CME

Cost of Differentiated HIV Antiretroviral Therapy Delivery Strategies in Sub-Saharan Africa: A Systematic Review

D. Allen Roberts, MPH,^a Nicholas Tan, BS,^b Nishaant Limaye, BA,^b Elizabeth Irungu, MBChB, MPH,^b and Ruanne V. Barnabas, MBChB, DPhil^{a.b.c}

Background: Efficient and scalable models for HIV treatment are needed to maximize health outcomes with available resources. By adapting services to client needs, differentiated antiretroviral therapy (DART) has the potential to use resources more efficiently. We conducted a systematic review assessing the cost of DART in sub-Saharan Africa compared with the standard of care.

Methods: We searched PubMed, Embase, Global Health, EconLit, and the grey literature for studies published between 2005 and 2019 that assessed the cost of DART. Models were classified as facility-vs. community-based and individual- vs group-based. We extracted the annual per-patient service delivery cost and incremental cost of DART compared with standard of care in 2018 USD.

Results: We identified 12 articles that reported costs for 16 DART models in 7 countries. The majority of models were facility-based (n = 12) and located in Uganda (n = 7). The annual cost per patient within DART models (excluding drugs) ranged from \$27 to \$889 (2018 USD). Of the 11 models reporting incremental costs, 7 found DART to be cost saving. The median incremental saving per patient per year among cost-saving models was \$67. Personnel was the most common driver of reduced costs, but savings were sometimes offset by higher overheads or utilization.

Conclusions: DART models can save personnel costs by task shifting and reducing visit frequency. Additional economic evidence from community-based and group models is needed to better understand the scalability of DART. To decrease costs, programs will need to match DART models to client needs without incurring substantial overheads.

Key Words: cost, antiretroviral therapy, differentiated care, Africa, HIV

(J Acquir Immune Defic Syndr 2019;82:S339–S347)

INTRODUCTION

In sub-Saharan Africa, over 25 million people are living with HIV of whom only 60% are on life-saving antiretroviral therapy (ART).¹ Although additional scale-up of ART is needed, donor funding is expected to remain flat or decline.² Thus, efficient and scalable models for ART delivery are needed to maximize health outcomes with available resources and reduce ongoing transmission. These strategies must increase access to high-quality care and ensure long-term retention while addressing challenges such as health care worker shortages, clinic crowding, and other resource constraints.³

Differentiated service delivery (DSD) is "a clientcentered approach that simplifies and adapts HIV services across the [HIV care] cascade, in ways that both serve the needs of [people living with HIV] better and reduce unnecessary burdens on the health system."⁴ Differentiated ART (DART) models may alter the provider, intensity, location, or frequency of ART services for specific populations.⁵ Rather than a "one-size-fits-all" approach, DART models strive to allocate resources more effectively by tailoring delivery strategies to the needs of diverse groups of clients. DART models have been implemented across sub-Saharan Africa that differ from standard clinic-based care and are often targeted to stable patients (eg, with undetectable viral loads) on ART.^{6,7} These approaches are classified into either group-based, in which the care of multiple clients is coordinated, or individual models.8 Models can be further classified into facility-based models that leverage existing infrastructure but tailor treatment services to different subgroups and community-based models that deliver ART closer to clients (Fig. 1). Examples of DART models include multimonth prescribing, task shifting, community drug distribution points, and adherence clubs.

With an increasing number of models available, countries must assess factors such as client preference, quality of care, scalability, and efficiency to develop national strategies. Because DART models often require fewer professional staff and fewer, faster clinic visits, these models have the potential to be cost-saving compared with more intensive traditional models; however, it is unknown how often DART models actually decrease costs in practice. Cost is a key outcome in implementation science frameworks and directly affects intervention acceptability and adoption.^{9–11} In the context of limited funding for HIV programs,¹² the evidence on the cost of implementing differentiated models for ART delivery is necessary to inform policymakers deciding how to improve ART coverage while operating

J Acquir Immune Defic Syndr • Volume 82, Supplement 3, December 2019

From the ^aDepartments of Epidemiology; ^bGlobal Health; and ^cMedicine, University of Washington, Seattle, WA.

This work was funded by a grant from the Bill & Melinda Gates Foundation (OPP1152764). D.A.R. is supported by the National Institutes of Health/ Health and Human Services T32 GM007266/GM/NIGMS.

Data from this manuscript were presented at the 22nd International AIDS Conference (AIDS 2018; July 23–27, 2018; Amsterdam, Netherlands). The authors declare no conflicts of interest.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.jaids.com).

Correspondence to: Ruanne V. Barnabas, MBChB, DPhil, University of Washington, Global Health and Medicine, Epidemiology International Clinical Research Center, HMC # 359927, 325 9th Avenue, Seattle, WA 98104-2499 (e-mail: rbarnaba@uw.edu).

Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

		₩НΟ							
	_	INDIVIDUAL	GROUP						
	FACILITY	Facility-Based Individual Models	Facility-Based Group Models						
RE		 Fast Track ART Refills Appointment Spacing Multi-Month Scripting and Dispensing 	 Facility ART Refill Group Facility-Based Adherence Group Facility Teen Clubs 						
WHERE	ТΥ								
3	OMMUNITY	Community-Based Individual Models	Community-Based Group Models						

FIGURE 1. Differentiated ART delivery framework (courtesy of ICAP at Columbia University⁴⁷).

under constrained budgets. Our overall aim was to assess the cost of DART services compared with the standard of care. To address this aim, we conducted a systematic review to assess and summarize the available evidence for the cost of DART models in sub-Saharan Africa.

METHODS

We conducted this review following the Cochrane Collaboration and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.¹³

Eligibility Criteria

We considered articles with study data from 2005 or later describing the cost of differentiated ART models implemented in sub-Saharan Africa. Eligible DART models altered the service provider (eg, task shifting), location of services (eg, community-based ART delivery), or frequency of ARV (antiretroviral drug) refills (eg, multi-month prescribing) compared with standard of care. We included studies that collected primary costing data; modeling studies without an empirical costing component were excluded. We restricted our review to articles reporting annual per-patient treatment costs and/or annual incremental per-patient treatment costs compared with standard of care. We extracted costs as implemented; modeled scenarios of staff substitution, price changes, or increased efficiency were excluded. We included costs from the provider perspective; therefore, our review does not include costs to the recipient of care. The review focuses on DART delivery models and does not include studies comparing laboratory monitoring procedures (eg, CD4 vs. viral load testing) and client support.

Search Strategy

We searched PubMed, Embase, Global Health Database, and EconLit for articles published between January 1, 2005, and May 23, 2019. We compiled keywords and MeSH terms related to ART, service delivery models, cost, and sub-Saharan Africa. Full search terms for each database are provided in the Tables S1–S4, Supplemental Digital Content, http://links.lww. com/QAI/B382. We hand-searched the grey literature, including conference abstracts, reports from HIV funding agencies, nongovernmental organizations, program implementers, and HIV treatment consortia websites. We also cross-referenced citations in articles included in this analysis and consulted subject matter experts to identify additional references.

Data Extraction and Analysis

Three researchers (D.A.R., N.L., and N.T.) screened titles and abstracts identified in the search. Two researchers (D.A.R. and N.L.) reviewed references identified for full-text screening. Discrepancies related to study inclusion were resolved through discussion with a third researcher (R.V.B.).

Using a standardized form, we extracted key program features, including DART classification (facility- vs. community-based and individual- vs. group-based), country, year, client eligibility criteria, provider, ARV refill frequency, location of ART services, cost estimation method, nominal annual ARV drug costs per patient, and nominal fully loaded annual treatment costs per patient. To compare costs, we first subtracted ARV drug costs from total ART costs due to sharp declines in drug prices over the review period (see Figure S1, Supplemental Digital Content, http://links.lww.com/QAI/ B382). We then inflated the remaining costs to 2018 US dollars (USD) using US gross domestic product implicit price deflators.¹⁴ We also report incremental costs (when available) in 2018 USD by subtracting the annual treatment cost per patient per year (excluding drugs) under standard of care from that under DART. For studies describing multiple models, we reported results from each program separately.

RESULTS

Our search identified 2328 records, of which 673 were removed as duplicates (Fig. 2). Of the 1655 records remaining, we assessed 68 full-text articles for eligibility. Of these, we included 12 articles describing 16 DART models in the review (Table 1). Models were most commonly reported from Uganda (7 models) and South Africa (4 models). Two studies (describing 4 models) included data from 2016, or later. Most studies estimated annual costs per patient by multiplying unit costs by the quantities of resources utilized over 12 months; by contrast, one study divided the total cost incurred in a calendar year by the total number of patients in care at midyear.¹⁵ Among reported models, drug and nondrug costs reported for both DART models and comparator models declined over time in nominal and real USD, respectively (see Figs. S1-S3, Supplemental Digital Content, http://links.lww. com/QAI/B382). The annual cost per patient within DART models (excluding drugs) ranged from \$27 to \$889 (2018 USD). Of the 11 models reporting incremental costs, 7 found

S340 | www.jaids.com

Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

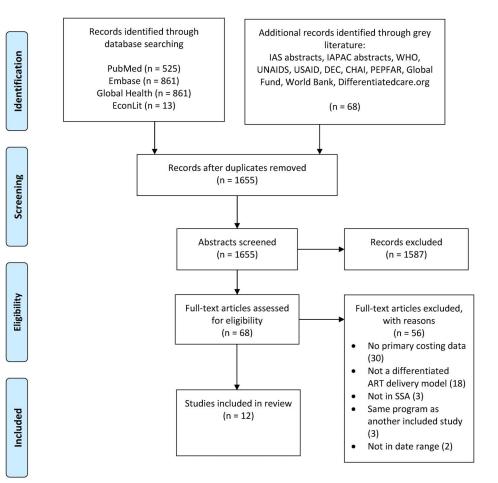


FIGURE 2. PRISMA¹³ flow diagram for the selection of studies on the cost of differentiated ART delivery strategies in sub-Saharan Africa.

DART to be cost-saving (Table 2, see Fig. S4, Supplemental Digital Content, http://links.lww.com/QAI/B382). The median incremental savings per patient per year among costsaving models was \$67, whereas the median incremental cost per patient per year among DART models with higher costs compared with standard of care was \$56 (2018 USD).

Facility-Based Individual Models

Eleven of the 16 models identified in the review are classified as facility-based individual models (Table 1). Eight analyses examined task-shifting. Six of these compared task shifting from doctors to either nurses, pharmacists, or both.¹⁶⁻²¹ In 2 of these studies, nurse-led care occurred after referral to a lower-tier health facility.^{19,21} A study from South Africa by Foster et al. involved task shifting from pharmacists to either nurses or indirectly-supervised pharmacist assistants, and another model from Malawi (Prust et al) described dispensing by health surveillance assistants instead of a nurse or pharmacy staff.^{22,23} Three models increased the drugprescribing interval from 1 to 3 months.^{23,24} Of these, 1 program in Malawi (Prust et al²³) additionally enabled stable clients to alternate clinical consultations with refill-only visits (fast-tracked refills). Six models explicitly included only stable clients (although definitions varied),16-19,21,23 one model analyzed costs for both stable clients as well as clients initiating ART,¹⁷ and the rest did not specify client eligibility criteria.^{15,18,22,24}

The annual per-patient HIV treatment costs reported by included studies are shown in Table 2. In an analysis from Malawi of multi-month prescribing and fast-track refills (Prust et al²³), the cost per patient (excluding drugs) in 2018 USD was estimated to be \$28 and \$27, respectively. By contrast, a 2012 study in Uganda of a nurse-driven stream-lined ART delivery found costs (excluding drugs) of \$889 (as observed, which included low volumes during study initiation) and \$494 (at steady state, once full enrollment had been achieved) per patient per year.¹⁸ This study had high salaries due to the employment of research staff in the provision of care; modeled scenarios involving government personnel and increased efficiency projected costs as low as \$236 (2018 USD, excluding ARVs) and \$143 (without viral load testing).¹⁸

Eight studies of facility-based individual models reported incremental costs with respect to standard of care. Of these, 4 models reported reduced costs in the DART model due to lower personnel costs, which were achieved through task shifting to a lower cadre in 2 models,^{16,21} reducing visit frequency in 1 model (Prust et al,²³ multi-month prescribing), and both in 1 model (Prust et al,²³ fast-track refills). The

Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

www.jaids.com | S341

Author (Dub Veer)	Model	Comit	Study	DART Fligibility Critoria	D	E ₂	I/*
(Pub Year)	Description	Country	Years	Eligibility Criteria	Provider	Frequency	Location
Babigumira et al (2011) ¹⁶	Task shifting	Uganda	2005–2007	Facility-based individual Stable clients defined based on CD4, adherence, retention, disclosure to partner, and clinical status	Pharmacy nurse vs. doctor	Monthly	Regional HIV treatment cente
Barton et al (2013) ¹⁷	Task shifting	South Africa	2007–2010	Cohort 1 = CD4 < 350, not on ART; cohort 2 = on ART \ge 6 months	Nurse vs. doctor	Monthly	Primary care clinic
Foster and McIntyre (2012) ²²	Task shifting	South Africa	2009–2010	None given	Indirectly supervised pharmacist assistant vs. nurse	Monthly for 1 yr, then every 2 mo	Primary care clinic
Jain et al (2015) ¹⁸	Task shifting	Uganda	2011–2015	Patients with CD4 \geq 350 and asymptomatic clinical status	Nurse instead of doctor	Monthly for first 2 mo, then every 3 mo	Health center
Johns et al (2014) ²⁰	Task shifting	Ethiopia	2008–2009	None given	Nurse or clinical officer vs. doctor for treating drug side effects and switching regimens	Not specified	Hospitals and health centers
Johns and Baruwa (2016) ¹⁹	Down-referral and task shifting	Nigeria	2010-2012	ART for at least 1 year	Nurse/pharmacist at spoke facility vs. doctor at hub facility	Not specified	Hospitals (hub) an health centers (spoke)
Long et al (2011) ²¹	Down-referral and task shifting	South Africa	2008–2009	Stable clients defined based on retention, clinical status, CD4 count, and viral load	Nurses instead of doctor	Every 2 mo	Hospital or primar health clinic
Prust et al (2017) ²³	Multi-month scripting	Malawi	2016	Stable clients defined based on age, retention, clinical status, adherence, and viral load	Consultation by nurse or clinician; dispensing by pharmacist	Every 3 mo instead of monthly	Hospital, health center, or clini
Prust et al (2016) ²³	Fast-track refills	Malawi	2016	Stable clients defined based on age, retention, clinical status, adherence, and viral load	Consultation by a nurse or clinician; dispensing by a health surveillance assistant	Every 3 mo instead of monthly	Hospital, health center, or clini
Shade et al (2018) ²⁴	Multi-month scripting	Uganda, Kenya	2015–2016	All HIV-positive patients in study communities	Nurse-driven care with physician consultation if necessary	Every 3 mo instead of monthly	Health facilities
Vu et al (2017) ¹⁵	Task shifting (Uganda cares)	Uganda	2012	None given Community-based individual	Nurse-driven care with physician referral	Every 1-2 mo	Health facilities
Jaffar et al $(2009)^{25}$	Home-based delivery	Uganda	2005–2009	None given	Community health workers supported by counsellors and medical officers	Monthly	Home
Vu et al (2016) ¹⁵	Community distribution points (TASO)	Uganda	2012	Stable clients	Nurses and expert clients with supervision by doctors	Every 2-3 mo	Community locations
Vu et al (2016) ¹⁵	Community-based delivery (Kitovu mobile)	Uganda	2012	None given	Expert clients with supervision by doctors	Every 1–2 mo	Community locations
				Facility-based group			
Bango et al (2016) ³⁰	Adherence clubs	South Africa	2007–2011	Stable clients defined based on retention, CD4 count, viral load, and clinical status	Groups of 25–30 patients receive symptom screening, education, and medication refills from lay counsellor. Annual clinical check-ups done by nurse.	Every 2 mo instead of monthly	Clinic
Prust et al (2017) ²³	Community ART groups	Malawi	2016	Community-based group Stable clients defined based on age, retention, CD4 count, viral load, and clinical status	Peer-led groups manage drug distribution and peer discussion. Nurse/clinician provides facility consultation for visiting member	One group member visits each month; each individual attends ~ every 6 months	Community locations and health facility

TARIE 1	Service Delivery	/ Models I	ncluded in	the S	vstematic I	Review
TADLL I.	Service Deliver	/ IVIOUEIS I	nciudeu in	uic J	ystematic i	VCAICAN

 $S342 \mid \mathsf{www.jaids.com}$

Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

Author (Pub Year)	Model Description	Country	USD Year	Annual DART Cost per Patient (Nominal USD)	Annual DART Cost per Patient, excluding ARVs (2018 USD)	Annual Incremental Cost per Patient (DART–Comparator) (2018 USD)*	Drivers of Incremental Cost
				Facility-based i	ndividual		
Babigumira et al (2011) ¹⁶	Task shifting	Uganda	2009	\$496	\$294	-\$132	Personnel
Barton et al $(2013)^{17}$	Task shifting	South Africa	2009	\$400 (cohort 1); \$481 (cohort 2)	\$326 (cohort 1); \$233 (cohort 2)	\$101 (cohort 1); \$69 (cohort 2)	Personnel, visit length and frequency, start- up, supervision
Foster and McIntyre (2012) ²²	Task shifting	South Africa	2010	NA	ISPA: \$71 nurse- driven: \$114	ISPA vs. pharmacist: \$12 nurse-driven vs. pharmacist: \$56	Number of visits, personnel
Jain et al (2015) ¹⁸	Task shifting	Uganda	2012	\$987 (baseline), \$628 (steady state)	\$889 (baseline), \$494 (steady state)	NA	Personnel, lab testing
Johns et al (2014) ²⁰	Task shifting	Ethiopia	2011	\$216	\$106	\$8	Reduced personnel costs offset by higher costs for training, supervision, and drugs
Johns and Baruwa (2016) ¹⁹	Down-referral and task shifting	Nigeria	2011	\$265 (site 1); \$324 (site 2)	\$165 (site 1), \$247 (site 2)	\$62 (site 1), -\$166 (site 2)	Personnel
Long et al $(2011)^{21}$	Down-referral and task shifting	South Africa	2009	\$486	\$260	-\$91	Personnel, lab tests, fixed costs
Prust et al $(2017)^{23}$	Multi-month scripting	Malawi	2016	\$121	\$28	-\$15	Personnel
Prust et al $(2017)^{23}$	Fast-track refills	Malawi	2016	\$121	\$27	-\$15	Personnel
Shade et al (2018) ²⁴	Multi-month scripting	Uganda, Kenya	2016	\$270 (Uganda), \$309 (Kenya)	\$166 (Uganda); \$178 (Kenya)	NA	NA
Vu et al ¹⁵	Task shifting (Uganda cares)	Uganda	2009	\$257	\$76	NA	NA
				Community-bas	ed individual		
Jaffar et al (2009) ²⁵	Home-based delivery	Uganda	2008	\$793	\$438	-\$51	Personnel
Vu et al (2016) ¹⁵	Community distribution points (TASO)	Uganda	2012	\$322	\$201	NA	NA
Vu et al (2016) ¹⁵	Community-based delivery (Kitovu mobile)	Uganda	2012	\$404	\$258	NA	NA
				Facility-based g	roup		
Bango et al (2016) ³⁰	Adherence clubs	South Africa	2011	\$300	\$178	-\$83	Personnel
				Community-bas	ed group		
Prust et al (2017) ²³	CAGs	Malawi	2016	\$122	\$29	-\$14	Personnel

TABLE 2. Economic Results From Included Studies

Costs are reported from the provider's perspective.

*Negative values indicate DART model costs less than comparator. Positive values indicate DART model costs more than comparator.

ISPA, indirectly-supervised pharmacist assistant; USD, United States Dollar.

incremental savings ranged from \$15 to \$132 per patient per year (2018 USD).^{16,23} All of the models reporting incremental savings were evaluated among stable clients. Babigumira et al¹⁶ found that a pharmacy-based refill program implemented in Uganda could save \$132 per patient per year (2018 USD) by task shifting from doctors to pharmacy staff. An

analysis by Long et al in South Africa found that stable patients who were down-referred from doctor-led care at central hospitals to nurses at primary health centers incurred lower personnel, laboratory testing, and non-ARV drug costs.²¹ The authors attributed increased drug and laboratory test costs to doctors' power to prescribe beyond what is

Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

www.jaids.com | S343

mandated by guidelines. In comparison, 3 studies reported higher costs in the task-shifted model, with incremental costs ranging from \$8 to \$101 per patient per year (2018 USD).^{17,20,22} In 2 of these, additional start-up and supervision costs offset the lower per-visit personnel costs in the taskshifted model.^{17,20} In a randomized trial of nurse-led vs. doctor-led care in South Africa (Barton et al¹⁷), nurse-led care resulted in more frequent and longer clinical visits. Among clients with CD4 \leq 350 who had not yet initiated ART, nurseled care also resulted in more doctor visits, which the authors hypothesized reflected closer adherence to physician referral procedures. Combined with set-up and implementation costs incurred in the nurse-led model, nurse-led care resulted in higher costs per patient for both new clients (cohort 1, \$101 per patient per year) and existing clients (cohort 2, \$69 per patient per year). A study by Foster et al²² also reported increased visit frequency in the task-shifted DART model, such that despite a lower cost per visit using either indirectlysupervised pharmacist assistants or nurses compared with pharmacists, the overall cost per year was higher. The authors predicted that annual costs in the task-shifted models, which were implemented in newer facilities, would decrease over time as the proportion of stable patients (who have longer refill intervals) increased. An analysis from Nigeria (Johns et al¹⁹) compared nurse-led care at primary health centers with doctor-led care hospitals and found mixed results, with one state (Cross Rivers) having increased costs (\$66 higher per patient per year in the decentralized model) and the other (Kaduna) having lower costs (\$166 lower per patient per year in the decentralized model). The hospital in Cross Rivers had relatively low salaries and involved counselors in treatment, reducing the personnel cost savings that could be achieved through decentralization. Furthermore, the hospital operated at high volumes, so scale economies may explain the lower per-patient costs as compared with the primary health center. By contrast, labor costs per visit in the hospital in Kaduna were over 5 times higher than those in the hospital in Cross Rivers. As a result, task shifting to nurses in the decentralized facility in Kaduna resulted in substantial savings despite increased visit frequency.

Community-Based Individual Models

Two studies described 3 community-based individual models, all in Uganda.^{15,25} In a randomized trial from 2005 to 2009, participants in the home-based arm initiated ART at a clinic and then received monthly refills and symptom screening at home, returning to the clinic every 6 months for a clinical consultation with a medical officer.²⁵ In an economic evaluation conducted concurrently with the trial, the annual cost per patient enrolled in home-based care was estimated to be \$51 (2018 USD) lower than under facility-based care. Although transportation, overheads (costs not directly attributable to a patient's medical care), and capital costs were higher in the home-based arm, these were offset by lower personnel costs using lay health workers for refills rather than nurses and clinical officers at the health facility.

Another study in Uganda described 2 community-based models of ART delivery that both used a combination of

nurses and expert clients for service delivery.¹⁵ One program implemented by The AIDS Support Organization (TASO, a Ugandan nongovernmental organization) used communitybased drug distribution points (CDDPs) for ARV refills. The CDDPs were supported by central clinics and allowed nurses and expert clients to dispense drugs to stable patients. In a more decentralized model implemented by Kitovu Mobile, mobile units of expert clients provided drug refills and adherence counseling at 111 nonfacility-based community locations in 10 districts in southwestern Uganda. This model incurred a higher annual per-patient cost (\$258 in 2018 USD, excluding drugs) than the CDDP model (\$201), which the authors attributed to increased refill location flexibility and higher numbers of visits per patient per year in the mobile unit model compared with CDDPs. The analysis did not cost facility-based care but noted that both models had comparable costs to facility-based estimates from other studies.²⁶⁻²⁹

Group Models

Two articles analyzed group-based models. A study by Bango et al³⁰ of a Médecins Sans Frontières (MSF) program in South Africa described facility-based adherence clubs that included groups of 25-30 stable clients managed by a lay counselor. Groups met at the health facility and received symptom screening and fast-tracked ART refills every 2 months as well as an annual clinical consultation with a nurse. Compared with standard facility-based care, the annual per patient cost in the adherence club was \$83 lower (2018 USD) due to lower personnel unit costs and fewer annual visits. In Malawi, Prust et al²³ described a community ART group (CAG) model for stable clients in which one client visits the health facility each month to receive a clinical consultation and to pick up ART refills for the entire group. Refills are distributed to the rest of the group in a community setting with peer-led discussion. By rotating who picks up the medication, each client travels to the facility about once every 6 months. The analysis found that the CAG model saved \$14 per client (2018 USD) per year by reducing the number of encounters with facility personnel.

DISCUSSION

In this systematic review, we found that DART models often but not always reduced costs relative to standard of care. Personnel costs were the most common driver of cost savings due to task-shifting client encounters to lower cadres or for multi-month prescribing or CAGs, reducing clinic visit frequency. However, several studies reported that taskshifted and decentralized models incurred higher costs due to increased numbers of visits or significant start-up and supervision costs. Although the importance of start-up and supervision costs may be diminished over time since implementation, these results highlight the importance of conducting empirical costing studies to both measure resource utilization and capture costs above service delivery incurred in DART programs.

Differences in the reported annual per-patient treatment cost between studies may be attributed to several factors,

S344 | www.jaids.com

Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

which restrict the generalizability of the findings. The studies included in this review took place across a range of years and countries, limiting comparability and the utility of a summary measure of the incremental cost of differentiated care. For example, the lowest cost was reported from a study in Malawi, which has lower personnel costs compared with other sub-Saharan African countries.²⁷ In addition, as HIV care has become increasingly decentralized and task shifted over time,^{31,32} lower costs (after excluding ARV drug costs) reported in more recent studies of DART models (see Fig. S2, Supplemental Digital Content, http://links.lww.com/QAI/ B382) may reflect decreases in the cost of standard of care (see Fig. S3, Supplemental Digital Content, http://links.lww. com/OAI/B382). If standard of care per-patient costs are declining over time, then the potential savings per patient under DART may diminish. Nevertheless, DART implementation could still translate to substantial reductions in overall spending if models can be successfully scaled to a large number of patients or if improved retention and adherence can impact ongoing transmission and prevent new HIV cases. A modeling study estimated that widespread implementation of DART models based on age and clinical stability could save nearly 18% of costs over a 5-year period.33 Furthermore, DART models may address other health system constraints that are not necessarily reflected in unit costs, such as human resource shortages and clinic crowding.34

This review also identified several evidence gaps. The majority of studies reported care models for stable clients, but DART models are also needed for unstable patients who could benefit from more intensive care as well as for key populations who might benefit from alternative service delivery strategies.³⁵ Several models did not report client eligibility criteria or client characteristics, which limits our understanding of the potential generalizability and scalability of the model. The 2 studies that evaluated multi-month prescribing only considered intervals of up to 3 months, whereas the WHO guidelines recommend intervals of up to 6 months for stable clients.³⁶ Economic evaluations from ongoing studies of 6-month dispensing intervals will help fill this gap.^{37,38} We identified relatively few community-based individual models that spanned a spectrum of decentralization of ART delivery, from home to CDDPs. Health systems considering community-based ART delivery will need to optimize the tradeoff between accessibility and cost of implementation, which will vary by context and deserves evaluation. In addition, we found only 2 group-based models that reported costs, indicating that additional economic evidence is needed to inform scale-up of such models. The per-patient cost of CAGs in Malawi was similar to fast-tracked refills and multi-month prescribing, but only 6% of eligible patients were enrolled in CAGs compared with over 70% in the other 2 models.²³ Although several studies have demonstrated high retention in pilot studies of group-based models,^{39,40} a recent randomized trial reported high dropout from club-based care within 2 years of enrollment.⁴¹ Assessing the cost-effectiveness of group-based models will require further research into scalability and long-term sustainability.

This review has several limitations. Although most studies of the incremental cost of DART models in this review found lower costs under DART implementation, it is possible that findings of higher costs of DART models are less likely to be published. Our review focused only on provider-level costs, but DART models also can impact client costs and outcomes. A previous review found that all identified studies reported decreased client costs in DART models compared with standard of care.⁷ Decisions about DART implementation must consider client benefits in addition to provider costs. Cost-effectiveness analyses should consider how the benefits of DART are distributed across the population to ensure equity in access to high-quality HIV care.⁴² Finally, differences in costs across included studies could reflect variation in methodology and reporting practices. Standardized methods for estimating and reporting the cost of HIV programs are needed to improve the comparability and utility of cost data.43 Using these data, facilities and programs can tailor DART models for their patient population and context. In addition to routine monitoring of program outcomes indicators,^{44,45} we recommend programs collect a minimum economic data set, including above servicedelivery costs such as supervision, administration, and training, and report key indicators of cost and efficiency (Table 3). These data also have the potential to inform budget impact analyses.46

The results from this review have implications for future implementation science studies. Researchers and program implementers designing DART models should consider factors such as personnel cadre and refill interval to maximize ART service efficiency. The dearth of economic evidence from community- and group-based models hinders comparisons with facility-based individual approaches. When

	Cost Inputs			
Category	Examples	Program Scale	Cost Indicators	
Personnel	Clinical service providers, outreach workers, community mobilizers, program administrators, data and IT staff	Client eligibility criteria	Average number of clinical encounters per client per year	
		Participant characteristics	Average clinical encounter time	
		Number of eligible clients	Average client wait time	
Recurrent	Drugs, laboratory tests, fuel, recurrent training	Number of clients enrolled in model	Average cost to client per clinical encounter AVERAGE ANNUAL COST PER CLIENT	
Capital	Laboratory equipment, vehicles, start-up costs			
Patient costs	Transportation, out-of-pocket expenses, lost work time			

Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

www.jaids.com | S345

feasible, head-to-head comparisons of DART models can help decision makers select efficient strategies for local contexts. Finally, resource utilization should be compared with health outcomes in economic evaluations to identify cost-effective service delivery strategies.

In conclusion, the majority of economic evidence for DART models comes from facility-based individual models. DART models can save personnel costs by task shifting and reducing visit frequency, but these savings may be offset by increased start-up and supervision costs. Additional economic evidence from community-based and group models is needed to better understand the scalability and sustainability of differentiated ART delivery.

ACKNOWLEDGMENTS

The authors thank Dr. Miriam Rabkin and Dr. Wafaa El-Sadr for scientific input and guidance, Diana Louden for assistance in designing the search strategy, and the Bill & Melinda Gates Foundation for support.

REFERENCES

- UNAIDS. Global HIV and AIDS Statistics: 2018 Fact Sheet; 2018. Available at: http://www.unaids.org/en/resources/fact-sheet. Accessed April 11, 2019.
- Henry J Kaiser Family Foundation and UNAIDS. Donor Government Funding for HIV in Low- and Middle-Income Countries in 2018; 2019. Available at: http://files.kff.org/attachment/Report-Donor-Government-Funding-for-HIV-in-Low-and-Middle-Income-Countries-in-2018.
- Boyd MA, Cooper DA. Optimisation of HIV care and service delivery: doing more with less. *Lancet.* 2012;380:1860–1866.
- Grimsrud A, Bygrave H, Doherty M, et al. Reimagining HIV service delivery: the role of differentiated care from prevention to suppression. J Int AIDS Soc. 2016;19:21484.
- Duncombe C, Rosenblum S, Hellmann N, et al. Reframing HIV care: putting people at the centre of antiretroviral delivery. *Trop Med Int Health.* 2015;20:430–447.
- Davis N, Kanagat N, Sharer M, et al. Review of differentiated approaches to antiretroviral therapy distribution. *AIDS Care*. 2018;30:1010–1016.
- Hagey JM, Li X, Barr-Walker J, et al. Differentiated HIV care in sub-Saharan Africa: a scoping review to inform antiretroviral therapy provision for stable HIV-infected individuals in Kenya. *AIDS Care*. 2018;30:1477–1487.
- Grimsrud A, Barnabas RV, Ehrenkranz P, et al. Evidence for scale up: the differentiated care research agenda. J Int AIDS Soc. 2017;20(suppl 4):22024.
- Damschroder LJ, Aron DC, Keith RE, et al. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implement Sci.* 2009;4:50.
- Proctor E, Silmere H, Raghavan R, et al. Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda. *Adm Policy Ment Heal Ment Heal Serv Res.* 2011;38:65–76.
- Padian NS, Holmes CB, McCoy SI, et al. Implementation science for the US president's emergency plan for AIDS relief (PEPFAR). JAIDS J Acquir Immune Defic Syndr. 2011;56:199–203.
- Global Burden of Disease Health Financing Collaborator Network. Spending on health and HIV/AIDS: domestic health spending and development assistance in 188 countries, 1995-2015. *Lancet.* 2018; 391:1799–1829.
- Moher D, Liberati A, Tetzlaff J, et al; PRISMA Group. Preferred reporting Items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009;6:e1000097.
- U.S. Energy Information Administration. GDP Implicit Price Deflator; 2019. Available at: https://www.eia.gov/opendata/qb.php? category=1039997&sdid=STEO.GDPDIUS.A. Accessed June 7, 2019.
- Vu L, Waliggo S, Zieman B, et al. Annual cost of antiretroviral therapy among three service delivery models in Uganda. *J Int AIDS Soc.* 2016; 19(5 suppl 4):20840.

Babigumira JB, Castelnuovo B, Stergachis A, et al. Cost effectiveness of a pharmacy-only refill program in a large urban HIV/AIDS clinic in Uganda. van Baal P, ed. *PLoS One.* 2011;6:e18193.

- Barton GR, Fairall L, Bachmann MO, et al. Cost-effectiveness of nurseled versus doctor-led antiretroviral treatment in South Africa: pragmatic cluster randomised trial. *Trop Med Int Health.* 2013;18:769–777.
- Jain V, Chang W, Byonanebye DM, et al. Estimated costs for delivery of HIV antiretroviral therapy to individuals with CD4+ T-cell counts >350 cells/uL in rural Uganda. *PLoS One.* 2015;10:e0143433.
- Johns B, Baruwa E. The effects of decentralizing anti-retroviral services in Nigeria on costs and service utilization: two case studies. *Health Policy Plan.* 2016;31:182–191.
- Johns B, Asfaw E, Wong W, et al. Assessing the costs and effects of antiretroviral therapy task shifting from physicians to other health professionals in Ethiopia. J Acquir Immune Defic Syndr. 2014;65:e140–e147.
- Long L, Brennan A, Fox MP, et al. Treatment outcomes and costeffectiveness of shifting management of stable ART patients to nurses in South Africa: an observational cohort. Ford N, ed. *PLoS Med.* 2011;8: e1001055.
- Foster N, McIntyre D. Economic evaluation of task-shifting approaches to the dispensing of anti-retroviral therapy. *Hum Resour Health.* 2012;10:32.
- 23. Prust ML, Banda CK, Nyirenda R, et al. Multi-month prescriptions, fasttrack refills, and community ART groups: results from a process evaluation in Malawi on using differentiated models of care to achieve national HIV treatment goals. J Int AIDS Soc. 2017;20(suppl 4):21650.
- Shade SB, Osmand T, Luo A, et al. Costs of streamlined HIV care delivery in rural Ugandan and Kenyan clinics in the SEARCH Studys. *AIDS*. 2018;32:2179–2188.
- Jaffar S, Amuron B, Foster S, et al. Rates of virological failure in patients treated in a home-based versus a facility-based HIV-care model in Jinja, southeast Uganda: a cluster-randomised equivalence trial. *Lancet.* 2009; 374:2080–2089.
- Menzies NA, Berruti AA, Berzon R, et al. The cost of providing comprehensive HIV treatment in PEPFAR-supported programs. *AIDS*. 2011;25:1753–1760.
- Tagar E, Sundaram M, Condliffe K, et al. Multi-country analysis of treatment costs for HIV/AIDS (MATCH): facility-level ART unit cost analysis in Ethiopia, Malawi, Rwanda, South Africa and Zambia. *PLoS One.* 2014;9:e108304.
- Galárraga O, Wirtz VJ, Figueroa-Lara A, et al. Unit costs for delivery of antiretroviral treatment and prevention of mother-to-child transmission of HIV. *Pharmacoeconomics*. 2011;29:579–599.
- Larson BA, Bii M, Henly-Thomas S, et al. ART treatment costs and retention in care in Kenya: a cohort study in three rural outpatient clinics. *J Int AIDS Soc.* 2013;16:18026.
- Bango F, Ashmore J, Wilkinson L, et al. Adherence clubs for long-term provision of antiretroviral therapy: cost-effectiveness and access analysis from Khayelitsha, South Africa. *Trop Med Int Health.* 2016;21: 1115–1123.
- Zachariah R, Ford N, Philips M, et al. Task shifting in HIV/AIDS: opportunities, challenges and proposed actions for sub-Saharan Africa. *Trans R Soc Trop Med Hyg.* 2009;103:549–558.
- Callaghan M, Ford N, Schneider H. A systematic review of taskshifting for HIV treatment and care in Africa. *Hum Resour Health*. 2010;8:8.
- Barker C, Dutta A, Klein K. Can differentiated care models solve the crisis in HIV treatment financing? Analysis of prospects for 38 countries in sub-Saharan Africa. *J Int AIDS Soc.* 2017;20(suppl 4):21648.
- Mikkelsen E, Hontelez JAC, Jansen MPM, et al. Evidence for scaling up HIV treatment in sub-Saharan Africa: a call for incorporating health system constraints. *PLOS Med.* 2017;14:e1002240.
- 35. World Health Organization. Key Considerations for Differentiated Antiretroviral Therapy Delivery for Specific Populations: Children, Adolescents, Pregnant and Breastfeeding Women and Key Populations; 2017. Available at: https://www.who.int/hiv/pub/arv/hiv-differentiatedcare-models-key-populations/en/.
- 36. World Health Organization. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection; 2016. Available at: https://www.who.int/hiv/pub/arv/arv-2016/en/.
- 37. Fatti G, Ngorima-Mabhena N, Chirowa F, et al. The effectiveness and cost-effectiveness of 3- vs. 6-monthly dispensing of antiretroviral treatment (ART) for stable HIV patients in community ART-refill groups

S346 | www.jaids.com

Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

in Zimbabwe: study protocol for a pragmatic, cluster-randomized trial. *Trials.* 2018;19:79.

- Hoffman R, Bardon A, Rosen S, et al. Varying intervals of antiretroviral medication dispensing to improve outcomes for HIV patients (The INTERVAL Study): study protocol for a randomized controlled trial. *Trials.* 2017;18:476.
- Decroo T, Koole O, Remartinez D, et al. Four-year retention and risk factors for attrition among members of community ART groups in Tete, Mozambique. *Trop Med Int Heal.* 2014;19:514–521.
- Vandendyck M, Motsamai M, Mubanga M, et al. Community-based ART resulted in excellent retention and can leverage community empowerment in rural Lesotho, a mixed method study. *HIV/AIDS Res Treat Open J.* 2015;2:44–50.
- 41. Hanrahan CF, Schwartz SR, Mudavanhu M, et al. The impact of community- versus clinic-based adherence clubs on loss from care and viral suppression for antiretroviral therapy patients: findings from a pragmatic randomized controlled trial in South Africa. Newell ML, ed. *PLoS Med.* 2019;16:e1002808.

- Verguet S, Kim JJ, Jamison DT. Extended cost-effectiveness analysis for health policy assessment: a tutorial. *Pharmacoeconomics*. 2016;34: 913–923.
- Vassall A, Sweeney S, Kahn J, et al. Reference Case for Estimating the Costs of Global Health Services and Interventions; 2017. Available at: https:// ghcosting.org/download/pdf/UCSR%20Methodology%20FINAL.pdf.
- 44. Ehrenkranz PD, Calleja JM, El-Sadr W, et al. A pragmatic approach to monitor and evaluate implementation and impact of differentiated ART delivery for global and national stakeholders. *J Int AIDS Soc.* 2018;21: e25080.
- Reidy WJ, Rabkin M, Syowai M, et al. Patient- and program-level monitoring of differentiated service delivery for HIV. AIDS. 2017;32:1.
- 46. Bilinski A, Neumann P, Cohen J, et al. When cost-effective interventions are unaffordable: integrating cost-effectiveness and budget impact in priority setting for global health programs. *PLOS Med.* 2017;14: e1002397.
- 47. Columbia University Mailman School of Public Health. *ICAP*. Available at: https://icap.columbia.edu/.