Alternative **M**odels of ART Delivery: Optimizing the **B**enef**IT**s

The **AMBIT** Project

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EXECUTIVE SUMMARY

To achieve global goals for the treatment of HIV, most high-prevalence countries are experimenting with and scaling up alternative service delivery approaches, or "differentiated models of care." 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, 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.

Fortunately, in the past half-decade, substantial groundwork has been laid for standardizing methods and indicators for evaluating the performance of alternative models 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. 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 targeted models of care, to help guide ministries of health, donor agencies, and others to make better decisions about what to scale up, where, and for whom.

The proposed, 30-month project, Alternative models of ART delivery: Optimizing the benefits (AMBIT), will be a set of data synthesis, data collection, data analysis, and modeling activities aimed at generating information for near- and long-term decision making and creating an approach and platform for ongoing evaluation of alternative models of HIV treatment delivery in the future. Primary data analysis will be conducted in three focus countries in sub-Saharan Africa: Malawi, Zambia, and South Africa. Activities will include literature reviews, analysis of retrospective data and implementation reports, cost estimates, surveys, modeling, and primary data collection.

AMBIT has five major components:

- Component 1: Coverage. This component captures the current extent of TMOC implementation under current guidelines and synthesizes what is known about the scale of implementation of targeted models at this time and existing targets and criteria for scale-up.
- Component 2: Allocation. This component develops a mathematical model to optimize distribution of alternative models to create an efficient plan for scaling up at national level.
- Component 3: Benefits and costs. This component collects and synthesizes information on the overall potential costs and benefits of large-scale adoption of TMOC in the focus countries, including clinical outcomes, non-clinical patient outcomes, clinic resources and costs, and healthcare worker experience.
- Component 4: Gaps. Component 4 comprises primary research in the focus countries to fill in high priority gaps in the evidence based, as revealed by components 1-3.
- Component 5: Partnerships and dissemination. Component 5 will integrate AMBIT with other ongoing projects involving targeted models of care, build partnerships, elicit input from stakeholders, and assure widespread dissemination of results.

I. PROBLEM STATEMENT

Background and rationale

To achieve global goals for the treatment of HIV, most high-prevalence countries are experimenting with and scaling up alternative service delivery approaches, or "differentiated models of care." 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. clinic visits) to remain stable, and are able to benefit from community-based service delivery that is closer to home[1]. 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 into the programs they support.

*For purposes of this proposal, we will refer to any approach to service delivery that is tailored to some aspect of patient needs as a "**targeted model of care (TMOC)**." The original model of clinic-based ART provision for all patients will be called "**traditional**" and any other model of care "**alternative**." A health system that optimizes the provision of approaches will offer one or more targeted 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) to patient characteristics (age, sex, condition). In this taxonomy, the traditional model of care may be adapted to serve patients who require traditional services, and it is thus a targeted model in itself (for example, Uganda regards "facility-based individual care" as one of its models). We will avoid using the phrase "differentiated model of care (DMOC)" because of its imprecise definition in the literature and differing definitions among countries.*

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 (e.g. ENHANCE, EQUIP, CommART). For most countries, though, we have little evidence on the "big picture." We cannot currently estimate such basic aggregate descriptive measures as the proportion of clinics offering alternative models, eligibility criteria and the proportion of patients considered eligible, the number of patients actually participating, 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—ICAP's CQUIN (https://cquin.icap.columbia.edu/) and PEPFAR's EQUIP (http://www.equiphealth.org/) among them—but their focus is on implementation rather than high-level evaluation or analysis of the phenomenon as a whole.

It is widely assumed that differentiated models of treatment delivery will secure a wide range of benefits for healthcare providers, payers, patients, and households. These include:

- Better or equivalent clinical outcomes (retention and viral suppression);
- Lower provider costs per patient served;
- Greater provider capacity to increase patient volume and/or quality of care, for HIV and other conditions;

- Greater patient and provider satisfaction; and
- Savings in out-of-pocket and opportunity costs to patients.

Despite a high level of confidence on the part of alternative model advocates and implementing countries and 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 relatively little 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 alternative models may certainly affect long-term retention in care. We also expect only modest potential for per-patient cost reductions, due in part to the large share of costs attributable to medications[7–9]. We have found no published evidence that moving HIV patients into alternative models increases the quality or quantity of services that clinics provide to other patients, whether the HIV patients left behind for traditional care or patients with non-HIV conditions.

Fortunately, in the past half-decade, substantial groundwork has been laid for standardizing methods and indicators for evaluating the performance of alternative models at the patient level. The most comprehensive efforts include CQUIN's monitoring and evaluation framework and the set of indicators proposed in Ehrenkranz (2018)[10]. 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. 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 targeted models of care, to help guide ministries of health, donor agencies, and others to make better decisions about what to scale up, where, and for whom.

In response to the BMGF draft TOR dated January 8, 2018, Boston University (PI: Sydney Rosen) and the Health Economics and Epidemiology Research Office (HE^2RO) at the University of the Witwatersrand (PI: Sophie Pascoe) propose the **AMBIT** Project (**A**lternative **M**odels of ART Delivery: Optimizing the **B**enef**IT**s). AMBIT will be a set of data synthesis, data collection, data analysis, and modeling activities aimed at generating information for near- and long-term decision making and creating an approach and platform for ongoing evaluation of TMOC in the future. Primary data analysis will focus on three project countries in sub-Saharan Africa, each representing a different level of economic development: Malawi (low income), Zambia (lower middle income), and South Africa (upper middle income). All three represent locations in which the project team from BU and HE^2RO have both extensive experience and strong local contacts, allowing the project to achieve its objectives in the requested 2.5 year time frame and proposed budget.

Related work by us and others

AMBIT will build on prior and ongoing evaluation work by ourselves and others. Some of the ongoing evaluations that we are aware of now include:

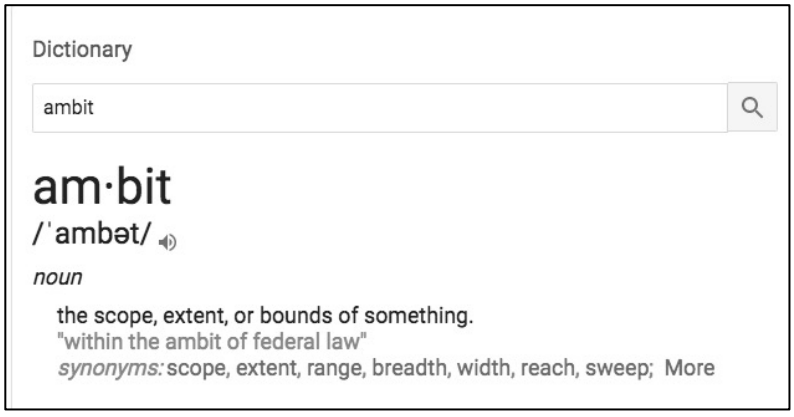
- Cost-outcome studies of alternative models of care in Uganda and Zambia conducted by BU/HE^2RO under USAID's EQUIP project
- Cluster-randomized cost-effectiveness evaluation of two alternative models of medication delivery in South Africa conducted by BU/HE^2RO under the World Bank-funded ENHANCE project[11]
- Cluster-randomized trials of multi-month ARV dispensing in Zambia, Malawi, Lesotho, and Zimbabwe, also under EQUIP[12] and with input from BU/HE^2RO.

- Cluster-randomized trial of alternative models in Zambia implemented by CIDRZ and supported by BMGF, including fast-track refills, same-day initiation, community adherence groups, and urban adherence groups (CommART)[13]
- Implementation studies currently underway within USAID's SOAR project
- Cost studies implemented by Avenir in Kenya, Malawi, and Tanzania in collaboration with the GHCC, supported by BMGF
- Cost studies in Malawi and Zambia conducted by CHAI with BMGF support
- Evaluations and implementation studies conducted by other PEPFAR projects, including CDC-supported work in Namibia and Kenya, USAID-supported work in South Africa, and DoD-supported work in Kenya.

There are also a number of older, published studies that can be mined for information relevant to TMOC today, such as that by Leisegang 2013[14]. In addition, the South African HIV Investment Case introduced novel methods for optimisation by cost-effectiveness under a budget constraint across 16 different HIV interventions, including adherence clubs, down referral to private general practitioners, and community-based adherence supporters[15]. The same BU/HE^{2}RO team is now developing a model to optimize placement of alternative models of care; preliminary work has begun under EQUIP.

In general, we expect to use the results of these studies, others to be identified, and modeling exercises as inputs to the activities described in this proposal. While AMBIT does include some primary research, we anticipate that most data will come from routine sources, existing aggregate reports, and published or unpublished research. For example, the EQUIP study in Zambia will produce a cost-effectiveness comparison of alternative models of care being implemented in that country. We will use these results and those of the CIDRZ CommART study to populate our mathematical model to optimize TMOC distribution and to understand some of the patient- and facility-level outcomes in our framework.

II. SCOPE AND APPROACH



Overview

The approach we propose for the AMBIT project is to evaluate the broad, national- or system-wide implications of targeted models of ART delivery in the context of health systems in sub-Saharan Africa, both to provide a better understanding of the status quo and to identify directions for research and

implementation support in the future. We have divided the project into five components, which will in turn determine the activities we propose to undertake.

- Component 1, **Coverage**, takes a big picture look at the status quo. This component captures the current extent of TMOC implementation under current guidelines and synthesizes what is known about the scale of implementation of targeted models at this time and existing targets and criteria for scale-up. We do not envision conducting a standard literature review on the effectiveness (clinical outcomes) of alternative models, as this has been ably done by differentiatedcare.org, the Global Fund, and the WHO. Instead, we will focus on published and unpublished evidence pertaining to the scale of national programs (proportions of patients covered by which models, etc.).

- Component 2, **Allocation**, expands the mathematical model we are currently developing, which we've dubbed MODULAR, to optimize distribution of alternative models to create an efficient plan for scaling up at national level. For the focus countries, the model will utilize all available data on patient numbers and characteristics, facility locations and capacity, transport infrastructure, and other variables to make recommendations about the most efficient combination(s) of TMOC to implement in each district or other geographic area (or, where possible, for each facility).

- Component 3, **Benefits and costs**, collects and synthesizes information on the overall potential costs and benefits of large-scale adoption of TMOC in the focus countries. For this component we have created the framework shown in Table 1. This framework aims to describe the full set of potential consequences that can be anticipated from large-scale implementation of TMOC. Using the four domains in the framework to guide our work, we will synthesize available data and modeling to improve stakeholders' understanding of what benefits and costs can be expected. We will also use this framework, along with the model created in Component 2, to identify and prioritize critical gaps in the evidence base, which can then be addressed in Component 4. Finally, under Component 3 we will develop a standardized methodology for national-level cost/outcome evaluation of TMOC using routinely collected data.

- Component 4, **Gaps**, is for generation of new evidence to fill priority gaps in current knowledge. Under this component, we expect to conduct one relatively small primary research study in each focus country. Topics for these studies will be identified in Components 1-3 and in collaboration with local and international stakeholders and partners.

- Component 5, **Partnerships and Dissemination**, will integrate AMBIT with other ongoing projects involving targeted models of care. In particular, collaboration with CQUIN and differentiatedcare.org seem essential for the dissemination of findings, identification of new questions, and synthesis of existing data. Component 5 includes a set of activities intended to build partnerships, elicit input from stakeholders, and assure widespread dissemination of results.

As mentioned above, several sets of practical monitoring and evaluation indicators for TMOCs have already been proposed. We take as our starting point that some of these indicators are already being collected and reported, or soon will be. While incorporating many of these indicators into our proposal, we also propose several new metrics that can help describe the system as a whole, rather than gauging progress or costs at individual sites or facilitating comparisons between models within countries.

We also note that demonstrating changes in our domains of interest implies that we will have reliable data on patients, facilities, costs, and other metrics prior to implementation of TMOC or from facilities

that have not yet implemented any alternative models. All of our focus countries are encouraging facilities and programs to adopt alternative models, and sharing of ideas from one site to another is common. We are thus not likely to be able to collect true comparison data sets, except to the extent allowed by retrospective data sources and already-published reports. We will instead use a combination of pre- and post-intervention data and modeling to estimate differences over time, as we have done with the World Bank-supported ENHANCE evaluation of alternatives models in South Africa[16].

For AMBIT, our overall approach will be to find and aggregate existing information, whether published, unpublished, or unanalyzed (e.g. routine clinical data sets). We will collect primary data where major gaps require or to fill in specific parameters required for models.

Component 1: Coverage

Many countries in sub-Saharan Africa are very rapidly scaling up alternative models of care for stable ART patients. There is currently no aggregate information about the kinds of models being offered, the numbers of patients eligible under current guidelines, the number of patients actually participating, and the proportion of clinics that offer alternatives to traditional care. There is also very little known about patients who do not meet criteria for stability, and whether the proportion of such patients is constant. Under Component 1, we will conduct a mapping exercise to collect and synthesize available information from the published literature and gray literature to report what is known about coverage in sub-Saharan Africa during the AMBIT project period. For the focus countries (Malawi, Zambia, South Africa), we will also collect primary data from ministries of health, treatment support partners, and funders to create a more comprehensive picture of the status quo. Where possible, this will include reviewing a sample of electronic patient-level data sets, as implementers' reports on implementation at site level and levels of participation are not always accurate.[*] Data on participation in alternative models is starting to be collected in Tier.Net nationally in South Africa, though the data files remain at each facility; in other countries we will aim to use samples of partners' program and patient-level data to estimate coverage. Data from Component 1 will also help us revise the remaining components as needed, based on data availability and geographic variation in coverage.

In Table 1 below, we list the data fields we aim to collect in Component 1. In the far right column, these fields are matched to the indicators proposed in Ehrenkranz (2018)[10], as shown in Figure 1. We have numbered these indicators for easy of reference in Table 1 and later tables.

[*]For example, for an evaluation being conducted by EQUIP, one implementing partner in Zambia told us that "information on adherence group utilization is in the patient files at the facilities." The facilities then informed us that "we don't keep track of adherence group utilization." Anecdotal evidence like this leads us to question the accuracy of information reported centrally.

Data field(s)	Potential availability and source(s)	Comments	JIAS indicator
% 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	Definition of stable varies by country. We expect to obtain at least some data for these fields in all focus countries. Will likely require some new analysis of electronic patient records.	n.a.
Geographic distribution and description of targeted models in use	Reports from existing implementers and technical support partners and MOH	To be confirmed with routine M&E data from sites, to the extent possible.	n.a.
Number (proportion) of patients in each model at time of data collection; patient-months enrolled in each model	Data from existing implementers and technical support partners, with quality assessment through primary data collection at a sample of sites	Anecdotal evidence indicates discrepancies between partner reports and actual practice. Amount of primary data collection required will depend on how large these discrepancies are.	n.a.
Location, duration, and frequency of dispensing for alternative models	Electronic medical record data; pharmacy data	May require new analysis of patient record databases and/or pharmacy dispensing databases.	1
Number of facility visits per patient per year, by model of care	Electronic medical record data	Data are likely available in routinely kept patient records but may be difficult to match to models of care	2
Number of viral load tests per patient per year, by model of care	Electronic medical record data	Data are likely available in routinely kept patient records but may be difficult to match to models of care	n.a.

Table 1. Data sought for Component 1

JIAS proposed indicators for monitoring and evaluation of alternative models of care (Ehrkranz 2018)

Domain	Proposed indicators
Coverage of differentiated ART delivery	1. # of visits at which medication pickup occurs/PLHIV currently on treatment/12 month period 2. # of clinical visits/PLHIV currently on treatment/12 month period
Experience of PLHIV and HCWs	3. PLHIV experience, including experience of those who disengaged from treatment 4. HCW experience
Clinical outcomes	5. # and % PLHIV virally suppressed/12 month period[1] 6. # and % PLHIV retained in care/12 month period[1] 7. # and % PLHIV lost to follow up/12 month period 8. # and % PLHIV who died/12 month period
Cost and efficiency of health care delivery from the perspective of the patient and the provider	9. Mean clinical consultation time/PLHIV/visit 10. Mean total time spent by the patient to receive HIV treatment services (including transportation)/PLHIV/visit 11. Mean out-of-pocket cost to patient to receive HIV treatment services (including clinic, medication, transportation)/PLHIV/visit 12. # of PLHIV receiving clinical consultations/day/HCW 13. # of patients (of any condition other than HIV) receiving clinical consultations/day/HCW[2] 14. Mean cost of treatment services from a provider perspective /PLHIV/year 15. Mean cost of treatment services from a provider perspective /virally suppressed PLHIV/year

Figure 1

As coverage is a moving target, with frequent shifts in both availability of models and patient utilization, we propose to estimate four specific sets of values:

- Proportion, geographic distribution, and characteristics of facilities at which at least one alternative model is functional for a full year and serves ≥20% of the eligible population. This is consistent with the CQUIN targets for scaling up differentiated models in participating countries. The thresholds may be increased over time, as new models are developed to serve other populations (e.g. unstable patients, co-infected patients, etc.).

- Percentage of ART patients eligible for an alternative model, under current guidelines. So far, most alternative models are limited to "stable" patients, with different definitions of stability applied. To the extent that representative cohort data are available, we will estimate the proportion of current patients who appear to meet each country's criteria and of those who do not.

- Patient-months enrolled in any alternative model of care and in each model. Anecdotal evidence suggests that patients shift from one model to another over the course of a year. It is thus useful to know what proportion of all patient-months of ART provided by a clinic fall under each model, to understand the true scale of operation.

- Location and duration/frequency of ARV dispensing and of facility/clinical visits in all models of care. These are perhaps the two most important characteristics of the models and, in at least some cases, should be available in routinely collected patient record data.

Estimating these values will require combining secondary data analysis (medical records and published reports) with a computer-based mapping exercise to stratify sites and models by setting and key characteristics. If data allow, we will be able to identify geographic regions (provinces, districts) with different levels of alternative model implementation and uptake and to describe how alternative models of care and traditional care are being combined in each focus country. We do not yet know how many of the fields in Table 1 we can populate with existing data. If existing data sources prove insufficient to achieve the goals of Component 1, we will reconsider our approach to this component, in consultation with BMGF and other stakeholders.

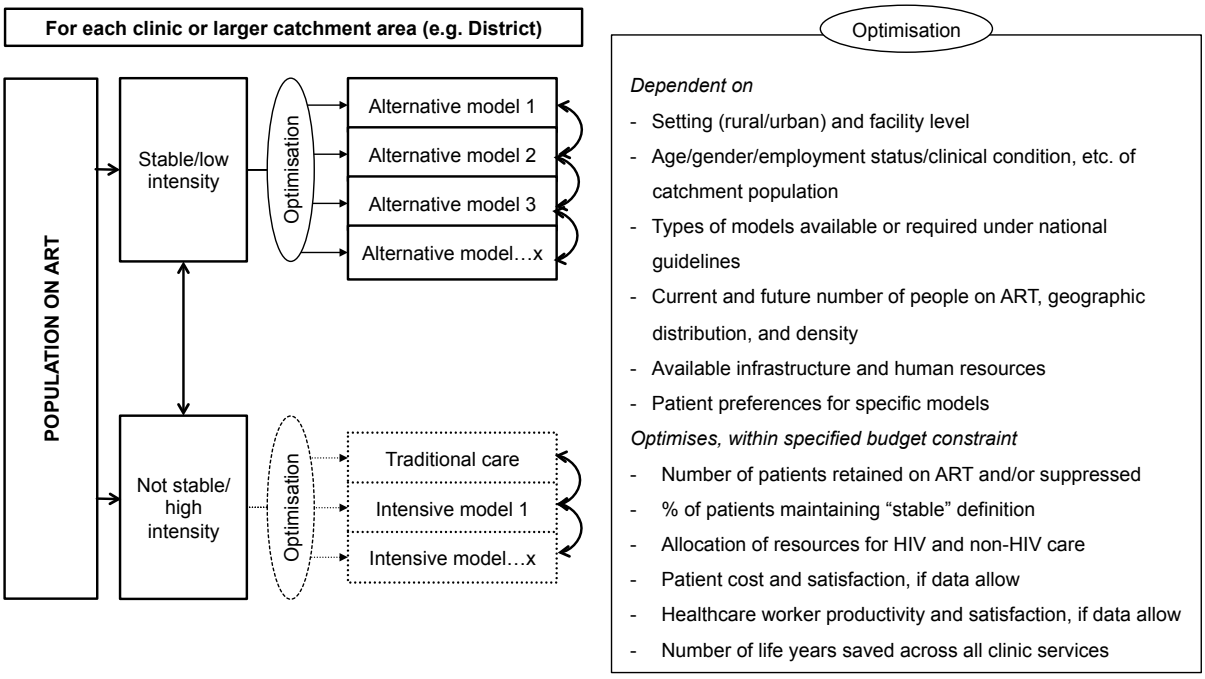
To some extent, the values described here overlap with Step 1c in the five-step process for building a differentiated care system as explained by differentiatedcare.org, which calls for "An initial broad mapping of differentiated ART delivery to determine what is being implemented in-country and the coverage of the models"[17]. They also overlap with items 2.3 and 2.4 in the CQUIN framework (uptake and coverage of alternative ART services among HIV patients). Work in Component 1 can thus complement the existing practical process proposed by IAS, ICAP, and others. ***(Terms of reference use case 1a)***

Component 2: Allocation

Present scale-up of TMOC generally offers patients one or more alternative models based on national choices for which models to support. There is little guidance on which models will be most efficient for which kinds of sites or patient populations. If patients live in low-density areas, for example, an adherence club might not be feasible for logistical reasons. Similarly, if facilities are extremely crowded, facility-based models may not be a reasonable approach. In all cases, costs are likely to vary with the menu of options available and how well they serve patient needs.

In Domain 2, we will continue to develop the mathematical model started under the EQUIP project (called MODULAR) to optimize the distribution of alternative and traditional models. To the extent that data allow, this model will take into account existing clinic infrastructure, roads and travel times for patients and test samples, and the clinical and geographic distribution of patients in a clinic's catchment area and/or patient cohort. As illustrated in Figure 2, the model will optimize for each facility (or district, as data permit) the distribution of existing and new patients into a set of targeted models (traditional and alternative) that will, at the least, maximize the number of ART patients who can be treated without increasing budgetary costs. Additionally, and depending on data generated in Component 3, we could also maximize retention and ART outcomes, for each clinic/ district and maximize clinical and non-clinical outcomes based on specific weights allocated to each.

Figure 2. Schematic of optimization model



In addition to allocation by site and patient characteristics, the question of "how many models is enough and how many is too many" has not been answered. It may be that the most efficient approach is to offer one alternative model for all stable ART patients and use an "opt-out" assignment procedure. Alternatively, offering patients choices may be essential for achieving goals. The mathematical model we create in Domain 2 will also help us to understand this question. Lastly, we will use the model to examine the question of whether alternative models should be restricted to ART patients defined as stable or should be open to any patient on ART, including the newly initiated and those with poor adherence, who may benefit the most from an easier way to obtain medications. **(*Use case 1d)***

Component 3: Benefits and costs

The universe of potential costs and benefits associated with scaling up alternative models of care extends beyond simple measures of viral suppression or retention and of incremental cost. In an effort to identify all the potential consequences of incorporating TMOC into the health system at large scale,

we have defined four domains in which benefits and costs may accrue. These domains are described in Table 2 and below. We note that these closely overlap the domains proposed in Ehrenkranz (2018), and Table 2 maps our domains to the indicators in that paper. We have also added data fields, however, that we would like to collect in AMBIT that are not likely to be collected for routine monitoring. **(*Use case 1b)***

Table 2: Potential benefits and costs of scaling up targeted models of ART delivery

Domain	Category	Goal	Data and measurement considerations	Comments	JIAS indicator
Domain 1: Clinical outcomes	90-90-90 outcomes for ART patients	Improve average outcomes for ART patient population served by clinic, without harming any specific group's outcomes.	Measure as: a) proportion of total patient-months in clinic's treated population (and in each model) for which ARVs are dispensed; b) proportion of 12-month intervals during which patients are retained or suppressed; and c) number and % of clinic population who meet the definition for stable over time.	Must include all ART patients, not just those meeting stability criteria for alternative models. Otherwise we are measuring suppression in the population known to be suppressed at baseline and most likely to stay suppressed. Non-inferiority of outcomes is acceptable; worse outcomes may not be. If targeted models achieve goals for improved quality of care, fewer patients on ART should be designated as unstable, over time. Comparison populations may be synthetic.	5, 6, 7, 8
	Clinical outcomes for non-ART patients	Ideally, better uptake of ART among HIV+ not yet on ART and higher rates of success for screening and treating TB and NCDs.	Standard indicators for these outcomes. Depends on having consistent patient records over time; will likely require site-level data collection.	Outcomes should improve or number of patients managed should increase due to more provider time/patient and other resources, unless there is a backlog of ART patients.	n.a.
Domain 2: Non-clinical patient outcomes	Costs to patients	Lower costs to patients for those enrolled in novel models with no increase for those remaining in traditional care (and potential reduction in opportunity costs for all).	Includes out-of-pocket (cash) costs and opportunity (time) costs, with valuation (labor productivity). Some data available; may require some new surveys.	These should decrease or stay the same but increases are possible. Visit or service fees should also be taken into account.	10, 11
	Patient satisfaction	Higher satisfaction and better quality of life for both novel and traditional model patients.	Can be determined through patient questionnaires and waiting time observations; comparison population may be difficult to identify.	Includes direct satisfaction with healthcare services, quality of life, and acceptability of novel models. Could include non-HIV patients as well.	3
Domain 3: Clinic resources and costs	Costs to provider	Reduced provider costs.	Average cost per ART patient, regardless of model (including traditional care). Take cost of ART program at site and divide by	Average cost per patient on ART and per patient suppressed could go up or down. Small decreases in average cost/patient in novel models could be offset by	14, 15

Domain	Category	Goal	Data and measurement considerations	Comments	JIAS indicator
			number of patients treated and number of patients suppressed.	increases in average cost/patient in traditional care—reallocation of costs but no true reduction. More patients retained on ART may increase overall treatment program cost, even if cost/patient falls.	
	Service delivery capacity	Increased or equivalent capacity unless there is an overall reduction resource availability (e.g. staff are transferred due to fewer visits/year).	Raw number of patients managed by sites, controlling for major resources allocated to sites (staff, space).	If novel models reduce number or duration of visits, clinic may have capacity to take on more clients for ART or non-ART care. Only relevant if there is unmet demand and if clinic's resources (staff) are unchanged.	12, 13
	Clinical quality	Improved outcomes for at least one group of patients, without worsening of outcomes for any.	Standard outcome metrics for HIV and chronic non-HIV patients.	Staff may have more time and other resources for complicated (non-stable) ART patients and/or non-HIV patients. Alternative is no change in staff time usage (longer breaks or shorter hours).	5, 6, 7, 8
	Resource availability and utilization	Ideally, resources matched to demand independent of model. Clinics should not be "punished" (lose resources) for becoming more efficient.	Changes in resources over time, as TMOC utilization expands. Should also report staff cadres utilized for ART patients, time-and-motion data, process and quality assessments, reduction in unplanned fluctuations in staff and stock availability given patient demand.	Resources available to clinic (e.g. staff) may stay the same, decrease, or increase as demand for facility-based services changes. Staff roles may also change, for example by shifting more tasks to lay HCW. Staff may have more time for data entry, training, stock management, etc. Alternative is no change in staff time usage (longer breaks or shorter hours).	9
	Facility performance	Improvements in overall performance (requires active leadership at senior level).	Composite aggregate metric using data described above (cost, capacity, quality, resource utilization) in a way that captures overall efficiency.	Metric for this measure does not exist. May need to create a scale or graph to incorporate multiple aspects of performance.	n.a.
Domain 4: Healthcare worker experience	Satisfaction	Higher satisfaction due to lower burden and potentially improved management.	Can only be determined through staff questionnaires, as staff retention is usually not voluntary.	HCWs may express more or less satisfaction with their work, which could be due to fewer clinic visits, happier patients, or general management improvements caused by TMOC.	4
	Guideline compliance	Better guideline compliance for HIV and non-HIV care.	Assessment of compliance with guidelines for a sample of patients.	If TMOC reduce pressure and burden on HCWs or improves training and support, guideline compliance could increase.	n.a.
	Productivity	Patient	Aggregate data per site	Through experience of TMOC,	12

Domain	Category	Goal	Data and measurement considerations	Comments	JIAS indicator
		load/provider increases without sacrificing outcomes.	(number of providers, number of successful patient outcomes).	HCWs could become more effective (produce an overall larger amount of health).	
	Task-shifting	Models utilize lowest cost cadre that can effectively provide services	Will need HR data to show the training and compensation levels of staff for both traditional and novel models.	There have been concerns raised that novel models rely heavily on lay staff who may or may not be paid; we have observed this in South Africa.	n.a.

Domain 1: Clinical outcomes

One of the reasons for targeting care, rather than remaining with a traditional model, is to improve or, minimally, maintain clinical outcomes for those on ART. For alternative models enrolling only stable patients, the extent to which improvements in health outcomes can occur is self-limiting, but these models must at least be non-inferior in terms of achieving retention and suppression. In addition, if a healthcare provider has more time to spend with unstable patients on ART, clinical outcomes may improve for those that remain in traditional care. Finally, if a healthcare provider has additional time, we may observe an increase in the successful diagnosis, treatment and/or prevention of other diseases such as tuberculosis (TB) or non-communicable diseases (NCDs).

In Domain 1 we will utilize existing ongoing studies and routine data in focus countries (Malawi, South Africa and Zambia) to analyze clinical outcomes of all patients on ART at a referring facility, including both those in alternative models and those in traditional care. It is important to look at the patient population as a whole, rather than solely those enrolled in alternative models, to capture the effect of TMOC on outcomes. It is particularly relevant because nearly all TMOC programs to date are limited to patients already determined to be stable on ART. There is thus little room for improvement among those enrolled in alternative models, while those remaining in traditional care are likely to have potential for better outcomes.

We will also utilize ongoing studies and partner reporting to assess the rates of diagnosis and treatment of TB and NCDs as an indication of a broad health systems improvement in clinical outcomes. Should these indicators not be regularly reported, site-level data extraction may be required at a subset of representative facilities.

In addition, where possible, we will collect information on the outcomes of patients lost to care from alternative models. A full assessment of outcomes after loss to follow up is beyond the scope of this proposal, as it would require extensive tracing and prospective (consented) data collection. Where available national electronic medical record systems are in place and sufficient, patients lost to follow up can be traced to other facilities. We are able to do this in South Africa using the National Health Laboratory Service database and Tier.net, the ART record system, though most searching must be done manually. We anticipate that some tracing of lost patients can be done electronically in Zambia and Malawi, though this is not certain. If prospective data collection is needed to explain unusually high loss rates for particular models or countries, we will consider incorporating such work into Component 4.

Quantity of care, or capacity to treat more HIV patients, may also increase upon large-scale uptake of alternative models of care. This may only happen in facilities where this is a backlog of patients or communities in which there is unmet demand. To measure the extent to which quantity of care

increases, the change in total number of patients on ART as the proportion in alternative models rises will be assessed. (***Use case 1b****)*

Domain 2: Non-clinical outcomes

A stated aim of targeted models of care (TMOC) is to provide services that are more closely aligned to the needs of the patients. Ultimately this may be seen in better clinical outcomes, but particularly for patients who are already stable and those facing adherence challenges, it is important to capture non-clinical outcomes as well. The cost to the patient of accessing care and treatment and their satisfaction with the services they access are two key non-clinical outcomes.

The economic cost to patients accessing care and treatment includes both the incurred financial cost (i.e. clinic fee, cost of transport) as well as the opportunity cost (i.e. time spent waiting, forgone wages). As TMOC are by design meant to be more patient-centric (i.e. closer to the patient population, have shorter queues, require fewer visits) the economic cost to patients is likely to decrease or remain the same. It is possible that the cost could increase (i.e. time spent accessing through a CAG is longer than going directly to the facility), but ultimately the patient should see some utility (benefit) from the TMOC either through decreased economic cost or increased satisfaction. This is why it is important to measure patient satisfaction in addition to patient cost.

There are a number of instruments and a body of supporting literature on the measurement of patient satisfaction with primary health care services. Some of the features that have been found to drive patient satisfaction are the continuity, comprehensiveness, accessibility, cost, and humaneness of services. If the TMOC are meeting their goals of providing patient-centered services then it would be expected that patients would report an improvement in satisfaction within at least one of these areas. The targeted nature of the interventions coupled with the diverse patient population means that it is unlikely that patients would report an improvement in all areas from a single model (some may remain constant or even worsen). While it is conceivable to create a composite patient satisfaction index, this would not provide policy makers or program implementers clear guidance on what parts of the program are having a positive impact at a patient level. Instead, for this domain we will look at data collected from surveys and qualitative studies, existing and new, about specific aspects of patient satisfaction.

Domain 3: Service delivery efficiency

The most challenging potential changes that may accompany scale-up of TMOC are those to service delivery procedures and resource allocation, rather than individual patient care and outcomes. In principle, the shifting of ART patients, who in many cases comprise a substantial share of all chronic patients in a clinic, from higher- to lower-intensity models of care should have profound effects on the availability of resources at the clinic, which could be used to improve HIV care, improve care for other conditions, or increase the number of patients served. The belief that alternative models will save money per patient enrolled, for example, is a major driver of current scale-up efforts.[17]

Measuring such changes is difficult, however, for several reasons.

- First, in many areas alternative models have not yet been implemented widely enough, consistently enough, or for a large enough proportion of patients that impacts on clinic efficiency should be expected. A clinic that offers community medication delivery but has only a handful of patients

signed up for it, for example, will not likely see facility-level resource effects. Many intervention evaluations of alternative models face the same limitation.

- Second, not all the alternative models free up resources as intended. If a pharmacist still has to review scripts, package medications, and complete records for all individual patients, the location of pickup may make little difference to the staff time required.

- And third, metrics for capturing changes to clinic efficiency are highly problematic due to the many ways in which "freed up" resources can be used. Clinic staff may spend more time per HIV or non-HIV patient remaining in facility care, thereby potentially improving the quality of care for the same number of patients. Alternatively, the clinic may be able to serve a larger number of patients (HIV and/or non-HIV) at the same level of quality as in the past. Freed-up time may be used to improve clinic-wide functions such as record-keeping, training, or stock management. Conversely, freed-up time may not be utilized productively at all, but instead lead to longer breaks during the day or shorter working hours. This is likely to be the case if clinic managers do not actively monitor and adapt to the new models. Documenting facility managers' reactions to the redistribution of patients to alternative models of care is thus also important.

Domain 3 attempts to evaluate a number of potential efficiency changes that scale-up of TMOC could produce, in four areas: a) clinical outcomes, b) non-clinical outcomes, c) resource allocation and cost, and d) provider experience. We note the importance of taking a clinic-wide view of efficiency to avoid incorrect conclusions[†]. If the cost per patient enrolled in an alternative model decreases, for example, this may or may not indicate a cost saving for the clinic's ART program. By leaving the most expensive patients in traditional care, the alternative model may simply cause a reallocation of costs among all targeted models, rather than an absolute decrease. For the categories in this domain, we will use existing data to the extent possible, but we anticipate that some new data will need to be generated for a sample of sites in the focus countries. **(*Use cases 1c, 3a-d, and 4a-b)***

In addition to the activities described above, under Component 3 we will develop a standardized methodology for national-level cost/outcome evaluation of TMOC using routinely collected data. This model will be aligned with the GHCC's costing reference case and with the approach we developed a number of years ago for stratifying outcomes and costs. An important element of the methodology we will propose is that it will take into account all ART patients, not only those assigned to alternative models, and thereby incorporate cost data into a measure of overall cost-effectiveness. The new methodology will build on our existing HCOM (Healthcare Costs and Outcomes Model) tool, available at http://www.heroza.org/researchtools/the-healthcare-cost-and-outcomes-model-hcom.

Domain 4: Healthcare worker experience

Finally, Domain 4 considers the impacts of TMOC scale-up on healthcare workers, both clinical and lay. This includes HCW roles (task-shifting), productivity as indicated by number of visits per provider at each level, compliance with prevailing treatment guidelines for ART and other conditions, and job satisfaction for affected cadres of staff. We anticipate that the first two measures (roles and productivity) can be collected or inferred from existing information and/or routinely collected data. Compliance with

[†]In fact, a district- or system-wide view of efficiency would be ideal, as rollout of TMOC could ultimately affect allocation of resources beyond any single clinic. Such an analysis is not currently feasible, however.

guidelines will be more challenging, given the array of guidelines in use. To evaluate compliance, we will look at previous studies on this topic and, as needed, collaborate with clinicians who are able to compare patient records with guideline recommendations. Finally, job satisfaction will require surveys of a sample of providers in the focus countries. ***(Use cases 1c and 3b)***

Component 4: Gaps

We anticipate that Components 1-3 of AMBIT will identify a large number of gaps in the evidence base on TMOC, both large and small. As time and resources allow, we will conduct up to three primary data studies (total) in the focus countries to help fill the highest priority gaps. Priority will be determined from consultations with stakeholders and by the model developed in Component 2, which will point to where improvements in estimates of parameters from additional data would be most important. We expect these to be small studies, lasting no more than 1.5 years and with modest budgets. Under Component 4, we will also produce a list of priority research questions about TMOC that remain, updating and adding specificity to the 2017 research agenda paper[18]. **(All use cases)**

Component 5: Partnerships and Dissemination

We have grouped under Component 5 the cross-cutting tasks of integrating AMBIT with other ongoing projects, eliciting stakeholder input, and disseminating results. We anticipate that key organizations with which we will initially interact, in addition to Ministries of Health in the target countries, are the WHO, PEPFAR (including CDC, USAID, OGAC), the Global Fund, the IAS, and ICAP (for CQUIN). We expect that this list will expand as the work progresses and we identify other key potential stakeholders. We will ask each of these organizations to designate one person to serve as the liaison with AMBIT for purposes of communication and coordination.

To facilitate AMBIT's work, we propose to create a small (≈15 persons) technical network of data advisors to guide us on locating existing data sets to use for the analyses described below. In each focus country, we will identify 2-3 individuals with strong contacts and knowledge of HIV-related data sources to participate in this network. To the extent possible, at least one network participant per country will represent the ministry of health, to ensure a communications channel with policy makers. The network will also include the liaison mentioned above from each key stakeholder organization that may be aware of data availability, such as ICAP, OGAC, IAS, etc. The network will be informal, to provide input as needed. We do not anticipate holding in-person meetings of the full network, but will instead take advantage of existing conferences, other project travel, and electronic meeting technology. As requested in the terms of reference for this project, we will also designate an AMBIT representative to participate in existing forums, such as the CDC/WHO process for refining indicators.

Products of AMBIT will be disseminated widely using conference presentations, published articles, and policy briefs. In addition, we will try to include within our data advisor network at least one individual per target country who participates in that country's technical working group (or similar body) responsible for targeted models of service delivery. Our experience suggests that most countries do have such groups, typically organized by the Ministry of Health, National AIDS Council, or a similar national agency.

Rather than re-creating any wheels (or websites), we will aim to collaborate with PEPFAR (USAID, CDC, OGAC), the Global Fund, WHO, ICAP, IAS, the GHCC, and other relevant organizations or websites to utilize their existing communications platforms as fully as possible for AMBIT dissemination. Instead of building a new, publicly-accessible dashboard to disseminate key findings, as is proposed in the TOR, we strongly prefer to utilize existing web-based dissemination platforms, such as differentiatedcare.org and CQUIN's website, that have already established a user base and appropriate technology. We will work with these other projects to confirm that they are willing to help disseminate AMBIT outputs and, if appropriate, how to present these on the sites. All AMBIT products will also be posted on the website of HE^{2}RO, our South African partner (www.heroza.org), which has sections for different kinds of publications and tools/models, and be announced in HE^{2}RO's quarterly newsletter.

We expect that many of the activities described below will take place in the focus countries, with our offices in Boston and Johannesburg serving as headquarters and data analysis/report writing centers. An early step in all the focus countries will be to meet with PEPFAR and Global Fund representatives to learn what alternative models of care each agency is supporting and to request introduction to their implementing partners, as needed. Involvement of these partners will thus also happen at country level, and not solely as communication among head offices.

Finally, through the network and partners mentioned above, as well as our own contacts within EQUIP and other projects, we will promote the use of standard indicators for evaluating TMOCs to the extent that we are able. In our experience, this is a relatively challenging task, as standardization is not necessarily regarded as a virtue in the research community, implementers often have to meet multiple objectives when collecting M&E data, and constraints vary by country. We also note that practical indicators have already been proposed in the literature and that development of monitoring indicators is part of the CQUIN project. We hope that AMBIT's primary contribution in this regard will be to demonstrate the value of standardized indicators through the work we produce, so that others will want to use the same approaches.

III. ACTIVITIES AND DELIVERABLES

To achieve the goals described in AMBIT components 1-5, we propose to undertake activities and produce deliverables described in Table 3 over AMBIT's 2.5-year duration. Where relevant, we have noted the overlap of these activities with the original deliverables described by BMGF. We expect to collaborate with local partners for nearly all activities, as appropriate. We also expect some of the activities and deliverables to evolve as the project progresses, as certain items may become more or less relevant or feasible and new ideas may emerge that take priority over those currently envisioned. In particular, some reports may be replaced with presentations or articles or combined with others to maximize the value of each product.

Table 3. Proposed activities and deliverables

Activity		Deliverable
Component 1: Coverage		
1.1	Literature review of existing evidence on the coverage of alternative models of care in sub-Saharan Africa, including gray literature but excluding primary data, emphasizing but not limited to focus countries.	Report, possible publication if sufficient newly published information is available.

Activity		Deliverable
1.2	Analysis of retrospective, routinely collected primary data in focus countries, based on existing reports from ministries, implementers, and funders. We will contact these potential sources and aggregate whatever data can be obtained to put together a picture of the status of TMOC in each focus country.	Report and publication.
1.3	Identification of major data gaps and expected value of specific new data. To support Components 2 and 4, we will also identify key gaps in the evidence base in terms of coverage and propose ways to filling them in.	Component of reports in 1.1 and 1.2.
Component 2: Allocation		
2.1	Detailed description of status quo in each focus country – mapping facility and treatment pick-up locations offering TMOC, capacity at these locations, and transport infrastructure. Data will come from a combination of existing information from providers and implementers, external sources (e.g. transport routes and clinic locations from maps), patient distribution from MOH, etc.	Report, possible publication if information justifies it. ***(Key deliverable 3i)***
2.2	Development and dissemination of a mathematical model for optimizing the distribution of alternative models of care, taking into account patient distribution, settings, infrastructure, etc.	Model (full and simpler user-friendly versions) and results for focus countries. ***(Key deliverable 3ii)***
Component 3: Benefits and costs		***(Key deliverable 3ii)***
Domain 1: Clinical outcomes		
3.1	Synthesis of existing published and reported data on clinical outcomes, by model of care	Report(s), publication(s) if justified
3.2	If data allow, pooled data meta-analysis of clinical outcomes by model of care	
3.3	Evidence on outcomes of patients remaining in traditional care, using routine retrospective data in focus countries.	
3.4	Evidence on outcomes of non-ART chronic care, if routine retrospective data allow (TB, NCDs).	TBD based on data
Domain 2: Non-clinical outcomes		
3.5	Review of existing evidence on patient costs, including estimates of labor productivity costs or savings from alternative models.	Report(s), publication(s) if justified
3.6	Review of existing evidence on patient satisfaction if data allow. Provide a feasible plan for collecting these data if not.	
Domain 3: Efficiency		
3.7	Develop and disseminate user-friendly mathematical model for evaluating the costs and outcomes of ART delivery services incorporating traditional and alternative models of care.	Methodology, software, user manual ***(Key deliverable 1)***
3.8	Compile country-specific ART delivery costs to determine alternative model costs to providers, using existing published and unpublished estimates.	Report, possible publication if information is sufficient
3.9	Using longitudinal aggregate data, estimate numbers over time of chronic patients (ART and non-ART) managed by sites in focus countries, controlling for major resources allocated to sites (staff, inventory, space).	TBD based on data
3.10	If longitudinal data are available, describe changes in clinic resources (staff and other) over time as alternative models are scaled up.	
3.11	Review duties and time-and-motion estimates for HCWs and lay staff if available. Propose feasible plan for collecting these data if not.	TBD based on data

Activity		Deliverable
3.12	Estimate HCW productivity using patient load/provider data at facility level, by HCW cadre.	
3.13	If data can be obtained, map HCW cadre (clinical and lay) to targeted models of care in focus countries.	
3.14	Develop a performance metric that captures multiple measures of efficiency related to scaling up TMOC.	Methodology
Domain 4: Healthcare worker experience		
3.15	Compile existing information on healthworker satisfaction, if any. Propose feasible plan for collecting these data if needed.	TBD based on data
3.16	Review guidelines for treatment in focus countries and evaluate aggregate evidence of compliance; record review and interviews will be needed for full report.	Report
Component 4: Gaps		
4.1	Identify critical data gaps in scaling up TMOC	Report and publication if update to existing paper[18] is warranted ***(Key deliverable 3iii)***
4.2	Develop proposals and protocols for 1-2 appropriate research studies in each country to further understand and address priority gaps	Concept notes, protocols, and approvals ***(Key deliverable 4)***
4.3	Conduct studies identified in 4.2 through subawards to in-country partners	Reports and publications as appropriate ***(Key deliverable 4)***
Component 5: Partnerships and dissemination		
5.1	Participate in a sub-group of M+E experts led by WHO and CDC to further clarify the definitions of the clinical indicators	Contributions to subgroup ***(Key deliverable 1i)***
5.2	Establish small data advisory network to help identify data sources in the focus countries and contribute to AMBIT more generally (input, ideas, results dissemination, etc.), with ≤15 members.	Network meetings and communications ***(Key deliverable 1ii, 5)***
5.3	Synthesis of information and data collected in components 1 to 4 into relevant reports for dissemination through appropriate channels and upload to repositories such as differentiatedcare.org	Contributions to existing dissemination platforms ***(Key deliverables 2, 6)***
5.4	Country-specific policy briefs for focus countries as well as policy briefs with regional/global perspective.	At least 3 briefs per focus country and a set of global briefs ***(Key deliverable 5)***
5.5	Stakeholder meetings in focus countries and with relevant funding organizations to disseminate and discuss information from data collected in components 1 to 4.	In-person and electronic meetings and workshops as needed ***(Key deliverable 7)***
5.6	Manuscripts and conference presentations for submission regionally and internationally	Publications and slide presentations ***(Key deliverable 5)***

IV. TIMELINE

We estimate that a period of 30 months (2.5 years) will be needed to complete the scope of work described here.

V. BUDGET

We estimate that the budget for the AMBIT investment will be approximately _____. These funds will be divided among the primary recipient (Boston University), the lead sub-recipient (HE^2RO in South Africa), and two local partner organizations implementing Component 4 in Zambia and Malawi.

VI. 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. 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
8. 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
9. 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
10. 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
11. 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;8: e019680. doi:10.1136/bmjopen-2017-019680
12. Clinicaltrials.gov. INTERVAL: Varying Intervals of ART to Improve Outcomes in HIV.
13. Clinicaltrials.gov. Differentiated care for improved health systems efficiency and health outcomes in Zambia (CommART).

14. Leisegang R, Maartens G, Hislop M, Sargent J, Darkoh E, Cleary S. A novel Markov model projecting costs and outcomes of providing antiretroviral therapy to public patients in private practices versus public clinics in South Africa. PLoS One. 2013;8: e53570. doi:10.1371/journal.pone.0053570
15. National Department of Health, South African National AIDS Council. South African HIV and TB Investment Case: Reference report phase 1 [Internet]. 2016. Available: http://sanac.org.za/2016/03/22/investment-case-report/
16. Fox MP, Pascoe SJ, Huber AN, Murphy J, Phokojoe M, Gorgens M, et al. Short-term outcomes from a cluster randomized evaluation of adherence clubs as part of differentiated HIV care in South Africa. J Acquir Immune Defic Syndr. 2018;In press.
17. differentiatedcare.org. DIFFERENTIATED CARE FOR HIV: A DECISION FRAMEWORK FOR ANTIRETROVIRAL THERAPY DELIVERY. Unpublished. Durban; 2016.
18. Grimsrud A, Barnabas R V., Ehrenkranz P, Ford N. Evidence for scale up: The differentiated care research agenda. J Int AIDS Soc. 2017;20: 1–6. doi:10.7448/IAS.20.5.22024