volume 25 no 12 pp 1553–1567 december 2020

Provider- and patient-level costs associated with providing antiretroviral therapy during the postpartum phase to women living with HIV in South Africa: A cost comparison of three postpartum models of care

Lucy Cunnama[1], Elaine J. Abrams[2,3], Landon Myer[4], Tamsin K. Phillips[4], Caitlin M. Dugdale[5], Andrea L. Ciaranello[5], Allison Zerbe[2], Victoria Iyun[4], Kim MacQuilkan[1], Vanessa Daries[1] and Edina Sinanovic[1]

1 *Health Economics Unit, School of Public Health & Family Medicine, University of Cape Town, Cape Town, South Africa*
2 *ICAP at Columbia University, Mailman School of Public Health, Columbia University, New York, USA*
3 *Department of Pediatrics, Vagelos College of Physicians & Surgeons, Columbia University, New York, USA*
4 *Division of Epidemiology & Biostatistics and Centre for Infectious Diseases Epidemiology & Research, University of Cape Town, Cape Town, South Africa*
5 *Division of Infectious Diseases, Medical Practice Evaluation Center, Massachusetts General Hospital, Boston, USA*

Abstract

objective To compare the unit and total costs of three models of ART care for mother–infant pairs during the postpartum phase from provider and patient's perspectives: (i) local standard of care with women in general ART services and infants at well-baby clinics; (ii) women and infants continue to receive care through an integrated maternal and child care approach during the postpartum breastfeeding period; and (iii) referral of women directly to community adherence clubs with their infants receiving care at well-baby clinics.

methods Capital and recurrent cost data (relating to buildings, furniture, equipment, personnel, overheads, maintenance, medication, diagnostic tests and immunisations) were collected from a provider's perspective at six sites in Cape Town, South Africa. Patient time, collected via time-and-motion observation and questionnaires, was used to estimate patient perspective costs and is comprised of lost productivity time, time spent travelling and the direct cost of travelling.

results The cost of postpartum ART visits under models I, II and III was US $13, US $10 and US $7 per visit for a mother–infant pair, respectively, in 2018 US$. The annual costs for the mother–infant pair utilising the average visit frequencies (a mean of 4.5, 6.9 and 6.7 visits postpartum for models I, II and III, respectively) including costs for infant immunisations, visits, medication and diagnostic tests for both mothers and infants were: I – US $222, II – US $335 and III – US $249. Sensitivity analysis to assess the impact of visit frequency on visit cost showed that Model I annual costs would be most costly if visit frequency was equalised.

conclusion This comparative analysis of three models of care provides novel data on unit costs and insight into the costs to provide ART and care to mother–infant pairs during the delicate postpartum phase. These costs may be used to help make decisions around integrated services models and differentiated service delivery for postpartum WLH and their children.

keywords cost analysis, retention, prevention of mother-to-child transmission of HIV, Sub-Saharan Africa, antiretroviral therapy, postpartum care, low/middle-income country

Sustainable Development Goals (SDGs): SDG 3 (good health and well-being), SDG 17 (partnerships for the goals)

Introduction

The last 20 years has witnessed substantial increases in the coverage of antiretroviral therapy (ART) among women living with HIV (WLH) who are pregnant and breastfeeding, with consequent declines in mother-to-child transmission (MTCT) of HIV [1]. However, there are widespread concerns about the ability of existing health services to retain postpartum WLH in care and maintain the high levels of treatment adherence required to maximise the benefits of ART for maternal and child health [2].

There is a need for innovative models of care to address these challenges. Since 2016, the WHO has suggested the use of alternative models to deliver ART ('differentiated care') to cater for patients needs, promote retention, unload clinics and promote accessibility for patients such as stable postpartum mothers [3-5]. The International AIDS (acquired immunodeficiency syndrome) Society categorises ART service delivery into four main types: 'facility-based individual models'; 'out-of-facility individual models'; 'healthcare worker-managed groups'; and 'client-managed groups' [6,7]. Some examples of specific ART delivery models within these four broad categories are as follows: fast track systems for ART collection within clinics such as in Malawi; community pharmacy collection in Nigeria; pick up points outside of healthcare facilities in the Democratic Republic of the Congo; collection by family members in Zimbabwe; teen ART clubs in Malawi and Swaziland; community adherence clubs in South Africa; and ART care integrated with other healthcare services such as for depression as is being studied in Malawi and Zimbabwe [6,8-14]. WHO and UNICEF particularly recommend supporting the adherence of mothers during the postpartum period as part of the third and fourth part, of a four-component strategic approach to the prevention of mother-to-child transmission of HIV (PMTCT) [15,16]. Explicitly, these components of the strategic approach are to prevent: 'HIV transmission from a woman living with HIV to her infant' and to provide 'appropriate treatment, care and support to mothers living with HIV and their children and families' [16].

Multiple limiting and enabling factors have been found to assist successful delivery of ART. Identified enablers from a qualitative study in South Africa are care being focused on the patient and clear support and guidance from the National Department of Health, which aids the adoption of context-specific models of care which in turn facilitate flexibility for patients [8]. Barriers include stigma and discrimination and lack of resources (such as physical space and personnel capacity due to their high workload and staff turnover) [8,17].

Although several models have been put forward, including the approaches used in this paper, the costs of these different approaches have received little attention. Two trials were conducted in the same population to examine the impact of models of care on retention and viral suppression and collect associated cost data for each model from the provider and patient's perspectives. The three models in the postpartum period were the local standard of care of referral of women to general ART services and infants to well-baby clinics (Model I – Routine Care); women and infants continue to receive care through an integrated maternal and child care approach during the postpartum breastfeeding period (Model II – Integrated Care); and referral of women directly to a community-based adherence club (CAC) and infants to well-baby clinics (Model III – Community Care). The effectiveness of these three models of care is reported in detail elsewhere [18-21]. Furthermore, the costs from this study were utilised to update the Cost-Effectiveness of Preventing AIDS Complications (CEPAC)-International and CEPAC-Pediatrics Models and inform the cost-effectiveness analysis that was undertaken and published [22]. Briefly, Model III was found to be the most effective in terms of retention of mother–infant pairs and maternal viral suppression (which was defined as HIV ribonucleic acid (RNA) <50 copies/mL) at 12 months postpartum with 84% of mother–infant pairs meeting these criteria [18-21]. Model I had a 56% and Model II had a 77% proportion of mother–infant pairs retained and virally suppressed at the 12-month mark [18-20]. Dugdale et al. (2019) found Model II to be cost-effective in comparison to Model I with an ICER of US $599 per year of life saved with the threshold being an ICER below US $903 per year of life saved [22]. Our detailed cost analysis fed into the study by Dugdale et al. (2019) and will lead into two separate upcoming papers [23,24], and for these reasons as well as the valuable content of this analysis, we felt this work necessitated a separate manuscript.

In this work, we aimed to compare the unit and total costs of three models of care for mother–infant pairs during the postpartum phase from the provider and patient's perspective.

Methods

Both the *Methods for the Economic Evaluation of Health Care Programmes* textbook and the *Reference Case for Estimating the Costs of Global Health Services and Interventions* were extensively consulted [25,26].

Parent studies

Three locally developed and policy relevant postpartum models of care were compared through two studies in South Africa: 1 – Strategies to Optimize ART Services for Maternal and Child Health (MCH-ART) study (NCT01933477; April 2013–December 2016) and 2 – Postpartum CACs to Enhance Support (PACER) study (NCT02417675; February 2015–October 2016) [18,20]. All institutions approved protocols, and there was individual written informed consent.

The MCH-ART study was a randomised controlled trial conducted in a subdistrict of Cape Town that evaluated two approaches to postpartum care for WLH who initiated ART antenatally and their breastfed children [19]. The trial enrolled women from an observational cohort (where all WLH seeking antenatal care services who were at least 18 years of age and eligible for ART initiation) were studied from their second antenatal care visit at Site A, located in a community with a high prevalence of HIV, until their first postpartum clinic visit (further details in Appendix S1 and cited papers) who were less than 6 weeks postpartum (median of 5 days postpartum) and who had started ART during their recently completed pregnancy [18,19,27]. In order to be eligible for trial enrolment, women had to be breastfeeding their infants at the time of screening. Mother–infant pairs (n = 471) enrolled in the trial were randomised to one of two arms. The control arm (n = 238), referred to here as Model I, consisted of immediate postnatal referral to local ART services after delivery, as per standard of care and paediatric care for infants at well-baby clinics (where they would receive routine immunisations and growth monitoring as well as HIV services including early infant diagnosis using polymerase chain reaction (PCR) testing and infant antiretroviral prophylaxis with nevirapine). In the intervention arm, referred to here as Model II (n = 233), women and infants continued to receive care in co-located maternal/paediatric care integrated in Maternal and Child Health (MCH) services through the postpartum breastfeeding period at Site A. The infants in Model II received the same care at Site A that they would in the well-baby clinic. Once breastfeeding ceased, women and infants were referred to local clinics for routine care (as per Model I). We selected five referral clinics nearest to Site A, where the majority of women were referred due to proximity to their homes, for cost data collection. Guidance on preferred ART regimens and routine monitoring was equivalent for Models I and II. The primary objective of the MCH-ART study was to evaluate the composite endpoint of maternal retention in ART services and viral suppression at 12 months postpartum by trial arm [19]. These women were followed for 12 months postpartum with study measurements at 6 weeks and then at 3, 6, 9 and 12 months postpartum [19].

The PACER study enrolled 129 postpartum breastfeeding WLH who initiated ART during their recently completed pregnancy, who met local criteria for CAC membership [20,21,28]. Eligible women were offered a choice for postpartum ART care: Model I (as described above) or Model III – referral directly to a CAC with their infants receiving care at well-baby clinics. These women were followed for 12 months postpartum with study measurement visits that paralleled the MCH-ART study methods. As in the MCH-ART study, the primary objective of the PACER study was to assess the composite endpoint of maternal retention in ART services and viral suppression at 12 months postpartum. The work presented here is a detailed costing study using bottom-up methodology performed alongside the MCH-ART and PACER studies. See Table 1 for a comparison of the three models of care.

Study setting

All study activities took place in a low-income area in Cape Town with high levels of poverty and HIV prevalence [29,30]. All women received antenatal care at the same large primary care antenatal clinic (Site A). Women referred out from Site A attended sites including Sites B-F. Women in Model III (n = 84) who chose to be referred to CACs received their care at a nearby Community Centre (Site G). Facility-level cost data were collected at Sites A-F and site-level costs at Site G (Table 2). We purposively selected the five clinics that were near to Site A and that were chosen by a large proportion of women.

Utilisation

Data regarding the mean number of visits were drawn from the study data, through medical record abstraction at the facilities. All women were seen in Site A in the postpartum phase before forming part of the models I, II or III cohorts. Those under Model II were transferred out to general ART services at the end of breastfeeding or at 12 months (if breastfeeding was continued for longer than a year) for routine care (as per Model I).

Cost analysis

Cost data

When referring to costs in this paper, we are referring to the economic costs collected through the quantification of the items (for instance the amount of time spent on a task) and assigning a value (price) to these items [25]. Economic costs differ from financial costs in that they include goods that may have been donated or services that have been volunteered [26]. A unit cost refers here to the average cost of a service; that is, the ‘cost per visit per mother–infant pair’ is the average cost of a single visit for postnatal care for both the mother–infant pair [25]. We costed the entire postpartum healthcare service rather than using an incremental costing approach, using both a provider and a patient perspective [25,26]. A mixture of top-down (i.e. gross costing, allocative method for overheads and maintenance) and bottom-up (i.e. microcosting, ingredients based methods for buildings,

Table 1 Comparison of key features of the three models of care [19,28,45,46]

Category	Model I – Routine Care	Model II – Integrated Care	Model III – Community Care
Setting	Clinic-based general ART services at Primary Care Clinics (PHC) and well-baby clinics	Clinic-based services at Midwife Obstetric Unit (MOU)	Community Adherence Club (CAC) and infants at well-baby clinics
Sites	B, C, D, E, F	A (Clinic-based)	G (Community-based [clinic-based for infants])
Units of care	Individual patient	Mother–infant pairs	Groups of 25–30 patients
Patient profile	Mother–infant pairs seen together in Sites C, D, E, F. In Site B, only mothers are seen	Mother–infant pairs	Mothers
Infants	Infants seen separately in well-baby clinics for mothers attending services in Site B		Infants seen separately in at well-baby clinics for mothers attending the CAC
Key personnel	Professional nurse/staff nurse (Site F only)/ counsellors	Professional nurse who is trained as a midwife as well as in PMTCT, HIV and paediatrics/ counsellors	Lay counsellors
Frequency of visits	1-2 monthly	1-2 monthly	2-4 monthly
Frequency of clinical consultations	1-2 monthly (every visit)	1-2 monthly (every visit)	12-monthly
Emphasis of patient contacts	Detecting clinical complications	Detecting clinical complications	Treatment adherence, patient wellness
Services offered to mothers	ART adherence counselling ART dispensed Breastfeeding and infant feeding advice Family planning (contraception)	ART adherence counselling ART dispensed Breastfeeding and infant feeding advice Family planning (contraception)	ART adherence counselling ART dispensed Peer support
Services offered to infants	Infant weighing Immunisations as per the National Childhood Immunisation Schedule Nevirapine refills PCR testing Anthropometry	Infant weighing Immunisations as per the National Childhood Immunisation Schedule Nevirapine refills PCR testing Anthropometry	Infants must attend separate well-baby clinic (as with Site B)
Peer-based support	No emphasis	No emphasis	Strong emphasis
Patient self-management	Minimal emphasis	Minimal emphasis	Strong emphasis
Frequency of laboratory monitoring for stable patients	3 monthly	3 monthly	12 monthly
Management of clinical complications	On-site	On-site	Up-referral to PHC
ART packing and dispensing	Packed at the clinic pharmacy, dispensed from pharmacy or during consultations. Patients collect ART themselves.	Packed at the clinic pharmacy, dispensed during consultations. Patients collect ART themselves.	Pre-packed by central dispensing unit, dispensed at CAC visit. ART can be collected by a treatment 'buddy'

furniture, equipment, personnel, medication, diagnostic tests and immunisations) costing methods was applied [25,31].

Provider costs comprised an estimation of total and unit costs based on collection of capital and recurrent costs for postpartum WLH and their infants (Table 3).

Table 2 Sites A-G

	Site A	Site B	Site C	Site D	Site E	Site F	Site G
Predominant model of care	Model I	Model II	Model II	Model II	Model II	Model II	Model III
	Midwife Obstetric Unit - MOU (Provincial)	Clinic 1 (Non-Governmental Organisation on same grounds as MOU)	Clinic 2 (City of Cape Town)	Clinic 3 (City of Cape Town)	Clinic 4 (City of Cape Town)	Clinic 5 (City of Cape Town)	Community Centre (Community Adherence Club – CAC)
MCH-ART study	✓	✓					
PACER study	✓						✓
Provider's perspective postpartum phase costs	✓	✓	✓	✓	✓	✓	✓
Patient perspective postpartum phase non-medical direct and direct costs	✓	✓					✓
Patient perspective postpartum phase indirect costs	✓	✓	✓	✓	✓	✓	✓
Provider's perspective infant costs	✓		✓	✓	✓	✓	
Example of staff complement directly involved in postpartum care*	2 nursing assistants, 3 professional nurses (including a focal nurse), 2 counsellors	2 professional nurses, 1 counsellor	2 professional nurses, 1 counsellor, 1 administration officer	3		professional nurses, 1 counsellor	2 professional nurses, 2 clerks
1 professional nurses, 2 enrolled nurses, 1 counsellor, 2 clerks	1 professional nurse, 4 counsellors, 1 coordinator, 3 data clerks						

*Those involved directly in postpartum services who complete timesheets for the study. These staff members spend more than 0% and less than 100% of their time on postpartum services. This list excludes support staff who did not fill in timesheets, but whose time was accounted for through allocation.

Direct non-medical patient cost data were collected in questionnaire form to assess the travel costs (transport time and out of pocket payment for transport) for Models I-III from Sites A (Model I), B (Model II) and G (Model III). All of the seven sites (see Table 2) are near Site A and so travel time collected for Sites A (Model I), B (Model II) and G (Model III) were representative. Time-and-motion studies were performed to evaluate the indirect patient costs in terms of loss of productive time by patients at all 7 sites (Sites A to G, for Models I-III see Table 2). Time-and-motion studies refer to a researcher observing workflow and keeping track of the time that the patients spent in the facility including the waiting time [32]. This was done through the use of small sheets of paper attached to the patient file on which the researcher recorded the time that the patient arrived at the facility (through asking the patient), the time the folder was drawn (observed) and the time of exiting the facility (when the folder was returned by the patient on leaving the facility). Costs are presented in 2018 United States dollars (US$) and were inflated where necessary using the South African Consumer Price Index [33]. The exchange rate of 1:13.24 United States dollars to South African Rands was used for 2018 (the average exchange rate for the 2018 year). Capital costs were annuitized using a standard discount rate of 3% [25,26] and an expected number of years of useful life of 30 years for buildings and 10 years for equipment [34].

Cost measures

Capital (buildings, furniture and equipment) and recurrent (personnel, overheads and maintenance) costs were estimated separately and summed to give the total cost at the health facility. The total costs were then apportioned using the total number of postnatal visits divided by the total clinic headcount for each input to value the total postpartum phase cost under each model. For the postpartum phase, the unit cost was defined as the 'cost per visit per mother–infant pair' from delivery to cessation of breastfeeding or 12 months postpartum. We multiplied the average number of visits made by mothers by the unit 'cost per visit' to calculate a 'cost per woman', with average medication and diagnostic costs added subsequently. The postpartum unit costs used the mother–infant pair to calculate an annual 'cost per mother–infant pair', with other per person costs of the average medication (for mothers and infants), diagnostic (for mothers and infants) and infant immunisation being added subsequently.

Postnatally, the PCR for early infant diagnosis at birth, 10 and 18 weeks and 9 months was added together and divided by 12 months. For postpartum diagnostic costs under Model I and II, initial CD4, haemoglobin and creatinine, and viral load testing at 3, 6, 9 and 12 months were added together and divided by 12 months. Under Model III, once yearly haemoglobin, creatinine and viral load testing were added and divided by 12.

Medication included ART for mothers (tenofovir/emtricitabine/efavirenz) and nevirapine syrup for infants. The daily unit cost for medication was multiplied by 30 days to get the per month cost for mother and infants separately. Immunisations as per the National Department of Health's Expanded Programme on Immunisation – EPI (SA) Revised Childhood Immunisation Schedule, included the prices of Bacillus Calmette-Guérin (BCG); oral polio vaccine (OPV); rotavirus vaccine (RV); diphtheria, tetanus, acellular pertussis, inactivated polio vaccine, haemophilus influenzae type B and hepatitis B combined (DTaP-IPV-Hib-HBV); pneumococcal conjugated vaccine (PCV); and the measles vaccine according to the schedule (up to 12 months), added together and divided by 12 months (Table 4).

Cost data collection

As part of this undertaking, the sites were mapped and measured (in metres squared), and an inventory of furniture and equipment was made. All the staff that provided services during the postpartum phase under the three models completed timesheets to ascertain the percentage of their time dedicated to the various tasks for women in the postpartum phase, as well as for infants. For instance, these tasks included consulting, adherence training and educating, dispensing medication, management of services, record keeping and administration.

Salary information, patient utilisation and overhead costs, were provided by Site G, City of Cape Town and Western Cape Government Health administrators. The prices of equipment and furniture were sought from local medical equipment and furniture suppliers. Some utilisation data were sourced through the project records. The Council for Scientific and Industrial Research (CSIR) supplied building replacement costs. Diagnostic cost data were furnished by the South African National Health Laboratory Services, while immunisation and medication costs were provided by Pharmacy Services in Western Cape Government Health [35,36].

Patient costs

Patient-level data were collected in terms of direct costs, which relate to the transport costs incurred by the patients. In addition, indirect costs were collected which cover lost productivity time and transport time. These costs were collected during the MCH-ART and PACER Studies through questionnaires administered at 6 months postpartum. The questionnaires provided information that could be separated easily into the three models of care as the control arm of MCH-ART represented postpartum mother–infant pairs in Model I, the intervention arm represented postpartum mother–infant pairs in Model II and the intervention arm of PACER represented postpartum mother–infant pairs in Model III. A convenience sample of 355 consecutive women had additional information collected using a time-in-motion tool. The time-and-motion tool was used to document the time that patients spent at the seven sites in terms of productive time lost. These time-in-motion studies followed three separate postpartum mother–infant pairs, that is postpartum mother–infant pairs in Model I, II and III, respectively. A minimum wage of $1.52 per hour (for 2018) was used to calculate the cost of transport and productive time lost [37]. Income information was collected through the resource questionnaires; however, the information received was very sparse and may have biased the valuation of productivity losses and so the choice was made to use minimum wage.

Sensitivity analyses assessed the change in cost if the number of visits was equalised between the models of care, using the scenario where mother–infant pairs attended sites on a monthly basis for the year (i.e. 12 times) during the postpartum phase. In addition, we assumed that the cost for infants seen in well-baby clinics was the same whether a mother was seen in Model I or III.

Results

Costs for postpartum phase

During the postpartum phase, the mother–infant pair received care in either Model I, II or III. The unit cost of a visit for a mother–infant pair from a provider perspective was US $13, US $10 and US $7 in Models I, II and III, respectively. The average annual total costs for visits for the mother–infant pair from a provider perspective

Table 3 Impact Inventory (adapted from the Second Panel on Cost-Effectiveness in Health and Medicine [47])

Sector	Type of impact	Perspective		Notes
		Provider	Patient	
	Formal healthcare sector			
Health	*Medical costs*			
	Paid for by healthcare sector	Costs of visits were collected as well as diagnostic, immunisation and medication costs. This was done through collection of utilisation data/ quantities as well as prices	Not collected	Timesheets were used to quantify healthcare provider time spent on tasks
	Informal healthcare sector			
Health	Patient time costs	N/A	Patient time for waiting was collected through time-in-motion	
	Unpaid caregiver time costs	N/A	Not collected	
	Transport costs	N/A	Direct transport costs collected through questionnaires Indirect transport costs linked to time travelling to and from the clinic was also included	
	Non-healthcare sectors			
Productivity	Labour market earnings lost	N/A	Attempt to collect via a questionnaire however very sparsely completed	
	Cost of unpaid lost productivity due to illness/ inability to work	N/A	Calculated using the minimum wage ($1.52 per hour) [37]	This method has the draw-back in that the women attending are likely to earn less income on average than the minimum wage, however their time is important for other reasons and so it can be argued that this monetary evaluation of time does not do the valuation justice
	Cost of uncompensated household production	N/A	Not collected	

were US $222, US $335, US $249 when medication, diagnostic tests (for infants and mothers) and infant immunisations were included for Models I, II and III, respectively, or US $54, US $75 and US $48 for the mother–infant visit only (indicated in the yellow bars of Figure 1). Visit costs accounted for 24% (average of 4.5 visits), 22% (average of 6.9 visits) and 19% (average of 6.7 visits) of the average annual postpartum care costs per mother–infant pair in each model (Figure 2). Unit costs per visit from the patient perspective (to and from their residence) were US $7 for Model I, US $4 for Model II and US $5 for Model III, respectively (see Table 5 – For the direct and indirect cost of transport time, there were 462 responses). Annually, this amounted to between US $29-54, US $23-44 and US $75 from a patient perspective for Models I, II and III, respectively (Figure 1).

Sensitivity analysis

In order to look at the impact of different visit loads, we assessed what the cost would be if the mother–infant pair

Table 4 Unit and total costs for the postpartum phase in 2018 US$

Postpartum phase unit costs	Visit cost (mother and infant)	Cost of medication per month (infant)	Cost of medication per month (mother)	Cost of diagnostic tests per month (mother and infant)	Immunisation costs per month (infants)	Total number mothers enrolled	Assumed number infants enrolled	Mean number of visits	Total clinic visit costs	Average annual total cost per mother–infant pair	Total cost for annual postpartum care cost
Model I– Routine Care	*$13*	$1	$9	$9	$10	238	238	4.49†	*$12 808*	**$222**	**$52 940**
Model II – Integrated Care	*$10*	$1	$9	$9	$10	233	233	6.94‡	*$17 396*	**$335**	**$78 124**
Model III –				Community Care	$7	$1	$9	$10	*$10*	84	84
6.73§	*$4 019*	**$249**	**$20 933**								

†Women were retained for an average of 1.04 visits in Site A, before being transferred to Model I where they attended 3.45 visits on average.
‡Women attended an average of 5.5 visits in Model II, once they ceased breastfeeding, they were transferred to Routine Care (Model I) for an average of 1.44 visits.
§Women were retained for an average of 1.04 visits in Site A, before being transferred to Model III where they attended 5.69 visits on average.

received the same number of visits (12 visits) under each of the models (holding the initial number of visits constant (1.44 Routine Care visits after transferring out for Model II; 1.04 visits in Site A for Model I and III; see Table 6 and Figure 1 (light blue dotted bars)). The percentage increase for Model I would be 180% from the provider's perspective, making it the most costly model of care when assessing annual postpartum care visit costs per mother–infant pair (increasing from US $54 to US $151).

Patient time

Patient time at the facility/community centre from arriving to exiting across the three models (n = 355 patients) was 3 h on average (standard deviation 1 h 34 min). For Model I (n = 250), the average time at the facility was 3 h 33 min (standard deviation (SD) 1 h and 28 min); the average time for Model II (n = 52) was 1 h 27 min (SD 60 min); the average time for Model III (n = 53) was 2 h 1 min (SD 53 min).

Input proportions

The two main recurrent inputs in visit costs were personnel and overheads (including maintenance). Personnel made up the largest proportion of visit costs for all three models: Model I – 80%; Model II – 69%; and Model III – 78%. Overheads and maintenance accounted for I – 18%; II – 27%; and III – 20%. While the capital inputs for buildings accounted for less than 4% (I – 2%; II 4%; and III – 2%) across the three models and equipment and furniture less than 1%.

Discussion

Understanding the costs of care for postpartum WLH and their children is critical for programme planning and optimisation of ART services during the postnatal period. We took the approach of considering the costs for the mother–infant pair with the trialled models of care specifically assessing maternal (and infant) outcomes. In the PACER and MCH-ART studies, Model III was found to be the most effective in terms of retention of mother–infant pairs and maternal viral suppression at 12 months postpartum with 84% of mother–infant pairs meeting these criteria [18-21]; Model I had a 56%; and Model II had a 77% proportion [18-20]. As the population of adults living with HIV is not homogeneous, there is a need to consider having a combination of different models depending on the characteristics of the population or individual's phase of life.

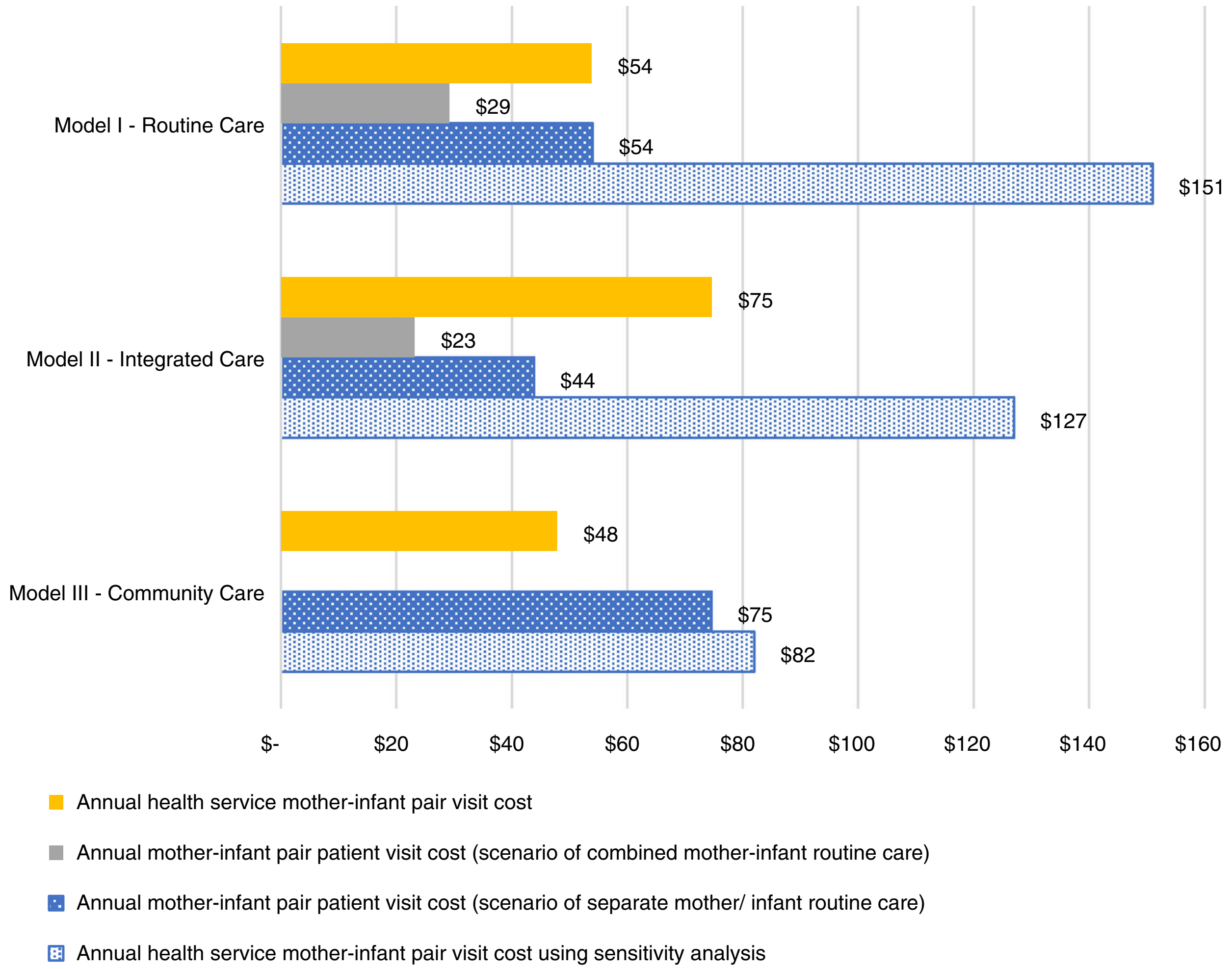

Figure 1 Annual provider and patient visit costs (including costs from the sensitivity analysis) per mother–infant pair in the postpartum phase in 2018 US$. The x-axis in the figure is the cost in 2018 US$, while the y-axis shows the three models. The yellow bars show the annual provider cost for a mother–infant pair for visits only. A range is provided for Model I and II, where the lower amount is shown in grey bars and the upper amount is shown in dark blue dotted bars. The grey bar shows the annual patient cost for a mother–infant pair visit under the scenario of combined routine care for mothers and infants (both mother and infant in the same consultation). The dark blue dotted bars display the annual patient cost for a mother–infant pair for visits only, where routine care is provided under the scenario of mother and infants being seen in separate consultations, that is not at the same site or on separate days. The costs from the sensitivity analysis for the annual provider for a mother–infant pair visit, shown here in light blue dotted bars are described in more detail in Table 6 – they show the cost of equalising the number of visits between models for the annum. [Colour figure can be viewed at wileyonlinelibrary.com]

A large proportion of HIV care costs are attributable to service delivery. As ART services expand to achieve population-level coverage, building costs are unlikely to substantially increase, unless they reach capacity. However, healthcare provider time costs may go up significantly as larger numbers of patients receive care in the clinic or community. Initially, there are economies of scale at play, where staff can care for more patients with the same resources; however, when the capacity of the healthcare workers is reached additional staff (and other resources) will be needed [25]. As the costs of ART medications continue to come down, the relative contribution of service delivery-related costs (e.g. provider time, clinic building costs/overheads) increase. With costs driven by service delivery elements, detailed costing data such as provided in this study are key to understanding the costs of different models of care.

Mother–infant pairs may have different needs in terms of the care they require. The clinical presentation of

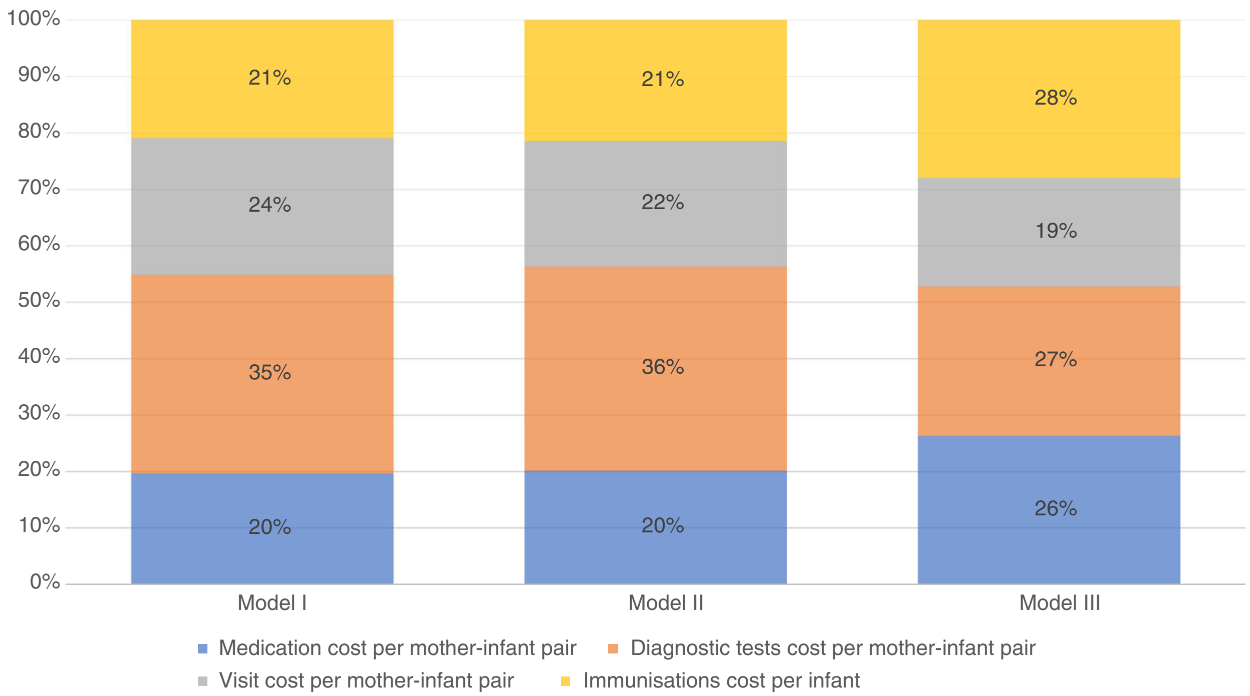

Figure 2 Proportion of average annual cost for postpartum care per mother–infant pair by category (medication, diagnostics, immunisation and visit cost). [Colour figure can be viewed at wileyonlinelibrary.com]

mothers may be that they are well or not well; this could be the first time that they are starting ART or they could have experience in taking ART [38]. Prior ART experience could mean that mothers access to care was previously negatively impacted, for instance that they were lost to follow up at some point in the treatment cascade or defaulted. Further to this different patient needs can be addressed by the distinctive models, a crucial underpinning of the idea of differentiated care [4,39]. For instance, not all patients will be eligible for CACs and may be better suited to care under Model I or II. CAC inclusion criteria being that patients should be adults, who have been on ART for 6-12 months, be stable with a suppressed viral load, not be pregnant and should not require frequent clinical management for adherence issues or comorbidities [21]. For those eligible and attending a CAC, the less frequent visit requirement of CACs (see Table 1) and ability to send a treatment 'buddy' to collect ART may aid WLH who are working or who would be unable to come to the clinic as regularly [40]. This flexibility is appreciated by those in CACs [8,40]. Integrated Care has the benefit of prolonging the time that the mother–infant pair are kept together which may limit (at least initially) the loss to follow up during transfer to another model [41]. Postpartum WLH were also found to breastfeed for a longer time in Model II, which in turn could positively impact their infant's health [19]. Further evolution of these models may include combining ideas such as integrating peer support into facility-based models such as Mother to Mothers (M2M), which has been done elsewhere in South Africa and extending ART refill times decreasing the visit frequency limiting face-to-face interaction especially in a time of COVID-19 [17,39].

In assessing these three models of care, we were interested in considering whether community-based care can be a desirable alternative to facility-based care from a cost perspective, given the potential increase in patient numbers with expanded ART services. The provider's perspective annual costs are the highest for Model II – Integrated Care (women and infants continue to receive care through an integrated maternal and child care approach during the postpartum breastfeeding period), then Model III – Community Care (referral of women directly to CACs and Model I – Routine Care (local standard of care of referral of women to general ART services and infants to well-baby clinics). Both the costs from the provider and patient's perspectives are affected by the structure of the services provided. The important differences from a costing standpoint between the models are that: under Model II mother–infant pairs are seen

Table 5 Direct and indirect patient costs for the three models of care in 2018 US$

		Indirect patient cost Mean waiting time/ lost productivity cost using time-in-motion	Non-medical indirect patient cost Cost of transport time/ time to clinic (at 6 months)	Non-medical direct patient cost Out of pocket payment for transport to the clinic (at 6 months)	Total per patient visit cost Total indirect and direct (including transport to the clinic)	Total per patient visit cost Total indirect and direct (including transport to and from the clinic)
Model I – Routine Care	Number of observations	*n* = 250	*n* = 175	*n* = 175		
	Mean (SD)	*5.41 (2.23)*	*0.49 (0.35)*	0.40 (0.29)	**6.3**	**7.19**
Model II – Integrated Care	Number of observations	*n* = 52	*n* = 178	*n* = 178		
	Mean (SD)	*2.21 (1.51)*	*0.54* (0.47)	0.46 (0.36)	**3.21**	**4.21**
Model III – Community Care	Number of observations	*n* = 53	*n* = 109	*n* = 109		
	Mean (SD)	*3.07 (1.34)*	*0.50 (0.35)*	0.54 (1.05)	**3.11**	**5.15**

together during the breastfeeding period (before transferring out to routine care (as per Model I); under Model I, mothers and infants are seen separately, but depending on the facility this may be within the same site or even in the same consultation as we observed in four facilities; and for Model III, mothers and infants are seen separately at separate sites. This has impact particularly on the patient costs, because one integrated visit as opposed to two visits reduces the productive time lost, time spent on transport and the direct transport costs. In Model II, we saw a positive impact on travel costs, with the lowest mother–infant pair patient visit cost (see Figure 1) as only one visit is required for the pair. The observed waiting time for patients in Model III is relatively long as patients still arrive well before their medication is dispensed (or even before the community centre is opened), first listening to wellness talks given by the counsellors. This is counter to the rationale of a CAC, which aims to minimise the time spent by patients collecting medication [20].

Immunisation costs per infant and diagnostic cost per mother–infant pair are the highest drivers of cost for Model III. However, the proportion of the annual cost for Model III specifically for mother's diagnostic testing accounts for only 3%, whereas it represents 17% and 18% in Model I and II. These higher proportions in Model I and II can be attributed to the extra monitoring performed in these models, specifically more frequent viral load testing. For Models I and II diagnostic cost per mother–infant pair is the main cost driver (35% and 36% of the annual costs). Personnel costs, which relate to time of healthcare professionals, were the major cost driver in the visit costs for each of the three models, more so in Model I (19% of the annual cost) and less so in Model II and III (15% of the annual cost in each model respectively). Care in Model I, is delivered by a mix of professional nurses, nursing assistants and counsellors; Model II is mainly delivered by a focal nurse in conjunction with counsellors, while Model III is delivered primarily by a counsellor. The profession of the staff and by implication the salary level, as well as the time staff spent on postpartum care tasks all influence the personnel cost. In addition, there may be other value added such as in information exchange between counsellors and patients as this cadre of staff may help to de-medicalise information and reduce use of jargon (Model III), and more holistic care of the mother–infant pair when treated together (Model II). In the PACER study 78% of WLH who chose to stay in the control arm, reported a preference for attending a health facility [21]. Zerbe et al. (2020) also note a movement of WLH from CACs back into health facilities with these WLH showing poorer outcomes [21]. Hence, there are nuances to the three models of care and many factors to weigh up aside from costs and outcomes.

In an evaluation of CAC costs (comparable to those used in the Model III) in a similar setting in South Africa, Bango et al. [11] (costs have been inflated from 2011 to 2018 US$ for comparison using US $ Consumer Price Index [42]) found higher annual costs of US $418 for standard of care (compared to Model I – US $114 for mothers' care only) and US $335 for the CACs

Table 6 Sensitivity analysis, normalising the number of visits between models of care (2018 US$)

	Provider's perspective (as per study visits)	Provider's perspective (12 visits)	Percentage increase
Model I: 12 visits Mean of 1.04 visits at Site A (in Model II – Integrated Care) remains constant; Model I visits increased to 10.96	*$54*	$151	180%
Model II: 12 visits Model II visits increased to 10.56; mean of 1.44 visits in the general ART clinic for routine care (as per Model I) after referral out from Model II – Integrated Care, stays the same	*$75*	$127	70%
Model III: 12 visits Mean of 1.04 visits at Site A (in Model II – Integrated Care) remains constant; Model III visits increased to 10.96†	*$48*	$82	72%

†An important part of CACs service delivery is that stable patients in the CACs can collect medication less frequently than in a standard of care setting, so in reality we would not want to increase the number of visits; however, this is being done to be able to compare cost equally across the three models.

(compared to Model III – US $90 for mothers' care only). One of the factors that has affected the difference in values in the current study compared to the study by Bango et al. [11] is the reduction in ART medication cost by approximately one third. Another is the utilisation rate, which is higher in the study by Bango et al. [11] than for Model I in this work (10.3 versus 4.5 visits per year in the current study). The average number of clinic visits is an integral part of the annual cost and varies between the three models in this paper from 4.6 and 6.9.

Although these three models have been presented separately, there is a level of interdependence between the models and need for thought as to how patients flow through these models in order to ensure mothers and infants are retained in suitable care. For instance, as the models currently function, all mother–infant pairs continue to receive care in Site A for approximately one visit (or while breastfeeding in Model II) before either moving to routine clinic-based ART care or community-based care in the form of a CAC, where infants transfer to being cared for in well-baby clinics. To this end, we do not suggest that one model is superior to another. We also found that in reality four of the five clinics in Model I were consulting with mothers and infants in the same visit and in two of the facilities were also dispensing medication during that consultation. The total unit costs are also affected by assessing only the mother in isolation or by ignoring the patient costs, hence our approach of assessing the mother–infant pairs.

The unit costs from this study could be generalised to the wider population in South Africa, taking note of the specific peri-urban setting and way the services are offered. Further work is needed to look into the outcomes and cost-effectiveness of the different models of care to make judgments on which model of care or mix of models of care are best suited to the healthcare system and to inform what these models would cost at scale. In low- and middle-income countries where unit cost estimates are not available, these costs could assist in planning similar programmes or models.

Limitations

One limitation of this study could be the comparison of Model III, as the CAC is intended only for women who are already stable on ART, whereas Models I and II have no requirements for inclusion. In the case of the PACER study, all women enrolled had the prerequisite of having started ART during pregnancy, currently breastfeeding their infant, with evidence of viral suppression after three months of ART (VL < 1000 copies/ mL) and no comorbidities that require frequent clinical review [21]. As one of the goals of CACs service delivery model is that visits are less frequent for stable patients, we are not suggesting that the number of visits be increased as we have done in our sensitivity analysis, but rather are looking at the effect on cost when we equalise the number of visits. This is particularly relevant in light of the WHO's recommendation to extend refills for clinically stable patients to between three and six months [43]. An ongoing South African clinical trial is aiming to assess the impact of less frequent refills within the CAC setting which will aid policy going forward [44]. It is important to note that these costs are most applicable to the population of women who started ART in pregnancy and may differ for those who have been stable on ART prior to conception. Another limitation is that the cost of care may vary from clinic to clinic, though our sample is representative and we present average unit costs. Also for Site A, we used the average number of visits in the study per woman to inform the number of visits for postnatal care as the facility did not have utilisation data for this. The largest number of time-and-motion studies was completed for Model I across different clinics, and this may have biased the time data as Models II and III had fewer time-and-motion studies.

Conclusions

Novel data on unit costs to provide ART to mother–infant pairs during the postpartum phase and insight into the cost drivers has been provided through this comparative analysis of three models of care. The unit costs of the two new models of care, using Integrated Care (Model II) and Community Care approaches (Model III), respectively, are more expensive; however, they are also more effective in terms of retention of mother–infant pairs and viral suppression at 12 months postpartum as shown by the MCH-ART and PACER studies. These costs may be used to help make decisions around integrated services models and differentiated service delivery for postpartum WLH and their children. Importantly, these costs will be useful for informing budgeting for postpartum care and have already fed into a cost-effectiveness analysis comparing Integrated Care (Model II) to Routine Care (Model I). This work will feed into another cost-effectiveness analysis comparing all three models of care and a budget impact analysis for the South African setting.

Acknowledgments

We would like to acknowledge the women that comprised these cohorts and staff that tirelessly care for them. Funding: CMD receives a NIH T32 grant, NIAID T32 AI007433, and ALC receives a NIH Research Project Grant, R01 HD 079214.

References

1. Luzuriaga K, Mofenson LM. Challenges in the elimination of pediatric hiv-1 infection. *N Engl J Med* 2016: **374**: 761–770.
2. Phillips TK, Myer L. Shifting to the long view: engagement of pregnant and postpartum women living with HIV in lifelong antiretroviral therapy services. *Expert Rev Anti Infect Ther* 2019: **17**: 349–361.
3. World Health Organization. *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach - Second Edition*. World Health Organization: Geneva, Switzerland, 2016.
4. 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.
5. World Health Organization. *Key considerations for differentiated antiretroviral therapy delivery for specific populations: children, adolescents, pregnant and breastfeeding women and key populations*. Switzerland: Geneva, 2017.
6. International AIDS Society. *Supplement: Leveraging differentiated art delivery models for stable clients to scale up TB preventive therapy*. 2019.
7. International AIDS Society. *Differentiated care for HIV: Decision Framework for differentiated antiretroviral therapy delivery for children adolescents and pregnant and breastfeeding women*. 2017.
8. Sharer M, Davis N, Makina N, Duffy M, Eagan S. Differentiated antiretroviral therapy delivery. *J Assoc Nurses AIDS Care* 2019: **30**: 511–520.
9. Grimsrud A, Barnabas RV, Ehrenkranz P, Ford N. Evidence for scale up: the differentiated care research agenda. *J Int AIDS Soc* 2017: **20**: 22024.
10. Asieba IO, Oqua DA, Wutoh AA *et al*. Antiretroviral therapy in community pharmacies - Implementation and outcomes of a differentiated drug delivery model in Nigeria. *Res Social Adm Phar* 2020. https://doi.org/10.1016/j.sapharm.2020.06.025
11. Bango F, Ashmore J, Wilkinson L, van Cutsem G, Cleary S. 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.
12. Moudachirou R, Van Cutsem G, Chuy RI *et al*. Retention and sustained viral suppression in HIV patients transferred to community refill centres in Kinshasa, DRC. *Public Health Action* 2020: **10**: 33–37.
13. Nyamayaro P, Bere T, Magidson JF *et al*. A task-shifting problem-solving therapy intervention for depression and barriers to antiretroviral therapy adherence for people living with HIV in Zimbabwe: case series. *Cognitive Behavioral Practice* 2020: **27**: 84–92.
14. Stockton MA, Udedi M, Kulisewa K *et al*. The impact of an integrated depression and HIV treatment program on mental health and HIV care outcomes among people newly initiating antiretroviral therapy in Malawi. *PLoS One* 2020: **15**: e0231872.
15. World Health Organization. *Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations 2016 update*. World Health Organization: Geneva, Switzerland, 2016.
16. WHO UNICEF. *Guidance on Global Scale-Up of the Prevention of Mother to Child Transmission of HIV: Towards Universal Access for Women, Infants, and Young Children and Eliminating HIV and AIDS Among Children*. Inter-Agency Task Team on Prevention of HIV Infection in

Pregnant Women, Mothers and their Children. World Health Organization; Geneva, Switzerland, 2007.
17. Mutabazi JC, Gray C, Muhwava L *et al*. Integrating the prevention of mother-to-child transmission of HIV into primary healthcare services after AIDS denialism in South Africa: perspectives of experts and health care workers - a qualitative study. *BMC Health Ser Res* 2020: **20**: 1-18.
18. Myer L, Phillips TK, Zerbe A *et al*. Optimizing Antiretroviral Therapy (ART) for Maternal and Child Health (MCH): rationale and design of the MCH-ART study. *J Acquir Immune Defic Syndr* 2016: **72**: S189–S96.
19. Myer L, Phillips TK, Zerbe A *et al*. Integration of postpartum healthcare services for HIV-infected women and their infants in South Africa: a randomised controlled trial. *PLoS Med* 2018: **15**: 1-21.
20. Myer L, Iyun V, Zerbe A *et al*. Differentiated models of care for postpartum women on antiretroviral therapy in Cape Town, South Africa: a cohort study. *J Int AIDS Soc* 2017: **20**: 32–40.
21. Zerbe A, Brittain K, Phillips TK *et al*. Community-based adherence clubs for postpartum women on antiretroviral therapy (ART) in Cape Town, South Africa: a pilot study. *BMC Health Serv Res* 2020: **20**: 1-12.
22. Dugdale CM, Phillips TK, Myer L *et al*. Cost-effectiveness of integrating postpartum antiretroviral therapy and infant care into maternal & child health services in South Africa. *PLoS One* 2019: **14**: e0225104.
23. Cunnama L, Abrams EJ, Myer L*et al*.Cost-effectiveness analysis of three postpartum models of care for women living with HIV in Cape Town, South Africa. Upcoming.
24. Cunnama L, Myer L, Sinanovic E.Scaling up postpartum models of care for mother-infant pairs in South Africa: A budget impact analysis. Upcoming.
25. Vassall A, Sweeney S, Kahn JG *et al*. Reference case for estimating the costs of global health services and interventions. *Global Health Cost Consortium* 2017. https://ghcosting.org/pages/standards/reference_case
26. Drummond M, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. *Methods for the Economic Evaluation of Health Care Programmes* (4th edn), Oxford University Press: UK, 2015.
27. Haas AD, Tenthani L, Msukwa MT *et al*. Retention in care during the first 3 years of antiretroviral therapy for women in Malawi's option B+ programme: an observational cohort study. *The Lancet HIV* 2016: **3**: e175–e82.
28. Trafford Z, Gomba Y, Colvin CJ *et al*. Experiences of HIV-positive postpartum women and health workers involved with community-based antiretroviral therapy adherence clubs in Cape Town, South Africa. *BMC Public Health* 2018: **18**: 935.
29. Strategic Development Information and GIS Department. *City of Cape Town – 2011 Census*. City of Cape Town: Cape Town, 2013.
30. Phillips TK, Clouse K, Zerbe A, Orrell C, Abrams EJ, Myer L. Linkage to care, mobility and retention of HIV-positive postpartum women in antiretroviral therapy services in South Africa. *Journal of the International AIDS Society*. 2018: **21**: e25114.
31. Cunnama L, Sinanovic E, Ramma L *et al*. Using Top-down and Bottom-up Costing Approaches in LMICs: The Case for Using Both to Assess the Incremental Costs of New Technologies at Scale. *Health Econ* 2016: **25**: 53–66.
32. Lopetegui M, Yen PY, Lai A, Jeffries J, Embi P, Payne P. Time motion studies in healthcare: what are we talking about? *J Biomed Inform*. 2014: **49**: 292–9.
33. Statistics South Africa. Consumer Price Index 2018 (Available from: http://www.statssa.gov.za/publications/P0141/P0141March2018.pdf). [07 Sept 2020]
34. National Treasury. *Local Government Capital Asset Management Guideline*. Republic of South Africa: Pretoria, South Africa, 2009.
35. Berrie L. *National Priority Programmes*. National Health Laboratory Service: Johannesburg, South Africa, 2016.
36. Johnson Y. Pharmacy Services, Western Cape Government. *Health* 2017.
37. Mywage.co.za. Minimum wages in South Africa. 2016.
38. Rosen S, Grimsrud A, Ehrenkranz P, Katz I. Models of service delivery for optimizing a patient's first six months on antiretroviral therapy for HIV: an applied research agenda. *Gates Open Res* 2020: **4**: 116.
39. Wilkinson L, Grimsrud A. The time is now: expedited HIV differentiated service delivery during the COVID-19 pandemic. *J Int AIDS Soc* 2020: **23**: e25503.
40. Venables E, Towriss C, Rini Z *et al*. Patient experiences of ART adherence clubs in Khayelitsha and Gugulethu, Cape Town, South Africa: A qualitative study. *PLoS One* 2019: **14**: e0218340.
41. Luzuriaga K, Mofenson LM. Challenges in the elimination of pediatric HIV-1 infection. *N Engl J Med* 2016: **374**: 761–770.
42. United States Bureau of Labor Statistics. Consumer Price Index (Available from: https://www.bls.gov/regions/mid-atlantic/data/consumerpriceindexhistorical_us_table.htm) [25 Aug 2020].
43. World Health Organization. *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach* (2nd edn), World Health Organization: Geneva, 2016.
44. Wilkinson L, Grimsrud A, Cassidy T *et al*. A cluster randomized controlled trial of extending ART refill intervals to six-monthly for anti-retroviral adherence clubs. *BMC Infect Dis* 2019: **19**: 1-9.
45. Grimsrud A, Lesosky M, Kalombo C, Bekker L-G, Myer L. Community-based adherence clubs for the management of stable antiretroviral therapy patients in Cape Town, South Africa: a cohort study. *J Acquir Immune Defic Syndr* 2016: **71**: e16–e23.
46. Zerbe A, Iyun VO, Chihana M *et al*. editors. Differentiated models for delivery of antiretroviral therapy to HIV-infected women in the postpartum period in Cape Town,

South Africa (Poster #LBPE037). *8th international workshop on HIV pediatrics, AIDS*. 2016; Durban.

47. Neumann PJ, Sanders GD, Russell LB, Siegel JE, Ganiats, TG. *Cost-Effectiveness in Health and Medicine* (2nd edn), United States of America: Oxford University Press: New York, 2017.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Parent studies.

Corresponding Author Lucy Cunnama, Health Economics Unit, Faculty of Health Sciences, University of Cape Town, Anzio Road, Observatory, Cape Town, 7925. Tel.: +27214066754; E-mail: Lucy.Cunnama@uct.ac.za

