings

The results of this study will be disseminated as widely as possible in the study countries and globally. A full report will be made to local stakeholders and will be circulated widely and posted on our website. We will also develop a short briefing document to send to the Ministry of Health, donor agencies, and other interested organizations, and we will present the results at relevant conferences domestically and internationally. One or more journal manuscripts will be submitted to an appropriate peer-reviewed international journal.

8. ETHICAL CONSIDERATIONS

The evaluation will require ethics approval from the Institutional Review Board of Boston University and the University of the Witwatersrand's Human Ethics Research Committee and the National Health Sciences Research Committee (NHSRC) of Malawi.

a. Potential Risks

The study team will not collect any biomedical samples specifically for this study and will not have any interaction with study subjects. Both biomedical and clinical data for the study will be drawn from existing data. We therefore believe that our study poses no physical risks to subjects.

The only risk that we believe is posed by this study is that of loss of confidentiality. We will collect data indicating individuals' HIV status and other sensitive health information. A high level of stigmatization continues to inhibit the disclosure of HIV status in the study population. A breach of confidentiality, for example through inadvertent loss of a storage device or paper files, would thus pose a risk to subjects.

b. Protections Against Risks

We will protect against the risk and repercussions of loss of confidentiality in two main ways. First, patient identifiers will be collected and stored separately from all other individual data. As explained above, names, national identification numbers, and other identifying information will be used only for the purposes of linking disparate sources of data for the same patient. Identifiers will be separated from the rest of each data set and stored in encrypted, password protected files. As soon as a specific source document has been linked to the patient of interest, data from it will be entered in a record containing the Study ID number only. Analytic data sets will not contain any identifiers.

Second, all study data will be stored in secure locations. Password-protected laptops used on site will be kept in locked and secure locations when not in use. Patient data extracted from electronic patient systems will be extracted in a password protected double-encrypted format and will be uploaded to a secure server at the HE^2RO office via a dedicated secure VPN. For all patient data extracted from paper files and registers, we anticipate entering all data onto electronic case report forms on tablets on site, so that paper forms do not need to be removed from the study clinics. Once patient information is captured on the tablet, the information will be immediately sent to a highly secure cloud server and wiped from the tablet. If data transfer is required, the data will be transferred through a secure cloud-based system. The data will be encrypted, uploaded to the relevant location and then removed from the cloud as soon as the recipient confirms receipt of the data. Study staff will not be permitted to download de-identified data sets for cleaning or analysis except with the explicit permission of a co-investigator, and data sets will not be stored on individual hard drives when not in use. Upon completion of the study, computer files containing study data will be retained for five years and then destroyed.

All study staff will be trained in Good Clinical Practice, research ethics, and study procedures to ensure that they understand both research confidentiality requirements and study confidentiality procedures. Study investigators will monitor data collection on an ongoing basis. They will report to the BU IRB the Wits HREC, and NHSRC (Malawi) any breaches in confidentiality identified. In the event that a breach in confidentiality does occur, staff will be retrained on human subjects protection and confidentiality if possible or removed from the study if the either the breach is too serious or if the PI feels the staff member cannot be sufficiently retrained. Staff will be made aware of this condition on employment.

c. Direct Benefits

There are no direct benefits to study subjects enrolled in this study.

d. Indirect (Societal) Benefits

The indirect benefits of this study are expected to be large. Differentiated service delivery models are being scaled up across sub-Saharan Africa and will ultimately affect hundreds of thousands, if not millions, of patients. Generating information about coverage, allocation, costs and benefits of these programs has the potential to make the DSD models more effective nationwide. The evaluation will also assist the MOH to target and tailor its interventions and allocate its resources to the patients at greatest need and/or most likely to benefit and help project budgetary needs in future years.

e. Risk to Benefit Ratio

Because the indirect benefits of the study are large and the risks to human subjects are minimal, we are confident that the risks to subjects are reasonable in relation to anticipated benefits.

f. Recruitment Procedures

As explained above, we will not generate any new (not yet collected) data for this study, nor will we have any interaction with study subjects. We will therefore not have an active recruitment procedure. We will enroll in the study all current and former ART patients accessing HIV care from January 1, 2014 to February 28, 2021. No screening of study subjects will be conducted.

g. Informed Consent

We do not intend to seek informed consent for this study which is a retrospective record review only and poses minimal risk to study subjects. We therefore request a Waiver of Informed Consent.

h. Subject Confidentiality

As explained above, we will take multiple steps to protect subject confidentiality. These are detailed in the paragraph entitled “Potential Risks and Protections.”

i. Destruction of Identifiers

The linking files will be kept until all data collection for each individual study subject is complete, the data set has been closed, and all data has been linked. Once the linking is complete, the linking file will be destroyed. All data collection files will be coded using patient ID numbers and not contain subject identifiers. We note that some data sets, such as those from completed trials, will be closed (no further updates expected) when we receive them, and these data can be de-linked soon after receipt. Other data sets, like longitudinal electronic medical record data, will not be closed until the study is completed, as we anticipate receiving updated EMR data sets periodically throughout the project.

j. Costs and Payments

Study subjects will not incur any costs from study participation or receive any payments for it.

k. Data Safety Monitoring Plan

This study is not greater than minimal risk. Unanticipated problems, adverse events, and protocol deviations will be reported to the BU IRB, Wits HREC, and NHSRC as required by each institution’s policies. The study monitor will be the Principal Investigator at Boston Medical Center/BU Medical Campus and will report all adverse events and Unanticipated Problems to the IRB in compliance with IRB policy, Federal/State regulations, and sponsor requirements (as applicable).

9. REFERENCES

1. Grimsrud A, Bygrave H, Doherty M, Ehrenkranz P, Ellman T, Ferris R, et al. Reimagining HIV service delivery : the role of differentiated care from prevention to suppression. J Acquir Immune Defic Syndr. 2016; 10–12. doi:10.7448/IAS.19.1.21484
2. Kolawole GO, Gilbert HN, Dadem NY, Genberg BL, Agaba PA, Okonkwo P, et al. Patient Experiences of Decentralized HIV Treatment and Care in Plateau State, North Central Nigeria: A Qualitative Study. AIDS Res Treat; 2017. doi:10.1155/2017/2838059
3. Prust ML, Banda CK, Nyirenda R, Chimbwandira F, Kalua T, Jahn A, et al. Community ART groups: results from a process evaluation in Malawi on using differentiated models of care to achieve national HIV treatment goals. J Int AIDS Soc. 2017;20: 41–50. doi:10.7448/IAS.20.5.21650
4. Wilkinson L, Harley B, Sharp J, Solomon S, Jacobs S, Cragg C, et al. Expansion of the Adherence Club model for stable antiretroviral therapy patients in the Cape Metro, South Africa 2011-2015. Trop Med Int Heal. 2016; doi:10.1111/tmi.12699
5. Vogt F, Kalenga L, Lukela J, Salumu F, Diallo I, Nico E, et al. Decentralizing ART supply for stable HIV patients to community-based distribution centres: Programme outcomes from an urban

context in Kinshasa, DRC. J Acquir Immune Defic Syndr. 2016;74: 1. doi:10.1097/QAI.0000000000001215

6. Geldsetzer P, Francis JM, Ulenga N, Sando D, Lema IA, Mboggo E, et al. The impact of community health worker-led home delivery of antiretroviral therapy on virological suppression: a non-inferiority cluster-randomized health systems trial in Dar es Salaam, Tanzania. BMC Health Serv Res. BMC Health Services Research; 2017;17: 1–12. doi:10.1186/s12913-017-2032-7

7. Fox MP, Pascoe SJ, Huber AN, Murphy J, Phokojoe M, Gorgens M, et. al. Assessing the impact of the National Department of Health's National Adherence Guidelines for Chronic Diseases in South Africa using routinely collected data: a cluster-randomised evaluation. BMJ Open. 2018 Jan 21;8(1):e019680. doi: 10.1136/bmjopen-2017-019680.

8. Fox MP, Pascoe SJS, Huber AN, Murphy J, Phokojoe M, Gorgens M, et al. Effectiveness of interventions for unstable patients on antiretroviral therapy in South Africa: results of a cluster-randomised evaluation. Trop Med Int Health. 2018 Dec;23(12):1314-1325. doi: 10.1111/tmi.13152. Epub 2018 Oct 24.

9. Jere L, Cheelo C, Mukumbwa-Mwenechanya M, Mwamba C, Nkwemu S, Sharma A, Bolton C, Topp S, Mutale W. Healthcare workers' and patients' experiences during implementation of the Fast Track model: Piloting differentiated ART service delivery in Zambia [abstract]. In: 22nd International AIDS Conference (AIDS 2018); 2018 July 23–27; Amsterdam, Netherlands. Abstract nr THPEE696.

10. Prust ML, Banda CK, Nyirenda R, Chimbwandira F, Kalua T, Jahn A et al. Multi-month prescriptions, fast-track refills, and community ART groups: results from a process evaluation in Malawi on using differentiated models of care to achieve national HIV treatment goals. Journal of the International AIDS Society 2017, 20(Suppl 4):21650

11. Bango F, Ashmore J, Wilkinson L, van Cutsem G, Cleary S. Adherence clubs for long-term provision of anti-retroviral therapy: Cost-effectiveness and access analysis from Khayelitsha, South Africa. Trop Med Int Heal. 2016; doi:10.1111/tmi.12736

12. Mcbain RK, Petersen E, Tophof N, Dunbar EL, Kalanga N, Nazimera L, et al. Impact and economic evaluation of a novel HIV service delivery model in rural Malawi. AIDS. 2017;31: 1999–2006. doi:10.1097/QAD.0000000000001578

13. Miyano S, Syakantu G, Komada K, Endo H, Sugishita T. Cost - effectiveness analysis of the national decentralization policy of antiretroviral treatment programme in Zambia. Cost Eff Resour Alloc. BioMed Central; 2017; 1–10. doi:10.1186/s12962-017-0065-8

14. Ehrenkranz PD, Calleja JM, El-Sadr W, Fakoya AO, Ford N, Grimsrud A, et al. A pragmatic approach to monitor and evaluate implementation and impact of differentiated ART delivery for global and national stakeholders. J Int AIDS Soc. 2018;21: e25080. doi:10.1002/jia2.25080

15. Ministry of Health, Malawi. 3rd Edition of the Malawi Guidelines for Clinical Management of HIV in Children and Adults. 2016, Lilongwe, Malawi

16. UNAIDS Country Factsheet – Malawi 2017. Reference: Accessed April 4 2019 from

http://www.unaids.org/en/regionscountries/countries/malawi.