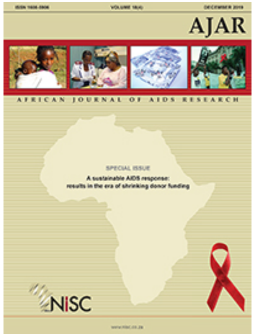

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Research Article

A meta-analysis approach for estimating average unit costs for ART using pooled facility-level primary data from African countries

Diego Cerecero-García[1], Carlos Pineda-Antunez[1], Lily Alexander[2], Drew Cameron[3], Gisela Martinez-Silva[1], Carol Dayo Obure[4], Elliot Marseille[5], Lung Vu[6], James G Kahn[7], Anna Vassall[8], Gabriela Gomez[8], Lori Bollinger[9], Carol Levin[10], and Sergio Bautista-Arredondo[1]*

[1]*National Institute of Public Health, Cuernavaca, Mexico*
[2]*HIV AIDS TB Research Consortium CISIDAT, Cuernavaca, Mexico*
[3]*Health Policy, University of California Berkeley, Berkeley, USA*
[4]*African Development Bank Group, Abidjan, Tunis*
[5]*Center for Global Surgical Studies, University of California San Francisco, San Francisco, USA*
[6]*Population Council, Washington, USA*
[7]*Institute for Health Policy Studies, University of California San Francisco, San Francisco, USA*
[8]*London School of Hygiene and Tropical Medicine, London, UK*
[9]*Avenir Health, Glastonbury, USA*
[10]*Department of Global Health, University of Washington, Seattle, USA*
**Corresponding author email: sbautista@insp.mx*

Objective: **To estimate facility-level average cost for ART services and explore unit cost variations using pooled facility-level cost estimates from four HIV empirical cost studies conducted in five African countries .**
Methods: **Through a literature search we identified studies reporting facility-level costs for ART programmes. We requested the underlying data and standardised the disparate data sources to make them comparable. Subsequently, we estimated the annual cost per patient served and assessed the cost variation among facilities and other service delivery characteristics using descriptive statistics and meta-analysis. All costs were converted to 2017 US dollars ($).**
Results: **We obtained and standardised data from four studies across five African countries and 139 facilities. The weighted average cost per patient on ART was $251 (95% CI: 193–308). On average, 46% of the mean unit cost correspond to antiretroviral (ARVs) costs, 31% to personnel costs, 20% other recurrent costs, and 2% to capital costs. We observed a lot of variation in unit cost and scale levels between countries. We also observed a negative relationship between ART unit cost and the number of patients served in a year.**
Conclusion: **Our approach allowed us to explore unit cost variation across contexts by pooling ART costs from multiple sources. Our research provides an example of how to estimate costs based on heterogeneous sources reconciling methodological differences across studies and contributes by giving an example on how to estimate costs based on heterogeneous sources of data. Also, our study provides additional information on costs for funders, policy-makers, and decision-makers in the process of designing or scaling-up HIV interventions.**

Keywords: HIV, treatment, efficiency, cost variatio

Introduction

In 2017, 36.9 million people were living with HIV worldwide, with 1.8 million new infections in that year alone (UNAIDS, 2019). Africa carries a disproportionate burden of the HIV/AIDS epidemic, with 25.7 million people living with HIV (PLHIV) on the continent. This region also accounts for over two-thirds of new HIV infections globally (UNAIDS, 2019; WHO, 2019). In 2014, the Joint United Nations Programme on HIV/AIDS (UNAIDS) launched the 90–90–90 targets. The aim was to diagnose 90% of all HIV-positive persons, provide antiretroviral therapy (ART) to 90% of those who know their status, and achieve viral suppression in 90% of those treated by 2020 (UNAIDS, 2017). However, as of 2018, it was estimated that 70% of PLHIV know their status globally, 77% of PLHIV who know their status are receiving treatment, and 82% of people on treatment are virally suppressed (UNAIDS, 2017). In the case of eastern and southern Africa, 81% of PLHIV know their status, 66% are receiving treatment, and only 52% of those treated have suppressed viral loads (UNAIDS, 2019).

To reach the 90–90–90 goals, — especially for ART coverage and viral suppression — an intense mobilisation of technical and financial resources is needed. Programme planners, policy-makers, and funders need accurate and relevant cost information to help them plan and implement efficient ART programs that maximise the health impact of the scarce resources available. Thus, identifying empirical cost data is imperative to efficiently and realistically allocate resources and identify inefficiencies within HIV treatment and care programmes.

There is evidence of the costs of delivering ART in African countries. The estimates have ranged from \$116 to \$1 700 per year (Duong et al., 2014; Larson et al., 2013; Rosen, Long, & Sanne, 2008). Unfortunately, one limitation of these studies is that many included only one health facility (Jain et al., 2015; Jouquet et al., 2011; Riviere et al., 2014; Siregar et al., 2015), while others relied on small, convenience samples (Larson et al., 2013; Marseille et al., 2012; Vu et al., 2016). Due to this significant limitation, such studies are unable to demonstrate how unit costs vary across contexts, which is essential to predict and understand the needs at national level, as well as to assess levels of efficiency observed across units of implementation. As a result, policy-makers have had to make policy and programmatic decisions based on weak and unspecific cost estimates.

Yet a handful of studies have shown that HIV programme costs vary significantly across facilities, even within countries, and that such variation is a function of several service delivery characteristics, including the scale or size of the programmes (Bautista-Arredondo, Colchero, et al., 2018; Bautista-Arredondo, Sosa-Rubi, et al., 2018; Bollinger et al., 2014). For example, one study exploring the costs of ART in Nigeria with a sample size of 80 facilities across the country found that facility-level average cost per patient varied across the type of facility and the scale (Bautista-Arredondo, Colchero, et al., 2018). However, studies like this are scarce — lack of funding and time constraints often compromise the ability to sample a relatively large and representative sample of facilities in costing studies.

Using a meta-analysis approach in this study, we pooled facility-level cost estimates from four HIV empirical cost studies conducted in five African countries in order to estimate average costs for ART and we explored the variation of facility-level ART unit cost, as well as the cost composition across countries.

Methods

Overview

We identified relevant ART cost studies through a systematic literature review. To be eligible, the results reported in the papers had to be based on facility-level cost data and rely on more than one facility. We contacted the authors of all suitable articles to request the primary data underlying their published results. We pooled and standardised the data to estimate average unit costs across different service delivery platforms. Finally, we estimated weighted average ART unit costs through meta-analysis.

Data collection and study sample

The data collection process began with a systematic review of all studies that estimated cost of HIV/AIDS interventions between January 2006 and July 2018, including published studies and gray literature. The literature search identified 54 different HIV interventions — including prevention, treatment and care, testing, enablers, and health systems. A total of 49 published studies included ART costs. Among those, 16 papers included facility-level cost data and a sample size greater than one facility. We requested the underlying data from the authors. We offered modest financial support to authors if they needed to prepare and transfer the data. We received data from four studies (168 facilities) conducted in five African countries: Kenya, Uganda, Eswatini, Zambia, and Nigeria (Bautista-Arredondo, Colchero, et al., 2018; Marseille et al., 2012; Obure et al., 2015; Vu et al., 2016).

Standardisation

To compare unit costs across studies, we standardised the aggregated data according to a multi-step process. First, we transformed all the costs reported in local currencies to USD using the average exchange rate of the year of data collection. Then, using the US GDP deflator, we inflated all the costs to 2017 US dollars (\$). We obtained exchange rates and year-specific GDP deflators from the World Bank (World Bank, 2019).

Second, we formatted all the variables to standardised dummy variables to facilitate comparability across studies. We present the definitions of these variables in Table 1.

Third, for facilities with missing information on urbanicity, we conducted a web search based on the facility name to attempt to fill in this missing information. If urbanicity was still unknown after the previous step, we used demographic data of the area to categorise them as rural ($<$1000 person/km^2) or

Table 1: Description of standardised variables

Variable	Description
Facility type	A binary variable indicating if the facility is a clinic (including health centers, integrated clinics, and clinics) or a hospital
Facility provider	A binary variable that distinguishes sources of funding. A facility is considered to be public if funding came from government and private if funding came from profit-non-profit organisations
Urbanicity	A binary variable for the area where the facility was located: urban or rural
Total cost	The total ART cost expressed as the sum of recurrent costs, capital costs, personnel costs, and ARVs costs
Unit cost	The total ART cost divided by the number of patients treated in a year
Recurrent costs	The total recurrent cost (sum of all: medical supplies, consultations, and laboratories)
Capital costs	The total capital cost (sum of all: administrative equipment, furnishings, laboratory equipment, medical equipment, vehicles)
Personnel costs	The total annual personnel salaries (sum of all: physicians, nurses, others)
Income level	Level income of country according to the World Bank classification
Scale	Annual number of patients treated

urban (≥1000 person/km²). From the sample, we eliminated 29 facilities for which we were not able to identify whether the facility was publicly or privately financed. All of the eliminated facilities were from Nigeria and come from the same study (Bautista-Arredondo, Colchero, et al., 2018). In order to explore whether this elimination introduced any biases in the sample, we compared the distribution of the other facility characteristics and found no difference with those that remained in the analytical sample.

Finally, based on the Global Health Cost Consortium (GHCC) Reference Case, we allocated input costs according to four main cost categories: capital costs, recurrent costs, personnel costs, and antiretroviral drugs (ARVs). All the studies included in our analysis reported disaggregated cost categories. One study included above-facility costs, which were removed from the total cost to ensure consistency across studies (Marseille et al., 2012).

Service delivery platforms

Once costs were standardised, we estimated unit costs (i.e. the facility-level average cost per patient) across six site-specific characteristics, including scale, facility type, ownership, urbanicity, GDP per capita, and ARV costs. "Scale" was defined as the annual number of patients on ART per facility. Facility type indicates whether the facility was a clinic (this category includes clinics, health centres, and integrated clinics) or hospitals. Ownership distinguishes between public and private (NGOs, faith-based health facilities, and other non-profit for-profit sites) facilities. Urbanicity designates a facility as urban or rural based on its geographic location. We identified income level from the World Bank sources (World Bank, 2019). For the ARV cost variable, we pooled reported ARV costs by country and created terciles to classify countries to "low," "medium," or "high" ARV costs categories.

Definition of unit costs

To measure ART unit costs, we included four broad input cost categories — capital, recurrent, personnel, and ARVs. We defined capital costs as non-consumable supplies such as equipment and vehicles. Recurrent costs included consumables, maintenance, utilities, training, laboratory costs (CD-4 lymphocyte counts)**,** and non-ARV drugs such as TB drugs. Personnel consisted of salaries of direct medical staff (physicians and nurses), and non-medical staff (managers, supervisors, and ancillaries). The final category was ARV costs. We subsequently estimated unit costs by adding capital, recurrent, personnel, and ARV costs and divided by the number of patients on ART, as follows:

$$UC_j = \frac{\sum_{i=1}^{i=4} IC_{ij}}{P_j}$$

where UC represents the unit cost at facility j. The term IC_{ij} represents the total annual cost of input category i at facility j, for input categories: 1: capital, 2: recurrent, 3: personnel, and 4: ARVs. P_j represents the annual number of ART patients for facility j.

Descriptive analysis of unit costs

We explored the variation of unit costs across different service delivery platforms: scale, facility type, ownership, urbanicity, income level, and ARV costs. We categorised scale into three levels according to observed terciles of the number of patients treated within each country: small (from 13 to 258 clients), medium (from 259 to 2 559 patients), and large (from 2 560 to 12 690 patients). We also explore the distribution of unit cost and other facility characteristics by the different levels of scale.

Finally, to explore the unit cost composition, we disaggregated average unit costs by the four categories of input costs (capital, recurrent, personnel, and ARVs) to explore the proportion represented by each category. We also investigated economies of scale by exploring the correlation between unit costs and scale.

Meta-analysis

We used a meta-regression approach to estimate unit cost averages while accounting for random effects (Bower et al., 2003). We opted for a random effect analysis following the assumption that costs vary by implementation characteristics (Bautista-Arredondo, Sosa-Rubi, et al., 2018). This method gives more weight to studies with a lower sampling variability, a process known as inverse variance weighting (Bower et al., 2003). A test for heterogeneity was also conducted to determine the most appropriate model.

Results

After excluding 29 facilities, our sample included 139 facilities across four studies and five countries. Table 2 presents the descriptive statistics of the sample. Fifty-six per

Table 2: Description of the facility-level cost data acquired

Characteristics	ART	
Observations	139	
Breakdown of observations by study		
Vu et al. (2012)	4 (3%)	
Bautista et al. (2014)	51 (37%)	
Marseille et al. (2010)	45 (32%)	
Obure et al. (2011)	39 (28%)	
Urbanicity		
Rural facilities	44	
Urban facilities	56	
Ownership		
Private facilities	36	
Public facilities	64	
Facility type		
Hospitals	54	
Clinics	46	
ARVs cost (tertiles)		
Low	32	
Medium	33	
High	35	
Unit cost	Mean (SE)	Median (IQR)
Unit cost per client (USD)	275	187
Average number of clients	1 828	
Average ART coverage in 2017	54%	
Number of studies	4	
Countries	5	

cent of the clinics were located in urban areas, and almost two-thirds were public facilities. The mean annual cost per client on ART was $275 (median $187). The average number of clients was 1 828 per year, and the average country-level ART coverage in 2017 was 54 per cent.

In Table 3, we break down the average ART unit cost by country and service delivery characteristics. Facilities in lower-middle-income countries showed a higher unit cost compared with those in low-income countries ($277 vs $201). Clinics showed higher unit costs than hospitals ($337 vs $221). Facilities in rural areas had higher average ART unit costs than urban facilities ($320 vs $239), and public facilities had higher unit costs than private facilities ($280 vs $258). The average unit costs decreased by 39% when comparing medium to small facilities, and by 59% when comparing large to small clinics. These differences were mainly due to personnel costs. We also stratified our sample by terciles of scale and explored the distribution of unit costs by facility characteristics. Those facilities with large levels of scale consistently had lower unit costs than those with medium or low levels of scale (Table A1 appendix).

We observed substantial variation in unit cost estimations across studies. Figure 1 shows the weighted unit cost estimates from the meta-analysis. The weighted average unit cost per client served was $250 (95% CI: 193–308). We stratified our sample by study and country to explore variations in unit cost composition in both, absolute and relative terms (Figure 2). The right panel of the graph shows the relative unit cost composition. On average, capital costs made up 2 per cent of the unit costs, recurrent costs made up 20 per cent, personnel costs 31 per cent, and ARVs represented 46 per cent. However, we observed substantial heterogeneity in the relative composition of the unit cost across countries. For example, in countries like Zambia, Kenya, and Eswatini the input with higher relative weight in unit costs was ARVs (64%, 63%, and 44% respectively) while in others like Nigeria more than half of the unit cost corresponded to personnel (56%). In the case of Uganda, personnel and other recurrent costs made up to two-thirds of the unit cost (68%). When comparing the cost profiles for each country in absolute terms (Figure 2, left panel), we observed differences in personnel costs — Eswatini and Nigeria had twice the personnel costs of Kenya and Uganda. We also observed higher ARV unit costs in Eswatini compared with the other countries.

Table 3: ART unit costs by implementation characteristics, 2017

	ART		
	Mean	Median	SD
Income level			
Low	201	200	37
Low-middle	277	187	260
Facility characteristics			
Hospital	221	162	204
Clinic	337	207	296
Urban	239	184	151
Rural	320	191	342
Public	280	186	276
Private	258	189	178
Level of scale			
Low	425	249	365
Middle	259	189	230
Large	174	164	68

In Figure 3, we show the variation in unit cost (panel A) and scale (panel B) by country. Each dot in the graph represents a facility. We observed variation both within and between countries. In panel A we observed that Kenya and Eswatini reported the highest cost variation within countries, with costs ranging from 56 to 635 in Kenya, and 65 to 1440 in Eswatini. We also found heterogeneity in the number of patients served between and within countries. Nigeria had the highest variation in scale, with an average number of clients ranging from 13 to 12 690 across facilities and Uganda was the country with the higher volume of patients ranging from 4 602 to 6 969.

To explore the relationship between scale and unit cost we show, in Figure 4, a scatterplot between these variables. We represented the facilities within a country with a particular shape and colour. We also included a non-linear regression line to show the statistical relationship between these variables. We observed a negative and significant association between unit cost and scale. We also found that almost 15% of the variability in the unit costs is explained by scale (see the *R*-square coefficient at the bottom of Figure 4).

Discussion

In this article, we used facility-level primary data to create a pooled dataset with ART unit costs and facility characteristics in five countries. With this strategy, we sought to emulate a study with a relatively large sample of facilities and countries to obtain robust estimations of ART unit costs and capture unit cost variation. Our meta-analysis approach showed that the weighted average annual cost per patient on ART was $250 (95% CI: 193–308). We also identified variations in costs across studies, countries, and service delivery characteristics. Our findings suggest that these variables may be important drivers of unit cost variations. Future studies should explore the individual effects of these variables on costs. We also explored the composition of unit costs, finding substantial heterogeneity across studies and countries. ARV costs, however, seemed to consistently make up the highest proportion of unit costs across settings. In absolute terms, we found substantial differences in the cost of ARVs between countries. These differences could be explained by the number of patients receiving treatment in each facility and also due to changes in prices and guidelines which should be taken into account when performing additional analyses.

Our study has several limitations. First, although we used facility-level primary data and standardised cost categories to ensure comparability, we were unable to control for study design and measurement methods. Additionally, we had an unbalanced sample of facilities. While some studies contributed with a large sample of facilities within countries, other studies only included a couple of observations. We addressed this limitation by estimating average unit costs using a meta-analysis approach. This approach reduces the bias by giving more weight to cost estimates with lower standard errors. Second, not all of the studies included in our analysis came from representative samples of facilities.

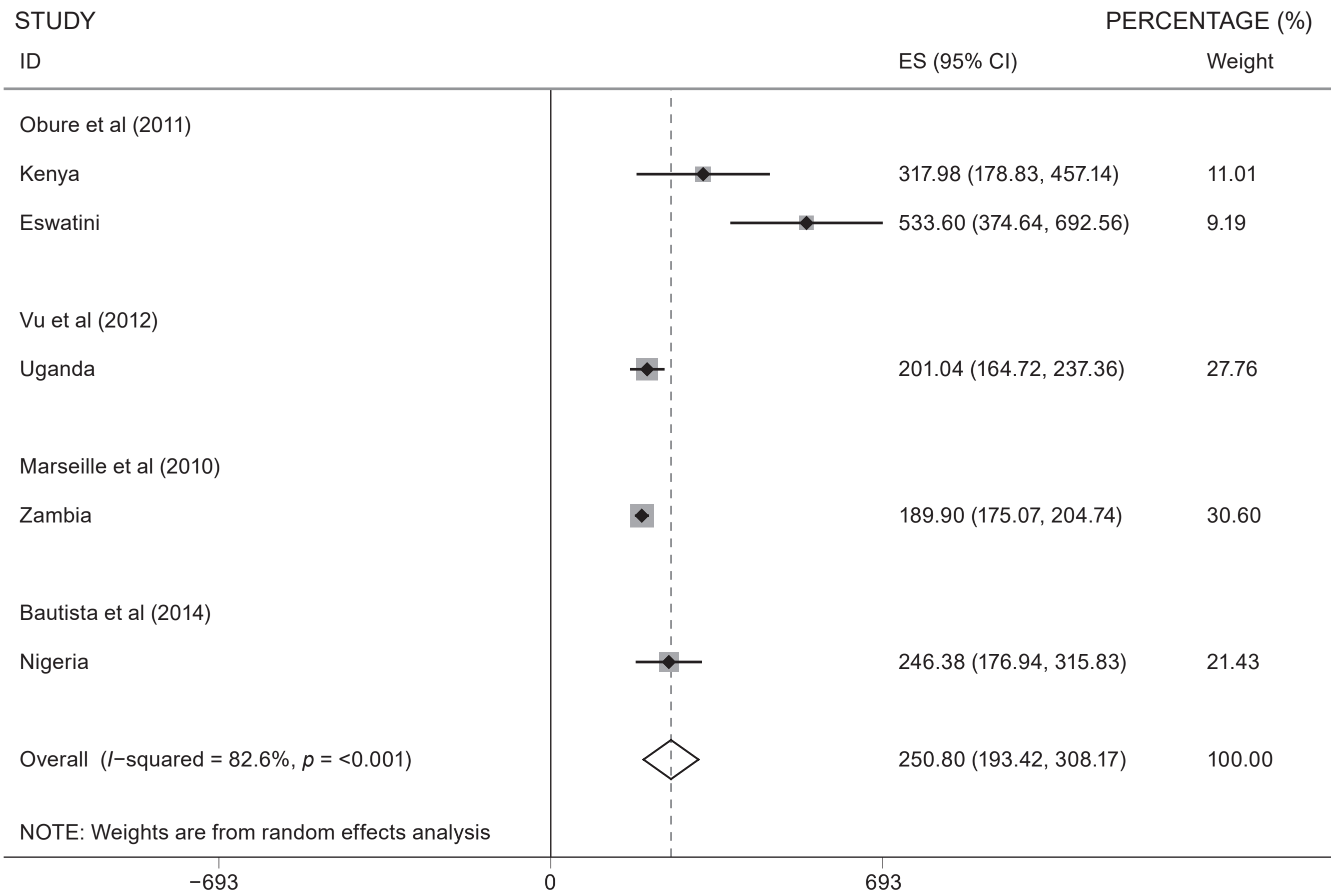

Figure 1: Estimation of ART average unit costs

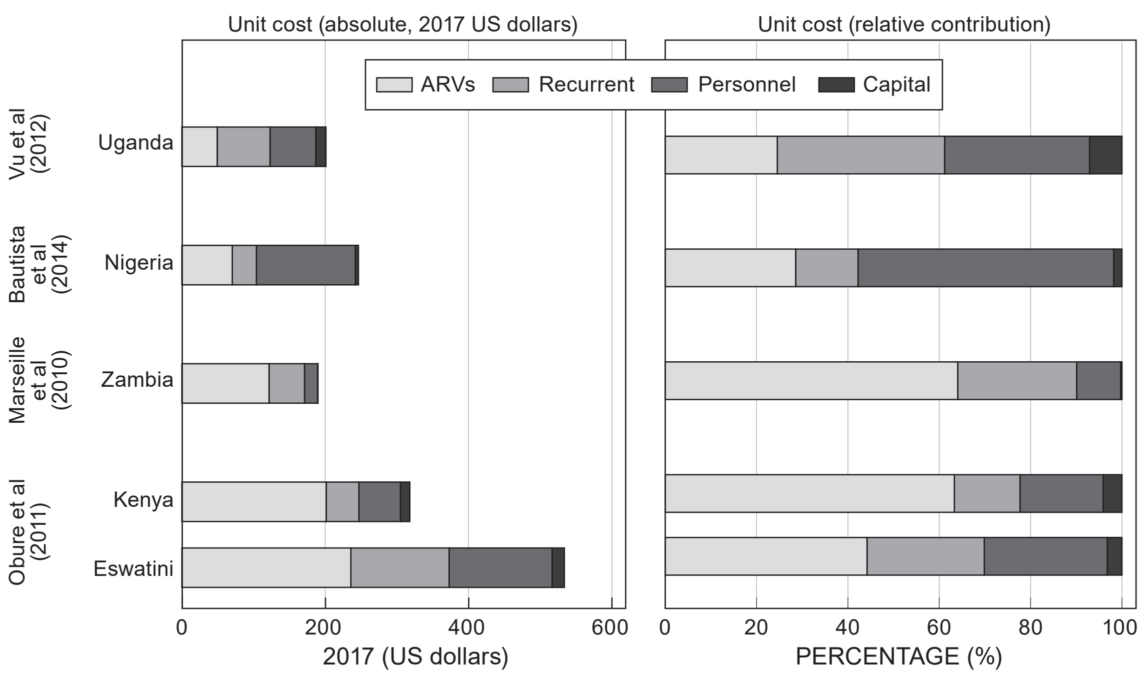

Figure 2: ART unit cost breakdown by study and country

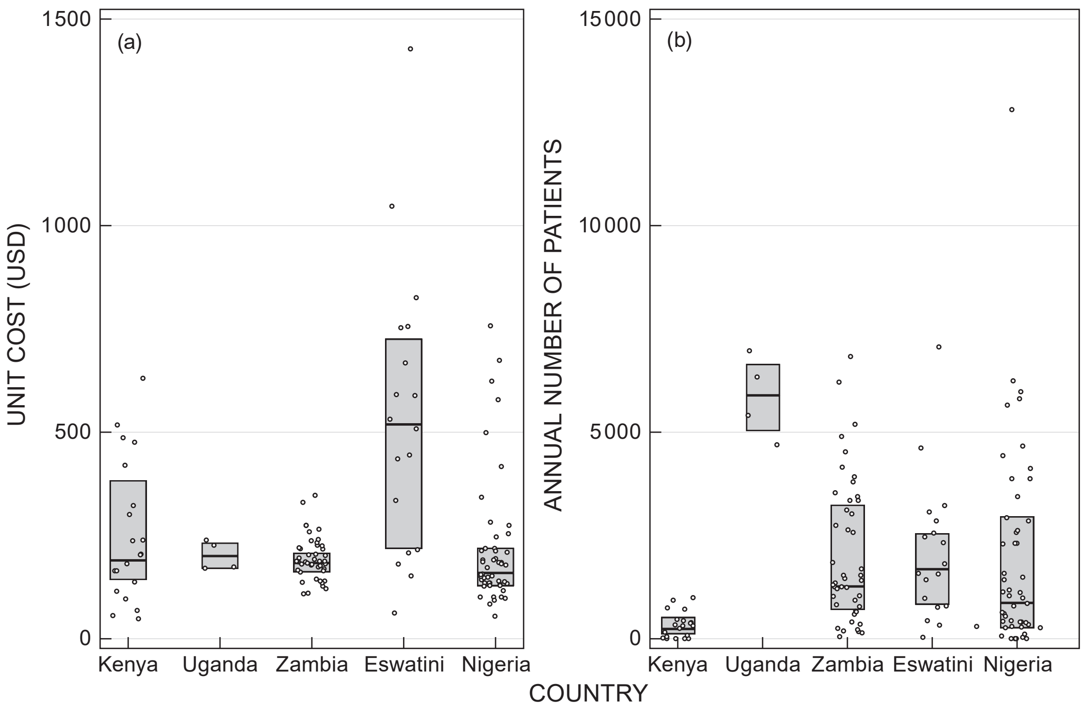

Figure 3: Variation in ART unit costs and scale by country

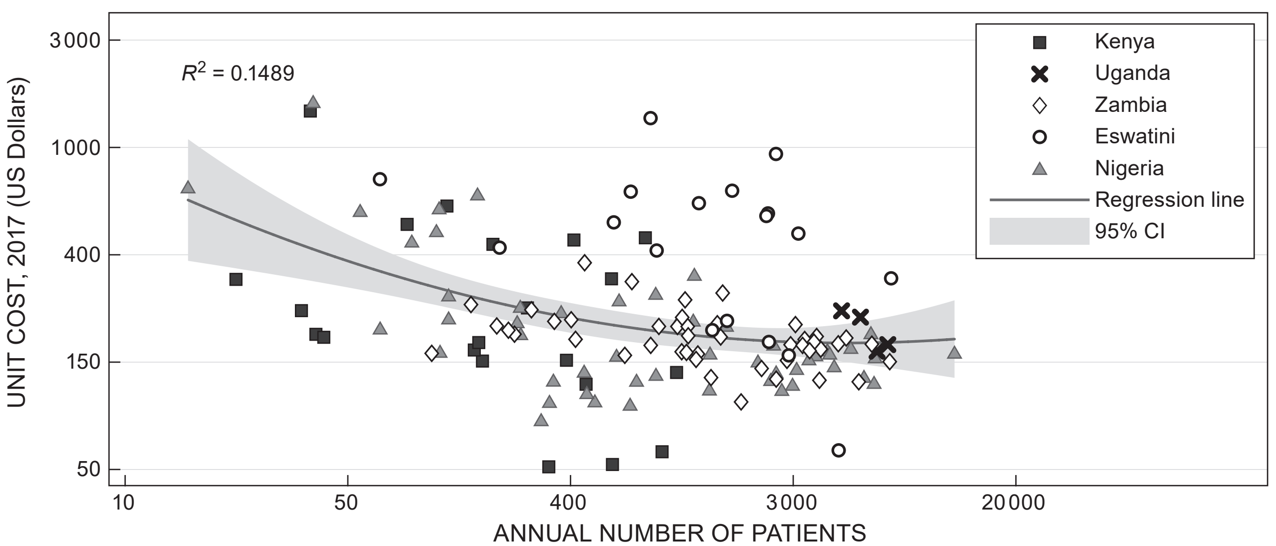

Figure 4: Relationship between ART unit costs and scale

For example, the study from Uganda (Vu et al., 2016) included a very small sample of sites and is therefore, not representative of ART costs for that particular country. For this particular case, we could not determine the extent to which the cost we estimated can be extrapolated to most facilities within that country. This is not the case for all the other studies included. One of them collected information from a representative sample of facilities in Nigeria (Bautista-Arredondo, Colchero, et al., 2018), while the Zambian study collected information from all the clinics operated by the Zambian Centre for Infectious Disease Research in Zambia (CIDRZ) which provides a complete overview of this type of service delivery model. The study conducted within Kenya and Eswatini collected information retrospectively from a sample of three different services delivery models of HIV services in these countries (Obure et al., 2015).

Third, we excluded above site costs from the analysis given that these type of costs were measured in one of the studies included in the sample only (Marseille et al., 2012). Above service level activities can contribute substantially to overall costs of services — particularly fixed costs (Johns, Baltussen, & Hutubessy, 2003). Given the importance of such costs, future costing studies should focus specifically on these costs.

Fourth, the data included in this study are derived from different years and as such, there may be variations in costs, especially in ARV costs, due to changes in guidelines and prices of these drugs. Another factor to consider is that we were not able to separate first line and second-line ARV costs — although in some cases, second line ARV regimens represent a small proportion of clients served. To assess these limitation, future analysis should take into account changes in technology, guidelines, and costs of ARVs. It is also important to note that this work will benefit from including more recent costing studies on ART since it will improve our ability to extrapolate these costs to a variety of contexts.

Since this is a descriptive study, we were not able to identify statistically significant cost drivers. This is the first of a series of papers using pooled facility level primary data to explore unit cost variations for ART services. The analyses open the door for future research exploring multivariate approaches to unpack underlying causes of the variation on costs we observed and to generate useful information for decision makers and programme planners.

Conclusion

Our study explores the variability of ART cost linked to service delivery platform characteristics. We take advantage of a relatively large and diverse sample of clinics, allowing us to explore the unit cost variation and some potential drivers of such variation. Our results suggest that identifying the individual effects of facility-level characteristics on unit costs using econometric methods is a potentially fruitful area for future research. It is also important to consider additional potential drivers of unit cost variation at a country level. Country-specific structural factors as well as epidemic and health system variables should be explored as potential predictors of unit costs. Our approach provides additional information on ART unit costs by estimating weighted average unit costs based on a relatively large sample of facilities and with a multi-country perspective. Also, our work contributes by providing an example of how to estimate costs based on heterogeneous sources of data. Efficient resource utilisation is essential for maximising the impact of ART programmes in the current context of severely constrained resources. Policy-makers and programme planners need accurate cost information in a timely fashion to plan resource allocation and program scale-up. Our research aims to provide a proof of concept for an approach to estimate costs for ART services based on a variety of empirical costs and highlight the potential of these methods to generate robust information as more data come available.

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Appendix A

Table A1: ART unit costs by implementation characteristics and terciles of scale

Facility characteristics	Terciles of scale Mean (SD)		
	Low scale	Middle scale	Large scale
Hospital	415 (389)	178 (92)	176 (89)
Clinics	433 (357)	382 (311)	171 (38)
Urban	430 (437)	297 (305)	159 (38)
Rural	418 (212)	226 (129)	178 (75)
Public	445 (422)	269 (244)	174 (75)
Private	381 (200)	220 (170)	172 (41)