The incremental cost of switching from Option B to Option B+ for the prevention of mother-to-child transmission of HIV

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Objective To estimate the incremental cost over 5 years of a policy switch from the Option B to the Option B+ protocol for the prevention of mother-to-child transmission (PMTCT) of the human immunodeficiency virus (HIV).

Methods Data from cost studies and other published sources were used to determine the cost, per woman and per cohort (1000 breastfeeding and 1000 non-breastfeeding women), of switching from Option B (maternal triple antiretroviral [ARV] regimen during pregnancy and breastfeeding plus daily nevirapine for the infant for 6 weeks) to Option B+ (maternal triple ARV regimen initiated during pregnancy and continued for life). The variables used to model the different scenarios were maternal CD4+ T lymphocyte (CD4+ cell) count (350–500 versus > 500 cells/μl), rate of decline in CD4+ cells (average, rapid, slow), breastfeeding status (yes, no) and breastfeeding duration (12, 18 or 24 months).

Findings For women with CD4+ cell counts of 350–500 cells/μl, the incremental cost per 1000 women was 157 345 United States dollars (US$) for breastfeeding women and US$ 92 813 for non-breastfeeding women. For women with CD4+ cell counts > 500 cells/μl, the incremental cost per 1000 women ranged from US$ 363 443 to US$ 484 591 for breastfeeding women and was US$ 605 739 for non-breastfeeding women.

Conclusion From a cost perspective, a policy switch from Option B to Option B+ is feasible in PMTCT programme settings where resources are currently being allocated to Option B.

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

Introduction

In July 2011, a United Nations political declaration called for greater efforts to eliminate human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS). It established commitments and targets, including eliminating new HIV infections among children and substantially reducing AIDS-related maternal deaths by 2015.[1] Nevertheless, in 2012 there were 260 000 new paediatric HIV infections globally and 40% of pregnant women in 20 countries with a high burden of HIV infection did not receive antiretrovirals (ARVs) to prevent the vertical transmission of HIV.[2,3]

The optimal way to structure programmes for the prevention of mother-to-child transmission (PMTCT) of HIV has not yet been determined. Countries with a high burden of HIV infection are left to decide what PMTCT options are feasible and most effective for their own contexts. In its 2010 revision of *Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: recommendations for a public health* approach,[4] the World Health Organization (WHO) recommended that HIV+ pregnant women who are eligible for antiretroviral therapy (ART) [based on a CD4+ T lymphocyte (CD4+ cell) count of ≤ 350 cells/μl, or on the presence of WHO stage 3 or 4 disease] receive lifelong triple ARV treatment. The guidelines also recommended that HIV+ pregnant women not eligible for lifelong ART be placed on one of two PMTCT protocols – Option A or Option B – beginning as early as the 14th week of gestation to reduce the risk of vertical transmission of HIV during pregnancy, delivery and the postpartum period, including breastfeeding. The protocol known as Option A comprised giving zidovudine (AZT) to the mother prophylactically during pregnancy; single-dose nevirapine (NVP) to both the mother and the neonate at delivery; maternal AZT and lamivudine (3TC) to the mother during the first week postpartum; and NVP daily to the infant throughout breastfeeding. Option B comprised a triple ARV regimen, typically consisting of the recommended first-line ART for the mother during pregnancy and throughout breastfeeding, plus 6 weeks of daily NVP for the infant, regardless of infant feeding method.

In its 2013 *Consolidated guidelines on general HIV care and the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach*,[5] WHO no longer recommends Option A. In addition to Option B, which remains a recommended PMTCT option, WHO has endorsed a new option known as Option B+ that consists of a triple ARV regimen initiated during pregnancy and continued for life.[6] Option B+ has already been implemented in Malawi and is now actively being considered globally as a simpler and more effective PMTCT approach.[6,7]

Several clinical trials have shown Options A and B to be equally efficacious in preventing vertical HIV transmission.[8–11] However, concerns have arisen about the implementation and effectiveness of Option A in programmatic settings because: (i) the drugs used for prophylaxis and treatment are not the same and the therapeutic ARV regimen must be changed during pregnancy and in the intrapartum and postpartum periods; (ii) a CD4+ cell count is needed to determine if a woman is eligible for treatment. It has been suggested that these factors have made it difficult to scale up PMTCT programmes based on Option A.[5] Option B may be easier to implement, as the same triple ARV regimen used prophylactically during pregnancy can be used to initiate subsequent treatment and because a CD4+ cell count is not required before commencing prophy-

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(*Submitted: 16 April 2013 – Revised version received: 7 October 2013 – Accepted: 9 October 2013 – Published online: 10 January 2014*)

laxis. The newly proposed Option B+ may be even easier to implement, for it possesses the same advantages as Option B and the same triple ARV regimen initiated during gestation is used to maintain treatment as patients graduate from the PMTCT programme and transition to adult care and treatment programmes. In addition, Option B+ may confer benefits by not delaying treatment initiation among mothers and by reducing sexual transmission among those who have a serodiscordant partner.[12] However, the higher cost of a triple ARV regimen can be a limiting factor in implementing either Option B or Option B+ in some countries.

With the evidence surrounding PMTCT regimens constantly evolving, countries must ensure that their PMTCT programmes are effective. A December 2012 snapshot of PMTCT regimens approved by ministries of health in 22 countries with a high burden of HIV infection revealed that 10 countries had in place an Option A regimen policy (although three of them had piloted Option B+ in select districts); six had an Option B policy; and six had an Option B+ policy.[13] (A PMTCT regimen policy reportedly approved by the health ministry may not entirely reflect the PMTCT regimen actually implemented in a country.) With WHO's recent endorsement of Option B+, other countries may start to shift their PMTCT policies and will need to plan their resources accordingly.

Given the respective mandates of the United Nations Millennium Development Goals and the *Global plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive 2011–2015*, of the Joint United Nations Programme on HIV/AIDS,[14,15] countries with a high burden of HIV infection are trying to scale up their PMTCT programmes and implement the most effective PMTCT ART strategies, especially in the context of limited domestic and international financial resources and donor funding. WHO's 2010 PMTCT guidelines[4] emphasized the importance of considering the short- and long-term feasibility and cost implications of scaling up programmes. WHO's 2012 *Programmatic update: use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: executive summary*[6] points to a decrease in the costs of triple ARVs as an encouraging trend; however, it did not include an analysis of programme costs.

Although initial drug costs are a driving factor in decision-making, an in-depth understanding of programme costs over time, including the ongoing costs of drugs and non-ARV care, is also needed. The objective of this study was to estimate the incremental programme cost, over 5 years, of switching from policy Option B to Option B+.

Methods

We used cost data from the ART cost study of the United States President's Emergency Plan for AIDS Relief (PEPFAR),[16] WHO's *Global price reporting mechanism* (GPRM)[17] and other published sources to derive study estimates.[18–21] In our main analyses we examined the cost per woman (individual analysis) and the cost per cohort of women (cohort analysis). We also conducted sensitivity analyses to examine the effect on costs of varying ARV prices and postpartum rates of decline in CD4+ cell count.[18] The analysis was based on a five-year time frame and employed a programmatic cost perspective.

We compared the costs of Option B and Option B+ under two scenarios: breastfeeding and absence of breastfeeding. In the breastfeeding scenario, we assumed a breastfeeding duration of 12 months, as recommended by WHO,[22] for the main analyses, although we also considered breastfeeding durations of 18 and 24 months. We assumed that (i) a woman following the Option B protocol who stopped ARV prophylaxis because she was no longer breastfeeding would go through the same process for initiating ART as any patient initiating ART at a care and treatment facility (i.e. on the basis of a CD4+ cell count of ≤ 350 cells/μl);[6] (ii) a woman following the Option B+ protocol would be maintained on ART for the full 5-year postpartum period.

In the non-breastfeeding scenario, a woman following Option B would be followed through the period in which she was in care after the cessation of ARVs at delivery and until becoming ART-eligible in her own right (i.e. the pre-ART period), at which time she would be initiated on ART and then transitioned into the ART maintenance phase. A woman following the Option B+ protocol would be maintained on ART for the full 5-year postpartum period.

Because no standard guidelines exist for operationalizing Option B+, different applications of Options B and B+ are possible in different settings. We assumed that the cost of providing Option B was similar to the cost of providing Option B+ during pregnancy and in the intrapartum period, so in our analyses we considered only the variation in costs incurred during the postpartum period. We did not consider the costs associated with Option B prophylaxis during subsequent pregnancies that might have occurred within the 5-year postpartum period. To calculate drug costs we used non-fixed-dose ARV pricing for our main analyses and included fixed-dose ARV pricing in our sensitivity analyses. We calculated the cost for a 12-month period of the generic ARV drugs used in the recommended first-line regimen: tenofovir (TDF), 3TC and efavirenz (EFV). For this calculation we used the individual prices of these drugs and the currently available fixed-dose prices for sub-Saharan Africa as obtained from the 2011 WHO GPRM.[17] For non-ARV drugs, we obtained the annual cost per patient in care, the annual cost per patient for the first 12 months on ART, and the annual cost per patient after their first year on ART (maintenance) from the PEPFAR ART costing study, which was based on 43 care and treatment sites.[16]

To adjust costs for inflation we used an average annual rate of inflation (2.4%) based on the US Consumer Price Index from 2009 to 2011.[23] All costs are reported in 2011 United States dollars (US$). All model inputs are presented in Table 1.

Individual analysis

The cost per woman in care was defined as the annual cost per woman of all care received in the pre-ART period (i.e. cotrimoxazole prophylaxis, routine clinical monitoring and laboratory services). The cost per woman on ART (first 12 months on ART or in maintenance) comprised the costs of ARVs and non-ARV drugs, routine clinical monitoring and laboratory services.

We derived the total cost per woman of each PMTCT option as the sum of drug and non-drug costs per patient. In the breastfeeding scenario, the total cost of Option B per woman comprised the sum of the costs of following the woman through four phases totalling 5 years: the breastfeeding

Table 1. **Model inputs – and their sources – for study of the incremental cost of switching from Option B to Option B+ for the prevention of mother-to-child transmission of HIV**

Model input	Value	Source
Median postpartum CD4+ cell count, cells/µl		
Lower: 350–500	425	Ekouevi, 2012[19]
Higher: > 500	613	Ekouevi, 2012[19]
CD4+ cell count for ART eligibility, cells/µl	≤ 350	WHO, 2010[22]
Monthly decline in CD4+ cell count postpartum, cells/µl		
Breastfeeding woman	3.2 (1.5, 4.9)[a]	Otieno, 2007[18]
Non-breastfeeding woman	4.4 (2.7, 6.0)[a]	Otieno, 2007[18]
Average[b]	3.9	Estimated
Cost per patient per year, US$		
ART		
TDF + 3TC + EFV	167.31	WHO, GPRM, 2011[17]
Pre-ART period		
Co-trimoxazole, routine clinical monitoring and laboratory services	211.81	Menzies, 2011[16]
First 12 months on ART		
Non-ARV drugs, routine clinical monitoring and laboratory services	378.54	Menzies, 2011[16]
Maintained on ART		
Non-ARV drugs, routine clinical monitoring and laboratory services	246.42	Menzies, 2011[16]

3TC, lamivudine; ART, antiretroviral therapy; ARV, antiretroviral; EFV, efavirenz; TDF, tenofovir; US$, United States dollars; WHO, World Health Organization.
[a] Values in parentheses were used to simulate a slow and a rapid monthly decline in CD4+ cell count.
[b] Breastfeeding and non-breastfeeding women.

phase, the pre-ART period in care, the first 12 months on ART, and the period of being maintained on ART. The total cost of Option B+ per woman in this scenario was estimated as the cost of being maintained on ART for the full 5-year postpartum period. In the non-breastfeeding scenario, the total cost of Option B per woman comprised the sum of the costs of following the woman through three phases totalling 5 years: the pre-ART period in care, the first 12 months on ART and the period of being maintained on ART. The total cost of Option B+ per woman in this scenario was also estimated as the cost of being maintained on ART for the full 5-year postpartum period.

For each scenario, we estimated the incremental cost of a policy switch from Option B to Option B+ by calculating the difference in the total costs of the two options. Table 2 outlines the time spent by breastfeeding and non-breastfeeding women in each phase of the 5-year postpartum period for Option B and Option B+.

Cohort analysis

We considered a hypothetical cohort of HIV+ pregnant women and followed them for the first 5 years postpartum. For each PMTCT option, 1000 women were breastfeeding and 1000 were non-breastfeeding. Within Option B there were two subpopulations: (i) women who were ART-eligible at the beginning of the postpartum period (based on the CD4+ cell eligibility threshold of ≤ 350 cells/µl) and who were maintained on ART throughout the 5-year postpartum period; and (ii) women who stopped ARV prophylaxis at delivery (non-breastfeeding women) or after breastfeeding and who became ART-eligible at a later date. Based on CD4+ cell count distribution and the rates of CD4+ cell count decline among HIV+ women, we assumed – on the basis of the distribution of CD4+ cell counts among HIV+ women and the rate of CD4+ decline over time – that 40% of the women in the Option B cohort would be ART-eligible at the beginning of the postpartum

Table 2. **Time spent per woman in Option B[a] or Option B+[b] over 5 years postpartum**

Breastfeeding status and duration	CD4+ count 350–500 cells/µl			CD4+ count > 500 cells/µl		
	Months spent in care (pre-ART)	First 12 months on ART	Remaining months on ART	Months spent in care (pre-ART)	First 12 months on ART	Remaining months on ART
Breastfeeding						
12 months	23[c]	12	13	48	0	0
18 months	23[c]	12	7	42	0	0
24 months	23[c]	12	1	36	0	0
No breastfeeding	17	12	31	60	0	0

ART, antiretroviral therapy.
[a] Option B comprises a maternal triple antiretroviral (ARV) regimen, typically consisting of the recommended first-line ART, during pregnancy and throughout breastfeeding, in combination with 6 weeks of daily nevirapine for the infant, regardless of infant feeding method.
[b] Option B+ comprises a triple ARV regimen initiated during pregnancy and continued for life.
[c] Includes duration of breastfeeding.

Table 3. **Incremental cost[a] per woman of Option B+[b] relative to Option B[c] over 5 years postpartum**

Breastfeeding status and duration	CD4+ count 350–500 cells/μl			CD4+ count > 500 cells/μl		
	Total cost Option B+	Total cost Option B	Incremental cost	Total cost Option B+	Total cost Option B	Incremental cost
Breastfeeding						
12 months	2069	1814	255	2069	1261	808
18 months	2069	1814	255	2069	1362	707
24 months	2069	1814	255	2069	1463	606
No breastfeeding	2069	1915	154	2069	1059	1010

[a] All costs are given in 2011 United States dollars.
[b] Option B+ comprises a triple antiretroviral (ARV) regimen initiated during pregnancy and continued for life.
[c] Option B comprises a maternal triple ARV regimen, typically consisting of the recommended first-line antiretroviral therapy (ART), during pregnancy and throughout breastfeeding, in combination with 6 weeks of daily nevirapine for the infant, regardless of infant feeding method.
Note: Within each CD4+ cell count stratum, the time to ART treatment eligibility was the same regardless of breastfeeding duration; however, the time in treatment varied across breastfeeding duration categories.

Table 4. **Incremental cost[a] per 1000 women of Option B+[b] relative to Option B[c] over 5 years postpartum**

Breastfeeding status and duration	CD4+ count 350–500 cells/μl			CD4+ count > 500 cells/μl		
	Total cost Option B+	Total cost Option B	Incremental cost	Total cost Option B+	Total cost Option B	Incremental cost
Breastfeeding						
12 months	2 068 627	1 911 282	157 345	2 068 627	1 584 036	484 591
18 months	2 068 627	1 911 282	157 345	2 068 627	1 644 609	424 017
24 months	2 068 627	1 911 282	157 345	2 068 627	1 705 183	363 443
No breastfeeding	2 068 627	1 975 814	92 813	2 068 627	1 462 888	605 739

[a] All costs are given in 2011 United States dollars.
[b] Option B+ comprises a triple antiretroviral (ARV) regimen initiated during pregnancy and continued for life.
[c] Option B comprises a maternal ARV regimen, typically consisting of the recommended first-line antiretroviral therapy, during pregnancy and throughout breastfeeding, in combination with 6 weeks of daily nevirapine for the infant, regardless of infant feeding method.
Note: Within each CD4+ cell count stratum, the time to ART eligibility was the same regardless of breastfeeding duration; however, the time in treatment varied across breastfeeding duration categories.

period[20,21] and that the remaining 60% would spend time in pre-ART care before becoming ART-eligible. Scenarios with cohorts containing varying CD4+ cell counts (350–500 cells/μl and > 500 cells/μl) were also considered.

Sensitivity analyses

We conducted univariate sensitivity analyses by varying the monthly rates of postpartum decline in CD4+ cell count and the costs of ARV drugs. We used published estimates of the monthly rates of decline in CD4+ cell counts by breastfeeding status (Table 1) in our modelling.[18] We first assumed that CD4+ cell count declined at an average monthly rate of 3.9 cells/μl, regardless of breastfeeding status. We then estimated the impact on the incremental cost of switching from Option B to Option B+ for women with a rapid and a slow rate of decline in CD4+ cell count, defined as follows: in breastfeeding women, rapid decline, 4.9 cells/μl; slow decline, 1.5 cells/μl; in non-breastfeeding women, rapid decline, 6.0 cells/μl/month; slow decline, 2.7 cells/μl. We also examined the impact on the incremental cost of Option B+ of doubling and halving the prices of ARV drugs.

Results

Individual analysis

The total cost of Option B+ was US$ 2069 per woman over 5 years, regardless of CD4+ cell count, breastfeeding status or breastfeeding duration (Table 3). For a breastfeeding woman with a CD4+ cell count between 350 and 500 cells/μl, the incremental cost per woman of Option B+ versus Option B was US$ 255; for a non-breastfeeding woman, the incremental cost was US$ 154. For a breastfeeding woman with a higher CD4+ cell count (i.e. > 500 cells/μl), the incremental cost per woman of Option B+ versus Option B ranged from US$ 606 to US$ 808, depending on breastfeeding duration. For a non-breastfeeding woman with CD4+ cell count > 500 cells/μl, the incremental cost of Option B+ relative to Option B was US$ 1010 (Table 3).

Cohort analysis

For breastfeeding women with a CD4+ cell count between 350 and 500 cells/μl, the incremental cost of Option B+ relative to Option B per 1000 women was US$ 157 345, regardless of breastfeeding duration (Table 4); for non-breastfeeding women, the incremental cost per 1000 women was US$ 92 813. For breastfeeding women with a CD4+ cell count > 500 cells/μl, the incremental cost of Option B+ ranged from US$ 363 443 to US$ 484 591, depending on breastfeeding duration. The incremental cost per 1000 non-breastfeeding women was US$ 605 739 (Table 4).

Sensitivity analyses

Varying the rate of CD4+ cell decline

When a single rate of decline in CD4+ cell count (3.9 cells/μl/month) was ap-

Table 5. **Incremental cost[a] per woman of Option B+[b] relative to Option B[c] over 5 years postpartum, by CD4+ cell count and breastfeeding status, for varying rates of decline in CD4+ cell count**

Breastfeeding status	CD4+ count 350–500 cells/μl			CD4+ count > 500 cells/μl		
	Total cost Option B+	Total cost Option B	Incremental cost	Total cost Option B+	Total cost Option B	Incremental cost
Breastfeeding (12 months)						
Rate of CD4+ cell decline						
Average[d]	2069	1814	255	2069	1261	808
Rapid[e]	2069	1948	121	2069	1261	808
Slow[f]	–	1261	808	–	1261	808
ARV price						
Doubled	2905	2330	575	2905	1428	1477
Halved	1650	1556	94	1650	1177	473
No breastfeeding						
Rate of CD4+ cell decline						
Average[d]	2069	1915	154	2069	1059	1010
Rapid[g]	2069	1982	87	2069	1460	609
Slow[h]	–	1730	339	–	1059	1010
ARV price						
Doubled	2905	2514	391	2905	1059	1846
Halved	1650	1615	35	1650	1059	591

ARV, antiretroviral.
[a] All costs are given in 2011 United States dollars (US$).
[b] Option B+ comprises a triple antiretroviral (ARV) regimen initiated during pregnancy and continued for life.
[c] Option B comprises a maternal triple ARV regimen, typically consisting of the recommended first-line antiretroviral therapy, during pregnancy and throughout breastfeeding, in combination with 6 weeks of daily nevirapine for the infant, regardless of infant feeding method.
[d] 3.9 cells/μl/month.
[e] 4.9 cells/μl/month.
[f] 1.5 cells/μl/month.
[g] 6.0 cells/μl/month.
[h] 2.7 cells/μl/month.
Sources: CD4+ cell count declines for breastfeeding and non-breastfeeding women were obtained from Otieno;[18] the full price of ARVs was obtained from WHO GPRM.[17]

plied in the model for women with a CD4+ cell count between 350 and 500 cells/μl, regardless of breastfeeding status or duration, the incremental cost per woman of switching from Option B to Option B+ was US$ 255 (Table 5).

When a rapid rate of decline in CD4+ cell count was modelled for women with CD4+ cell counts between 350 and 500 cells/μl, Option B remained the least costly option for both breastfeeding and non-breastfeeding women. The incremental cost of switching from Option B to Option B+ per woman was US$ 87 for non-breastfeeding women and US$ 121 for breastfeeding women (Table 5). Regardless of CD4+ cell count, when a slow rate of decline in CD4+ cell count was modelled, Option B was again a less costly option than Option B+ in both breastfeeding and non-breastfeeding women. The incremental cost of switching from Option B to Option B+ per woman was US$ 339 in non-breastfeeding women and US$ 808 in breastfeeding women with CD4+ cell counts between 350 and 500 cells/μl (Table 5).

Varying the price of ARV

Doubling the price of the ARV had the following effect on the incremental cost per woman of switching to Option B+, regardless of breastfeeding status: for women with CD4+ cell counts between 350 and 500 cells/μl, it more than doubled the cost; for women with a CD4+ cell count > 500 cells/μl, it increased the cost by about 80%. Halving the price of the ARV had the following effect on the incremental cost: for breastfeeding women with CD4+ cell counts between 350 and 500 cells/μl, it resulted in a decrease of 63%; for women with CD4+ cell count between 350 and 500 cells/μl who were not breastfeeding, it resulted in a decrease of 77%; for women with a CD4+ cell count > 500 cells/μl, regardless of breastfeeding status, it resulted in a decrease of 41% (Table 5).

In sensitivity analyses with fixed-dose pricing of generic ARVs (TDF + 3TC + EFV) for women with CD4+ cell counts between 350 and 500 cells/μl, the incremental cost per woman of Option B+ increased by 9% and 10% in breastfeeding and non-breastfeeding women, respectively. For women with a CD4+ cell count > 500 cells/μl, the incremental cost per woman increased by 6%, regardless of breastfeeding status (Table 6).

Discussion

Using data available from the literature and basic assumptions about the movement of women through the continuum of care as they progress towards ART eligibility, we estimated the 5-year incremental costs, per woman and per 1000 women, of a policy switch from Option B to Option B+ for a cohort of HIV+ postpartum women.

We chose a 5-year time frame because it is readily understandable and relevant for many budgeting and planning cycles. However, planners should

Table 6. **Percentage change in incremental cost[a] per woman of Option B+[b] relative to Option B[c] over 5 years postpartum, by CD4+ cell count and for fixed-dose and non-fixed-dose pricing of antiretrovirals**

Breastfeeding status and duration	CD4+ count 350–500 cells/μl			CD4+ count > 500 cells/μl		
	Incremental cost, non-fixed-dose pricing (US$)	Incremental cost, fixed-dose pricing (US$)	Percentage change	Incremental cost, non-fixed-dose pricing (US$)	Incremental cost, fixed-dose pricing (US$)	Percentage change
Breastfeeding						
12 months	255	277	9	808	853	6
18 months	–	–	9	707	746	6
24 months	–	–	9	606	640	6
No breastfeeding	154	170	10	1010	1066	6

[a] All costs are in 2011 United States dollars (US$).
[b] Option B+ comprises a triple antiretroviral (ARV) regimen initiated during pregnancy and continued for life.
[c] Option B comprises a maternal triple ARV regimen, typically consisting of the recommended first-line antiretroviral therapy, during pregnancy and throughout breastfeeding, in combination with 6 weeks of daily nevirapine for the infant, regardless of infant feeding method.

not simply divide the 5-year incremental costs by five to estimate the annual incremental cost because it is unlikely that costs will be accrued equally across this time frame; it is more reasonable to expect that higher costs will be incurred during the initial years of a policy switch. Although these estimates cannot be used to directly compare the costs of switching from Option A to Option B+, this analysis is also relevant for policy-makers considering a switch from Option A to either Option B or Option B+.

We believe that a policy switch from Option B to Option B+ is feasible from a cost perspective in PMTCT programme settings where resources are currently being allocated to Option B as the standard practice or where Option B is being actively considered, even before considering the additional benefits of Option B+. This study provides a realistic perspective for policy-makers who are faced with the immediate question of how much more Option B+ would cost than Option B. Our analyses not only address the initial cost requirements of a change in policy, but they also look at a 5-year time frame during which cohorts of breastfeeding and non-breastfeeding women would progress towards ART initiation. Our sensitivity analysis indicates that a 50% reduction in ARV drug costs would decrease the 5-year incremental cost of transitioning from Option B to Option B+ by 41 to 77%. Given the encouraging trend of decreasing first-line ART costs,[24] the incremental 5-year programme cost of Option B+ is likely to decrease further.

Our analysis has several limitations. We did not consider the cost of Option B prophylaxis in subsequent pregnancies. Including subsequent pregnancies in the analyses would have decreased the incremental costs of Option B+ over Option B because women following the Option B+ protocol would have already been receiving triple ARVs and would have therefore avoided the costs associated with ART initiation. Another limitation of our analysis is that it lacks longitudinal evidence about patient adherence/compliance and drug resistance as they relate to Option B+. We did not consider the resource implications of either non-adherence to the ART regimen or drug resistance as a result of being initiated on lifelong ART. Considering that 0.2% of patients routinely fail first-line treatment (by 12 months post-initiation) and are moved onto second-line treatment,[25] we have potentially underestimated the overall costs of both Option B and Option B+. In addition, some have expressed concern that, with widespread access to ARVs, the benefits of lifelong treatment may be offset by risk compensation in the form of risky sexual behaviour and the use of illicit injected drugs. However, evidence suggests that HIV+ patients receiving ART do not demonstrate more risky sexual behaviour than HIV+ patients not receiving ART.[26,27]

Further evidence is beginning to emerge about the cost implications of a policy switch to Option B+. A recent study from Malawi showed that, when averted infant infections and maternal survival were considered, Option B+ was more cost-effective than the WHO 2010 PMTCT practices being employed.[7] Additionally, a model using Zimbabwean data revealed Option B+ to be more cost-effective than Option B in terms of the years of maternal life saved.[16] A Rwandan study suggested that Option B was more cost-effective than dual ARV therapy; however, Option B+ was not considered in that analysis.[17]

The recent endorsement of Option B+ by WHO provides high-burden countries with another regimen to consider for scaling up their PMTCT programmes and meeting elimination targets by 2015. We hope that our study's preliminary financial considerations will assist countries contemplating a policy switch from Option B to Option B+ in determining their resource needs.

To better estimate the potential cost savings associated with Option B+, researchers need to develop additional cost-effectiveness models informed by field data based on experiences with Option B and Option B+. These data should consider the operational issues surrounding each PMTCT option and the potential benefits of Option B+, including improved maternal health and the reduced risk of sexual transmission of HIV in serodiscordant couples.

A small number of studies have begun to formally evaluate the cost of Option B+;[7,28,29] however, in-depth programme data are still lacking in this area – although, in theory, existing evidence about the cost of initiating adults on highly-active ARV therapy can provide insight into the potential costs of implementing Option B+. In the absence of primary programme data on costs and effectiveness, published

models such as ours provide the opportunity to estimate these costs. Cost data should be routinely collected as part of programme planning, implementation and evaluation to enhance the evidence base surrounding Option B+. ■

Acknowledgements
The authors thank Harrell Chesson, Margarett Davis, Elena Ghanotakis, Naoko Ishikawa, Elizabeth McCarthy and Larissa Stabinski for their help. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the US Centers for Disease Control and Prevention.

Competing interests: None declared.

ملخص

التكلفة الإضافية للتحول من الخيار ب إلى الخيار ب+ للوقاية من انتقال فيروس العوز المناعي البشري من الأم إلى الطفل

الغرض تقدير التكلفة الإضافية لتحول السياسة من بروتوكول الخيار ب إلى الخيار ب+ على مدار 5 سنوات للوقاية من انتقال فيروس العوز المناعي البشري من الأم إلى الطفل.

الطريقة تم استخدام البيانات المستمدة من دراسات التكلفة وغيرها من المصادر المنشورة لتحديد تكلفة التحول من الخيار ب (نظام مضادات الفيروسات القهقرية الثلاثي للأم أثناء الحمل والرضاعة الطبيعية بالإضافة إلى نفيرابين الذي يعطى للرضع يومياً لمدة 6 أسابيع) إلى الخيار ب+ (بدء نظام مضادات الفيروسات القهقرية الثلاثي للأم أثناء الحمل واستمراره مدى الحياة)، لكل سيدة ولكل مجموعة (1000 سيدة تستخدمن الرضاعة الطبيعية و1000 سيدة لا تستخدمن الرضاعة الطبيعية). وكانت المتغيرات المستخدمة لنمذجة السيناريوهات المختلفة هي إحصاء الخلايا اللمفاوية التائية المساعدة (CD4+) للأم (350–500 مقابل أكبر من 500 خلية/ ميكرولتر) ومعدل الانخفاض في الخلايا اللمفاوية التائية المساعدة (متوسط وسريع وبطيء) وحالة الرضاعة الطبيعية (نعم أو لا) ومدة الرضاعة الطبيعية (12 أو 18 أو 24 شهراً).

النتائج بالنسبة للنساء اللاتي تراوح إحصاء الخلايا اللمفاوية التائية المساعدة (CD4+) لديهن من 350 إلى 500 خلية/ ميكرولتر، كانت التكلفة الإضافية لكل 1000 سيدة 157345 دولاراً أمريكياً للنساء اللاتي يستخدمن الرضاعة الطبيعية و92813 دولاراً أمريكياً للنساء اللاتي لا يستخدمن الرضاعة الطبيعية. وبالنسبة للنساء اللاتي يزيد إحصاء الخلايا اللمفاوية التائية المساعدة (CD4+) لديهن عن 500 خلية/ ميكرولتر، تراوحت التكلفة الإضافية لكل 1000 سيدة من 363443 دولاراً أمريكياً إلى 484591 دولاراً أمريكياً بالنسبة للنساء اللاتي يستخدمن الرضاعة الطبيعية وكانت 605739 دولاراً أمريكياً بالنسبة للنساء اللاتي لا يستخدمن الرضاعة الطبيعية.

الاستنتاج من منظور التكلفة، فإن تحول السياسة من الخيار ب إلى الخيار ب+ مجد في بيئات برنامج الوقاية من انتقال فيروس العوز المناعي البشري من الأم إلى الطفل حيث يتم تخصيص الموارد في الوقت الراهن للخيار ب.

摘要

从选项 B 切换到选项 B+ 预防母婴艾滋病传播的增量成本

目的 评估 5 年来预防艾滋病病毒（HIV）母婴传播（PMTCT）政策从选项 B 切换到选项 B+ 所增加的成本。

方法 使用来自成本研究和其他发表来源的数据确定从选项 B（在怀孕和母乳喂养期间母亲三重抗逆转录病毒 [ARV] 疗法以及婴儿每天服用奈韦拉平 6 周）切换到选项 B+（母亲怀孕期开始并终身接受三重 ARV 疗法）每名妇女和每个同生群（一千名母乳哺育和一千名非母乳哺育女性）的成本。不同场景建模使用的变量为：母亲 CD4+ T 淋巴细胞（CD4+ 细胞）数（350-500 对比 >500 细胞 / μl）、CD4+ 细胞衰退率（平均、快速和缓慢）、母乳哺育状态（是、否）和母乳哺育时长（12、18 或 24 个月）。

结果 对于 CD4+ 细胞数为 350-500 细胞 / μl 的女性，每千名母乳喂养女性的成本增加 157345 美元（US$），每千名非母乳哺育女性的成本增加 92813 美元。对于 CD4+ 细胞数为 >500 细胞 / μl 的女性，每千名母乳哺育女性的成本增加范围为 363443 至 484591 美元（US$），每千名非母乳哺育女性的成本增加 605739 美元。

结论 从成本角度看，在目前资源调配给选项 B 的 PMTCT 计划环境中，进行选项 B 至选项 B+ 的政策切换是可行的。

Résumé

Surcoût du passage de l'Option B à l'Option B+ pour la prévention de la transmission du VIH de la mère à l'enfant

Objectif Estimer le surcoût sur 5 ans d'un changement de politique, avec le passage du protocole de l'Option B à celui de l'Option B+ dans le cadre de la prévention de la transmission de la mère à l'enfant (PTME) du virus de l'immunodéficience humaine (VIH).

Méthodes Des données issues d'études de coûts et d'autres sources publiées ont été utilisées pour déterminer le coût, par femme et par cohorte (1000 femmes qui allaitent et 1000 femmes qui n'allaitent pas), du passage de l'Option B (traitement par trithérapie antirétrovirale [ARV] de la mère pendant la grossesse et l'allaitement, et administration quotidienne de névirapine à l'enfant pendant 6 semaines) à l'Option B+ (traitement par trithérapie ARV initié pendant la grossesse et ensuite pris à vie). Les variables utilisées pour modéliser les différents scénarios ont été la numération des lymphocytes T CD4+ (cellules CD4+) chez la mère (350–500 contre > 500 cellules/µl), la vitesse de la baisse des cellules CD4+ (moyenne, rapide, lente), la situation au regard de l'allaitement maternel (oui, non) et la durée de l'allaitement (12, 18 ou 24 mois).

Résultats Pour les femmes présentant une numération des cellules CD4+ de 350–500 cellules/µl, le surcoût pour 1000 femmes était de 157 345 dollars pour les femmes qui allaitent et de 92 813 dollars pour les femmes qui n'allaitent pas. Pour les femmes présentant

une numération des cellules CD4+ > 500 cellules/µl, le surcoût pour 1000 femmes était compris entre 363 443 dollars et 484 591 dollars pour les femmes qui allaitent et de 605 739 dollars pour les femmes qui n'allaitent pas.

Conclusion En termes de coûts, un changement de politique de l'Option B à l'Option B+ est possible dans le cadre du programme PTME où les ressources sont actuellement affectées à l'Option B.

Резюме

Дополнительные издержки перехода от Варианта B к Варианту B+ для предотвращения передачи ВИЧ от матери к ребенку

Цель Оценить дополнительные издержки перехода от политики использования протокола Варианта B к политике использования протокола Варианта B+ для предотвращения передачи ВИЧ (вируса иммунодефицита человека) от матери к ребенку за период, равный пять лет.

Методы Для оценки издержек перехода от Варианта B (режим тройной комбинации антиретровирусных препаратов для женщин во время беременности и кормления грудью плюс ежедневный прием невирапина новорожденным в течение 6 недель) к Варианту B+ (режим тройной комбинации антиретровирусных препаратов для женщин, начинающийся во время беременности и продолжающийся в течение всей жизни) на каждую женщину и на группу (1000 кормящих и 1000 не кормящих грудью женщин) использовались данные анализов издержек и других общедоступных источников. Для моделирования различных сценариев использовались следующие переменные: уровень лимфоцитов CD4+ T (клеток CD4+) у матерей (350–500 против > 500 клеток/мкл), скорость снижения уровня клеток CD4+ (средняя, высокая, низкая), наличие или отсутствие грудного вскармливания (да, нет) и продолжительность грудного вскармливания (12, 18 или 24 месяца).

Результаты Среди женщин с уровнем клеток CD4+ 350–500 клеток/мкл дополнительные издержки на 1000 женщин составили 157 345 долларов США для женщин, кормящих грудью, и 92 813 долларов США для женщин, не кормящих грудью. Среди женщин с уровнем клеток CD4+ > 500 клеток/мкл дополнительные издержки на 1000 женщин варьировались от 363 443 до 484 591 долларов США для женщин, кормящих грудью, и достигли 605 739 долларов США для женщин, не кормящих грудью.

Вывод С точки зрения издержек политика перехода от Варианта B к Варианту B+ в рамках программы предотвращения передачи ВИЧ от матери к ребенку, ресурсы которой в настоящий момент используются для обслуживания Варианта B, является оправданной.

Resumen

El coste adicional del cambio de la opción B a la opción B+ para la prevención de la transmisión del VIH de madre a hijo

Objetivo Estimar el coste adicional en 5 años de un cambio en la política del protocolo de la opción B a la opción B+ para la prevención de la transmisión de madre a hijo (PTMI) del virus de inmunodeficiencia humana (VIH).

Métodos Se emplearon datos de estudios de costes y otras fuentes publicadas para determinar el coste, por mujer y por cohorte (1000 mujeres lactantes y 1000 mujeres no lactantes), al cambiar de la opción B (régimen antirretroviral triple materno [ARV] durante el embarazo y la lactancia materna junto con nevirapina diaria para el lactante durante 6 semanas) a la opción B+ (régimen antirretroviral triple ARV iniciado durante el embarazo y tomado de por vida). Las variables empleadas para modelar los diversos escenarios fueron el recuento de linfocitos (CD4 + células) CD4 + T maternos (350–500 frente a > 500 células/µl), la tasa de disminución de CD4 + células (media, rápida, lenta), el estado de lactancia materna (sí, no) y la duración de la lactancia materna (12, 18 o 24 meses).

Resultados En las mujeres con un recuento de CD4 + de 350–500 células/µl, el coste adicional por 1000 mujeres fue 157 345 dólares de los Estados Unidos (US$) para las mujeres lactantes y US$ 92 813 para las mujeres no lactantes. En las mujeres con un recuento de CD4 + células de > 500 células/µl, el coste adicional por 1000 mujeres varió de US$ 363 443 a US$ 484 591 en las mujeres lactantes y US$ 605 739 en las mujeres no lactantes.

Conclusión Desde el punto de vista de los costes, un cambio en la política de la B opción a la opción B+ es factible en la configuración del programa de PTMI, en el que en la actualidad los recursos se están destinando a la opción B.

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