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Health care costs associated with clinic visits for prevention of mother-to-child transmission of HIV in Dar es Salaam, Tanzania

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Abstract

Early and appropriate antenatal care (ANC) is key for the effectiveness of prevention of mother-to-child transmission (PMTCT) of human immunodeficiency virus (HIV). We evaluated the importance of ANC visits and related service costs for women receiving option B^+ to prevent mother-to-child transmission (MTCT) of HIV in Tanzania.

A cost analysis from a health care sector perspective was conducted using routine data of 2224 pregnant women newly diagnosed with HIV who gave birth between August 2014 and May 2016 in Dar es Salaam, Tanzania. We evaluated risk of infant HIV infection at 12 weeks postnatally in relation to ANC visits (<4 vs ≥4 visits). Costs for service utilisation were estimated through empirical observations and the World Health Organisation Global Price Reporting Mechanism.

Mean gestational age at first ANC visit was 22 (±7) weeks. The average number of ANC/prevention of MTCT visits among the 2224 pregnant women in our sample was 3.6 (95% confidence interval [CI] 3.6–3.7), and 57.3% made ≥4 visits. At 12 weeks postnatally, 2.7% (95% CI 2.2–3.6) of HIV exposed infants had been infected. The risk of MTCT decreased with the number of ANC visits: 4.8% (95% CI 3.6–6.4) if the mother had <4 visits, and 1.0% (95% CI 0.5–1.7) at ≥4. The adjusted MTCT rates decreased by 51% (odds ratio 0.49, 95% CI 0.31–0.77) for each additional ANC visit made. The potential cost-saving was 2.2 US$ per woman at ≥4 visits (84.8 US$) compared to <4 visits (87.0 US$), mainly due to less defaulter tracing.

Most pregnant women living with HIV in Dar es Salaam initiated ANC late and >40% failed to adhere to the recommended minimum of 4 visits. Improved ANC attendance would likely lead to fewer HIV-infected infants and reduce both short and long-term health care costs due to less spending on defaulter tracing and future treatment costs for the children.

Abbreviations: AIDS = acquired immunodeficiency syndrome, ANC = antenatal care, ART = antiretroviral therapy, CD4 = cluster of differentiation 4, CI = confidence interval, CTC = care and treatment clinic, DNA-PCR = deoxyribonucleic acid polymerase chain reaction, EID = early infant diagnosis, GA = gestational age, HEI = HIV-exposed infant, HIV = human immunodeficiency virus, MDH = management and development for health, MTCT = mother-to-child transmission, OR = odds ratio, PMTCT = prevention of mother-to-child transmission, WHO = World Health Organisation.

Keywords: antenatal care, antiretroviral, health care cost, human immunodeficiency virus prevention, low and middle-income countries, prevention of mother-to-child transmission, vertical transmission, women

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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1. Introduction

Nearly 90% of the 160,000 infants estimated to be have been human immunodeficiency virus (HIV)-infected in 2020 through mother-to-child transmission (MTCT) reside in Africa.[1] Delays in the initiation of antenatal care (ANC), poor adherence to regular clinic visits, and high defaulter rates throughout the prevention of MTCT (PMTCT) cascade are the main barriers to reaching an acquired immunodeficiency syndrome (AIDS)-free generation.[2] In low and middle-income countries[3,4] half of all pregnant women living with HIV are lost between their ANC/PMTCT registration and postpartum follow-up care.[5]

In an effort towards the elimination of MTCT, the World Health Organization (WHO) released a program update in 2012 suggesting that all pregnant women living with HIV should receive lifelong antiretroviral therapy (ART), a strategy called PMTCT option B+.[6] In September 2015, this became WHO official recommendation.[7] In Tanzania, PMTCT option B^+ was rolled out from September 2013, and by the end of 2018, 93% of pregnant women living with HIV received ART.[8] Despite a reduction in the incidence of HIV in children, the current MTCT rate at 10% remains a major public health concern in Tanzania[1] as well as in many other sub-Saharan African settings.

The integrated ANC/PMTCT care model in Tanzania offers an opportunity for accessing PMTCT option B^+, since 98% of pregnant women attend ANC at least once and 90% accept to be tested for HIV.[9,10]

ANC services in Tanzania aim for 4 ANC visits in low-risk pregnancies, and more visits for those with complicating conditions including HIV infection.[11] However, even to achieve the 4 ANC visits has been an uphill task regardless of HIV status.[3,4,12,13]

In Tanzania, as much as one third of pregnant women delay their first ANC visit until the sixth month of pregnancy and only 51% complete a minimum of 4 ANC visits.[9] This delay and poor uptake reduces the opportunity for counselling on HIV status disclosure and infant feeding, ART initiation/refill, and adherence monitoring and support.[10]

Given the above-mentioned shortcomings, Tanzania failed to achieve the Joint United Nations Programme on HIV/AIDS elimination of MTCT target by 2020.[14] Thus, we need an enhanced understanding of the reasons behind this and strategies required for universal access to prevention and care including interventions to promote program retention and ART adherence throughout the PMTCT period and beyond. Some of these strategies involve the use of differentiated ART service delivery models, for example, that women living with HIV who are clinically stable on ART at conception, could receive a 3 to 6 month prescription to allow health systems to focus their PMTCT resources on women newly diagnosed with HIV.[15] In line with this reasoning, the number of ANC visits would be reduced, in theory reducing health care costs as well as the workload for overstretched health workers, for example, in Tanzania, where only 22% of the WHO-recommended minimum of 23 health workers per 10,000 people is available to deliver essential maternal and child health services.[16]

On the other hand, the WHO has recommended at least 8 ANC visits for all women to improve the quality of care,[17] and at the moment Tanzanian guidelines are being updated to accommodate these changes that are also in line with the country's recommended number of visits for pregnant women living with HIV.[10]

To realize the full life-saving potential of option B^+, pregnant women must be tested for HIV, initiated on ART and retained in care from the first trimester to the end of the breast-feeding period and beyond.[13,18]

This analysis evaluates the health care cost associated with adherence to the ANC schedule of at least 4 visits compared to fewer than 4 visits, with respect to MTCT among newly diagnosed pregnant women living with HIV who were treated under PMTCT option B^+ in Dar es Salaam, Tanzania.

2. Material and methods

2.1. Study design

A cost analysis using a health care sector perspective and a longitudinal cohort of women newly diagnosed with HIV in Dar es Salaam, Tanzania.

2.2. Setting

Dar es Salaam is Tanzania's most prominent commercial city with a population of 4.4 million people.[19] The city receives technical support for HIV and PMTCT care services from the United States Government-President's Emergency Plan for AIDS Relief through the management and development for health (MDH) organization. The MDH supports the HIV program including ART/PMTCT care, clinical and laboratory patient monitoring and health system strengthening. Patients including pregnant women are monitored through the care and treatment clinic (CTC) card number 2 (CTC-2) and, the HIV-exposed infant (HEI) government databases. Since its initiation in 2002 by the Government with The United Nations Children's Fund support,[20] ANC and PMTCT care has been integrated and provided at ANC clinics all weekdays from 8 AM to 4 PM throughout the country. In each facility, at least 1 health care provider is dedicated to providing PMTCT services.

Demographic information and clinical data of all pregnant women living with HIV is registered in the CTC-2 database using a unique identification number. If and when polymerase chain reaction (PCR) testing for HIV (so called early infant diagnosis [EID]) is carried out at 4 to 6 weeks postnatally, a unique HEI identification number is assigned and used to register the infant in the HEI database. The CTC-2 and HEI databases are linked using the mother's identification number. The databases are updated at each patient visit. Data quality assessment is done by the MDH team on a quarterly basis in selected health facilities and on a yearly basis at each facility to validate the consistency of the information in the databases with the actual patient cards.

2.3. Patient sample and data collection

To estimate MTCT outcomes, we extracted records of pregnant women living with HIV who delivered their infants between August 2014 and May 2016 from CTC-2 database. Our target population was pregnant women newly diagnosed with HIV, as they are at higher risk for late ANC initiation and often have fewer visits compared to those who are already on ART.[4,21,22] We extracted information regarding the infants' date of birth, date of HIV deoxyribonucleic acid (DNA)-PCR test, and test results from the HEI database. We used infant HIV DNA-PCR test results that had been performed within 12 weeks of age.

From the CTC-2 database, we extracted information on the date of each ANC/PMTCT clinic visit, demographic characteristics, cluster of differentiation 4 (CD4) cell count, WHO stage for HIV disease, self-reported ART adherence (at least 95% of prescribed antiretrovirals taken yes/no), and infant-feeding practice. The duration of ANC follow-up was estimated as the difference between the date of the first ANC visit and date of delivery for each pregnant woman living with HIV. We also collected information on any missed scheduled visits during the follow-up period.

Viral load was not included in this analysis as this was not routinely tested and viral load results were only available for a few women suspected to have treatment failure.

A total of 4450 mothers residing in Dar es Salaam who delivered their infants between August 2014 and May 2016 were identified. We excluded women who already were on ART at the time of their first ANC booking (N=2014), mother–infant pairs missing information on infant date of birth (N=100), ANC visit dates (N=85) or and those missing an infant DNA-PCR test result (N=27) as shown (Fig. 1).

2.4. Outcomes

Pregnant women treated under PMTCT option B^+ were divided into 2 scenarios: the first scenario included women who made at least 4 ANC visits, and the second scenario included women who made fewer than 4 ANC visits. The outcome, defined as the effectiveness of the PMTCT program up to EID, was estimated as the difference between the number of infants infected with HIV through MTCT observed at 12 weeks postnatally among mothers who made ≥4 ANC visits compared to the number of MTCT events in infants born to mothers who made <4 ANC visits.

2.5. Costing and unit costs

Costs were evaluated from a health care sector perspective using a micro-costing approach, first assessing the average cost of services (health provider salaries, costs of laboratory tests, and medication) consumed per individual patient[23] and then assessing the average time spent on each PMTCT activity, by using data obtained from a time–motion study that we conducted in 26 PMTCT clinics across Dar es Salaam during the same time period.[24] This time–motion study observed the actual time a provider normally spends with a pregnant woman during her first ANC/PMTCT visit, as well as during a typical ANC/PMTCT follow-up visit. Health care provider costs for each clinic visit were then estimated from their monthly salaries taking the time spent on each activity associated with a particular type of visit into account.[24] In most of these facilities, the health attendants (who earned around $175 per month)[24] clean and prepare the clinical room for about 20 minutes. Thus, a cost equivalent to 20 minutes salary of a health attendant (0.37 US dollars [US$]) was

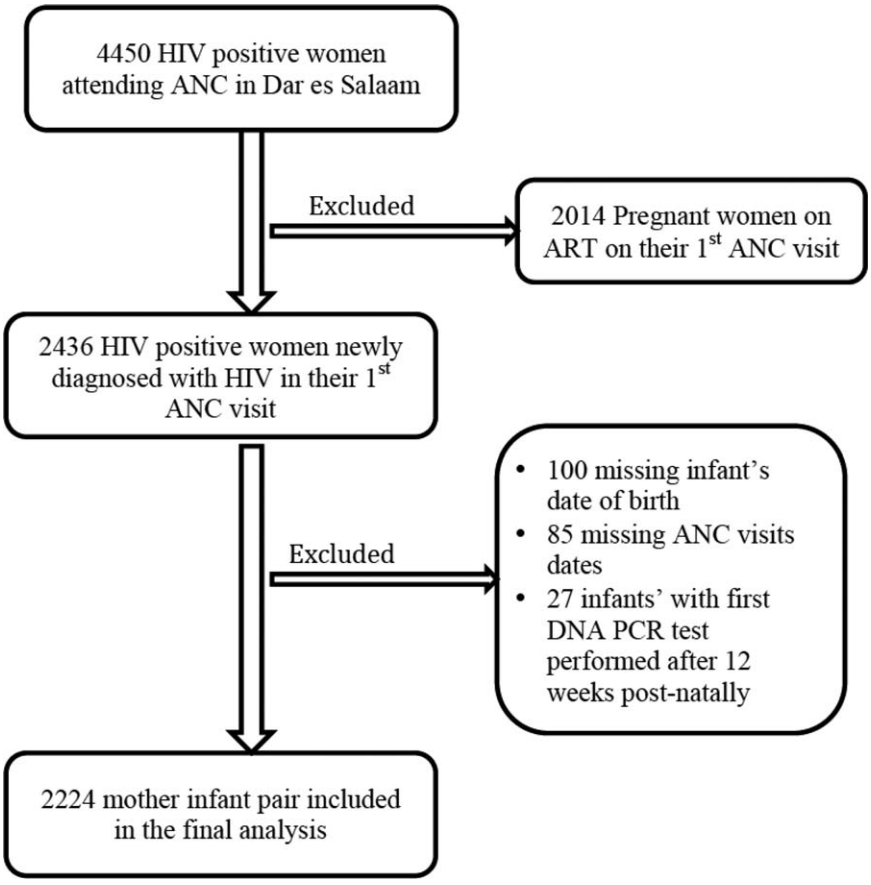

Figure 1. Study flow chart showing inclusion and exclusion of pregnant women living with HIV in Dares Salaam 2014–2016 in the study analysis. ANC = antenatal care, ART = antiretroviral therapy, DNA-PCR = deoxyribonucleic acid polymerase chain reaction, HIV = human immunodeficiency virus.

added to the cost of each visit. Fixed expenditures such as rental and utilities (ie, water and electricity, estimated at 2.5 US$ per patient/year) were derived from a previous study done at HIV treatment clinics in Dar es Salaam.[25] All of this information was thereafter converted into cost per service unit (Table 1).

The cost for tracing patients defaulting from PMTCT care was estimated using the average time spent on standard tracing procedures that include health care providers' phone calls and home visits as observed in other empirical studies involving adults living with HIV in Dar es Salaam, Tanzania.[26,27]

Monthly costs of medication included both the price of the antiretroviral drugs and cotrimoxazole (used to prevent opportunistic infections), and the provider time spent on dispensing the medicines. We obtained the unit price for standard ART regimens recommended for PMTCT option B^+ during the study period in Tanzania (tenofovir + lamivudine + efavirenz), from the 2017 WHO global price reporting mechanism. The global price reporting mechanism contains the drug price, strength, dosage form, destination country, shipment method, and price of shipments in an international development context.[28] The price of cotrimoxazole was obtained from the Tanzanian 2017 Medical Store Department catalogue.[29]

The cost of laboratory tests was based on the actual cost of performing these tests (HIV antibody, CD4 cell count, liver and kidney function, and haemoglobin) at HIV clinics in Dar es Salaam (Table 1), as reported in an empirical study conducted in 2017.[26] All costs were expressed in US$ and in the 2017 prices adjusted for inflation using a GDP deflator-based calculator.[30]

2.6. Ethical approval

Ethical clearance was obtained from the research and publication ethics committee of Muhimbili University of Health and Allied Sciences, Tanzania (Ref No 2017-08-11/AEC/Vol.XII/67).

2.7. Data analysis

Univariable analysis for categorical data was conducted with the Pearson Chi-Square test and Fisher exact test for sparse data. Two-sample comparisons of continuous data were conducted with the Student *t* test.

The percent of missing data was 71.5% for self-reported adherence 62.8% for CD4 cell count, and 25.2% for marital status. About 55% with missing CD4 count results and 60% with missing values on self-reported adherence made 4 or more ANC visits.

We evaluated the potential effect of missing values on the observed outcome (MTCT) based on 10 imputed datasets using multiple imputations by chained equations[31] under the assumption of missing at random.

In cost analysis, the difference in total PMTCT health care costs between the group of women with ≥4 ANC visits and those with <4 ANC visits was calculated. Since the time horizon for the analysis was within 1 year, costs and effects were not discounted.

A one-way sensitivity analysis of cost was performed, involving analysis of one cost parameter at a time while keeping the other constant, and the choice of the sensitivity range was based on the upper and lower range of the unit cost of the services utilized.

The statistical analyses were performed using Stata, release 14 (College Station, TX: Stata Corp LP and cost data was analysed using Microsoft Excel 2010).

3. Results

3.1. Patient characteristics

A total of 2224 pregnant women living with HIV were eligible for analysis. Most (95.9%) of women were in WHO disease stage I and II, 68.4% had CD4 ≥ 350 cells per μL and 96.5% self-reported good adherence to ART. Nearly three quarters of the women (72.2%) made their first ANC/PMTCT visit in their

Table 1

Cost and service utilization parameter values and ranges for the prevention of mother to child transmission of HIV in Tanzania based on previous studies and market price of antiretroviral therapy according to Tanzania medical store price list.

Item	Resource use	Mean unit cost [range] US$	Source
Personnel cost			
First PMTCT/ANC visit	53.5 [41.8–55.2] min/visit	2.27 [1.80–2.37]	Naburi et al (2017)[24]
Follow-up PMTCT/ANC visit	15.0 [13.5–16.6] min/visit	0.65 [0.58–0.71]	Naburi et al (2017)[24]
First mother–infant visit (DNA-PCR test)	28.9 [26.2–31.6] min/visit	1.28 [1.15–1.39]	Naburi et al (2017)[24]
Adherence counselling	7.4 [4.4–10.4] min/session	0.32 [0.19–0.47]	Naburi et al (2017)[24]
Cost of tracing a woman who missed her appointment	Tracing (call or home visit)/client	7.00 [3.00–15.00]	Lema et al (2014)[27] Kimaro et al (2015)[26]
Cost of laboratory tests			
CD4 cell count	1 test	15.76 [14.75–16.72]	Kimaro et al (2015)[26]
Alanine aminotransferase	1 test	0.88 [0.84–0.91]	Kimaro et al (2015)[26]
Serum creatinine	1 test	0.31 [0.28–0.35]	Kimaro et al (2015)[26]
Haemoglobin	1 test	0.85 [0.81–0.89]	Kimaro et al (2015)[26]
Medication cost			
TDF+ 3TC + EFV	30 combination tablets	8.00 [7.50–8.25]	WHO-GPRM[28]
Cotrimoxazole prophylaxis	One monthly dose (60 tablets)	0.60 [0.40–0.81]	MSD (2017)[29]
Fixed costs			
Rent and utilities		2.5/client/yr	Shayo et al (2015)[25]

Haemoglobin level, renal function test (serum creatinine), and liver function test (alanine aminotransferase are not HIV-specific tests but recommended in routine care before a patient is started on ART. 3TC = lamivudine, ANC = antenatal care, ART = antiretroviral therapy, CD4 = cluster of differentiation 4, DNA-PCR = deoxyribonucleic acid polymerase chain reaction, EFV = effavirenz, MSD = medical store department, PMTCT = prevention of mother-to-child transmission of HIV, TDF = tenofovir disoproxil fumarate, WHO-GPRM = WHO global price reporting mechanism.

second trimester. The overall MTCT rate by 12 weeks of life was 2.7% (N = 59/2224) (Table 2).

3.2. Factors associated with fewer number of ANC/PMTCT visits

The average number of ANC/PMTCT visits before delivery was 3.7 (95% confidence interval [CI] 3.6–3.7). Women who made fewer than 4 visits had an average of 1.7 visits (95% CI 1.6–1.8), while those who made a minimum of 4 visits had an average of 5.1 visits (95% CI 5.0–5.2). Unsurprisingly, women who made fewer than 4 visits, also booked their first ANC/PMTCT visit later than women with 4 or more visits (mean gestational age [GA] 27.8 vs 18.6 weeks, $P < .001$), and they also initiated ART later (mean GA at ART initiation was 27.9 vs 19.0 weeks, $P < .001$) (Table 2).

Bivariate analyses using number of ANC visits as the outcome variable, showed that women who made fewer than 4 visits were more likely to be cohabiting (6.7% vs 6.0%) or to have an advanced WHO stage of disease (III or IV) (5.7% vs 3.0%) than women who made at least 4 visits. Furthermore, 5.1% of women who made fewer than 4 visits reported poor adherence to ART, compared to 1.9% among those who made at least 4 visits during pregnancy (Table 2).

3.3. Factors associated with MTCT

The MTCT rate at 12 weeks postnatally decreased significantly with the number of ANC visits, being 4.8% (N = 46/949) for mothers who made <4 ANC visits, while it was only 1.0% (N = 13/1275) among those with a minimum of 4 ANC visits (Table 3). There was a significant difference in mean CD4 cell

Table 2

Characteristics of 2224 pregnant women newly diagnosed with HIV in Dar es Salaam Tanzania 2014 to 2016 in relation to their antenatal care clinic visits.

Variables Continuous variables	Overall N = 2224 Mean (95% CI)	<4 ANC visits 949 (42.7%) Mean (95% CI)	≥4 ANC visits 1275 (57.3%) Mean (95% CI)	*P*-value
Gestational age at first visit	22.0 (21.7–22.3)	27.8 (27.3–28.3)	18.6 (18.3–18.8)	<.001*
Gestational age at ART initiation	22.4 (22.1–22.7)	27.9 (27.4–28.4)	19.0 (18.7–19.2)	<.001*
Number of visits	3.7 (3.6–3.7)	1.7 (1.6–1.8)	5.1 (5.0–5.2)	<.001*
Categorical variables	N (%)	N (%)	N (%)	
Woman's age at ANC/PMTCT enrollment (yr)				
≤25	489 (22.2)	219 (23.2)	270 (21.4)	.25
26 to 30	665 (30.2)	276 (29.3)	389 (30.8)	
31 to 35	618 (28.0)	250 (26.5)	368 (29.2)	
>35	433 (19.6)	198 (21.0)	235 (18.6)	
Marital status				
Married	1094 (65.7)	452 (64.4)	642 (66.7)	.01
Single	441 (26.5)	184 (26.2)	257 (26.7)	
Cohabiting	105 (6.3)	47 (6.7)	58 (6.0)	
Divorced/widowed	25 (1.5)	19 (2.7)	6 (0.6)	
Facility level				
Dispensary	1300 (58.5)	587 (61.9)	713 (55.9)	.02
Health centre	723 (32.5)	286 (30.1)	437 (34.3)	
Hospital	201 (9.0)	76 (8.0)	125 (9.8)	
WHO disease stage				
I or II	2125 (95.9)	891 (94.3)	1234 (97.0)	.001
III or IV	92 (4.1)	54 (5.7)	38 (3.0)	
CD4 cell count				
<350 cells per μL	261 (31.6)	107 (32.8)	154 (30.7)	.53
≥350 cells per μL	566 (68.4)	219 (67.2)	347 (69.3)	
Self-reported adherence*				
Good	611 (96.5)	296 (94.9)	315 (98.1)	.03
Poor	22 (3.5)	16 (5.1)	6 (1.9)	
Infant-feeding options				
Exclusive breastfeeding	1430 (70.9)	632 (73.1)	798 (69.1)	.10
Formula feeding	224 (11.1)	83 (9.6)	141 (12.2)	
Mixed feeding	364 (18.0)	149 (17.3)	215 (18.6)	
MTCT status at 12 wk postnatally				
Positive	59 (2.7)	46 (4.8)	13 (1.0)	<.001
Negative	2165 (97.3)	903 (95.2)	1262 (99.0)	
Gestational age at first ANC visit				<.001
0 to 12 wk (1st trimester)	177 (8.7)	12 (1.6)	165 (12.9)	
13 to 27 (2nd trimester)	1471 (72.2)	371 (48.6)	1101 (86.4)	
28+ (3rd trimester)	389 (19.1)	380 (49.8)	9 (0.7)	

Self-reported adherence: good (at least 95% of prescribed pills taken), poor (<95% of prescribed pills taken).

ANC = antenatal care clinic, CD4 = cluster of differentiation 4, CI = confidence interval, HIV = human immunodeficiency virus, MTCT = mother-to-child transmission of HIV, PMTCT = prevention of mother-to-child transmission, WHO = World Health Organisation.

* Student *t* test.

count at the first ANC visit between women whose children became infected with HIV as compared to those whose children remained HIV negative up to 12 weeks (mean CD4 330; 95% CI: 230–423 vs mean CD4 485; 95% CI: 465–501 cells per μL). Women, whose children became infected, were more likely to be cohabiting (14.3% vs 6.1%) or have higher GA (25.6 vs 21.9 weeks) when they made their first ANC visit. Similarly, women whose children became infected were more likely to have made <4 visits (78% vs 41.7%) or to have initiated ART at later GA (24.9 vs 22.3 weeks) (Table 3).

In a univariable analysis, the number of ANC visits before delivery was inversely related to MTCT risk (odds ratio [OR] 0.60, 95% CI 0.52–0.70). GA at first ANC visit (OR 1.06, 95% CI 1.02–1.10) was positively associated with MTCT risk. In a multivariable model we included CD4 cell count, marital status, GA at ART initiation, GA at first visit and number of visits before delivery. The adjusted MTCT rate, decreased by 51% (OR 0.49, 95% CI 0.31–0.77) for those who made 4 or more ANC visits compared to those who made fewer than 4 ANC visits (Table 4). Furthermore, no cases of MTCT were observed when 7 or more ANC visits were made (Fig. 2).

Results from a complete case analysis were overall similar to that of the multiple imputations model. For example, the adjusted MTCT risk decreased by 51% (OR 0.49, 95% CI 0.37–0.65) for those who made 4 or more ANC visits compared to those who made fewer than 4 ANC visits (Table S1, Supplemental Digital Content, http://links.lww.com/MD/G477).

Table 3

Characteristics of 2224 women, comparing mother–infant couples where mother-to- child transmission of HIV had occurred vs not occurred at 12 weeks postnatally.

Variables	MTCT positive 59 (2.7%)	MTCT negative 2165 (97.3%)	*P*-value
Continuous variables	Mean (95% CI)	Mean (95% CI)	
Gestational age at first ANC visit	25.6 (22.7–27.9)	21.9 (21.6–22.3)	.001*
Overall number of ANC visits	1.8 (1.3–2.2)	3.7 (3.6–3.8)	<.001*
Gestational age at ART initiation	24.9 (21.8–27.4)	22.3 (22.0–22.6)	.030*
CD4 count at 1st ANC visit (cells/μL)	330.4 (230.9–423.5)	485.8 (465.5–501.1)	.005*
Categorical variables	59 (2.7%)	2165 (97.3%)	*P*-value†
Woman's age at ANC/PMTCT enrollment (yr)			
≤25	12 (21.4)	477 (22.2)	.71
26 to 30	14 (25.0)	651 (30.3)	
31 to 35	16 (28.6)	602 (28.0)	
>35	14 (25.0)	419 (19.5)	
Marital status			
Married	26 (61.9)	1068 (65.8)	.04
Single	8 (19.0)	433 (26.7)	
Cohabiting	6 (14.3)	99 (6.1)	
Divorced/widowed	2 (4.8)	23 (1.4)	
Facility level			
Dispensary	41 (69.5)	1261 (58.1)	.25
Health centre	14 (23.7)	709 (32.8)	
Hospital	4 (6.8)	195 (9.1)	
WHO disease stage			
I or II	57 (98.3)	2068 (95.8)	.51
III or IV	1 (1.7)	91 (4.2)	
CD4 cell count			
<350 cells per μL	10 (50)	251 (31.1)	.20
≥350 cells per μL	10 (50)	556 (68.9)	
Self-reported adherence			
Good (at least 95% of prescribed pills taken)	14 (93.3)	597 (96.6)	.46
Poor (<95% of prescribed pills taken)	1 (6.7)	21 (3.4)	
Infant-feeding options			
Exclusive breastfeeding	39 (70.9)	1391 (70.9)	.85
Formula feeding	5 (9.1)	219 (11.2)	
Mixed feeding	11 (3.0)	353 (18.0)	
Clinic visits before delivery			
<4	46 (78.0)	903 (41.7)	<.001
>4	13 (22.0)	1262 (58.3)	
Gestational age at first ANC visit			
0 to 12 wk (1st trimester)	3 (7.3)	174 (8.7)	.06
13 to 27 (2nd trimester)	24 (58.5)	1448 (72.5)	
28+ (3rd trimester)	14 (34.2)	375 (18.8)	

ANC = antenatal care clinic, ART = antiretroviral therapy, CD4 = cluster of differentiation 4, CI = confidence interval, HIV = human immunodeficiency virus, MTCT = mother-to-child transmission of HIV, PMTCT = prevention of mother-to-child transmission, WHO = World Health Organisation.

* Student *t* test.

† Overall *P*-value, from Fisher exact test.

Table 4

Predictors of mother-to-child transmission of HIV among N = 2224 pregnant women newly diagnosed with HIV in Dar es Salaam Tanzania 2014–2016.

Variables	Crude OR (95% CI)	Adjusted OR (95% CI)
ANC visits before delivery	0.60 (0.52–0.70)	0.49 (0.31–0.77)
GA at 1st ANC visit	1.06 (1.02–1.10)	0.94 (0.89–1.00)
GA at ART initiation	1.04 (1.00–1.09)	0.92 (0.86–0.98)
Woman's age at ANC/PMTCT enrollment (yr)		
≤25	Reference	
26 to 30	0.86 (0.39–1.87)	
31 to 35	1.06 (0.50–2.26)	
>35	1.33 (0.61–2.92)	
Marital status		
Married	Reference	
Single	0.76 (0.34–1.69)	0.74 (0.41–0.73)
Cohabiting	2.49 (1.00–6.19)	2.49 (0.81–7.68)
Divorced/widowed	3.57 (0.80–15.95)	4.43 (0.93–21.10)
Facility level		
Dispensary	Reference	
Health centre	0.61 (0.33–1.12)	
Hospital	0.62 (0.22–1.76)	
WHO disease stage		
I & II	Reference	
III & IV	0.41 (0.06–2.98)	
CD4 cell count		
<350 cells per μL	Reference	Reference
≥350 cells per μL	0.45 (0.19–1.10)	1.3 (0.30–5.70)
Self-reported adherence*		
Good	Reference	
Poor	0.49 (0.06–3.92)	
Infant-feeding options		
Exclusive breastfeeding	Reference	
Formula feeding	0.81 (0.32–2.09)	
Mixed feeding	1.11 (0.56–2.19)	
GA age at 1st ANC visit		
0 to 12 weeks	Reference	
13 to 27	0.96 (0.29–3.23)	
28+	2.17 (0.06–7.63)	

* Good = At least 95% of prescribed pills taken; poor = <95% of prescribed pills taken).
ANC = antenatal care, ART = antiretroviral therapy, CD4 = cluster of differentiation 4, CI = confidence interval, GA= gestation age, HIV = human immunodeficiency virus, OR = odds ratio, PMTCT = prevention of mother-to-child transmission, WHO = World Health organisation.

3.4. Difference in costs

The overall health care cost utilized by the entire cohort of 2224 women from their first ANC visit up to time of the first infant HIV test visit, was estimated to US$ 190,727.48.

This cost includes medication, laboratory tests, and time spent by staff providing ANC services both during the first and the follow-up visits, as well as time spent on defaulter tracing (Table 5). The average cost per woman incurred by those who made at least 4 visits was US$ 84.82, with the highest amount spent on ART and staff salaries (time spent by health care providers to provide services to women during their ANC/PMTCT visits). The average cost per patient incurred by those who made <4 visits was US$ 87.02 (Table 5). This implies that more ANC visits would not incur additional health care costs but rather the opposite, with potential cost savings (for the entire pregnancy period) of 2.2 US$ per woman who makes at least 4 visits, compared to women who make fewer visits (Table 5).

3.5. Sensitivity analysis

The average (per patient) cost difference between those who made at least 4 visits and those who made <4 visits was not sensitive to changes in the pricing of ART but rather to changes in the cost of tracing PMTCT defaulters. Varying the unit cost of ART from the lowest and highest range according to the available literature, making at least 4 ANC visits, would always result in a cost reduction, which varied between US$ 1.95 and US$ 2.70, respectively relative to a scenario of <4 ANC visits. However, variations in the cost of defaulter tracing were more important: the average cost reduction when making at least 4 ANC visits relative to fewer than 4 visits would be US$ 26.0 if the unit cost of defaulter tracing was set to its maximum value. However, it appeared to be US$ 9.8 costlier per patient if the cost of defaulter tracing was set to its minimum value simply because the tracing cost will be slightly lower compared to the cost for actual clinic visit 3.00 vs 3.60 US$. The average cost difference estimated in the base case analysis changed just slightly when the other parameters were varied in the sensitivity analysis (Fig. 3).

4. Discussion

This study examined the MTCT outcomes in relation to the cost of adhering to a minimum of 4 intergraded ANC/PMTCT visits among pregnant women newly diagnosed with HIV in the era of PMTCT option B^+ in Tanzania. We found that those who attended <4 ANC visits during pregnancy had an increased risk of MTCT of HIV at 12 weeks postnatally. Furthermore, we observed no MTCT at all when a woman made 7 or more ANC visits before delivery.

We observed relatively low overall vertical transmission rate (2.7%) at 12 weeks of life among newly diagnosed women living with HIV, initiated on option B+. Since advanced maternal HIV disease is an important risk factor for MTCT[32–34], this observation could have been contributed by the fact that most of the newly diagnosed women in this real-life cohort, were in an early HIV disease stage. Given that ART adherence has been shown to often drop significantly with time postdelivery,[35] this MTCT rate does not reflect the final MTCT rate at the end of the breastfeeding period.

Option B^+ for PMTCT, is considered as a cost-effective strategy for ensuring universal access to ART for women living with HIV.[36] We observed that among these women who were newly diagnosed with HIV, those who made fewer ANC visits were more likely to start ANC/PMTCT later, therefore initiating ART later. This implies that, those who registered late were more likely to have missed out on important ANC visits where PMTCT interventions offered could have made a difference.

Furthermore, although majority of women in this cohort made their first ANC visit during their second trimester, MTCT was less likely if the first visit was as early as 22 weeks GA than if it was later than 25 weeks of gestation. Thus, high GA at PMTCT initiation could have influenced the MTCT outcomes. However, although, both the number of ANC visits and GA at ART initiation remained significant predictors of MTCT, the number of ANC visits was a more important predictor. Thus in order to optimize the benefits of option B^+, early ANC booking and early ART initiation, must be accompanied with retention in the PMTCT cascade, ensuring good ART adherence.

Previous studies have shown that adherence to prenatal visits are often linked to high retention in postnatal PMTCT care,

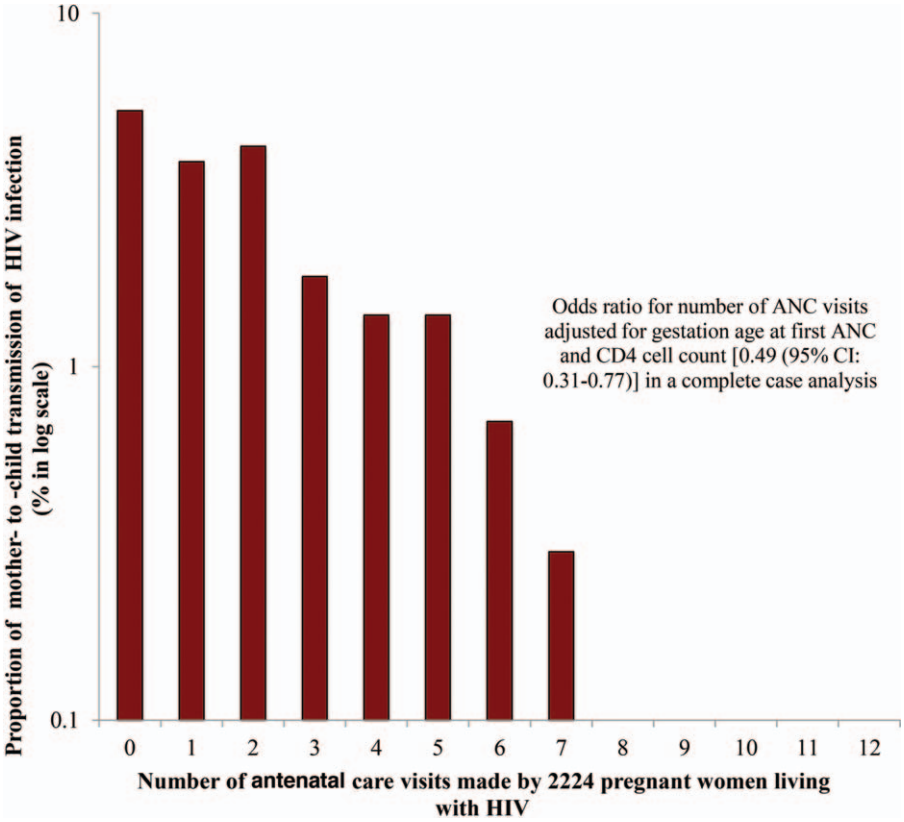

Figure 2. Proportion of mother-to- child transmission of HIV in relation to antenatal care visits among 2224 pregnant women living with HIV in Dar es Salaam 2014–2016. ANC = antenatal care, CD4 = cluster of differentiation 4, CI = confidence interval, HIV = human immunodeficiency virus.

including high ART adherence.[37] For instance, in Rwanda, the number of ANC visits was directly related to postnatal ART adherence, such that 1, 2, 3, and 4 ANC visits corresponded to postnatal ART adherence rates of 56%, 77%, 81%, and 83%, respectively.[37] Similarly, in Malawi, ANC visits between 1 to 2 and 3 to 4 corresponded to ART adherence rates of 49% and 72%, respectively.[37]

Assuming that the observed relationship between ANC visit frequency and MTCT rate is causal, our observations indicate that timing of ANC booking and most importantly the number of

Table 5

Difference in costs of antenatal care visit and the risk of mother-to-child transmission of HIV among 2224 pregnant women treated under option B+ in Dar es Salaam, Tanzania, who made at least 4 antenatal clinic visits compared to those who made fewer than 4 visits.

Variables		<4 visits (N = 949)			4 or more visits (N = 1275)		
PMTCT service components	Unit cost US$	No. of units*	No. of patients	Overall cost (US$)	No. of units*	No. of patients	Overall cost (US$)
First ANC/PMTCT visit	5.23	1	949	4963.27	1	1275	6668.25
CD4 cell count tests	15.76	1	949	14,956.24	1	1275	20,094.00
PMTCT follow-up visits	3.60	2	949	6832.8	5	1275	22,950.00
Defaulter tracing	7.00	3	949	19,929	0	1275	0.00
Antiretroviral medication	8.00	4	949	30,368	5	1275	51,000.00
Haemoglobin test	0.88	1	949	835.12	1	1275	1122.00
Serum creatinine test	0.32	1	949	303.68	1	1275	408.00
Alanine transferase test	0.91	1	949	863.59	1	1275	1160.25
Cotrimoxazole syrup	0.62	6	949	3530.28	6	1275	4743.00
Total cost for PMTCT care			82,581.98		108,145.50		
No. MTCT events/total number of women in each group			46/949		13/1275		
Average cost/patient (US$)†			82,581.98/949 = 87.02 US$		108,145.5/1275 = 84.82 US$		

ANC = antenatal clinic, CD4 = cluster of differentiation 4, MTCT = mother-to-child transmission, PMTCT = prevention of mother-to-child transmission of HIV.

* Number of units = number of services utilised.

† Average cost/patient (US$): total cost of PMTCT services/number of patients for each group.

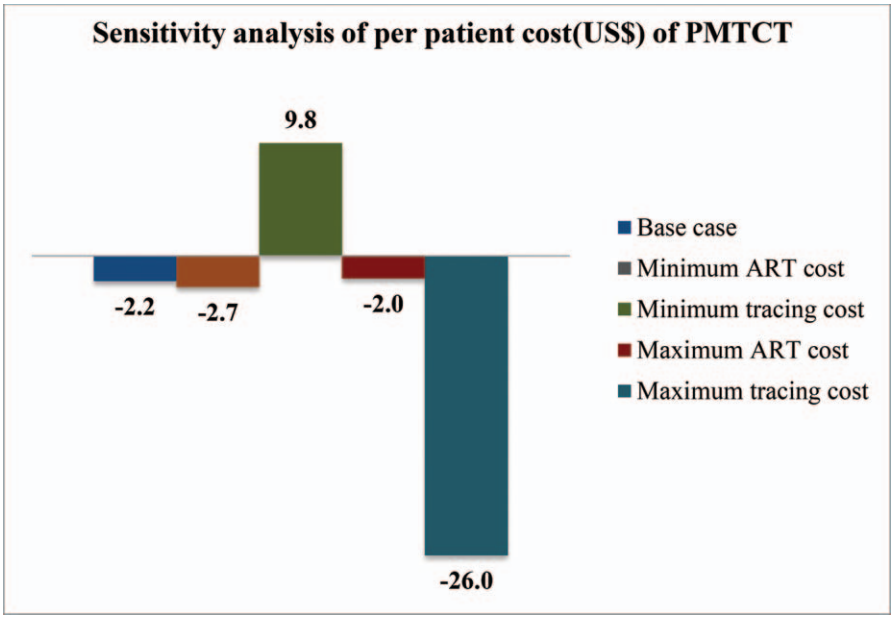

Figure 3. Sensitivity analysis of average incremental cost (US$) relative to the base case for at least 4 antenatal clinic visits vs <4 visits for 2224 pregnant women living with HIV in Dar es Salaam using a low vs high range of costs for ART and defaulter tracing. ART = antiretroviral therapy, HIV = human immunodeficiency virus, PMTCT = prevention of mother-to-child transmission.

ANC visits could be an important warning indicator of women at higher risk of MTCT.

Although viral load and resistance testing was not routinely performed and thus not available during the study period, studies have shown that poor adherence to clinical follow-up visits is linked to poor adherence to ART, in turn closely associated with poor viral load suppression.[38,39] Missing an ANC visit could mean missing out on both ART refill and adherence counselling, both crucial elements for achieving good PMTCT outcomes.

Studies have also shown that adequate viral suppression in the mother can prevent most perinatal MTCT cases[40,41] Viral load suppression before delivery is achievable in most pregnant women who are living with HIV if they are initiated on efficacious ART in early pregnancy.[42] However, persistent viremia combined with sub-optimal ART adherence can lead to drug resistance and ART failure, and increase the risk of MTCT.[43] Although a small proportion of pregnant women may have pre-existing resistance mutations,[44] most drug resistance is linked to poor adherence to ART and clinic visits.[43]

Although most women in this cohort included in the analysis self-reported good ART adherence, we cannot confidently conclude that they had good medication adherence since a majority had missing values on this variable. It is known that inadequate prenatal care limits the likelihood of receiving adequate ART refill and counselling, and subsequently impacts viral suppression at delivery.[38] Thus, extra efforts such as task-shifting to community health workers may be required to encourage early ANC booking and retention in PMTCT care.[27]

This study indicates that investing in more and earlier ANC visits for a pregnant woman living with HIV may be cost-effective. Losses along the PMTCT treatment cascade resulting from delays or gaps in receiving ART and thus inadequate viral suppression may have a deleterious impact on achieving the full health impact of option B+. More visits can increase the cost related to service utilization (medication costs and health care providers' time). However, adding defaulter tracing to the workload of already overstretched health care providers, also means incurring additional costs as high as $15 per person per visit for a PMTCT client who misses an appointment. Thus, where possible, the need for defaulter tracing should be minimised or avoided by encouraging women to adhere to the scheduled clinic visits in order to reduce health care cost.

Since more ANC visits was associated with fewer children becoming HIV-infected by their mothers, future health care costs for treating these children, including lifelong ART, regular clinic visits, clinical monitoring, and laboratory tests, should also be taken into account when considering future cost saving potentials through better ANC adherence. It has been estimated that even with the reduced ART cost, an average of between $440 and $580 per patient per year would be required to treat 1 HIV-positive African child initiated on LPV/r-based ART (the current paediatric standard regimen in Tanzania).[45,46] Thus the additional cost for reaching ANC visits above 4 is far lesser that the cost of potentially having an MTCT child and the antecedent costs.

Our sensitivity analysis revealed that changes in the unit price of ART and the cost of tracing a PMTCT defaulter were the main drivers of the difference in cost. Thus, as less expensive ART formulations become available, encouraging early ANC and retention in PMTCT care can significantly reduce both MTCT, future HIV treatment costs as well as costs related to the tracing of defaulters.

ANC uptake can be improved, for example, by using community health workers to do sensitization in communities[27]. However, retention in PMTCT care requires addressing health system barriers (by ensuring good quality of care,[47,48] and easier access to health facilities and to family planning)[48,49] and as well as the strengthening of longer-term individual factors including education, household wealth and employment.[49]

Thus, to improve both uptake and retention, multifaceted and multilevel interventions are required involving multiple stakeholders such as community health workers, midwives, and families.

This study had some limitations. Firstly, we focussed entirely on the added costs related to PMTCT care during pregnancy and did not consider the cost of delivery at a health facility or other non-HIV-related pregnancy care costs. Thus, in that respect the reported cost is not a complete estimate of total prenatal ANC/PMTCT costs. Secondly, our analysis takes a provider perspective and does not include patient time and travel costs. Thirdly, some observations had missing values making it difficult to draw solid conclusions. Fourthly, women who did not bring their babies for EID before month 3 postnatally were excluded from our analysis, and this may have underestimated the true MTCT rate. Also, we limited our analysis to women newly diagnosed with HIV, since these are known to have a higher risk of MTCT than women on ART at time of conception. Despite these limitations, it nonetheless helps us to roughly estimate service utilization during pregnancy and impact on patient outcomes at 12 weeks postnatally and associated health system costs.

5. Conclusions

This study indicates that most pregnant women living with HIV in Dar es Salaam initiated ANC late and >40% failed to adhere to the recommended minimum of 4 visits. The additional cost for reaching ANC above 4 is far lesser that the cost of potentially having an MTCT child and the antecedent costs. Thus, investing in earlier ANC and ensuring that pregnant women living with HIV complete at least the recommended number of ANC visits may reduce health care costs, as it does not increase health care spending in the short-term but may significantly reduce long-term spending on HIV care by reducing the risk of MTCT.

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Author contributions

HN, AME, PM, CK, GL, RU, and TB contributed to the study conceptualization and methodology; HN conducted the field study, linked the databases and extracted the required data; HN analysed the data and drafted the original manuscript; NO worked with HN on formal analysis; AME, GB, NO, PM, CK, TB, KM, and NZ contributed to the project administration, writing (review and editing), data visualization, supervision and funding acquisition. All authors have seen and approved their contributions and the final version of the manuscript.

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