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Cost-effectiveness of the optimal mix of differentiated service delivery models for HIV care and treatment in Zambia: a mathematical modelling study

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Cost-effectiveness of the optimal mix of differentiated service delivery models for HIV care and treatment in Zambia: a mathematical modelling study

A Research report submitted to the School of Public Health, Faculty of Health Sciences, University of Witwatersrand

In partial fulfilment of the requirements for the degree of Masters of Public Health in the field of Health Economics, submitted by

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30 October 2024

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DECLARATION

I, Nkgomeleng Abel Lekodeba, student number: 1706844, declare that this research report is my own work, I wrote the protocol, cleaned data and collected secondary data, performed all the analysis, wrote the first draft and received critical comments from all co-authors. It has not been submitted before to any university or for any degree or examination.

signature of the candidate  Date: 30 October 2024

PUBLICATION

This research report is submitted in the submissible format following the guidelines required by the School of Public Health, faculty of health sciences, University of Witwatersrand.

The manuscript presented in the submissible format has been co-submitted to the PLOS Medicine for publication and at MedRxiv (https://www.medrxiv.org/content/10.1101/2024.06.17.24309039v1) as a preprint. The submissible paper has been written to meet the target journal submission requirements.

ABSTRACT

Background: Zambia has scaled up differentiated service delivery (DSD) models for antiretroviral treatment (ART) to provide more client-centric care and increase service delivery efficiency. The current DSD landscape includes multiple models of care based on guidelines, resources, partner inputs, and other factors. We used local data to identify cost-effective combinations of DSD models that will maximize benefits and/or minimize costs to guide future DSD expansion.

Methods: We developed a mathematical Excel-based model using retrospective retention and viral suppression data from a national cohort of ART clients (≥15 years) between January 2018-March 2022 stratified by age, sex, setting (urban/rural), and model of ART delivery. Outcomes (viral suppression and retention in care), provider costs, and costs to clients for each model were estimated from the cohort and previously-published data. For different combinations of the nine DSD models in use, we evaluated the incremental cost to the health system per additional ART client virally suppressed on treatment compared to the 2022 base case. To assess uncertainty in our model parameters, we conducted univariate and multivariate deterministic sensitivity analysis on key model input parameters.

Results: Of the 125 scenarios evaluated, six were on the cost-effectiveness frontier: 1) six-month dispensing (6MMD)-only; 2) 6MMD and adherence groups (AGs); 3) AGs-only; 4) fast track refills (FTRs) and AGs; 5) FTRs-only; and 6) AGs and home ART delivery. 6MMD-only was cost-saving compared to the base case, increased the proportion of clients retained in care by 1.2% (95% CI, 0.7; 1.8), virally suppressed by 1.6% (95% CI, 1.0;2.6), and decreased costs to clients by 12.0% (95% CI, -10.8; -12.4). The next two scenarios on the cost-effectiveness frontier, 6MMD + AGs and AGs-only, each cost an additional $245 per person virally suppressed, increased the total number of individuals suppressed on treatment by 2.8% (95% CI, 2.2; 3.3) and 4.0% (95% CI, 3.5; 4.0) and increased costs to clients by 20.1% (95% CI, 9.5; 28.1) and 52.3% (95% CI, 29.8; 68.7), respectively. Under the base case, and scenarios on the cost-effectiveness frontier, cost of ART and laboratory tests were the most influential model parameters to the total health system costs and ICER, respectively.

Conclusions: Mathematical modelling using existing data can identify cost-effective mixes of DSD models and allocations of clients to these models, while ensuring that all client sub-populations are explicitly considered. In Zambia, providing 6MMD to all eligible clients is likely to be cost-saving, while health outcomes can be improved by allocating clients to selected models based on sub-population.

DEDICATION

I dedicate this study to my late father Makwena Mariba, my late grandmother Mokgadi Lekodeba, and my mother Moyanalo Lekodeba for their support throughout my academic journey.

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LIST OF ABBREVIATIONS

UNAIDS: United Nations Programme on HIV/AIDS

WHO: World Health Organization

HIV: Human immunodeficiency virus

ART: Antiretroviral therapy

DSD: Differentiated service delivery

ART: Antiretroviral therapy

ICER: Incremental cost-effectiveness ratio

6MMD: Six-months dispensing

FTRs: Fast track refills

AGs: Adherence groups

HAD: Home ART delivery

1. INTRODUCTION

This review synthesis evidence-based literature of differentiated service delivery (DSD) and conventional care models of HIV treatment delivery in sub-Saharan Africa. The four main sections are considered in this review, namely, the outline on overview and landscape of DSD in Zambia, provider and ART client's experiences of DSD models including conventional care, impact of DSD on health outcomes, and costs to clients and to health system (provider). The last part of this section outlines the research question, aim and objectives of the study.

1.1 BACKGROUND

In 2014, joint United Nations Programme on HIV/AIDS (UNAIDS) announced the 95-95-95 target to end the AIDS endemic by 2030 [1]. This targets aim to ensure that 95% of people living with HIV know their status and of those who know their status 95% are on antiretroviral (ART) treatment and for those who are on ART treatment, 95% of are virally suppressed by 2030 [1]. In 2016, the world health organisation (WHO) ART guideline acknowledged the adaptation of differentiated care for HIV services as necessary to fast-track the treat all recommendations [2]. The introduction of DSD has been widely viewed as a transition from the conventional care "one size-fits-all" model of HIV services to a differentiated care that seeks to accelerate sustainable access to health services for everyone [2]. DSD for HIV aim to provide a client-centered approach to HIV care along the treatment cascade, with clients established on treatment decanted to differentiated care [2,3]. In 2022, it was estimated that 39 million people were living with human immunodeficiency virus (HIV) globally [4]. As one of the components of strategy to achieve UNAIDS targets and manage high number of people on ART given low HIV budgets , Zambia [5] and other countries in sub-Saharan Africa adopted and are expanding DSD for HIV treatment [6].

Differentiated care differs from conventional care by location of services, frequency of interactions with the healthcare system, medication dispensing intervals, services provided and type of staff involved [7,8]. DSD models are tailored to provide client-centred approach to HIV treatment and are hypothesized to reduce the burden on the healthcare system, decongest healthcare facilities and reduce costs [8–10]. The client-centered approach includes variety of services tailored to different population groups such as after-hours medication collection services for the working groups or community adherence support meetings for the elderly [9,11]. WHO recommended a set of DSD enrolment criteria for ART clients to be considered eligible for DSD, also referred to "established on treatment" to be formulated as part of DSD guidelines by each implementing country [10].

In Zambia, variety of DSD models were designed and implemented, guided by the Ministry of Health DSD framework [12], with updated guideline introduced in 2022 [13]. In total, twelve DSD models were introduced, with a choice for which models to scale-up at each site entirely left at the discretion of implementing facilities [12,13]. However, there is a lack of evidence about the combination or the type of DSD models to prioritise that are likely to improve health outcomes and minimise costs compared to current distribution of ART delivery models. We conducted a cost-effective analysis of combination of DSD models to assist Zambia Ministry of Health to make informed choices about the type of DSD models to prioritise and scale-up at national level.

1.2. LITERATURE REVIEW

1.2.1. Overview and landscape of DSD models in Zambia

In 2013, DSD was introduced in Zambia as a form of standalone models that were mainly supported by the external implementing partners [5]. Since then, then Ministry of Health commissioned a DSD task force to oversee the implementation of DSD [5,12,13]. The first DSD framework was then developed and signed into policy in 2018, the framework outlined a set of eligibility criteria for DSD, services and the type of models to implement among eligible clients [12]. The eligibility criteria at the time of the first DSD framework for an ART client to be considered as "established on treatment" if they were virally suppressed with viral load of <1,000 copies/mL, on ART for at least 12 months and on first-line regimen [12]. The models that were adopted and scale-up included individual and group-based DSD models with on-site and off-site DSD interactions or health services led by ART clients and healthcare providers [12].

In 2022, a six-year DSD framework was introduced, under the updated framework, the time on ART for clients meeting other DSD eligibility criteria was reduced to six months with ART clients aged ≥2 years eligible for DSD [13]. The framework also recommends the adoption of unique DSD models for ART clients considered as high-risk, key Populations (i.e. men who have sex with men) and priority populations (i.e. pregnant and breastfeeding women and children) [13]. In 2022, it was reported that 100% of all facilities in Zambia achieved at least 10% DSD enrolment for all eligible clients in less-intensive models, with 59% of DSD clients receiving ≥6 months of medication dispensing [5]. In 2005, Zambia Ministry of Health introduced the SmartCare electronic medical record to capture continuity and routine medical information related to HIV services at about one-third of facilities [14]. Since then the rollout of SmartCare continued and was updated by adding data fields such as DSD variables [13]. To date it was estimated that about 75% percent of all ART clients are covered on SmartCare [15].

1.2.2. Provider and ART client's experiences of DSD

The implementation of DSD models is hypothesized to improve healthcare providers job satisfaction as well as ART client's satisfaction with the health services [16]. In a qualitative study conducted in Zambia, adoption of six-month dispensing (6MMD) model of ART delivery was perceived to decongest facilities due to reduced client's interaction with the healthcare system which resulted in decreased workload compared to three-months medication dispensing interval and conventional care model [16]. Provider perceived 6MMD as an ideal strategy to that may improve facility health services efficiency [16]. Similar experiences with the 6MMD where reported in Malawi, however, the risk of medication sharing due to increased supply was regarded as demotivator for seeking care amount ART clients who may require non-HIV services [17]. In contract, several clients reported that they were not involved in any medication sharing activities as their medication supply was aligned with their next medication refill visits [17]. Compared to clients in conventional care, clients enrolled in DSD models reported benefits such as decreased transport costs, reduced loss of wages due to time off work and less waiting time at facilities during their medication collection visits [17].

In a parallel convergent mixed-method study conducted in Ethiopia, DSD implementation was also perceived to improve quality of care, reduced provider workload and decongestion of facilities [18]. However, among the ART clients not enrolled in DSD models but receiving longer medication dispensing intervals (i.e. 3-months) and in contrast with other studies [17], increased medication supply was associated with increased risk of poor medication storage [18]. Healthcare workers reported that reduced workload enable the facilities to use the freed-up time to perform other activities such as administration duties which improved the records management and record-keeping at the facility [18]. In east central Uganda [19], and in South Africa [20] clients enrolled in DSD models experienced increased satisfaction of the health services than those not enrolled in DSD models. In contrast, a study conducted in Tanzania and other parts of Uganda found that quality of care and satisfaction with health services was similar regardless of ART model delivery [19].

1.2.3. Health outcomes

The most common measure of health outcomes for people living with HIV and on ART treatment are treatment adherence as measured by retention in care, viral load and CD4 cell count [21]. In many settings, retention in care is defined as not having missed a visit for more than 90 consecutive days for any clinical interaction or DSD events such as medication collection visits [8,19]. Retention in care is commonly measured every 12-months after treatment initiation or DSD model enrolment [8,19]. DSD Viral load measures the amount of HIV infection or how fast the HIV infection is reproducing in the body [21]. In interpreting the results of viral load measurement, three key categories are

recommended by the WHO; 1) unsuppressed viral load defined as >1,000 copies/mL; 2) suppressed viral load defined as ≤1,000 copies/mL, and undetected viral load were viral load is not detected by the test [21].In the past decades, in low and middle-income countries, CD4 count has been less preferred to viral load [11,21], some of the reasons includes the growing evidence that undetectable viral load reduces the risk of HIV sexual transmission [22], and viral load measure as requirement for DSD enrolment [3,9,23–25]. In a recent systematic literature review of DSD models and HIV outcome evaluation studies in Sub-Saharan Africa, it was found that retention in care was 5% more among clients enrolled in DSD models compared to those in conventional care [8]. In Zambia, retention in care was reported to have improved by 2% among clients enrolled in community adherence groups, 14% among those enrolled urban adherence groups [26]. Clients enrolled in DSD models were also associated with disengagement from care as in conventional care, 2% of ART clients enrolled in home ART delivery model and 13% in mobile ART model were not retained in care at the end follow-up period [26].

In line with the new DSD guidelines in Zambia [13], a recent study compared disengagement from care among clients enrolled in DSD model with <6 months on ART (early enrollers) to established enrollers defined as those enrolled in DSD with >6-months on ART treatment [23]. It was found that early DSD enrollers had a slightly lower rate of disengagement from care of 3.0% (95% CI 2.6%-3.5%) compared to established enroller with 4.5% (95% CI 4.3%-4.8%) [23]. Among clients enrolled in different DSD models tailored by location of services, the type of staff involved, it was found that health outcomes were similar for clients enrolled in different ART delivery models [27]. The retention in care, measured at 12-months was 98% for the overall sample included in the analysis ranging between 96% to 100%, and viral suppression was found to be 91% and ranged between 86% to 93% [27]. The findings of this studies showed that time to DSD enrolment and DSD model participation does not lead to improved health outcomes but rather may be associated with sustained health outcomes and low resource use such as staff time as a results of fewer health care interaction as opposed to conventional care model of ART delivery [23].

1.2.4. Costs to provider (health system costs) and to clients

Cost to clients and to health system are part of the key factors that influence healthcare service provision and utilisation [28]. In sub-Saharan Africa, many countries provides primary health care services at no cost to clients including HIV services such as testing and treatment, with involvement of donor funded external support [28,29]. The introduction of DSD models is considered as one of the strategies to reduce the burden on the health system and to clients through reduced health services interactions [28]. In Zambia, the DSD framework requires clients enrolled in DSD models to make

fewer ART/HIV related visit to the healthcare system per year compared to clients enrolled in conventional ART care [13]. However, DSD clients may still access other health services during the course of the year in the out-patient departments [13]. Over the years, a quite number of studies evaluated the cost of differentiated and conventional care from the perspective of the providers and of ART clients [8,28,30], and recent study from societal perspective [31]. From healthcare perspective, the common cost categories used in economic evaluations studies include staff costs, medications, laboratory services and overheads costs while cost to clients include transport costs, opportunity costs often measured as time spent seeking care [28,31,32].

Three studies, two prospective cluster randomized non-inferiority trial conducted in Lesotho [32], and Zimbabwe [33], and retrospective electronic record review conducted in Zambia [26], evaluated costs and outcomes of differentiated and conventional care. The study in Zambia used conventional as a comparator to community-based DSD models [26], while economic evaluations in Lesotho and Zimbabwe included both community- and facility-based DSD models from the perspective of the provider and to clients [32,33]. Community DSD models were reported to cost more than the conventional care, with an annual provider cost per person ranging from $116 to $199 for the DSD models, compared to $100 for conventional care [26]. In Both economic evaluations, in Lesotho and Zambia, DSD models evaluated were similar, the models included community ART refill groups with 3-month medication dispensing interval and community ART distribution/community adherence groups with 6-month medication dispensing intervals with clients in facility based conventional care receiving 3-months of medical supply [32,33].

DSD models were found to be less costly than conventional care but with similar health outcomes [32,33]. In Zambia annual provider costs per client retained in care were slightly similar for both DSD models, $173 compared to $201 for conventional care and annual cost to clients ranged from $4 to $5 per client per year [33]. In Lesotho, annual provider cost per client retained in care for both DSD models were 6% to 8% less compared to conventional care with provider cost of $126 and annual cost to clients ranged between $16 to $19 compared to $44 in clients enrolled in conventional care [32]. A pragmatic, cluster-randomised, unblinded, non-inferiority trial conducted in Zambia and Malawi showed that 6-month dispensing was cost-saving for both healthcare system and to clients retained in care at 12 months, compared to standard of care and 3-month ART dispensing [34]. A recent study in Mozambique compared DSD models implementation with hypothetical scenario where no DSD and found that DSD models was less-expensive [34]. The evidence from these studies show that DSD models may lead to reduced resource use such as staff time among clients enrolled.

1.3. PROBLEM STATEMENT

Rapid scale-up and expansion of DSD models for HIV treatment in Zambia resulted in the implementation of 11 different models of care [12,13]. The models are targeted to different population groups, age groups, sex, and different settings (rural/urban) with a mix of in-facility and out-of-facility models [9,12,13]. Although DSD implementation is guided by the country DSD framework, it is often up to facility DSD coordinator or facility managers to make decisions about which models to scale-up without evidence about the performance of the models in terms of costs and outcomes such as model effectiveness [8,26,28]. As Zambia scale-up DSD models for HIV treatment – questions arise about how many and which models to offer that maximise client's health outcomes and minimise costs (provider and costs to clients). There is little evidence about which models to scale-up, distribution and combination of models that are both cost saving and cost-effective at national level.

1.4. JUSTIFICATION

Many studies evaluated the costs and outcomes of DSD scale-up from facility level resources from both the perspective of the provider and to clients [23–25,28,35,36]. The national level impact of DSD scale-up and benefits have not been evaluated for the entire national-level ART program in Zambia [26,28,36], with a recent study comparing DSD models with hypothetical ART distribution scenario [31]. DSD models were found to be cost saving compared to conventional HIV care and lead to improved and sustained health outcomes such as retention rate and viral suppression rates at facility level [28,31]. While DSD models were introduced to provide more client-centered approach to HIV treatment and care, the design of each model differs by the type of services offered at DSD events and at routine clinical visit, the type of cadre involved –higher and lower paid cadre and the frequency of medication dispensing and intervals [9,24,25].

As a results, annual provider costs per client per year and cost to clients per year – services utilization costs differ for each model in use, including the health outcomes [26,28]. To assist in the prioritization and scale-up of cost-effective DSD models, we developed the Alternative Delivery of ART Optimization (ADAPT) model, an Excel-based mathematical model that provides a decision-making framework for scaling-up DSD for HIV treatment. We compared different DSD model implementation scenarios in terms of health outcomes (viral suppression) and costs (provider and costs to clients) at a national level.

1.5. RESEARCH QUESTION

What is the optimal mix of differentiated service delivery models for HIV care and treatment that maximize health outcomes and minimize costs in Zambia?

1.6. AIM

The aim of this study was to evaluate the cost-effectiveness of the optimal mix of differentiated service delivery models for HIV treatment among ART clients aged 15+ years in Zambia public healthcare facilities.

1.7. OBJECTIVES

Objective 1: To determine the combination of DSD models that maximizes retention and viral suppression among ART clients aged 15+ in Zambia public healthcare facilities in 2023.

Objective 2: To determine combinations of DSD models that minimize costs to ART clients and provider costs among ART clients aged 15+ in Zambia public healthcare facilities in 2023.

Objective 3: To determine the incremental cost-effectiveness ratio per ART clients aged 15+ suppressed on treatment in Zambia public healthcare facilities in 2023.

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2. MANUSCRIPT

Optimal mix of differentiated service delivery models for HIV treatment in Zambia: a mathematical modelling study

Short title: Optimizing differentiated service delivery for HIV treatment

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Abstract

Background: Zambia has scaled up differentiated service delivery (DSD) models for antiretroviral treatment (ART) to provide more client-centric care and increase service delivery efficiency. The current DSD landscape includes multiple models of care based on guidelines, resources, partner inputs, and other factors. We used local data to identify cost-effective combinations of DSD models that will maximize benefits and/or minimize costs to guide future DSD expansion.

Methods: We developed a mathematical Excel-based model using retrospective retention and viral suppression data from a national cohort of ART clients (≥15 years) between January 2018-March 2022 stratified by age, sex, setting (urban/rural), and model of ART delivery. Outcomes (viral suppression and retention in care), provider costs, and costs to clients for each model were estimated from the cohort and previously-published data. For different combinations of the nine DSD models in use, we evaluated the incremental cost to the health system per additional ART client virally suppressed on treatment compared to the 2022 base case. To assess uncertainty in our model parameters, we conducted univariate and multivariate deterministic sensitivity analysis on key model input parameters.

Results: Of the 125 scenarios evaluated, six were on the cost-effectiveness frontier: 1) six-month dispensing (6MMD)-only; 2) 6MMD and adherence groups (AGs); 3) AGs-only; 4) fast track refills (FTRs) and AGs; 5) FTRs-only; and 6) AGs and home ART delivery. 6MMD-only was cost-saving compared to the base case, increased the proportion of clients retained in care by 1.2% (95% CI, 0.7; 1.8), virally suppressed by 1.6% (95% CI, 1.0;2.6), and decreased costs to clients by 12.0% (95% CI, -10.8; -12.4). The next two scenarios on the cost-effectiveness frontier, 6MMD + AGs and AGs-only, each cost an additional $245 per person virally suppressed, increased the total number of individuals suppressed on treatment by 2.8% (95% CI, 2.2; 3.3) and 4.0% (95% CI, 3.5; 4.0) and increased costs to clients by 20.1% (95% CI, 9.5; 28.1) and 52.3% (95% CI, 29.8; 68.7), respectively. Under the base case, and scenarios on the cost-effectiveness frontier, cost of ART and laboratory tests were the most influential model parameters to the total health system costs and ICER, respectively.

Conclusions: Mathematical modelling using existing data can identify cost-effective mixes of DSD models and allocations of clients to these models, while ensuring that all client sub-populations are explicitly considered. In Zambia, providing 6MMD to all eligible clients is likely to be cost-saving, while health outcomes can be improved by allocating clients to selected models based on sub-population.

Keywords: Differentiated service delivery, HIV, antiretroviral treatment, cost-effectiveness, mathematical modelling, Zambia

2.1. Introduction

Many countries in sub-Saharan Africa are expanding differentiated service delivery (DSD) for HIV treatment to efficiently achieve national and global targets for treatment uptake and viral suppression [1,2]. DSD models for HIV treatment differ from conventional care in several ways: the location of service delivery, frequency of interactions with the healthcare system, types of services provided, and cadres of staff involved. They are designed to provide a more client-centred approach, aiming to improve outcomes of those on antiretroviral treatment (ART) and reducing costs to and improving the experiences of both clients and healthcare providers [1,2]. The World Health Organization has recommended the implementation of differentiated service delivery for HIV treatment since 2015 [3], and many countries, including Zambia, have incorporated DSD models into national HIV treatment guidelines [4].

In Zambia, a high HIV-prevalence country with an estimated 1.4 million people living with HIV [5], the Ministry of Health currently supports a range of "low intensity" DSD models that require fewer resources from both clients and providers than does conventional ART care [6,7]. Models described in national guidelines include 6-month dispensing of ART at facilities (6MMD), community medication pickup points, appointment spacing, fast-track dispensing at facilities, and other models targeted specific population groups, such as teen/scholar and extended clinic hours models. Conventional care typically entails 3-month dispensing of ART at health facilities, with a clinical consultation and medication pickup at each quarterly clinic visit. Each public sector HIV clinic offers some combination of these models, based on available resources and staff choices. In addition, non-governmental partner organizations support several other bespoke models at subsets of healthcare facilities.

As Zambia continues to improve differentiated service delivery to build the long-term sustainability of its HIV program, more attention is needed to the optimal combination of models that facilities should offer. Ideally, the allocation of models should reflect considerations of the trade-offs and synergies among health outcomes, costs and benefits to clients, and costs and benefits to the healthcare system. While some evidence is available about each of these factors [2,8–12], little is known about the cost-effectiveness of different combinations of DSD models, at any level. In most settings, in Zambia and elsewhere, the distribution of models across facilities and nationally is largely determined by national guidelines, which themselves are generally not tailored to local conditions, and by available facility and partner resources.

To assist in the prioritization and scale-up of cost-effective DSD models, we developed the Alternative Delivery of ART Optimization (ADAPT) model, an Excel-based mathematical model that provides a decision-making framework for scaling-up differentiated service delivery for ART. ADAPT compares

different DSD model implementation scenarios in terms of viral suppression and providers' and clients' costs at a national level. We parameterised ADAPT for Zambia, which has a rich endowment of both routine and research data sources, and then conducted a cost-effectiveness analysis of likely combinations of ART delivery models to demonstrate how model mix and allocation may affect achievement of HIV program goals.

2.2. Methods

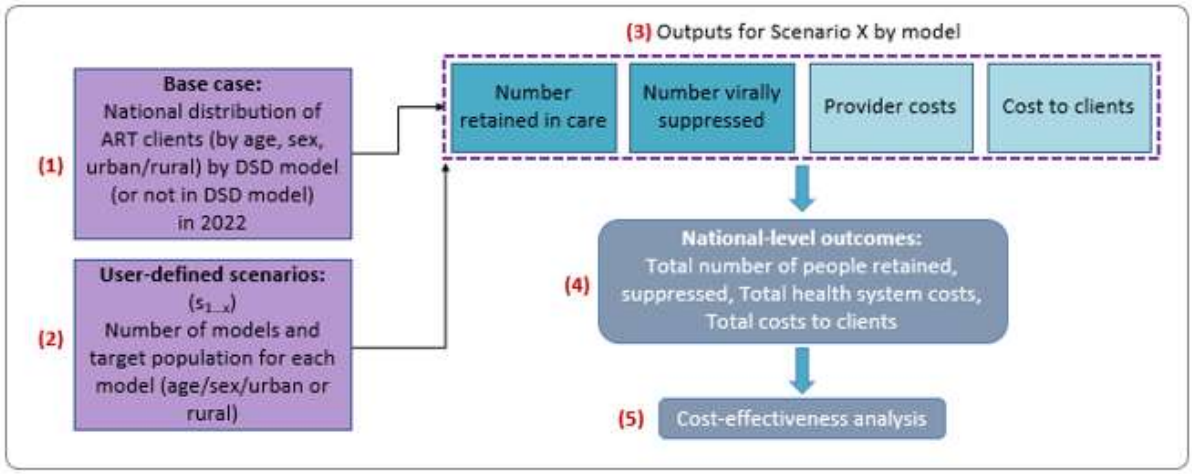
We developed and parameterised an Excel-based mathematical model of all ART clients in care in Zambia using de-identified, retrospective SmartCare electronic data from Zambia's national cohort of ART clients (aged ≥15 years) from January 2018 to March 2022 (Table 3) [13]. SmartCare, Zambia's public sector electronic medical record system for HIV, captures roughly 75% of all ART patients in Zambia [10,14]. It includes data fields indicating when an ART client enrolled in a DSD model, the specific model enrolled in, the number of months for which ART medications were dispensed at each event, treatment outcome, outcome date, and demographic characteristics [4,14].

2.2.1. Model structure and approach

To determine the expected impact and cost-effectiveness of the implementation of various combinations of DSD models and uptake in each model, we started with a base case representing the actual 2022 national distribution of ART clients among DSD models disaggregated by population sub-groups (age group, sex, urban or rural location). The health outcomes from this base case reflect the health outcomes observed in 2022 for all DSD models for each population sub-group.

We then constructed multiple hypothetical scenarios in which specific combinations of one or more DSD models can either be implemented across the entire population cohort or be targeted to specific sub-populations based on age, sex, and urban or rural setting. Each scenario reflected a specific distribution of ART clients among different models. The model then generated a total number of individuals virally suppressed and retained in care (sum of all individuals virally suppressed on treatment and retained in care by model of ART delivery for each scenario), and a total estimated cost to the provider and clients. The modelling approach, comprised of five distinct steps, is depicted in Figure 1.

Figure 1. ADAPT modelling structure



2.2.2. Cohort, eligibility and outcomes

The primary outcomes for this analysis were retention in care, viral suppression, provider costs, and cost to ART clients. Viral suppression and provider costs were combined into an incremental cost-effectiveness ratio for each model. Study cohort, eligibility criteria and outcomes are defined in Table 1. The window period for estimating 12-month retention and viral suppression rates was wide (11 to 24 months) to accommodate the limitations of the data, which consisted of annual snapshots of the ART cohort, as well as the annual viral load testing as per ART treatment guidelines [12].

Table 1. Definitions of study cohort, eligibility criteria and outcomes

Cohort, criterion, or outcome	Definition
Study cohort	
Study analytic cohort	The study analytical cohort comprised ART clients (aged ≥15 years) included in the SmartCare database in January 2018 to March 2022 and enrolled in differentiated or conventional care.
Criteria	
Eligibility for DSD enrollment	On ART for at least 12 months. (Because there were limited viral load data available, viral suppression could not be used as an eligibility criterion despite it being specified in DSD policy guidelines)
DSD model assignment	Each participant was assigned to the first DSD model they enrolled in during the first year after becoming eligible for DSD. Those who did not have any DSD model enrollment reported in the dataset were classified as remaining in conventional care
Outcomes	
Total health system costs	The sum of provider costs to the health system per year
Total costs to clients	The sum of cost to clients incurred accessing ART services per year
Retention in care at 12 months	The proportion of ART clients who had a clinic visit between 11 and 24 months stratified by age group, sex, setting (urban/rural), and model of ART delivery. Retention in care for clients enrolled in DSD model was estimated after they became eligible and were enrolled in DSD models.
Viral suppression at 12 months	The proportion of ART clients who had viral load test results of <1,000 copies/ml at 12 months, stratified by age group, sex, setting (urban/rural), and model of ART delivery. The viral load at 12 months is measured between 11 and 24 months.

Cohort, criterion, or outcome	Definition
Incremental cost-effectiveness ratio (ICER)	Healthcare system (provider) cost per additional ART client virally suppressed on treatment

2.2.3. ART delivery models

In the modelled scenarios we considered a total of 11 models of ART delivery for ART clients in 2022 (Table 2). Two were variations of conventional (non-differentiated) care: 3-month facility-based dispensing (3MMD), which is the current standard of care, and a study-defined model for clients observed to be receiving less than 3 months of medication at a time. Nine were DSD models [10,15]. At the time of the study, Zambia's criteria for being designated as "established on treatment" were a viral load of <1,000 copies/mL and a minimum of 6 months on ART. ART clients in conventional care went through all service points (registration, vitals, clinical consultation, pharmacy, etc.) within the facility at each quarterly visit.

The nine DSD models considered in the analysis were categorised as either in-facility or out-of-facility models and are described in detail in Table 2 [4]. We did not include models of care tailored to clients with viral loads >1,000 copies/ml, such as "high viral load clinics." Instead, cohort participants who did not meet DSD eligibility criteria were retained in conventional care in our mathematical model.

Table 2. Description of conventional and differentiated ART service delivery models

Category	ART delivery model	Description
In-facility models	Conventional care not eligible for DSD	Conventional care for ART clients who are shown in the database to receive <3-month refills of medications. Reasons for shorter dispensing intervals are not indicated in the database but may include insufficient experience on ART, unsuppressed viral loads, missed medication refills, uncontrolled co-morbidities; some clients may receive shorter refills at their own request or due to clinic stock limitations. ART clients receiving <3-months refills go through all service points (registration, vitals, clinical consultation, pharmacy, etc.) within the facility at each visit. (Note: "conventional care not eligible for DSD" was defined for this analysis to distinguish it from standard of care for clients who are eligible for DSD).
	Conventional care (3MMD)	Conventional care targeted to ART clients not yet enrolled in other models, declining other models, or not enrolled in DSD for some other reason.
	Fast-track refills (FTR)	Established clients access a separate shorter queue for medication collection visits; refill duration varies.
	Six-month dispensing (6MMD)	Clients are dispensed 6 months of ART medication at each clinic visit. Clinic visits are scheduled every 6 months, with no required interactions with the healthcare system between visits.
	Extended clinic hours models	ART clients aged ≥25 years enrolled in these models of care are eligible to collect medication outside facility operation hours (e.g. morning, evening, or weekends).
	Scholar/ adolescents models	Group model for teenagers and school-going population aged between 10 to 24 years. The groups meet 4-times a month to discuss

Category	ART delivery model	Description
		treatment adherence and 3 months ART medications are dispensed every 3-months during the group meetings.
Out-of-facility based models	Adherence groups (rural and urban)	Up to 30 members who meet with a healthcare worker every 1-3 months at the facility to collect pre-packed medications, share treatment experiences and reinforce medication adherence practices.
	Community ART distribution points	ART refills are provided at central location within the community such as in schools, churches, community halls, retail pharmacies, and health posts.
	Health posts	ART medications are dispensed at the health post which is linked to a main health care facility. These are usually situated in remote areas where access to health facilities may be limited. ART clients receive 3-6 months of ART medication at each.
	Mobile ART delivery	A clinical outreach team who are linked to a facility conducts 3-monthly clinical assessments in rural settings.
	Home ART delivery (HAD)	A trained healthcare worker visits ART client in their homes to conduct health screening, provide pre-packed medications and monitor adherence. ART clients eligible are those ≥25 years.

2.2.4. Input parameters and assumptions

Model input parameters, parameter values, client characteristics, and the base case distribution of clients that reflect the 2022 cohort are presented in Table 3. Health outcomes (retention in care and suppression rates) for each ART delivery model, stratified by sex, age, and setting, were estimated from the SmartCare database (Table 3, Table S1) [13].

Table 3. Baseline input parameters (N=917,749)

Parameter	Model value, n (%)	
Demographic characteristics [15]		
Sex (female)	584,509 (63.7%)	
Setting (urban)	636,597 (69.3%)	
Age group		
15-19 years	21,608 (2.4%)	
20-24 years	49,990 (5.4%)	
25-49 years	660,085 (71.9%)	
50+ years	186,066 (20.3%)	
Distribution of ART delivery models (n, %) [15]	*Male*	*Female*
Conventional care not eligible for DSD	17,914 (5.4%)	30,766 (5.3%)
Conventional care (3MMD)	47,302 (14.2%)	85,728 (14.7%)
Six months dispensing	231,153 (69.4%)	401,085 (68.6%)
Fast-track refills	29,096 (8.7%)	52,691 (9.0%)
Extended clinic hours	75 (<0.1%)	130 (<0.1%)
Scholar/adolescent model	92 (<0.1%)	110 (<0.1%)
Mobile ART distribution	583 (0.2%)	1,159 (0.2%)
Health post	691 (0.2%)	1,281 (0.2%)
Home ART delivery	1,366 (0.4%)	2,020 (0.3%)
Community ART distribution points	2,693 (0.8%)	4,989 (0.9%)
Adherence groups	2,275 (0.7%)	4,550 (0.8%)
Health outcomes [15]		
Retention rates	Outcomes dependent on DSD model type, age, sex and setting (urban/rural).	
Viral suppression rates		

2.2.5. Cost inputs

Provider costs using ingredients-based approach and costs to clients were estimated using previously published (Table 4) [16,17]. Provider costs per ART client per year included costs of staff time (facility visits and DSD interactions), medication costs, and laboratory testing costs (Table S2) [17]. Costs to clients are based on self-reported resource utilization collected during the SENTINEL survey [20]. Clients in each ART delivery models were asked to report the number of interactions (visits) with the healthcare system and the time spent accessing care at each study site [18]. Cost to clients included opportunity costs for time spent seeking care, estimated as time spent accessing care multiplied by Zambia's minimum daily wage ($1.99), and transport costs incurred for accessing ART services [17], taking into consideration the proportion of clients incurring transport costs in each ART delivery model (Table S3). Unit costs for the provider and costs to ART clients per year were updated to 2023 prices [16,17,19] and then converted from Zambian Kwacha (ZMW) to United States Dollars (USD) using the average 2023 exchange rate of 20.23 ZMW per = 1 USD [19].

Table 4. Cost inputs – provider costs and cost to client per year

Costs per year (mean) -2023 USD	**Average provider costs per client per year** [26]	**Average costs to clients per year** [35]		
		Lost wages (opportunity costs), (95% CI)	**Transport costs**	
			incurring any costs (%)	**Average cost (95% CI)** †
Conventional care not eligible for DSD	$119.23	$6.94 (5.60;8.28)	51.5%	$3.19 (1.98; 4.40)
Conventional care (3MMD)	$109.05	$5.01 (4.33; 5.70)	40.9%	$3.01 (0.89; 5.14)
Six-month dispensing	$99.72	$3.01 (2.50; 3.51)	36.4%	$2.80 (1.56; 4.04)
Fast-track refills	$105.90	$3.94 (2.94; 4.95)	42.5%	$1.32 (0.86; 1.77)
Extended clinic hours	$109.05	$2.35 (1.94; 2.76)	46.7%	$1.74 (0.56; 2.91)
Scholar/adolescent model	$109.05	$4.34 (3.19; 5.48)	26.8%	$1.66 (0.64; 2.68)
Mobile ART distribution	$125.56	$4.01 (2.10; 5.92)	0.0%	$0.0 (0.0; 0.0)
Health post	$107.27	$5.21 (3.94; 6.49)	51.4%	$1.71 (1.04; 2.38)
Home ART delivery	$132.51	$2.67 (2.19; 3.16)	40.0%	$2.98 (1.16; 4.81)
Community ART distribution points	$106.19	$5.21 (3.94; 6.49)	51.4%	$1.71 (1.04; 2.38)
Adherence groups	$104.33	$6.44 (4.45; 8.42)	34.8%	$2.09 (0.14; 4.31)

†among clients incurring any transport costs, the remainder likely walked.

2.2.6. Scenarios and input assumptions

As noted above, the base case was defined as the current national distribution of ART clients by age, sex, setting and ART delivery model type, under the current status quo, as determined by the SmartCare database (Table S1, Table 3). The analytic scenarios include 125 unique possible combinations of DSD models and model offerings tailored by age, sex, and setting. While most DSD models allow enrolment of any eligible ART patient, some are limited to specific population subgroups. These include the scholar/adolescent model (for ART clients aged ≤24 years), extended clinic hours

(for clients aged ≥25 years), and mobile ART delivery (available only in rural areas). We thus modelled two different sets of scenarios: 1) DSD models for the full population (excluding DSD models that are targeted to specific population subgroups); and 2) stratified scenarios which included age-specific DSD models for relevant subgroups and other DSD models for everyone else. For scenarios with two or more DSD models, we assumed equal distribution of the number of eligible ART clients allocated to each model.

Each scenario reflected a different allocation of eligible clients to the models included in the scenario. In most scenarios, 95% of ART clients were allocated to differentiated models (non-conventional care), with the rest remaining in conventional care. For example, in a fast track refills-only scenario, all eligible clients were enrolled in fast-track refills and the remainder were in conventional care. In a population specific scenario such as enrolling everyone eligible for DSD in a combination of scholar/adolescent model and extended clinic hours, eligible clients aged ≤24 years were enrolled in scholar/adolescent model and those aged ≥25 years enrolled in extended clinic hours. The details of mix of ART delivery models and client distribution by scenario are described in Table S4.

2.2.7. Cost analysis

ADAPT estimates costs over a one-year period after ART delivery model enrolment from the perspectives of the provider (Ministry of Health) and of clients enrolled in each model. The relatively short (1-year) time horizon was chosen because it matched the period of the health outcomes, and we wanted to ensure realistic estimates that could be used for short-term budget cycles relevant to the Ministry of Health's budget planning. For baseline and modelled scenarios, health system costs per model of ART delivery was estimated by multiplying the number of ART clients assigned to each model by average annual provider cost. Cost to clients were estimated by multiplying the number of clients assigned to each ART delivery model by the annual average costs incurred accessing ART services, including lost wages (opportunity costs) and transport costs.

2.2.8. Cost-effectiveness analysis

To estimate incremental cost effectiveness ratios, we first ranked total health system costs of each scenario from lowest to highest total costs [20]. We then determined and eliminated scenarios that were strongly dominated. A scenario was considered strongly dominated if it resulted in higher total costs to the healthcare system and fewer people virally suppressed on treatment to the next best scenario [20]. An ICER for each scenario was then calculated by dividing the difference in total health system costs (incremental cost) by the difference in viral suppression rate (incremental effect) of one scenario compared to the next best scenario. ICERs per additional person suppressed on treatment

were calculated by comparing scenarios to the to the next best scenario scenarios that was on the cost-effective frontier [20].

Next, we compared each scenario with the next best scenario, based on its ICER, and scenarios that were weakly dominated were identified and eliminated. A scenario was considered weakly dominated if it resulted in smaller effect (lower number of people virally suppressed) but had a higher ICER compared to the next highest ranked scenario [20,21]. These results were then used to establish the cost-effectiveness frontier, defined as graphical representation of interventions that increase the number of people virally suppressed on treatment compared to the current distribution of ART delivery model [22]. A full list of all scenarios analysed, with total effects, total costs, and ICERs, is provided in Table S5. Finally, for all interventions on the cost-effectiveness frontier, a sub-analysis was conducted to understand how health outcomes (viral suppression and retention rates) of each sub-group (by age, sex, and rural/urban setting) would be affected if the scenarios on the cost-effectiveness frontier were adopted at the national level, compared to base case distribution.

2.2.9. Sensitivity analysis

To assess uncertainty in our model parameters, we conducted univariate and multivariate deterministic sensitivity analysis for the total health system costs under the base case scenario and ICER per person suppressed on treatment for the scenarios on the cost-effectiveness frontier, respectively. We varied model input cost parameters using estimated lower and upper bounds from literature which included costs of ART, Laboratory test costs, DSD interaction and facility visits costs (Table S2), and modelling input assumptions – client distributions and number of visits or DSD interactions per year.

2.3. Results

2.3.1. Base case scenario

The base case cohort comprised a total of 917,749 ART clients, of whom roughly two thirds were female (63.7%) and two thirds live in an urban setting (69.3%) (Table 3). Most (72%) were aged between 25-49 years and another quarter were ≥50 years, leaving just 8% ≤24 years. In the base case, reflecting the status quo in 2022, less than a quarter of the cohort (20%) received conventional care, nearly 70% 6MMD, 9% fast track, and the remainder were enrolled in each of the other active models, which served fewer than 1% of clients each. The average provider cost ranged from $100 to $133 per client per year, while costs to clients ranged from $2.35 (95% CI, 1.94; 2.76) and $6.94 (95% CI, 5.60 ;8.28) per year for lost wages. Among the 39.2% of those who incur any transport costs, cost per client ranged from $1.32 (95% CI, 0.86; 1.77) to $3.19 (95% CI, 1.98; 4.40) per year (Table 5).

A total of 89.1% (95% CI, 85.7; 93.3) of the cohort were retained in care at 12 months in the base case scenario (Table 5). Among those retained in care, 94.1% (95% CI, 91.2; 96.2) were virally suppressed. Of the entire cohort, 80.2% (n=736,039) were enrolled in DSD models, 14.5% (n=133,031) were eligible for DSD but not enrolled, and 5.3% (n=48,679) were not eligible for DSD enrolment. The associated health system costs and costs to clients were $84,332,234 and $4,145,400 per year, respectively.

Table 5. Health outcomes and costs for the Zambia ART program at 12 months under the base case, 2022

Characteristics	National outcomes, n, %	% (95% CI)
Analytic cohort		
Total (N)	917,749	100% (n/a)
Retained in care	817,948 (95% CI, 786,510; 855,901)	89.1% (85.7; 93.3)
Suppressed on treatment	770,086 (95% CI, 717,521; 823,735)	94.1% (91.2; 96.2)
Costs (2023 USD)		
Health system costs	$84,332,234 (n/a)	n/a
Costs to clients	$4,145,400 (n/a)	n/a
DSD eligibility/enrolment†		
Conventional care not eligible for DSD	48,679 (5.3%)	n/a
Conventional care eligible for DSD but not enrolled	133,031 (14.5%)	n/a
Clients enrolled in DSD models	736,039 (80.2%)	n/a

† Clients enrolled in DSD models and those eligible but not enrolled can be allocated to any DSD model for the scenario analysis; clients not eligible for DSD must remain in conventional care.

2.3.2. Scenarios on the cost-effectiveness frontier

Results of all 125 scenarios analysed are reported in Table S5. Six of these scenarios were found to be on the cost-effectiveness frontier (Table 6 & 7, Fig 2). Five of the scenarios on the frontier improved outcomes but also resulted in greater health system costs and costs to clients, while one scenario—6-month dispensing for all eligible clients—both improved outcomes and reduced costs, compared to the current baseline. Scenarios on the cost-effectiveness frontier encompassed both facility-based models (6MMD, fast-track refills) and out-of-facility-based models (adherence groups, home ART delivery) for all those eligible for DSD enrolment. The only scenario on the cost-effectiveness frontier that included an approach that targeted specific sub-populations was the combination of adherence groups (AGs) (for those ≤24 years) and home ART delivery (HAD) (for those aged ≥25).

Table 6. Description of DSD scenarios on the cost-effectiveness frontier

Scenarios	Description
Base case	Current distribution of ART delivery models as indicated in the SmartCare database (80.2% enrolled in DSD, 14.5% enrolled in conventional care and eligible for DSD but not enrolled, and 5.3% in conventional care but not eligible for DSD).

Scenarios	Description
6MMD	94.7% (n=869,070) of all ART clients enrolled in 6MMD across all population groups (rural/urban, age, sex) (all of those eligible for DSD models), and 5.3% (n= 48,679) remains in conventional care (not eligible for DSD models).
6MMD & AGs	94.7% (n=869,070) of all ART clients distributed equally between a combination of two DSD models (6MMD & AGs) and 5.3% (n= 48,679) remain in conventional care (not eligible for DSD models).
AGs	94.7% (n=869,070) of all ART clients enrolled in AGs across all population groups (rural/urban, age, sex) and 5.3% (n= 48,679) remains in conventional care not eligible.
FTRs & AGs	94.7% (n=869,070) of all ART clients distributed equally between a combination of two DSD models (FTRs & AGs) across all population groups (rural/urban, age, sex) and 5.3% (n= 48,679) remain in conventional care (not eligible for DSD models).
FTRs	94.7% (n=869,070) of all eligible clients enrolled in FTRs only across all population groups (rural/urban, age, sex) and 5.3% (n= 48,679) remains in conventional care (not eligible for DSD models).
AGs & HAD	Population specific-scenario for all 94.7% (n= 869,070) eligible clients; enrolling 6.8% (n= n=62,106) of clients aged ≤24 years in AGs and 87.7% (n= 806,964) of clients aged ≥25 years in HAD across all population groups (rural/urban, age, sex) and 5.3% (n= 48,679) of all clients remain in conventional care (not eligible for DSD models).

6MMD, six-month dispensing; AGs, adherence groups; FTRs, fast track refills; HAD, home ART delivery

Table 7. Health outcomes, health system costs, and ICERs for the DSD scenarios on the cost-effectiveness frontier

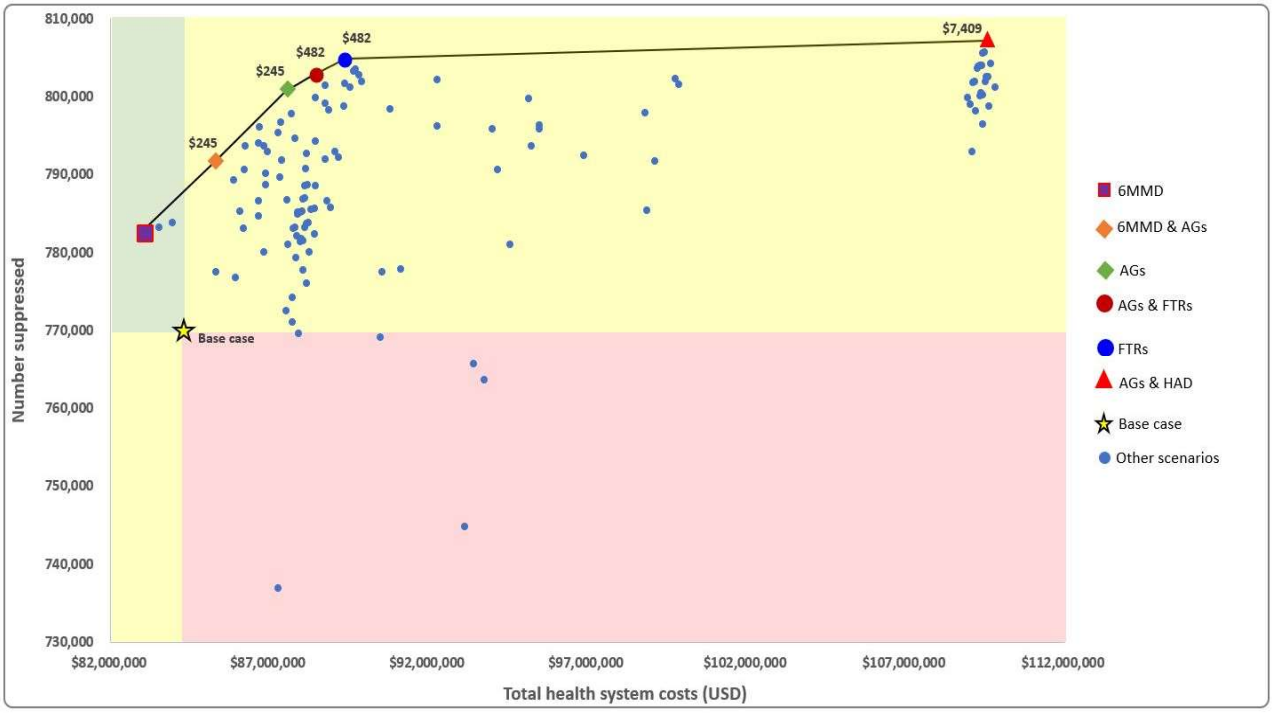
Scenarios	Total number of people retained, n, 95% CI (% change compared to base case)	Total number of people suppressed, n, 95% CI (% change compared to base case)	Total health system cost, USD (% change compared to base case)	ICER per additional person suppressed (USD)†
Base case	817,948 (786,510; 855,901) (n/a)	770,086 (717,521; 823,735) (n/a)	$84,332,234 (n/a)	n/a
6MMD	827,415 (792,037; 871,306) 1.2% (0.7; 1.8)	782,545 (724,788; 845,272) 1.6% (1.0; 2.6)	$83 095,136 (-1.5%)	Cost-saving (compared to base case)
6MMD & AGs	831,498 (797,906; 874,787) 1.7% (1.4; 2.2)	791,712 (733,632; 851,124) 2.8% (2.2; 3.3)	$85,336,549 (1.2%)	$245
AGs	835,581 (803,774; 878,268) 2.2% (2.2; 2.6)	800,878 (742,477; 856,975) 4.0% (3.5; 4.0)	$87,577,961 (3.8%)	$245
FTRs & AGs	838,225 (799,578; 886,582) 2.5% (1.7; 3.6)	802,755 (730,983; 865,189) 4.2% (1.9; 5.0)	$88,483,273 (4.9%)	$482
FTRs	840,869 (795,382; 894,895) 2.8% (1.1; 4.6)	804,632 (719,490; 873,403) 4.5% (0.3; 6.0)	$89,388,584 (6.0%)	$482
AGs & HAD	844,609 (800,208; 890,409) 3.3% (1.7; 4.0)	807,356 (736,649; 870,927) 4.8% (2.7; 5.7)	$109,574,215 (29.9%)	$7,409

†ICERs per additional person suppressed on treatment were calculated by comparing scenarios to the previous scenarios that was on the cost-effective frontier.

Scenarios	Total number of people retained, n, 95% CI (% change compared to base case)	Total number of people suppressed, n, 95% CI (% change compared to base case)	Total health system cost, USD (% change compared to base case)	ICER per additional person suppressed (USD)†
6MMD, six-month dispensing; AGs, adherence groups; FTRs, fast track refills; HAD, home ART delivery				

With the exception of 6-month dispensing, which was cost-saving, all other scenarios on the cost-effectiveness frontier resulted in an additional cost to the healthcare system per additional person virally suppressed, with ICERs ranging from $245 to $7,409. Compared to the base case, enrolling all eligible clients in 6MMD increased the number of individuals retained in care by 1.2% (95% CI, 0.7; 1.8) and the number virally suppressed by 1.6% (95% CI, 1.0; 2.6), while decreasing health system cost by 1.5%. As illustrated in Fig 2, the remaining scenarios on the frontier further improved treatment outcomes while also increasing total costs. The most expensive scenario on the cost-effectiveness frontier—AGs for young adults and HAD for everyone else—resulted in the greatest increase in retention by 3.3% (95% CI, 1.7; 4.0) and suppression by 4.8% (95% CI, 2.7; 5.7), at an increase in annual costs of nearly 30% compared to the current base case.

Figure 2. Total number of people suppressed on treatment by total health system costs for scenarios on the cost-effectiveness frontier

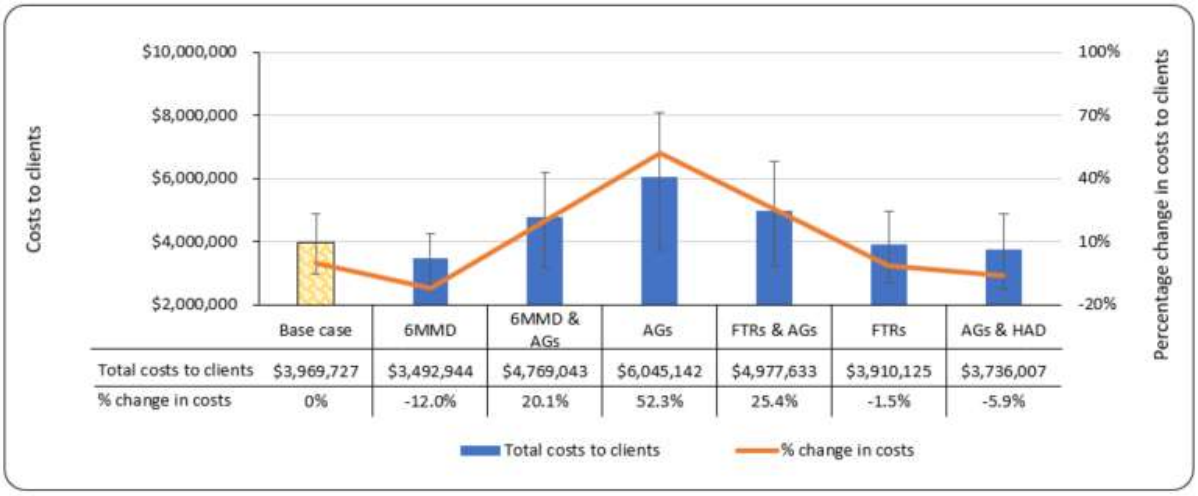


2.3.3. Costs to ART clients

Compared to the current base case ART distribution of DSD models, enrolling all clients eligible for DSD in 6MMD-only, FTRs-only and a combination of AGs and HAD scenario was cost-saving, while the other three scenarios on the cost-effectiveness frontier all resulted in an increased cost to clients per

year (Fig 3, Table S6). Compared to the base case, enrolling all eligible clients in 6MMD-only reduced cost to clients by 12.0% (95% CI, -10.8; 12.4), while a combination of 6MMD and AGs resulted in an increase in costs to clients per year of 20.1% (95% CI, 9.5; 28.1). The scenario on the cost-effectiveness frontier with the highest cost to ART clients was AGs-only for all eligible clients, which increased costs to clients by 52.3% (95% CI, 29.8; 68.7) compared to the current base case. A combination of fast-track refills (FTRs) and AGs for all eligible clients resulted in an annual increase of costs to clients of 86.4% compared to the base case. Enrolling all eligible clients in FTRs-only, and the age-specific scenario, which was a combination of AGs for those ≤24 years and HAD for those ≥25 years, reduced costs to clients per year by 1.5% (95% CI, -7.3; 3.3) and 5.9% (95% CI -15.6; 0,5), compared to the base case, respectively.

Figure 3. Cost to clients per year for the scenarios on the cost-effectiveness frontier (2023 USD)



	Base case	6MMD	6MMD & AGs	AGs	FTRs & AGs	FTRs	AGs & HAD
Total costs to clients	$3,969,727	$3,492,944	$4,769,043	$6,045,142	$4,977,633	$3,910,125	$3,736,007
% change in costs	0%	-12.0%	20.1%	52.3%	25.4%	-1.5%	-5.9%

2.3.4. Outcomes stratified by subpopulation

The relative impact of each scenario varied by age, sex, and setting (Table 8). For clients aged 25-49 years, who constituted over 70% of the ART population included in the analysis, all scenarios on the cost-effectiveness frontier resulted in increased retention compared to the base case. Retention was lower in female clients aged 15-19 years and male clients 15-24 in rural settings for all scenarios on the cost-effectiveness frontier except for 6MMD-only, which improved retention across all sub-populations. A scenario utilizing AGs-only had a low retention rate among clients aged ≥50+ in both urban and rural settings. Viral suppression increased for most subpopulations in most scenarios on the cost-effectiveness frontier, though 6MMD was slightly less successful for older clients and rural clients showed slightly lower suppression rates in several of the scenarios. 6MMD combined with adherence groups was associated with better viral suppression for the largest proportion of the subpopulations assessed except for male clients aged ≥50+ in rural settings.

Table 8. Retention(a) and viral suppression (b) rates for scenarios on cost-effectiveness frontier compared to the base case distribution by ART client sub-category

Sex/age/setting subgroup	Base case distribution	6MMD	6MMD & AGs	AGs	FTRs & AGs	FTRs	AGs & HAD
(a) Retention							
Total	89.1%	90.2%	90.6%	91.0%	91.3%	91.6%	92.0%
Male, 15-19, Rural	90.6%	91.7%	89.5%	87.2%	82.3%	77.3%	87.2%
Male, 20-24, Rural	88.6%	90.2%	92.7%	95.1%	92.1%	89.1%	95.1%
Male, 25-49, Rural	89.8%	91.1%	91.2%	91.3%	91.5%	91.8%	92.1%
Male, 50+, Rural	91.7%	92.5%	91.2%	89.9%	92.5%	95.2%	90.3%
Male, 15-19, Urban	87.8%	88.8%	87.8%	86.8%	87.1%	87.4%	86.8%
Male, 20-24, Urban	85.7%	87.5%	91.0%	94.5%	91.5%	88.5%	94.5%
Male, 25-49, Urban	87.8%	88.9%	90.0%	91.1%	91.2%	91.4%	89.9%
Male, 50+, Urban	90.1%	90.3%	90.1%	89.9%	91.2%	92.4%	91.5%
Female, 15-19, Rural	88.0%	89.0%	88.0%	87.1%	82.3%	77.5%	87.1%
Female, 20-24, Rural	85.9%	87.5%	91.4%	95.4%	92.3%	89.2%	95.4%
Female, 25-49, Rural	90.7%	91.8%	91.7%	91.5%	91.7%	91.9%	96.5%
Female, 50+, Rural	92.4%	93.1%	91.5%	90.0%	92.6%	95.3%	85.7%
Female, 15-19, Urban	86.3%	87.7%	87.1%	86.5%	86.8%	87.1%	86.5%
Female, 20-24, Urban	82.6%	85.5%	89.5%	93.4%	90.5%	87.6%	93.4%
Female, 25-49, Urban	88.8%	89.8%	90.5%	91.2%	91.4%	91.6%	93.9%
Female, 50+, Urban	90.8%	91.0%	90.5%	90.0%	91.3%	92.5%	84.2%
(b) Viral suppression							
Total	94.1%	94.6%	95.2%	95.8%	95.8%	95.7%	95.6%
Male, 15-19, Rural	80.3%	81.9%	86.7%	91.8%	91.3%	90.7%	91.8%
Male, 20-24, Rural	84.6%	87.3%	89.6%	91.7%	91.3%	90.9%	91.7%
Male, 25-49, Rural	94.3%	95.1%	94.6%	94.0%	93.7%	93.3%	92.6%
Male, 50+, Rural	95.3%	95.7%	95.0%	94.2%	93.8%	93.4%	92.8%
Male, 15-19, Urban	78.5%	78.9%	85.8%	92.8%	92.9%	92.9%	92.8%
Male, 20-24, Urban	80.5%	80.6%	87.2%	93.4%	93.3%	93.3%	93.4%
Male, 25-49, Urban	93.9%	94.2%	95.0%	95.8%	95.8%	95.9%	96.9%
Male, 50+, Urban	94.8%	94.7%	95.4%	96.0%	96.1%	96.1%	97.2%
Female, 15-19, Rural	80.2%	82.0%	87.8%	93.7%	93.1%	92.4%	93.7%
Female, 20-24, Rural	91.5%	93.4%	94.6%	95.8%	95.3%	94.7%	95.8%
Female, 25-49, Rural	95.2%	95.8%	96.2%	96.6%	96.0%	95.5%	92.7%
Female, 50+, Rural	96.3%	96.5%	96.6%	96.8%	96.2%	95.7%	92.8%
Female, 15-19, Urban	78.4%	79.3%	86.0%	92.7%	92.9%	93.0%	92.7%
Female, 20-24, Urban	90.0%	91.8%	93.4%	94.9%	95.0%	95.1%	94.9%
Female, 25-49, Urban	94.9%	95.2%	95.7%	96.2%	96.4%	96.5%	97.0%
Female, 50+, Urban	95.7%	95.5%	96.0%	96.5%	96.6%	96.7%	97.3%

†based on mid-point value of health outcomes (retention and viral suppression rate)
*Cells shaded green are greater than base case; cells shaded red are less than base case.

2.3.5. Sensitivity analysis

The main cost drivers of the total health system costs for the base case scenario were the cost of ART, the cost of VL test and cost of clinical follow-up. Cost of DSD interaction for HAD and AGs did not meaningfully affect the total health system costs (Fig 4). Under the 6MMD-only, a combination of 6MMD and AGs, AGs-only, and a combination of AGs and FTRs scenario, cost of laboratory tests (VL and CD4) and ART were the most influential parameters leading to all scenario with a potential of being cost-saving or resulting in addition cost to the healthcare system per person suppressed on treatment (Fig 5a-d). In addition, for FTrs-only scenario, cost of short-visit (fast-track visit) was also the most influential cost parameter (Fig 5e). For the most-expensive scenario on the cost-effectiveness frontier, Cost input parameters for cost of DSD interaction per year and number of DSD interaction for

were the most influential cost drivers for the ICER per person suppressed on treatment compared to other input parameters, with no potential of cost-saving (Fig 5f).

Figure 4. Sensitivity analysis of base case total health system costs

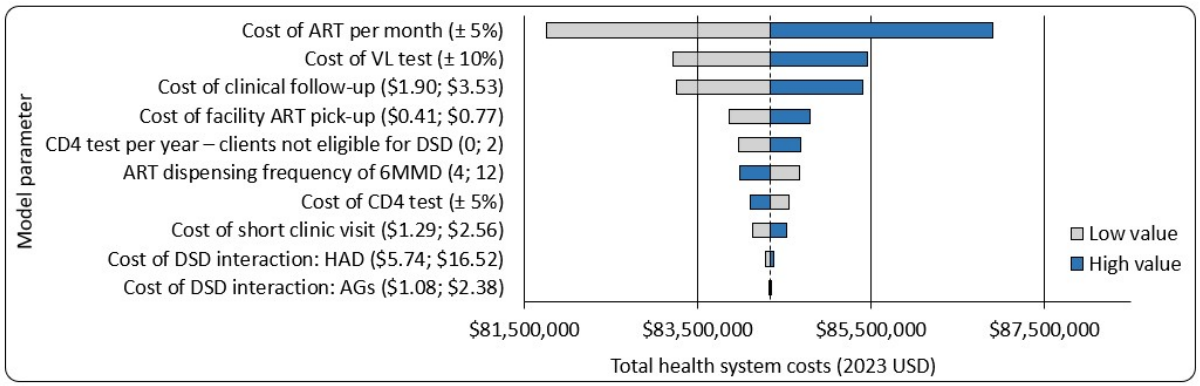
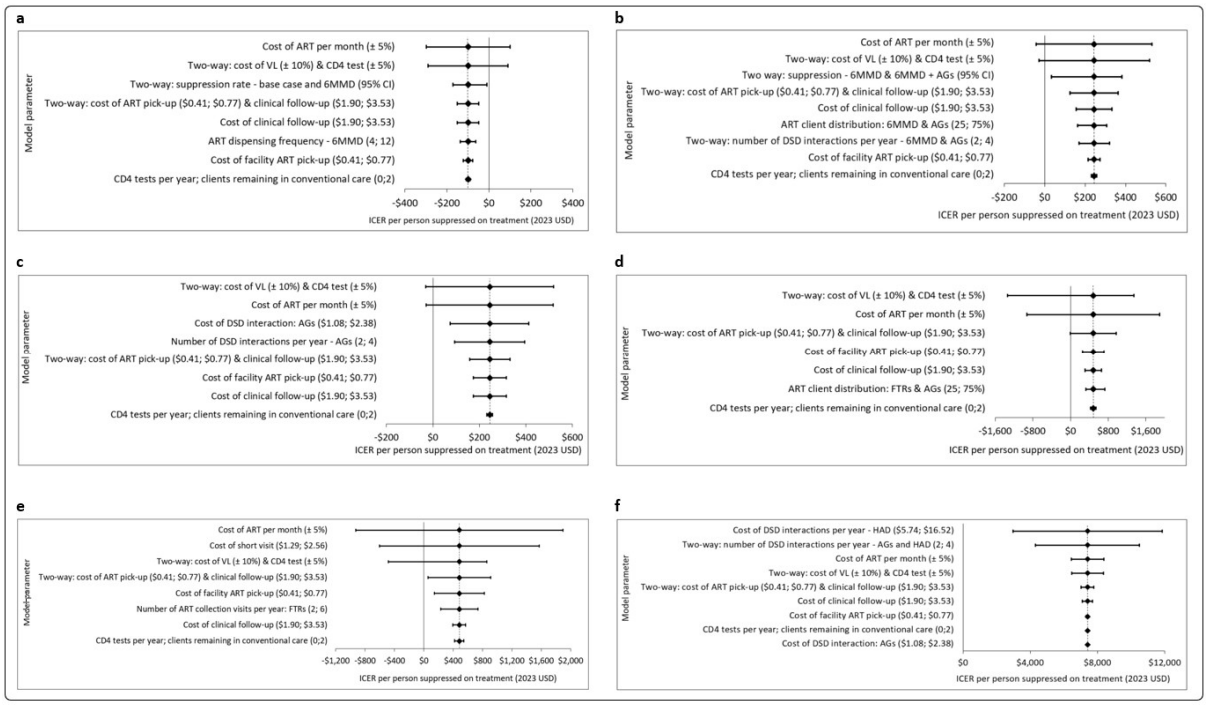


Figure 5. Sensitivity analysis of ICER per person suppressed on treatment for each of the scenario on the cost-effectiveness frontier



*The dashed line in figure 5 represent the uncertainty impact on the ICER under 6MMD-only (**a**), a combination of 6MMD and AGs (**b**), AGs-only (**c**), a combination of FTRs and AGs (**d**), FTRs-only (**e**), and a combination of AGs and HAD (**f**)

2.4. Discussion

In this modelling study, we identified several differentiated service delivery allocation scenarios that are likely to have better health outcomes than the current distribution of ART delivery models in Zambia and estimated the additional cost to the HIV program budget of implementing those scenarios. Enrolment of all eligible clients in 6MMD appeared to be cost-saving for both providers and clients, while still improving outcomes modestly. While not cost-saving, other combinations of DSD models on

the cost-effectiveness frontier could further increase retention in care and viral suppression, beyond rates estimated for 6MMD-only, by up to 4.8%. These scenarios come at an additional cost to both providers and clients, compared to the base case. This is not surprising in view of the base case distribution, in which nearly 70% of clients were enrolled in 6MMD. Since all other models of care are more expensive for both providers and clients than is 6MMD, any scenario that reduced total 6MMD coverage was bound to cost more than the base case. By increasing viral suppression, however, the combinations of DSD models on the frontier may have the longer-term benefit of reducing onward transmission, and therefore reducing both health system and client costs in the long term.

Our analysis found that a scenario tailored to specific sub-populations–adherence groups for those ≤24 years and home ART delivery for those ≥25+ years–can increase the number of people virally suppressed on treatment across all subgroups. In the 6MMD-only scenario, in contrast, retention and suppression rates increased for all subgroups except clients ≥50+ years in urban settings. DSD models tailored to subpopulations may thus still be required, rather than implementation of a single DSD scale-up strategy for all clients who are eligible. Sensitivity analysis showed that varying the model input parameters – costs ART and laboratory test was influential to the total health system costs, and ICERs for each of the most of scenarios while under a combination of AGs for ≤24 years and HAD for clients aged ≥25, the cost of DSD interaction for HAD and number of DSD interaction (both AGs & HAD) were the most influential model parameters.

To our knowledge, this is the first model to consider how the distribution of available differentiated service delivery models might affect overall cost-effectiveness of a national HIV treatment program. Other studies have investigated the outcomes, costs, and cost-effectiveness of individual DSD models, with a wide range of results depending on the country and specific model(s) of care being evaluated [2,9,23], or have compared the costs of the actual DSD landscape to a “no DSD” status quo [12]. Across multiple countries, reported retention and viral suppression rates in DSD models have broadly fallen within 5% of what was reported in the conventional care [2]. A retrospective electronic record review in Zambia reported higher cost of community DSD models compared to conventional care, with an annual provider cost per DSD ranged from $116 to $199 for the DSD models, compared to $100 in conventional care [16]. A pragmatic, cluster-randomised, unblinded, non-inferiority trial conducted in Zambia and Malawi showed that 6-month ART dispensing was associated with non-inferior retention rates and ART uptake to standard of care and 3-month ART dispensing [24]. In this trial, as in our modelled analysis, 6-month ART dispensing was found to be cost-saving for both healthcare system and to clients retained in care at 12 months, compared to standard of care and 3-month ART dispensing [24]. In two prospective cluster randomized non-inferiority trials conducted in Lesotho and Zimbabwe, community adherence groups with 3 months medication dispensing and 6-month

community dispensing were found to be less costly than conventional care [25,26], with similar health outcomes. Finally, a comprehensive analysis of the costs of existing DSD models in Mozambique concluded that, compared to a hypothetical scenario in which all clients received conventional care, DSD is less expensive than the comparison [12]. These studies support our finding that DSD models have a potential to improve health outcomes and minimise costs.

Although our results are specific to one country and point in time, we believe that they can broadly help inform policy-makers about how changes in DSD model offerings might affect health outcomes, costs, and the prioritisation of population specific DSD model combinations at an aggregate level and the trade-offs that must be made. If the goal of the healthcare system is to achieve optimal cost savings without diminishing health outcomes, for example, the implementation of 6MMD-only for all eligible ART clients appears to be a strategy that could achieve such goals. If the goal is to prioritise improvement of health outcomes while allowing the budget to increase modestly, scenarios that increase health outcomes but with lower ICERs may be optimal. The higher costs to clients associated with most non-conventional models of care, along with client preferences and concerns, must also be considered. Future research is required to understand the DSD model transition acceptability and cost implications from the perspective of the clients.

Key strengths of our study are the use of a large national-level dataset to quantify the expected outcomes of different DSD models in different sub-populations, local cost estimates, and the analysis of multiple hypothetical combinations of DSD models. Our study also had a number of limitations. First, we parameterised the model using retention and viral suppression rates from individuals enrolled in these models currently. Our results omit the effects and costs of moving from the current distribution to any other scenario. Moving individuals around among models, as is done in our analysis, is likely to result in different outcomes and costs from those observed for current enrollees, particularly if the base case reflects individual client preferences for service delivery, which the modelled scenarios ignore. For this reason, results should be regarded as illustrative of what can potentially be achieved through re-allocation, rather than a precise prediction of outcomes.

Second, we modelled only national level outcomes with stratification for rural and urban settings. We did not consider protentional provincial or other geographic differences and we acknowledge that the results may differ at provincial level especially between provincial with substantial difference in geographical settings and poor access to care. Third, because we did not have actual cost estimates for all the models of care included in our analysis, we assumed that models are implemented according to guidelines and utilized ingredients-based costing. Actual costs incurred may be either under- or over-estimated using this approach. Fourth, cost to clients were estimated from self-reported

frequency of visits, time spent at the facility, lost wages, and transport costs. Self-report may be subject to recall bias, reducing the accuracy of estimates. Fifth, we did not include any additional costs that might arise from the additional coordination and management required to operate multiple models of care at a single site, nor did we capture any costs above those at the facility (e.g. national or provincial planning, training, budgeting). Some facilities are likely to struggle with the simultaneous implementation of multiple models and require additional resources to do this successfully. We note that none of the scenarios on the cost-effectiveness frontier, however, required more than two non-conventional models of care, reducing our concerns about imposing excessive management and coordination burden.

Finally, we acknowledge that the results of this modelling analysis may not be generalizable beyond Zambia, as the factors that influence the cost-effectiveness of DSD allocation may be context dependent. For countries in southern Africa with relatively similar conditions as Zambia, the results we report may be adoptable locally. For most countries, though, it is the mathematical model itself, and the potential for running it with country-specific data, rather than using the Zambia-specific results, that we hope can help improve DSD allocation. We also emphasize that "cost savings" in a model like that presented here in fact reflect a reduced investment of resources, such as staff time, per ART client served, rather than a budgetary savings. The freed-up resources can be used for other purposes within the healthcare system, but budgetary reductions should not be expected.

2.5. Conclusions

With six years remaining towards achieving the global UNAIDS 95-95-95 targets in 2030, many countries in sub-Saharan Africa, such as Zambia, that have made progress towards achieving these goals may benefit from restructuring their DSD model offerings for ART distribution [27]. The model and overall approach demonstrated here can broadly allow for rapid evaluation of different model allocations in terms of health outcomes, cost to clients, and costs to the healthcare system, while ensuring that all client sub-populations are considered. Given the large scale of ART programs and the widespread adoption of differentiated service delivery in sub-Saharan Africa, even small improvements in service delivery efficiency can have large impacts. Applying a relatively simple mathematical model that relies largely on existing data may be one way to achieve such progress.

2.6. Funding

The project in which this study was conducted as part of was provided by the Bill & Melinda Gates Foundation through OPP1192640 to Boston University and INV-037138 to the Wits Health Consortium. The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

2.7. Ethics

This study protocol was approved by ERES Converge IRB (Zambia), protocol number 2019-Sep-030; the Human Research Ethics Committee (Medical) of the University of Witwatersrand (South Africa), protocol number M190453 and sub-study protocol number M231093; and the Boston University IRB (United States), protocol number H-38823.

2.8. Declaration of Interest

The authors report no competing interests. PM is the employee of the Ministry of Health in Zambia and thus have some supervisory authority over the ART program.

2.9. Authors' contributions

NL, SR, LJ, BP and BEN conceptualised the study. NL and LJ collected the cost data. LJ and BEN oversaw data collection. NL developed and parameterised the model. LJ and BEN oversaw the model development. NL did data analysis and had full access to the data. LJ and BEN oversaw data analysis. NL, SR, LJ and BEN verified underlying data assumptions. NL wrote the first draft. All authors contributed to reviewing and editing the manuscript for submission.

2.10. Acknowledgements

We would like to thank the staff of the Ministry of Health in Zambia for approving this research. We are particularly appreciative of the support of each country's Differentiated Service Delivery Technical Working Group.

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3. EXTENDED METHODS AND RESULTS

3.1. Extended methods

3.2. Introduction

This section outlines the extended methods used to estimate the distribution of ART health outcomes, unit cost used to estimate the provider costs per client per year, cost to clients per year and the distribution of clients among ART delivery models for the scenarios analysed.

3.3. Methods

The distribution of ART delivery model which reflect the 2022 cohort were estimated from the Zambia electronic medical record – SmartCare database [1]. The cohort was stratified by the ART model delivery, sex, settings (rural/urban), age groups and health outcomes (retention and suppression rate). The age groups for each model of ART delivery was categorised into four groups (15-19, 20-24, 25-49, and 50+) (Table S1).

3.3.1. Health outcomes by sex, setting, age and model of ART delivery

Table S1. Health outcomes – retention and viral suppression rates stratified by ART delivery model, sex, setting and age group

ART delivery model	Sex	Setting	Age	Retention rates	Suppression rates
Scholar/adolescents model	Female	Rural	15-19	94.4%	91.7%
Fast track refills	Female	Rural	15-19	76.5%	95.7%
Conventional care not eligible for DSD	Female	Rural	15-19	81.9%	67.6%
Six-month dispensing (6MMD)	Female	Rural	15-19	89.6%	83.3%
Adherence groups	Female	Rural	15-19	87.5%	96.8%
Community ART distribution points	Female	Rural	15-19	95.0%	75.0%
Health posts	Female	Rural	15-19	91.5%	100.0%
Mobile ART distribution	Female	Rural	15-19	94.9%	92.0%
Conventional care (3MMD)	Female	Rural	15-19	87.4%	76.2%
Scholar/adolescents model	Male	Rural	15-19	90.0%	91.7%
Fast track refills	Male	Rural	15-19	76.5%	93.5%
Conventional care not eligible for DSD	Male	Rural	15-19	80.7%	63.9%
Six-month dispensing (6MMD)	Male	Rural	15-19	92.5%	83.2%
Adherence groups	Male	Rural	15-19	87.5%	94.2%
Community ART distribution points	Male	Rural	15-19	95.0%	75.0%
Health posts	Male	Rural	15-19	89.9%	92.9%
Mobile ART distribution	Male	Rural	15-19	95.7%	87.5%
Conventional care (3MMD)	Male	Rural	15-19	90.4%	73.1%
Scholar/adolescents model	Female	Urban	15-19	93.0%	83.3%
Fast track refills	Female	Urban	15-19	88.2%	96.8%
Conventional care not eligible for DSD	Female	Urban	15-19	77.3%	66.0%
Six-month dispensing (6MMD)	Female	Urban	15-19	88.9%	80.9%

ART delivery model	Sex	Setting	Age	Retention rates	Suppression rates
Adherence groups	Female	Urban	15-19	87.5%	96.5%
Community ART distribution points	Female	Urban	15-19	95.0%	75.0%
Health posts	Female	Urban	15-19	89.0%	93.7%
Conventional care (3MMD)	Female	Urban	15-19	86.0%	74.4%
Scholar/adolescents model	Male	Urban	15-19	96.7%	83.3%
Fast track refills	Male	Urban	15-19	88.2%	96.2%
Conventional care not eligible for DSD	Male	Urban	15-19	79.2%	63.3%
Six-month dispensing (6MMD)	Male	Urban	15-19	89.7%	80.4%
Adherence groups	Male	Urban	15-19	87.5%	96.1%
Community ART distribution points	Male	Urban	15-19	95.0%	75.0%
Health posts	Male	Urban	15-19	87.0%	95.7%
Conventional care (3MMD)	Male	Urban	15-19	87.8%	74.7%
Scholar/adolescents model	Female	Rural	20-24	94.4%	91.7%
Fast track refills	Female	Rural	20-24	90.4%	95.7%
Conventional care not eligible for DSD	Female	Rural	20-24	74.6%	82.7%
Six-month dispensing (6MMD)	Female	Rural	20-24	88.5%	94.2%
Adherence groups	Female	Rural	20-24	97.2%	96.8%
Community ART distribution points	Female	Rural	20-24	88.9%	83.3%
Health posts	Female	Rural	20-24	91.5%	100.0%
Mobile ART distribution	Female	Rural	20-24	94.9%	92.0%
Conventional care (3MMD)	Female	Rural	20-24	84.0%	87.1%
Scholar/adolescents model	Male	Rural	20-24	90.0%	91.7%
Fast track refills	Male	Rural	20-24	90.4%	93.5%
Conventional care not eligible for DSD	Male	Rural	20-24	75.9%	63.0%
Six-month dispensing (6MMD)	Male	Rural	20-24	91.6%	89.4%
Adherence groups	Male	Rural	20-24	97.2%	94.2%
Community ART distribution points	Male	Rural	20-24	88.9%	83.3%
Health posts	Male	Rural	20-24	89.9%	92.9%
Mobile ART distribution	Male	Rural	20-24	95.7%	87.5%
Conventional care (3MMD)	Male	Rural	20-24	84.7%	76.4%
Scholar/adolescents model	Female	Urban	20-24	93.0%	83.3%
Fast track refills	Female	Urban	20-24	90.3%	96.8%
Conventional care not eligible for DSD	Female	Urban	20-24	64.9%	78.7%
Six-month dispensing (6MMD)	Female	Urban	20-24	87.9%	93.1%
Adherence groups	Female	Urban	20-24	97.2%	96.5%
Community ART distribution points	Female	Urban	20-24	88.9%	83.3%
Health posts	Female	Urban	20-24	89.0%	93.7%
Mobile ART distribution	Female	Urban	20-24	94.3%	96.5%
Conventional care (3MMD)	Female	Urban	20-24	80.0%	86.1%
Scholar/adolescents model	Male	Urban	20-24	96.7%	83.3%
Fast track refills	Male	Urban	20-24	90.3%	96.2%
Conventional care not eligible for DSD	Male	Urban	20-24	72.6%	69.3%
Six-month dispensing (6MMD)	Male	Urban	20-24	89.1%	81.8%
Adherence groups	Male	Urban	20-24	97.2%	96.1%
Community ART distribution points	Male	Urban	20-24	88.9%	83.3%
Health posts	Male	Urban	20-24	87.0%	95.7%
Conventional care (3MMD)	Male	Urban	20-24	81.8%	74.1%
Extended clinic hours	Female	Rural	25-49	82.4%	96.7%

ART delivery model	Sex	Setting	Age	Retention rates	Suppression rates
Fast track refills	Female	Rural	25-49	92.3%	95.7%
Conventional care not eligible for DSD	Female	Rural	25-49	80.5%	90.1%
Six-month dispensing (6MMD)	Female	Rural	25-49	92.2%	96.0%
Adherence groups	Female	Rural	25-49	91.9%	96.8%
Community ART distribution points	Female	Rural	25-49	92.1%	95.9%
Health posts	Female	Rural	25-49	91.5%	100.0%
Home ART delivery	Female	Rural	25-49	97.1%	92.8%
Mobile ART distribution	Female	Rural	25-49	94.9%	92.0%
Conventional care (3MMD)	Female	Rural	25-49	87.5%	92.4%
Extended clinic hours	Male	Rural	25-49	98.1%	100.0%
Fast track refills	Male	Rural	25-49	92.3%	93.5%
Conventional care not eligible for DSD	Male	Rural	25-49	77.7%	88.6%
Six-month dispensing (6MMD)	Male	Rural	25-49	91.7%	95.3%
Adherence groups	Male	Rural	25-49	91.9%	94.2%
Community ART distribution points	Male	Rural	25-49	92.1%	95.9%
Health posts	Male	Rural	25-49	89.9%	92.9%
Home ART delivery	Male	Rural	25-49	92.6%	92.8%
Mobile ART distribution	Male	Rural	25-49	95.7%	87.5%
Conventional care (3MMD)	Male	Rural	25-49	86.0%	91.6%
Extended clinic hours	Female	Urban	25-49	82.4%	96.7%
Fast track refills	Female	Urban	25-49	92.2%	96.8%
Conventional care not eligible for DSD	Female	Urban	25-49	76.1%	89.7%
Six-month dispensing (6MMD)	Female	Urban	25-49	90.4%	95.4%
Adherence groups	Female	Urban	25-49	91.9%	96.5%
Community ART distribution points	Female	Urban	25-49	92.1%	95.9%
Health posts	Female	Urban	25-49	89.0%	93.7%
Home ART delivery	Female	Urban	25-49	94.7%	97.3%
Conventional care (3MMD)	Female	Urban	25-49	86.7%	93.4%
Extended clinic hours	Male	Urban	25-49	98.1%	100.0%
Fast track refills	Male	Urban	25-49	92.2%	96.2%
Conventional care not eligible for DSD	Male	Urban	25-49	74.8%	88.1%
Six-month dispensing (6MMD)	Male	Urban	25-49	89.5%	94.5%
Adherence groups	Male	Urban	25-49	91.9%	96.1%
Community ART distribution points	Male	Urban	25-49	92.1%	95.9%
Health posts	Male	Urban	25-49	87.0%	95.7%
Home ART delivery	Male	Urban	25-49	90.7%	97.3%
Conventional care (3MMD)	Male	Urban	25-49	84.5%	92.0%
Extended clinic hours	Female	Rural	50+	82.4%	96.7%
Fast track refills	Female	Rural	50+	95.5%	95.7%
Conventional care not eligible for DSD	Female	Rural	50+	81.6%	93.2%
Six-month dispensing (6MMD)	Female	Rural	50+	93.2%	96.5%
Adherence groups	Female	Rural	50+	90.1%	96.8%
Community ART distribution points	Female	Rural	50+	91.8%	99.5%
Health posts	Female	Rural	50+	91.5%	100.0%
Home ART delivery	Female	Rural	50+	85.7%	92.8%
Mobile ART distribution	Female	Rural	50+	94.9%	92.0%
Conventional care (3MMD)	Female	Rural	50+	88.9%	94.4%
Extended clinic hours	Male	Rural	50+	98.1%	100.0%

ART delivery model	Sex	Setting	Age	Retention rates	Suppression rates
Fast track refills	Male	Rural	50+	95.5%	93.5%
Conventional care not eligible for DSD	Male	Rural	50+	80.1%	91.2%
Six-month dispensing (6MMD)	Male	Rural	50+	92.7%	95.8%
Adherence groups	Male	Rural	50+	90.1%	94.2%
Community ART distribution points	Male	Rural	50+	91.8%	99.5%
Health posts	Male	Rural	50+	89.9%	92.9%
Home ART delivery	Male	Rural	50+	90.5%	92.8%
Mobile ART distribution	Male	Rural	50+	95.7%	87.5%
Conventional care (3MMD)	Male	Rural	50+	88.2%	93.3%
Extended clinic hours	Female	Urban	50+	82.4%	96.7%
Fast track refills	Female	Urban	50+	92.6%	96.8%
Conventional care not eligible for DSD	Female	Urban	50+	83.5%	93.8%
Six-month dispensing (6MMD)	Female	Urban	50+	91.1%	95.5%
Adherence groups	Female	Urban	50+	90.1%	96.5%
Community ART distribution points	Female	Urban	50+	91.8%	99.5%
Health posts	Female	Urban	50+	89.0%	93.7%
Home ART delivery	Female	Urban	50+	84.2%	97.3%
Conventional care (3MMD)	Female	Urban	50+	89.6%	95.0%
Extended clinic hours	Male	Urban	50+	98.1%	100.0%
Fast track refills	Male	Urban	50+	92.6%	96.2%
Conventional care not eligible for DSD	Male	Urban	50+	81.8%	91.7%
Six-month dispensing (6MMD)	Male	Urban	50+	90.4%	94.8%
Adherence groups	Male	Urban	50+	90.1%	96.1%
Community ART distribution points	Male	Urban	50+	91.8%	99.5%
Health posts	Male	Urban	50+	87.0%	95.7%
Home ART delivery	Male	Urban	50+	91.7%	97.3%
Conventional care (3MMD)	Male	Urban	50+	88.5%	93.5%

3.3.2. Unit costs

Table S2. Unit costs (provider costs)

Cost Items	Mean unit cost (2023 USD)	Description
Laboratory (cost per test)		Assumed one test per person per year [37]
Viral load	$27.44	
CD4 count	$5.38	
HIV treatment		Assumed first-line regimen (Tenofovir/Lamivudine/ Dolutegravir) for all clients [37]
ART (per month)	$5.25	
Interaction costs	**Mean unit cost (range)**	
Facility visit (cost per visit)		Unit cost data were collected from previously published literature in Zambia and updated with 2023 public sector prices and staff costs [26]. Facility visit and DSD interaction costs include staff time, equipment, consumables, overheads, and training costs [26].
Clinical follow-up	$2.71 (1.90; 3.53)	
Short clinic visit	$1.93 (1.29; 2.56)	
Pharmacy visit	$0.59 (0.41; 0.77)	
DSD interaction (cost per interaction)		
Scholar/adolescent model	$1.11 (0.74; 1.49)	
Fast-track refills	$1.93 (1.29; 2.56)	
Adherence groups†	$1.73 (1.08; 2.38)	
Community ART distribution points‡	$2.35 (1.43; 3.28)	

Health post§	$2.71 (1.90; 3.53)	
Home ART delivery	$11.13 (5.74; 16.53)	
Mobile ART distribution	$8.81 (7.36; 10.26)	
† assumed similar resources use as Community Adherence groups and urban adherence groups ‡ assumed similar resources use as urban adherence groups § assumed similar resources use as clinical follow-up		

3.3.3. Cost to clients per year

Table S3. Average cost (2023 USD) to ART clients per year, stratified by ART delivery model

Model of care	N	Opportunity cost/RoC/year† (mean, SD)		Transport costs/RoC/year (mean, 95% CI)	
		Time spent (hours)	Mean cost (95% CI)	% RoC incurring any transport costs**	Travel costs/RoC incurring any transport costs
Conventional care not eligible for DSD	66	27.9	$6.94 (5.60; 8.28)	51.5%	$3.19 (1.98; 4.40)
Conventional care (3MMD)	66	20.28	$5.01 (4.33; 5.70)	40.9%	$3.01 (0.89; 5.14)
Six-month dispensing	118	12.16	$3.01 (2.50; 3.51)	36.4%	$2.80 (1.56; 4.04)
Scholar/adolescent model	41	17.55	$4.34 (3.19; 5.48)	26.8%	$1.66 (0.64; 2.68)
Adherence groups	23	26.06	$6.44 (4.45; 8.42)	34.8%	$2.09 (0.14; 4.31)
Community ART distribution points‡	37	21.10	$5.21 (3.94; 6.49)	51.4%	$1.71 (1,04; 2.38)
Extended clinic hours	15	9.52	$2.35 (1.94; 2.76)	46.7%	$1.74 (0.56; 2.91)
Fast track refills	31	15.96	$3.94 (2.94; 4.95)	45.2%	$1.32 (0.86; 1.77)
Mobile ART	9	16.23	$4.01 (2.10; 5.92)	0.0%	$0.00 (0.00; 0.00)
Home ART delivery	25	10.82	$2.67 (2.19; 3.16)	40.0%	$2.98 (1.16; 4.81)
Health post§	37	21.10	$5.21 (3.94; 6.49)	51.4%	$1.71 (1,04; 2.38)

Cost to clients data was collected and updated from previously collected data [35]
*Includes both clinical consult visits and ART medication pick up visits at the facility.
**Remainder likely walked, incurred no cash costs.
†Calculated opportunity cost based on the cost of time spent travelling and time at clinic visits or out-of-facility events. The minimum wage for Zambia of $1.98/day (adjusted to an hourly minimum wage using 8 working hours/day) as used to assign a monetary value to the time spent.
‡Community adherence access points are equivalent to external medication pickup points.
§ assumed similar resources use as Community ART distribution points

3.3.4. Distribution of clients among ART delivery models for the scenarios analysed

Table S4. Distribution of clients among ART delivery models for the scenarios analysed

Scenario number	Scenario name	Descriptions/DSD mix and distribution of ART clients
Base case	2022 ART distribution	The current ART program in Zambia which includes 10 ART delivery models plus conventional care (3MMD and frequent refills) distribution as indicated in 2022 SmartCare database. ▪ 80.2% DSD coverage, 14.1% in conventional care eligible for DSD but not enrolled, and 5.3% in conventional care not eligible for DSD.
Scenario 1-4: The scenarios tailored to clients based on model population-specific enrolment with different DSD coverage (e.g. scholar/adolescent model is tailored for clients aged ≤24 years).		

Scenario number	Scenario name	Descriptions/DSD mix and distribution of ART clients
1	Scholar/adolescent model-only	Enrolling all eligible clients aged ≤24 years in scholar/adolescent model ▪ 6.8% DSD coverage for clients aged ≤24 years, 90.1% conventional care (3MMD), and 3.1% remain in conventional care not eligible
2	MAD-only	Enrolling all eligible clients in rural settings in mobile ART delivery ▪ 29.3% DSD coverage of all clients in rural settings, 70.7% in conventional care (3MMD), and 3.1% remain in conventional care not eligible
3	HAD-only	Enrolling all eligible clients aged ≥25 years in Home ART delivery ▪ 87.9% DSD coverage for clients aged ≥25+, 9.0% conventional care (3MMD), and 3.1% remains in conventional care not eligible for DSD
4	ECH-only	Enrolling all eligible clients aged ≥25 years in extended clinic hours ▪ 87.9% DSD coverage for clients aged ≥25+, 9.0% conventional care (3MMD), and 3.1% remains in conventional care not eligible for DSD
Scenario 5-9: Scenarios for all eligible clients, utilising DSD models with no age/setting specific restrictions, enrolling all clients in one DSD model at a time. Clients distribution: 94.7% DSD coverage and 5.3% conventional care not eligible for DSD.		
5	FTRs-only	Enrolling all eligible clients in fast-track refills
6	6MMD-only	Enrolling all eligible clients in 6MMD
7	CADP-only	Enrolling all eligible clients in community ART distribution points
8	HP-only	Enrolling all eligible clients in health post
9	AGs-only	Enrolling all eligible clients in adherence groups
Scenario 10-19: Scenario 5-9: Scenarios for all eligible clients, utilising DSD models with no age/setting specific restrictions, enrolling all clients in two DSD models at a time - paired all possible combinations. Clients distribution: 94.7% DSD coverage and 5.3% conventional care not eligible for DSD.		
10	FTRs & 6MMD	Equal distribution of all eligible clients between fast track refills and 6MMD
11	FTRs & AGs	Equal distribution of all eligible clients between fast track refills and adherence groups
12	FTRs & CADP	Equal distribution of all eligible clients between fast track refills and community ART distribution points
13	FTRs & HP	Equal distribution of all eligible clients between fast track refills and health posts
14	6MMD & AGs	Equal distribution of all eligible clients between 6MMD and adherence groups
15	6MMD & CADP	Equal distribution of all eligible clients between 6MMD and community ART distribution points
16	6MMD & HP	Equal distribution of all eligible clients between 6MMD and health posts
17	AGs & CADP	Equal distribution of all eligible clients between adherence groups and community ART distribution points
18	AGs & HP	Equal distribution of all eligible clients between adherence groups and health posts
19	CADP & HP	Equal distribution of all eligible clients between community ART distribution points and health posts
Scenario 20-29: Scenarios for all eligible clients, utilising DSD models with no age/setting specific restrictions, enrolling all clients in three DSD models at a time - paired all possible combinations. Clients distribution: 94.7% DSD coverage and 5.3% conventional care not eligible for DSD.		

Scenario number	Scenario name	Descriptions/DSD mix and distribution of ART clients
20	FTRs, 6MMD & AGs	Equal distribution of all eligible clients between fast-track refills, 6MMD and adherence groups
21	FTRs, 6MMD & CADP	Equal distribution of all eligible clients between fast-track refills, 6MMD and community ART distribution points
22	FTRs, 6MMD & HP	Equal distribution of all eligible clients between fast-track refills, 6MMD and health posts
23	FTRs, AGs & CADP	Equal distribution of all eligible clients between fast-track refills, adherence groups and community ART distribution points
24	FTR, AGs & HP	Equal distribution of all eligible clients between fast-track refills, adherence groups and health posts
25	FTRs, CADP & HP	Equal distribution of all eligible clients between fast-track refills, community ART distribution points and health post
26	6MMD, AGs & CADP	Equal distribution of all eligible clients between 6MMD, adherence groups and community ART distribution points
27	6MMD, AGs & HP	Equal distribution of all eligible clients between 6MMD, adherence groups and health posts
28	6MMD, CADP & HP	Equal distribution of all eligible clients between 6MMD, community ART distribution points and health posts
29	AGs, CADP & HP	Equal distribution of all eligible clients between Adherence groups, community ART distribution points and health posts
Scenario 30-35: Scenarios for all eligible clients, utilising DSD models with no age/setting specific restrictions, enrolling all clients in four DSD models at a time - paired all possible combinations. Clients distribution: 94.7% DSD coverage and 5.3% conventional care not eligible for DSD.		
30	FTRs, MMD6, AGs & CADP	Equal distribution of all eligible clients between fast track refills, 6MMD, adherence groups and community ART distribution points
31	FTRs, MMD6, AGs & HP	Equal distribution of all eligible clients between fast track refills, 6MMD, adherence groups and health posts
32	FTRs, MMD6, CADP & HP	Equal distribution of all eligible clients between fast track refills, 6MMD, community ART distribution points and health posts
33	FTRs, AGs, CADP & HP	Equal distribution of all eligible clients between fast track refills, adherence groups, community ART distribution points and health posts
34	MMD6, AGs, CADP & HP	Equal distribution of all eligible clients between 6MMD, adherence groups, community ART distribution points and health posts
	Scenario 35: Scenario for all eligible clients, utilising DSD models with no age/setting specific restrictions, enrolling all clients in five DSD models at a time. Clients distribution: 94.7% DSD coverage and 5.3% conventional care not eligible for DSD.	
35	FTRs, MMD6, AGs, CADP & HP	Equal distribution of all eligible clients between fast track refills, 6MMD, adherence groups, community ART distribution points and health posts
Scenario 36-42: Age-specific scenarios - paired all possible combinations. Clients distribution: 94.7% DSD coverage (7.1% scholar/adolescent model & 92.9% in each of the DSD model) and 5.3% conventional care not eligible for DSD.		
36	Scholar/adolescent model & FTRs	Enrolling all eligible clients aged ≤24 years in scholar model and clients aged ≥25 years in fast tract refills
37	Scholar/adolescent model & 6MMD	Enrolling all eligible clients aged ≤24 years in scholar model and clients aged ≥25 years in 6MMD
38	Scholar/adolescent model & AGs	Enrolling all eligible clients aged ≤24 years in scholar model and clients aged ≥25 years in adherence groups
39	Scholar/adolescent model & CADP	Enrolling all eligible clients aged ≤24 years in scholar model and all clients aged ≥25 years in community ART distribution points
40	Scholar/adolescent model & HP	Enrolling all eligible clients aged ≤24 years in scholar model and clients aged ≥25 years in health posts

Scenario number	Scenario name	Descriptions/DSD mix and distribution of ART clients
41	Scholar/adolescent model & ECH	Enrolling all eligible clients aged ≤24 years in scholar model and clients aged ≥25 years in extended clinic hours
42	Scholar/adolescent model & HAD	Enrolling all eligible clients aged ≤24 years in scholar model and eligible clients aged ≥25 years in Home ART delivery
Scenario 43-47: scenarios enrolling all eligible clients in a mix of DSD model with age restrictions and models without age restrictions, distributing clients equally across- paired all possible combinations. Clients distribution: 94.7% DSD coverage (3.6% scholar/adolescent model & 96.4% in each DSD model) and 5.3% conventional care not eligible for DSD.		
43	Scholar/adolescent model & fast track refills	Equal distribution of clients aged ≤24 years between scholar/adolescent model and fast track refills and enrolling eligible clients aged ≥25 years in fast track refills
44	Scholar/adolescent model & 6MMD	Equal distribution of clients aged ≤24 years between scholar/adolescent model and fast track refills and enrolling eligible clients aged ≥25 years in 6MMD
45	Scholar/adolescent model & AGs	Equal distribution of clients aged ≤24 years between scholar/adolescent model and fast track refills and enrolling eligible clients aged ≥25 years in adherence groups
46	Scholar/adolescent model & CADP	Equal distribution of clients aged ≤24 years between scholar/adolescent model and fast track refills and enrolling eligible clients aged ≥25 years in community ART distribution points
47	Scholar/adolescent model & HP	Equal distribution of clients aged ≤24 years between scholar/adolescent model and fast track refills and enrolling eligible clients aged ≥25 years in health posts
Scenario 48-57: Age-specific scenarios - paired all possible combinations. Clients distribution: 94.7% DSD coverage (7.1% in each DSD models & 92.9% in either extended clinic hours and Home ART delivery) and 5.3% conventional care not eligible for DSD.		
48	FTRs & ECH	Enrolling all eligible clients aged ≤24 years in fast track refills and clients aged ≥25 years in extended clinic hours
49	AGs & ECH	Enrolling all eligible clients aged ≤24 years in adherence groups and clients aged ≥25 years in extended clinic hours
50	CADP & ECH	Enrolling all eligible clients aged ≤24 years in community ART distribution points and clients aged ≥25 years in extended clinic hours
51	HP & ECH	Enrolling all eligible clients aged ≤24 years in health posts and clients aged ≥25 years in extended clinic hours
52	6MMD & ECH	Enrolling all eligible clients aged ≤24 years in 6MMD and clients aged ≥25 years in extended clinic hours
53	FTRs & HAD	Enrolling all eligible clients aged ≤24 years in fast track refills and clients aged ≥25 years in home ART delivery
54	CADP & HAD	Enrolling all eligible clients aged ≤24 years in community ART distribution points and clients aged ≥25 years in home ART delivery
55	AGs & HAD	Enrolling all eligible clients aged ≤24 years in adherence groups and clients aged ≥25 years in home ART delivery
56	HP & HAD	Enrolling all eligible clients aged ≤24 years in health posts and clients aged ≥25 years in home ART delivery
57	6MMD & HAD	Enrolling all eligible clients aged ≤24 years in 6MMD and clients aged ≥25 years in home ART delivery
Scenario 58-87: Age-specific scenarios - paired all possible combinations. Clients distribution: 94.7% DSD coverage (7.1% of clients aged ≤24 in distributed equally in each of the two models & 92.9% of clients in either home ART delivery or extended clinic hours) and 5.3% conventional care not eligible for DSD.		
58	Scholar/adolescent model, FTRs & ECH	Equal distribution of client's eligible clients aged ≤24 years between scholar/adolescent model and fast track refills and clients aged ≥25 years in extended clinic hours

Scenario number	Scenario name	Descriptions/DSD mix and distribution of ART clients
59	Scholar/adolescent model, AGs & ECH	Equal distribution of clients aged ≤24 years between scholar/adolescent model and adherence groups and clients aged ≥25 years in extended clinic hours
60	Scholar/adolescent model, CADP & ECH	Equal distribution of clients aged ≤24 years between scholar/adolescent model and community ART distribution points and clients aged ≥25 years in extended clinic hours
61	Scholar/adolescent model, 6MMD & ECH	Equal distribution of clients aged ≤24 years between scholar/adolescent model and 6MMD and clients aged ≥25 years in extended clinic hours
62	Scholar/adolescent model, HP & ECH	Equal distribution of clients aged ≤24 years between scholar/adolescent model and health posts and clients aged ≥25 years in home ART delivery
63	FTRs, AGs & ECH	Equal distribution of clients aged ≤24 years between fast track refills and adherence groups and clients aged ≥25 years in extended clinic hours
64	FTRs, CADP & ECH	Equal distribution of clients aged ≤24 years between fast track refills and community adherence groups and clients aged ≥25 years in extended clinic hours
65	FTRs, 6MMD & ECH	Equal distribution of clients aged ≤24 years between fast track refills and 6MMD and clients aged ≥25 years in extended clinic hours
66	AGs, CADP & ECH	Equal distribution of clients aged ≤24 years between adherence groups and community adherence groups and clients aged ≥25 years in extended clinic hours
67	AGS, 6MMD & ECH	Equal distribution of clients aged ≤24 years between adherence groups and 6MMD and clients aged ≥25 years in extended clinic hours
68	CADP, 6MMD & ECH	Equal distribution of clients aged ≤24 years between community ART distribution points and 6MMD and clients aged ≥25 years in extended clinic hours
69	Scholar/adolescent model, HP & ECH	Equal distribution of clients aged ≤24 years between scholar/adolescent model and health posts and clients aged ≥25 years in extended clinic hours
70	FTRs, HP & ECH	Equal distribution of clients aged ≤24 years between scholar/adolescent model and health posts and clients aged ≥25 years in extended clinic hours
71	AGs, HP & ECH	Equal distribution of clients aged ≤24 years between adherence groups and health posts and clients aged ≥25 years in extended clinic hours
72	CADP, HP & ECH	Equal distribution of clients aged ≤24 years between community adherence groups and health posts and clients aged ≥25 years in extended clinic hours
73	6MMD, HP & ECH	Equal distribution of clients aged ≤24 years between 6MMD and health posts and clients aged ≥25 years in extended clinic hours
73	Scholar/adolescent model, FTRs & HAD	Equal distribution of clients aged ≤24 years between scholar/adolescent model and fast track refills and clients aged ≥25 years in home ART delivery
74	Scholar/adolescent model, AGS & HAD	Equal distribution of clients aged ≤24 years between scholar/adolescent model and adherence groups and clients aged ≥25 years in home ART delivery
75	Scholar/adolescent model, CADP & HAD	Equal distribution of clients aged ≤24 years between scholar/adolescent model and community ART distribution points and clients aged ≥25 years in home ART delivery
76	Scholar/adolescent model, 6MMD & HAD	Equal distribution of clients aged ≤24 years between scholar/adolescent model and 6MMD and clients aged ≥25 years in home ART delivery
77	FTRs, AGs & HAD	Equal distribution of clients aged ≤24 years between fast track refills and adherence groups and clients aged ≥25 years in home ART delivery
78	FTRs, CADP & HAD	Equal distribution of clients aged ≤24 years between fast track refills and community ART distribution points and clients aged ≥25 years in home ART delivery
79	FTRs, 6MMD & HAD	Equal distribution of clients aged ≤24 years between fast track refills and c and clients aged ≥25 years in home ART delivery

Scenario number	Scenario name	Descriptions/DSD mix and distribution of ART clients
80	AGs, CADP & HAD	Equal distribution of clients aged ≤24 years between adherence groups and community ART distribution points and clients aged ≥25 years in home ART delivery
81	AGs, 6MMD & HAD	Equal distribution of clients aged ≤24 years between adherence groups and 6MMD and clients aged ≥25 years in home ART delivery
82	CADP, 6MMD & HAD	Equal distribution of clients aged ≤24 years between community ART distribution points and 6MMD and clients aged ≥25 years in home ART delivery
83	Scholar/adolescent model, HP & HAD	Equal distribution of clients aged ≤24 years between scholar/adolescent model and health posts and clients aged ≥25 years in home ART delivery
84	FTRs, HP & HAD	Equal distribution of clients aged ≤24 years between fast track refills and health posts and clients aged ≥25 years in home ART delivery
85	AGs, HP& HAD	Equal distribution of clients aged ≤24 years between fast track refills and health posts and clients aged ≥25 years in home ART delivery
86	CADP, HP & HAD	Equal distribution of clients aged ≤24 years between community ART distribution points and health posts and clients aged ≥25 years in home ART delivery
87	6MMD, HP & HAD	Equal distribution of clients aged ≤24 years between 6MMD and health posts and clients aged ≥25 years in home ART delivery
Scenario 88-108: Age-specific scenarios - paired all possible combinations. Clients distribution: 94.7% DSD coverage (7.1% scholar/adolescent model & 92.9% each of the two models) and 5.3% conventional care not eligible for DSD.		
88	Scholar/adolescent model, FTRs & AGs	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in fast track refills and adherence groups.
89	Scholar/adolescent model, FTRs & CADP	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in fast track refills and community ART distribution points.
90	Scholar/adolescent model, FTRs & 6MMD	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in fast track refills and 6MMD.
91	Scholar/adolescent model, FTRs & HP	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in fast track refills and health posts.
92	Scholar/adolescent model, FTRs & HAD	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in fast track refills and home ART delivery.
93	Scholar/adolescent model, AGs & CADP	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in adherence groups and community ART distribution points.
94	Scholar/adolescent model, AGs & 6MMD	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in adherence groups and 6MMD.
95	Scholar/adolescent model, AGs & HP	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in adherence groups and health posts.
96	Scholar/adolescent model, AGs & HAD	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in community ART distribution points and home ART delivery.
97	Scholar/adolescent model, CADP & 6MMD	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in community ART distribution points and 6MMD.
98	Scholar/adolescent model, CADP & HP	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in community ART distribution points and health posts.
99	Scholar/adolescent model, CADP & HAD	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in community ART distribution points and home ART delivery.
100	Scholar/adolescent model, 6MMD & HP	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in 6MMD and health posts.
101	Scholar/adolescent model, 6MMD & HAD	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in 6MMD and home ART delivery.

Scenario number	Scenario name	Descriptions/DSD mix and distribution of ART clients
102	Scholar/adolescent model, HP & HAD	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in health posts and home ART delivery.
103	Scholar/adolescent model, FTRs & ECH	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in fast track refills and extended clinic hours.
104	Scholar/adolescent model, AGs & ECH	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in adherence groups and extended clinic hours.
105	Scholar/adolescent model, CADP & ECH	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in community ART distribution points and extended clinic hours.
106	Scholar/adolescent model, 6MMD & ECH	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in 6MMD and extended clinic hours.
107	Scholar/adolescent model, HP & ECH	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in health posts and extended clinic hours.
108	Scholar/adolescent model, HAD & ECH	Clients aged ≤24 years in scholar/adolescent and equal distribution of clients aged ≥25 years in home ART delivery and extended clinic hours.
Scenario 109-118: Settings-specific scenarios - paired all possible combinations. Clients distribution: 94.7% DSD coverage and 5.3% conventional care not eligible for DSD (30.9% mobile ART delivery & 69.1% in each of DSD models)		
109	MAD & FTRs	Equal distribution of clients in rural area between mobile ART delivery and fast track refills and clients in urban areas only in fast track refills.
110	MAD & MMD6	Equal distribution of clients in rural area between mobile ART delivery and 6MMD and clients in urban areas only in 6MMD.
111	MAD & AGs	Equal distribution of clients in rural area between mobile ART delivery and adherence groups and clients in urban areas only in adherence groups.
112	MAD & CADP	Equal distribution of clients in rural area between mobile ART delivery and community ART distribution points and clients in urban areas only in community ART distribution points.
113	MAD & HP	Equal distribution of clients in rural area between mobile ART delivery and health posts and clients in urban areas only in health posts.
114	MAD & FTRs	Enrolling all eligible clients in rural areas in mobile ART delivery and clients in urban areas in fast track refills.
115	MAD & 6MMD	Enrolling all eligible clients in rural areas in mobile ART delivery and clients in urban areas in 6MMD.
116	MAD & AGs	Enrolling all eligible clients in rural areas in mobile ART delivery and clients in urban areas in adherence groups.
117	MAD & CADP	Enrolling all eligible clients in rural areas in mobile ART delivery and clients in urban areas in community ART distribution points.
118	MAD & HP	Enrolling all eligible clients in rural areas in mobile ART delivery and clients in urban areas in health posts.
Scenario 119-125: Settings and age specific scenarios - paired all possible combinations. Clients distribution: 94.7% DSD coverage and 5.3% conventional care not eligible for DSD (4.8% scholar/adolescent model, 64.3% each of the DSD model & 30.9% mobile ART delivery).		
119	Scholar/adolescent model, MAD & FTRs	Enrolling all eligible clients aged ≤24 in urban areas in scholar/adolescent model and clients all clients in rural areas in mobile ART delivery and clients aged ≥25 years in urban settings in fast track refills.
120	Scholar/adolescent model, MAD & 6MMD	Enrolling all eligible clients aged ≤24 in urban areas in scholar/adolescent model and clients all clients in rural areas in mobile ART delivery and clients aged ≥25 years in urban settings in 6MMD.
121	Scholar/adolescent model, MAD & AGs	Enrolling all eligible clients aged ≤24 in urban areas in scholar/adolescent model and clients all clients in rural areas in mobile ART delivery and clients aged ≥25 years in urban settings in adherence groups.

Scenario number	Scenario name	Descriptions/DSD mix and distribution of ART clients
122	Scholar/adolescent model, MAD & CADP	Enrolling all eligible clients aged ≤24 in urban areas in scholar/adolescent model and clients all clients in rural areas in mobile ART delivery and clients aged ≥25 years in urban settings in community ART distribution points.
123	Scholar/adolescent model, MAD & HP	Enrolling all eligible clients aged ≤24 in urban areas in scholar/adolescent model and clients all clients in rural areas in mobile ART delivery and clients aged ≥25 years in urban settings in health posts.
124	Scholar/adolescent model, MAD & ECH	Enrolling all eligible clients aged ≤24 in urban areas in scholar/adolescent model and clients all clients in rural areas in mobile ART delivery and clients aged ≥25 years in urban settings in extended clinic hours.
125	Scholar/adolescent model, MAD & HAD	Enrolling all eligible clients aged ≤24 in urban areas in scholar/adolescent model and clients all clients in rural areas in mobile ART delivery and clients aged ≥25 years in urban settings in Home ART delivery.

3.4. Extended results

3.5. Introduction

The section provides a summary of the results of the cost-effectiveness analysis of all scenario analysed.

3.6. Results

The results for all the scenarios analysed are presented in Table S5.

3.6.1. Cost-effectiveness analysis of all scenarios

Table S5. Cost-effectiveness analysis of all scenarios

Scenario	Scenario name	Total number retained	Total number suppressed	Total Provider costs	Total cost to Clients	ICER
Base case	Current distribution	817,948	770,086	$84,332,234	$4,145,400	Strongly dominated
1	Scholar/adolescent model-only	798,346	736,820	$87,280,581	$5,581,838	Strongly dominated
2	MAD-only	813,319	744,752	$93,139,757	$4,743,071	Strongly dominated
3	HAD-only	837,820	792,967	$109,110,439	$5,050,269	Strongly dominated
4	ECH-only	802,451	774,257	$87,728,203	$2,891,995	Strongly dominated
5	FTRs-only	840,869	804,632	$89,388,584	$5,398,622	$482
6	6MMD-only	827,415	782,545	$83,095,136	$3,455,290	Cost-saving (*compared to base case)*
7	CADP-only	838,325	798,779	$89,350,068	$5,354,108	Strongly dominated
8	HP-only	813,234	772,556	$87,524,461	$5,195,471	Strongly dominated
9	AGs-only	835,581	800,878	$87,577,961	$10,056,934	$245
10	FTRs & 6MMD	834,142	793,588	$86,241,860	$4,426,956	Weakly dominated
11	FTRs & AGs	838,225	802,755	$88,483,273	$7,727,778	$482
12	FTRs & CADP	839,597	801,705	$89,369,326	$5,376,365	Strongly dominated
13	FTRs & HP	827,052	788,594	$88,456,522	$5,297,046	Strongly dominated
14	6MMD & AGs	831,498	791,712	$85,336,549	$6,756,112	$245
15	6MMD & CADP	832,870	790,662	$86,222,602	$4,404,699	Strongly dominated
16	6MMD & HP	820,325	777,551	$85,309,798	$4,325,380	Strongly dominated
17	AGs & CADP	836,953	799,829	$88,464,015	$7,705,521	Strongly dominated
18	AGs & HP	824,408	786,717	$87,551,211	$7,626,202	Strongly dominated
19	CADP & HP	825,779	785,668	$88,437,264	$5,274,789	Strongly dominated
20	FTRs, 6MMD & AGs	834,622	796,018	$86,687,227	$6,303,615	Weakly dominated

Scenario	Scenario name	Total number retained	Total number suppressed	Total Provider costs	Total cost to Clients	ICER
21	FTRs, 6MMD & CADP	835,536	795,319	$87,277,929	$4,736,006	Strongly dominated
22	FTRs, 6MMD & HP	827,173	786,578	$86,669,394	$4,683,127	Strongly dominated
23	FTRs, AGs & CADP	838,258	801,430	$88,772,204	$6,936,554	Strongly dominated
24	FTR, AGs & HP	829,895	792,689	$88,163,669	$6,883,675	Strongly dominated
25	FTRs, CADP & HP	830,809	791,989	$88,754,371	$5,316,067	Strongly dominated
26	6MMD, AGs & CADP	833,774	794,068	$86,674,388	$6,288,777	Weakly dominated
27	6MMD, AGs & HP	825,410	785,327	$86,065,853	$6,235,898	Strongly dominated
28	6MMD, CADP & HP	826,325	784,627	$86,656,555	$4,668,290	Strongly dominated
29	AGs, CADP & HP	829,047	790,738	$88,150,830	$6,868,838	Strongly dominated
30	FTRs, MMD6, AGs & CADP	835,548	796,709	$87,352,937	$6,066,238	Weakly dominated
31	FTRs, MMD6, AGs & HP	829,275	790,153	$86,896,535	$6,026,579	Strongly dominated
32	FTRs, MMD6, CADP & HP	829,961	789,628	$87,339,562	$4,850,873	Strongly dominated
33	FTRs, AGs, CADP & HP	832,002	794,211	$88,460,268	$6,501,284	Strongly dominated
34	MMD6, AGs, CADP & HP	828,639	788,690	$86,886,906	$6,015,451	Strongly dominated
35	FTRs, MMD6, AGs, CADP & HP	831,085	791,878	$87,387,242	$5,892,085	Strongly dominated
36	Scholar/adolescent model & FTRs	844,148	801,920	$89,919,547	$5,709,962	Strongly dominated
37	Scholar/adolescent model & 6MMD	830,515	783,863	$83,947,939	$3,895,498	Weakly dominated
38	Scholar/adolescent model & AGs	835,293	794,629	$87,823,118	$10,000,680	Strongly dominated
39	Scholar/adolescent model & CADP	840,242	803,475	$89,720,660	$5,658,795	Strongly dominated
40	Scholar/adolescent model & HP	816,012	769,660	$87,926,246	$5,505,595	Strongly dominated
41	Scholar/adolescent model & ECH	808,952	782,397	$88,437,136	$3,211,782	Strongly dominated
42	Scholar/adolescent model & HAD	844,321	801,106	$109,819,372	$5,370,056	Strongly dominated
43	Scholar/adolescent model & fast track refills	842,508	803,276	$89,654,065	$5,554,292	Strongly dominated
44	Scholar/adolescent model & 6MMD	828,965	783,204	$83,521,537	$3,675,394	Weakly dominated
45	Scholar/adolescent model & AGs	835,437	797,753	$87,700,540	$10,028,807	Strongly dominated
46	Scholar/adolescent model & CADP	839,283	801,127	$89,535,364	$5,506,451	Strongly dominated
47	Scholar/adolescent model & HP	814,623	771,108	$87,725,354	$5,350,533	Strongly dominated
48	FTRs & ECH	805,673	785,109	$87,906,174	$2,900,441	Strongly dominated
49	AGs & ECH	809,240	788,646	$88,191,979	$3,268,035	Strongly dominated
50	CADP & ECH	807,034	777,701	$88,066,544	$2,907,095	Strongly dominated
51	HP & ECH	806,174	785,293	$88,035,351	$2,901,658	Strongly dominated
52	6MMD & ECH	805,851	781,080	$87,584,333	$2,771,574	Strongly dominated
53	FTRs & HAD	841,042	803,818	$109,288,410	$5,058,716	Strongly dominated
54	CADP & HAD	841,220	799,789	$108,966,569	$4,929,848	Strongly dominated
55	AGs & HAD	844,609	807,356	$109,574,215	$5,426,310	$7,409
56	HP & HAD	842,403	796,410	$109,448,780	$5,065,369	Strongly dominated
57	6MMD & HAD	841,543	804,002	$109,417,587	$5,059,933	Strongly dominated
58	Scholar/adolescent model, FTRs & ECH	807,313	783,753	$88,171,655	$3,056,111	Strongly dominated
59	Scholar/adolescent model, AGs & ECH	809,096	785,522	$88,314,558	$3,239,909	Strongly dominated
60	Scholar/adolescent model, CADP & ECH	807,993	780,049	$88,251,840	$3,059,438	Strongly dominated
61	Scholar/adolescent model, 6MMD & ECH	807,401	781,738	$88,010,735	$2,991,678	Strongly dominated
62	Scholar/adolescent model, HP & ECH	807,457	786,878	$88,049,076	$3,084,238	Strongly dominated
63	FTRs, AGs & ECH	806,354	781,405	$87,986,359	$2,903,768	Strongly dominated
64	FTRs, CADP & ECH	805,762	783,094	$87,745,254	$2,836,008	Strongly dominated
65	FTRs, 6MMD & ECH	808,137	783,174	$88,129,262	$3,087,565	Strongly dominated
66	AGs, CADP & ECH	807,546	784,863	$87,888,156	$3,019,805	Strongly dominated
67	AGS, 6MMD & ECH	806,443	779,390	$87,825,439	$2,839,334	Strongly dominated
68	CADP, 6MMD & ECH	807,563	783,845	$88,236,244	$3,056,720	Strongly dominated
69	Scholar/adolescent model, HP & ECH	805,924	785,201	$87,970,762	$2,901,050	Strongly dominated
70	FTRs, HP & ECH	807,707	786,970	$88,113,665	$3,084,847	Strongly dominated
71	AGs, HP & ECH	806,604	781,497	$88,050,947	$2,904,376	Strongly dominated
72	CADP, HP & ECH	806,013	783,186	$87,809,842	$2,836,616	Strongly dominated
73	6MMD, HP & ECH	842,681	802,462	$109,553,891	$5,214,386	Strongly dominated
74	Scholar/adolescent model, FTRs & HAD	844,465	804,231	$109,696,793	$5,398,183	Strongly dominated
75	Scholar/adolescent model, AGS & HAD	843,362	798,758	$109,634,076	$5,217,713	Strongly dominated
76	Scholar/adolescent model, CADP & HAD	842,770	800,448	$109,392,971	$5,149,952	Strongly dominated
77	Scholar/adolescent model, 6MMD & HAD	842,826	805,587	$109,431,312	$5,242,513	Weakly dominated

Scenario	Scenario name	Total number retained	Total number suppressed	Total Provider costs	Total cost to Clients	ICER
78	FTRs, AGs & HAD	841,722	800,114	$109,368,595	$5,062,042	Strongly dominated
79	FTRs, CADP & HAD	841,131	801,804	$109,127,489	$4,994,282	Strongly dominated
80	FTRs, 6MMD & HAD	843,506	801,883	$109,511,497	$5,245,840	Strongly dominated
81	AGs, CADP & HAD	842,915	803,573	$109,270,392	$5,178,079	Strongly dominated
82	AGs, 6MMD & HAD	841,811	798,100	$109,207,675	$4,997,609	Strongly dominated
83	CADP, 6MMD & HAD	842,932	802,554	$109,618,479	$5,214,995	Strongly dominated
84	Scholar/adolescent model, HP & HAD	841,293	803,910	$109,352,998	$5,059,324	Strongly dominated
85	FTRs, HP & HAD	843,076	805,679	$109,495,901	$5,243,121	Strongly dominated
86	AGs, HP& HAD	841,973	800,206	$109,433,183	$5,062,651	Strongly dominated
87	CADP, HP & HAD	841,382	801,896	$109,192,078	$4,994,891	Strongly dominated
88	Scholar/adolescent model, FTRs & AGs	839,720	798,274	$88,871,333	$7,855,321	Strongly dominated
89	Scholar/adolescent model, FTRs & CADP	842,195	802,698	$89,820,103	$5,684,379	Strongly dominated
90	Scholar/adolescent model, FTRs & 6MMD	837,332	792,891	$86,933,743	$4,802,730	Strongly dominated
91	Scholar/adolescent model, FTRs & HP	830,080	785,790	$88,922,896	$5,607,778	Strongly dominated
92	Scholar/adolescent model, FTRs & HAD	844,234	801,513	$99,869,459	$5,540,009	Strongly dominated
93	Scholar/adolescent model, AGs & CADP	837,767	799,052	$88,771,889	$7,829,738	Strongly dominated
94	Scholar/adolescent model, AGs & 6MMD	832,904	789,246	$85,885,529	$6,948,089	Strongly dominated
95	Scholar/adolescent model, AGs & HP	825,652	782,144	$87,874,682	$7,753,137	Strongly dominated
96	Scholar/adolescent model, AGs & HAD	839,807	797,868	$98,821,245	$7,685,368	Strongly dominated
97	Scholar/adolescent model, CADP & 6MMD	835,379	793,669	$86,834,300	$4,777,146	Strongly dominated
98	Scholar/adolescent model, CADP & HP	828,127	786,568	$88,823,453	$5,582,195	Strongly dominated
99	Scholar/adolescent model, CADP & HAD	842,281	802,291	$99,770,016	$5,514,426	Strongly dominated
100	Scholar/adolescent model, 6MMD & HP	823,264	776,761	$85,937,093	$4,700,546	Strongly dominated
101	Scholar/adolescent model, 6MMD & HAD	837,418	792,485	$96,883,656	$4,632,777	Strongly dominated
102	Scholar/adolescent model, HP & HAD	830,166	785,383	$98,872,809	$5,437,825	Strongly dominated
103	Scholar/adolescent model, FTRs & ECH	826,550	792,158	$89,178,341	$4,460,872	Strongly dominated
104	Scholar/adolescent model, AGs & ECH	822,122	788,513	$88,130,127	$6,606,231	Strongly dominated
105	Scholar/adolescent model, CADP & ECH	824,597	792,936	$89,078,898	$4,435,288	Strongly dominated
106	Scholar/adolescent model, 6MMD & ECH	819,734	783,130	$86,192,538	$3,553,640	Strongly dominated
107	Scholar/adolescent model, HP & ECH	812,482	776,029	$88,181,691	$4,358,688	Strongly dominated
108	Scholar/adolescent model, HAD & ECH	826,636	791,752	$99,128,254	$4,290,919	Strongly dominated
109	MAD & FTRs	844,409	802,197	$92,280,254	$5,120,643	Strongly dominated
110	MAD & MMD6	831,633	780,024	$86,822,887	$3,473,242	Strongly dominated
111	MAD & AGs	840,344	798,362	$90,792,565	$9,060,995	Strongly dominated
112	MAD & CADP	842,674	796,220	$92,291,788	$5,085,661	Strongly dominated
113	MAD & HP	818,973	769,095	$90,481,332	$4,935,811	Strongly dominated
114	MAD & FTRs	847,949	799,763	$95,171,925	$4,842,665	Strongly dominated
115	MAD & 6MMD	835,851	777,502	$90,550,639	$3,491,194	Strongly dominated
116	MAD & AGs	845,106	795,845	$94,007,169	$8,065,055	Strongly dominated
117	MAD & CADP	847,024	793,661	$95,233,508	$4,817,215	Strongly dominated
118	MAD & HP	824,713	765,634	$93,438,203	$4,676,150	Strongly dominated
119	Scholar/adolescent model, MAD & FTRs	849,742	796,324	$95,484,499	$5,048,018	Strongly dominated
120	Scholar/adolescent model, MAD & 6MMD	838,126	777,829	$91,140,416	$3,785,923	Strongly dominated
121	Scholar/adolescent model, MAD & AGs	845,007	790,668	$94,180,566	$8,028,637	Strongly dominated
122	Scholar/adolescent model, MAD & CADP	848,365	795,783	$95,487,386	$5,021,027	Strongly dominated
123	Scholar/adolescent model, MAD & HP	827,013	763,581	$93,754,323	$4,886,029	Strongly dominated
124	Scholar/adolescent model, MAD & ECH	826,467	781,074	$94,573,568	$3,325,743	Strongly dominated
125	Scholar/adolescent model, MAD & HAD	848,478	798,981	$109,046,436	$4,805,072	Strongly dominated

6MMD, six months dispensing; MAD, Mobile ART delivery, HAD, Home ART delivery, ECH, extended clinic hours, FTRs, fast track refills; CADP, community ART distribution points, HP, health posts, AGs, adherence groups

4. RECOMMENDATIONS

4.1. Introduction

This section outlines the recommendations for the implementation and scale-up of DSD models in Zambia and other sub-Saharan African countries. Drawing from the evidence presented in this research, which is supported by the existing and growing literature of DSD expansion and evaluations. We therefore recommend the adaptation to the current DSD policy framework, continuation of population-specific DSD models and considering the potential expansion of DSD models beyond HIV treatment.

4.2. Recommendations

4.2.1. Adaptation of current DSD policy framework

The findings presented in this research shows that compared to the current ART distribution of clients in Zambia and implementation of different DSD models, our modelled approach to DSD implementation may result in better health outcomes and minimise costs. We also show that the implementation and prioritisation of DSD models that improve health outcomes may bring the country closer to achieving UNAIDS HIV global 95-95-95 targets. In addition, the country may benefit from decongested facilities due to reduced frequency of clinic-based interactions with more clients enrolled in DSD models, particularly 6MMD, as a result of increased dispensing intervals. The current DSD framework is not explicit on the type of DSD models that should be prioritised for scale-up and implementation [13]. As indicated, it is often up to the implementing partners and facility managers to decide on which models to offer among a set of models outlined in the DSD framework [9,13].

In our analysis, six scenarios were on the cost-effectiveness frontier. While cost-saving, 6MMD also improved health outcomes, other scenarios improved retention and increased number of people virally suppressed on treatment but thus come at an additional cost to the health system. The model also shows that within sub-population groups, DSD models tailored by age groups may result in better outcomes. However, implementation of such scenarios is likely to depend on the availability of resources compared to current distribution. Within the current five-year DSD framework [13], we recommend the inclusion of a policy framework to encourage the prioritisation and rapid scale-up of the six scenarios presented in this report. We also recommend the use of a mathematical model to guide the future implementation and evaluation of DSD scale-up. ADAPT findings and methods presented here offer the Ministry of Health in Zambia and other countries in sub-Saharan Africa an opportunity to evaluate and potentially restructure their DSD programs in order to improve health

outcomes and save costs. The evaluations may be conducted on an annual basis, informed by routinely-collected data, and integrated or as part of strategic five-year plan for goal settings.

4.2.2. Continuation of population specific DSD models

The current DSD programme in Zambia and other sub-Saharan African countries includes a set of DSD models that are targeted to specific population groups (e.g. teens enrolled in scholar/adolescent model) [8,9,19]. The results presented here support the growing evidence that DSD models targeted to specific population groups are important in ensuring continuity of care and improved outcomes with the HIV cascade [19].

The one size-fits-all approach may not provide sustainable continuation of care for all DSD eligible clients. In our analysis, part of the models on the cost-effectiveness frontier includes population-specific models. These models are: 1) adherence groups (which includes adherence support discussions among all eligible clients), and 2) home-ART delivery models (which includes the distribution of ART to the homestead of clients aged ≥25 years). However, as presented in this report, these models come at an additional cost to the health system while improving health outcomes for clients. We recommend the use of such population-specific models to offer continued support to clients enrolled in such models. Furthermore, we recommend a task-shifting of less clinic duties such as leading adherence group meetings or completing DSD related administration duties to less specialised healthcare providers such as enrolled or staff nurses. This type of task-shifting may enable healthcare providers to spend their time and resources on providing HIV services to clients requiring more care, such as with clients showing poor treatment outcomes.

4.2.3. Potential expansion of DSD beyond HIV treatment

The findings of this analysis suggest positive impact of DSD models for HIV treatment on health outcomes. As DSD implementation expands, we recommend potential expansion of the DSD beyond HIV treatment. This can be done through the integration of HIV services with health services for conditions such as hypertension, diabetes or family planning. The integration of differentiated care been achieved elsewhere [38]. For example, the Chronic Central Medication Dispensing and Distribution (CCMDD) programme in South Africa that offers differentiated care for other chronic conditions such as hypertension or diabetes [10]. Given limited resources in Zambia and a high demand for health services [39]. We therefore recommend the implementation to follow a stepwise approach, integrating one or two chronic conditions at a time, with continuous evaluation to ensure the success of integration. Furthermore, we encourage the evaluation of acceptability and satisfaction of integrated services from the perspective of the provider and clients.

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6. APPENDICES

6.1. Plagiarism declaration

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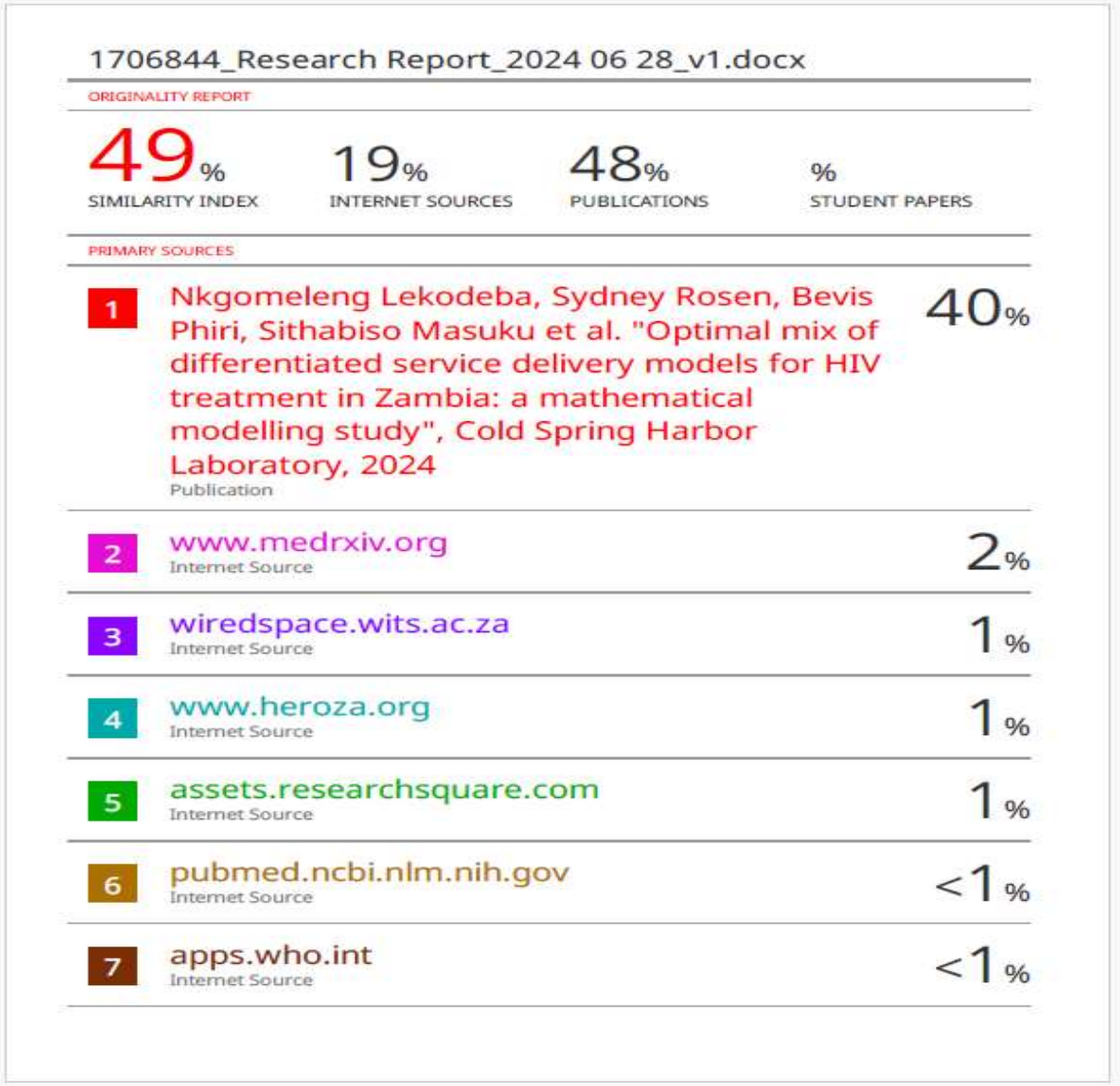
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1	Nkgomeleng Lekodeba, Sydney Rosen, Bevis Phiri, Sithabiso Masuku et al. "Optimal mix of differentiated service delivery models for HIV treatment in Zambia: a mathematical modelling study", Cold Spring Harbor Laboratory, 2024 Publication	40%
2	www.medrxiv.org Internet Source	2%
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We, supervisors and student acknowledge a high similarity index (49%) as a result of the submissible paper co-submission to the PLOS MEDICINE journal and MedRxiv as a preprint which occurred before the Turnitin submission. We also confirm that that we checked the Turnitin report and there is no plagiarism.

Signatures:

Prof. BE Nichols
Date: 30/10/2024

Dr. L Jamieson
Date: 30/10/2024

Mr. NA Lekodeba
Date: 30/10/2024

6.3. Ethics clearance certificate

Page 1 of 2

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research and Innovation)

TO: Mr NA Lekodeba
School of Public Health
Medical School
University

E-mail: 1706844@students.wits.ac.za

CC: Supervisor: Drs B Nichols and L Jamieson
Brooke.Nichols@finddx.org
and <HREC-Medical Research Office@wits.ac.za>

FROM: Mr Iain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: Iain.Burns@wits.ac.za

DATE: 20 November 2023

REF: R14/49

PROTOCOL NO: **M231093** (This is your ethics application reference number. Please quote it in all enquiries, oral or written, relating to this study.)

PROJECT TITLE: *Cost-effectiveness of the optimal mix of differentiated sevice delivery models for HIV care and treatment in Zambia: a mathematical modelling study*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to Government funding of the University.

MSWorks2000/Iain0007/Clearscan.wps

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R49 Mr NA Lekodeba

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M231093

NAME: (Principal and Co-Investigators)	Mr NA Lekodeba	**DEGREE:** MPH
DEPARTMENT:	School of Public Health Medical School University	
PROJECT TITLE:	*Cost-effectiveness of the optimal mix of differentiated sevice delivery models for HIV care and treatment in Zambia: a mathematical modelling study*	
DATE CONSIDERED:	Ad hoc	
DECISION:	Approved unconditionally	
CONDITIONS:	Sub-study under M19/04/53	
NOTE:	If contact information regarding student study participants is required, please contact the Registrar's office - <Nicoleen.Potgieter@wits.ac.za>	
SUPERVISOR:	Drs B Nichols and L Jamieson	
APPROVED BY:	Professor P Ruff, Chairperson, HREC (Medical)	
DATE OF APPROVAL:	20 November 2023	**EXPIRY DATE:** 19 November 2028

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report** in the format available at https://wits.ac.za/research/researcher-support/research-ethics/ethics-committees/. This report is due annually, for the duration of the Clearance Certificate, beginning on the first anniversary of Date of Approval above. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator

23 November 2023
Date

6.4. Journal guidelines for authors

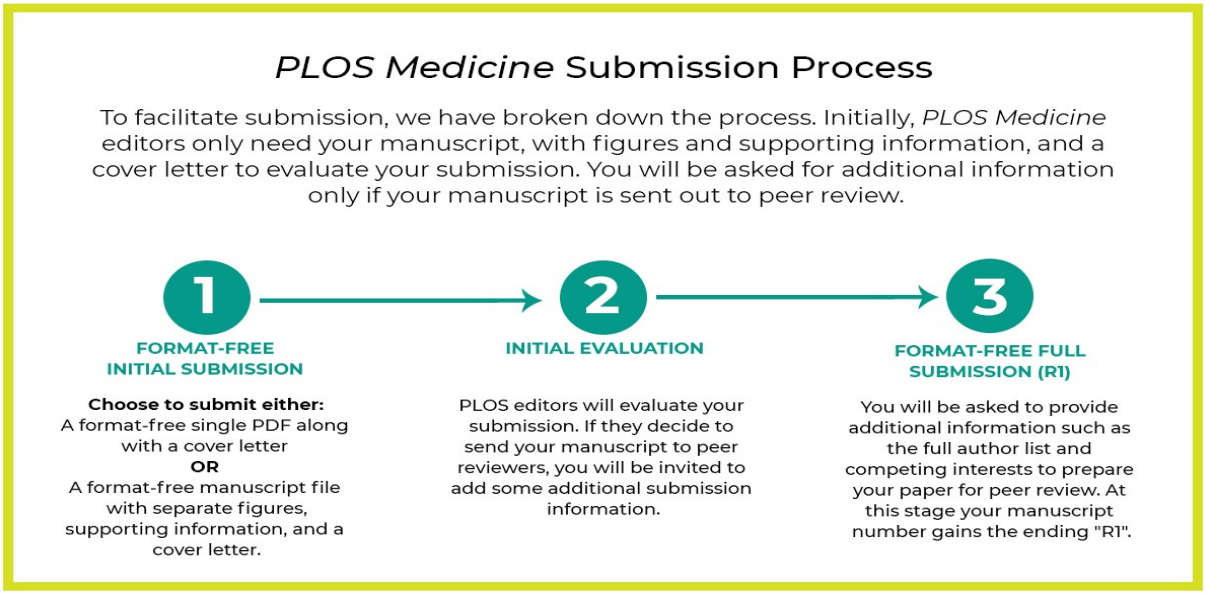
PLOS MEDICINE author submission guideline

About the Journal

PLOS Medicine publishes original research articles of outstanding medical importance. We will consider manuscripts of any length; we encourage the submission of both substantial full-length bodies of work and shorter manuscripts that report novel findings that might be based on a more limited range of experiments.

The writing style should be concise and accessible, avoiding jargon so that the paper is understandable for readers outside a specialty or those whose first language is not English. Editors will make suggestions for how to achieve this, as well as suggestions for deletions or additions that could be made to the article to strengthen the argument. Our aim is to make the editorial process rigorous and consistent, but not intrusive or overbearing. Authors are encouraged to use their own voice and to decide how best to present their ideas, results, and conclusions.

About the Submission Process



Format-free initial submission

PLOS Medicine uses the initial submission process, allowing authors to quickly submit to the journal and obtain rapid feedback from the editors. If the editors decide that the work is suitable for peer review, authors will be asked to provide a full submission with additional information.

Qualifying article types	This process applies to all article types submitted to *PLOS Medicine*.
Submission elements	Corresponding author information Manuscript (with title page containing full author list) Cover letter Figures

	Supporting information
Submission format	A single PDF file containing manuscript, figues and supporting information files, with a separate cover letter (recommended for ease of initial submission) OR If preferred, upload figure files alongside a PDF or Word manuscript file, with a separate cover letter

Creating an initial submission is the most efficient way to obtain feedback from the journal. Authors who email with an inquiry will be asked to submit the manuscript as an initial submission.

Format-free full submission

If you receive an initial decision from the journal committing to peer review, you will be asked to complete a full submission with additional information including: Full author list and author details, Details of the availability of data generated in the study, Details of any ethical approvals, Details of clinical trials registration, if applicable

Style and Format

File format	Submit the manuscript file in DOC, DOCX, RTF, or PDF format. Your file should not be locked or protected. If you have written your manuscript in LaTeX, please submit as a PDF. Read the LaTeX guidelines.
Length	Manuscripts can be any length. There are no restrictions on word count, number of figures, or amount of supporting information. We encourage you to present and discuss your findings concisely.
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Headings	Limit manuscript sections and sub-sections to 3 heading levels. Make sure heading levels are clearly indicated in the manuscript text.
Layout and spacing	Manuscript text should be double-spaced. Do not format text in multiple columns.
Page and line numbers	Include page numbers and line numbers in the manuscript file. Use continuous line numbers (do not restart the numbering on each page).
Footnotes	Footnotes are not permitted. If your manuscript contains footnotes, move the information into the main text or the reference list, depending on the content.
Language	Manuscripts must be submitted in English. You may submit translations of the manuscript or abstract as supporting information. Read the supporting information guidelines.
Abbreviations	Define abbreviations upon first appearance in the text. Do not use non-standard abbreviations unless they appear at least three times in the text. List all non-standard abbreviations (with definitions) in alphabetical order in a separate section at the beginning of the manuscript. Keep abbreviations to a minimum.
Reference style	PLOS uses “Vancouver” style, as outlined in the ICMJE sample references. See reference formatting examples and additional instructions below.

<table>
<tr><td>Equations</td><td>We recommend using MathType for display and inline equations, as it will provide the most reliable outcome. If this is not possible, Equation Editor or Microsoft's Insert→Equation function is acceptable. Please do not embed equations as images.
Avoid using MathType, Equation Editor, or the Insert→Equation function to insert single variables (e.g., “$a^2 + b^2 = c^2$”), Greek or other symbols (e.g., β, Δ, or ′ [prime]), or mathematical operators (e.g., x, ≥, or ±) in running text. Wherever possible, insert single symbols as normal text with the correct Unicode (hex) values.
Do not use MathType, Equation Editor, or the Insert→Equation function for only a portion of an equation. Rather, ensure that the entire equation is included. Equations should not contain a mix of different equation tools. Avoid “hybrid” inline or display equations, in which part is text and part is MathType, or part is MathType and part is Equation Editor.</td></tr>
<tr><td>Nomenclature</td><td>Use correct and established nomenclature wherever possible.<table>
<tr><td>Units of measurement</td><td>Use SI units. If you do not use these exclusively, provide the SI value in parentheses after each value. Read more about SI units.</td></tr>
<tr><td>Drugs</td><td>Provide the Recommended International Non-Proprietary Name (rINN).</td></tr>
<tr><td>Species names</td><td>Write in italics (e.g., Homo sapiens). Write out in full the genus and species, both in the title of the manuscript and at the first mention of an organism in a paper. After first mention, the first letter of the genus name followed by the full species name may be used (e.g., H. sapiens).</td></tr>
<tr><td>Genes, mutations, genotypes, and alleles</td><td>Write in italics. Use the recommended name by consulting the appropriate genetic nomenclature database (e.g., HGNC for human genes; we strongly recommend using this tool to check against previously approved names). It is sometimes advisable to indicate the synonyms for the gene the first time it appears in the text. Gene prefixes such as those used for oncogenes or cellular localization should be shown in roman typeface (e.g., v-fes, c-MYC).</td></tr>
<tr><td>Allergens</td><td>The systematic allergen nomenclature of the World Health Organization/International Union of Immunological Societies (WHO/IUIS) Allergen Nomenclature Sub-committee should be used for manuscripts that include the description or use of allergenic proteins. For manuscripts describing new allergens, the systematic name of the allergen should be approved by the WHO/IUIS Allergen Nomenclature Sub-committee prior to manuscript publication. Examples of the systematic allergen nomenclature can be found at the WHO/IUIS Allergen Nomenclature site.</td></tr>
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</table>

Manuscript Organization

Most manuscripts should be organized as follows. Instructions for each element appear below.

Title

Authors

Affiliations

Abstract

Introduction

Methods (or Methods and Materials)

Results

Discussion

Acknowledgments

References

Supporting information captions

Other elements

Upon revision, figure files should be uploaded separately from the manuscript, and each figure caption should be inserted in read order after the first paragraph where the figure is cited. Read more information about our figure requirements during each stage of editorial review. Tables are inserted immediately after the first paragraph in which they are cited.

Supporting information files are uploaded separately.

Parts of a Submission

Title

Include a full title and a short title for the manuscript.

Title	Length	Guidelines	Examples
Full title	200 characters	Specific, descriptive, concise, and comprehensible to readers outside the field	Impact of cigarette smoke exposure on innate immunity: A *Caenorhabditis elegans* model Solar drinking water disinfection (SODIS) to reduce childhood diarrhoea in rural Bolivia: A cluster-randomized, controlled trial
Short title	70 characters	State the topic of the study	Cigarette smoke exposure and innate immunity SODIS and childhood diarrhoea

Titles should be written in sentence case (only the first word of the text, proper nouns, and genus names are capitalized). Avoid specialist abbreviations if possible. For clinical trials, systematic reviews, or meta-analyses, the subtitle should include the study design.

Author list

Authorship requirements

All authors must meet the criteria for authorship as outlined in the authorship policy. Those who contributed to the work but do not meet the criteria for authorship can be mentioned in the Acknowledgments. Read more about Acknowledgments. The corresponding author must provide an ORCID iD at the time of submission by entering it in the user profile in the submission system. Read more about ORCID.

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During initial submission, enter author names on the title page of the manuscript. If your manuscript is selected for peer review, you will also add author details to the submission system. On the title page, write author names in the following order:

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Middle name (or initials, if used)

Last name (surname, family name)

Each author on the list must have an affiliation. The affiliation includes department, university, or organizational affiliation and its location, including city, state/province (if applicable), and country. Authors have the option to include a current address in addition to the address of their affiliation at the time of the study. The current address should be listed in the byline and clearly labeled "current address." At a minimum, the address must include the author's current institution, city, and country.

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Contributions will be published with the final article, and they should accurately reflect contributions to the work. The submitting author is responsible for completing this information at full submission, and we expect that all authors will have reviewed, discussed, and agreed to their individual contributions ahead of this time. All authors will be contacted via email upon Full Submission to ensure that they are aware of and approve the submission of the manuscript, its content, authorship, and order of authorship. Articles will not be published unless all authors have provided their assent to publication.

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Upload a cover letter as a separate file in the online system. The cover letter should address the following questions: Why is this manuscript suitable for publication in *PLOS Medicine*?

Why will your study inspire researchers or clinicians, and how will it improve patient care or public health, or drive the understanding of disease forward?

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The title, authors, and affiliations should all be included on a title page as the first page of the manuscript file.

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The Abstract comes after the title page in the manuscript file. The abstract text is also entered in a separate field in the submission system. The research article Abstract is divided into the following three sections: Background, Methods and Findings, and Conclusions. It should contain all the following elements (items in square brackets are needed only for some study types).

PLOS Medicine prefers abstract submissions not exceed 300 words, with a maximum of 500 words allowed.

Background

This section should clearly describe the rationale for the study. It should end with a statement of the specific study hypothesis and/or study objectives.

Methods and Findings

Describe the study participants or what was studied (e.g., patient population, cell lines; be as specific as possible, including numbers of individuals studied). Describe the study design, intervention if applicable, main methods used, primary outcome measure(s), and length of follow up if applicable. [If appropriate, include how many participants were assessed out of those enrolled. For survey research, include the response rate.]. [If critical to the understanding of the paper, describe how results were analyzed, i.e., which specific statistical tests were used.]. Describe the main outcomes and quantify the results using a measure of precision (e.g., 95% confidence interval). Describe any adverse events. Describe the main limitations of the study.

Conclusions

Provide a general interpretation of the results with any important recommendations for future research. [For a clinical trial, provide any trial identification number(s) and name(s) (e.g., trial registration number, protocol number or acronym).]

Introduction

The introduction should put the focus of the manuscript into a broader context. As you compose the Introduction, think of readers who are not experts in this field. Include a brief review of the key literature. If there are relevant controversies or disagreements in the field, they should be mentioned so that a non-expert reader can delve into these issues further. The Introduction should conclude with a brief statement of the overall aim of the experiments and a comment about whether that aim was achieved.

Methods

The Methods should provide enough detail for reproduction of the findings. Protocols for new methods should be included, but well-established methodological procedures may simply be referenced. A full description of the methods should be included in the manuscript itself rather than in a supplemental file.

Methods should also include a section with descriptions of any statistical methods used. The description should conform to the criteria outlined by the Uniform Requirements, as follows:

Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to judge its appropriateness for the study and to verify the reported results. When possible, quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals). Avoid relying solely on statistical hypothesis testing, such as P values, which fail to convey important information about effect size and precision of estimates. References for the design of the study and statistical methods should be to standard works when possible (with pages stated). Define statistical terms, abbreviations, and most symbols. Specify the statistical software package(s) and versions used. Distinguish prespecified from exploratory analyses, including subgroup analyses.

Submit detailed protocols for newer or less established methods. Well-established protocols may simply be referenced. Protocol documents for clinical trials, observational studies, and other non-laboratory investigations may be uploaded as supporting information. We recommend and encourage you to deposit laboratory protocols in protocols.io, where protocols can be assigned their own persistent digital object identifiers (DOIs). To include a link to a protocol in your article: Describe your step-by-step protocol on protocols.io. Select Get DOI to issue your protocol a persistent digital object identifier (DOI). Include the DOI link in the Methods section of your manuscript using the following format provided by protocols.io: http://dx.doi.org/10.17504/protocols.io. [PROTOCOL DOI]

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The Results section should include all primary and secondary outcome measures analyzed. The section may be divided into subsections, each with a concise subheading. Tables and figures central to the study should be included in the main paper. The Results section should be written in past tense. PLOS

journals require authors to make all data underlying the findings described in their manuscript fully available without restriction, with rare exception.

Large data sets, including raw data, may be deposited in an appropriate public repository. See our list of recommended repositories. For smaller data sets and certain data types, authors may provide their data within Supporting Information files accompanying the manuscript. Authors should take care to maximize the accessibility and reusability of the data by selecting a file format from which data can be efficiently extracted (for example, spreadsheets or flat files should be provided rather than PDFs when providing tabulated data). For more information on how best to provide data, read our policy on data availability. PLOS does not accept references to "data not shown."

As outlined in the Uniform Requirements: *Give numeric results not only as derivatives (for example, percentages) but also as the absolute numbers from which the derivatives were calculated, and specify the statistical significance attached to them, if any. Restrict tables and figures to those needed to explain the argument of the paper and to assess supporting data. Use graphs as an alternative to tables with many entries; do not duplicate data in graphs and tables. Avoid nontechnical uses of technical terms in statistics, such as "random" (which implies a randomizing device), "normal," "significant," "correlations," and "sample."*

Discussion

The Discussion should be concise and tightly argued. It should start with a brief summary of the main findings. It should include paragraphs on the generalizability, clinical relevance, strengths, and limitations of your study. You may wish to discuss the following points also: How do the conclusions affect the existing knowledge in the field? How can future research build on these observations and what are the key experiments that must be done?

Acknowledgments

Those who contributed to the work but do not meet our authorship criteria should be listed in the Acknowledgments with a description of the contribution. Authors are responsible for ensuring that anyone named in the Acknowledgments agrees to be named. PLOS journals publicly acknowledge the indispensable efforts of our editors and reviewers on an annual basis. To ensure equitable recognition and avoid any appearance of partiality, do not include editors or peer reviewers—named or unnamed—in the Acknowledgments. Do not include funding sources in the Acknowledgments or anywhere else in the manuscript file. Funding information should only be entered in the financial disclosure section of the submission system.

References

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Ensure that your reference list includes full and current bibliography details for every cited work at the time of your article's submission (and publication, if accepted). If cited work is corrected, retracted, or marked with an expression of concern before your article is published, and if you feel it is appropriate to cite the work even in light of the post-publication notice, include in your manuscript citations and full references for both the affected article and the post-publication notice. Email the journal office if you have questions. References are listed at the end of the manuscript and numbered in the order that they appear in the text. In the text, cite the reference number in square brackets (e.g., "We used the techniques developed by our colleagues [19] to analyze the data"). PLOS uses the numbered citation (citation-sequence) method and first six authors, et al. Do not include citations in abstracts. Make sure the parts of the manuscript are in the correct order *before* ordering the citations.

Formatting references

Because all references will be linked electronically as much as possible to the papers they cite, proper formatting of references is crucial. PLOS uses the reference style outlined by the International Committee of Medical Journal Editors (ICMJE), also referred to as the "Vancouver" style. Example formats are listed below. Additional examples are in the ICMJE sample references. A reference management tool, EndNote, offers a current style file that can assist you with the formatting of your references. If you have problems with any reference management program, please contact the source company's technical support. Journal name abbreviations should be those found in the National Center for Biotechnology Information (NCBI) databases.

Source	Format
Published articles	Hou WR, Hou YL, Wu GF, Song Y, Su XL, Sun B, et al. cDNA, genomic sequence cloning and overexpression of ribosomal protein gene L9 (rpL9) of the giant panda (Ailuropoda melanoleuca). Genet Mol Res. 2011;10: 1576-1588. Devaraju P, Gulati R, Antony PT, Mithun CB, Negi VS. Susceptibility to SLE in South Indian Tamils may be influenced by genetic selection pressure on TLR2 and TLR9 genes. Mol Immunol. 2014 Nov 22. pii: S0161-5890(14)00313-7. doi: 10.1016/j.molimm.2014.11.005. Note: A DOI number for the full-text article is acceptable as an alternative to or in addition to traditional volume and page numbers. When providing a DOI, adhere to the format in the example above with both the label and full DOI included at the end of the reference (doi: 10.1016/j.molimm.2014.11.005). Do not provide a shortened DOI or the URL.
Accepted, unpublished articles	Same as published articles, but substitute "Forthcoming" for page numbers or DOI.
Online articles	Huynen MMTE, Martens P, Hilderlink HBM. The health impacts of globalisation: a conceptual framework. Global Health. 2005;1: 14. Available from: http://www.globalizationandhealth.com/content/1/1/14
Books	Bates B. Bargaining for life: A social history of tuberculosis. 1st ed. Philadelphia: University of Pennsylvania Press; 1992.
Book chapters	Hansen B. New York City epidemics and history for the public. In: Harden VA, Risse GB, editors. AIDS and the historian. Bethesda: National Institutes of Health; 1991. pp. 21-28.
Deposited articles (preprints, e-prints, or arXiv)	Krick T, Shub DA, Verstraete N, Ferreiro DU, Alonso LG, Shub M, et al. Amino acid metabolism conflicts with protein diversity. arXiv:1403.3301v1 [Preprint]. 2014 [cited 2014 March 17]. Available from: https://128.84.21.199/abs/1403.3301v1 Kording KP, Mensh B. Ten simple rules for structuring papers. BioRxiv [Preprint]. 2016 bioRxiv 088278 [posted 2016 Nov 28; revised 2016 Dec 14; revised 2016 Dec

Source	Format
	15; cited 2017 Feb 9]: [12 p.]. Available from: https://www.biorxiv.org/content/10.1101/088278v5 doi: 10.1101/088278
Published media (print or online newspapers and magazine articles)	Fountain H. For Already Vulnerable Penguins, Study Finds Climate Change Is Another Danger. The New York Times. 2014 Jan 29 [Cited 2014 March 17]. Available from: http://www.nytimes.com/2014/01/30/science/earth/climate-change-taking-toll-on-penguins-study-finds.html
New media (blogs, web sites, or other written works)	Allen L. Announcing PLOS Blogs. 2010 Sep 1 [cited 17 March 2014]. In: PLOS Blogs [Internet]. San Francisco: PLOS 2006 - . [about 2 screens]. Available from: http://blogs.plos.org/plos/2010/09/announcing-plos-blogs/.
Masters' theses or doctoral dissertations	Wells A. Exploring the development of the independent, electronic, scholarly journal. M.Sc. Thesis, The University of Sheffield. 1999. Available from: http://cumincad.scix.net/cgi-bin/works/Show?2e09
Databases and repositories (Figshare, arXiv)	Roberts SB. QPX Genome Browser Feature Tracks; 2013 [cited 2013 Oct 5]. Database: figshare [Internet]. Available from: http://figshare.com/articles/QPX_Genome_Browser_Feature_Tracks/701214
Multimedia (videos, movies, or TV shows)	Hitchcock A, producer and director. Rear Window [Film]; 1954. Los Angeles: MGM.

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Example caption: S1 Text. Title is strongly recommended. Legend is optional.

In-text citations: We recommend that you cite supporting information in the manuscript text, but this is not a requirement. If you cite supporting information in the text, citations do not need to be in numerical order. Read the supporting information guidelines for more details about submitting supporting information and multimedia files.

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6.5. Signed letter stating the contribution of the candidate to the manuscript

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Sunnyside Office Park, Building C, First Floor
Princess of Wales Terrace
Parktown, Johannesburg
2193
30 October 2024

School of Public Health,
Faculty of Health Sciences
University of Witwatersrand

To whom it many concern

Subject: Contribution of the candidates to the manuscript

We are pleased to write this letter to state the candidate's contribution to the manuscript attached entitled "Optimal mix of differentiated service delivery models for HIV treatment in Zambia: a mathematical modelling study". Submitted by Nkgomeleng Lekodeba (student no: 1706844) to the School of Public Health, Faculty of Health Sciences, University of Witwatersrand in partial fulfilment of the requirements for the degree of Masters of Public Health in the field of Health Economics.

NL, SR, LJ, BP and BEN conceptualised the study. NL collected the cost data. LJ and BEN oversaw data collection. NL developed and parameterised the model. LJ and BEN oversaw the model development. NL did data analysis and had full access to the data. LJ and BEN oversaw data analysis. NL, SR, LJ and BEN verified underlying data assumptions. NL wrote the first draft. All authors contributed to reviewing and editing the manuscript for submission.

By signing this declaration, the supervisors and the student on behalf of the co-authors agree to the use of the manuscript by the student as part of his research report.

Yours sincerely,



Prof. BE Nichols



Dr. L Jamieson



Mr. NA Lekodeba