



RESEARCH ARTICLE

Do differentiated service delivery models for HIV treatment in sub-Saharan Africa save money? Synthesis of evidence from field studies conducted in sub-Saharan Africa in 2017-2019

[version 1; peer review: 1 approved, 1 approved with reservations]

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Abstract

Introduction: “Differentiated service delivery” (DSD) for antiretroviral therapy (ART) for HIV is rapidly being scaled up throughout sub-Saharan Africa, but only recently have data become available on the costs of DSD models to providers and patients. We synthesized recent studies of DSD model costs in five African countries.

Methods: The studies included cluster randomized trials in Lesotho, Malawi, Zambia, and Zimbabwe and observational studies in Uganda and Zambia. For 3-5 models per country, studies collected patient-level data on clinical outcomes and provider costs for 12 months, and some studies surveyed patients about costs they incurred. We compared costs of differentiated models to those of conventional care and identified drivers of cost differences. We also report patient costs of seeking care.

Results: The studies described 22 models, including facility-based conventional care. Of these, 13 were facility-based and 9 community-based models; 15 were individual and 7 group models. Average provider cost/patient/year ranged from \$100 in Zambia to \$187 in Zimbabwe, in both cases for facility-based conventional care. Conventional care was less expensive than any other model in the Zambia observational study, more expensive than any other model in Lesotho, Malawi, and Zimbabwe, and in the middle of the range in the Zambia trial and the observational study in Uganda. Models

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view

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incorporating 6-month dispensing were consistently less expensive to the provider per patient treated. Savings to patients were substantial for most models, with patients' costs roughly halved.

Conclusion: In five field studies of the costs of DSD models for HIV treatment, most models within each country had relatively similar costs, except for 6-month dispensing models, which were slightly less expensive. Most models provided substantial savings to patients. Research is needed to understand the effect of DSD models on the costs of ART programmes as a whole.

Keywords

Antiretroviral therapy; HIV; Africa; costs; differentiated service delivery

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Introduction

Throughout sub-Saharan Africa, governments are rapidly scaling up “differentiated service delivery” (DSD) for antiretroviral therapy (ART) for HIV. DSD tailors the location, frequency, and other characteristics of treatment delivery to specific patient populations, with the goal of making treatment both more patient-centric and more efficient for service providers¹. DSD is intended to improve the “conventional” model of service delivery, in which all ART patients received the same, resource-intensive, clinic-based care regardless of their conditions, constraints, or preferences. Examples of DSD models for ART delivery include medication pickup points at convenient locations in the community, multi-month dispensing of medications that minimize the frequency of required clinic visits, and adherence clubs that bring groups of patients together either at a healthcare facility or in the community for medication refills and social support.

Among other anticipated benefits, DSD models are expected to reduce the cost of service delivery per ART patient for providers and the cost of accessing ART for patients themselves². This expectation follows logically on the notion that DSD models are designed to be “less intensive” than conventional care, and therefore presumably utilize fewer resources per patient served³. Until very recently, however, few empirical data drawn from DSD models implemented in routine care settings have been available to compare the costs of differentiated service delivery to conventional, facility-based care⁴.

Between 2017 and 2019, we conducted or participated in five studies of DSD model costs and patient outcomes in sub-Saharan Africa, in Lesotho, Malawi, Uganda, Zambia, and Zimbabwe. All were sponsored by the U.S. Agency for International Development and the U.S. President’s Emergency Program for AIDS Relief (PEPFAR) under the EQUIP Health project. Clinical outcomes and costs of these studies have previously been reported^{5–11}. All utilized primary healthcare clinics and/or hospital outpatient clinics to implement and evaluate between three and six differentiated models of delivery of antiretroviral therapy for stable, adult patients. All estimated provider costs; several also estimated costs to recipients of treatment. Each reported, for each DSD model in the study, the proportion of patients achieving a primary outcome of retention in care 12 months after study enrollment, an average cost per patient enrolled, an average cost per patient retained or suppressed, and, for those that included patient costs, an average cost incurred by each patient per year of care. In this paper, we aggregate and synthesize these data to provide a larger picture of the resource utilization and costs of DSD models in the sub-Saharan region.

Methods

In each country, an analysis was conducted of the outcomes and costs of DSD models that were mandated in national guidelines and/or introduced by nongovernmental treatment partners in collaboration with local ministries of health. Three of the analyses were cluster-randomized trials; the

remaining two were observational cohort studies of routine care. One of the cluster-randomized trials was conducted in two countries and reported costs by country; we include each country separately here, giving us a total of six sets of country-level results for our analysis.

In [Table 1](#), we describe each of the study sites, designs, populations, and costing methods. The five studies utilized similar but not identical methods. Methods are described in detail in the previous reports for each study, cited above. Each analysis collected individual patient-level data on the clinical outcomes of patients enrolled in DSD models for at least 12 months and the costs of the resources used to treat the patients during that period. In each country, the analysis included conventional, clinic-based care as one of the study models. Most models enrolled only “stable” adult patients, typically ≥ 18 years old, with at least six months experience on ART and with evidence of a suppressed viral load, except where indicated in [Table 1](#). For all studies except that in Uganda, the period of observation corresponded with patients’ first 12 months enrolled in a DSD model; in Uganda, study participants had already participated in the models for a median of one year at study enrollment, and we report results for months 13–24 after study enrollment. We note that each of the papers included in this synthesis contains some stratification of results by patient and/or facility characteristics which we do not present here.

In addition to the average cost per patient enrolled, each study also reported the average cost per patient achieving a primary outcome of retention 12 months after study enrollment. Definitions of retention varied somewhat among the studies and are included in [Table 1](#).

For this synthesis, we collated provider cost results per patient for each model of care from each country, with resources and costs broken down into six categories: ARV medications, non-ARV medications, laboratory tests, facility visits, DSD-model interactions distinct from full facility visits, and infrastructure and fixed costs. Most of the studies included some but not all of these categories. DSD interactions included all meetings of providers and patients that occurred away from the clinic, group meetings of patients both at and away from clinics, and individual facility visits that were designed specifically for a differentiated model, such as a “fast track visit”. In some studies, costs for infrastructure and other fixed resources were allocated per visit and included in the estimated cost/visit, rather than as a separate category, and we note where this occurs.

We note major exclusions from cost/patient estimates for each study. We also compare observed, average numbers of clinic visits and DSD interactions completed by each patient with the numbers recommended in each model’s guidelines. Finally, we report patient costs per year in care, divided into out-of-pocket (cash) costs, such as transport, and opportunity costs, valued at the country’s minimum wage for the time required per healthcare system interaction.

Table 1. Studies included in the analysis.

| Country and sources | Study design | Population enrolled | Period of enrollment and follow up or observation | Definition of retention in care | Costs included | Costs excluded | Patient costs captured? |
|---------------------------------|--|---|--|---|---|--|-------------------------|
| Lesotho ^{6,11} | Prospective cluster randomized trial at 30 healthcare facilities | Adults on first line ART ≥6 months with suppressed viral load | Aug 2017- July 2019; first 12 months of model participation for each patient | Not having missed a scheduled clinic visit or DSD interaction for >90 consecutive days | ARVs, viral load tests, clinic visits and off-site DSD model interactions, infrastructure, transport equipment, transport | Non-ARV medications, other laboratory tests, above-site costs | Yes |
| Malawi (INTERVAL) ⁵ | Prospective cluster randomized trial at 15 healthcare facilities | Adults on first line ART ≥ 6 months with suppressed viral load | May 15, 2017-April 30, 2018; first 12 months of model participation for each patient | No period of >60 days without possession of ARVs, based on dates and quantities dispensed | ARVs, outpatient clinic visits that included ARV refills, and infrastructure | Laboratory tests, clinic visits that did not include an ARV refill, above-site costs | Yes |
| Uganda ⁸ | Observational cohort using retrospective, routinely collected medical record data from 20 healthcare facilities, many of which offered multiple models of care | Adults on first or second line ART; included new, non-suppressed, and advanced disease patients in some models | Jan 1, 2017-Dec 31, 2018; 24 months follow up for all patients (outcomes for months 13-24 reported here) | Not having missed a scheduled clinic visit or DSD interaction for >90 consecutive days; this study also reported viral suppression at 12 months | ARVs and other medications (with supply chain costs), laboratory tests, clinic visits and off-site DSD model interactions, infrastructure, equipment, transport, training, administration, above-site costs | | No |
| Zambia ¹⁷ | Observational cohort using retrospective, routinely collected medical record data from 20 healthcare facilities | Adults on first line ART ≥6 months with suppressed viral load (excluding mobile ART model); many model enrollees did not have a record of a suppressed viral load | Jan 1, 2015-Dec 31, 2017; first 12 months of model participation for each patient | Having a recorded clinic visit between 9 and 15 months after enrollment in the DSD model (all models required a minimum of one visit every 12 months) | ARVs and other medications, laboratory tests (except for mobile model), clinic visits and off-site DSD model interactions, infrastructure, transport | Above-site costs; lab costs excluded for mobile ART model | No |
| Zambia2 (INTERVAL) ⁵ | Prospective cluster randomized trial at 15 healthcare facilities | Adults on first line ART ≥ 6 months with suppressed viral load | May 15, 2017-April 30, 2018; first 12 months of model participation for each patient | No period of >60 days without possession of ARVs, based on dates and quantities dispensed | ARVs, outpatient clinic visits that included ARV refills, and infrastructure | Laboratory tests, clinic visits that did not include an ARV refill, above-site costs | Yes |
| Zimbabwe ^{9,10} | Prospective cluster randomized trial at 30 healthcare facilities | Adults on first line ART ≥6 months with suppressed viral load | Aug 2017-Feb 2018; first 12 months of model participation for each patient | Not having missed a scheduled clinic visit or DSD interaction for >90 consecutive days | ARVs, clinic visits and off-site DSD model interactions, viral load tests | Other laboratory tests, above-site costs | Yes |

No ethics review was required for this synthesis analysis, as all data used were previously published in the sources cited.

Results

Models and study populations

The five studies included patient outcomes and cost results for 22 models of care, including conventional models in each country. In [Table 2](#), we list the individual DSD models included in the studies in each country, the numbers of participants observed (sample sizes), and the proportion achieving the common outcome of retention in care at 12 months and compare the models based on their location of services, duration of dispensing, and group or individual approach. We note that, with the exception of Uganda and the conventional care models, all the models in the studies were designed and implemented by external parties—either nongovernmental organizations or researchers—and not by the healthcare systems themselves. In Uganda, in contrast, all models evaluated were part of the national DSD strategy.

Provider cost per patient

The average cost per patient included in the analysis and per patient retained at the 12-month endpoint, by country and model, is shown in [Table 3](#), with the breakdown into cost categories in [Table 4](#). We include the 95% confidence interval or standard deviation for each cost estimate as provided by the original publications.

If we assume that patients in Malawi had an average of one viral load test per year, adding roughly \$19 to the cost/patient year, then average costs/patient for the 12-month observation period ranged from a low of \$100/patient for conventional, facility-based care in Zambia to a high of \$187 for conventional, facility-based care in Zimbabwe. Importantly, we note that these values are not adjusted to reflect differences in purchasing power across countries. Each country pays different procurement prices for commodities such as medications and has different salary scales ([Table S1](#)). As a result, differences in cost/patient between countries are generally larger than the differences among models within countries, and comparisons between countries are less informative than comparisons within countries. We focus on cost differences between models within countries for the remainder of this paper, while also comparing resource utilization across countries where possible.

Conventional, facility-based care was less expensive than any other model in the observational study in Zambia, more expensive than any other model in the trials in Lesotho, Malawi, and Zimbabwe, and in the middle of the range for the trial in Zambia and the observational study in Uganda. Models incorporating six-month dispensing were consistently the least expensive per patient treated. In most of the countries, most models cost slightly less per patient than did conventional care. The exception to this is Zambia¹, where all the DSD models were estimated to cost more than SOC. Cost differences between the least and most expensive models within each country were smaller for the cluster-randomized trials (2–14%)

but more substantial for the two observational studies (15% in Uganda and 32% in Zambia). This was in part because the observational studies, which reflect use of DSD models in routine care, included varying numbers of patients on expensive second line therapy and/or in their first 6 months on ART, a period that tends to be resource-intensive; healthcare system interactions per patient also diverged from guidelines more in the observational studies than in the trials, as reported below.

Allocation of costs to cost categories

Reasons for cost differences between models in the same countries become apparent in [Table 4](#) and [Table 5](#), which provide a breakdown of average utilization of healthcare system interactions and of costs per patient by resource category.

In the cluster randomized trials (Lesotho, Malawi, Zambia², Zimbabwe), utilization of facility visits and DSD interactions was roughly consistent with guidelines for each DSD model, though even under trial conditions, patients were likely to interact with the healthcare system (either through facility visits or DSD interactions) more often than guidelines recommended. Most of the DSD models reduced the number of clinic visits/patient/year substantially compared to conventional care, from at least four in conventional care to three, two, or even one per year in the DSD models. Some of the models were designed to replace multiple clinic visits with an even larger number of DSD interactions; others reduced the overall burden of healthcare system interactions faced by most patients. In general, patient interaction with the healthcare system was minimized in six-month dispensing models and was relatively frequent in group models.

In the observational studies (Uganda and Zambia¹), average numbers of facility visits and DSD interactions diverged somewhat more widely from guideline recommendations, with some models experiencing more and others fewer healthcare system interactions than expected. This variation appears to reflect a combination of patients' choices, providers' preferences, and model design. Patients are always permitted to make more clinic visits than suggested by guidelines, based on individual needs; in some cases, extra interactions likely indicate shorter dispensing intervals, forcing patients to return more often for medication refills. Fewer interactions may suggest that patients are experiencing lapses in medication adherence or may, in contrast, reflect longer dispensing intervals. Six-month dispensing models are designed to require only 2 interactions per year, but all of the studies in [Table 4](#) showed an average of 2.5–3.0 interactions (combined facility visits + DSD interactions) per year, indicating that patients interacted with the healthcare system more often than model designers intended and making these models slightly more expensive than was likely anticipated.

The differences among models within countries for ARV costs per patient largely reflect loss to follow up—patients who did not receive 12 months of medications cost less and

Table 2. Description of models and sample included in each study.

| Model name | Description of model | Number of model participants in study | % retained at 12 months | Location | | Refill duration | | | Approach | |
|--|---|---------------------------------------|-------------------------|----------|-----------|-----------------|-------|-------|------------|-------|
| | | | | Facility | Community | 1-2 mos | 3 mos | 6 mos | Individual | Group |
| Lesotho | | | | | | | | | | |
| Facility enhanced conventional care ^{††} | Standard facility-based care with 4 visits/year and 3-month refills | 1,898 | 97.1% | ✓ | | | ✓ | | ✓ | |
| Community ART groups with 3-month refills (CAGs) | Group of 6-12 patients in same geographic area; groups meet 4 times/year in community, with 1 member collecting medications for all members from clinic once/quarter and 3-month refills | 1,558 | 96.5% | | ✓ | | ✓ | | | ✓ |
| Community distribution points with 6-month refills | 6-month dispensing alternating between clinic and community pickup point; 1 clinic visit + 1 pickup point visit/year | 1,880 | 94.7% | | ✓ | | | ✓ | ✓ | |
| Malawi | | | | | | | | | | |
| Facility conventional care | Standard of care; dispensing intervals varied with provider's discretion, availability of stock, etc. from 1-3 months, with 4-12 clinic visits/year. | 1,532 | 89.7% | ✓ | | | | | | |
| Facility dispensing with 3-month refills | Patients consistently received 3-month supplies of ARVs, with 4 clinic visits/year. No other changes to model of care. | 1,430 | 90.2% | ✓ | | | ✓ | | ✓ | |
| Facility dispensing with 6-month refills | Patients consistently received 6-month supplies of ARVs, with 2 clinic visits/year. No other changes to model of care. | 1,588 | 93.2% | ✓ | | | | ✓ | ✓ | |
| Uganda* | | | | | | | | | | |
| Facility conventional care | Standard of care referred to as "Facility-based individual model"; generally required 4 clinic visits/year with varying dispensing intervals. Note: This was considered a differentiated model for new and complicated patients but continued to function as conventional care for patients not in other models | 128 | 97% (88%*) | ✓ | | | ✓ | | ✓ | |
| Facility-based groups | Groups of patients requiring additional care or adherence support, with varying numbers of visits and dispensing intervals.** | 129 | 96% (94%) | ✓ | | | ✓ | | | ✓ |
| Fast-track drug refills | Accelerated medication pickup at facilities for stable first- and second-line patients; varying dispensing intervals. | 133 | 99% (90%) | ✓ | | | ✓ | ✓ | ✓ | |

| Model name | Description of model | Number of model participants in study | % retained at 12 months | Location | | Refill duration | | | Approach | |
|--|--|---------------------------------------|-------------------------|----------|-----------|-----------------|-------|-------|------------|-------|
| | | | | Facility | Community | 1-2 mos | 3 mos | 6 mos | Individual | Group |
| Client-led ART delivery (CAGs) | Groups of stable patients meet in the community, with 1 member collecting medications from the clinic for all members; varying frequency of meetings and dispensing intervals. | 131 | 98% (90%) | | ✓ | ✓ | ✓ | | | ✓ |
| Community drug distribution points | Stable patients pick up medications from a community location, including private pharmacies; dispensing intervals varied but most patients had 1 clinic visit and 6 medication pickup interactions per year. | 132 | 100% (92%) | | ✓ | ✓ | | | ✓ | |
| Zambia 1 (observational) | | | | | | | | | | |
| Facility conventional care | Standard of care; generally requires 4 full clinic visits/year with 1-3 month dispensing intervals. For study, selected a matched sample of DSD model-eligible patients not enrolled in DSD models. | 1,174 | 80.7% | ✓ | | ✓ | | | ✓ | |
| Community adherence groups (CAGs) | Group of approximately 6 patients meet monthly in the community; 1 member collects medications for all members. 2 full clinic visits/year. | 754 | 83.2% | | ✓ | ✓ | | | | ✓ |
| Urban adherence groups | Group of 20-30 patients meet as a group at clinic to receive services every 2-3 months. Urban areas only. | 193 | 94.8% | ✓ | | ✓ | | | | ✓ |
| Home ART delivery | Community health workers visit patients' homes to deliver medications and monitor treatment. 2 full clinic visits/year. Rural areas only. | 169 | 79.3% | | ✓ | ✓ | | | ✓ | |
| Mobile ART services† | Clinical team from district hospital visits rural health posts every 2 weeks to provide services. Requires 6 patient interactions/year. | 216 | 68.5% | | ✓ | ✓ | | | ✓ | |
| Zambia 2 | | | | | | | | | | |
| Facility conventional care | Standard of care; dispensing intervals vary with provider's discretion, availability of stock, etc. from 1-3 months, with 4-12 clinic visits/year. | 1,480 | 74.6% | ✓ | | ✓ | | | ✓ | |
| Facility dispensing with 3-month refills | Patients consistently receive 3-month supplies of ARVs, with 4 clinic visits/year. No other changes to model of care. | 1,296 | 82.3% | ✓ | | | ✓ | | ✓ | |

| Model name | Description of model | Number of model participants in study | % retained at 12 months | Location | | Refill duration | | | Approach | |
|---|--|---------------------------------------|-------------------------|----------|-----------|-----------------|-------|-------|------------|-------|
| | | | | Facility | Community | 1-2 mos | 3 mos | 6 mos | Individual | Group |
| Facility dispensing with 6-month refills | Patients consistently receive 6-month supplies of ARVs, with 2 clinic visits/year. No other changes to model of care. | 1,393 | 89.7% | ✓ | | | | ✓ | | ✓ |
| Zimbabwe | | | | | | | | | | |
| Facility enhanced conventional care ^{††} | Standard facility-based care with 4 clinic visits/year and 3-month refills | 1,919 | 93.0% | ✓ | | | ✓ | | | ✓ |
| Community ART groups with 3-month refills | Group of 6–12 patients in same geographic area; groups met 4 times/year in community, with 1 member collecting medications for all members from clinic once/quarter and 3-month refills; 1 annual clinical consultation/year on same day for entire group. | 1,335 | 94.8% | | | | | ✓ | | ✓ |
| Community ART groups with 6-month refills | Group of 6–12 patients in same geographic area; groups met 4 times/year in community, with 1 member collecting medications for all members from clinic once/quarter and 6-month refills; 1 annual clinical consultation/year on same day for entire group. | 1,546 | 95.5% | | | | | ✓ | | ✓ |

*Uganda results reported were from the second 12-month observation period (months 13–24 reported in published paper). Outcome in parentheses is viral suppression.

** Facility groups included in study were for pregnant and post-partum women only.

†Model includes newly-initiated patients; outcomes reflect high early attrition during period when patients are not eligible for all other DSD models.

††Conventional models in Lesotho and Zimbabwe were an enhanced version of standard of care in which providers were asked to dispense 3-month supplies of ARVs, rather than whatever duration they otherwise would have and patients received 4 clinical consultations per year, rather than 1.

Table 3. Average annual cost and cost per patient retained at 12 months, by country and model, in USD.

| Country and model | Mean annual cost per patient (SD or 95% CI where reported) | Mean annual cost per patient retained for 12 months (SD or 95% CI where reported) | % difference from SOC model (mean annual cost per patient) |
|--|--|---|--|
| Lesotho (2018 USD) | | | |
| Facility care with 3-month refills (SOC) | \$122.28 (23.91) | \$125.99 (24.64) | |
| Community ART groups with 3-month refills (CAG) | \$114.20 (23.03) | \$118.38 (23.87) | -6.6% |
| Community distribution points with 6-month refills | \$112.58 (21.44) | \$118.83 (22.63) | -7.9% |
| Malawi (2018 USD)* | | | |
| Facility conventional care (SOC) | \$86.50 (84.50-88.42)* | \$96.15 | |
| Facility dispensing with 3-month refills | \$86.00 (83.99-87.91)* | \$94.87 | -0.6% |
| Facility dispensing with 6-month refills | \$84.60 (82.62-86.54)* | \$90.76 | -2.2% |
| Uganda (2018 USD) | | | |
| Facility-based individual management (SOC) | \$152.49 (72.04) | \$173 | |
| Facility groups (pregnant/post-partum) | \$141.29 (33.70) | \$150 | -7.3% |
| Fast-track drug refills | \$166.48 (82.51) | \$185 | +9.2% |
| Client-led ART delivery (CAG) | \$150.07 (54.94) | \$167 | -1.5% |
| Community drug distribution points | \$146.42 (59.52) | \$159 | -3.9% |
| Zambia1 (2018 USD) | | | |
| Facility conventional care (SOC) | \$100.09 (61.59) | \$124 | |
| Community adherence groups (CAG) [‡] | \$116.25 (67.83) | \$140 | +16.1% |
| Urban adherence groups [‡] | \$147.01 (57.15) | \$155 | +46.9% |
| Mobile ART services* | \$122.46 (70.10) | \$179 | +22.3% |
| Home ART delivery [‡] | \$137.18 (57.02) | \$173 | +37.1% |
| Zambia2 (2018 USD)* | | | |
| Facility conventional care (SOC) | \$132.00 (130.43-134.35)* | \$177.00 | |
| Facility dispensing with 3-month refills | \$134.00 (132.09-136.02)* | \$162.87 | +1.5% |
| Facility dispensing with 6-month refills | \$128.00 (125.64-129.57)* | \$142.41 | -3.0% |
| Zimbabwe (2020 USD) | | | |
| Facility dispensing with 3-month refills (SOC) | \$187.04 (185.31-188.78) | \$195.06 (194.11-195.99) | |
| Community ART groups with 3-month refills | \$177.83 (176.19-179.46) | \$182.81 (181.80-183.83) | -6.3% |
| Community ART groups with 6-month refills | \$167.40 (165.44; 169.36) | \$172.81 (171.30; 174.31) | -11.4% |

*Excludes cost of laboratory tests, for which the authors did not have data; one viral load test per year, as called for by national guidelines, would add approximately \$19 to the mean annual cost per patient per year.

[‡]Table shows results from lower cost scenario reported by source publication.

brought the average down—and differing proportions of patients on second-line regimens, which are more expensive than first-line regimens. In most models, patients received <1 viral load test per year; the average quantity of viral load

Table 4. Average number of healthcare system interactions per patient per year, guideline and observed, and average ARV dispensing duration.

| Country and model | Clinic visits/year | | DSD interactions/year | |
|--|-------------------------|----------|-----------------------|----------|
| | Guidelines [†] | Observed | Guidelines | Observed |
| Lesotho | | | | |
| Facility care with 3-month refills (SOC) | 4 | 4.19 | 0 | 0.00 |
| Community ART groups with 3-month refills | 1 | 1.00* | 4 | 4.65 |
| Community distribution points with 6-month refills | 1 | 1.49 | 1 | 0.96 |
| Malawi | | | | |
| Facility conventional care (SOC) | 4-12 | 5.4 | 0 | 0.00 |
| Facility dispensing with 3-month refills | 3 | 4.9 | 0 | 0.00 |
| Facility dispensing with 6-month refills | 2 | 2.9 | 0 | 0.00 |
| Uganda | | | | |
| Facility-based individual management (SOC) | 4-12 | 7.63 | 0 | 0.00 |
| Facility groups (pregnant/post-partum) | 2 | 9.05 | 2-4 | 6.6 |
| Fast-track drug refills | 4 | 5.82 | 0 | 0.00 |
| Client-led ART delivery | 2 | 5.92 | 2 | 2.00 |
| Community distribution points | 1 | 6.07 | 4 | 1.92 |
| Zambia 1 | | | | |
| Facility conventional care (SOC) | 4 | 2.55 | 0 | 0.00 |
| Community adherence groups | 2 | 2.64 | 12 | 10.02 |
| Urban adherence groups | 2 | 3.06 | 4 | 4.54 |
| Mobile ART services | 0 | 0.00 | 6 | 4.87 |
| Home ART delivery | 1 | 1.01 | 6 | 3.34 |
| Zambia 2 | | | | |
| Facility conventional care (SOC) | 4-12 | 4.6 | 0 | 0.00 |
| Facility dispensing with 3-month refills | 3 | 4.7 | 0 | 0.00 |
| Facility dispensing with 6-month refills | 2 | 2.8 | 0 | 0.00 |
| Zimbabwe (2020 USD) | | | | |
| Facility dispensing with 3-month refills (SOC) | 4 | 5.02 | 0 | 0.00 |
| Community ART groups with 3-month refills | 1 | 1.99* | 4 | 3.05 |
| Community ART groups with 6-month refills | 1 | 1.98* | 2 | 1.18 |

*Assumed based on source authors' calculations.

†Patients are always permitted to make additional clinic visits as needed; guidelines should be regarded as the minimum number of clinic visits/year.

tests utilized per patient per year ranged from 0.22 to 1.15. Costs of clinic visits and DSD interactions varied widely, as would be expected, since this is the characteristic of treatment that DSD models change most (though it is also a relatively inexpensive resource).

One of the major differences among DSD models for HIV treatment is dispensing interval (number of months of ARV medications dispensed at a time). All of the cluster randomized trials specified dispensing interval as a characteristic of the model. Actual dispensing intervals are reported for only two

Table 5. Breakdown of cost per patient at 12 months, by model (cost and percentage of total mean cost/patient).

| Country and model | ARVs | | Non-ARV medications | | Lab tests | | Clinic visits | | DSD interactions | | Infrastructure and fixed costs | |
|--|----------|-----|---------------------|-----|----------------------|-----|---------------|-----|------------------|-----|--------------------------------|----|
| Lesotho | | | | | | | | | | | | |
| Facility care with 3-month refills (SOC) | \$84.37 | 69% | * | | \$12.00 | 10% | \$25.91 | 21% | \$0 | 0% | † | |
| Community ART groups with 3-month refills | \$86.10 | 75% | * | | \$8.93 | 8% | \$5.78 | 5% | \$13.59 | 12% | † | |
| Community distribution points with 6-month refills | \$87.08 | 77% | * | | \$10.29 | 9% | \$9.60 | 9% | \$5.59 | 5% | † | |
| Malawi¶ | | | | | | | | | | | | |
| Facility conventional care (SOC) | \$77.54 | 87% | * | | ‡ | | \$8.19 | 9% | \$0 | 0% | \$3.32 | 4% |
| Facility dispensing with 3-month refills | \$77.65 | 88% | * | | ‡ | | \$7.43 | 8% | \$0 | 0% | \$3.32 | 4% |
| Facility dispensing with 6-month refills | \$78.18 | 91% | * | | ‡ | | \$4.42 | 5% | \$0 | 0% | \$3.32 | 4% |
| Uganda** | | | | | | | | | | | | |
| Facility-based individual management (SOC) | \$115.33 | 76% | \$9.99 | 7% | \$13.04 | 9% | \$5.00 | 3% | \$0.00 | 0% | \$9.12 | 6% |
| Facility groups (pregnant/post-partum) | \$96.88 | 69% | \$13.13 | 9% | \$14.85 | 11% | \$6.90 | 5% | \$0.06 | 0% | \$9.46 | 7% |
| Fast-track drug refills | \$133.96 | 80% | \$11.10 | 7% | \$11.75 | 7% | \$4.77 | 3% | \$0.00 | 0% | \$4.89 | 3% |
| Client-led ART delivery | \$103.20 | 69% | \$20.10 | 13% | \$11.21 | 7% | \$2.55 | 2% | \$0.17 | 0% | \$12.84 | 9% |
| Community distribution points | \$112.76 | 77% | \$10.12 | 7% | \$11.40 | 8% | \$1.47 | 1% | \$0.17 | 0% | \$10.51 | 7% |
| Zambia1§ | | | | | | | | | | | | |
| Facility conventional care (SOC) | \$86.04 | 86% | \$0.13 | 0% | \$4.61 | 5% | 9.31 | 9% | \$0 | 0% | † | |
| Community adherence groups | \$89.01 | 77% | \$0.10 | 0% | \$6.92 | 6% | \$9.63 | 8% | \$9.92 | 9% | † | |
| Urban adherence groups | \$101.87 | 69% | \$0.18 | 0% | \$23.24 | 16% | \$11.16 | 8% | \$10.68 | 7% | † | |
| Mobile ART services | \$73.30 | 60% | \$3.45 | 3% | ‡ | | \$0.00 | 0% | \$45.71 | 37% | † | |
| Home ART delivery | \$87.96 | 64% | \$0.18 | 0% | \$4.56 | 3% | \$3.70 | 3% | \$40.78 | 30% | † | |
| Zambia2¶ | | | | | | | | | | | | |
| Facility conventional care (SOC) | \$109.65 | 76% | * | | ‡ | | \$31.75 | 22% | \$0 | 0% | \$2.20 | 2% |
| Facility dispensing with 3-month refills | \$106.71 | 75% | * | | ‡ | | \$32.69 | 23% | \$0 | 0% | \$2.20 | 2% |
| Facility dispensing with 6-month refills | \$109.45 | 83% | * | | ‡ | | \$19.48 | 15% | \$0 | 0% | \$2.20 | 2% |
| Zimbabwe¶ | | | | | | | | | | | | |
| Facility dispensing with 3-month refills (SOC) | \$164.17 | 84% | * | | \$6.90 | 4% | \$23.98 | 12% | \$0 | 0% | † | |
| Community ART groups with 3-month refills | \$163.45 | 89% | * | | \$6.43 | 4% | \$9.23 | 5% | \$3.70 | 2% | † | |
| Community ART groups with 6-month refills | \$161.08 | 93% | * | | \$1.08 ^{§§} | 1% | \$9.22 | 5% | \$1.42 | 1% | † | |

*Non-ARV medication costs not captured.

†Infrastructure and other fixed costs included in clinic visit costs.

‡Laboratory costs not captured; one viral load test per year, as called for by national guidelines, would add approximately \$19 to the mean annual cost per patient per year.

§For Zambia1, on-site pharmacy costs were included in clinic visit costs.

¶Costs for Malawi, Zambia2, and Zimbabwe are only for those who were retained at 12 months.

**For Uganda, 1) medication costs include supply chain costs, not solely procurement of products; 2) lab tests included tests other than viral loads; and 3) infrastructure and fixed costs included some costs incurred by implementing partners above the level of the individual healthcare facility.

§§In Zimbabwe, facilities in the study arm with community ART groups with 6 month refills were more likely to be located in districts that did not have access to viral load testing technology. As a result, far fewer patients received viral load tests than in the other arms (Table 4), and average cost per patient was low.

studies. In the INTERVAL trial (Malawi and Zambia²), participants received the expected supply of ARVs roughly 90% of the time; some patients in the 3-month dispensing arm received more or fewer than 3 months' supply at some or all visits, and some patients in the 6-month dispensing arm received fewer than 6 months at some or all visits. In Uganda, the average dispensing interval ranged from 1.3 to 2.1 months per medication pickup, helping to explain the relatively high number of healthcare system interactions observed for the models in Uganda.

Patient costs

Table 6 presents estimates of costs borne by patients for the studies that included a patient survey. Total costs/patient/year depend heavily on how individuals' time is valued and the estimated or assumed duration of an average clinic visit or DSD interaction, but in general, savings to patients were

substantial for almost all of the differentiated models, equivalent to several days' minimum wage in each country. All of the studies in Table 6 compared three- and six-month dispensing to conventional care, either without making any other changes (Malawi and Zambia²) or using community-based models (Lesotho and Zimbabwe). Patient savings were large for all the six-month models, while savings for the three-month models likely depended on the visit frequency required by conventional care, relative to the quarterly interaction frequency required by three-month dispensing.

Discussion

In this synthesis of five previously reported studies, we pull together the average cost per patient treated for HIV and per patient retained in care for a variety of differentiated service delivery models in Lesotho, Malawi, Uganda, Zambia, and Zimbabwe. In most, but not all, cases, the DSD models

Table 6. Average costs to patients per year in care, by model.

| Country and model | Transport | Opportunity cost | Total cost | % difference from SOC model (mean total cost per patient) | Minimum wage reported for country [‡] |
|--|-----------|----------------------|------------|---|--|
| Lesotho | | | | | |
| Facility care with 3-month refills | \$11.45 | \$32.97* | \$44.42 | | \$7.10 |
| Community ART groups with 3-month refills | \$2.62 | \$13.73* | \$16.34 | -63.2% | |
| Community distribution points with 6-month refills | \$4.83 | \$13.94* | \$18.77 | -57.7% | |
| Malawi | | | | | |
| Facility conventional care | \$1.59§ | \$5.30 [†] | \$6.89 | | \$1.33 |
| Facility dispensing with 3-month refills | \$1.59§ | \$6.63 [†] | \$8.22 | +19.3% | |
| Facility dispensing with 6-month refills | \$2.27§ | \$3.98 [†] | \$6.25 | -9.3% | |
| Zambia 2 | | | | | |
| Facility conventional care | \$1.67§ | \$15.00 [†] | \$16.67 | | \$4.99 |
| Facility dispensing with 3-month refills | \$1.58§ | \$20.00 [†] | \$21.58 | +29.5% | |
| Facility dispensing with 6-month refills | \$1.19§ | \$9.98 [†] | \$11.17 | -33.0% | |
| Zimbabwe | | | | | |
| Facility care with 3-month refills | \$2.51 | \$7.52 | \$10.03 | | \$3.39** |
| Community ART groups with 3-month refills | \$0.99 | \$4.12 | \$5.12 | -49.0% | |
| Community ART groups with 6-month refills | \$0.99 | \$3.41 | \$4.40 | -56.1% | |

*Assumed full day for facility visit and ¼ day for DSD interaction at minimum wage for Lesotho.

[†]Assumed half or full day at minimum wage for country, depending on total number of minutes reported by patients.

[‡]As reported by each study.

**There is no minimum wage in Zimbabwe. Authors' calculations based on 2021 "most typical annual salary" reported at <https://www.averagesalariesurvey.com/zimbabwe>.

§Average across entire cohort. In both Malawi and Zambia², only 23–46% of participants incurred any travel costs. Average cost/participant who did incur travel costs was thus substantially higher than is shown here.

achieved roughly the same 12-month retention rates as did conventional care or were reported as non-inferior to conventional care, a finding that likely reflects both the efficacy of the DSD models and the fact that most enrolled only stable patients who had already demonstrated their ability to adhere to treatment and remain in care. Some models did slightly better than conventional care in terms of retention; few did worse. We found that within countries, most models of care had relatively similar costs, except for resource-intensive models such as home ART delivery, which were more expensive, and, to a lesser extent, 6-month dispensing models, which were slightly less expensive.

We note that although provider costs varied widely among countries, from a low of \$100 per patient per year in Zambia per year to a high of \$187 per patient per year in Zimbabwe—both for conventional, facility-based care—these differences primarily reflect larger differences between countries in prices of inputs. Examples of such differences are provided in Table 5 and Table S1: the daily minimum wage in Malawi is \$1.93, while in Lesotho it is \$7.10, 3.8 times more; in Malawi, first-line ARVs averaged \$6.30/month, while in Zimbabwe they cost \$13.81/month, more than twice as much.

Unlike the differences among countries, the differences among models within countries are informative. The average cost per patient for each model reflects that model's particular combination of location of service delivery, interaction frequency, provider cadre, and, in Uganda, proportions of patients on second-line regimens. Models that offered six-month dispensing, whether at the facility or in the community, consistently cost less than those with shorter dispensing durations, though the savings were modest in magnitude. The small differences in total cost/patient between models within countries highlight the large share of costs attributable to antiretroviral medications, whose cost does not vary with model of care. ARVs accounted for 60–92% of the total per patient, and laboratory tests (typically one viral load test/year) another 5–10%, on average. There is thus relatively little room for DSD models to reduce overall treatment costs.

For all the models, fidelity to model guidelines varied, with patients receiving more or fewer months of ARVs, viral load tests, and healthcare system interactions than guidelines recommended and often receiving different dispensing intervals than the model called for. These discrepancies, which were particularly noticeable in viral load test and clinic visit numbers (Table S2), affected the total resource utilization, and thus total cost, per patient. It is unclear whether strict fidelity to guideline recommendations is desirable for purposes of patient management, as clinical discretion may be preferable to guideline recommendations in some cases, and some patients may benefit from, for example, making more or fewer clinic visits than called for. In any case, increases in guideline compliance may cause costs either to rise or to fall, depending on the status quo.

The studies included in this synthesis differed from one another in several ways that are important to interpretation of their

results. The models compared in the randomized trials are potentially substitutes for one another, enrolling the same populations in the same settings. In the two observational studies, in contrast, models should not be regarded as potential substitutes, because the settings, populations served, and other model characteristics varied widely by model. It is likely that a mix of models, including those that cost more and those that cost less than average, will be needed to provide access to a country's entire ART patient cohort.

While most DSD models in most of the studies cost slightly less than conventional care, the models observed in Zambia were all somewhat more expensive than conventional care. This can largely be explained by the design of the models. In Zambia, all four of the DSD models observed required more healthcare system interactions than did conventional care. These models were thus not “less intensive” than conventional care, and did not utilize fewer resources. In these models, resource allocation shifted from the clinic to the DSD model but did not diminish.

More striking than the cost implications to healthcare providers were the sharp reductions in costs to patients themselves. Patients reported cutting their own out-of-pocket and/or opportunity cost expenditures by between a quarter and a half per year, generally due to the reduced number of full clinic visits required by DSD models. Savings to patients may help improve long-term retention in care, as patient costs are often cited as a reason for interrupting treatment¹². Spending less time and money in seeking healthcare also provides an immediate improvement to patients' quality of life.

Our study had a number of limitations. First, costing methods and resources included in the analysis differed between the studies, such that each “total cost per patient” estimate represents a slightly different set of inputs. Although we have noted inclusions and exclusions as fully as possible, the variation in input data and costing methods and the previously noted differences in national price levels argue for caution in comparing results between studies. Second, implementation of nearly all the models in the study was relatively recent, and costs may not reflect the operational efficiency that may be gained from experience. Third, observational studies in Uganda and Zambia were conducted prior to the scaleup of 6-month dispensing in these countries. Both countries now recommend 6-month dispensing, alone or in combination with other models, whenever possible, a development that is likely to reduce the costs of their models.

Fourth, we also are aware that the unit costs used for some categories of provider resources, such as labor and infrastructure, may not correctly capture the value of these resources to the health system. If a DSD model reduces the number of hours of a nurse's time required per patient, for example, the cost estimates included here will reflect that as the product of the nurse's salary and the estimated number of hours saved. From a health systems perspective, however, the value of that saved time will depend entirely on what the nurse does instead—be it seeing more patients,

spending more time with the same number of patients, completing more administrative tasks, or taking longer breaks and working shorter hours. The provider must pay that nurse's full-time salary regardless of how the "saved" time is spent. Effective management of human and physical resources is thus needed for DSD models to realize the apparent cost savings reported by these studies.

Finally, an important limitation to all of the studies reported here is that, for the most part, costs are limited to clients who are stable on ART and therefore eligible for DSD models. These clients are likely to cost the health system less than average even when in conventional care; shifting them to DSD models may leave the more expensive clients in conventional care, simply reallocating overall health system costs, rather than reducing them. Future research is needed to understand the role of DSD models in improving health outcomes and lowering per-patient costs of ART programmes

as a whole. Research is also needed to explore the integration of DSD models for HIV treatment with service delivery for other chronic needs, to optimize clinic efficiency and minimize the overall burden of healthcare access on patients.

Data availability

Figshare. Supplementary tables.docx. DOI: <https://doi.org/10.6084/m9.figshare.17096678.v1>¹³

Data are available under the terms of the [Creative Commons Zero "No rights reserved" data waiver](#) (CC BY 4.0 Public domain dedication).

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 **Michael J. Vinikoor** 

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Summary:

This article uses already published research on DSD models of HIV care across multiple Southern and East African countries to report on whether costs are reduced through this intervention that is now widely implemented. The justification for synthesizing these data could be better stated including the value of showing variability in cost savings across countries and by study design. The findings are limited by the fact that data came from research studies and not routine implementation by government systems, which will be using DSD for decades to come. Even in light of these limitations, this paper is significant in providing an informative view into the economics of DSD and would be useful to policymakers adopting and implementing DSD.

Background:

- In paragraph 1, the authors might want to add a sentence to state that the “conventional” model led to increasingly over-crowded clinics and this stretched staffing and led to queues, less patient-centered experiences with increased retention losses.
- Was saving cost one of the proposed outcomes of DSD? It would be good to state that it was never pitched as cost-saving or that in fact it was.
- Could you also reference that the term DSD could also be used to intensify services, such as for high HIV VL, advanced HIV, etc. Not all DSD should be for “less intensive” - I think it goes both ways (more and less intense, more and less costly) depending on need.
- In the last paragraph the authors could mention that DSD for stable patients was compared to convention model costs and outcomes for each site (assuming it was).

- Is this like a systematic review or meta analysis of published papers? How is this justified as the data are already published? Please explain further. Maybe you should mention that the cost outcomes and CE may differ across settings?

Methods:

- No ethics review: were all the data publically available via data sharing websites?
- Please comment on whether the costs of care before DSD/conventional approach were also collected as well as those from patients in conventional. Were those captured at the same time as DSD (to avoid calendar time biases)?
- Maybe having a column in Table 1 to indicate if the convention model was included in the data collection could be considered

Results:

- I note from Table 6, costs to patients, for several countries, moving from conventional care to 3 and then 6-month refills didn't lead to a stepwise reduction in total costs. Why is that? In one case, Zambia, 3-month refills was more costly than conventional while 6-month was less. Please explain.

Discussion:

- As the DSD studies were implemented by NGOs, etc. and not by government, what are the implications of these findings? People often say that the government can find ways to do things cheaper than NGOs so perhaps we need additional data in the real world when the government is in charge of this.
- You comment that costs of DSD were highest in observational cohorts where second-line and people in first 6 months were included - didn't this overall analysis focus on stable patients, which I though meant 1st line and >6 months on ART? What is the meaning of this? Especially as trials (where you state the costs of DSD were more reduced) often don't translate to the real world.
- It's very interesting that most of the overall cost is due to ARVs and labs; hence DSD can have that much impact on cost. I suggest highlighting this more.
- You ought to clearly answer the question posed in the title in the first paragraph of the discussion. Do you consider DSD to save money?

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: infectious diseases, behavioral science, implementation science

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 18 Feb 2022

Sydney Rosen, Boston University School of Public Health, Boston, USA

We are glad that the Reviewer found our paper useful despite its limitations, which we also acknowledge.

In paragraph 1, the authors might want to add a sentence to state that the “conventional” model led to increasingly over-crowded clinics and this stretched staffing and led to queues, less patient-centered experiences with increased retention losses.

Thank you, a good suggestion. We have added this sentence.

Was saving cost one of the proposed outcomes of DSD? It would be good to state that it was never pitched as cost-saving or that in fact it was.

Yes, it was. We have stated this in the first sentence of the second paragraph and provided a reference.

Could you also reference that the term DSD could also be used to intensify services, such as for high HIV VL, advanced HIV, etc. Not all DSD should be for “less intensive” - I think it goes both ways (more and less intense, more and less costly) depending on need.

You are right and this is an important point. Almost all of the models in the papers we synthesized were intended to “less intensive,” with the exception of facility-based individual care in Uganda (which is for patients not eligible for less intensive models) and possibly of home and mobile ART delivery Zambia¹. More intensive models designed for advanced HIV disease would not be expected to cost less. We have added a note about this to the first paragraph of the Introduction.

In the last paragraph the authors could mention that DSD for stable patients was compared to convention model costs and outcomes for each site (assuming it was).

We assume that this refers to the last paragraph of the Introduction. We have added a note about this there.

Is this like a systematic review or meta analysis of published papers? How is this justified as the data are already published? Please explain further. Maybe you should mention that the cost outcomes and CE may differ across settings?

We present it as a synthesis of published papers, rather than a systematic review or meta analysis, on the grounds that pulling together all the results of these papers into a single manuscript, where they are presented in a standard format and can be compared and contrasted, has value to readers. We have added a sentence about costs and outcomes varying across settings to the second to last paragraph of the introduction.

Methods:

No ethics review: were all the data publically available via data sharing websites?

Yes, all the data used in the manuscript have either been published in open access journals or posted on an open access pre-print server. All are fully referenced in the manuscript.

Please comment on whether the costs of care before DSD/conventional approach were also collected as well as those from patients in conventional. Were those captured at the same time as DSD (to avoid calendar time biases)?

While it would have been ideal to have data from prior to DSD implementation, to allow a pre-post or difference-in-differences comparison, all the papers were written after implementation of DSD models at the study sites. We sought retrospective or previously published data that would serve as a pre-period comparison but were unable to find it. All the models within each of the studies were observed at the same chronological time, to avoid calendar time biases. Table 1 indicates the dates of enrollment for each study, in case readers are concerned about secular changes underway during the study periods.

Maybe having a column in Table 1 to indicate if the convention model was included in the data collection could be considered

In Table 2, a conventional care model is included and described for each study.

Results:

I note from Table 6, costs to patients, for several countries, moving from conventional care to 3 and then 6-month refills didn't lead to a stepwise reduction in total costs. Why is that? In one case, Zambia, 3-month refills was more costly than conventional while 6-month was less. Please explain.

Good catch. We also noted that apparent discrepancy. As shown in Table 4, the number of visits made to the facility in Malawi and Zambia² are roughly the same for conventional care

and 3-month dispensing. What isn't evident from Table 4 is that the time spent per visit was higher for 3-month dispensing than for conventional care in both Malawi and Zambia. This is reported in the original paper in Appendix 2 and evident in Table 6, where patient opportunity (time) costs for 3MD are larger than for conventional care in these two studies. We cannot explain why the visits were longer, unfortunately.

Discussion:

○ As the DSD studies were implemented by NGOs, etc. and not by government, what are the implications of these findings? People often say that the government can find ways to do things cheaper than NGOs so perhaps we need additional data in the real world when the government is in charge of this.

At this point in time, NGO partners with donor support, primarily but not solely from PEPFAR or the Global Fund, support a large number public sector healthcare facilities in much of sub-Saharan Africa. These sites are typically the countries' highest-volume facilities and generally have better data collection than do sites without partner support, and new models of care are often initially introduced at these sites. As a result, these are the sites where research is done, particularly if the research is also donor-funded, as was the case for the studies included in this manuscript. While it's likely that NGO partners increase costs in some cases, they do not do so in all. For example, for Malawi and Zambia², the INTERVAL trial did not increase intervention costs beyond what would be required if no research partner or NGO were involved.

Importantly, we cannot know that patient outcomes would be the same if the partners were not involved, and the logic of costing methodology suggests that all resources used to achieve an outcome should be included in cost estimates, including partner support. Based on the papers that were used to pull together these results, it appears that only the Uganda study attempted to capture any "above site" or partner expenses, and these were combined with infrastructure and fixed costs. These may well be equivalent to the costs that a government district health office would incur to supervise the implementation of DSD models in the district. For all these reasons, we're not convinced that costs would be lower if implementation was done only by government, and we don't have the data to make a case either way.

○ You comment that costs of DSD were highest in observational cohorts where second-line and people in first 6 months were included – didn't this overall analysis focus on stable patients, which I thought meant 1st line and >6 months on ART? What is the meaning of this? Especially as trials (where you state the costs of DSD were more reduced) often don't translate to the real world.

This was a challenge in interpreting the observational studies. Unlike the trials, the observational studies included some DSD models that permitted patients on second line therapy and/or in their first 6 months on ART to enroll. We could not clearly exclude these patients in doing our synthesis. We have added a note about this to the limitations writeup in the Discussion. As you note, the trials, which could exclude all but stable patients, were not as close a reflection to real world conditions as were the observational studies.

○ It's very interesting that most of the overall cost is due to ARVs and labs; hence DSD can have that much impact on cost. I suggest highlighting this more.

(We assume you mean that "DSD can NOT have much impact on cost.") Thank you for highlighting this point. It is important. We have emphasised it again in the Discussion where we contrast savings to providers with savings to patients.

○ You ought to clearly answer the question posed in the title in the first paragraph of the discussion. Do you consider DSD to save money?

Good point! We have added an answer to this question in the last paragraph of the manuscript.

Competing Interests: No competing interests were disclosed.

Reviewer Report 10 January 2022

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Ingrid Eshun-Wilson 

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This important paper is an excellent comparison of costs of DSD models and standard care across multiple settings in sub-Saharan Africa, demonstrating overall comparable costs across all models and SOC, but with some reduced costs noted for 6MMD models, which highlights the importance of strengthening supply to allow 6M dispensations in several settings. The authors make a note of the importance of within country comparisons of models and provide extensive detail in very clear tables in the results section. Another critical finding is how guidelines for DSD model visit frequency do not necessarily match up with visit frequency in practice. The authors also highlight the key limitations of the analysis. The abstract can be strengthened to better articulate the main findings of the paper.

I suggest accepting for indexing with minor revisions.

Abstract:

The results in the abstract are not entirely clear, this might be the result of the word count restrictions however, re-wording could aid understanding for the reader, currently the results of the study are hard to glean from the abstract alone and one must read the full paper to understand the abstract. I also recommend including a few more results in the abstract:

- It would be helpful if the authors could simplify/clarify the sentence “average provider cost/patient/year ranged from 100 -187 for conventional care, in both cases for facility-based conventional care”. Was this average cost assessed for conventional care only? Consider simplifying and rephrasing to: “The average provider cost/patient/year for conventional care ranged from 100-187.” Although Table 3 suggests that this ranged from 86 to 187.

- I recommend re-wording: “Conventional care was less expensive than any other model in the Zambia observational study, more expensive than any other model in Lesotho, Malawi, and Zimbabwe, and in the middle of the range in the Zambia trial and the observational study in Uganda.”

It is hard to determine what the synthesis is here, it is more a list of the results of individual studies, it would help the reader if the top-line points are made here.

Consider a synthesized statement – e.g.: The majority of DSD models had comparable costs to SOC with the % difference in mean annual cost per patient ranging from 11.4% less to 9.2% more, with the exception of observational data from Zambia which showed much higher costs for DSD models compared to SOC (16-37% higher).

- I recommend rephrasing this sentence “Models incorporating 6-month dispensing were consistently less expensive to the provider per patient treated.” to include the comparison. Was this in comparison to all other models or compared to conventional care, compared to 3 month models? Based on reviewing the results in the paper one could rephrase as such: e.g. “Models incorporating 6-month dispensing were consistently less expensive to the provider per patient treated compared to all other models, including SOC (% difference range: -11.4% to -2.2%).”

This section is repeated in the main results of the paper and should be clarified in the main text results as well.

- The abstract conclusion could also be more specific by including a comparison statement. “In five field studies of the costs of DSD models for HIV treatment, most models within each country had relatively similar costs [to each other or conventional care or all], except for 6-month dispensing models, which were slightly less expensive.”
- The term “provider cost” throughout the abstract and manuscript is somewhat confusing as providers are frequently considered to be health providers in this setting rather than the health system/government/ngo, on reading the methods it is clear that it is related to most aspects of ART health service provision but possibly not staff salaries – consider changing it to “health service cost” or other term to avoid assumptions regarding what “provider” means.
- Ideally include the main study limitations in the abstract, particularly that what was included in unit cost estimates was quite variable across studies.

Methods, Results & discussion:

Thank you for the overall clarity of the presentation of the methods and results.

- Lowest cost is cited as \$100 in the abstract and conclusions, but from tables appears to be \$86.

- Of note the cost of personnel which is a significant health care expenditure stands out as missing from the assessments in the main paper. Based on the reviewing the discussion section and supplementary materials, salaries were considered variably in the estimation of unit costs across studies and how they should be considered is unclear. It would however still be worthwhile being explicit and including in the main methods sections some detail about what a “clinic visit or off-site DSD visit” cost was comprised of and point out that salary may or may not have been included. This is in the footnotes of S1 Table, but I recommend mentioning briefly in main methods.
- In the patient costs section, it is worth clarifying why the total patient costs for Malawi and Zambia are higher for the 3-month models compared to SOC which is generally 1-2/3monthly. It appears from other tables that this may be related to more actual visits than in the guideline but this still doesn't seem to account for the big % difference that is seen. It would be worth specifying in the text the specific reason, as ~50% savings to patients is one of the main conclusions of the paper.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Infectious Diseases, Implementation Science, Systematic reviews, Epidemiology, Preference Elicitation, Mixed Methods

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 18 Feb 2022

Sydney Rosen, Boston University School of Public Health, Boston, USA

We thank the reviewer for the positive overview.

Abstract

The results in the abstract are not entirely clear, this might be the result of the word count restrictions however, re-wording could aid understanding for the reader, currently the results of the study are hard to glean from the abstract alone and one must read the full paper to understand the abstract.

We have attempted to clarify the abstract, in line with the suggestions below.

I also recommend including a few more results in the abstract:

○ It would be helpful if the authors could simplify/clarify the sentence “average provider cost/patient/year ranged from 100 -187 for conventional care, in both cases for facility-based conventional care”. Was this average cost assessed for conventional care only? Consider simplifying and rephrasing to: “The average provider cost/patient/year for conventional care ranged from 100-187.” Although Table 3 suggests that this ranged from 86 to 187.

We thank the reviewer for catching these discrepancies and have corrected these results in the abstract.

○ I recommend re-wording: “Conventional care was less expensive than any other model in the Zambia observational study, more expensive than any other model in Lesotho, Malawi, and Zimbabwe, and in the middle of the range in the Zambia trial and the observational study in Uganda.” It is hard to determine what the synthesis is here, it is more a list of the results of individual studies, it would help the reader if the top-line points are made here. Consider a synthesized statement – e.g.: The majority of DSD models had comparable costs to SOC with the % difference in mean annual cost per patient ranging from 11.4% less to 9.2% more, with the exception of observational data from Zambia which showed much higher costs for DSD models compared to SOC (16-37% higher).

We have accepted the reviewer’s suggestion for revising this sentence.

○ I recommend rephrasing this sentence “Models incorporating 6-month dispensing were consistently less expensive to the provider per patient treated.” to include the comparison. Was this in comparison to all other models or compared to conventional care, compared to 3 month models? Based on reviewing the results in the paper one could rephrase as such: e.g. “Models incorporating 6-month dispensing were consistently less expensive to the provider per patient treated compared to all other models, including SOC (% difference range: -11.4% to -2.2%).”

This section is repeated in the main results of the paper and should be clarified in the main text results as well.

We have clarified this comparison in the abstract and the main text.

○ The abstract conclusion could also be more specific by including a comparison statement.

“In five field studies of the costs of DSD models for HIV treatment, most models within each country had relatively similar costs [to each other or conventional care or all], except for 6-month dispensing models, which were slightly less expensive.”

We have clarified this sentence in the abstract.

○ The term “provider cost” throughout the abstract and manuscript is somewhat confusing as providers are frequently considered to be health providers in this setting rather than the health system/government/ngo, on reading the methods it is clear that it is related to most aspects of ART health service provision but possibly not staff salaries – consider changing it to “health service cost” or other term to avoid assumptions regarding what “provider” means.

“Provider cost” is a standard term in the health economics literature and is intended to distinguish costs to the healthcare system (the provider) from costs to patients themselves. We have added a definition to the methods section of the main text to address this. Space limitations prevent further explanation in the abstract.

○ Ideally include the main study limitations in the abstract, particularly that what was included in unit cost estimates was quite variable across studies.

We have noted the most important limitation in the abstract. The limitation on abstract word count precludes providing any more detail.

Methods, Results & discussion:

Thank you for the overall clarity of the presentation of the methods and results.

○ Lowest cost is cited as \$100 in the abstract and conclusions, but from tables appears to be \$86.

As explained in the paragraph immediately after Table 4, we assumed that each Malawi cost/patient should be increased by \$19 to reflect an average of one viral load test per year. Once \$19 is added to each Malawi value, the lowest cost is then for conventional care in Zambia¹, at \$100/year. We have tried to clarify this in the text.

○ Of note the cost of personnel which is a significant health care expenditure stands out as missing from the assessments in the main paper. Based on the reviewing the discussion section and supplementary materials, salaries were considered variably in the estimation of unit costs across studies and how they should be considered is unclear. It would however still be worthwhile being explicit and including in the main methods sections some detail about what a “clinic visit or off-site DSD visit” cost was comprised of and point out that salary may or may not have been included. This is in the footnotes of S1 Table, but I recommend mentioning briefly in main methods.

Thank you for this suggestion. In fact, salaries, which as you note are an important contributor to cost, are included in all the estimates. We have added a sentence to explain

this in the Methods section.

○ In the patient costs section, it is worth clarifying why the total patient costs for Malawi and Zambia are higher for the 3-month models compared to SOC which is generally 1-2/3monthly. It appears from other tables that this may be related to more actual visits than in the guideline but this still doesn't seem to account for the big % difference that is seen. It would be worth specifying in the text the specific reason, as ~50% savings to patients is one of the main conclusions of the paper.

As shown in Table 4, the number of visits made to the facility in Malawi and Zambia² are roughly the same for conventional care and 3-month dispensing. What isn't evident from Table 4 is that the time spent per visit was higher for 3-month dispensing than for conventional care in both Malawi and Zambia. This is reported in the original paper in Appendix 2 and evident in Table 6, where patient opportunity (time) costs for 3MD are larger than for conventional care in these two studies.

Competing Interests: No competing interests were disclosed.