RETHINKHIV

Perspective Paper

Prevention of Non-Sexual Transmission of HIV: Mother-to-child transmission

Mira Johri

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FUNDING DISRUPTIVE IDEAS AGAINST HIV

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Prevention of Non-Sexual Transmission of HIV: Mother-to-child transmission

Mira Johri[1]

[1] Associate Professor, International Health Unit (USI) and Department of Health Administration (DASUM), University of Montreal.
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RethinkHIV: The Project

2011 marks the 30-year anniversary since the Centers for Disease Control and Prevention introduced the world to the disease that became known as AIDS. Despite 30 years of increasing knowledge about transmission, prevention, and treatment, and current annual spending of $15 billion, every day around 7,000 people are infected with the HIV virus and two million die each year. The HIV/AIDS epidemic has had its most profound impact in sub- Saharan Africa, which accounts for 70 percent of new worldwide infections and 70 percent of HIV-related deaths, 1.8 million new infections in children each year, and has 14 million AIDS orphans.

Humanitarian organizations warn that the fight against HIV/Aids has slowed, amid a funding shortfall and donor fatigue. Yet HIV is still the biggest killer of women of reproductive age in the world, and of men aged 15-59 in sub-Saharan Africa. Time is ripe for a reassessment of current policy and expenditure.

The Rush Foundation has asked the Copenhagen Consensus Center to commission a group of leading health academics to analyze HIV policy choices and identify the most effective ways to tackle the pandemic across sub-Saharan Africa.

RethinkHIV identifies effective interventions in the fight against HIV/Aids across sub-Saharan Africa. It applies cost-benefit analysis to highlight investments and actions that can make a significant difference.

The Copenhagen Consensus Center has commissioned eighteen research papers by teams of top health economists, epidemiologists, and demographers who examine the cost-effectiveness of a range of responses to HIV/AIDS in sub- Saharan Africa under the following topics:

- Efforts to Prevent Sexual Transmission
- Efforts to Prevent Non-Sexual Transmission
- Treatment and Initiatives to Reduce the Impact of the HIV/AIDS Epidemic
- Research and Development Efforts
- Social Policy Levers
- Initiatives to Strengthen Health Systems

A panel of five eminent economists, including recipients of the Nobel Prize, convenes in the fall of 2011 to carefully consider the research and engage with the authors. The Expert Panel is tasked with answering the question:

If we successfully raised an additional US$10 billion over the next 5 years to combat HIV/AIDS in sub-Saharan Africa, how could it best be spent?

After deliberating in a closed-door meeting, the Nobel Laureate Expert Panel provides their answer, highlighting investments and actions that could be most effective avenues for additional funding. Their findings and reasoning are released in the fall of 2011, and published in full alongside all of the research in a collated volume in 2012.

RethinkHIV will generate global discussion regarding responses to HIV/AIDS in sub-Saharan Africa. To participate in a dialogue on the research and findings within sub-Saharan Africa, a Civil Society Conference and forums for youth are held following the Expert Panel meeting in late 2011.

The Civil Society Conference is a means of creating a dialogue with African civil society and to agree on a set of bold new actionable priorities with society politicians, civil society organizations, influential thought-leaders, and others within sub-Saharan Africa.

It is hoped that the project will motivate donors to direct more money to the investments and actions that are demonstrated to be most effective to curtail the pandemic in sub-Saharan Africa.

All of the research papers, and many different perspectives on priorities can be found online at the project's website:
www.rethinkhiv.com

You are invited to join the dialogue and provide your own perspective on priorities for action in Africa.

The Copenhagen Consensus Center

The Copenhagen Consensus Center is a Danish state-funded think- tank that commissions and promotes research highlighting the most effective responses to global challenges. The Center is led by author Bjorn Lomborg, named 'one of the 100 Top Global Thinkers' by Foreign Policy in 2010, 'one of the world's 75 most influential people of the 21st century' by Esquire in 2008, and 'one of the 50 people who could save the planet' by the Guardian in 2008. The Copenhagen Consensus Center is implementing the project, which follows the format of past projects such as Copenhagen Consensus 2004, Consulta de San José in 2007, Copenhagen Consensus 2008, and Copenhagen Consensus on Climate in 2009.
www.copenhagenconsensus.com

The Rush Foundation

The Rush Foundation, based in Lausanne, is dedicated to providing fast, effective funding for innovative thinking addressing the HIV/AIDS epidemic in sub-Saharan Africa. The Rush Foundation is the sponsor of the project. The Rush Foundation was launched in 2010 to fund sustainable projects in sub-Saharan Africa focused on alleviating the pandemic through innovative thinking, and to shake up the status quo in HIV thinking by spearheading thought leadership projects and debates that will help reframe HIV policy. Among other initiatives, the Rush Foundation is currently designing a grant programme with ActionAid in Africa aimed at generating new, sustainable HIV initiatives on the ground.
www.rushfoundation.org

The Papers

The body of research for RethinkHIV comprises 18 research papers. The series of papers is divided into Assessment Papers and Perspective Papers. Each Assessment Paper outlines the costs and benefits of at least three of the most promising responses, interventions, or investments to HIV/AIDS in Sub-Saharan Africa within the respective category. Each Perspective Paper reviews the assumptions and analyses made within the Assessment Paper. In this way, a range of informed perspectives are provided on the topic.

Contents

Overview

This perspective paper focuses on a single mode of non-sexual HIV transmission, mother-to-child transmission of HIV (MTCT), currently responsible for about 20% of new HIV infections annually in sub-Saharan Africa. Specifically, it examines the Assessment Paper (AP) proposal to evaluate the costs and benefits of a single strategy to prevent MTCT, consisting of WHO Option A delivered to over 90% of pregnant women by 2015 via a pattern of linear scale up from current levels (Bollinger 2011). The paper is structured in four parts. (1) The first section presents some general comments on the methods and findings of the AP. The critical assessment of HIV MTCT is then developed in three steps. (2) The second section reviews the reasoning surrounding the choice of WHO Option A as the sole MTCT strategy. It assesses representation of Option A in the analysis and finds that it is unlikely fully to capture costs. It also demonstrates that methodological and modelling choices lead to a truncated assessment of benefits, such that potentially relevant differences among therapeutic options A, B and B+ are not considered. The section concludes that analysis of a more comprehensive range of MTCT intervention options is required, including family planning, reproductive counselling, cotrimoxazole prophylaxis, early infant diagnosis, maternal ART for women requiring therapy for their own health, and WHO Options A, B and B+. (3) The third section examines the assumption of linear programme scale-up. The production function for an intervention is rarely described in economic evaluations and results are usually given without regard to programme scale. The costs and cost-effectiveness of Preventing Mother-to-Child-Transmission (pMTCT) programmes are substantially affected by variations in HIV prevalence and health system infrastructure. Within countries, existing MTCT programmes are generally located in settings of higher HIV prevalence and better health infrastructure, with the result that the costs of scale-up are likely to be importantly non-linear. The term pMTCT "cascade" has been used to describe the sequence of steps required to deliver antiretroviral-based MTCT interventions to HIV+ mothers and their infants. It is argued that, at the population level, health system performance at each step of the cascade is likely to be the single most important factor for determining the number of infections in children. (4) The final section sketches four additional MTCT intervention strategies that are likely to offer good value for money in some contexts and have received less attention to date. These include interventions to improve health system performance, HIV screening in the labour ward, and interventions to interrupt MTCT for HIV+ women not delivering in a health facility. Most importantly, this section highlights the potential of an emerging "leapfrog" technology, multiplex point-of-care diagnostics, to overcome the problems outlined in section 3. This technology could play a decisive role in increasing access to the pMTCT cascade while providing good value for money and thus, in synergy with health system improvements, in elimination of new infant HIV infections. Prevention of HIV transmission from mother-to-child is a high leverage intervention with implications for health and development. It is an opportunity too important to miss.

General comments

Methods of the assessment

The main purpose of an economic evaluation is to inform judgments about the relative worth or "value for money" of two or more alternative interventions or strategies. The assessment paper (AP) takes two distinct approaches to this task. For each of the four sets of interventions valued in the paper, the AP first performs a cost-effectiveness analysis (CEA) in which outcomes are measured in natural (health) units. It then performs a cost-benefit analysis (CBA), which assesses the net monetary benefits accruing from an intervention. A third type of evaluation design, cost-

utility analysis (CUA), uses a generic outcome measure such as a QALY or a DALY to permit decision makers to make broad comparisons across different conditions and interventions. CUA is described but not implemented in the AP.

The analysis has several important strengths, including use of the AIDS impact model in Spectrum and the Goals Express model to project HIV infections averted. These models have been extensively used for research and programmatic objectives and facilitate use of up-to-date country-validated data. I have three concerns relating to assessment methods.

- Interpretation of the ICER for CEA estimates: To evaluate the four categories of prevention intervention using a CEA design, the AP assesses the incremental costs of averting one HIV infection. This is an appropriate approach for CEAs of HIV prevention interventions due to the importance of an HIV infection averted as a health outcome and the availability and high quality of the associated data. My concern relates specifically to the interpretation of results. One of the recognised disadvantages of a CEA design is that it does not facilitate the comparison of interventions across different conditions because of its reliance on one natural measure of health.(Drummond, Sculpher et al. 2005; 2006) In the AP, the incremental cost-effectiveness ratio (ICER) is calculated for a CEA where the measure of effectiveness "E" represents an HIV infection prevented. There are no established cost-effectiveness standards that pertain to this unit. Notwithstanding, the AP compares ICERs expressing cost per HIV infection averted to three commonly used international benchmarks developed by the World Health Organization (WHO) Commission on Macroeconomics and Health (CMH) and used by the WHO CHOosing Interventions that are Cost Effective (CHOICE) project, which classify interventions costing less than GDP per capita as very cost-effective, those under two times GDP as cost-effective, and those costing three or more times GDP per capita as cost-ineffective. (World Health Organization 2001; Tan-Torres Edeger, Baltussen et al. 2003) In the published literature, the term "cost-effectiveness analysis" is often used to refer to economic evaluations in general, rather than to a specific study design. In fact, because the WHO initiatives seek to make general comparisons across all types of interventions and conditions, the proposed thresholds are defined in relation to a CUA measure of effectiveness; specifically, the cost per DALY averted.(World Health Organization 2001; Tan-Torres Edeger, Baltussen et al. 2003) To properly apply these benchmarks, interventions must therefore be expressed in terms of cost per DALY, and not cost per a specific health outcome such as HIV infections averted. Cost per life years gained may be an acceptable approximation to the DALY under some conditions. Under all reasonable assumptions about quality-adjusted life expectancy in sub-Saharan Africa (SSA) and intervention timing, each HIV infection averted should represent many DALYs. Interventions will hence be substantially more cost-effective than stated by the CEA component of the AP. As the AP analysis focuses on CBA estimates, this point does not affect the central results presented.
- Comprehensiveness of the CBA: The CBA translates the preceding CEA results into monetary terms. The measure of net benefit calculated considers the costs of providing the intervention, and the benefits in monetary terms associated with an HIV infection averted. Benefits accrue from two sources. First, HIV infections averted are translated into an estimate of life years gained, and these life years are valued at levels recommended by RethinkHIV. Second, the analysis considers savings in treatment costs associated with HIV infections averted; specifically, expenditure averted for provision of antiretroviral therapy and treatment of opportunistic infections.

  Although not commonly used in health care settings, CBA is the only form of economic evaluation that directly addresses allocative efficiency (efficiency between sectors) and it can consider dimensions not included in standard cost-effectiveness analyses. However, the AP analysis does not take up the opportunity to address the broader economic and social benefits of the interventions studied, such as productivity gains, impact on household poverty, orphaned children, catastrophic expenditure, impact on epidemic spread, educational attainment, fertility patterns, and macroeconomic impact. Data on these broader impacts may be difficult

to assemble in a convincing way, and the complexity of the causal chains introduces additional difficulties for modelling of consequences. Nonetheless, it is important to note that the CBA analysis of benefits in the AP is driven entirely by the outcome of an HIV infection averted. I will return to the issue of comprehensiveness below, in the context of pMTCT.

- Savings due to treatment costs averted: Treatment costs averted due to prevention of an infection are included only in the CBA. These costs could legitimately be considered in any CEA or CUA; it is not clear why they were restricted to the CBA.

Auto-disposable syringes for safe medical injection and IDU

Unsafe medical injections figure as an important source of HIV infection in sub-Saharan Africa, and contaminated needles are an important source of infection in injecting drug users (IDU). Auto-disposable syringes represent a promising strategy to reduce unsafe injections and to prevent HIV. Although not all unsafe injections carry the HIV virus, effective HIV prevention requires that all injections be safe. The assessment paper therefore outlines a universal strategy for injection safety in sub-Saharan Africa. Benefits extend beyond HIV to other blood borne pathogens such as hepatitis B and hepatitis C; however only HIV impact is considered.

The key intervention studied is introduction of auto-disposable (AD) syringes. AD syringes have been introduced in immunisation programmes worldwide and are very effective in preventing syringe reuse; however, they do come with drawbacks. In addition to the higher cost of the syringes, AD syringes require considerably greater volume in the supply, distribution and storage chain(Battersby, Feilden et al. 1999; Drain, Nelson et al. 2003) and yield greatly increased volumes of used injection materials.(Tamplin, Davidson et al. 2005) In many developing countries, approaches to clinical waste disposal are not well established and scavenging of disposal sites is common practice.(Tamplin, Davidson et al. 2005)

WHO defines a safe injection as one that does no harm to the healthcare worker administering it, to the patient receiving it, or to the environment where disposal might occur. (Battersby, Feilden et al. 1999) With respect to medical waste disposal, AD syringes introduce the challenge of balancing public health, financial and environmental goals to ensure that the procedures and technologies used in the disposal process do not themselves constitute a danger to public health.

The AP analysis considers a variety of costs associated with AD syringe introduction. It estimates not only the incremental cost of the AD syringes (valued at USD $0.02 per syringe), but also the costs of training, public information, and waste disposal. The costs of the latter three components are evaluated at $0.01 per injection, based on a personal communication from a WHO staff member involved in injection safety cited in an advocacy report by an NGO.(Koska and Baker 2007) The method of waste disposal for which costs are given is not described, and no information about the method of cost assessment is offered. On this basis, the incremental cost per syringe is evaluated at USD $0.03.

There are an expanding number of options for AD syringe disposal. Incineration of medical waste is an established strategy but is increasingly seen as a less-than-ideal solution, due to its infrastructure requirements, lack of portability to rural areas, potentially hazardous emissions, and environmental impact.(Tamplin, Davidson et al. 2005) A number of alternative technologies have been developed, including point-of-use needle-remover technologies suitable for use in

rural and remote settings, each with specific characteristics and costs.(Tamplin, Davidson et al. 2005; Program for Appropriate Technology in Health (PATH) 2011) As additional costs to storage and distribution facilities are not considered in the AP and the method for waste disposal is not clearly described or valued, the costs associated with AD introduction are likely to represent underestimates. The AP also provides benefit-cost estimates associated with a doubling of costs from USD $0.03 to USD $0.06 per injection. Without additional detail, it is difficult to know what a reasonable range for cost estimates should be. A recent analysis of resource needs for an effective response to HIV/AIDS applied a cost of USD $0.22 per safe injection for sub-Saharan Africa.(Schwartländer, Stover et al. 2011)

Prevention of mother-to-child transmission of HIV

Access to services to prevent MTCT has increased worldwide, leading to a steep drop in the number of children newly infected with HIV. Incident cases of paediatric HIV are 24% lower in 2009 as compared to five years earlier,(United Nations Joint Programme on HIV/AIDS (UNAIDS) 2010) an unprecedented achievement that has lead to calls for virtual elimination of HIV transmission from mother-to-child.(United Nations Joint Programme on HIV/AIDS (UNAIDS) 2011) Despite these successes, an estimated 370 000 [95% CI: 230 000 to 510 000] children were newly infected in 2009.(United Nations Joint Programme on HIV/AIDS (UNAIDS) 2010) Twenty-two countries have the highest burden of HIV positive pregnant women and therefore account for almost 90% of all new infant HIV infections. Twenty- one are in sub-Saharan Africa (SSA).(United Nations Joint Programme on HIV/AIDS (UNAIDS) 2010)

Comprehensive versus narrow approaches to pMTCT

Earlier this year, UNAIDS released a global plan to eliminate new HIV infections among children and to keep their mothers alive.(United Nations Joint Programme on HIV/AIDS (UNAIDS) 2011) The plan is based on two targets: (1) reducing the number of new HIV infections among children by 90%; and (2) reducing the number of AIDS-related maternal deaths by 50%.(United Nations Joint Programme on HIV/AIDS (UNAIDS) 2011) The strategy is multifaceted, consistent with the UN comprehensive approach to prevent MTCT based on four components: (1) primary prevention of HIV infection among women of childbearing age; (2) preventing unintended pregnancies among women living with HIV; (3) preventing HIV transmission from a woman living with HIV to her infant; and (4) providing appropriate treatment, care and support to mothers living with HIV and their children and families.[12] With respect to component 3, the virtual elimination goal specifies that MTCT be reduced to below 5% in breastfeeding populations, and 2% in non-breastfeeding populations. (Mahy, Stover et al. 2010; United Nations Joint Programme on HIV/AIDS (UNAIDS) 2011)

Like virtually all cost-effectiveness analyses to date, the AP focuses only on “component 3” of the recommended four-prong MTCT strategy; that is, prevention of HIV transmission from a woman living with HIV to her infant.(Johri and Ako-Arrey 2011) In policy terms, this focus appears too narrow, as prongs 1, 2, and 3 are synergistic and necessary to achieve the targeted 90% reduction in child HIV infections, and prongs 1 and 2 have received less support and success to date.(Reynolds, Janowitz et al. 2006; Halperin, Stover et al. 2009; Mahy, Stover et al. 2010) Although I recognise that this focus is to some extent imposed by the division of topics mandated by RethinkHIV for this assessment of HIV/AIDS, it is important to take note of this choice from the outset and to trace its implications for the analysis.

Prevention of HIV transmission from mother to child: intervention options

Virtually all HIV-infected children acquire the infection through mother-to-child transmission (MTCT), which can occur during pregnancy, labour and delivery, or through breastfeeding. In the absence of any intervention an estimated 15 - 30% of mothers with HIV infection will transmit the infection during pregnancy and delivery, and breastfeeding by an infected mother increases the risk by a further 5 - 20% to 20 - 45% overall.(2010; World Health Organization 2010; UNAIDS Reference Group on Estimates Modelling and Projections 2011)

Interventions to prevent transmission from an HIV+ mother to her child (component 3 of the comprehensive pMTCT strategy) can dramatically reduce this risk, and have succeeded in virtually eliminating MTCT in high-income countries (HICs).[2] At number of intervention options exist, each with different resource requirements and levels of associated clinical benefit. All involve administration of antiretroviral drugs to mother and infant. For low- and middle-income countries (LMICs), new WHO guidelines introduced in 2010 depart from previous approaches in emphasising the importance of treating eligible pregnant women living with HIV requiring treatment for their own health (the suggested criterion is a CD4 cell count of less than 350 cells/µl) with triple combination antiretroviral therapy (ART).[3] (World Health Organization 2010) The guidelines also recommend two equivalent options of antiretroviral prophylaxis to prevent MTCT for women with CD4 cell counts greater than 350 cells/µl, and for the first time make provision for prophylaxis to the mother or child during breastfeeding.(World Health Organization 2010) "Option A" is based on a less intensive medications antiretroviral prophylaxis regimen (ARV) during pregnancy and breastfeeding, while "Option B" is based on triple drug prophylaxis (ART) during pregnancy and breastfeeding.(World Health Organization 2010) An additional strategy now under discussion, "Option B+" proposes that all HIV+ women be given lifelong ART, regardless of CD4 count or disease stage.(National Institutes of Health: IMPAACT Trial Network 2010; Schouten, Jahn et al. 2011)

Of these therapeutic options, Option A has the lowest medication costs. Moreover, the effectiveness of these strategies in preventing MTCT in the perinatal period and during breastfeeding is considered equivalent.(2010; World Health Organization 2010; UNAIDS Reference Group on Estimates Modelling and Projections 2011) The AP therefore chooses to evaluate the costs and benefits of a single strategy, consisting of Option A delivered to over 90% of pregnant women by 2015. The analysis of costs associated with Option A includes counselling and testing, medication and service delivery, and a laboratory component, drawn from a recent investment framework analysis by Schwartländer and colleagues.(Schwartländer, Stover et al. 2011) The AP analysis of costs associated with Option A may be underestimated in two ways. First, it seems to consider that all HIV+ women in fact receive Option A. However, approximately 48% of HIV+ women are expected to have a CD4 cell count <=350(2010), and should therefore receive ART. Costs associated with provision of ART for a woman's own health were treated as a separate pMTCT component in the investment framework analysis.(Schwartländer, Stover et al. 2011) It is not clear whether and how they were considered in the AP. Second, laboratory facilities are often lacking and the investment framework analysis explicitly does not include the costs of laboratory start up and infrastructure.(Schwartländer, Stover et al. 2011) Appropriate laboratory infrastructure costs may be assessed elsewhere within the CCC HIV/AIDS exercise.

[2] Country income classifications are taken from the World Bank.The World Bank. (2009). "2008 Country ClassificationTables." Data & Statistics: Country Classification Retrieved September 25, 2009, from http://go.worldbank.org/K2CKM78CC0.

[3] Following emerging practice, this paper uses "ARV" to refer to any single or dual antiretroviral drug regimen used for pMTCT, and "ART" to refer to three-drug combination therapy (whether used for pMTCT or treatment of maternal HIV disease). "Prophylaxis" refers to the situation where ARV or ART is administered for purposes of pMTCT and is contrasted with "treatment" which refers to the situation where ART is administered for a woman's health.

More importantly, selection of an appropriate MTCT intervention option may not be as simple as the AP presents. Countries must make decisions that balance a wide range of factors and in the face of considerable uncertainty. In terms of effectiveness in preventing infant infections, the current estimates should be viewed as provisional as no studies report specifically on all components of the ARV interventions recommended in either Options A or B in the population for whom the option is recommended.(UNAIDS Reference Group on Estimates Modelling and Projections 2011) Furthermore, no empirical study has as yet provided a comparison of Options A and B.(UNAIDS Reference Group on Estimates Modelling and Projections 2011) Option B+ has not yet been directly studied. A number of studies now in the field are soon expected to contribute new information. (Mofenson 2010) Operationally, Option A requires a CD4 cell count reading to initiate therapy. The laboratory infrastructure required to provide a CD4 cell count is often lacking. Provision of Option A to breastfeeding mothers with CD4 counts 200-350 is not recommended; however, this situation may arise where the infrastructure needed to perform CD4 counts is not in place.(UNAIDS Reference Group on Estimates Modelling and Projections 2011) Option B requires a CD4 reading only to stop therapy, leaving time for travel or transport of specimens to be arranged. Option B+ proposes to guide therapy with minimal laboratory monitoring. In terms of safety to mothers, there are concerns about nevirapine-induced rash associated with Option A, provision of ART to healthy women associated with Options B and B+, and the impact on maternal health of the ART initiation and discontinuation strategies required by Option B.(Mofenson 2010) In terms of safety to infants, Options B and B+ also raise unanswered questions about potential adverse pregnancy outcomes associated with receipt of ART, and potential teratogenicity associated with unintentional use of Efavirenz during the first trimester.(Mofenson 2010) All three options are likely to stimulate resistance in infants who are infected during breastfeeding, making it necessary to foresee the use of second line therapies.(Mofenson 2010) Despite these concerns, there are important factors favouring Options B and B+.

Study conclusions can be importantly influenced by methodological and modelling choices. (Brisson and Edmunds 2006) The AP uses a static natural history model to depict the process of HIV transmission from mother to child, focussing on the outcome of averting an infant HIV infection. The analysis is potentially truncated in several ways, such that potentially relevant differences among options are not captured.

- Maternal health and child survival: The WHO 2010 guidelines for pMTCT introduce new therapeutic strategies that promote use of ART for a woman's own health and antiviral regimens during the breastfeeding period to prevent HIV transmission from mother to child. (World Health Organization 2010) The most important gains of the new strategy are likely to be through impact on maternal health and child survival, which are not considered in the AP nor in any cost-effectiveness models of pMTCT published to date.(Johri and Ako-Arrey 2011) With respect to child survival, the proposed interventions (Options A or B, including ART as required for a woman's health) are designed to make breastfeeding a good option for HIV infected mothers as opposed to formula feeding. This is one of the greatest benefits of the new strategy, as it substantially reduces infection of HIV-exposed infants during the breastfeeding period. In addition, infants who are able to breastfeed safely are thereby protected against other major causes of mortality such as diarrhoea, pneumonia and malnutrition.(World Health Organization 2010) Also of relevance to assessment of the new 2010 pMTCT strategies is the effect of ART on maternal survival and the downstream effect of maternal survival on child survival. Cost-effectiveness estimates that fail to capture these dimensions are likely to be inaccurate and to underestimate the full benefits of pMTCT interventions.
- In addition, focus on an infant HIV infection averted may fail to capture potentially relevant differences among specific intervention options. For example, therapeutic options may have

different impacts on maternal health. A model-based comparison of the effectiveness of Options A, B, and B+ contextualised to Zimbabwe found that projected maternal and infant life expectancy was highest for Option B+.(Ciaranello, Perez et al. 2011) This finding is limited by lack of data and cannot be considered conclusive at this juncture. However, it illustrates the importance of capturing differences in the survival of mothers and infants in the analysis.

- Analytic timeframe: Published cost-effectiveness studies of pMTCT have been based on a cohort perspective and consider a short time frame bounded by the initiation of Antenatal Care (ANC) and cessation of breastfeeding.(Johri and Ako-Arrey 2011) Fertility is very high in SSA and it is of relevance that a woman who is detected as HIV+ during pregnancy is likely to have children in future. MTCT rates are substantially lower for women taking ART prior to pregnancy, such that Option B+ may be of substantial benefit to future children of an HIV infected mother. (Schouten, Jahn et al. 2011) Consideration of a longitudinal perspective would clarify this point and likely suggest a different ranking of strategies.

Table 1. Comparison of recommended therapeutic options in women with CD4 >350 who do not require therapy for their own health[1]

Criterion	Option A: Maternal AZT and Infant daily NVP	Option B: Maternal Triple ARV Prophylaxis	Option B+: Lifelong Maternal Triple ARV Prophylaxis
Efficacy in preventing MTCT[2]	**Peripartum 2% Postpartum 0.2% per month**	**Peripartum 2% Postpartum 0.2% per month**	**Peripartum 2% Postpartum 0.2% per month**
Feasibility	**CD4 monitoring required to initiate therapy**	**ART initiated for all HIV infected pregnant women CD4 monitoring needed to determine when to stop ART**	**ART for all HIV infected pregnant women**
Protection against forward (adult-to-adult) transmission of the HIV virus?	**No**	**Yes, during pregnancy and breastfeeding**	**Yes**
Optimal protection against HIV transmission for future pregnancies?[3]	**No**	**No**	**Yes Pre-pregnancy ART Tx rates Peripartum 0.5% Postpartum 0.16% per month**

[1] This table does not consider clinical criteria relating to the possible differential impact of therapeutic options on maternal and child health, as the key issues are as yet unresolved.

[2] All three strategies are viewed as identical in efficacy at the present time. These are estimates for MTCT transmission rates peripartum, and per month of postpartum HIV exposure through breastfeeding. Estimates are based on expert consensus synthesising data from studies using similar regimens. There are no studies that report specifically on all components of the ARV interventions recommended in either Options A or B in the population for whom the option is recommended.(UNAIDS Reference Group on Estimates Modelling and Projections 2011) Option B+ has not yet been studied.

[3] These are expert consensus estimates for MTCT transmission rates in women taking ART prior to pregnancy. Rates are given separately for the peripartum period, and per month of postpartum HIV exposure through breastfeeding. (UNAIDS Reference Group on Estimates Modelling and Projections 2011)

- Impact on forward transmission: Receipt of ART by an HIV+ person reduces HIV viral load, which has been demonstrated to provide protection against transmission of the virus to non-HIV-infected partners.(Anglemyer, Rutherford et al. 2011) Option B+, which offers lifelong ART, may therefore have a positive impact on epidemic transmission.(Schouten, Jahn et al. 2011) However, the dynamics of infection and transmission in the general population are not considered in this model.

A broader comparison of therapeutic options A, B, and B+ is presented in Table 1. Questions remain about the comparative efficacy and safety of the three options; however, from a population health perspective, the "test and treat" approach reflected in Option B+ has the potential to offer substantially higher health benefits. The advantages it offers are likely to be particularly important when HIV prevalence is high, fertility rates are high, and health system infrastructure limited. Medications costs associated with Option B+ are higher, but potentially offset by lower laboratory costs and enhanced feasibility leading to greater uptake. In some contexts, Option B+ may thus have a more favourable cost-benefit profile.

In sum, the AP's exclusive focus on Option A as the intervention of choice seems premature. All three options are of live policy importance. Of the 17 of the 21 sub-Saharan African high burden countries that have chosen a policy option, 10 (Cameroon, Kenya, Lesotho, Mozambique, Namibia, South Africa, Swaziland, Uganda, Zambia, Zimbabwe) have chosen Option A, 5 (Botswana, Burundi, Chad, Côte d'Ivoire, Ghana) have chosen Option B, 1 (Nigeria) has chosen a combination of Options A (rural) and B (urban), and 1 (Malawi) has chosen Option B+.(UNICEF 2011) Both Options A and B were considered in a recent analysis of investment needs for HIV.(Schwartländer, Stover et al. 2011) A more comprehensive range of MTCT intervention options is required.

Scale-up of interventions to prevent transmission from HIV+ mother to child: key challenges

Interventions to prevent transmission from a woman living with HIV to her infant (component 3 of the comprehensive pMTCT strategy) are simple, modest in cost, and highly effective interventions backed by strong technical guidance, and as such, ideal candidates for widespread scale-up. (Yamey 2011) While acknowledging the importance of additional investment in infrastructure for reproductive and child health (considered in a separate paper for this HIV/AIDS exercise), the AP models a linear scale up pattern for the proposed pMTCT strategy, starting from contemporary levels and increasing linearly until 90% coverage is reached in 2015. It is useful to examine factors likely to affect the linearity of scale up, particularly with respect to costs.

The costs of preventing transmission from a woman living with HIV to her child can be divided into two categories: the cost of detecting a case of HIV in a pregnant woman, and the cost of administering appropriate interventions to prevent MTCT once detected. These costs depend on two factors:

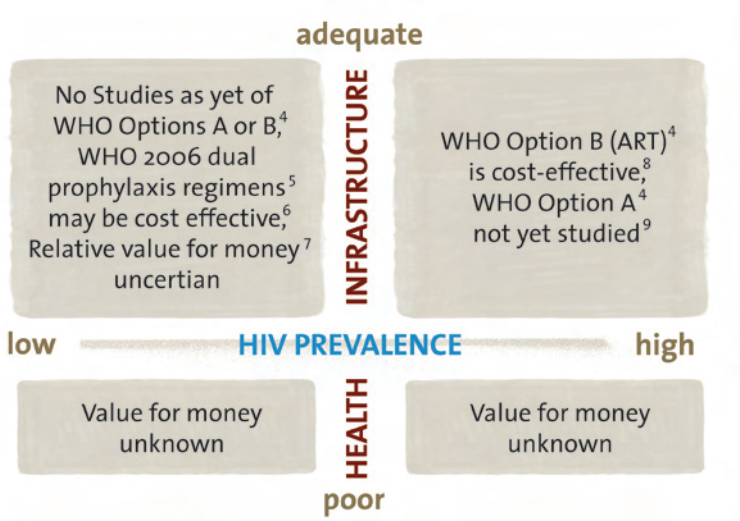
- HIV prevalence: Currently recommended interventions to prevent paediatric infections have been found to be cost-effective in a variety of LMIC settings as measured against accepted international benchmarks (Orlando, Marazzi et al. 2010; Robberstad and Evjen-Olsen 2010; Johri and Ako-Arrey 2011; Shah, Johns et al. 2011); however, there are challenges for efficient delivery of these interventions in low HIV prevalence settings.(Rely, Bertozzi et al. 2003; Kumar, Birch et al. 2006; Johri and Ako-Arrey 2011) In settings of low HIV prevalence, the costs of case finding may be high relative to health benefits obtained. Collectively, the published literature suggests that, in settings where HIV prevalence in the general population is low, MTCT strategies based

on universal or targeted testing of pregnant women may not compare well against cost-effectiveness benchmarks, or may satisfy formal criteria for cost-effectiveness but offer a low relative value in relation to competing interventions to improve population health.(Johri and Ako-Arrey 2011)

- Health system infrastructure: Published evaluations of pMTCT cost-effectiveness in LMICs have been based on decision models of hypothetical patient cohorts, with the exception of two studies, which used modelling in conjunction with data drawn from specific patient cohorts in Malawi (Orlando, Marazzi et al. 2010) and Tanzania (Robberstad and Evjen-Olsen 2010). With rare exceptions (Sweat, O'Reilly et al. 2004; Reynolds, Janowitz et al. 2006), modelling studies have generally assumed that the infrastructure required to provide the interventions under consideration is currently in place. The two studies using data from specific patient cohorts (Orlando, Marazzi et al. 2010; Robberstad and Evjen-Olsen 2010) take place in fully functioning centres, such that operational costs are considered, but infrastructure investments to create new facilities are not.

The production function for the intervention is rarely known in economic evaluations, and CEA estimates are usually given without specifying the degree of programme scale.(Moatti, Marlink et al. 2008) Some populations are more difficult to reach or to help. Variations in HIV prevalence principally affect the costs of case finding, while variations in infrastructure increase the costs of case finding and potentially also treatment. The costs and cost-effectiveness of HIV pMTCT is likely to be non-linear in these dimensions. These factors should be considered in interpreting CEA results (Figure 1).

Figure 1. Value for money of "component 3" pMTCT interventions in LMICs[1, 2]



[1] Updated summary of a systematic review of HIV pMTCT cost-effectiveness in low- and middle-income countries (LMICs) (Johri and Ako-Arrey 2011).

[2] These are interventions to prevent transmission from a woman living with HIV to her infant(World Health Organization 2010c)

[3] For empirical studies, we refer to the infrastructure of the study location, not necessarily of the country. Modelling studies generally take infrastructure as given or linearly scalable.

[4] Currently recommended WHO pMTCT regimens. (World Health Organization 2010b) Option B+ has not yet been studied.

[5] Formerly recommended WHO pMTCT antiretroviral prophylaxis regimens focussing on the last trimester of pregnancy.(World Health Organization 2006)

[6] Associated studies(Kumar et al. 2006; Rely et al. 2003).

[7] This is relative value as compared to competing interventions to improve population health.

[8] Associated studies(Orlando et al. 2010; Robberstad and Evjen-Olsen 2010; Shah et al. 2011).

[9] Option A should be at least as cost-effective as Option B for models considering only impact on infant HIV transmission, as Option A is considered to be lower in cost and equal in effectiveness to Option B in terms of preventing infant HIV transmission.

To guide strategic planning and programming for HIV prevention, UNAIDS and other agencies advocate the use of data on disease burden and programmatic response to match resources to need, reflected in the principles "know your epidemic; know your response."(United Nations Joint Programme on HIV/AIDS (UNAIDS) 2007; The Global Fund to Fight HIV 2011; UNICEF 2011) Table 2 presents key indicators for the 44 sub-Saharan African countries included in the analysis.

Several points are worth noting.

- HIV prevalence varies substantially. Eight countries (Senegal, Niger, Mauritania, Madagascar, Eritrea, Comoros, Mauritius, Mali) have HIV prevalence of less than 1%, and in an additional six countries HIV prevalence lies between 1-2% (Benin, Guinea, Burkina Faso, Ghana, Ethiopia, Democratic Republic of the Congo). Even in the 21 high burden countries, HIV prevalence ranges from just 1-2% in Ghana and the Democratic Republic of the Congo, to almost 26% in Swaziland. HIV prevalence also varies widely within countries. In Ethiopia, for example, HIV prevalence is estimated at 8% in the urban population and 1% in the rural population. The efficiency of interventions can be improved by targeting resources according to need. However, even in areas with very high need, HIV prevalence varies substantially. Moreover, targeting resources only to areas of high prevalence is insufficient to meet the elimination goal for infant HIV infections.
- Family planning is an important entry point to reducing infant HIV infections. Fertility rates are very high in SSA and unmet needs for family planning substantial, demonstrating the strategic importance of family planning, reproductive counselling, and potentially Option B+ for reducing infant infections.
- Health system infrastructure is often lacking. The term pMTCT "cascade" has been used to describe the sequence of steps required to deliver antiretroviral-based MTCT interventions to HIV+ mothers and their infants.(Barker, Mphatswe et al. 2011) A simplified three-step version is used for illustrative purposes.(Barker, Mphatswe et al. 2011) The first step in the pathway involves access to antenatal care (ANC). As Table 1 demonstrates, access to ANC is highly variable in the countries in the analysis, ranging from 26% to 98%. Moreover, populations arrive in ANC at 22 weeks on average, while antiretroviral regimens are to start at 14 weeks. Timing is an important determinant of therapeutic effectiveness. (2010) The second step in the pathway involves access to HIV (and CD4) testing, to enable a woman to know her HIV status. The percentage of pregnant women receiving an HIV test was also highly variable, ranging from 6% to over 95%. The third step is provision of antiretroviral treatment to women living with HIV and their infants. This also ranged from 6% to over 95% among the countries in our analysis.

At the population level, access to the pMTCT "cascade" is likely to be the single most important factor for determining the number of infections in children.(2010; Mahy, Stover et al. 2010; Mofenson 2010; Barker, Mphatswe et al. 2011) The vast majority of MTCT occurs in women who receive no treatment. Triple regimens will be important in reducing transmission in mother-infant dyads but, at a population level, will not have a large impact on MTCT rates. A study modelling the impact of the WHO Option B regime in Nigeria as compared to WHO 2006 dual prophylaxis found that at current coverage rates (10% of HIV infected mothers) expected values for mother-to-child HIV transmission were 24.3% with WHO 2006 and 23.7% with Option B – a difference of 0.6%. (Shah, Johns et al. 2011) Introduction of more effective combination ARV regimens will yield only marginal reductions in childhood HIV infections and mortality unless health systems achieve high performance at each step of the pMTCT pathway.(Barker, Mphatswe et al. 2011) What is required is to ensure high coverage at each step of the cascade, and to avoid losses to follow up occurring at each linkage point.(2010; Mahy, Stover et al. 2010; Mofenson 2010; Barker, Mphatswe et al. 2011)

Table 2. Key indicators[1]

Country	High burden?[2]	HIV prevalence (adult)[3]	2010 HDI[4]	Total Fertility Rate[5]	< 5 mortality (per 1000)	Maternal mortality (per 100 000)	Unmet need for family planning	1 ANC visit (%)	Skilled birth attendance (%)	% ANC with pMTCT services	HIV testing in pregnant women %	ARV coverage for pMTCT (mothers. %)[6]	ARV coverage for pMTCT (infants. %)[7]
Angola	1	2	146	5.79	161	610	30	80	8	23	26	19	15
Benin	0	1.2	134	5.49				84	78		49	46	
Botswana	1	24.8	98	2.90	57	190		94.5	97	100	93	>95	>95
Burkina Faso	0	1.2	161	5.95			29	85	54		42	32	
Burundi	1	3.3	166	4.66	166	970	29	92	34	41	40	12	9
Cameroon	1	5.3	131	4.67	154	600	20	80	63	79	41	27	25
CAR	0	4.7	159	4.85				69	53		28	34	
Chad	1	3.4	163	6.20	209	1200	23.3	39	14	8	6	6	4
Comoros	0	0.1	140	5.08				94			5		
Congo	0	3.4	126	4.64			16	86	86		23	12	
Cote d'Ivoire	1	3.4		4.65	119	470		85	57	44	47	54	33
Djibouti			147	3.95				92	93		39	10	
DRC	1	1.2-1.6	168	6.07	199	670	24	85	74	8	9	6	6
Equatorial Guinea	0	5	117	5.36							63	26	
Eritrea	0	0.8		4.68							25	34	
Ethiopia	1	1.5	157	4.60	104	470	22	28	6	86	16	18	15
Gabon	0	5.2	93	3.35							23	30	
Gambia	0	2	151	5.10				98	57		50		
Ghana	1	1.8	130	4.34	69	350	35	90	57	19	51	27	13
Guinea	0	1.3	156	5.45			21	88	46		10	17	
Guinea-Bissau	0	2.5	164	5.27				78	39		21	24	
Kenya	1	6.3	128	4.80		530	26	92	44	58	63	73	49
Lesotho	1	23.6	141	3.37	84	530	31	92	62	86	50	64	33
Liberia	0	1.5	162	5.42			36	79	46		22	16	
Madagascar	0	0.2	135	4.83			19	86	44		20		
Malawi	1	11	153	6.00	100	510	28	92	54	95	52	58	41
Mali	0	1	160	6.46			31	70	49		16		
Mauritania	0	0.7	136	4.71				81	61		6		
Mauritius	0	1	72	1.67					99.5		83		
Mozambique	1	11.5	165	5.11	142	550	18	89	55	78	77	70	43

Country	High burden?[2]	HIV prevalence (adult)[3]	2010 HDI[4]	Total Fertility Rate[5]	< 5 mortality (per 1000)	Maternal mortality (per 100 000)	Unmet need for family planning	1 ANC visit (%)	Skilled birth attendance (%)	% ANC with pMTCT services	HIV testing in pregnant women %	ARV coverage for pMTCT (mothers. %)[6]	ARV coverage for pMTCT (infants. %)[7]
Namibia	1	13.1	105	3.40	48	180	7	95	81	86	90	93	88
Niger	0	0.8	167	7.19			16	46	33		19		
Nigeria	1	3.6	142	5.61	138	840	20.2	58	39		13	22	8
Rwanda	0	2.9	152	5.43			38	96	52		71	65	
Senegal	0	0.9	144	5.03			32	87	52		35		
Sierra Leone	0	1.6	158	5.22			28	87	42		74	19	
Somalia	0			6.40				26	33		<1		
South Africa	1	17.8	110	2.55	62	410	14	92	91	95	95	88	56
Swaziland	1	25.9	121	3.57	73	420	24	85	69	79	73	88	82
Tanzania	1	5.6	148	5.58	108	790	21.8	76	43	72	66	70	51
Togo	0	3.2	139	4.30				84	62		20	26	
Uganda	1	6.5	143	6.38	128	430	41	94	42	51	64	53	28
Zambia	1	13.5	150	6.20	141	470	27	94	47	64	>95	69	39
Zimbabwe	1	14.3	169	3.47	90	790	13	93	60	55	46	56	35

[1] For the 21 high burden countries (note 2), all data is taken from UNICEF unless otherwise specified.(UNICEF 2011) For other countries, data comes from the WHO Global Health Observatory unless otherwise specified. (World Health Organization 2010a) Data may be from different years, leading to some inconsistencies. Empty cells reflect missing information.

[2] These are the 22 countries (21 in Sub-Saharan Africa) that have the highest burden of HIV positive pregnant women and therefore account for almost 90% of all new infant HIV infections.(United Nations Joint Programme on HIV/AIDS (UNAIDS) 2011)

[3] HIV prevalence in adults ages 15-49, as reported in the 2010 UNAIDS Epidemic Update.(United Nations Joint Programme on HIV/AIDS (UNAIDS) 2010)

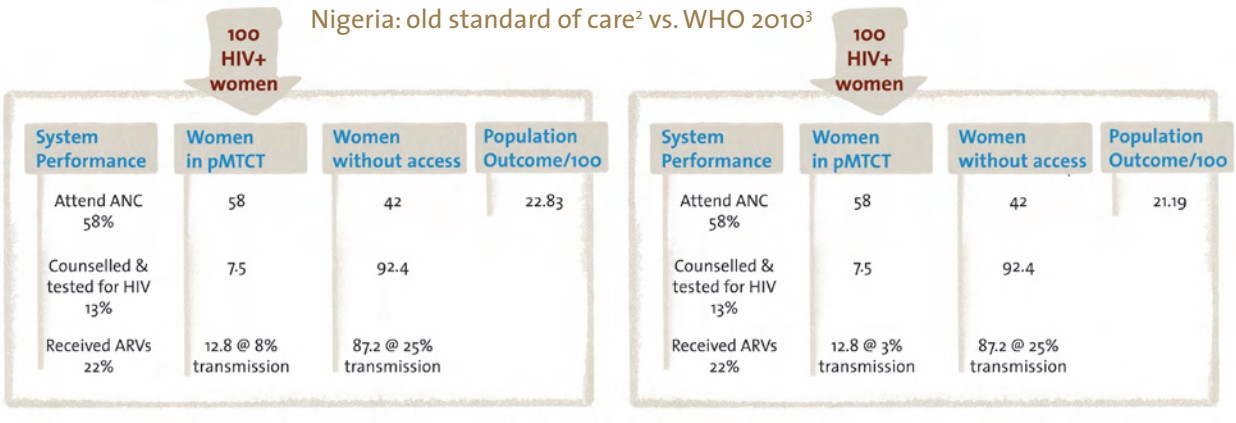
[4] The Human Development Index (HDI) provides a composite measure of three basic dimensions of human development: health, education and income. This is the country rank for 2010 out of 169 countries with comparable data.(United Nations Development Program (UNDP) 2011)

[5] The average number of children a hypothetical cohort of women would have at the end of their reproductive period if they were subject during their whole lives to the to the fertility rates of a given period and if they were not subject to mortality. It is expressed here as children per woman for the period 2005-2010.(United Nations Department of Economic and Social Affairs 2010)

[6] The percentage of HIV-infected pregnant women who received antiretroviral medicines to reduce the risk of mother-to-child transmission, among the estimated number of HIV-infected pregnant women.

[7] The percentage of HIV-exposed infants who received antiretroviral medicines to reduce the risk of mother-to-child transmission, among the estimated number of HIV-exposed infants.

Figure 2. Impact of health system performance on childhood HIV infections[1]



[1] Adapted from (Barker et al. 2011). System performance data are taken from Table 2. Due to inconsistencies in the data, the % of HIV+ women attending ANC is multiplied directly by the % of HIV+ women receiving to obtain the number of women benefitting from pMTCT. All transmission rates in this figure are for illustration only.

[2] Older antiretroviral prophylaxis regimens focussing on the last trimester of pregnancy(World Health Organization 2006) are estimated to reduce infant transmission from the natural history rate of 25% to 8% and are shown on left. Under this scenario, we expect almost 23 infant infections per 100 HIV+ women.

[3] Currently recommended WHO pMTCT regimens (World Health Organization 2010b) are estimated to reduce infant transmission from the natural history rate of 25% to 3% and are shown on right. Under this scenario, we expect 21 infant infections per 100 HIV+ women.

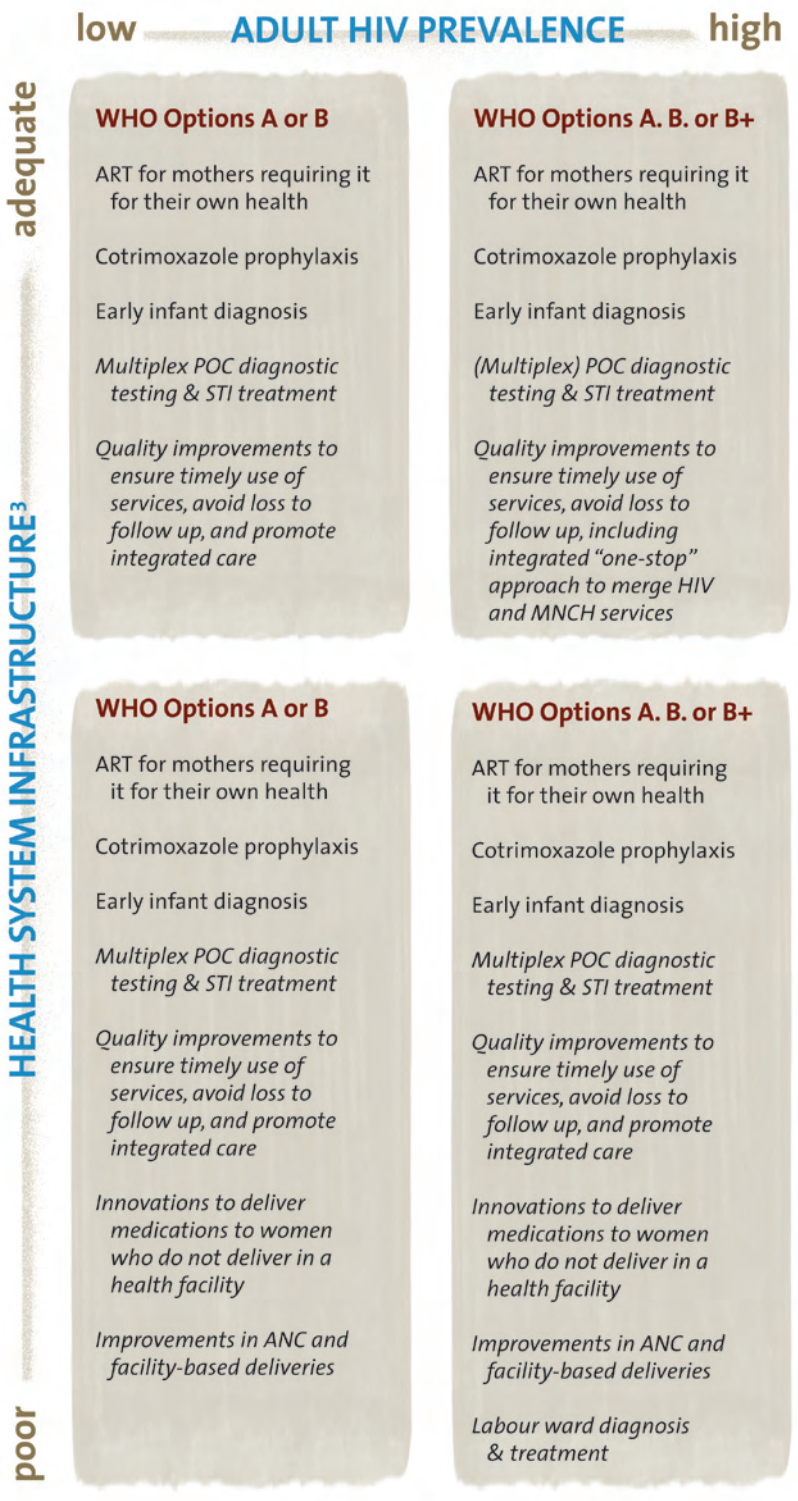
A final insight emerging from this situational analysis relates to concerns for fair distribution of health benefits. Efficiency and equity are widely recognized as vital, independent goals for health systems.(World Health Organization 2000) Almost all countries in the analysis document substantial inequities in access by wealth quintile and area of residence, with poor and rural populations having less access.(UNICEF 2011) Achieving an equitable distribution of the benefits of enhanced pMTCT services will require substantial improvements to infrastructure and enhancements to access.

Within countries, existing MTCT programmes are generally located in settings of higher HIV prevalence and better health infrastructure. Scale-up of pMTCT initiatives is likely to be highly non-linear in terms of costs, and resolution of health systems issues will be of paramount importance in achieving elimination goals for new infant HIV infections. We should anticipate that future scale-up might require new means to provide access for more difficult to reach populations.

Scale-up of interventions to prevent transmission from HIV+ mother to child: solutions

To prevent transmission from a woman living with HIV to her infant (component 3 of the comprehensive pMTCT strategy) the AP proposes that we adopt Option A.(Bollinger 2011) A recent investment framework analysis by Schwartländer and colleagues considered a broader range of interventions for pMTCT, including family planning, reproductive counselling, cotrimoxazole prophylaxis, early infant diagnosis, and Options A, B and maternal ART for women requiring therapy for their own health. (Schwartländer, Stover et al. 2011) These interventions are similar to those considered in the UNAIDS global plan to eliminate new infant HIV infections.(United Nations Joint Programme on HIV/AIDS (UNAIDS) 2011) I have argued above that Option B+ also be given serious consideration. In addition to these strategies, I next sketch four additional "solutions" not yet discussed.

Figure 3. Innovative "component 3" strategies to prevent mother-to-child transmission[1, 2]



[1] These are interventions to prevent transmission from a woman living with HIV to her infant(World Health Organization 2010c)

[2] This table highlights strategies likely to offer good value for money in different epidemic and health system contexts. Strategies in italics highlight dimensions that have received less attention to date.(Bollinger 2011; Schwartlander et al. 2011; United Nations Joint Programme on HIV/AIDS (UNAIDS) 2011).

- Interventions to improve health system performance: Interventions to improve uptake at each step in the pMTCT cascade have the potential to confer substantial improvements in maternal and child survival.(Youngleson, Nkurunziza et al. 2010; Barker, Mphatswe et al. 2011) Moreover, efforts to reduce losses to follow up help to counter stigma and promote equity, since those who are lost to care are often among the most vulnerable. Health system improvements are feasible and can be achieved at reasonable cost.(Youngleson, Nkurunziza et al. 2010)
- Screening in the labour ward: Rapid point of care HIV screening in the labour ward can serve as an alternative pMTCT entry point. It is important for at least three reasons: (1) Many women in sub-Saharan Africa do not receive an HIV test during ANC and present at labour with undocumented HIV status. (2) The highest rates of HIV transmission from mother to child are associated with new infections acquired during pregnancy and breastfeeding. Rates have been estimated at 30% (13-30%) for peripartum transmission, and 28%(14.3-56%) during the postnatal period.(UNAIDS Reference Group on Estimates Modelling and Projections 2011) (3) Male partners are more frequently present at the time of delivery than at ANC. Findings from clinical trials show that ARV prophylaxis given to mother during labour and neonate immediately after birth can reduce HIV MTCT by as much as 50%.(UNAIDS Reference Group on Estimates Modelling and Projections 2011) Although the effectiveness of this strategy is lower than for interventions delivered in ANC, in settings of high HIV prevalence and weak maternal-child health infrastructure, HIV screening in the labour ward has been demonstrated feasible and effective in capturing a large number of cases for which effective intervention is possible(Temmerman, Quaghebeur et al. 2003; Homsy, Kalamya et al. 2006; Sagay, Musa et al. 2006; Beltman, Fitzgerald et al. 2010; Bello, Ogunbode et al. 2011), and in encouraging couple counselling.(Homsy, Kalamya et al. 2006) Moreover, enabling a woman to have knowledge of her diagnosis provides her an opportunity to improve her own health and to promote more favourable outcomes in future pregnancies. It is hence plausible that this strategy represents good value for money in some settings.
- Innovations to deliver care to women not delivering in a health facility: In developing countries, most poor women deliver at home.(Montagu, Yamey et al. 2011) HIV-infected pregnant woman living far from a clinic may be unable to afford long, repeated trips for treatment. In addition, many clinics in SSA suffer from stock outs, further endangering continuity of care. For women who know their HIV+ status and are likely to deliver at home, innovative strategies have been developed to increase the uptake of more efficacious ARV prophylactic regimens for PMTCT in line with the most recent WHO guidelines.(World Health Organization 2010) For example, the Mother-Baby Pack developed by WHO and UNICEF gives pregnant women living with HIV a complete, pre-packaged set of drugs to prevent transmission of the virus to their children.

My final suggestion highlights the potential of an intervention currently under development and not yet discussed in the context of HIV pMTCT.

- Multiplex point-of-care (POC) diagnostic tests: Through its Grand Challenges program, the Bill and Melinda Gates Foundation has recently focussed attention on the need to develop point-of-care (POC) diagnostics that are easy to use, low cost, and suitable to assess conditions and pathogens at the point-of-care in a variety of settings.(The Bill and Melinda Gates Foundation 2011) Some initiatives involve multiplex tests, which provide diagnostic information on several conditions simultaneously. This is potentially a “leapfrog technology” for pMTCT as multiplex tests provide a means to circumvent both the health infrastructure problem and the HIV prevalence problem outlined above. (1) As we have seen, structural factors in country health systems, in particular, lack of access to ANC and HIV testing, are a critical factor in impeding pMTCT scale up. Our ability to affect MTCT transmission rates at the population level depends crucially on improving access to the PMTCT cascade. HIV POC tests can be implemented even in rural and remote areas and require less highly trained personnel, making them a vital tool to improve access and potentially appropriate timing of administration. (2) The ratio of costs to health benefits of single condition HIV POC tests depends on testing costs, and HIV prevalence. In settings where HIV prevalence in the general population is low, or costs of outreach are

high, MTCT strategies based on universal or targeted testing of pregnant women may offer low value for money as compared to competing interventions to improve population health. (Johri and Ako-Arrey 2011) Multiplex tests can be engineered to the epidemiology of the local context. Provided that testing costs can be kept low, it should therefore be possible to guarantee that diagnostic testing will detect a sufficient number of (HIV or non-HIV) cases to improve the value-to-money profile of universal antenatal screening. Multiplex POC diagnostic tests combining detection of HIV with several other conditions are ready to be tested in antenatal care populations in India.(Pai, Joseph et al. 2010)

Concluding remarks

I have argued that increasing coverage of prevention of mother-to-child transmission services to 90% for all childbearing women living with HIV to reach elimination of new child infections by 2015 will require a substantially more comprehensive set of options than that presented in the AP, and for that reason find the cost estimate of US $139 million to scale up pMTCT in SSA by 2015(Bollinger 2011) implausibly low. Two recent assessments may serve as useful comparisons. In its global plan towards virtual elimination of new HIV infections among children, UNAIDS evaluates resources required to increase coverage of a comprehensive set of pMTCT interventions to 90% of pregnant women in the 22 high burden countries that are home to nearly 90% of pregnant women living with HIV who need services. For these 22 priority countries (of which 21 lie in SSA and also figure in the AP analysis), UNAIDS evaluated the shortfall for pMTCT scale up at US$ 2.5 billion for the period 2011–2015.(United Nations Joint Programme on HIV/AIDS (UNAIDS) 2011) This resource needs estimate is of a similar order of magnitude to that identified in the investment framework by Schwartländer and colleagues, which also took a more comprehensive approach to MTCT and considered savings due to treatment costs offset.(Schwartlander, Stover et al. 2011) Like the CCC HIV/AIDS exercise, the analysis by Schwartländer and colleagues studies investments in health infrastructure and HIV treatment separately.(Schwartlander, Stover et al. 2011) All three analyses assess similar health benefits (90% coverage of pMTCT for all pregnant women) over a similar time period (2011-2015).[4]

The key question posed by RethinkHIV is, "If we successfully raised an additional US$10 billion over the next 5 years to combat HIV/AIDS in Sub-Saharan Africa, how could it best be spent?" Prevention of HIV transmission from mother-to-child is a high leverage intervention with implications for health and development. The new therapeutic strategies for pMTCT introduced in the WHO 2010 guidelines (World Health Organization 2010) yield important benefits for maternal survival via use of ART for a woman's own health. They also confer important benefits for child survival as antiretroviral interventions can interrupt mother-to-child transmission, enable HIV-exposed infants to benefit from the protection against competing sources of child mortality afforded by safe breastfeeding, and contribute indirectly to child survival through enhanced maternal survival. Cost-effectiveness estimates that fail to capture these dimensions are likely to be inaccurate and to underestimate the full benefits of pMTCT interventions. Even at substantially higher cost, a comprehensive approach to pMTCT has the potential to make a decisive contribution to achievement of Millennium Development Goal (MDG) 6 (Combat HIV/AIDS, malaria and other diseases), MDG 4 (reduce child mortality) and MDG 5 (improve maternal health), thereby yielding high value for money and return on investment. Simply put, scale-up of pMTCT is an opportunity too important to miss.

[4] Schwartländer and colleagues evaluate resource requirements for a broader set of countries, but data is available by region. Similar to RethinkHIV, their investment framework does not include infrastructure costs nor primary prevention of HIV in the pMTCT component, but considers these elements separately. Schwartlander, B., J. Stover, et al. (2011). "Towards an improved investment approach for an effective response to HIV/AIDS." Lancet 377(9782): 2031-2041.

A successful pMTCT strategy will be comprehensive and consider all four pillars of the recommended approach.(World Health Organization 2010) Some of the related interventions, such as primary prevention of HIV in women and girls, and improvements to health infrastructure, are described in other components of the RethinkHIV exercise.

Currently recommended antiretroviral-based options for pMTCT provide an excellent value for money under certain conditions. However, the costs and cost-effectiveness of pMTCT programmes are substantially affected by variations in HIV prevalence and health system infrastructure. Within countries, existing MTCT programmes are generally located in settings of higher HIV prevalence and better health infrastructure, with the result that scale-up of interventions is likely to pose challenges in terms of feasibility and efficiency. Since most transmission occurs in women who do not receive treatment, at the population level, access to the pMTCT "cascade" may be the single most important factor for determining the number of new HIV infections in children.

While many of the most important interventions to reduce MTCT rates lie at the level of health systems, leapfrog technologies can help to change the rules of the game. An innovative way of increasing access to the pMTCT cascade may come by means of an emerging technology, multiplex point-of-care diagnostics. POC diagnostics allow one to partially bypass weak maternal and child health infrastructure, ensuring that diagnostic testing in pregnancy can be conducted without advanced laboratory facilities or highly skilled technicians, and thereby facilitating entry to the initial phase of the pMTCT cascade. While POC HIV tests have been in the field for several years, multiplex POC tests that provide results for several conditions simultaneously are still in the development pipeline. The additional and essential contribution of multiplex tests lies in their potential to increase the value for money associated with antenatal screening, by offering on average more health benefits per test due to detection and treatment of a wider range of health conditions. This will be particularly important in contexts where HIV prevalence is low, or costs of outreach are high. This technology could play a decisive role in increasing access to an HIV diagnosis during pregnancy and thus, in synergy with interventions to improve health system performance throughout the pMTCT cascade, in elimination of new infant HIV infections.

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