Universal combination antiretroviral regimens to prevent mother-to-child transmission of HIV in rural Zambia: a two-round cross-sectional study

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Objective To evaluate if a pilot programme to prevent mother-to-child transmission (PMTCT) of the human immunodeficiency virus (HIV) was associated with changes in early childhood survival at the population level in rural Zambia.

Methods Combination antiretroviral regimens were offered to pregnant and breastfeeding, HIV-infected women, irrespective of immunological status, at four rural health facilities. Twenty-four-month HIV-free survival among children born to HIV-infected mothers was determined before and after PMTCT programme implementation using community surveys. Households were randomly selected and women who had given birth in the previous 24 months were asked to participate. Mothers were tested for HIV antibodies and children born to HIV-infected mothers were tested for viral deoxyribonucleic acid. Multivariable models were used to determine factors associated with child HIV infection or death.

Findings In the first survey (2008–2009), 335 of 1778 women (18.8%) tested positive for HIV. In the second (2011), 390 of 2386 (16.3%) tested positive. The 24-month HIV-free survival in HIV-exposed children was 0.66 (95% confidence interval, CI: 0.63–0.76) in the first survey and 0.89 (95% CI: 0.83–0.94) in the second. Combination antiretroviral regimen use was associated with a lower risk of HIV infection or death in children (adjusted hazard ratio: 0.33, 95% CI: 0.15–0.73). Maternal knowledge of HIV status, use of HIV tests and use of combination regimens during pregnancy increased between the surveys.

Conclusion The PMTCT programme was associated with an increased HIV-free survival in children born to HIV-infected mothers. Maternal utilization of HIV testing and treatment in the community also increased.

Abstracts in عربي, 中文, Français, Русский and Español at the end of each article.

Introduction

In recent years, studies have shown unequivocally that the use of combination antiretroviral regimens, for either treatment or prophylaxis, during the antenatal, intrapartum and breastfeeding periods in women with human immunodeficiency virus (HIV) infections can reduce the rate of transmission to their infants to less than 5%.[1–3] The World Health Organization (WHO) has endorsed this approach to the prevention of mother-to-child transmission (PMTCT) of the human immunodeficiency virus (HIV), which it terms the Option B strategy. It is relatively simple, is aligned with adult HIV treatment guidelines, is associated with a reduction in comorbid conditions related to acquired immunodeficiency syndrome (AIDS), and can limit HIV transmission to uninfected partners.[4,5] In fact, this approach has been extended in many settings into what has been termed Option B+, where antiretroviral therapy (ART) is started during pregnancy for all HIV-infected pregnant women and continued for life.[6]

Although maternal antiretroviral regimens have been shown to be highly effective in clinical trials, the results are difficult to replicate fully in real world settings,[7] largely because of inefficiencies in health systems.[8] For example, incomplete uptake of health-care services in a community can result in poor coverage of proven biomedical interventions.[9,10] In addition, delays in screening patients for their eligibility for antiretroviral prophylaxis or treatment can result in late drug administration.[11] There is also growing evidence in the literature suggesting that, after therapies have been started, treatment adherence and programme retention may be poor among HIV-infected pregnant and breastfeeding women.[12–14]

Research on the implementation of antiretroviral programmes for PMTCT is needed to extend our understanding of the efficacy of these interventions in individuals to their effectiveness in the general population.[15,16] This broader understanding is urgently needed by policy-makers and programme managers who are planning to adopt or optimize maternal combination antiretroviral regimens for PMTCT in various settings.[6,17,18] The aim of this study was to evaluate, at the population level, a pilot PMTCT programme similar to Option B in rural Zambia (Table 1). Cross-sectional household surveys were performed before and after implementation of the programme to determine whether early childhood survival in the community changed during this time.

Methods

The pilot programme

In April 2009, we implemented a pilot PMTCT programme at four health-care facilities in the rural Kafue district of Zambia using a phased approach. With support from the Zambian Ministry of Health, we offered standard combination antiretroviral regimens to all HIV-infected pregnant women,

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Table 1. **Characteristics of a pilot programme to prevent mother-to-child transmission (PMTCT) of the human immunodeficiency virus (HIV) in the Kafue district of Zambia, 2009–2011, and the World Health Organization's strategies**

Characteristic	Zambian pilot programme	WHO strategy	
		Option B[4]	Option B+[5]
CD4+ T-cell count measured before starting ART	Yes	Yes	Optional
Maternal combination antiretroviral regimen during pregnancy and labour	Yes	Yes	Yes
Gestational age at regimen initiation	28 weeks or later	14 weeks or later	14 weeks or later
Timing of infant prophylaxis with zidovudine or nevirapine	First week of life	First 6 weeks of life	First 6 weeks of life
Maternal combination antiretroviral regimen during breastfeeding	Yes	Yes	Yes
Continuation of combination antiretroviral regimens after cessation of breastfeeding	Only for those eligible for HIV treatment according to adult guidelines	Only for those eligible for HIV treatment according to adult guidelines	Lifelong HIV treatment for all women

ART: antiretroviral therapy; WHO: World Health Organization.

irrespective of immunological status. A detailed description of the clinical services provided has been presented elsewhere.[19] Briefly, consistent with the standard of care in Zambia, all pregnant women who sought antenatal care were offered opt-out HIV counselling and testing; those who tested positive underwent clinical and immunological (i.e. CD4+ T-cell count) screening. These evaluations were required by national treatment guidelines and were used to determine whether the maternal ART should be continued after breastfeeding. In addition, since virological monitoring was not routinely available, these baseline data were also important for assessing treatment responses. Women who met Zambian national guideline criteria for HIV treatment (i.e. a CD4+ T-cell count less than 350 cells/μl or WHO clinical stage 3 or 4) immediately started lifelong antiretroviral therapy.[20]

In our programme, we also offered three-drug combination regimens to women who did not meet these eligibility criteria, starting at 28 weeks' gestation and continuing until the cessation of breastfeeding. The regimens were based on the nucleoside reverse transcriptase inhibitors zidovudine and lamivudine, which were combined with either nevirapine or efavirenz. (At the time, Zambian PMTCT guidelines recommended zidovudine monotherapy for HIV-infected pregnant women from 28 weeks' gestation until delivery and nevirapine peripartum for mother and neonate but no antiretrovirals during breastfeeding.)[21] Although we implemented this pilot programme before 2010, when WHO first recommended antiretroviral prophylaxis during breastfeeding, this regimen closely resembles Option B, as described in later WHO guidelines (Table 1).[4]

Household surveys

To measure changes associated with the PMTCT programme at the population level, we conducted two household surveys in the catchment areas of the four health-care facilities taking part. We used the methods first introduced in the four-country study to measure the 24-month HIV-free survival in children born to HIV-infected mothers.[22] We assessed survival using methods similar to those used in Demographic and Health Surveys conducted in many African countries.[23] The sampling method was established in the first survey, which was conducted between November 2008 and May 2009, before implementation of the pilot PMTCT programme. Government-demarcated catchment areas were mapped and we randomly selected zones within these communities. These zones were used by each health-care facility's Neighbourhood Health Committee for community outreach. We identified a central point in each zone and used a spin-the-bottle approach to select the starting point for enumeration.[24] Individual residences were then selected at a predefined spacing interval, which was based on the estimated population of each catchment area. The residences were sampled in a clockwise direction until the whole zone had been canvassed. Team members then went to the next zone on the list and started the process anew. In the first survey, sampling continued until 387 eligible households, as defined below, had been surveyed in each community. If the target number was reached midway through a zone, sampling was completed for that zone. The second survey was conducted in the same zones, used the same predefined residence spacing intervals and took place between March and December 2011, at least two years after the PMTCT programme had been introduced at each health-care facility. However, since the starting point for canvassing households in each zone was randomly selected, the two surveys did not necessarily include the same households.

At each household, trained enumerators identified the head of the household and administered a screening questionnaire. If a household member was reported to have given birth in the last two years, written consent was requested for the use of an additional questionnaire with 165-questions to collect more data on the demographic and socioeconomic characteristics of the household and on the medical history of the child's mother. Separate written consent was also requested for the collection of blood specimens from eligible mothers and children. Maternal samples were tested for HIV antibodies and specimens from children who were exposed to HIV (i.e. because their mothers were seropositive) were tested for HIV deoxyribonucleic acid using polymerase chain reaction. In households in which a newborn child had died within the past two years, survey staff administered a comprehensive verbal autopsy questionnaire.[25] If members of a selected household were not available at the time of the initial visit, enumerators returned up to three times and scheduled appointments to meet with either the head of the household or the child's mother or both.

The primary outcome measure was the proportion of HIV-exposed children that were alive and HIV-uninfected at 24 months of age (i.e. 24-month HIV-free survival). We hypothesized

that the proportion would increase between the two surveys from 50% to 75%.[26] To achieve a power of 80% with an α of 0.05 using the χ^2 test, we needed to enrol 58 HIV-exposed children born within the last two years from each of the four study sites. Assuming an estimated prevalence of HIV infection of 15%, we calculated that we needed to include a minimum of 387 households with a child under the age of two years in each community.

Statistical methods

We compared participants in the two surveys. Differences in categorical variables were assessed using Pearson's χ^2 test after we confirmed that the test's assumptions were valid in each case. Differences in continuous variables were assessed using nonparametric Wilcoxon rank-sum tests. The overall HIV-free survival rate in HIV-exposed children was derived for each survey using a parametric survival model with a Weibull distribution. A Weibull model was considered appropriate following graphical exploration of the baseline hazard. We also examined differences in HIV-free survival between the two surveys in each individual community using the same approach. Further, we identified factors associated with HIV infection or death by calculating adjusted hazard ratio (aHR) using Weibull regression with interval censoring and adjustment for clustering. The variables selected a priori for inclusion in our multivariable models were the PMTCT therapy, maternal age, parity, educational level and marital status, institutional antenatal care, institutional delivery and infant breastfeeding. In addition, a binary variable for whether the data were collected in the first or second household survey (i.e. before or after programme implementation) was included to take into account unmeasured time trends between the surveys. Because extensive information was collected in the household questionnaires, the multivariable models included socioeconomic and children's health factors that were associated with HIV-free survival at a statistical significance level of $P < 0.10$. A factor was excluded if it did not appear to be independent of other factors included in the proposed model. We controlled for the survey site using the strata option in Stata version 12.1 (StataCorp. LP, College Station, United States of America). Further, to correct for possible correlations within sites, we employed a sandwich estimator to obtain robust standard errors using the *vce(robust)* option. In addition, because we were interested in the detailed effect of the pilot PMTCT programme on programme outcomes, we used Pearson's χ^2 test to compare the utilization of specific PMTCT services between respondents who took part in the first and second surveys. For all analyses, we considered $P < 0.05$ to be statistically significant.

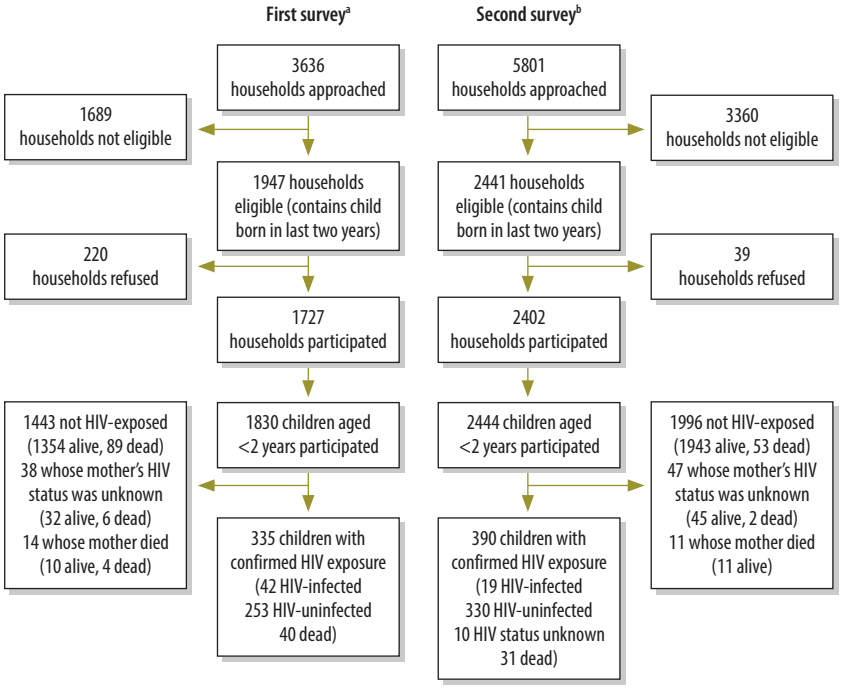
The study was approved by the Biomedical Research Ethics Committee of the University of Zambia and the institutional review boards of the University of North Carolina at Chapel Hill and of the University of Alabama at Birmingham in the United States.

Results

In total, 31 zones were visited in each of the two surveys: seven in Chipapa, six in Kafue Estates, nine in Kafue Missions and nine in Mount Makulu. In the first survey, 3636 households were approached, 1947 (53.5%) of which were found to be eligible (Fig. 1). Information about maternal HIV status was available for 1778 (97.2%) of the 1830 children aged under two years in these households; 335 (18.8%) were found to be HIV-exposed. In the second survey, 5801 households were approached, 2441 (42.1%) of which were found to be eligible. Information about maternal HIV status was available for 2386 of 2444 (97.6%) children aged under two years and 390 (16.3%) were found to be HIV-exposed. The geographical distribution of eligible households sampled in the second survey is shown in Fig. 2 – comparable data were not collected in the first survey.

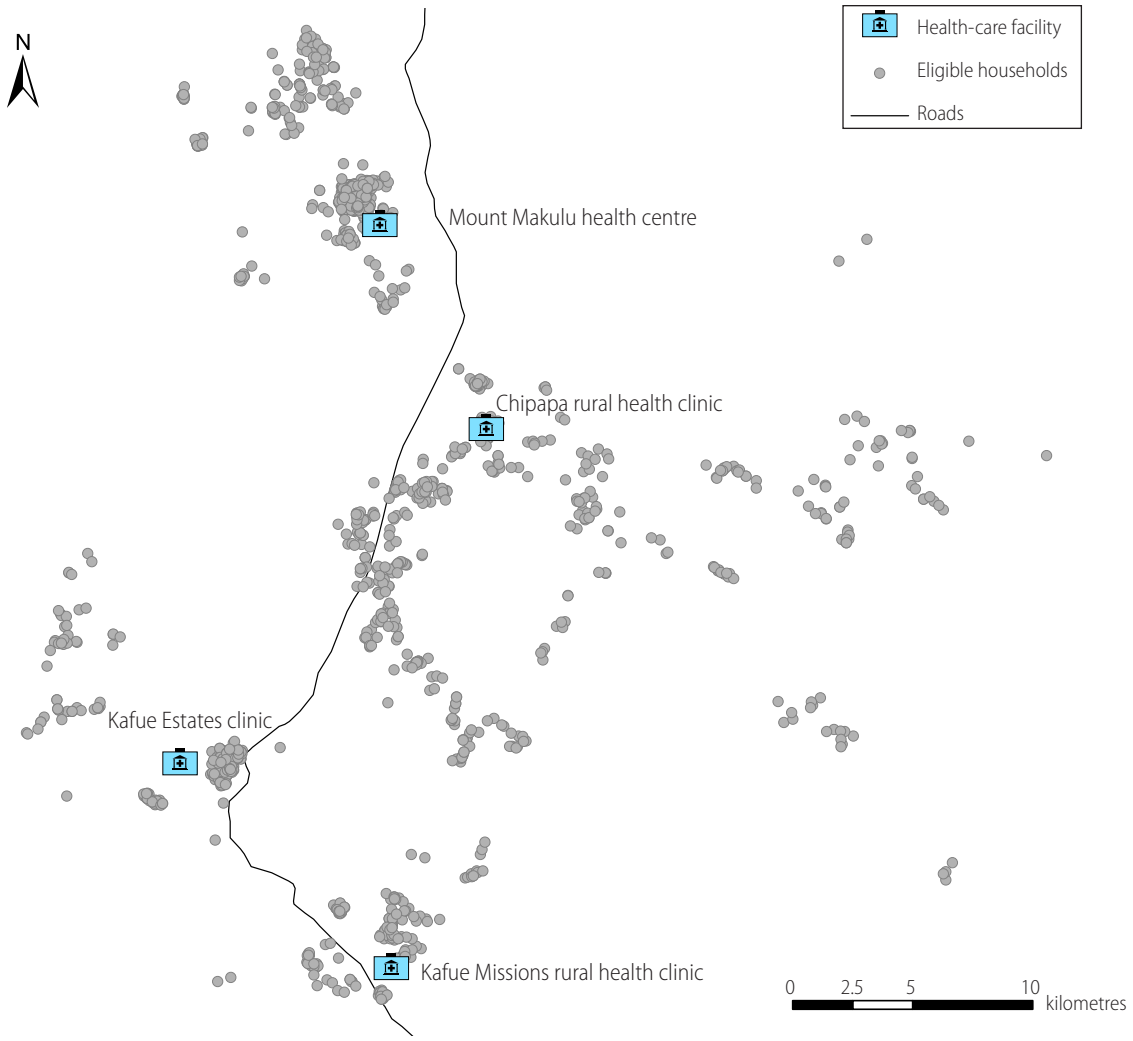
There were significant differences in household and maternal characteristics between the two surveys (Table 2). Socioeconomic conditions were better in the second survey than the first: households in the second survey were significantly more likely to report having a water supply, a finished floor, electricity, a refrigerator, a television and a mobile phone ($P < 0.0001$ for all). The prevalence of HIV infection among mothers appeared to decline between the surveys, from 18.8% to 16.3% ($P < 0.071$), and the proportion of women who gave birth

Fig. 1. **Community surveys before and during the pilot programme to prevent mother-to-child transmission (PMTCT) of the human immunodeficiency virus (HIV) in the Kafue district of Zambia, 2009–2011**



[a] The first survey was conducted between November 2008 and May 2009, before implementation of the PMTCT pilot programme.
[b] The second survey was conducted between March and December 2011, at least two years after the PMTCT pilot programme had been introduced.

Fig. 2. **Geographical distribution of eligible households in the second community survey[a] during the pilot programme to prevent mother-to-child transmission (PMTCT) of the human immunodeficiency virus (HIV) in the Kafue district of Zambia, 2009–2011**



[a] Comparable data were not collected in the first survey.
Source: map produced using ArcGIS® (Esri, Redlands, United States of America) and shapefile of roadmap.[27]

at a health-care facility increased from 58.0% to 67.8% ($P < 0.0001$). The children's' characteristics appeared similar in the two surveys. In particular, there was no significant difference in their median age: 10.9 months in the first survey versus 10.8 months in the second ($P = 0.081$, Table 2).

The cumulative estimated 24-month survival in HIV-exposed children was significantly higher in the second survey than the first: 0.97 (95% confidence interval, CI: 0.95–0.99) versus 0.87 (95% CI: 0.84–0.95), respectively (Fig. 3). The difference in the estimated 24-month HIV-free survival was even more pronounced: 0.89 (95% CI: 0.83–0.94) in the second survey versus 0.66 (95% CI: 0.63–0.76) in the first (Fig. 4). These trends were consistent across all four communities. Multivariate analysis showed that the risk of HIV infection or death was significantly lower in the children of mothers who started a combination antiretroviral regimen during pregnancy than in those whose mothers had no antiretroviral prophylaxis (aHR: 0.33, 95% CI: 0.15–0.73). Moreover, even after adjustment for potential demographic and socioeconomic confounders, children in the second survey were less likely to acquire an HIV infection or die than those in the first (aHR: 0.52, 95% CI: 0.34–0.80; Table 3).

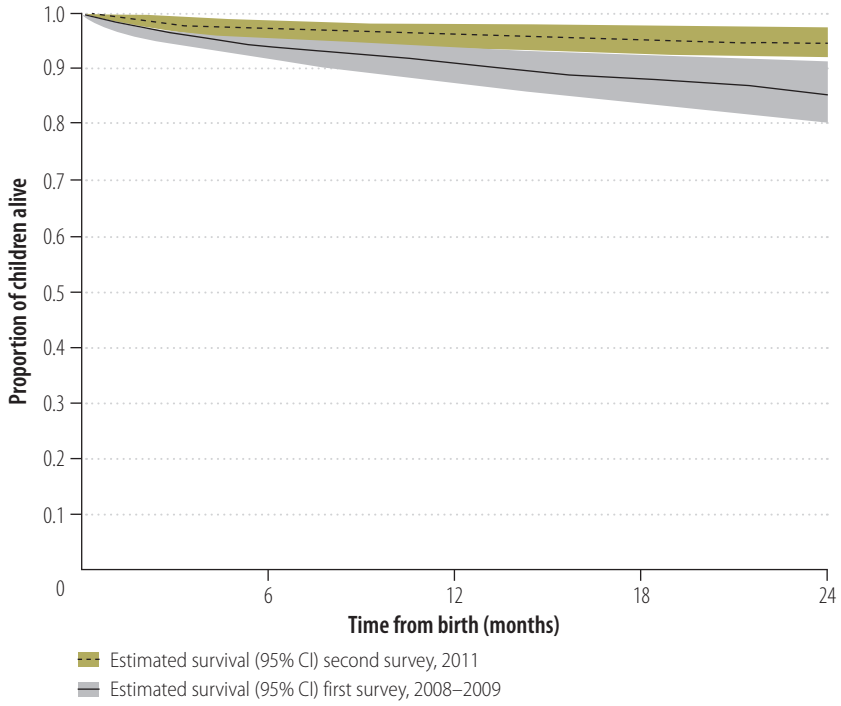
To assess the contribution of the pilot PMTCT programme to the observed improvement in the HIV-free survival rate in children, we examined differences in the utilization of specific PMTCT services between the surveys. Increases were observed between the first and second surveys in four key indicators in HIV-infected mothers (i.e. those who tested positive at the time of the survey): (i) the proportion who knew their HIV status (from 74.4% to 91.9%, $P < 0.0001$; Fig. 5, available at: http://www.who.int/bulletin/volumes/92/8/13-129833); (ii) the proportion who were tested for HIV during their last pregnancy (from 76.4% to 88.1%, $P < 0.0001$; Fig. 6, available at: http://www.who.int/bulletin/volumes/92/8/13-129833); (iii) the proportion who reported using any antiretroviral prophylaxis during their last pregnancy (from 42.5% to 67.5%, $P < 0.0001$; Fig. 7, available at: http://www.who.int/bulletin/volumes/92/8/13-129833); and (iv) the proportion who reported using combination antiretroviral regimens

Table 2. **Characteristics of households, mothers and children in a pilot programme to prevent mother-to-child transmission (PMTCT) of the human immunodeficiency virus (HIV) the Kafue district of Zambia, 2009–2011**

Characteristic[a]	No. (%) of households, mothers or children[a]		*P*[d]
	First survey[b] (*n* = 1830)	Second survey[c] (*n* = 2444)	
Household characteristics			
Water supply			< 0.0001
Piped water to house	256 (14.0)	401 (16.4)	
Piped water outside but available within grounds	437 (23.9)	516 (21.1)	
Public tap	379 (20.7)	704 (28.8)	
Other	758 (41.4)	823 (33.7)	
Toilet facilities			0.026
Flush toilet or pit latrine	1600 (87.4)	2161 (88.4)	
None	230 (12.6)	283 (11.6)	
Main floor material			< 0.0001
Finished floor (i.e. cement, tiles, wood or planks)	1094 (59.8)	1672 (68.4)	
Natural floor (i.e. earth, mud, dung or sand)	735 (40.2)	758 (30.9)	
Data missing	1 (0.1)	17 (0.7)	
Electricity	581 (31.7)	1032 (42.2)	< 0.0001
Refrigerator	353 (19.3)	641 (26.2)	< 0.0001
Television	705 (38.5)	1079 (44.1)	< 0.0001
Mobile phone	1103 (60.3)	1990 (81.4)	< 0.0001
Maternal characteristics			
Age at survey in years, median (IQR)	26 (21–31)	25 (21–30)	0.003
Parity, median (IQR)	2 (1–4)	2 (1–3)	0.0002
Marital status			0.075
Married or cohabitating	1531 (83.7)	2093 (85.6)	
Other	299 (16.3)	351 (14.4)	
Educational level			0.034
Primary schooling or none at all	924 (50.5)	1314 (53.8)	
Secondary or higher	906 (49.5)	1130 (46.2)	
Currently employed	697 (38.1)	1068 (43.7)	< 0.0001
HIV status (laboratory data; *n* = 1778 and *n* = 2386)[e]			0.071
Positive	335 (18.8)	390 (16.3)	
Negative	1443 (81.2)	1996 (83.7)	
Enrolled for antenatal care during last pregnancy	1729 (94.5)	2392 (97.9)	< 0.0001
Gestational age when antenatal care started, in weeks (*n* = 1720 and *n* = 2393), median (IQR)	20 (16–24)	20 (16–24)	0.488
Delivery in a health-care facility	1061 (58.0)	1658 (67.8)	< 0.0001
Child's characteristics			
Age at survey in months, median (IQR)	10.9 (4.6–16.9)	10.8 (5.2–17.3)	0.081
Birth weight in grams (*n* = 1179 and *n* = 1791),[e] median (IQR)	3000 (2800–3500)	3050 (2700–3400)	0.144
Birth weight ≤ 2500 g	193 (10.5)	300 (12.3)	< 0.0001
Feeding method in first 6 months of life (children aged > 6 months only, *n* = 1256 and *n* = 1747)[e]			
Exclusively breastfed	1088 (86.6)	1660 (95.0)	< 0.0001
Mixed feeding	148 (11.8)	34 (1.9)	
Formula feeding only	14 (1.1)	21 (1.2)	
Data missing	6 (0.5)	32 (1.8)	

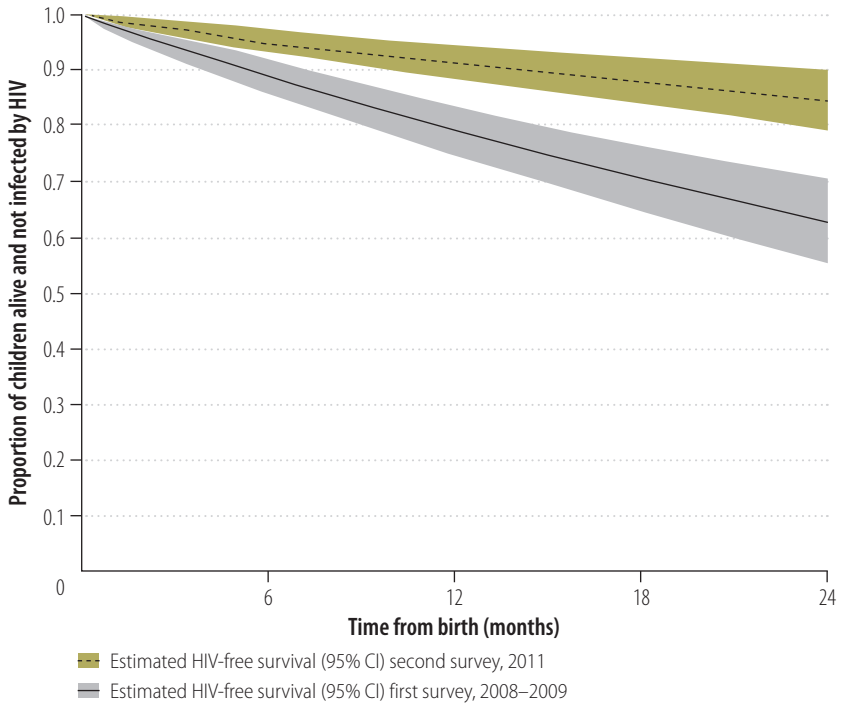
IQR: interquartile range.
[a] No. (%) unless otherwise stated in row headers.
[b] The first survey was conducted between November 2008 and May 2009, before implementation of the PMTCT programme.
[c] The second survey was conducted between March and December 2011, at least two years after the PMTCT programme had been introduced.
[d] Categorical variables were compared using Pearson's χ^2 test and continuous variables were compared using the Wilcoxon rank-sum test.
[e] The number of women or children for whom the information was available in the first and second surveys, respectively.

Fig. 3. **Estimated survival of children born to HIV-infected mothers before and after the pilot programme to prevent mother-to-child transmission (PMTCT) of the human immunodeficiency virus (HIV) in the Kafue district of Zambia, 2009–2011**



CI: confidence interval.

Fig. 4. **Estimated HIV-free survival of children born to HIV-infected mothers before and after the pilot programme to prevent mother-to-child transmission (PMTCT) of the human immunodeficiency virus (HIV) in the Kafue district of Zambia, 2009–2011**



CI: confidence interval.

during their last pregnancy (from 13.3% to 45.3%, $P < 0.0001$; Fig. 8).

Discussion

Our study used before and after household surveys to assess the changes, at the population level, associated with a pilot PMTCT programme similar to WHO's Option B. We observed a dramatic increase in the 24-month HIV-free survival rate among children born to HIV-infected mothers in our four targeted communities. However, because our study was not randomized and did not include a control group, we were not able to attribute this improvement to the provision of combination antiretroviral regimens to HIV-infected pregnant women in our pilot programme. Nevertheless, our findings indicate that increased investment in PMTCT can have a positive effect on early childhood health outcomes at the population level even though it was difficult to quantify the influence of individual components of the programme.

Our study had several other limitations in addition to the absence of randomization and the lack of a control group. First, the significant differences observed between our two survey populations, particularly in household indicators of socioeconomic status, were unexpected and could have contributed to a general improvement in health. Although we attempted to adjust for these factors in our multivariate analysis, there remained a risk of residual confounding. Moreover, other studies carried out in these communities between 2008 and 2011 may also have contributed to improved health outcomes.[28–30] Second, the number of HIV infections and deaths among HIV-exposed children was relatively small. However, the use of statistical models to estimate the 24-month HIV-free survival rate in children increased the precision of our estimates. Finally, in this analysis we did not explore reasons for the lower than expected uptake of maternal ART during pregnancy in the four communities. We plan to carry out a secondary analysis using the survey data to address this issue. However, given the likely heterogeneity of participants' characteristics between the study communities, more extensive qualitative research may be needed.

Table 3. **Factors associated with HIV infection or death before 24 months in children born to HIV-infected mothers, Kafue district of Zambia, 2009–2011**

Factor	Hazard ratio for HIV infection or death (95% CI)[a]	
	Unadjusted	Adjusted
Reported PMTCT therapy		
Combination antiretroviral regimen	0.24 (0.11–0.52)	0.33 (0.15–0.73)
Other therapy	1.30 (0.85–2.00)	1.39 (0.87–2.23)
No antiretroviral prophylaxis	1.0	1.0
Maternal age at time of survey, years		
15 to < 25	1.0	1.0
25 to < 35	1.52 (0.72–3.22)	1.67 (0.94–2.96)
≥ 35	0.53 (0.16–1.75)	1.10 (0.49–2.44)
Parity		
0–1	1.0	1.0
2–3	1.08 (0.53–2.21)	0.62 (0.35–1.10)
≥ 4	0.38 (0.17–0.82)	0.54 (0.29–0.99)
Educational level		
No schooling or primary	1.32 (0.72–2.39)	1.13 (0.74–1.73)
Secondary or higher	1.0	1.0
Marital status		
Married or cohabitating	1.0	1.0
Single or widowed	0.79 (0.33–1.89)	1.07 (0.65–1.75)
One or more institutional antenatal care visits		
Yes	1.0	1.0
No	0.14 (0.06–0.31)	0.59 (0.23–1.52)
Institutional delivery		
Yes	1.0	1.0
No	1.65 (0.89–3.08)	1.28 (0.83–1.96)
Infant breastfed at birth		
Yes	1.0	1.0
No	0.30 (0.12–0.76)	0.66 (0.24–1.76)
Survey		
First (before PMTCT programme)	1.0	1.0
Second (after PMTCT programme)	0.38 (0.20–0.72)	0.52 (0.34–0.80)

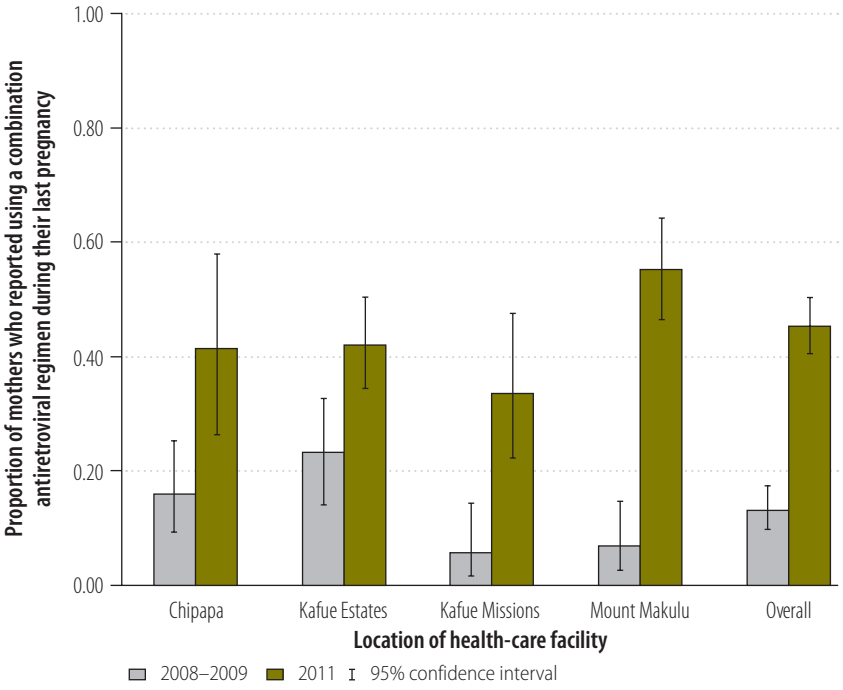
CI: confidence interval; HIV: human immunodeficiency virus; PMTCT: prevention of mother-to-child transmission.

[a] In the multivariate analysis, adjustment was made for the health-care facility in which the programme was implemented.

Although we observed a more than threefold increase in the utilization of combination antiretroviral regimens between the first and second surveys, the rates were modest, at 13.3% and 45.3%, respectively. Since fewer than half of HIV-infected pregnant women received this intervention, it is unlikely that the pilot PMTCT programme alone could have produced such a dramatic increase in HIV-free survival in children. Better survival could, however, be explained by increased coverage of PMTCT and HIV treatment services in our target communities. It is possible that investment at our pilot sites may have resulted in both a greater supply of PMTCT services and an increase in demand. Indeed, we observed that the proportion of HIV-infected women who knew their HIV status during pregnancy increased between the two surveys, as did the proportion who reported HIV testing during their last pregnancy and the proportion that started any form of antiretroviral prophylaxis. It is certainly plausible that community outreach efforts and additional human resources associated with the pilot programme benefited all HIV-infected pregnant women, whether or not they eventually started combination antiretroviral regimens. This broader influence of PMTCT services should be considered when national programmes seek to scale up the implementation of Option B or Option B+.[31] Each step of the PMTCT cascade must be addressed at the health systems level if we are to maximize the effect of interventions implemented during pregnancy and breastfeeding.[32]

This study assessed the effectiveness of the pilot PMTCT programme using community-based household surveys, which is one of five approaches endorsed by WHO.[33] However, we encountered several unanticipated challenges. The proportion of eligible households that refused to participate in the first survey was much higher than in the second: 11.3% versus 1.6%, respectively (Fig. 1). The number of refusals declined at each of the four study sites; the greatest difference was noted in the Kafue Missions catchment area, where the proportion decreased from 22.2% to 1.2%. There was anecdotal evidence that our first survey coincided with the circulation of negative rumours about clinical research, which may explain the high refusal rate. It is important, therefore, that extensive, sustained outreach work be carried out during study implementation. We failed to collect information about which mothers participated in both surveys. However, the overlap is likely to be low because the latest demographic and health survey in Zambia indicated that only 15.2% of women with a recent pregnancy reported the delivery of another child within the previous 24 months.[34] Moreover, since our surveys took place more than two years apart, no HIV-exposed child aged under 24 months could have been included in both surveys. In addition, we acknowledge that our estimates of HIV-free survival have not been validated against a gold standard metric, as could be achieved by longitudinal follow-up of HIV-exposed infants over time. Currently, this is being remedied in a study funded by the United States National Institutes of Health (clinicaltrials.gov ID: NCT01951794). While the precision of our estimates for HIV-free survival requires confirmation, we believe our comparisons are valid because we used the same methods in both surveys.

Fig. 8. **Proportion[a] of HIV-infected mothers who reported using a combination antiretroviral regimen during their last pregnancy, by health-care facility, before and after the pilot programme to prevent mother-to-child transmission (PMTCT) of the human immunodeficiency virus (HIV) in the Kafue district of Zambia, 2009–2011**



In conclusion, this pilot PMTCT programme in rural Zambia was associated with an increase in the 24-month HIV-free survival in children born to HIV-infected mothers; however, we were unable to quantify the contribution of specific programme features to health outcomes. Increased investment at the pilot sites probably contributed to the observed improvements in health by increasing both the supply of and demand for PMTCT services. Countries planning to incorporate WHO's Option B or Option B+ strategy for PMTCT into their national PMTCT policies should bear in mind the importance of health systems capacity to support the effective incorporation of more efficacious regimens. ■

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ملخص

نظم العلاج التوليفي الشامل بمضادات الفيروسات القهقرية لتوقي انتقال فيروس العوز المناعي البشري من الأم إلى الطفل في المناطق الريفية في زامبيا: دراسة متعددة القطاعات من جولتين

الغرض تقييم ما إذا كان البرنامج التجريبي لتوقي انتقال فيروس العوز المناعي البشري من الأم إلى الطفل مرتبطاً بالتغيرات في البقاء على قيد الحياة في مرحلة الطفولة المبكرة على صعيد السكان في المناطق الريفية في زامبيا.

الطريقة تم تقديم نظم العلاج التوليفي بمضادات الفيروسات القهقرية إلى النساء الحوامل والمرضعات المصابات بعدوى فيروس العوز المناعي البشري، بغض النظر عن حالتهن المناعية، في أربعة مرافق صحية ريفية. وتم تحديد بقاء الأطفال في سن 24 شهراً على قيد الحياة دون الإصابة بفيروس العوز المناعي البشري بين الأطفال الذين ولدوا لأمهات مصابات بعدوى فيروس العوز المناعي البشري قبل تنفيذ برنامج توقي الانتقال من الأم إلى الطفل وبعده باستخدام دراسات استقصائية مجتمعية. وتم اختيار الأسر المعيشية عشوائياً ومطالبة النساء اللاتي ولدن خلال الأربع والعشرين شهراً السابقة بالمشاركة. وتم اختبار الأمهات للكشف عن أضداد فيروس العوز المناعي البشري، وتم اختبار الأطفال الذين ولدوا لأمهات مصابات بفيروس العوز المناعي البشري للكشف عن الحمض الريبي النووي منزوع الأكسجين الفيروسي. وتم استخدام نماذج متعددة المتغيرات لتحديد العوامل المرتبطة بإصابة الطفل بعدوى فيروس العوز المناعي البشري أو وفاته.

النتائج كانت نتيجة اختبار 335 سيدة من إجمالي 1778 سيدة (18.8 ٪) في الدراسة الاستقصائية الأولى (من 2008 إلى 2009) إيجابية لفيروس العوز المناعي البشري. وكانت نتيجة اختبار 390 سيدة من إجمالي 2386 سيدة (16.3 ٪) في الدراسة الاستقصائية الثانية (2011) إيجابية. وكان بقاء الأطفال في سن 24 شهراً على قيد الحياة دون الإصابة بفيروس العوز المناعي البشري في الأطفال المعرضين لفيروس العوز المناعي البشري 0.66 (فاصل الثقة 95 ٪، فاصل الثقة: 0.63 –0.76) في الدراسة الاستقصائية الأولى و0.89 (فاصل الثقة: 95 ٪، فاصل الثقة: 0.83 –0.94) في الدراسة الاستقصائية الثانية. وكان استخدام نظام العلاج التوليفي بمضادات الفيروسات القهقرية مرتبطاً بانخفاض مخاطر الإصابة بعدوى فيروس العوز المناعي البشري أو الوفاة في الأطفال (نسبة المخاطر المصححة: 0.33، فاصل الثقة: 95 ٪، فاصل الثقة: 0.15 –0.73). وازدادت معرفة الأمهات بحالة فيروس العوز المناعي البشري واستخدام اختبارات فيروس العوز المناعي البشري واستخدام نظم العلاج التوليفي أثناء الحمل بين الدراسات الاستقصائية.

الاستنتاج ارتبط برنامج توقي الانتقال من الأم إلى الطفل بازدياد بقاء الأطفال الذين ولدوا لأمهات مصابات بعدوى فيروس العوز المناعي البشري على قيد الحياة دون الإصابة بفيروس العوز المناعي البشري. وازداد كذلك استخدام الأمهات لاختبارات فيروس العوز المناعي البشري وعلاجه في المجتمع المحلي.

摘要

预防赞比亚农村地区艾滋病毒母婴传播的普及联合抗逆转录病毒疗法：两轮横断面研究

目的 评估赞比亚农村防止艾滋病毒（HIV）母婴传播的试点计划（PMTCT）是否在人口水平上与儿童早期存活的改变有关。

方法 在四个农村卫生设施，对于处于怀孕和哺乳期并感染艾滋病毒的妇女，无论其免疫状态如何均提供联合抗逆转录病毒治疗方案。使用社区调查确定PMTCT计划实施之前和之后HIV感染母亲生育的孩子中24月无HIV存活情况。随机选择家庭，并要求在之前24个月生育的妇女参与调查。母亲接受HIV抗体检测，HIV感染母亲所生婴儿接受病毒脱氧核糖核酸检测。使用多变量模型确定与儿童HIV感染或死亡相关的因素。

结果 在第一次调查中（2008－2009年），1778名妇女中有335名（18.8%）检测HIV阳性。在第二次调查中（2011年），2386名中有390（16.3%）名检测阳性。在第一次调查中HIV暴露儿童中24月无HIV存活率为0.66（95%置信区间，CI：0.63－0.76），在第二次中为0.89（95% CI：0.83－0.94）。使用联合抗逆转录疗法与更低HIV感染或儿童死亡风险相关（校正危险比：0.33，95% CI：0.15－0.73）。在两次调查之间，母亲HIV知识的状态、使用HIV检测和在怀孕期间使用联合治疗方案的情况有所增强。

结论 PMTCT计划与HIV感染母亲所生儿童更高的无HIV生存率有关。社区中母亲使用HIV检测和治疗也有增加。

Résumé

Thérapies antirétrovirales combinées universelles pour prévenir la transmission mère-enfant du VIH en Zambie rurale: une étude transversale en deux tours

Objectif Évaluer si un programme pilote pour prévenir la transmission mère-enfant (PTME) du virus de l'immunodéficience humaine (VIH) est associé à des changements en matière de survie du jeune enfant au sein de la population dans les régions rurales de la Zambie.

Méthodes Des thérapies antirétrovirales combinées ont été proposées à des femmes infectées par le VIH, enceintes et allaitantes, indépendamment de leur statut immunologique, dans quatre centres de santé ruraux. La survie sans VIH à 24 mois chez les enfants nés de mères infectées par le VIH a été déterminée avant et après la mise en œuvre du programme PTME à l'aide d'enquêtes communautaires. Les ménages ont été choisis de manière aléatoire, et il a été demandé aux femmes qui avaient accouché au cours des 24 derniers mois, d'y participer. On a testé la présence d'anticorps anti-VIH chez les mères et d'acide désoxyribonucléique viral chez les enfants nés de mères infectées par le VIH. Des modèles à variables multiples ont été utilisés pour déterminer les facteurs associés à l'infection par le VIH ou au décès de l'enfant.

Résultats Dans la première étude (2008–2009), 335 femmes parmi 1778 (18,8%) ont été testées positives à l'infection par le VIH. Dans la deuxième étude (2011), 390 femmes parmi 2386 (16,3%) ont été testées positives. La survie sans VIH à 24 mois chez les enfants exposés au VIH était de 0,66 (intervalle de confiance de 95%, IC: 0,63–0,76) dans la première étude et de 0,89 (IC de 95%: 0,83–0,94) dans la seconde. La combinaison de la thérapie antirétrovirale était associée à un risque inférieur d'infection par le VIH ou de décès chez les enfants (rapport de risques ajusté: 0,33, IC de 95%: 0,15–0,73). La connaissance du statut VIH des mères, l'utilisation des tests de dépistage du VIH et des traitements combinés pendant la grossesse ont augmenté entre les études.

Conclusion Le programme PTME était associé à une augmentation de la survie sans VIH chez les enfants nés de mères infectées par le VIH. L'utilisation par les mères du dépistage et du traitement contre le VIH a également augmenté au sein de la communauté.

Резюме

Схемы универсальной комбинированной антиретровирусной терапии для предотвращения передачи ВИЧ от матери к ребенку в сельских районах Замбии: двухэтапное поперечное исследование

Цель Определить, связана ли пилотная программа по предотвращению передачи от матери к ребенку (ППМР) вируса иммунодефицита человека (ВИЧ) с изменениями в уровне выживаемости в раннем детском возрасте в сельских районах Замбии.

Методы В четырех сельских медицинских учреждениях беременным и кормящим ВИЧ-инфицированным женщинам предлагалась комбинированная антиретровирусная терапия вне зависимости от их иммунологического статуса. До и после реализации программы ППМР на основе исследований общин были определены уровни 24-месячной выживаемости без ВИЧ среди детей, рожденных от ВИЧ-инфицированных матерей. Домохозяйства выбирались случайным образом, и женщинам, родившим в течение последних 24 месяцев, предлагалось принять участие в исследовании. Матери были протестированы на наличие антител к ВИЧ, а дети, рожденные от ВИЧ-инфицированных матерей, были проверены на наличие ДНК ВИЧ. Для определения факторов, связанных с инфицированием детей ВИЧ или смертью, использовались многопараметрические модели.

Результаты В первом исследовании (2008–2009 гг.) 335 из 1778 женщин (18,8%) имели положительный результат на ВИЧ. Во втором исследовании (2011 г.) положительный результат показали 390 из 2386 (16,3%) обследованных женщин. Уровень 24-месячной выживаемости без ВИЧ у детей, подверженных ВИЧ, составил 0,66 (95% доверительный интервал, ДИ: 0,63–0,76) в первом исследовании и 0,89 (95% ДИ: 0,83–0,94) – во втором. Применение комбинированной антиретровирусной терапии сопровождалось более низким риском инфицирования ВИЧ или смерти у детей (скорректированное отношение рисков: 0,33, 95% ДИ: 0,15–0,73). Осведомленность матерей о ВИЧ-статусе, использование тестов на ВИЧ и применение комбинированной терапии во время беременности возросло в период между исследованиями.

Вывод Программа ППМР сопровождалась увеличением выживаемости без ВИЧ у детей, рожденных от ВИЧ-инфицированных матерей. Также увеличилось число матерей в сельских общинах, проходящих проверку и лечение ВИЧ-инфекции.

Resumen

Tratamientos antirretrovirales de combinación universal para prevenir la transmisión maternoinfantil del VIH en las zonas rurales de Zambia: un estudio transversal de dos vueltas

Objetivo Evaluar si un programa piloto para prevenir la transmisión maternoinfantil (PTMI) del virus de la inmunodeficiencia humana (VIH) está asociado a cambios en la supervivencia en la primera infancia a nivel de población en las zonas rurales de Zambia.

Métodos Se ofreció una combinación de tratamientos antirretrovirales a mujeres embarazadas y lactantes infectadas por el VIH, independientemente de su estado inmunológico, en cuatro centros de salud rurales. Mediante encuestas en la comunidad se determinó una supervivencia sin VIH de veinticuatro meses entre los niños nacidos de madres infectadas por el VIH antes y después de la implementación del programa PTMI. Los hogares se seleccionaron al azar y se pidió que participaran las mujeres que habían dado a luz en los 24 meses anteriores. Las madres se sometieron a una prueba para detectar los anticuerpos contra el VIH y se realizó una prueba del ácido desoxirribonucleico viral a los niños nacidos de madres infectadas con VIH. Se utilizaron modelos multivariables para determinar los factores asociados con la infección o muerte por VIH del niño.

Resultados En la primera encuesta (2008–2009), 335 de 1778 mujeres (18,8 %) dieron positivo en el VIH. En la segunda (2011), dieron positivo 390 de 2386 (16,3 %). La supervivencia sin VIH de 24 meses en los niños expuestos al VIH fue del 0,66 (intervalo de confianza del 95 %, IC: 0,63–0,76) en la primera encuesta y del 0,89 (IC del 95 %: 0,83–0,94) en la segunda. La combinación de un tratamiento antirretroviral se asoció con un menor riesgo de infección por VIH o muerte en los niños (razón de riesgo ajustada: 0,33, IC del 95 %: 0,15–0,73). El conocimiento de las madres de su estado serológico, el uso de pruebas para el VIH y los tratamientos combinados durante el embarazo aumentaron en el tiempo transcurrido entre las encuestas.

Conclusión El programa PTMI estuvo asociado a un aumento de la supervivencia sin VIH en los niños nacidos de madres infectadas por el VIH. La utilización materna de la prueba y el tratamiento del VIH en la comunidad también aumentó.

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Fig. 5. **Proportion[a] of HIV-infected mothers who knew their HIV status, by health-care facility, before and after the pilot programme to prevent mother-to-child transmission (PMTCT) of the human immunodeficiency virus (HIV) in the Kafue district of Zambia, 2009–2011**

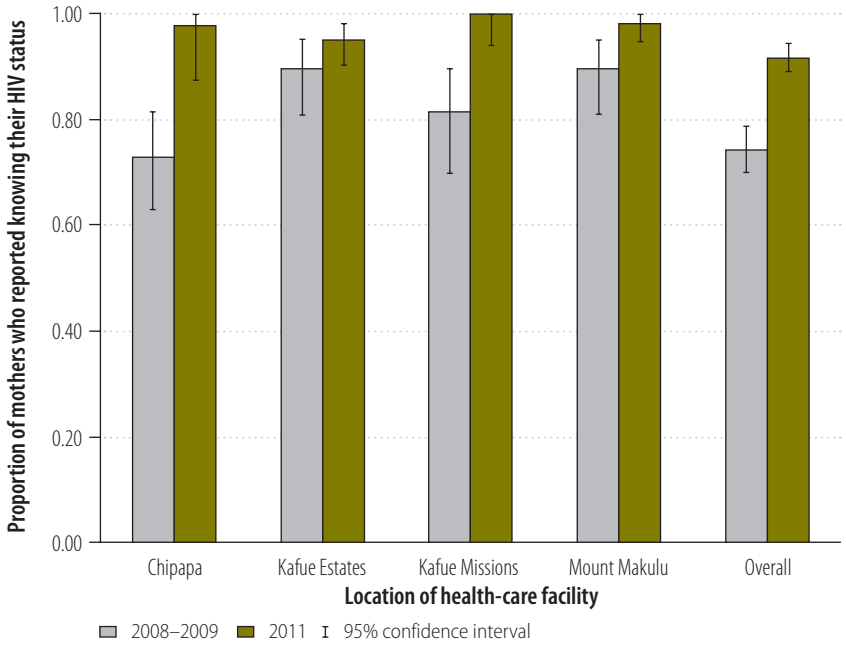

Fig. 6. **Proportion[a] of HIV-infected mothers tested for HIV during their last pregnancy, by health-care facility, before and after the pilot programme to prevent mother-to-child transmission (PMTCT) of the human immunodeficiency virus (HIV) in the Kafue district of Zambia, 2009–2011**

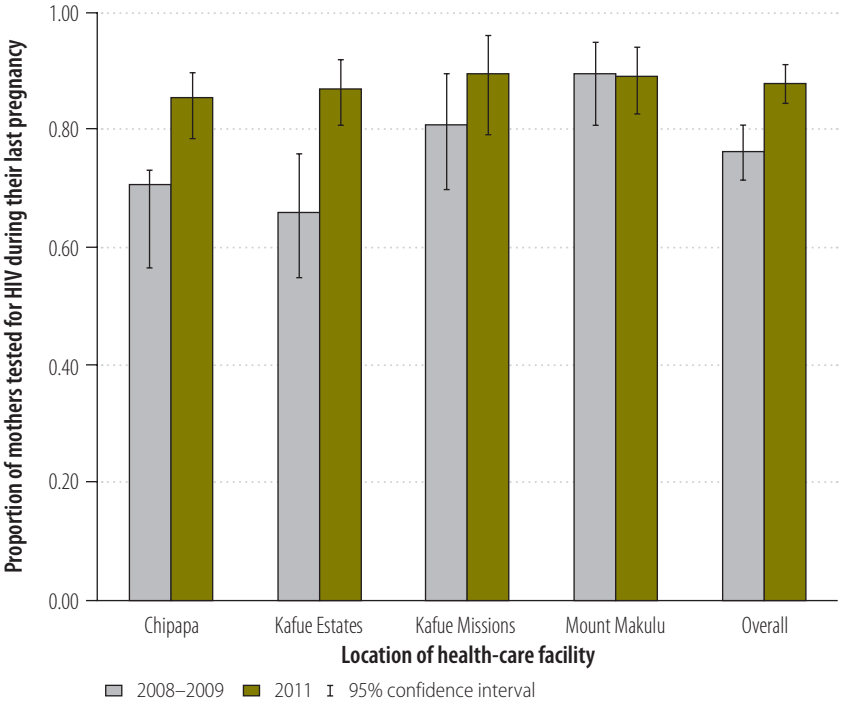

Fig. 7. **Proportion[a] of HIV-infected mothers who reported using any antiretroviral prophylaxis during their last pregnancy, by health-care facility, before and after the pilot programme to prevent mother-to-child transmission (PMTCT) of the human immunodeficiency virus (HIV) in the Kafue district of Zambia, 2009–2011**