1. Assumptions regarding perinatal transmission of human immunodeficiency virus (HIV)

The assumed proportions of women who receive different forms of prophylaxis are based on a 2010 survey of South African women who were interviewed and tested for HIV at immunization clinics (Kate Kerber, personal communication).1 The assumed combined in utero (IU) and intrapartum (IP) transmission risk is based on various studies that have evaluated the efficacy of different forms of antiretroviral prophylaxis, reviewed elsewhere.2,3 The fraction of this transmission that is IU and therefore detectable at birth is estimated from published literature, with a focus on landmark studies and those with larger cohorts that used standardized testing technologies in the context of prevention of mother-to-child (PMTCT) regimens similar to South African guidelines.4-10 The assumed parameter values are specified in Table 1 of the main text.

2. Assumptions regarding postnatal transmission of HIV

It is assumed that 20% of HIV-infected pregnant women choose not to breastfeed, 55% choose exclusive breastfeeding (EBF) and 25% practise mixed feeding. These rates of breastfeeding are higher than those observed historically6 because of recent changes to South Africa’s policy on infant feeding.11 For women who choose EBF, the duration of breast feeding is randomly assigned by sampling from an exponential distribution with a median of 2 months and resetting any sampled values greater than 6 months to 6 months (the assumed maximum duration of EBF). Similarly, the duration of mixed feeding is randomly assigned by sampling from an exponential distribution with a median of 7 months and limiting the maximum duration to 36 months. These assumptions reflect the actual feeding durations observed in HIV-diagnosed mothers12,13 rather than the recommended durations. In women electing to practise EBF, 30% are assumed to practise abrupt weaning at the end of the simulated EBF period and the remaining 70% switch to mixed feeding. These breastfeeding assumptions for HIV-infected women are based on various South African data sources, reviewed elsewhere.2

The monthly probability of transmission through breast milk is assumed to be 1.0% for mothers who practice mixed feeding in the absence of maternal or infant antiretroviral prophylaxis.14 The transmission probability is assumed to be reduced by 50% if the mother practices EBF. The rate of transmission is assumed to be reduced by 80% if the mother is receiving antiretroviral therapy (ART)15 and by 60% if the child is receiving daily-dose nevirapine (NVP) prophylaxis.16-18 The proportion of breastfeeding women who receive ART is assumed to be the same as the proportion of women who receive
ART antenatally (33%). It is assumed that 40% of children who are breastfed and whose mothers are not receiving ART would receive NVP for the entire duration of breastfeeding, though no data are available to support this assumption.

It is believed that few HIV-exposed children access testing post weaning. Since there is little current data, it is conservatively assumed that 10% of exposed children undergo a post-weaning test and as with routine polymerase chain reaction (PCR) screening, it is assumed that 66% of these children receive their test results.

3. Assumptions regarding sensitivity of HIV PCR testing

It is assumed that a birth PCR test would not detect HIV-infections that have been acquired IP. In addition, the sensitivity of PCR testing for detecting HIV-infection from 6 weeks of age is assumed to be reduced in children receiving daily-dose NVP, as recent studies have found delayed diagnosis of HIV-infection beyond 4 to 6 weeks of age in the context of prolonged and/or multi-drug prophylactic regimens. The sensitivity of PCR testing for detecting IU-infections at 6 weeks of age is assumed to be 85% in the context of daily-dose NVP, based on previous findings of 83% sensitivity at 2 weeks of age among IU-infected infants receiving single-dose NVP. A lower 6-week sensitivity of 70% is assumed for IP-infections based on the findings of the HPTN 040 Study, as these infections are being established at the time of daily-dose NVP and would therefore be more susceptible to NVP’s viral load lowering effect. PCR sensitivity is assumed to recover over time as NVP resistant strains accumulate (see Table 2 of the main text).

4. Assumptions regarding survival of HIV-infected children and calculation of life years saved by PCR screening

ART-naïve children are assumed to progress through 2 disease stages prior to dying from Acquired Immune Deficiency Syndrome (AIDS): an early disease stage and a late disease stage, the latter corresponding to children who have met the clinical or immunological criteria previously used to determine ART eligibility in the 2006 World Health Organization pediatric ART guidelines. Children starting ART when in the late disease stage are assumed to be at a high risk of AIDS mortality during the first 3 months of treatment, but then experience a 90% lower mortality rate once they have stabilized on ART. Perinatally infected children starting ART when in the early disease stage do not go through an initial ‘high risk’ phase. Parameters are set to match the observed difference in mortality between early ART and deferred ART groups in the CHER trial. The maximum age in the model is 100 years and non-HIV mortality assumptions are obtained from the ASSA2008 AIDS and Demographic model. A more detailed description of the model of HIV survival is provided elsewhere.
The approach for calculating p-values for the savings in life years by PCR screening at different ages is likely to underststate the true significance, as it assumes zero correlation between untreated and treated HIV survival and therefore overstates the variance of the survival difference when comparing scenarios with different levels of ART uptake.

References


FIGURE S1. PCR testing at different ages in the 'WHO Option B' scenario. A: Effectiveness of PCR testing for identification of perinatally HIV-infected infants. B: Effectiveness of PCR testing for saving life years. C: Efficiency of PCR testing for identification of perinatal HIV-infection per additional PCR. PCR, Polymerase Chain Reaction.
FIGURE S2. PCR testing at different ages in the 'No loss in PCR sensitivity due to NVP' scenario. A: Effectiveness of PCR testing for identification of perinatally HIV-infected infants. B: Effectiveness of PCR testing for saving life years. C: Efficiency of PCR testing for identification of perinatal HIV-infection per additional PCR. PCR, Polymerase Chain Reaction.
FIGURE S3. PCR testing at different ages in the 'Lower mortality if infected intrapartum' scenario. A: Effectiveness of PCR testing for identification of perinatally HIV-infected infants. B: Effectiveness of PCR testing for saving life years. C: Efficiency of PCR testing for identification of perinatal HIV-infection per additional PCR. PCR, Polymerase Chain Reaction.