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WORKING PAPER

**Modelling the Impact of Stigma on
HIV and AIDS Programmes:
Preliminary Projections for
Mother-to-Child Transmission**

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Acknowledgments

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This is a working paper in progress, and we would appreciate feedback from experts in the field that will inform future revisions to the model.

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Executive summary

Although many studies document the pervasiveness and perniciousness of HIV stigma and discrimination, no research to date has attempted to quantify how stigma might undermine HIV programmes or explored the potential benefits of stigma reduction programmes. These are important evidence gaps. Decisions about the scale, intensity and investment of HIV programme efforts require better information about the influences of stigma. Without this knowledge, we cannot adequately address stigma and discrimination experienced by people living with HIV and cannot achieve optimal effectiveness of HIV programmes in prevention, care and treatment.

This analysis estimates the potential impact of stigma on mother-to-child transmission outcomes. It represents an initial step toward addressing these evidence gaps. Although prevention programmes have the potential to minimize transmission of HIV from mothers to infants, substantial levels of dropout and lack of adherence to prescribed drug and feeding protocols compromise results. This is due to many factors, including problems related to the accessibility of services, the continuity of tests and drug supplies, the costs of accessing care, and whether women traditionally deliver in health facilities. A review of current evidence highlights that HIV stigma and women's fear of violence if their status becomes known is an important barrier. This analysis employs a mathematical model to project the impacts of stigma on service use and infant infections under different scenarios, including varying levels of stigma, HIV prevalence among women accessing antenatal care services, and health system capacity.

The findings suggest that stigma might have a large impact on mother-to-child transmission, and programmes that can effectively reduce stigma would be beneficial to women and children. Findings suggest that stigma might be responsible for more than half of mother-to-child infections in some settings. A highly effective stigma reduction programme could reduce infant infections by as much as 33 percent. Based on these findings, investments of between \$1 and \$10 per woman attending antenatal care services could be cost-effective, with higher levels of investment merited in settings with higher levels of HIV prevalence.

Since this work is exploratory, the estimates provided are best viewed as an initial step in providing concrete information for decision making and a practical framework for further research. The impact projections depend on assumptions about the extent to which stigma influences the uptake of and adherence to prevention of mother-to-child transmission programmes, and assumptions about potential improvements resulting from stigma reduction programmes. The model inputs are based upon a limited body of available data and, in a number of cases, reflect best-guess estimates. The model also considers general scenarios rather than modelling specific health systems and settings.

Although exploratory, the findings nonetheless illustrate that investment in stigma reduction could be an important and cost-effective addition to current prevention of mother-to-child transmission programming. The model indicates how the loss of individuals at each service point in mother-to-child prevention programming has substantial and cumulative effects, increasing the likelihood of transmission and morbidity. To date, a large focus of prevention of mother-to-child transmission programming has been on strengthening the delivery of the medical components of programming. This modelling exercise highlights the importance of investment in addressing the social barriers to service use as well, particularly stigma, as part of mother-to-child HIV prevention programmes.

Introduction

Researchers have widely documented the pervasiveness of HIV stigma and discrimination, and the damage these inflict on people living with HIV and their families. Yet, to date, no research has attempted to quantify how stigma, in its various forms, might undermine HIV prevention, treatment and care programmes. This is a critical evidence gap. Decisions on the intensity and scale of programme efforts are increasingly based on cost and cost-effectiveness data. Without these data, it might be difficult to secure funding for an expanded response to stigma and discrimination, resulting in inadequate programming in these areas.

This analysis, which quantifies the potential effects of stigma on mother-to-child transmission, or vertical transmission, is a preliminary step toward addressing this evidence gap. Although programmes to prevent mother-to-child transmission have the potential to minimize infant HIV infections, programme dropout and inadequate adherence to prescribed drug and feeding regimens compromise results. HIV stigma and discrimination are important factors, along with other gender factors like inequality and violence against women, in deterring service use and adherence, which contributes to transmission and morbidity. This working paper uses a mathematical model to project the potential magnitude of the effects of stigma on programme outcomes and mother-to-child transmission of HIV. The findings below describe the model's approach, structure and results.

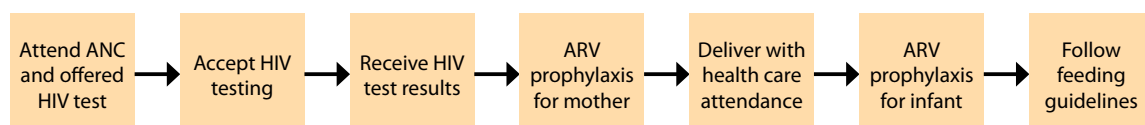
Methods: modelling stigma and prevention of mother-to-child transmission

Development of the modelling approach involved multiple stages. We first reviewed current evidence on the impact of stigma on different forms of HIV programming. Based on this review, the authors developed draft model structures for programming and analysis. The authors agreed to focus on stigma and HIV programming for prevention of mother-to-child transmission (PMTCT) because of the growing recognition of the effect of stigma on PMTCT programs, the serious implications for the health of mother and infants, and the clear pathways through which stigma affects each step in the PMTCT service delivery process.

How does stigma influence PMTCT: model structure

PMTCT is a comprehensive, multistep prevention programme that follows women from antenatal care (ANC) through postdelivery services. **Figure 1** describes, in a simplified, linear fashion, the optimal steps of PMTCT that HIV-positive pregnant women follow. The process begins with attending ANC, being offered and accepting an HIV test. Next, women and infants take antiretroviral medications (ARVs) and then follow feeding guidelines to reduce transmission during infant feeding.¹ This process is often described as the "PMTCT cascade," because women are frequently lost to follow-up at different stages of the process or are not able to adhere to some components of the recommended guidelines (such as following feeding guidelines).

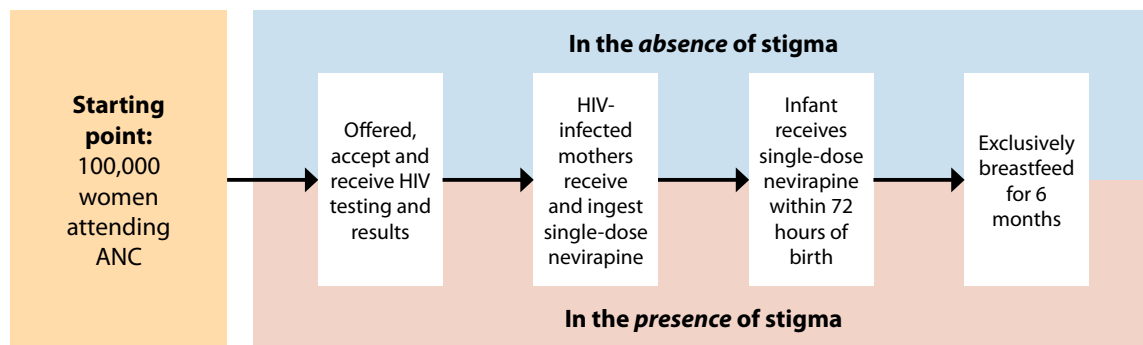
Figure 1. Typical PMTCT process



Over the past decade, as new evidence has become available, the specific guidelines and service delivery practices at each point in the PMTCT process have evolved. The World Health Organization (WHO) issued new PMTCT guidelines in November 2009.^{*2;3} However, for the purpose of this modelling exercise, we have followed what has been, until recently, the commonly recommended practice in many parts of sub-Saharan Africa around drug prophylaxis (single-dose nevirapine for mother at onset of labour and for infant within 72 hours of birth) and infant feeding (exclusive breastfeeding for the first six months).

In addition, to facilitate the modelling exercise, we combined several of the steps (see **Figure 2**). Specifically, being offered, accepting and receiving an HIV test result were combined into one step. After testing, the next step is the mother's receiving and taking single-dose nevirapine (with the assumption that the dose is taken at the prescribed time). Whether or not delivery occurs in a health facility, which has been shown to increase adherence,⁴ is factored into two steps in our model—whether the mother takes single-dose nevirapine, and whether the infant receives dosing within 72 hours. Next, the model looks at a mother's ability to exclusively breastfeed for six months. Finally, the model considers the effect of stigma on these four points in the PMTCT service delivery process, as illustrated by the two shaded areas in **Figure 2**.

Figure 2. Specific PMTCT process considered in the model



Throughout this linear course, attrition occurs at each stage of PMTCT. At each step of the cascade, women face barriers to following the recommended actions and may not complete the process, thereby increasing morbidity and the potential for infant infection.

Figure 3 illustrates the pathways of women who are and are not HIV infected when in the PMTCT process, as defined for this modelling exercise. It shows how these pathways filter into the model's two main outcomes of interest: vertical infections and knowledge of HIV status. For women entering ANC, the first branch in the pathway is refusing or accepting (and receiving) an HIV test. Women who accept the test follow the top trajectory initially, while those who do not, whether HIV positive or negative, follow the bottom one. Women who accept a test and are HIV negative then fall out of the top pathway and are included in the model calculations only to explore the impacts of stigma on the numbers of women who know their HIV status.

The top pathway then follows pregnant women who know they are HIV positive. Women may or may not take up single-dose or short-course nevirapine, and their infant may or may not be given

* WHO issued new PMTCT guidelines in November 2009 related to ARV treatment and infant feeding. The guidelines suggest pregnant women with severe or advanced clinical HIV infection, or a CD4 cell count below 350 cells/mm³ regardless of symptoms, initiate lifelong antiretroviral therapy. In addition, WHO recommends all HIV-positive mothers begin a daily zidovudine or a three-drug regimen at 14 weeks and continue through the end of the breastfeeding period. In addition, ARV prophylaxis, specifically, daily single-dose nevirapine, is recommended for the infant during breastfeeding. As for feeding practices, WHO is developing guidance for national authorities to promote either exclusive breastfeeding with ARV prophylaxis or exclusive replacement feeding, depending on the quality of water available and the accessibility of formula. In conditions where breastfeeding is the better option, WHO strongly recommends exclusive breastfeeding for the first six months of life and continued breastfeeding through 12 months.

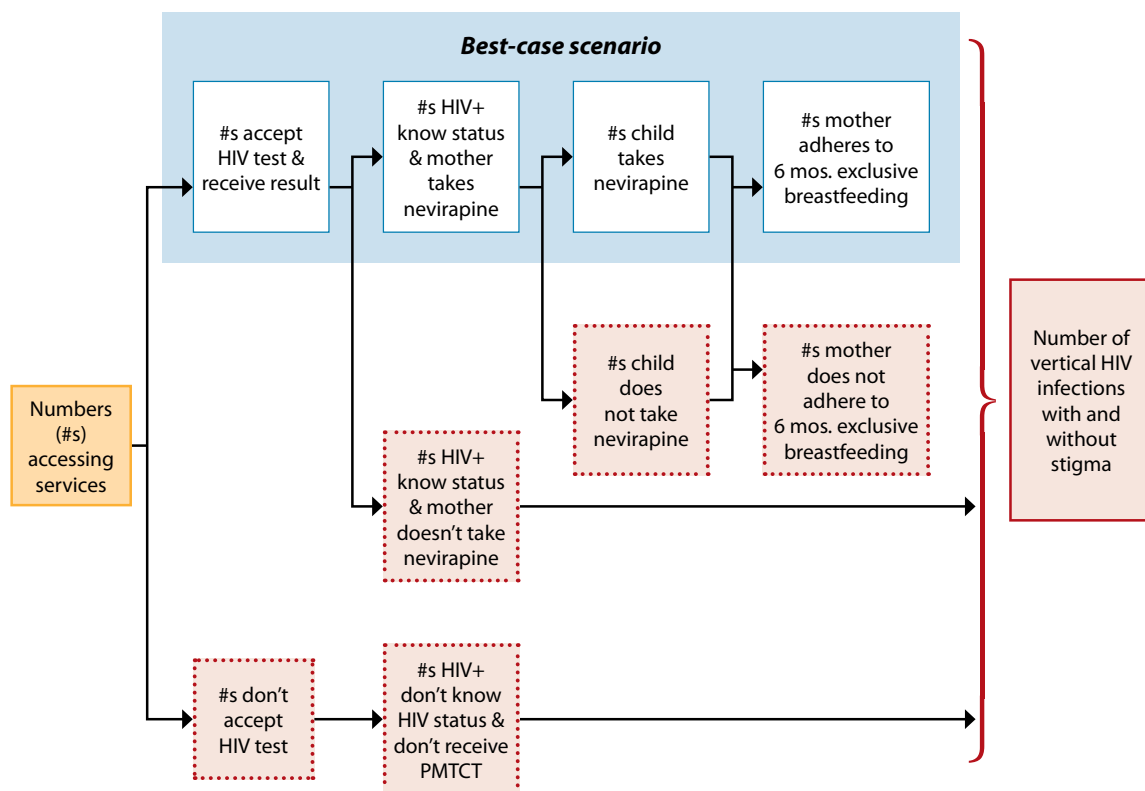
single-dose nevirapine within 72 hours after birth. Finally, women may or may not adhere to six months of exclusive breastfeeding. The uppermost stream (upper solid-line boxes) of the top pathway shows the ideal intervention pathway for women who are HIV positive, in which women and infants are provided with and adhere to medication, as well as to feeding guidelines. For these women, the resulting risk of mother-to-child HIV infection is substantially reduced in contrast to HIV-positive women in any of the lower pathways.

Women in the lower pathway of the top stream (middle dashed-line boxes) represent women who adhere to one or more initial steps in the PMTCT process but are not able to participate fully in all the steps. The lowest pathway for HIV-positive women (lower dashed-line boxes) indicates women who did not test for HIV, and hence do not know whether they are HIV positive.

When using the model, pregnant women will diverge across different pathways during PMTCT depending on the underlying prevalence of HIV in the population of women accessing ANC and the degree to which they are affected by HIV stigma and other factors, including the strength of the local health care system.

All HIV-positive women, no matter which pathway they take, are factored into the calculations for the model outcome on number of vertical transmissions. HIV-negative women are not factored into this outcome. For the model outcome—number of women who know their HIV status—all women are included.

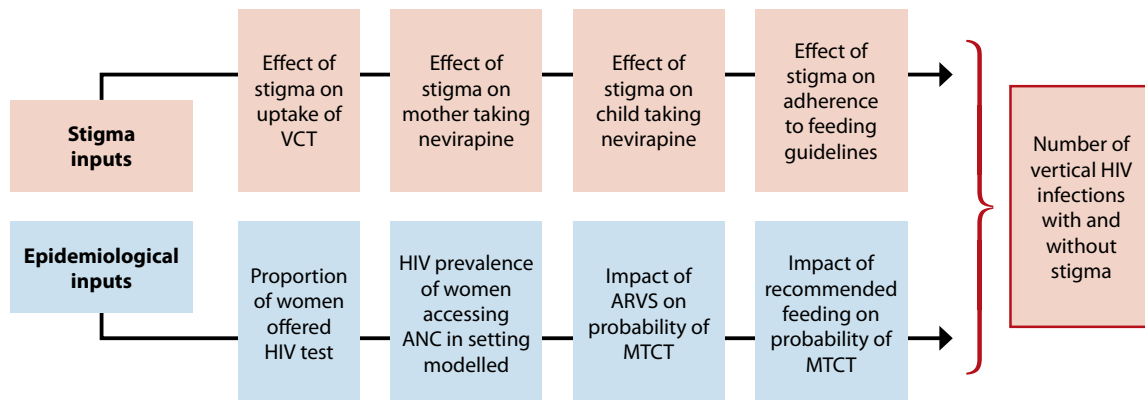
Figure 3. Pathways of pregnant women through PMTCT model



Model parameterisation

The modelling process considered both epidemiological inputs and inputs describing the estimated effects of different levels of stigma (stigma inputs) for each step in the PMTCT cascade. These inputs were used to project the number of mother-to-child (vertical) HIV infections. **Figure 4** shows how these epidemiological and stigma inputs are utilised in the model.

Figure 4. Model inputs



Notes: VCT, voluntary counselling and testing; MTCT, mother-to-child transmission.

General inputs for size and levels of HIV infection among the population of women accessing antenatal care

The model requires general inputs about the particular ANC population that is being considered. These inputs are the number of women attending antenatal services, the levels of HIV infection in the ANC population, and the percentage of women who either die or lose their child during pregnancy or in first year of life. For this modelling exercise, the authors assume an initial cohort of 100,000 women entering ANC, a range of potential levels of HIV infection among women attending antenatal services (15%, 10%, 5%), and a 5% mortality rate.

Epidemiological inputs on the probability of mother-to-child transmission

The model incorporates five epidemiological inputs that describe the probability of vertical transmission in different levels of adherence to the PMTCT cascade (**Table 1**). The probabilities are based on a review of current evidence of transmission probabilities in various prevention scenarios. The highest transmission probability is in the absence of PMTCT and when the mother is not able to undertake six months of exclusive breastfeeding. The lowest transmission probability is when both the mother and child receive nevirapine and the mother is able to adhere to six months of exclusive breastfeeding. It is worth noting that lower transmission probabilities for best-case scenarios are achievable if the mother receives antenatal ART and post-natal ART during breastfeeding.

Table 1. Probability of transmission from HIV-infected mother to child in first year of life

<i>Probability description</i>	<i>%</i>	<i>References</i>
Probability of vertical transmission in absence of PMTCT	32%	5-7
Probability of vertical transmission when mother receives nevirapine, child does not, and mother is not able to adhere to feeding guidelines	20%	8,9
Probability of vertical transmission when mother receives nevirapine, child does not, and mother is able to adhere to feeding guidelines	13%	9,10
Probability of vertical transmission when mother and child receive nevirapine and mother is not able to adhere to feeding guidelines	8%	11-14
Probability of vertical transmission when mother and child receive nevirapine and mother is able to adhere to feeding guidelines	5%	12,14-16

Stigma inputs

A key element of the model is the incorporation of numerical inputs describing how stigma may reduce women's ability to adhere to different components of the PMTCT programme, such as receiving her HIV test result, receiving the necessary medication, or being able to consistently follow the feeding guidelines.

Based upon our review of existing evidence, the model assumes that the greater the level of stigma in a setting, the greater the challenges for PMTCT programming. However, this is difficult to quantify accurately; and following initial feedback from experts, we decided to have the model compare the potential impact of four different levels of stigma (*none, low, medium and high*).

This approach makes it possible to estimate the proportion of vertical infections due to stigma and to explore how reductions in stigma could influence transmission levels. For example, the model can indicate how many infections might be averted by reducing stigma from *high* to *medium* or from *medium* to *low*. The stigma model inputs reflect the influence of different levels of stigma* on mother-to-child HIV transmission through the proportions of HIV-positive and HIV-negative women who follow different pathways. In addition, the inputs take into account the range of health system, economic and cultural influences. These include the accessibility of services, the continuity of tests and drug supplies, the costs of accessing care, and whether women traditionally deliver in health facilities. Each will also impact uptake of and adherence to PMTCT.

The effect of other non-stigma-related factors, such as service accessibility, that might impact uptake and adherence are represented in the parameter values used for the *no stigma* scenario under each step in the process. The values used for the *low, medium and high stigma* scenarios represent the combined effect of these other factors *and* the impact of stigma. In addition, two service delivery contexts (higher and lower functioning—see **Table 2**) are modelled to reflect the different impact stigma will have on vertical transmission, depending on how well the service delivery system functions.

* In this model we are considering stigma that occurs in the family, in the community and at the health care setting, as well as internalized, or self-, stigma.

Table 2. Description of higher- and lower-functioning health care system settings

<i>Higher-functioning health system setting</i>	<i>Lower-functioning health system setting</i>
<ul style="list-style-type: none"> ANC services routinely offer PMTCT services opt-out HIV testing protocol—HIV testing is routinely provided to all patients unless the client chooses not to be tested pre- and posttest counselling rapid testing (women receive test results before leaving the clinic same day) sufficient number of test kits and medication nevirapine to women when they receive a positive test result good access to PMTCT services higher proportions of women delivering at the health care facility 	<ul style="list-style-type: none"> testing is not always offered by the health care provider rapid testing may or may not be available stock-outs of test kits and ARV medications occur women must return to the facility for nevirapine dispensing limited access to facilities that offer PMTCT less likelihood of delivery in the health facility

To estimate the specific stigma inputs (see **Table 3**) for each of the four PMTCT steps in the model, the authors conducted an extensive literature review examining published and grey literature* on women's participation along the PMTCT service delivery cascade^{10–13;17–30} and women's reasons (stigma- and non-stigma-related) for nonparticipation in services.^{4;31–51}

It should be noted that the literature describing women's perspectives on PMTCT programmes and factors affecting their ability to initiate and adhere to the full PMTCT protocol (from testing through infant feeding) is small and largely qualitative.^{4;31;33–35;44–46;48–50} Research into the relative roles of various factors influencing adherence is even sparser.^{31;33–35;39;45;49} Quantitative data on the relative importance of factors influencing uptake and adherence are unavailable. Because of this scarcity of quantitative data on stigma and other factors affecting uptake, the authors made best-guess estimates of the stigma parameters, which were generally based on qualitative data. The literature reviewed and the process for arriving at the stigma parameter estimates for the four steps in the PMTCT process are described below.

Specifically, the stigma estimates (**Table 3**) for each step were achieved via the following process. To begin, we considered the *no stigma* scenario, which is estimated to reflect all nonstigma factors affecting uptake. To arrive at this estimate, we considered the available literature (qualitative and quantitative) documenting barriers to uptake (other than stigma), and participation rates across PMTCT programs in a range of contexts for each particular step (e.g., accepting an HIV test). Based on the influence of non-stigma-related factors and participation rates, we selected a value on the high end of participation as our starting point for the *no stigma* estimate in the higher-capacity settings, and on the lower end for the *no stigma* estimate for low-capacity setting.

The next step was to consider how this participation rate might drop in the presence of high levels of stigma. Available literature suggests that stigma is a large barrier to uptake and adherence. Combining the qualitative evidence with the sparse quantitative data, the authors estimated the parameters conservatively with respect to the influence of stigma on uptake, choosing parameter values in the middle to low end, rather than on the higher end. Next, as data available do not

* A search was conducted on PubMed and Google Scholar using combined phrases of *PMTCT* or *mother-to-child transmission* with *stigma*, *discrimination*, *retention*, *adherence*, *drop out* and *participation*. A search for grey literature was conducted with similar terms on Web sites of multilateral organizations, such as UNAIDS and WHO; bilateral organizations, such as DFID and PEPFAR; and international nonprofit organizations, such as Family Health International and Elizabeth Glaser Pediatric AIDS Foundation. The references sections of all articles found were consulted for additional relevant literature. A total of 65 articles were reviewed.

distinguish between levels of stigma, we estimated values for *low stigma* and *medium stigma* by evenly distributing the point difference between *high stigma* and *no stigma*.*

Finally, we assume that the only difference between the high- and low-functioning service delivery settings is in the starting point (the *no stigma* estimate), which reflects the differing impact of health systems factors on uptake and adherence. The relative effect of each level of stigma (*low, medium, high*) is assumed to remain the same across both high- and low-functioning service delivery settings.

Table 3. PMTCT stigma inputs

	Lower Functioning Health System Setting				Higher Functioning Health System Setting			
	No stigma	Low stigma	Medium stigma	High stigma	No stigma	Low stigma	Medium stigma	High stigma
1. Proportion of women attending ANC who are offered and accept HIV test and receive results	83%	80%	77%	74%	98%	95%	92%	89%
2. Proportion of women who test HIV positive, find out status and take nevirapine	75%	65%	55%	45%	95%	85%	75%	65%
3. Proportion of women who test HIV positive and receive nevirapine whose infant receives infant dose	40%	33%	27%	20%	82%	75%	69%	62%
4. Proportion of women who test HIV positive, receive ART and are able to adhere to feeding guidelines	35%	25%	15%	5%	65%	55%	45%	35%

Note: ART, antiretroviral therapy.

1. Proportion of women attending ANC who are offered and accept an HIV test

To estimate the *no stigma* inputs for the proportion of women attending ANC and accepting an HIV test, the authors reviewed available monitoring data from several PMTCT service sites.[†] From this data, we ascertained the testing rates of pregnant women under different testing protocols. The authors also reviewed the available literature on reasons (other than stigma) that pregnant women might refuse an HIV test or be unwilling to accept a hypothetical test. Based on this review, factors that may hinder or facilitate testing among pregnant women include knowledge of mother-to-child transmission, awareness of and access to available PMTCT services, educational level of the mother, and availability of test kits and medication at ANC facilities. In Tanzania, for example, only 53% of women sampled knew about the availability of medications and other services that can prevent mother-to-child transmission.⁵² In Nigeria, only 27% of 804 women attending antenatal services knew about the possibility of mother-to-child transmission.³¹

* For example, if 75% of women are estimated to participate in the *no stigma* setting, and 45% are estimated to participate in the *high stigma* setting, the difference between these two extremes would be divided evenly between the *low* and *medium stigma* parameters to arrive at 65% for the *low stigma* setting and 55% for the *medium stigma* setting.

† We reviewed data for opt-out testing, in which an HIV test is routinely given unless the patient states otherwise; rapid testing, in which testing and diagnosis occur within 20–30 minutes; and voluntary counselling and testing (VCT), in which health providers may counsel the patient to receive an HIV test but the process is entirely voluntary.

Because the lack of knowledge about mother-to-child HIV transmission and problems accessing HIV testing services appear to hinder pregnant women from HIV testing, experts believe that reducing these barriers will increase testing and participation in PMTCT services. It should be noted that the advent of rapid testing and opt-out testing in PMTCT settings is, in fact, improving testing rates, as a much higher proportion of women are testing and receiving their test result. As demonstrated by Botswana's national "routine testing" campaign, with an opt-out rapid-testing initiative started in 2004, testing among the general population, particularly among women, has skyrocketed.⁵³ Recent data from 2005 to 2007 show that more than 95% of pregnant women in Botswana accepted HIV testing at antenatal clinics.⁵⁴ Monitoring data from PMTCT sites administered by the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) also indicate increases in testing among pregnant women after instituting opt-out testing procedures. From 2000 to 2007, before opt-out testing was implemented, 94% of pregnant women were counselled and 78% accepted testing at EGPAF sites. From 2007 to 2008, after opt-out testing was made standard practice, 100% of women were counselled and 90% of pregnant women accepted testing.²⁷

Based on this information, and the assumption that most PMTCT programs have or are shifting to rapid testing and opt-out protocols, the *no stigma* parameter for the high-functioning service delivery setting is estimated at 98%. The estimate is based on the assumption that, in the absence of stigma and in a high-functioning service delivery system, the majority of women (close to 100%) will be offered and accept a test and receive their results.

In a low-capacity setting in which knowledge and awareness of PMTCT and access to PMTCT services are lower, and opt-out testing and rapid testing may not always be offered, the parameter for *no stigma* is estimated at 83%. This estimate is based on monitoring data from EGPAF sites prior to 2007, in which 78% of pregnant women were tested and 72% of women retrieved their results.²⁷ The authors assume that a portion of test refusal and not receiving test results is due to stigma and therefore add to 78% an additional 5 percentage points, a portion of what we estimate for the *high stigma* setting (9%). Because the sites included in the study varied across settings and countries, the authors assume the degree of stigma present within the communities also varied between low and high prevalence.

To estimate how the proportion of women receiving testing and test results would change in the context of high stigma, the authors reviewed literature on women's fears of involuntary disclosure and doubts about confidentiality of results, their anticipation of stigma and discrimination, and negative responses to a positive test result. Research demonstrates fear of stigma and discrimination impedes a woman's decision to seek or accept an HIV test. Pregnant women are fearful of receiving a positive result and the negative reactions they may incur from health care workers, family, friends and/or the community.⁵⁰ In Nigeria, 8% of women explained that their unwillingness to take an HIV test was due to feeling uncertain in their clinic's ability to maintain confidentiality and privacy. The same study also showed that pregnant or postpartum women were significantly less willing to accept an HIV test if their perception of social support from family and community was low.³¹ In Uganda, 7% of women who were offered an HIV test were fearful of a partner's reaction and refused testing.³⁵ Similarly, women who refused testing in Botswana were more likely to affirm the statement "it is better to die without treatment than for other people to know you are HIV positive" than were those women who accepted an HIV test.³⁴

Based on this literature and the monitoring data (discussed above) that shows 2% to 19% gaps between rates in testing acceptance and test result retrieval (the parameter for *high stigma*), it is conservatively estimated that 9% fewer women would be tested and receive their results in the *high stigma* setting compared with the *no stigma* setting. In a high-functioning service delivery setting, the testing rate among pregnant women attending ANC in the *absence of stigma* is estimated at 98%, while in a *high stigma* setting the estimate is 89%. Similarly, the estimates for the low-functioning service delivery setting are 83% in the *absence of stigma*, but in the presence of *high stigma* it is 74%.

2. Proportion of women who take single-dose or short-course nevirapine

Researchers have proposed several non-stigma-related reasons for why women are unable to adhere to ARV prophylaxis. These include the severity of drug side effects and the lack of confidence in the efficacy of ARV prophylaxis.⁴¹ However, others found no evidence to support these two theories.³⁹ It has also been proposed that the complex dosing schedule and/or the specific time for ingestion may confuse women into missing their proper dosage.²⁹ Data from Zambia indicate some women do not take their prescribed single-dose nevirapine because they “do not want to prevent their babies from getting HIV if there is no maternal treatment available.”⁵⁵ A study in Rwanda found a pregnant woman’s nonadherence is associated with an unmarried status, a lower educational level and less frequent ANC visits.³⁷ In addition, women may have difficulty travelling to the closest facility that offers PMTCT services, as demonstrated in a study of Malawi’s highly centralized PMTCT service delivery system.⁴² In Zambia, nonadherence of mothers was associated with home births (OR=3.15, 95% CI: 1.34 to 7.38).⁴ Similarly, in Rwanda, adherence was higher for health care facility delivery: 86% of adherent women delivered at the hospital, but only 28% of nonadherent women delivered at a health facility.³⁷ Nonstigma- (e.g., distance, cost) and stigma- (fear of disclosure of status) related factors could influence whether a delivery takes place in a health facility.

In addition to research examining potential reasons for nonadherence, the authors examined literature documenting rates of nevirapine uptake. From 2007 to 2008, EGPAF increased ARV uptake by expectant mothers at its PMTCT service delivery sites from 75% to 86% by dispensing nevirapine during posttest counselling.²⁷ Research from South Africa indicates 95% of women attending health facilities received nevirapine, and in Rwanda, 94% of women who received single-dose nevirapine understood health care providers’ ingestion instructions.^{29;37} Based on these data, and assuming that in the high-functioning health setting the vast majority of women will receive and take nevirapine (largely because they are delivering in the health facility where they received ANC testing and nevirapine), 95% of women in a high-functioning system who test positive are estimated to take nevirapine in the absence of stigma.

Data from the PEARL study, a multicountry study of PMTCT service delivery in Zambia, Cote d’Ivoire, Cameroon and South Africa, and from PMTCT service delivery sites administered by EGPAF prior to 2007, formed the basis for the *no stigma* estimate in the low-functioning setting. These data show that on average, across all 43 sites of the PEARL study, 71% of women received nevirapine, and across EGPAF sites prior to 2007, 75% received nevirapine.^{20;27} Although these numbers come from settings where stigma is probably high, they are used as the basis for the *no stigma* estimates because it is assumed that stigma is more likely to influence whether women ingest the drug rather than whether they simply receive it. Based on this, 75% of women in low-functioning settings who know their HIV status are estimated to adhere to nevirapine in the absence of stigma.

Both the qualitative and quantitative research highlights the association between HIV stigma and low drug adherence among pregnant women. Nondisclosure of status to partners, other family members and friends is considered a key factor related to both. Fearing negative reactions, women are selective regarding to whom they disclose. They choose most often to disclose to individuals who they feel have been supportive in the past.⁵⁶ In a study from Zimbabwe, only 44% of pregnant women shared their positive status with siblings, and only 30% disclosed to their parents because they feared both involuntary disclosure and rejection if their status was disclosed. A total of 78% of participating women disclosed their positive status to their spouse. Of the 22% who did not disclose to their spouse, 35% feared the marriage would suffer, 28% feared accusations of infidelity and 14% feared domestic violence.⁵⁷ In a study that analysed data from Rwanda’s national PMTCT programme, disclosure to family members or friends was significantly lower among nonadherent women than adherent women (62% vs. 82%, $P < 0.001$).³⁷ Similarly, results from a study in Lusaka,

Zambia, show that women who deliver at home and have not disclosed their HIV status to their partner are significantly less likely to adhere to single-dose nevirapine than women who have disclosed to their partner (OR=5.33, 95% CI: 1.09 to 26.01).⁴

Based on the above literature, and drawing specifically on figures from the PEARL study and the evaluation of Rwanda's national PMTCT initiative, the parameter for *high stigma* was set at 30% below the *no stigma* setting. The PEARL study, which collected cord blood samples to analyse single-dose nevirapine ingestion in participating women, demonstrated that of the women who received nevirapine and returned to deliver in a health facility (71%), only 57% had nevirapine in their cord blood. The range in this figure across sites was large, from 5% to 87%, and this represents a best-case scenario in which women returned to the health facility to deliver.²⁰ In Rwanda, of the women delivering at home, about 14% of women who been dispensed single-dose nevirapine but did not ingest it, expressed they were "afraid," and another 10% explained that someone who did not know their status was present.³⁷ Therefore, taking into account nonadherence due to stigma inside and outside the health facility, in a high-functioning setting, in the *absence of stigma* 95% of women who know their HIV status are estimated to take nevirapine, and in the presence of *high stigma* the estimate is 65%. In a low-functioning setting, in the *absence of stigma* 75% of women who know their status will take nevirapine, but in the presence of *high stigma* the estimate is 45%.

3. Proportion of infants who receive single-dose nevirapine within 72 hours after birth

To estimate the proportion of infants born to HIV-positive mothers who are administered single-dose nevirapine within the recommended 72 hours after delivery in the *no stigma* scenario, the authors reviewed literature on infant dosing rates and reasons that some infants do not receive treatment. Explanations for low levels of adherence among newborn infants include poor neonatal health, perhaps associated with a mother's low socioeconomic status or inadequate prenatal care⁴; delivery outside of a health care facility^{4,37}; and a mother's own nonadherence to nevirapine^{37,39}; the latter two could also be due to stigma. In a study in Rwanda, 90% of infants born in a health facility received single-dose nevirapine, while 15% of infants delivered at home were brought to the clinic to receive nevirapine.³⁷ Given the strong link between health facility delivery and adherence to infant dosing,⁴ rates of health care facility delivery among HIV-positive women are also taken into account. In studies from Zimbabwe and Zambia, 88% and 90% of HIV-positive women delivered at a health care facility, respectively.^{4,26}

In a high-functioning setting, the assumption is that most women will deliver in a health facility and, in instances where women deliver at home, access to a nearby facility for infant dosing will be available. Based on this assumption and the above data, the parameter for *no stigma* in a high-service-delivery setting was estimated as follows: 90% of women will deliver in a health facility, and of these women, 90% of their babies will receive infant dosing; or, 81% of infants born to HIV-positive mothers will be delivered in a health facility and receive dosing within 72 hours of delivery. In addition, we estimate that of the 10% of women who deliver at home, 15% of their infants will be brought to a facility and receive single-dose nevirapine within 72 hours of delivery. Adding these two groups together, 82% of infants born to HIV-positive women in the high-functioning, *no stigma* setting are estimated to receive infant ARV prophylaxis.

For the low-functioning setting, where access to a health facility may be limited and travel may be difficult to facilitate infant dosing, we estimate a significant decrease in the proportion of women delivering in a health care facility. Manzi et al. estimate 60% to 90% of all deliveries in rural sub-Saharan Africa occur at home.⁴² Therefore, in the absence of stigma for a low-functioning setting and assuming 60% of women deliver in a health care facility, the parameter for *no stigma* and low functioning is estimated at 40%.

To estimate the parameters for infant adherence in the presence of high levels of stigma, the authors considered research that demonstrates how the fear of disclosure impedes a mother's choice to deliver in a health facility and share her HIV status with health care providers, a factor that is significantly associated with whether or not an infant is administered prophylaxis. Pregnant adolescent girls in South Africa voiced their fear of judgmental, unsympathetic health care workers who would gossip about their patients' status, and as a result, hid their positive status from hospital staff by not bringing their ANC card, which indicates their HIV status, to the health facility or by swapping their ANC card with a friend who was HIV negative.⁵⁰ Additionally, qualitative data from Kenya suggests that women will avoid antenatal and delivery facilities in favour of traditional birth attendants at home because they fear disapproval and discrimination from health care providers.⁴⁸ Because an infant's uptake of nevirapine is related to whether the mother delivers at home or in a health facility, we make the assumption that if 24% of women who delivered at home in Rwanda could not adhere to ARV prophylaxis due to fears of involuntary disclosure (as stated in the previous section), a similar proportion of women would not obtain infant prophylaxis for their newborn due to the same reason. In fact, in the same study, 18% of the women who delivered at home and did not receive nevirapine for their newborn explained that they did not have any assistance to bring the child into the health facility,³⁷ a reason that might be due to nondisclosure to family and friends. Therefore, in both the low- and high-functioning settings, we have estimated a 20-point difference between the proportion of infants who receive single-dose nevirapine in the *absence of stigma* and the proportion of infants who receive single-dose nevirapine in the presence of *high stigma*. Therefore, in a high-functioning setting, 82% of infants receive nevirapine in the *absence of stigma*, but the estimate is 62% in the presence of *high stigma*. In a low-functioning setting, 40% of infants receive nevirapine in the *absence of stigma*, but the estimate is 20% in the presence of *high stigma*.

4. Proportion of women who take nevirapine and adhere to feeding guidelines

To estimate the parameters for the *no stigma* scenarios, the authors reviewed literature documenting rates of exclusive breastfeeding among different populations and examining reasons that HIV-positive women are not able to follow exclusive breastfeeding guidelines. Because best practice feeding guidelines in the context of HIV transmission have varied greatly over the past 10 years, mixed messaging and confusion are reasons some women do not adhere to the exclusive feeding guidelines. Researchers in South Africa and Malawi have documented the confusion women feel over which feeding practice—formula feeding or breastfeeding—is in the best interest of their newborn child.^{33;45;47} Low rates of exclusive breastfeeding among HIV-positive women are common in most African nations, with the exception of South Africa. In a survey of mothers attending antenatal services in Tanzania and Uganda, researchers found 19% and 48% of women, respectively, exclusively breastfeed their infant through age 4 months.²⁸ In South Africa, within the first week of the infant's life, the rate of exclusive breastfeeding is higher, reaching 56% among HIV-positive women and 61% among HIV-negative women.⁵⁸

Based on the proportions of women who exclusively breastfeed in different African countries and women's additional HIV support and knowledge associated with a high-functioning health system setting, the parameter estimate for exclusive breastfeeding in the *absence of stigma* is set at 65%. This number is estimated to drop to 35% in a low-functioning setting, based on the ranges presented above and the assumption that counselling on feeding practices is more likely to be unclear or absent in a low-functioning setting.

Fear of involuntary disclosure and pressures from the family can influence a woman's ability to adhere to six months of exclusive breastfeeding; therefore, to estimate the parameters for *high stigma*, the authors examined available data on the effects of women's disclosure on their ability to exclusively breastfeed. In Malawi, Sibeko et al. found that mothers who had not disclosed their status were less able to adhere to exclusive breastfeeding or exclusive formula feeding and

were most likely to mixed feed,⁴⁵ a practice that has been found to have the greatest risk of HIV transmission.^{15;59} Research from South Africa confirms the findings from Malawi. Of the women who intended to exclusively breastfeed, 80% introduced other liquids into their newborn's diet because of pressure from family members. Sixty-four percent of women who intended to breastfeed exclusively did not adhere because they had not disclosed their status to their family.⁴⁰ If a woman does not disclose her HIV status and is fearful of involuntary disclosure, it may be more difficult for her to adhere to one exclusive method of feeding practice. In general, community or family beliefs about early childhood nutrition dictate a new mother's infant feeding behaviour.^{6;13;40} Not following the cultural norms or her family's recommendations on how best to support her child's early nutrition could potentially signify she is HIV positive.

Because there is little data that quantify the association between disclosure and exclusive breastfeeding, the authors also looked at the proportion of HIV-positive women who intended to exclusively breastfeed in comparison with how many of those women successfully sustained the practice for six months. In Cote d'Ivoire, 32% of postpartum HIV-positive women who decided to breastfeed intended to breastfeed exclusively. After six months, the proportion of women exclusively breastfeeding fell to 3 percent.¹⁷ Similarly, in South Africa, 78% of HIV-positive women initially intended to exclusively breastfeed, and only 38% sustained this practice for six months.¹³ Based on this limited data and the authors' best estimate, the parameter for the *high stigma* scenario is estimated at 30% lower than that of the *no stigma* scenario. Therefore, in high-functioning health system settings, in the *absence of stigma* 65% of HIV-positive women will adhere to exclusive breastfeeding for six months, but in the presence of *high stigma* the estimate would be only 35%. In low-functioning health system settings, in the *absence of stigma* 35% of women will adhere to exclusive breastfeeding for six months, but in the presence of *high stigma* this number is estimated to fall to 5%.

Model impact projections

The model was then used to calculate how the different levels of stigma, with their associated impact, affect rates of participation at the different steps of PMTCT, from HIV testing through to infant feeding.

Table 4 shows the model projections of the impact of stigma in the low- and high-functioning delivery systems for varying assumptions about HIV prevalence levels among women accessing antenatal care services (15%, 10%, 5%).

In the high-functioning setting, for example, it is projected that where ANC HIV prevalence is 15% and stigma is *high*, there would be 2,827 vertical HIV infections, but there would only be 1,342 infections if there was *no stigma*. This suggests that more than half (53%) of vertical infections are attributable to stigma. The model projects proportionately smaller numbers of HIV infections averted in the 10% and 5% prevalence scenarios. In each case, the same percentage of HIV infections is due to stigma.

In the lower-functioning setting, with more challenges to the delivery of PMTCT services, the projected impact of stigma is still substantial. If the ANC HIV prevalence is 15% and stigma is *high*, the model projects that there would be 3,940 vertical HIV infections, while there would only be 2,902 vertical transmission if there was *no stigma*—26% fewer infections. The model projects there would be 3,684 infections in the *medium stigma* scenario, and 3,303 infections in the *low stigma* scenario. Again, the proportion of HIV infections due to stigma does not vary by HIV prevalence.

Figure 5 and **Figure 6** illustrate another way of viewing the potential impact of stigma in higher- and lower-functioning settings along the PMTCT cascade.

Table 4. Projected impact of stigma for different stigma, health sector and HIV prevalence scenarios

Health system functioning	ANC HIV prevalence	Projected number vertical infections, by level of stigma, per 100,000 women attending ANC services				Percentage of vertical infections due to stigma	Reduction in number vertical HIV infection if stigma reduced per 100,000 women attending ANC services			Percentage reduction in vertical HIV infections if stigma reduced		
		No stigma	Low stigma	Medium stigma	High stigma		High to low	High to medium	Medium to low	High to low	High to medium	Medium to low
High	15%	1,342	1,887	2,382	2,827	53%	940	445	495	33%	19%	21%
Low	15%	2,902	3,303	3,648	3,940	26%	637	292	345	16%	8%	9%
High	10%	895	1,258	1,588	1,885	53%	627	297	330	33%	19%	21%
Low	10%	1,935	2,202	2,432	2,627	26%	425	195	230	16%	8%	9%
High	5%	447	629	794	942	53%	313	148	165	33%	19%	21%
Low	5%	967	1,101	1,216	1,313	26%	212	97	115	16%	8%	9%

Figure 5. Proportion of HIV positive women completing PMTCT cascade, high-functioning health system

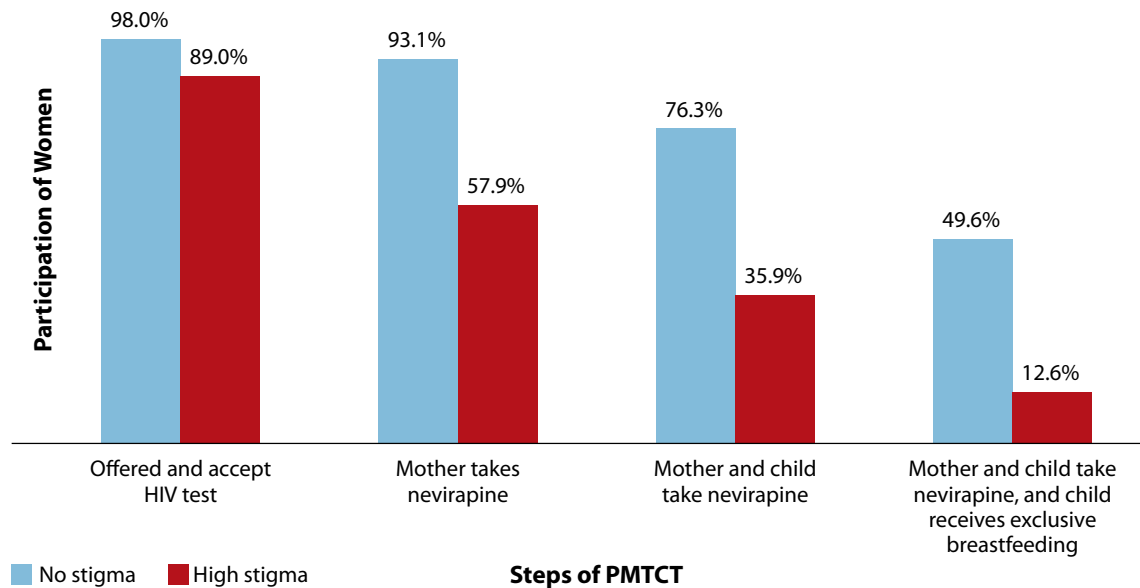
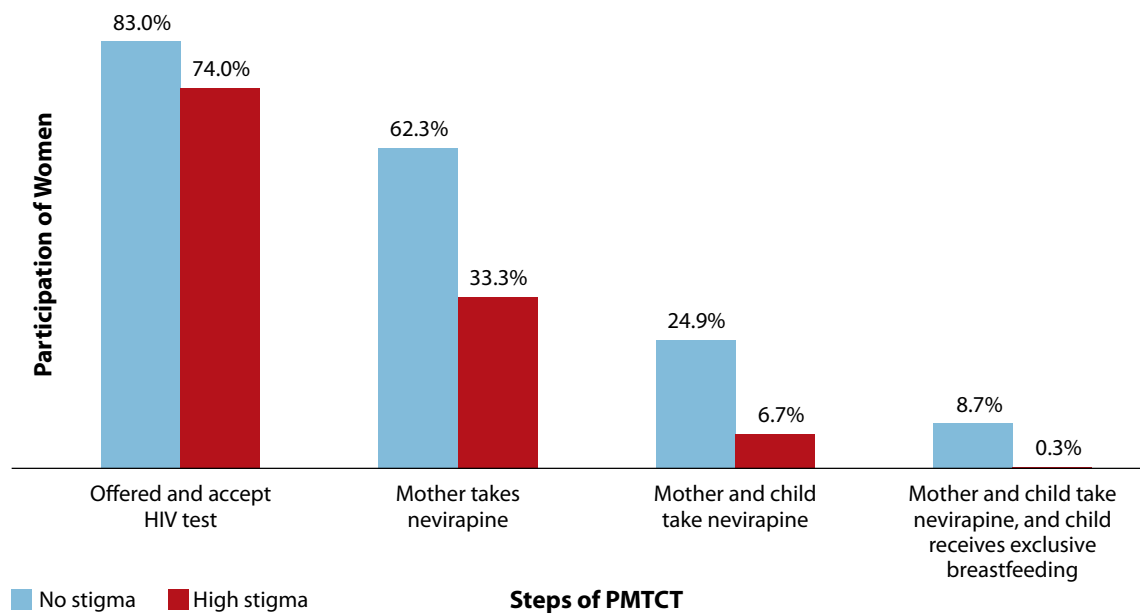


Figure 6. Proportion of HIV positive women completing PMTCT cascade, low-functioning health system



In the lower-functioning health service scenario, we project a larger number of potential HIV infections than in the higher health service setting, but a smaller percentage of infant infections attributable to stigma. This is because, in the lower-functioning setting, many other factors also contribute to transmission. This does not mean that stigma reduction programmes are less important in these settings but rather that a range of other important service improvements could also reduce transmission.

The model can also be used to explore how many HIV infections might be averted by reducing the levels of stigma in a community. This is done by comparing the number of HIV infections that would occur if levels of stigma were reduced from *high* to *low*, from *high* to *medium* or from *medium* to *low*.

For example, in a high-functioning setting with a 15% HIV prevalence, if a highly successful stigma reduction programme was able to reduce the level of stigma from *high* to *low*, the model suggests that 940 vertical infections might be averted (a reduction from 2,827 in *high stigma* to 1,887 in *low stigma*)—33% fewer HIV infections (also shown in the results in **Table 4**). Even a reduction in stigma from *high* to *medium* would reduce infections by 19%—translating to 445 fewer infections.

As would be expected, the projected number of HIV infections is influenced by the underlying levels of HIV infection in the ANC population, with twice as many babies potentially becoming HIV infected, for example, in settings where twice as many pregnant women are HIV infected. However, the percentage projections of the contribution of stigma to vertical transmission, and the percentage reduction in vertical HIV transmission associated with reduction of stigma, do not depend upon HIV prevalence because these are relative measures of impact.

Projected thresholds for cost-effectiveness investment in stigma reduction

The question that will inevitably arise among donors and programme managers is whether addressing stigma is cost-effective compared with other forms of investment. To explore this issue, drawing upon recent reviews of the cost-effectiveness of HIV prevention and recommendations from the World Bank regarding appropriate cost-effectiveness thresholds, we used a conservative cost-effectiveness threshold of US\$1,000 per HIV infection averted.^{60,61} Based on this threshold, it is then possible to use the impact figures (shown in Table 4) to estimate what level of investment in stigma reduction would be cost-effective, assuming that this investment would result in the specified improvements in service delivery (**Table 5**).

Table 5. Levels of resources that could be invested in stigma reduction, using a cost-effectiveness threshold of \$1,000 / HIV averted, for specified reductions in stigma effects

Health system functioning	ANC HIV prevalence	Reduction in number vertical HIV infection if stigma reduced (per 100,000 women attending ANC services)			Possible investment in stigma reduction that would be cost-effective (per 100,000 women accessing PMTCT), using a cost-effectiveness threshold of \$1000 / HIV infection averted, assuming investment results in specified reductions in stigma			Per capita investment in stigma reduction that would be cost-effective (per woman accessing PMTCT), using a cost-effectiveness threshold of \$1000 / HIV infection averted, assuming investment results in specified reductions in stigma		
		High to low	High to medium	Medium to low	High to low	High to medium	Medium to low	High to low	High to medium	Medium to low
High	15%	940	445	495	\$940,000	\$445,000	\$495,000	\$9.40	\$4.45	\$4.95
Low	15%	637	292	345	\$637,000	\$292,000	\$345,000	\$6.37	\$2.92	\$3.45
High	10%	627	297	330	\$626,667	\$296,667	\$330,000	\$6.27	\$2.97	\$3.30
Low	10%	425	195	230	\$424,667	\$194,667	\$230,000	\$4.25	\$1.95	\$2.30
High	5%	313	148	165	\$313,333	\$148,333	\$165,000	\$3.13	\$1.48	\$1.65
Low	5%	212	97	115	\$212,333	\$97,333	\$115,000	\$2.12	\$0.97	\$1.15

The results suggest that stigma reduction investments of between \$1 and \$10 per woman attending ANC services would be cost-effective, with higher levels of investment merited in higher-HIV-prevalence settings or if stigma reduction programmes are able to achieve large reductions in stigma (say from *high* to *low*). In practice, it is likely that stigma reduction programmes will need both a health sector and a community focus to ensure that women feel able to be HIV tested, to access treatment and to follow recommended HIV treatment guidelines.

Although these cost projections are speculative, because they depend upon the assumption that the projected stigma reduction impacts can be achieved, they nonetheless illustrate that an investment in stigma reduction programming might be an important and cost-effective addition to current PMTCT programming.

Limitations of the models

While the epidemiological modelling presented offers important insights about potential interactions between stigma and HIV, modelling such as this has a number of important limitations.

The most fundamental limitation is the challenge of trying to realistically quantify the different dimensions of stigma for use in mathematical models. While some stigma-related behaviours (e.g., enacted stigma or discrimination) are overt, many are subtle (e.g., psychological reactions or interpersonal relations), making them complex to “measure.” The current absence of data on stigma makes it difficult to determine the level of stigma, for example, *no*, *low*, *medium* or *high*. Similarly, it is difficult to estimate how patterns of behaviour and/or service use could change if stigma was reduced or if there was *no stigma*. Although it is easy to hypothesise that the situation would improve in the absence of stigma, other constraints to service use might nevertheless remain, including other gender-related factors like male involvement. For this reason, the *no stigma* inputs should be used to reflect the effects of other constraints on delivery of services.

For simplicity, this model also does not consider women who seroconvert while attending ANC services, that is, those who initially test as HIV negative but become HIV positive during pregnancy and therefore might transmit HIV to their infant. However, because these women would not be identified by an initial PMTCT intervention, the number of resulting vertical infections that occur due to this is unlikely to differ between the *stigma* and *no stigma* scenarios and therefore will not affect the final model outcomes.

Our analysis was based upon common PMTCT practise in many developing country settings over the past years and does not reflect the new (2010) WHO guidance.^{2,3} However, since this guidance recommends moving away from single-dose nevirapine to a daily zidovudine or three-drug regimen starting at 14 weeks of pregnancy and continuing through breastfeeding and daily nevirapine for the infant while breastfeeding, if anything, the current model underestimates the potential impact of stigma.

However, even using these “best guess” inputs and general scenarios, it is possible to gain important insights about the compounding impact of stigma. The structure of the models themselves demonstrates how the loss of individuals at each stage (e.g., those deterred by stigma) will have multiplying effects, increasing the likelihood of transmission and morbidity. The modelling of plausible scenarios presented here, which have been informed by existing research on stigma, also suggests that the impact of stigma might be substantial. Indeed, where possible, in our modelling we sought to take a conservative approach. For example, the PMTCT model only considers those women who present at ANC services (versus the universe of pregnant women) and does not take into account how stigma might negatively affect uptake or timing of presentation

at services. Furthermore, the model focuses on quantifying the impact of stigma on vertical HIV transmission and does not quantify the potential broader benefits to women of finding out their HIV status during the PMTCT care process.

Implications and conclusions

The model findings suggest that stigma has a large impact on mother-to-child transmission of HIV and that programmes that can effectively reduce levels of stigma might reap many benefits. To date, an appropriately large focus in PMTCT has been on strengthening the delivery of the medical components of PMTCT programming. This modelling highlights the additional importance of also investing in addressing stigma and other gender and social barriers to PMTCT.

This working paper has focused on the impact of stigma on the vertical transmission of HIV. However, it is important to recognise that the benefits of reducing stigma at a community level will spread across most aspects of HIV programming. Investment in stigma reduction interventions alongside more “traditional” medical services programs will have a multiplying effect within communities, which will impact not only PMTCT programmes but also ART programmes and other forms of HIV prevention and care. These benefits might be far reaching, as stigma is such an important structural driver of the HIV epidemic and its consequences.

With potentially as many as half of vertical transmissions attributable to stigma, more investment in responding to stigma is an urgent need. Research is needed to increase understanding of women's perspectives on PMTCT and how stigma and other gender-related factors impact participation in each step of the PMTCT process and to support evidence-based programming to respond effectively to these factors.

Appendix: PMTCT stigma model technical description

The spreadsheet model estimates the number of vertical HIV infections that would occur for different assumptions about the levels of stigma and their impact on PMTCT service delivery.

The model has the following inputs related to the ANC population being considered:

- Number of women accessing ANC services – N
- HIV prevalence among women accessing ANC services – p
- Percentage of women who lose child during pregnancy or in first year of life – d

The model also has inputs describing the probability of vertical transmission in the first year of life:

- Probability of mother-to-child HIV transmission in absence of PMTCT – p_0
- Probability of MTCT when mother receives nevirapine but child does not, and not able to adhere to feeding guidelines – p_1
- Probability of MTCT when mother receives nevirapine but child does not, and able to adhere to feeding guidelines – p_2
- Probability of MTCT when mother and child receive nevirapine, and not able to adhere to feeding guidelines – p_3
- Probability of MTCT when mother and child receive nevirapine, and able to adhere to feeding guidelines – p_4

The four sets of stigma inputs are as follows:

- Proportion of women attending ANC who are offered and accept HIV test – a_i
- Proportion of women who find out status, test HIV positive and take nevirapine – b_i
- Proportion of women testing HIV positive and receiving nevirapine whose baby receives infant dose – c_i
- Proportion of women testing HIV positive and receiving ART who are able to adhere to feeding guidelines – d_i

Where i ranges from 0 to 3, it denotes the associated level of stigma ($i = 0$, *no stigma*; 1 , *low stigma*; 2 , *medium stigma*; and 3 , *high stigma*).

For a specified level of stigma, i , the number of mother-to-child HIV infections (C_i) is given by the sum of infections from the following numbers of HIV-infected women whose babies do not die in the first year of life:

- May or may not test, do not receive any PMTCT intervention, and do not follow the recommended feeding guidelines:

$$Np(1 - d)[a_i(1 - b_i) + (1 - a_i)]p_0$$

- Test and receive nevirapine, child does not receive the infant dosage, and do not follow recommended feeding guidelines:

$$Np(1 - d) a_i b_i (1 - c_i) (1 - d_i) p_1$$

- Test and receive nevirapine, child does not receive the infant dosage, and follow recommended feeding guidelines:

$$Np(1 - d)a_i b_i (1 - c_i) d_i p_2$$

- Test and receive nevirapine, child receives the infant dosage, and do not follow recommended feeding guidelines:

$$Np(1 - d)a_i b_i c_i (1 - d_i) p_3$$

- Test and receive nevirapine, child receives the infant dosage, and follow recommended feeding guidelines:

$$Np(1 - d)a_i b_i c_i d_i p_4$$

That is, for $i = 0$ to 3,

$$C_i = Np(1 - d)\{[a_i(1 - b_i) + (1 - a_i)]p_0 + a_i b_i (1 - c_i)(1 - d_i)p_1 + a_i b_i (1 - c_i) d_i p_2 + a_i b_i c_i (1 - d_i) p_3 + a_i b_i c_i d_i p_4\}$$

The percentage of vertical HIV infections due to stigma is then calculated as follows:

- High stigma = $100(C_3 - C_0) / C_3$
- Medium stigma = $100(C_2 - C_0) / C_3$
- Low stigma = $100(C_1 - C_0) / C_3$

Similarly, the percentage reduction in vertical HIV infections that would occur following reductions in stigma are calculated as follows:

- High to medium stigma = $100(C_3 - C_2) / C_3$
- High to low stigma = $100(C_3 - C_1) / C_3$
- Medium to low stigma = $100(C_2 - C_1) / C_3$.

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