January 2013

Cost-Effectiveness Of Antiretroviral Therapy Regimens For Hiv-Positive Pregnant Women In Ghana: A Case For Option B-Plus

Adam Joseph Vandeusen
Yale University, avandeusen@gmail.com

Cost-Effectiveness of Antiretroviral Therapy Regimens for HIV-Positive Pregnant Women in Ghana

A Case for Option B-Plus

Adam VanDeusen
Master of Public Health Candidate
Yale School of Public Health
May 1, 2013

Thesis Readers:
Dr. A. David Paltiel, Yale School of Public Health
Dr. Elisa Long, Yale School of Management

Abstract

Background: Mother-to-child transmission (MTCT) of HIV continues to fuel the the HIV epidemic in resource-limited countries, especially in sub-Saharan Africa. To minimize MTCT, the World Health Organization (WHO) recommends a range of therapy guidelines – including Options B and B-Plus. Option B indicates that HIV-positive pregnant women in developing countries who are early in disease progression receive antiretroviral therapy (ART) during pregnancy and breastfeeding. An enhanced therapy recommendation, Option B-Plus, advises that all HIV-positive pregnant women initiate lifetime ART during their first pregnancy, regardless of disease progression. This study seeks to compare health outcomes and cost-effectiveness of adopting Option B-Plus versus Option B in Ghana.

Methods: A retrospective review of 817 medical records of HIV-infected women treated at two hospitals in Kumasi, Ghana was performed to obtain clinical values, including baseline CD4 count, fertility rate, and timing of antenatal care access, that were used in analysis. Using additional data from published literature, including changes in CD4 count and HIV-related costs, a decision-analytic model was developed to estimate quality-adjusted life expectancy for mothers and all future children following Option B-Plus or Option B. The model captures the probability of MTCT prenatally and during breastfeeding, both in the current and future pregnancies. Additional ART and healthcare cost calculations were performed to compare the cost-effectiveness of the regimens. Sensitivity analyses on model parameters were performed. Outcome values were evaluated against WHO benchmarks for cost-effectiveness.

Results: The average age at first pregnancy was 22.8 years (SD 5.0) and women had an average of 2.3 children (SD 1.3). Option B costs 6,038 USD over a woman's lifetime and yields 9.8 quality-adjusted life years (QALYs) to the mother and 62.2 QALYs to each child. Option B-Plus costs 16,727 USD and yields 16.3 QALYs to the mother and 67.6 QALYs to each child. Compared to Option B, Option B-Plus costs 625 USD per QALY gained, which would be considered "very cost-effective" by WHO benchmarks. If implemented on a national level, Option B-Plus could prevent nearly 1,000 HIV infections among children in Ghana each year, compared to Option B.

Results: Option B-Plus substantially reduces MTCT in current and future pregnancies, and is a very cost-effective use of limited resources. This cost-effectiveness remained over robust sensitivity analyses. Further, Option B-Plus demonstrates a substantial increase in both maternal and children QALYs. We recommend the implementation of policies supporting Option B-Plus in Ghana and other resource-limited countries affected by HIV.

Acknowledgements

I would like to thank the faculty at Yale University for their incredible guidance and evaluation of my thesis. Their encouragement and support have helped ensure I have received a complete public health education and without them, this thesis would not have been possible. Thank you to Dr. Elisa Long and Dr. Elijah Paintsil, for serving as outstanding mentors throughout the Downs Fellowship and beyond. Thank you to Dr. Long and Dr. David Paltiel for serving as my thesis readers. Their feedback is critical not only to this document, but also to my development as a public health professional.

Thank you also to those in Ghana who have supported this project. In particular, thank you to Dr. Thomas Agyarko-Poku for serving as an advisor while in Ghana. Additionally, thank you to the Ghana Health Service, the National AIDS/STI Control Programme, the Otomfuo Osei Tutu II Charity Foundation, and the staffs at the Suntreso Government Hospital and the Kumasi South Hospital.

I am extremely grateful to the Downs Fellowship Committee and the Yale School of Medicine Office of Student Research for the financial and logistical support of my summer internship that allowed me to execute this project.

Contents

Introduction

Global efforts to reduce mother-to-child transmission (MTCT) of HIV have made substantial progress with 400,000 fewer new infections occurring in children between 2009 and 2011, in large part due to improved access to antiretroviral therapy (ART) among pregnant women (1). Despite this considerable progress, approximately 13% of all new HIV infections occur among children, with 330,000 children newly infected each year, 90% of whom live in sub-Saharan Africa (1). To achieve an "AIDS-Free Generation," programs that improve access to treatment for HIV-positive pregnant women must be prioritized.

In Ghana, the prevalence of HIV among adults aged 15 to 49 is approximately 1.8% (2). In addition to those adults, nearly 30,000 children who were infected from MTCT are now living with HIV (1). HIV prevalence among pregnant women in Ghana ranges from 2.0-4.2% (2, 3). MTCT can occur during pregnancy, birth, or breastfeeding, yet much of this transmission is preventable with appropriate treatment (4). In 2011, 64% of pregnant women in Ghana received ART to reduce the incidence of MTCT, a substantial increase from just 28% in 2009 (5). With more than 80% of pregnant women having access to antenatal care, achieving the Millennium Development Goal of reducing or eliminating MTCT by 2015 is within reach in Ghana (6, 7).

Rates of MTCT in Ghana of HIV vary between studies, but range from 14-42%, depending largely on access and adherence to treatment(8). Current World Health Organization (WHO) recommendations endorse antiretroviral prophylaxis that begins early in gestation and continues through breastfeeding stages for women with a CD4 cell count above 350 cells/mm^3, and recommend lifetime ART for women with a CD4 cell count below 350 cells/mm^3. These guidelines, commonly known as "Option B," have the potential to reduce rates of MTCT to as low as 1%, assuming high access to antenatal services (9). Option B has the potential to significantly reduce MTCT and improve the health of HIV-positive mothers, yet it is significantly more expensive than the previously recommended prevention option of a single dose of Nevirapine during delivery (9).

Although Option B improves HIV-positive maternal health outcomes, more extensive regimens with fewer treatment interruptions between pregnancies may provide greater benefits. An enhanced recommendation, commonly referred to as "Option B-Plus," proposes that all HIV-positive pregnant women receive lifelong ART beginning at first pregnancy to improve overall health outcomes, regardless of CD4 cell count. This strategy may improve maternal health through reduced morbidity and mortality, and reduce overall MTCT, especially in settings with high fertility rates(10). Avoiding HIV infection in children reduces HIV-related mortality and the subsequent costs of pediatric HIV care. Option B-Plus may be challenging to implement in resource-limited settings like Ghana and further evaluation is needed to assess its budgetary impact and cost-effectiveness. In this study, we summarize primary data collected from two hospitals in Ghana. A key component of our analyses is the inclusion of all pregnancies likely to occur in a woman's lifetime. To the best of our knowledge, no prior study has included

pregnancy recurrence in cost-effectiveness evaluation of Option B-Plus. Including pregnancy recurrence in a model fully captures the impact of therapy regimens on HIV-positive women in developing countries, many of whom have more than one child. We utilized data collected onsite with epidemiologic, demographic, and clinical data from previous studies, and apply a decision-analytic model to evaluate the costs, health benefits – to both the mother and children – and cost-effectiveness of Option B versus Option B-Plus in Ghana. The primary objective of this analysis is to evaluate the cost-effectiveness of these two guidelines and a secondary objective is to utilize cost-effectiveness information to inform global recommendations for HIV therapy among pregnant women in resource-limited countries like Ghana.

Methods

We developed a state-transition model to compare the lifetime costs and benefits of two strategies to prevent MTCT in Ghana. When possible, data were collected from local Ghanaian sources. Ages of pregnancy and antenatal care access patterns were obtained from a review of medical charts of HIV-positive women at two government hospitals in Kumasi, Ghana (Table 1). Transmission rates, life expectancies, adherence rates and HIV care access patterns were obtained through documents issued by the Ghana Health Service. Costs, utilities, CD4 change patterns, CD4 testing patterns, and resistance values were obtained through previously published studies.

Patient Characteristics

The patient population included in the model is HIV-positive pregnant women in Ghana, who are pregnant with their first child. The chart review consisted of abstracting data from paper medical charts at two government hospitals in Kumasi, Ghana. These hospitals serve a range of women from Kumasi and its surrounding region. Their patient bases were considered demonstrative of the overall population by representatives from the Ghana Health Service.

Based on the chart review of HIV-positive pregnant women, estimates of average baseline CD4 count at time of antenatal care were obtained. Age of first pregnancy, lifetime number of children per woman, and time between successive pregnancies were also estimated through chart review. Maternal life expectancy was evaluated using medical charts and death records at each hospital.

Definition of Options

Option B and Option B-Plus are two of three options recommended for the prevention of MTCT by the WHO. Under both options, an HIV-positive woman who has CD4 count less than 350 cells/mm^3 is pregnant, she is immediately treated with a triple-ART that continues through life. However, under Option B, women with CD4 count greater than 350 cells/mm^3 receive ART beginning at 14 weeks into gestation and continued throughout pregnancy and after birth until breastfeeding ceases. Alternatively, under Option B-Plus, all women receive lifetime ART, even

if CD4 count is greater than 350 cells/mm^3. Under both options, infants born to HIV-positive women receive daily ART from birth through the age of 4-6 weeks(11).

Model Parameters

Fertility Rates

A key consideration when evaluating the cost-effectiveness of continual ART versus interrupted therapy is the time between successive pregnancies. Because Option B implies that a pregnant woman ceases ART following completion of breastfeeding, she may not receive ART at the optimal starting point (the end of the first trimester) of her next pregnancy, especially because only 12% of women in our sample received antenatal care during their first trimester. With Option B-Plus, she remains continually on ART, so there is no window during a pregnancy when she is not receiving prophylactic therapy.

Based on medical chart review, a hazard model was fit to estimate the rate and time distribution of future pregnancies following the first pregnancy. Each pregnancy recorded from the chart review was considered an event and the age at which these events occurred was included in the model. This hazard model produced the probability of a pregnancy occurring at each age in a woman's lifetime. The model was developed in SAS 9.3.

Access to Antenatal Care, Adherence, and Transmission

The overall fraction of pregnant women in Ghana who receive antenatal care at some point in their pregnancy was determined based on a national survey (6). In more detailed analysis, the proportions of pregnant women who accessing antenatal care, by month of pregnancy, were estimated through medical chart review. Estimates of ART adherence and the probability of mother-to-child transmission during pregnancy, delivery, or while breastfeeding were obtained from annual reports on antenatal care and MTCT issued by the Ghana Health Service (6, 12). Under Option B, a woman who does not qualify for lifetime therapy at their first pregnancy (by having a CD4 cell count < 350 cells/mm^3) can initiate ART during her lifetime when her CD4 cell count decreases below 350 cells/mm^3 (9). Our model accounts for this by tracking CD4 cell count throughout a woman's lifetime and initiating ART when the 350 cells/mm^3 threshold is reached.

Reports on transmission rates among women receiving Option B consider ideal conditions (i.e., a pregnant woman receives therapy from the beginning of her first trimester through six months of breastfeeding).However, these ideal conditions are not achievable if antenatal care is obtained beyond the first trimester of pregnancy. To achieve a more realistic transmission rate on Option B, we multiplied the percentage of women accessing antenatal care during a specific month of pregnancy – the values for which were obtained through chart review – by a scaled rate of transmission. This scaled rate of MTCT was determined by considering an ideal rate of 1.0% if a woman accessed antenatal care in the first 3 months of pregnancy, and gradually increasing rates if care was accessed in each subsequent month, with a 20.3% rate of MTCT under the least ideal

conditions (access to antenatal care in the 9th month of pregnancy). See the Appendix for a more detailed depiction of data used in this value generation.

Quality of life Adjustments, Costs, CD4 Changes, and other Parameters

Additional values not obtained through chart review were acquired through review of previously published studies. All costs are reported in US Dollars (1 USD = 1.93 Ghana Cedi, abbreviated as GHS) and incorporate all facets of HIV/AIDS care following diagnosis, including ART, medical personnel wages, and CD4 count and viral load testing. In particular, we assume the annual cost of HIV/AIDS care with first-line ART to be 385 USD (744 GHS), but we consider variations of this assumption in sensitivity analysis (13, 14).

Changes in CD4 cell count were modeled from previously published works and the rate of CD4 change was determined by a woman's ART utilization and whether ART is interrupted or continuous (15-17). Women incurred a CD4 cell count increase of 153 cells/mm^3 at the initiation of therapy (18). Adjustments for quality of life while living with HIV were considered on as a yearly quality adjustment for adults and a lifetime adjustment for children. Adult women living with HIV were assumed to have 0.8 times the quality of life of otherwise healthy women (19). Children born HIV-positive were attributed this same 0.8 quality of life adjustment, applied across life expectancy and discounted by an annual discount rate of 0.3 (20, 21).

Model Structure, Outcomes & Analysis

The state-transition model was developed in TreeAge Pro (2012 version). The model tracks a woman's age, CD4 count, and number of past pregnancies when evaluating transition probabilities to future states. Similar to Markov models, our model incorporates several states with transition probabilities between each state. However, values like CD4 count and number of previous pregnancies may impact these transition probabilities, thereby not following the assumed memoryless property of a Markov model, in which all transition probabilities are independent of past or current states.

The health states of the model were "Pregnant," "Breastfeeding HIV+ Child," "Breastfeeding HIV- Child," "Not Pregnant", and "Dead", where certain transition probabilities between states differed between treatment regimens. A basic model schematic is shown in Figure 1. Each cycle of the model represented 3 months of time. Sensitivity analyses were conducted on several variables. Ranges utilized in the sensitivity analyses are indicated in Table 1.

Primary outcomes of the model were costs and quality-adjusted life years (QALYs) for each therapy option. All costs and QALYs are discounted to the present using a 3% annual discount rate (22). Costs and QALYs of Option B and Option B Plus were then compared using an incremental cost-effectiveness ratio (ICER):

$$ICER = \frac{Cost_{Option\ B\ Plus} - Cost_{Option\ B}}{QALYs_{Option\ B\ Plus} - QALYs_{Option\ B}}$$

ICER values are measured in cost per QALY gained under Option B-Plus compared to Option B. These values were compared to benchmarks established by the WHO Commission on Macroeconomics for Health. These benchmarks indicate that a cost-effective alternative to current guidelines has an ICER value of less than 3 times the country's gross domestic product (GDP) per capita. An alternative recommendation with ICER less than 1 times the country's GDP per capita is considered "very cost-effective" (23). The GDP per capita in Ghana was 3,300 USD (6,369 GHS) in 2012 (24).

Results

Population Demographics

During the chart review, 817 medical charts were reviewed – 418 at Suntreso Government Hospital and 399 at Kumasi South Hospital. Key results of this chart review are trimester during which women access antenatal care, age of first pregnancy, and average number of children. The average age of first pregnancy was 22.78 years (± 4.97 years) and the average lifetime number of children per woman was 2.34 (± 1.27 children). Among women whose timing of antenatal care access was known, 12% accessed care in their first trimester, 40% in their second trimester, and 48% in their third trimester. Detailed results of this chart review can be found in Table 1.

Pregnancy Recurrence

The hazard model established probability of pregnancy at each age following a woman's first pregnancy. The probability associated with a second pregnancy at each year following the first pregnancy, as taken directly from chart review data, can be found in Figure 2. Approximately 32% of the women in our sample did not have a second pregnancy, while 4% became pregnant within one year following their first pregnancy and 19% became pregnant within two years. The average time between the first and second pregnancies was 4.56 years (± 3.05 years).

Reduction in Mother-to-Child Transmission

Approximately 10,800 births occur to HIV-positive women in Ghana each year (25). Under Option B, HIV transmission rate is 10.19% during pregnancy or delivery and 1% during breastfeeding, suggesting that approximately 1,209 new cases of HIV are due to MTCT each year. Under Option B-Plus, HIV transmission rate is 1% during pregnancy or delivery and 1% during breastfeeding, resulting in 216 new MTCT HIV cases each year. Thus, offering all pregnant women in Ghana Option B-Plus instead of Option B could theoretically prevent 993 HIV cases among newborn babies in Ghana each year.

Cost-Effectiveness

Option B has lifetime cost of 6,038 USD while Option B-Plus has a lifetime cost of 16,727 USD. Option B yields 11.91 QALYs to the mother and Option B-Plus yields 16.28 QALYs, an increase of 35%. Further, Option B yields 62.17 QALYs per child, while Option B-Plus yields 67.57 QALYs per child. Considering the QALYs attributed to the mother in addition to the

QALYs collectively attributed to all of the mother's children, Option B yields 165.2 QALYs and Option B-Plus yields 182.3 total QALYs. These values lead to an incremental cost-effectiveness ratio (ICER) of 625.1 USD per QALY gained. If quality-of-life weights are ignored, an ICER value of 1,039 USD per life-year gained is obtained. Table 3 contains detailed baseline results of the primary outcomes.

Sensitivity Analyses

A detailed sensitivity analysis was performed on all model parameters, to test for robustness and identify key parameters impacting cost-effectiveness results. Of all variables examined, cost-effectiveness was most sensitive to the probability of MTCT during pregnancy or delivery under Option B. However, even when this probability was decreased to 0%, the model's ICER value was only 1,553 USD per QALY gained, which is still below the Ghanaian GDP per capita of 3,300 USD. This increase in ICER is likely due to transmission rates among the two options becoming more similar, thus decreasing the cost-effectiveness of Option B-Plus as compared to Option B.

A tornado diagram (Figure 3) shows that the cost-effectiveness of Option B-Plus was also sensitive to specific variables in the model including life expectancies, cost of HIV care with first-line ART, access to antenatal care, and fertility rates.

One-way sensitivity analyses of several variables display each variable's relationship to the model ICER value (Figure 4). As the probability of accessing antenatal care is increased from 0.50 to 0.95, Option B-Plus becomes more cost-effective compared to Option B, yet ICER values only reach 1,108 USD per QALY gained. Similarly, ICER values decrease as the fertility rate in the model is ranged from 0.75 to nearly 5 children born to an HIV-positive woman, but the ICER only ranges from 507-874 USD per QALY gained over this range of fertility rate. Finally, as life expectancy on Option B is modified from 6-30 remaining life years after first pregnancy, ICER values increase approximately linearly. As women are estimated to live longer under Option B, their life expectancies are not only more similar to the life expectancies under Option B-Plus, thereby making Option B less cost-effective compared to Option B-Plus.

Discussion

The goal of this analysis was to evaluate the cost-effectiveness of Option B versus Option B-Plus therapy regimens among HIV-positive pregnant women in Ghana. Option B-Plus improves both maternal and child outcomes, and we find that the additional cost of such a program is likely warranted given its favorable cost-effectiveness. Option B-Plus helps ensure that women who would otherwise not initiate ART until the second or third trimester under Option B can receive continual therapy during their index pregnancy and all subsequent pregnancies. Our model was unique in its ability to account for multiple pregnancies. Our study also has important implications for helping policymakers allocate limited HIV resources effectively and efficiently.

A secondary objective was to inform global policy on recommendations for HIV therapy among pregnant women in resource-limited countries. Our results indicate that although Option B costs approximately one-third the cost of Option B Plus, the latter yields approximately 17 more QALYs to the mother and her children.

Comparing Option B Plus to Option B, we obtain an ICER value of 625 USD per QALY gained (1,206 GHS per QALY gained). This value is in line with other HIV interventions shown to be cost-effective in low- and middle-income countries, such as male circumcision in sub-Saharan Africa (26-28).The 2012 gross domestic product per capita in Ghana was approximately 3,300 USD (6,369 GHS) (24). Based on recommendations by the WHO Commission on Macroeconomics in Health, Option B Plus is considered very cost-effective compared to Option B (23). Additionally our sensitivity analysis demonstrates that our cost-effectiveness results were robust to wide ranges of parameter assumptions, which suggests that Option B-Plus is very likely cost-effective in a setting with similar resources and epidemiologic characteristics to Ghana. Our results are generally consistent with other studies that use model-based analyses to estimate the cost-effectiveness of Option B-Plus in Zimbabwe and Nigeria (9, 29). These previous analyses provide significant contributions to understanding the cost-effectiveness of Option B-Plus and our analysis expands this understanding further by incorporating the opportunity for multiple pregnancies over a woman's lifetime as well as primary data utilization. Our findings are also consistent with other cost-effectiveness analyses of HIV prevention methods in Ghana, including voluntary HIV counseling and blood donation screening (8, 30).

An outcome not directly related to this model that is critical to consider for larger policy implications is the percentage of HIV-positive pregnant women who qualify for lifetime therapy according to recommendations from the WHO Commission on Macroeconomics for Health (23). As Table 1 indicates, 52.9% of HIV-positive pregnant women qualify for lifetime therapy at the time of their first pregnancy. Considering this figure, the overall cost to scale up to Option B-Plus throughout the country is less expensive.

Our modeling study has several limitations. First, because Option B Plus is a newly devised intervention, updates on its efficacy and impact on maternal disease progression and survival are evolving; however, we have explored variations in parameter assumptions with robust sensitivity analysis. Second, the model does not explicitly consider horizontal HIV transmission; however, we believe this is a valid assumption because an HIV-positive pregnant woman likely has a regular partner who is also HIV-positive (31). We also estimated the expected costs and QALYs associated with Option B and Option B Plus, but the model simplifies complex clinical outcomes, such as viral load, development of opportunistic infections, or variability in HIV progression in children. Future projects related to this analysis could include comparing MTCT rates, by the trimester during which a mother first accesses antenatal care under Option B. Although our model captures this variability in transmission, more precise values should be examined.

In resource-limited settings such as Ghana, systematically comparing the potential health benefits and costs of competing HIV programs can illuminate where additional investment should be prioritized. Option B-Plus provides considerable health benefits to HIV-positive women and their children, even when opportunities for multiple pregnancies are considered, and represents good value. With wide implementation of Option B-Plus, we estimate that approximately 1,000 more children could potentially be born without HIV in Ghana *every year*, and preventing these infections now is a key step towards reducing the burden of HIV in the future.

Tables and Figures

Table 1. Population Demographics

Parameter	Value (Standard Deviation or % of total)*
Charts Reviewed	817
Suntreso Government Hospital	418 (51.2%)
Kumasi South Hospital	399 (48.8%)
Age of first pregnancy	22.78 years (±4.97 years)
Number of children (HIV+)	2.34 children (±1.27 children)
Number of children (overall)	4.12 children**
Pregnant when diagnosed HIV-positive	223 (27.3%)
Baseline CD4 count	471 cells/mm^3
CD4 <350 cells/mm^3 when pregnant and diagnosed	118 (52.9%)
Known timing of pregnancy when first accessing care (n=92)	
1st trimester	11 (12.0%)
Month 1	1 (1.1%)
Month 2	4 (4.4%)
Month 3	6 (6.5%)
2nd trimester	37 (40.2%)
Month 4	11 (12.0%)
Month 5	14 (15.2%)
Month 6	12 (13.0%)
3rd trimester	44 (47.8%)
Month 7	19 (20.7%)
Month 8	19 (20.7%)
Month 9	6 (6.5%)

*Percentages may not add to 100% due to rounding.
**Source: United States Central Intelligence Agency World Factbook(24)

Table 2. Model Parameters

Variable	Base-Case Value	Range	Source
Demographic variables			
Maternal life expectancy			
Option B	40 years	28-52 years	Ghana Health Service(6)
Option B Plus	56 years	44-68 years	Ghana Health Service(6)
Number of children	2.34	1-5	Chart review
Probabilities			
Access to care	82%	50-95%	Ghana Health Service(6)
Access to CD4 testing	33%	20-60%	When To Start Consortium (32)
Adherence to ART	90%	50-95%	Ghana Health Service(6)

Resistance to ART after stopping therapy	40%	-	Ghana Health Service(12)
Transmission during pregnancy			
No therapy/non-adherence	22%	15-30%	Ghana Health Service(12), De Cock 2000 (33)
Option B	10%[†]	0-15%	Ghana Health Service(12)
Option B-Plus	1%	0-5%	Ghana Health Service(12)
Transmission during breastfeeding			
No therapy/non-adherence	10%	5-20%	Ghana Health Service(12), De Cock 2000 (33)
Option B	1%	0-5%	Ghana Health Service(12)
Option B-Plus	1%	0-5%	Ghana Health Service(12)
Changes to CD4 Count			
No therapy (every 3 months)	- 12.75 cells/mm^3	5-20 cells/ mm^3	Fidler 2007(16), Holmes 2006(17)
Initiate therapy	+ 153 cells/mm^3	100-400	Deeks 1999(18)
Continue therapy (every 3 months)			
Previously interrupted therapy	-0.063659* [Current CD4]	-	Ickovics et al. 2001(15)
Continuous therapy	- 0.0099853* [Current CD4]	-	Ickovics et al. 2001(15)
Costs (USD[GHS])			
Mother (Annual Cost of HIV Care)			
Care with First-Line ART	385.45 [743.91]	191-580.31	WHO 2011(14); Rosen, J., and F. Asante. 2010(13)
Care with Second-Line ART	848.33 [1,637.28]	-	WHO 2011(14); Rosen, J., and F. Asante. 2010(13)
Child HIV Care (Lifetime costs)	10,665.49 [20,584.40]	5,181-15,544	WHO 2011(14); Rosen, J., and F. Asante. 2010(13)
Utility			
HIV-positive adult (quality of life)	0.8	0.50-1.0	Tengs T.O., Lin T.H. 2002(19)

HIV-positive child (lifetime QALYs)	20.2[††]	10-30	UN Impact of AIDS 2004(20)
HIV-negative child (lifetime QALYs)	62.7	50-70	UN Impact of AIDS 2004(20)
Discount rate	0.03	0.00-0.05	Weinstein et al. 1996(21)

*Sensitivity analyses performed on age of first pregnancy were performed by changing values manually due to variable structure in the decision-analytic model.

[†] Probability of transmission during pregnancy/delivery while on Option B was determined by applying the distribution of when women accessed antenatal care (found through chart review) with ideal conditions of Option B (beginning therapy at the beginning of the second trimester) indicated by the Ghana Health Service and WHO.

[††] Lifetime QALYs for an HIV-positive child assume a life expectancy at birth of 47.1 years (Source: UN "The Impact of AIDS" publication 2004) with a yearly utility of 0.82 and a discount rate of 0.03.

Table 3. Baseline Results of Primary Outcomes

Treatment Strategy	Lifetime Cost (GHS)	Lifetime Cost (USD)	Life-Years*	QALYs*[†]	ICER*[†]
Option B	11,654	6,038	186.4	165.2	
Mother	2,424	1,256	11.9	9.8	
Children	9,230	4,783	174.5	155.4	
Per Child	3, 692	1,913	69.8	62.2	
Option B-Plus	32,283	16,727	196.7	182.3	625.1
Mother	19,230	9,964	16.3	13.4	
Children	13,053	6,763	180.4	168.9	
Per Child	5,221	2,705	72.2	67.6	

*All life-years/QALYs discounted by 3% annual rate.

[†] QALY = Quality-Adjusted Life-Year; ICER = Incremental Cost-Effectiveness Ratio. All QALYs are calculated using an adjustment of 0.82 utility per year when living with symptomatic HIV and an annual discount rate of 0.03. The ICER value is calculated as follows: $ICER=([Cost_{B\text{-}Plus}-Cost_B]/[QALY_{B\text{-}Plus}-QALY_B])$.

Figure 1. State Transition Model Overview

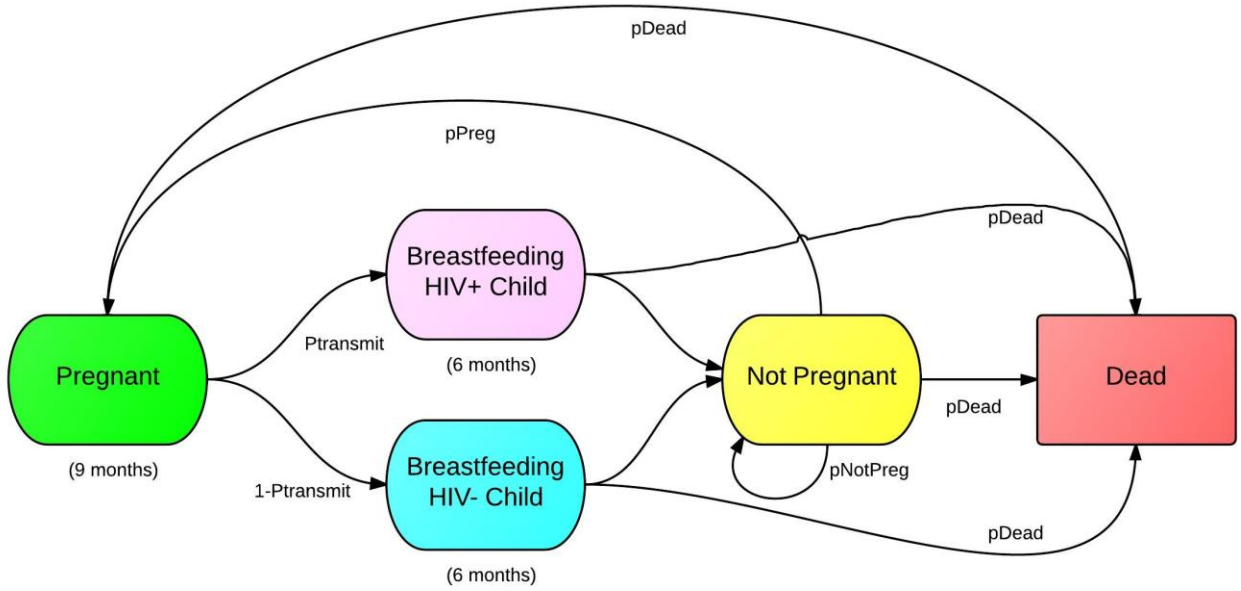
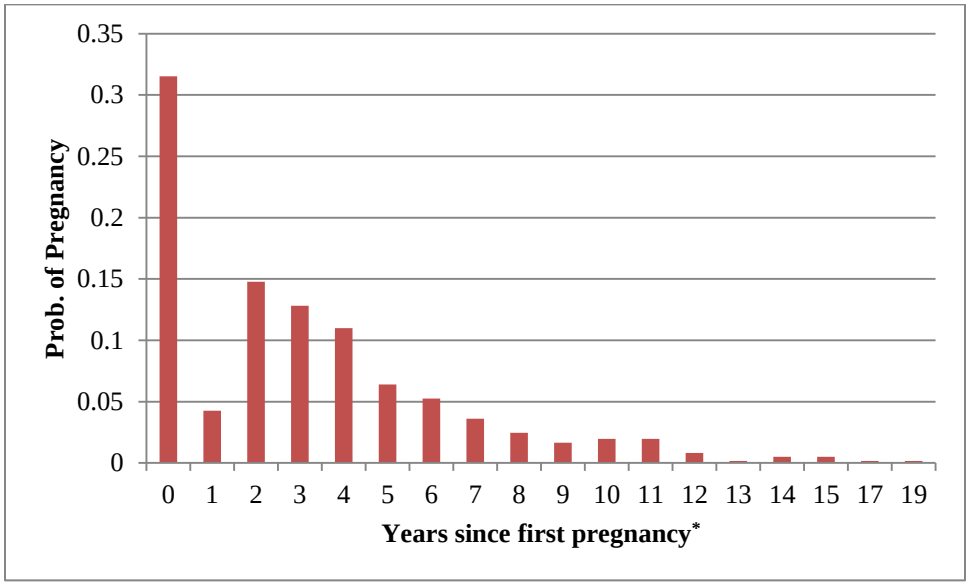


Figure 2. Probability of time between 1st and 2nd pregnancy



*0 years since first pregnancy indicates the mother does not have more than one child.

Figure 3. Tornado Diagram

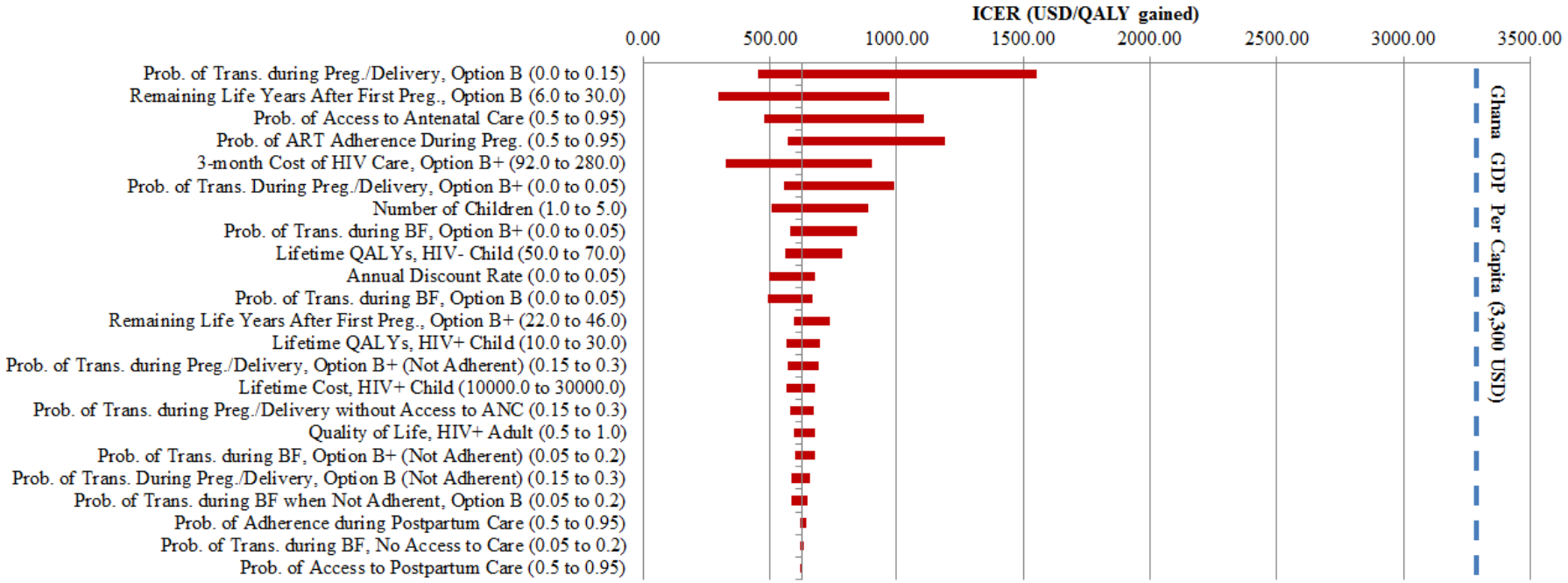
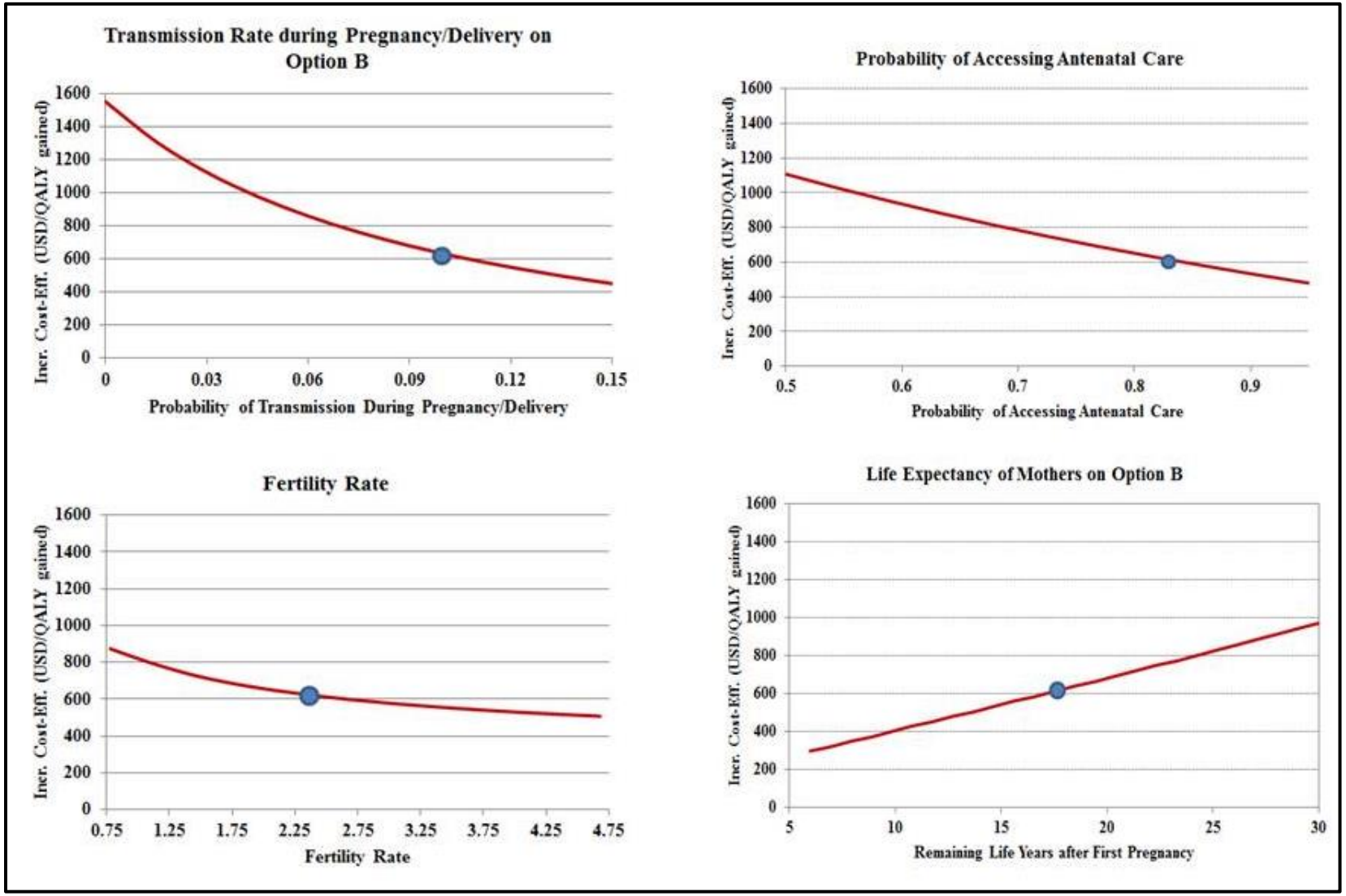


Figure 4. One-Way Sensitivity Analyses



● = Base Case

Appendix

Chart Review – Full Results

	N (% of total)
Total	817 (100%)
Location (n=817)	
Suntreso Government Hospital	418 (51.2%)
Kumasi South Hospital	399 (48.8%)
Pregnancy Status (n=588)	
Pregnant	221 (37.6%)
Not pregnant	367 (62.4%)
First Access of Antenatal Care (n=92)	
First trimester	11 (12.0%)
Second trimester	37 (43.5%)
Third trimester	44 (47.8%)
Age (n=811)	
18-24	64 (8.1%)
25-29	186 (23.4%)
30-34	179 (22.5%)
35-39	138 (17.4%)
40-44	85 (10.7%)
45-49	54 (6.8%)
50+	88 (11.1%)
Marital Status (n=804)	
Single	100 (12.4%)
Cohabiting	111 (13.8%)
Married	383 (47.6%)
Separated	30 (3.7%)
Divorced	85 (10.6%)
Widow	95 (11.8%)
Occupational Status (n=807)	
Full Time	614 (76.1%)
Part Time	10 (1.2%)
On Leave	13 (1.6%)
Unemployed	170 (21.1%)
Education Level (n=795)	
Nil	162 (20.4%)
Primary	155 (19.5%)
JSS/MSLC	391 (49.2%)
Sec/Tech	65 (8.2%)
Tertiary	22 (2.8%)
Vertical Transmission (n=641)	
Positive	25 (3.9%)
Negative	50 (7.8%)
Positive/Negative	5 (0.8%)
Don't Know	561 (87.5%)
HIV Type (n=453)	
Type I	411 (90.7%)
Type II	7 (1.5%)
Types I/II	35 (7.7%)
HIV Symptoms (n=738)	
0	137 (18.6%)
1	160 (21.7%)
2	107 (14.5%)
3	106 (14.4%)
4	88 (11.9%)

5	79 (10.7%)
6+	61 (8.3%)
Other Diseases (n=770)	
0	278 (36.1%)
1	276 (35.8%)
2	130 (16.9%)
3+	86 (11.2%)
Sexually Active (n=417)	346 (66.9%)
Contraception Use (n=323)	130 (40.2%)
Contraception Type (n=189)	
Condoms	151 (79.9%)
Injection	28 (14.8%)
Pill	10 (5.3%)
Diagnosis Year (n=811)	
2005	6 (0.7%)
2006	23 (2.8%)
2007	130 (16.0%)
2008	162 (20.0%)
2009	248 (30.6%)
2010	149 (18.4%)
2011	72 (8.9%)
2012	21 (2.6%)
Disclosure (n=746)	609 (81.6%)
WHO Status (n=718)	
I	181 (25.2%)
II	158 (22.0%)
III	296 (41.2%)
IV	83 (11.6%)
On ART (n=761)	597 (78.4%)
Malaria (n=770)	278 (36.1%)
Tuberculosis (n=770)	40 (5.2%)
Sexually Transmitted Infection (n=770)	57 (10.9%)
Respiratory Tract Infection (n=770)	84 (7.4%)
Depression (n=770)	13 (1.7%)
Anemia (n=770)	66 (8.6%)
Hypertension (n=770)	31 (4.0%)
Heart Disease (n=770)	16 (2.1%)
Gastrointestinal Disease (n=770)	34 (4.4%)

Calculation of Option B Transmission Rate

Month of ANC access	1	2	3	4	5	6	7	8	9
% of women in population (p_{month})	1.1	4.3	6.5	12.0	15.2	13.0	20.7	20.7	6.5
MTCT probability ($rate_{month}$)	1.0	1.0	1.0	2.8	6.3	9.8	13.3	16.8	20.3

$$Option\ B\ Transmission\ Rate = \sum_{month=1}^{9} p_{month} * rate_{month}$$

References

1. UNAIDS. World AIDS Day Report. UNAIDS, 2012.
2. Unicef. At a Glance: Ghana - Statistics. Unicef, 2007.
3. Ghana Health Service. Estimating National HIV Prevalence in Ghana Using Sentinel Surveillance Data. National AIDS/STI Control Programme, 2000.
4. WHO. PMTCT Strategic Visions 2010-2015: preventing mother-to-child transmission of HIV. World Health Organization, 2010.
5. Ghana AIDS Commission. Ghana - Country AIDS Progress Report. Reporting Period: January 2010-December 2011. UNAIDS, 2012.
6. Ghana Health Service. PMTCT Annual Report. Kumasi, Ghana: National AIDS/STI Control Programme, Office KR; 2011.
7. United Nations. The Millenium Development Goals Report. New York: United Nations, 2005.
8. Baiden F, Baiden R, Williams J, Akweongo P, Clerk C, Debpuur C, et al. Review of Antenatal-Linked Voluntary Counseling and HIV Testing in Sub-Saharan Africa: Lessons and Options for Ghana. Ghana medical journal. 2005 Mar;39(1):8-13. PubMed PMID: 17299534. Pubmed Central PMCID: 1790809.
9. Shah M, Johns B, Abimiku A, Walker DG. Cost-effectiveness of new WHO recommendations for prevention of mother-to-child transmission of HIV in a resource-limited setting. Aids. 2011 May 15;25(8):1093-102. PubMed PMID: 21505317.
10. WHO. Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants: Towards Universal Access - Recommendations for a public health approach. World Health Organization, 2010.
11. Unicef. Options B and B+: Key Considerations for Countries to Implement an Equity-Focused Approach. 2012.
12. Ghana Health Service. PMTCT Training Package for Health Care Providers Participant Manual. In: Service GH, editor. 2010.
13. Rosen J, and F. Asante. Cost of HIV & AIDS Adult and Pediatric Clinical Care and Treatment in Ghana. Washington, DC: Futures Group, Health Policy Initiative, 2010.
14. WHO. Global Price Reporting Mechanism Report. AIDS Medicines and Diagnostics Service, WHO, 2011.
15. Ickovics JR, Hamburger ME, Vlahov D, Schoenbaum EE, Schuman P, Boland RJ, et al. Mortality, CD4 cell count decline, and depressive symptoms among HIV-seropositive women: longitudinal analysis from the HIV Epidemiology Research Study. JAMA : the journal of the American Medical Association. 2001 Mar 21;285(11):1466-74. PubMed PMID: 11255423.
16. Fidler S, Fox J, Touloumi G, Pantazis N, Porter K, Babiker A, et al. Slower CD4 cell decline following cessation of a 3 month course of HAART in primary HIV infection: findings from an observational cohort. Aids. 2007 Jun 19;21(10):1283-91. PubMed PMID: 17545704.
17. Holmes CB, Wood R, Badri M, Zilber S, Wang B, Maartens G, et al. CD4 decline and incidence of opportunistic infections in Cape Town, South Africa: implications for prophylaxis and treatment. Journal of acquired immune deficiency syndromes. 2006 Aug 1;42(4):464-9. PubMed PMID: 16810113.
18. Deeks SG, Grant RM. Sustained CD4 responses after virological failure of protease inhibitor-containing therapy. Antiviral therapy. 1999;4 Suppl 3:7-11. PubMed PMID: 16021865.
19. Tengs TO, Lin TH. A meta-analysis of utility estimates for HIV/AIDS. Medical decision making : an international journal of the Society for Medical Decision Making. 2002 Nov-Dec;22(6):475-81. PubMed PMID: 12458977.

20. United Nations. The Impact of AIDS. United Nations, Department of Economic and Social Affairs PD; 2004.
21. Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB. Recommendations of the Panel on Cost-effectiveness in Health and Medicine. JAMA : the journal of the American Medical Association. 1996 Oct 16;276(15):1253-8. PubMed PMID: 8849754.
22. Gold MR. Cost-effectiveness in health and medicine. New York: Oxford University Press; 1996. xxiii, 425 p. p.
23. World Health Commission on Macroeconomics and Health: Investing in Health for Economic Development. Geneva: World Health Organization Commission on Macroeconomics and Health, 2001.
24. United States Central Intelligence Agency. World Factbook - Ghana [updated March 29, 2013; cited 2013]. Available from: https://www.cia.gov/library/publications/the-world-factbook/geos/gh.html.
25. United Nations. Together We Will End AIDS. Joint United Nations Programme on HIV/AIDS, 2012.
26. Andersson KM, Owens DK, Paltiel AD. Scaling up circumcision programs in Southern Africa: the potential impact of gender disparities and changes in condom use behaviors on heterosexual HIV transmission. AIDS and behavior. 2011 Jul;15(5):938-48. PubMed PMID: 20924783. Pubmed Central PMCID: 3112296.
27. Kahn JG, Marseille E, Auvert B. Cost-effectiveness of male circumcision for HIV prevention in a South African setting. PLoS medicine. 2006 Dec;3(12):e517. PubMed PMID: 17194197. Pubmed Central PMCID: 1716193.
28. Long E, Stavert RR. Portfolios of Biomedical HIV Interventions in South Africa: A Cost-Effectiveness Analysis. Journal of general internal medicine. 2013;(in press).
29. Ciaranello AL, Perez F, Maruva M, Chu J, Engelsmann B, Keatinge J, et al. WHO 2010 guidelines for prevention of mother-to-child HIV transmission in Zimbabwe: modeling clinical outcomes in infants and mothers. PloS one. 2011;6(6):e20224. PubMed PMID: 21655097. Pubmed Central PMCID: 3107213.
30. van Hulst M, Sagoe KW, Vermande JE, van der Schaaf IP, van der Tuuk Adriani WP, Torpey K, et al. Cost-effectiveness of HIV screening of blood donations in Accra (Ghana). Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2008 Sep-Oct;11(5):809-19. PubMed PMID: 18489518.
31. Achana FS, Debpuur C, Akweongo P, Cleland J. Postpartum abstinence and risk of HIV among young mothers in the Kassena-Nankana District of Northern Ghana. Culture, health & sexuality. 2010 Jun;12(5):569-81. PubMed PMID: 20432081.
32. When To Start Consortium, Sterne JA, May M, Costagliola D, de Wolf F, Phillips AN, et al. Timing of initiation of antiretroviral therapy in AIDS-free HIV-1-infected patients: a collaborative analysis of 18 HIV cohort studies. Lancet. 2009 Apr 18;373(9672):1352-63. PubMed PMID: 19361855. Pubmed Central PMCID: 2670965.
33. De Cock KM, Fowler MG, Mercier E, de Vincenzi I, Saba J, Hoff E, et al. Prevention of mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice. JAMA : the journal of the American Medical Association. 2000 Mar 1;283(9):1175-82. PubMed PMID: 10703780.