

The Cost Effectiveness of Voluntary Prenatal and Routine Newborn HIV Screening in the United States

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Objective: To evaluate the cost effectiveness of voluntary prenatal and routine postnatal HIV screening in the cohort of pregnant women and newborns in the United States.

Design: Cost-effectiveness analysis. We developed a decision model to analyze the cost effectiveness of enhanced prenatal screening and routine newborn screening for HIV. We also analyzed the incremental cost effectiveness of routine newborn screening when improved voluntary prenatal screening is already in place.

Participants: Analysis of the cohort of pregnant women and newborns in the United States.

Interventions: Enhanced prenatal screening, or routine newborn screening for HIV.

Main Outcome Measures: Infections averted, life expectancy, costs, and incremental cost effectiveness.

Results: Improved participation in voluntary prenatal HIV screening would result in an additional 1.1 million women being screened annually, would identify an additional 527 HIV-infected mothers annually, would avert 150 infections in newborns, and would cost \$8,900 U.S. per life-year gained. Routine newborn HIV screening would test 3.9 million infants annually, would identify 1061 HIV-infected mothers, would avert 266 infections in newborns, and would cost \$7,000 U.S. per life-year gained. If improved voluntary prenatal screening is already in place, routine newborn screening would avert an additional 135 infections in newborns, at an incremental cost of \$10,600 U.S. per life-year gained. The screening programs are likely to be cost effective over a wide range of assumptions regarding key factors in the analysis.

Conclusions: Improved voluntary prenatal HIV screening of women and routine screening of newborns are cost effective. Routine newborn screening becomes less attractive as the rate of voluntary prenatal screening increases. Improved participation in voluntary prenatal screening has the added benefit that mothers maintain their right to determine whether they are tested for HIV.

Key Words: HIV—Cost effectiveness—HIV screening.

Each year, approximately 6500 infants in the United States are born to women infected with HIV (1). AIDS Clinical Trial Group Study 076 (ACTG 076) demon-

strated that vertical HIV transmission could be decreased from about 25% to about 8% if HIV-infected women were treated with zidovudine during pregnancy (2). Some published data indicate that vertical transmission rates are falling and could decrease even further with new antiretroviral treatments (3,4). Yet, researchers have estimated that approximately one third of HIV-infected

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women do not know their infection status before becoming pregnant (5).

Several organizations, including the U.S. Centers for Disease Control and Prevention (CDC), the American College of Obstetricians and Gynecologists (ACOG), and the American Academy of Pediatrics have supported voluntary HIV testing as part of prenatal care (6). However, participation in such screening has been <100%. In one large health maintenance organization, only about two thirds of women seeking prenatal care consented to voluntary HIV screening (7). ACOG has recently recommended that efforts be made to increase the rate of voluntary prenatal screening, so that every pregnant woman is screened for HIV (8).

As an alternative, several U.S. state and federal legislators have proposed routine HIV testing of all newborns (9–16). Routine testing of newborns will become a requirement for continued federal funding of HIV programs in states where perinatal HIV transmission in the year 2000 has not decreased substantially from 1996 levels (12). A controversial policy change has already occurred in New York state, which for several years has conducted universal HIV screening of newborns for epidemiologic monitoring. Previously, the results of the infants' HIV screening tests were not released to patients or public-health authorities; now, both mothers and government officials are notified of each newborn's serostatus (16).

Routine HIV screening of newborns could decrease vertical HIV transmission if an abbreviated routine of antiretroviral drugs given immediately postpartum reduces vertical transmission or if avoidance of breastfeeding reduces postpartum transmission (17–20). Other benefits come from early identification and treatment of HIV-infected mothers and infants. However, such programs may be expensive if newborn screening is performed for infants of women who have already undergone voluntary screening during pregnancy (21). Some have argued that mandatory screening of newborns is a de facto nonconsensual test of a woman's HIV status because infants can only acquire antibodies to HIV from their mothers. Other critics have expressed concern that fear of mandatory newborn screening could decrease the number of women seeking prenatal care or could strain the patient-physician relationship (6,11). Routine newborn screening is controversial in the medical community as well; the American Medical Association is in favor of such programs (22), whereas the American Academy of Pediatrics is not (1).

We examined the potential health benefits and economic costs and savings associated with two hypothetical programs aimed at reducing perinatal HIV transmis-

sion in the United States: 1) a program to increase rates of voluntary prenatal HIV screening as part of prenatal care programs, and 2) a program of routine mandatory HIV screening of newborns. We also investigated how the costs and benefits of routine newborn screening might be influenced by increased rates of voluntary prenatal screening. Public decision making about such programs should consider many factors, including social, legal, and ethical ramifications of the interventions, in addition to cost effectiveness. Nonetheless, understanding the costs and benefits of these programs is essential: if the programs provide little benefit, or if the benefit is attainable only at a cost that exceeds available resources, then further debate may not be needed. Conversely, if the programs provide substantial benefits with an affordable investment, then the social, legal and ethical questions deserve a full hearing.

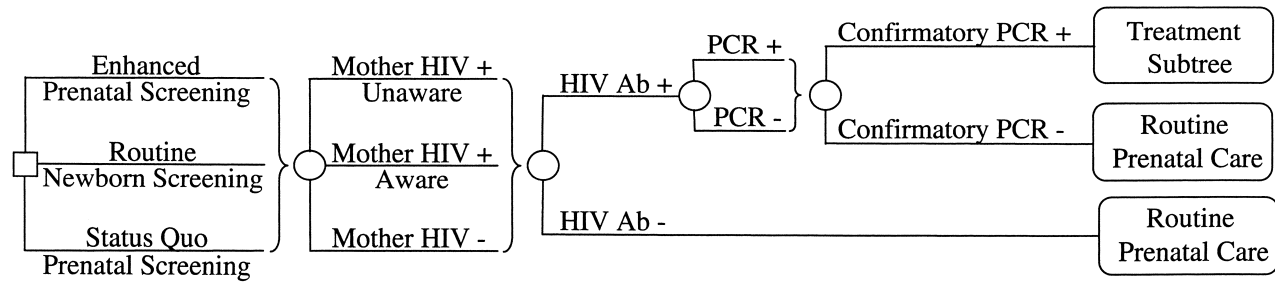
METHODS

We used a decision model to estimate the incremental costs and benefits of two programs in the cohort of pregnant women and newborns in the United States: an enhanced prenatal screening program in which mothers are voluntarily screened during pregnancy (with no routine screening of newborns), and a routine newborn screening program in which all infants are screened at birth (Fig. 1). We analyzed the incremental cost effectiveness of each program compared with the status quo, in which women are screened at current participation rates. We also analyzed the incremental cost effectiveness of routine newborn screening when enhanced voluntary prenatal screening is already in place.

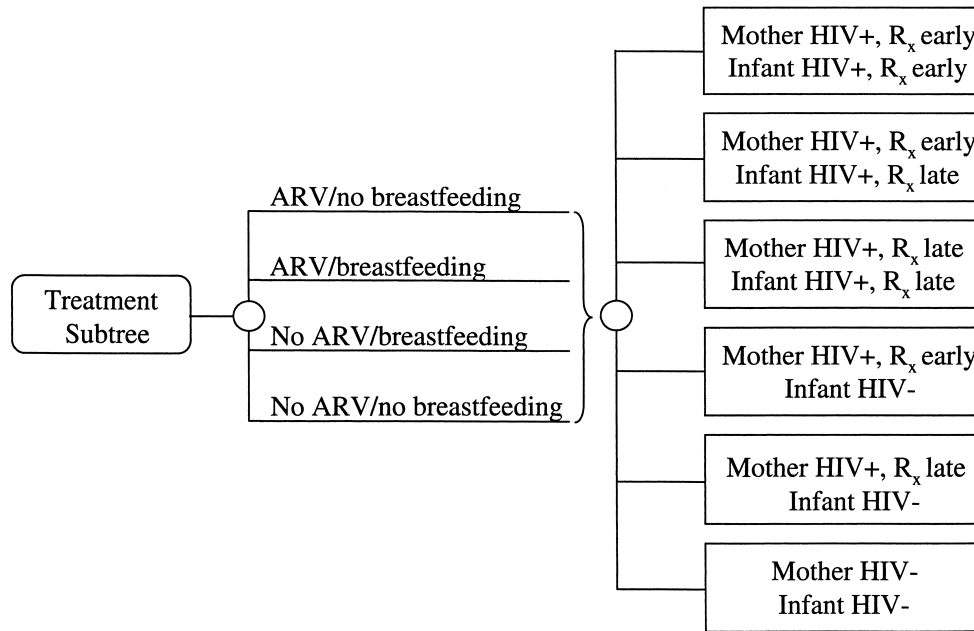
Our analyses take a societal perspective. We included the health benefits that accrue to mothers and infants from perinatal use of antiretroviral drugs, from avoidance of breastfeeding, and from early initiation of antiretroviral treatment. We included the incremental costs of screening, counseling, and treatment associated with the programs, as well as savings in future health care costs for averted infant HIV infections. We obtained estimates of test sensitivity and specificity (23), the probability of vertical HIV transmission (2,18,24–26), costs (19,23,27–36), demographic and behavioral data (5,7,37–62), and health benefits of early identification and treatment from the literature and expert opinions (Table 1).

We divided the cohort of mothers into three groups: women who are HIV infected and aware of their infection status, women who are HIV infected but unaware of their infection status, and women who are not HIV infected (Fig. 1). HIV-infected women were aware of their status if they had been voluntarily screened before becoming pregnant, or if they sought prenatal care and consented to screening as part of prenatal care.

Prenatal HIV-testing programs will have the greatest impact in women who are HIV infected but not identified as such. The CDC has estimated that two thirds of HIV-infected residents of the United States have been tested (5); we assumed that the same rate applies to HIV-infected pregnant women. For the remaining one third to be identified during pregnancy, they must seek prenatal care and consent to HIV testing. Although over 97% of women in the general population have been found to receive some prenatal care (40,42,44,46,58,59), HIV-infected women have sought prenatal care at lower rates (56). An



A



B

FIG. 1. (A) Schematic diagram of decision model. The small square represents the decision to implement enhanced prenatal screening, routine newborn screening, or to continue current screening programs. Circles represent chance events. The model divides women into three groups based on infection status and knowledge of infection. Initial HIV testing is performed with a human immunodeficiency virus (HIV) antibody test in all strategies. For the routine newborn screening strategy, if infants are antibody positive (Ab+), they are subsequently tested with the polymerase chain reaction (PCR). PCR can be either positive (PCR+) or negative (PCR-). If an infant is identified as having HIV, subsequent events are shown in the treatment subtree. (B) Schematic diagram of the treatment subtree. The tree shows the combination of treatment possibilities and outcomes. Women and infants may be treated with antiretroviral drugs (ARV) and women may or may not choose to breastfeed their infants. Rectangles represent the possible health outcomes for both mother and infant. Rx indicates ARV treatment. Rx early indicates that either mother or infant were treated earlier than they would have been in the absence of a screening program.

observational study of HIV-infected Medicaid recipients in New York found that 20% received no prenatal care (48) (Medicaid is a program funded by the U.S. federal government that is administered by states). One survey in four states estimated this proportion to be 12% to 15% (57). A study in North Carolina found that 2% of HIV-infected mothers received no prenatal care (61). We assumed that 95% of HIV-uninfected mothers and 80% of HIV-infected mothers seek prenatal care. We varied these rates in sensitivity analyses.

Rates of accepting voluntary prenatal screening were found to range from 6% to 88% in Great Britain, depending on how the tests were offered (63). Rates between 74% and 83% were observed in Brooklyn, New York (64). Based on a large observational cohort (7), we assumed for the base case that 65% of all women who sought prenatal care accepted HIV screening, and that acceptance was similar regardless of HIV status. Thus, we assumed that current prenatal screening programs would identify about half of all HIV-infected women who were un-

aware of their infection ($80\% \times 65\% = 52\%$), which is slightly higher than the proportion observed in a study in New York (60). HIV-infected women know of their status before delivery if they knew their status before pregnancy, or if they did not know before pregnancy but sought prenatal care and consented to HIV screening as part of prenatal care. Thus, our model predicts that 84% of women will know their status before childbirth ($\frac{2}{3}$ knew status + $\frac{1}{3}$ did not know \times 80% sought prenatal care \times 65% accepted HIV screening as part of care = 84%), compared with 81% observed in another study (57).

Health Benefits of Early Identification

For newborns of HIV-infected mothers, early identification allows for prompt treatment and avoidance of breastfeeding, which could avert some HIV infections. One study found that 75% of HIV-infected preg-

TABLE 1. Input variables and sources

Parameter	Base/case estimate (range)	Reference
Vertical transmission parameters		
Breastfeeding relative-risk ratio ^a	1.66 (1.00–2.00)	18
Risk-reduction benefit of antiretroviral therapy after birth	84.4% (10.0%–100.0%)	See text
Probability of vertical transmission with no antiretroviral therapy, and with no breastfeeding	26.6%	19
Probability of vertical transmission with no antiretroviral therapy, and with breastfeeding	44.2%	See text
Probability of vertical transmission with antiretroviral therapy after birth only, and with no breastfeeding	6.7%	See text
Probability of vertical transmission with antiretroviral therapy after birth only, and with breastfeeding	11.1%	See text
Probability of vertical transmission with antiretroviral therapy during pregnancy, and with no breastfeeding	3.0% (0%–8.5%) ^b	See text
Probability of vertical transmission with antiretroviral therapy during pregnancy, and with breastfeeding	5.0%	See text
Adherence		
Breastfeeding rate among HIV-infected women who are unaware of their status	30% (5%–30%)	51–55, 62
Breastfeeding rate among HIV-infected women who are aware of their status	2% (0.2%–2%)	38
Adherence with antiretroviral therapy during pregnancy	90% (50%–95%)	See text
Mothers' adherence with antiretroviral therapy after childbirth	90% (10%–100%)	See text
Newborns' adherence with antiretroviral therapy for first 6 weeks after birth	100%	Assumed
Demographic		
Prevalence of HIV among women of childbearing age	0.0017 (0.0010–0.0050)	34, 104
Number of babies born in United States annually	3,899,000	37
Proportion of HIV-infected women who are aware of their status prior to pregnancy	67% (25%–90%)	5
Prenatal care behavior		
Proportion of HIV-infected mothers who seek prenatal care	80% (25%–95%)	48
Proportion of mothers seeking prenatal care who consent to HIV screening, without enhanced prenatal screening	65% (25%–90%)	7
Proportion of mothers seeking prenatal care who consent to HIV screening, with enhanced prenatal screening	95% (70%–95%)	49, 50, 65
Proportion of HIV-uninfected mothers who seek prenatal care	95%	40, 42, 44, 46, 58, 65
Test characteristics		
Initial EIA TPR	.995	32
Initial EIA TNR	.994	32
Confirmatory test bundle TPR	.999994	32
Initial PCR TPR	.932	23
Initial PCR TNR	.932	23
Confirmatory PCR TPR	.982	23
Confirmatory PCR TNR	.982	23
Early treatment benefits: increased life expectancy		
Newborns	0 years (0–4) ^c	Assumed
Mothers, if infant tests positive, or if the infant is not tested but is HIV infected	0 years (0–4)	Assumed
Mothers, if infant tests negative, or if the infant is not tested and is not HIV infected	0 years (0–4)	Assumed
Life expectancies		
HIV-infected newborn	9.4 years	20, 50, 92
HIV-infected mother	8.4 years	32
HIV-uninfected newborn	76.3 years	37
Costs		
EIA test	\$5.00	34
PCR test	\$130.00	23
Confirmatory bundle of tests	\$48.00	32, 34
Pretest counseling cost for pregnant women ^d	\$12.35 (\$10.00–\$30.00)	Calculated
One-time counseling cost for women with a positive screening test, or whose infant had a positive screening test	\$64.00	32, 34
Infant formula	\$15.00/week	Assumed
Antiretroviral therapy, mothers ^e	\$291.00/week (\$179.00–\$410.00)	29, 33
Treatment of HIV-infected infants	\$192.00/week	28, 30, 31
Discounted lifetime health care costs for healthy newborns	\$30,000	37
Discounted lifetime health care costs for HIV-infected newborns	\$173,000 (\$100,000–\$400,000)	28, 30, 31
Discount rate	3% (0%–7%)	91

^a Increase in the risk of vertical transmission from breastfeeding.

^b In sensitivity analyses, we varied this probability as indicated. The other values for the probability of vertical transmission (e.g., with no antiretroviral therapy and no breastfeeding) depend on this value, as described in the text, and thus were implicitly varied when we varied this probability, as well as when we varied the breastfeeding risk ratio and the risk reduction benefit of antiretroviral therapy.

^c A recent study has found a survival advantage for infants treated with triple therapy (105), so we considered a survival advantage of up to 4 years in sensitivity analysis.

^d Assumes that counseling would take 15 minutes and would be done by a nurse earning \$30 U.S./hour (yielding a labor cost of \$8.50 U.S.); would incur a paperwork cost of \$1.00 U.S.; and that both of these costs would incur an additional 30% in associated overhead. This yields \$12.35 U.S. = (9.5) × (1.3).

^e \$281 U.S./week for drugs, plus \$178 U.S./year for viral load monitoring.

EIA, enzyme immunoassay; PCR, polymerase chain reaction; TPR, true-positive rate; TNR, true-negative rate. Amounts are shown in 1997 U.S. dollars.

nant women accepted perinatal zidovudine (60). A recent survey in four states found that 85% of HIV-infected pregnant women were offered antiretroviral therapy, and 95% accepted it (57). Another study found that 95% of HIV-infected mothers in North Carolina received some antiretroviral therapy (61). A four-state evaluation of medical records found that at least 90% of women offered zidovudine during pregnancy accepted it (65). A survey of 157 patients for self-reported adherence to antiretroviral therapy found that 11% had less than 80% adherence, 20% had 80% to 95% adherence, 29% had 95% to 99% adherence, and 64% claimed 100% adherence; a survey of the providers of these patients found that 4% of the patients had <80% adherence, 52% had adherence rates between 80% and 95%, and 44% had adherence rates of $\geq 95\%$ (66).

We assumed that all mothers identified as HIV infected would be offered antiretroviral therapy, and that 90% would adhere to antiretroviral treatment programs and accrue these benefits. We assumed that adherence rates with antiretroviral therapy for infants before and after the first 6 weeks were 100% and 90%, respectively. We assumed that treatment of infants during the first 6 weeks would take place in supervised settings, resulting in 100% adherence; however, after the first 6 weeks, adherence of infants would be the same as that of their mothers.

Studies of low-income, urban women have found breastfeeding rates ranging from 20% to 70% (51–55). A study of HIV-infected women revealed the breastfeeding rate to be 30% to 66% (62). We assumed a breastfeeding rate of 30% among HIV-infected women who were not aware of their serostatus, and 2% (38) among HIV-infected women who were aware of their serostatus. We varied these rates in sensitivity analysis.

We estimated that, with no screening, an asymptomatic HIV-infected woman who gave birth to an uninfected child would be identified as HIV-infected when she became symptomatic. We assumed that on average, women would give birth at the midpoint of a prolonged asymptomatic period and thus would not develop symptoms for another 3 years after giving birth (32). We assumed that an asymptomatic HIV-infected woman who gave birth to an HIV-infected child would be identified an average of 9 months' postpartum (30), when her child developed symptoms. Recent studies have shown a survival advantage associated with antiretroviral therapy; however, whether early initiation of therapy confers an additional survival advantage is unknown. We assumed no additional survival benefit to mothers from early identification and treatment as a result of newborn screening programs. We varied this benefit in sensitivity analyses. We assumed that a brief course of antiretroviral therapy causes no detrimental effects to the health of uninfected infants (67,68).

Enhanced Prenatal Screening

We assumed that, with an enhanced prenatal screening program, the proportion of HIV-infected mothers seeking prenatal care who consented to HIV screening would rise to 95% from the baseline rate of 65%. We varied the 95% rate in sensitivity analysis. The proportion of women who accept HIV testing has been increasing in several locations and may be as high as 91% (65). A program aimed at increasing HIV testing in an inner-city population achieved an acceptance rate of 96% using written information, trained interviewers, and a perinatal psychiatric nurse (50). A similar study yielded 97% voluntary acceptance of screening (49). We assumed that enhanced prenatal screening programs would cause HIV-infected women to consent to screening at the same rates as uninfected women. We assumed that additional counseling to explain the benefits and risks of HIV testing would only be offered to

those mothers who initially declined screening. This additional counseling constitutes the intervention to increase acceptance of prenatal screening. We assumed that rates of seeking prenatal care would not change with an enhanced prenatal screening program.

Women were identified by an enzyme immunoassay (EIA) for HIV antibodies and standard confirmatory tests if the EIA result was positive. HIV-positive women were offered multidrug antiretroviral therapy with two nucleoside reverse transcriptase inhibitors and one protease inhibitor and advised to avoid breastfeeding (4).

Routine Newborn Screening

With a routine newborn screening program, we assumed that all infants would be screened at birth with an EIA, followed by confirmatory tests if the EIA result was positive. If the newborn's confirmatory test results were positive, the newborn's mother was tested, offered antiretroviral therapy, and counseled to avoid breastfeeding. Infants with positive confirmatory test results were tested immediately and at 6 weeks with the polymerase chain reaction (PCR) for HIV-RNA. If an infant's initial PCR test was positive, mothers were advised to avoid breastfeeding (4), and antiretroviral therapy was administered to their infants for 6 weeks. If the confirmatory PCR test result at 6 weeks was positive, the infant's antiretroviral therapy was continued indefinitely; if the result was negative, antiretroviral therapy for the infant was stopped. We assumed that routine screening would cause all newborns to be screened, and all mothers whose infants had positive EIA results would agree to follow-up testing.

Vertical Transmission Rates

To evaluate the programs, we estimated the probability of vertical HIV transmission with and without antiretroviral therapy and with and without breastfeeding. Administration of zidovudine (ZDV) monotherapy to mothers during pregnancy and labor and to infants immediately after birth reduced the vertical HIV transmission rate from 25.5% to 8.3% among women who did not breastfeed (2). A subsequent study of 939 infants showed that abbreviated ZDV regimens could reduce the rate of vertical transmission from 26.6% in the absence of ZDV prophylaxis to 9.3% if initiated within 48 hours of birth (a reduction of 17.3%), and to 6.1% if initiated prenatally (a reduction of 20.5%) (19). Thus, we assumed that antiretroviral therapy initiated after birth would achieve 84.4% (17.3 of 20.5 = 84.4%) of the benefit achieved had it been initiated prenatally.

We assumed that pregnant women were treated with combination therapy including a protease inhibitor and two nucleoside reverse transcriptase inhibitors (4,26,69). A randomized clinical trial of 97 individuals on three different treatment regimens found that this more aggressive therapeutic regimen is more likely than other therapies to suppress serum HIV viral load levels (24). Some analyses have suggested that maternal viral load is strongly associated with the risk of HIV transmission (25,70–74). In one observational study of 92 HIV-infected mothers and 97 infants, no vertical HIV transmission was observed among 63 women with viral load levels <20,000 copies/ml, whereas the transmission rate for women with $\leq 50,000$ copies/ml was 6% (25). The goal of the Pediatrics AIDS Clinical Trial Group is to achieve a 2% transmission rate with new antiretroviral therapy (75). For our base case, we assumed that the vertical transmission rate with new antiretroviral therapy would be 3% (the average of the 0% and 6% values recently observed [25]). This rate is close to those observed in other studies for cases in which viral load was nearly undetectable (70,71); recent evidence from a study of sexual transmission of HIV

provides further evidence of decreased infectivity among subjects who have low viral load (76). To account for uncertainty regarding the exact impact of viral load on transmission rates (70–73,77–81), in sensitivity analyses we considered a wide range of estimates for the effect of antiretroviral drugs on vertical transmission.

We assumed that the increased risk of vertical transmission from breastfeeding was represented by a multiplicative risk ratio. Based on metaanalysis of six prospective studies (18), we assumed that breastfeeding resulted in a relative risk of HIV transmission of 1.66. In the metaanalysis, the transmission proportion was 55:205 among women who ever breastfed, and 253:1567 among women who never breastfed, indicating a risk ratio of $(55:205)/(253:1567) = 1.66$. This estimate is conservative relative to other studies that show risk ratios of 2.25 (82) and 2.55 (83). The increased risk from breastfeeding is often assumed to be 14%, in an additive risk model (18). We considered this possibility in sensitivity analyses.

The vertical transmission probabilities for mothers who did not breastfeed were 3% if antiretroviral therapy was initiated during pregnancy, 26.6% if neither the mother nor the infant received antiretroviral therapy, and $6.7\% = 26.6\% - (0.844 \times [26.6\% - 3\%])$ for abbreviated routines in which only the infant received antiretroviral therapy, and it was initiated postnatally. For mothers who did breastfeed, the vertical transmission rates were multiplied by the 1.66 risk ratio to obtain 5%, 44.2%, 11.1%, corresponding to antiretroviral therapy initiated during pregnancy, no therapy, and therapy initiated after birth, respectively.

Costs

We included the costs of the screening tests (23,32,34), the costs of counseling pregnant women (before testing) as part of enhanced prenatal screening, the costs of counseling for women who received a positive test result or whose infant received a positive test result (23, 32,34), the incremental treatment costs associated with earlier identification of HIV-seropositive newborns and HIV-infected mothers, and the future health care savings for infants saved from HIV infection as a result of the programs (27–31,33) (Table 1). The incremental prenatal counseling cost associated with enhanced prenatal screening was incurred by 35% of the 3.7 million women seeking prenatal care. Incremental treatment costs included incremental costs of baby formula and antiretroviral therapy for mothers and infants (27–31,33). For each HIV infection averted in a newborn, we estimated the monetary savings as the net present lifetime cost of treating a case of pediatric AIDS (27–31) minus the net present value of future lifetime health care costs of

a healthy person born today (37). All costs were expressed in 1997 U.S. dollars using a gross domestic product (GDP) deflator (84), and discounted at 3% (85).

RESULTS

The enhanced prenatal screening program would cause an additional 1.1 million women to be screened annually, would identify 527 HIV-infected women, and would avert 150 newborn infections annually relative to current programs (Table 2). The program would result in 3311 life-years gained (all among newborns). The annual net incremental cost of the program was \$29.4 million (all monetary amounts are given in current U.S. dollars). Enhanced prenatal screening cost approximately \$8,900 per life-year gained, or \$195,700 per case of HIV averted.

The newborn screening strategy would screen 3.9 million infants annually and avert 266 newborn HIV infections relative to current programs (Table 2). It would identify 1061 HIV-infected women and 74 HIV-infected infants who could potentially benefit from the early initiation of antiretroviral therapy. Routine newborn screening resulted in 5878 life-years gained (all among newborns). The annual net cost of the program was \$40.9 million (Table 2). Routine newborn screening cost approximately \$7,000 per life-year gained, or \$153,600 per case of HIV averted.

The benefits of routine newborn screening are diminished if the improved level of voluntary prenatal screening has already been achieved; in this situation, routine screening would avert an additional 135 infections per year and would result in 2975 life-years gained, with expenditures of \$10,600 per life-year gained (Table 2). Even if enhanced prenatal screening is in place, approximately 8% of HIV-infected women (or 540 women)

TABLE 2. Summary of annual screening benefits and costs

Costs and benefits	Enhanced prenatal screening ^a	Routine newborn screening	
		Without enhanced prenatal screening ^a	With enhanced prenatal screening already in place ^b
HIV infections averted	150	266	135
Life years gained			
Newborns	3311	5878	2975
Total	3311	5878	2975
Total costs	\$29,354,000	\$40,910,000	\$31,663,000
Marginal cost per life year gained	\$8,900	\$7,000	\$10,600
Marginal cost per HIV infection averted	\$195,700	\$153,600	\$234,800

^a Incremental costs and benefits compared to the status quo.

^b Incremental costs and benefits that accrue from routine newborn screening when enhanced prenatal screening is already in place.

Amounts shown in U.S. dollars.

would not know their HIV status, and they and their infants could thus benefit from routine newborn screening. The routine newborn screening program would identify 537 of 540 HIV-seropositive infants born to these women.

Details of the annual costs and savings associated with each strategy (Table 3) reveal that the cost of treating newly identified mothers comprises approximately one half to three fourths of the total screening and treatment costs for each program.

Sensitivity Analysis

We performed extensive one-way sensitivity analyses on key model parameters. Ranges considered are shown in Table 1. In all cases, the cost-effectiveness ratios were below \$36,000 per life-year gained. Results for parameters to which results were sensitive are shown in Table 4. Our model was not sensitive to other parameters in one-way sensitivity analyses.

Because of uncertainty in the estimates of the risk of HIV transmission from breastfeeding, we considered the possibility that the increased risk of vertical transmission due to breastfeeding is best represented by an additive model rather than a multiplicative model. When we assumed that breastfeeding increased the transmission risk by 14% (18), enhanced prenatal screening cost \$9,600 per life-year gained, while routine newborn screening cost \$7,300 per life-year gained. If enhanced prenatal

screening was already in place, routine newborn screening would cost \$11,500 per life-year gained.

We performed two-way sensitivity analyses on key factors. In the base case, we assumed that 80% of HIV-infected women seek care, and that counseling costs \$12.35 per woman, resulting in a cost-effectiveness ratio of \$8,900 per life-year gained. If 95% of HIV-infected mothers seek prenatal care (the same proportion as in the general population), and counseling costs \$10 per woman, the cost-effectiveness ratio is \$7,000 per life-year gained, or \$154,600 per infection averted (Table 5). If only 50% of HIV-infected women seek prenatal care, and counseling costs \$30 per woman, then the cost-effectiveness ratio rises to \$24,000 per life-year gained, or \$530,400 per infection averted.

Health benefits of routine newborn screening are attained primarily through the avoidance of breastfeeding and the administration of antiretroviral therapy to infants after birth. Even for moderate breastfeeding relative-risk ratios or small benefits associated with postnatal antiretroviral therapy, a program of routine newborn screening is likely to cost <\$50,000 per life-year gained. If there is no benefit to postpartum ZDV, then the incremental cost of routine newborn screening programs relative to the status quo is \$54,500 per life-year gained, and \$73,300 per life-year gained if enhanced prenatal screening is already implemented (Fig. 2). Although the proportion of HIV-infected women who breastfeed is likely to be low (38), it may vary among different populations (56). As the proportion of women who would breastfeed in the

TABLE 3. Annual costs and savings (in millions of U.S. dollars)

Annual costs and savings	Enhanced prenatal screening ^a	Routine newborn screening	
		Without enhanced prenatal screening ^a	With enhanced prenatal screening already in place ^b
Costs			
Screening by enzyme immunoassay	5.55	19.50	19.50
Confirmatory tests	0.58	2.50	2.50
Tests with polymerase chain reaction	0.14	0.28	0.15
Pretest counseling ^c	15.99	0.00	0.00
Posttest counseling ^d	0.39	0.42	0.42
Treatment of newborns	0.73	3.06	1.54
Infant formula	0.41	0.82	0.41
Treatment of mothers	26.92	52.47	26.45
Subtotal	50.83	79.10	50.97
Savings			
Health care costs avoided	(21.48)	(38.14)	(19.31)
Total	29.35	40.91	31.66

^a Incremental costs and savings compared to the status quo.

^b Incremental costs and savings that accrue from routine newborn screening when enhanced prenatal screening is already in place.

^c Represents additional prenatal counseling given to pregnant women seeking prenatal care who did not consent to HIV screening in the absence of enhanced prenatal screening.

^d Counseling for mothers who had a positive test result or whose infant had a positive test result.

TABLE 4. Summary of one-way sensitivity analyses for parameters to which results were sensitive

	Range considered		Cost per life-year gained ^a	
	Minimum value	Maximum value	CE at minimum value	CE at maximum value
Enhanced prenatal screening				
Probability of vertical transmission with antiretroviral therapy during pregnancy, and with no breastfeeding	0%	8.5%	\$7,500	\$12,300
Proportion of HIV-infected women who are aware of their status prior to pregnancy	25%	90%	\$5,000	\$24,900
Proportion of HIV-infected mothers who seek prenatal care	25%	95%	\$24,000	\$8,100
Proportion of mothers seeking prenatal care who consent to HIV screening, without enhanced prenatal screening	25%	90%	\$8,500	\$12,300
Proportion of mothers seeking prenatal care who consent to HIV screening, with enhanced prenatal screening	70%	95%	\$33,000	\$8,900
Adherence with antiretroviral therapy during pregnancy	50%	95%	\$9,700	\$8,800
Proportion of mothers who comply with no-breastfeeding recommendation	10%	99%	\$9,100	\$8,900
Breastfeeding rates among HIV-infected women who are unaware of their status and aware of their status, respectively ^b	5%, 0.3%	30%, 2%	\$11,700	\$8,900
Routine newborn screening without enhanced prenatal screening				
Breastfeeding relative-risk ratio	1.00	2.00	\$10,500	\$5,700
Proportion of HIV-infected women who are aware of their status prior to childbirth	84%	95%	\$7,000	\$15,600
Proportion of mothers who comply with no-breastfeeding recommendation	10%	99%	\$7,500	\$7,000
Breastfeeding rates among HIV-infected women who are unaware of their status and aware of their status, respectively ^b	5%, 0.3%	30%, 2%	\$9,800	\$7,000
Risk reduction benefit of antiretroviral therapy after birth	10%	100%	\$35,200	\$5,500

^a All numbers are rounded to the nearest \$100 U.S. All numbers are measured incremental to the status quo.

^b The numbers were varied simultaneously so that the ratio of the rates remained constant.

absence of counseling increases, the newborn screening strategy becomes more cost effective (Fig. 3). Routine newborn screening is most expensive when HIV prevalence is low among women who give birth and acceptance of prenatal screening is high. However, in all cases considered, the cost per life-year gained was <\$25,000 (Fig. 4). Similarly, two-way sensitivity analysis on the benefits to newborns of antiretroviral therapy and adherence to such therapy revealed that when therapy is only slightly effective in reducing transmission (10% risk reduction) but adherence is high (100%), the cost per life-year gained is \$35,200.

DISCUSSION

We assessed the cost effectiveness of two programs that can reduce vertical HIV transmission. We estimated that, compared with current practices, enhanced prenatal screening would avert 150 infections in infants annually at a cost of \$8,900 per life-year gained. Routine HIV screening of newborns nationwide would avert 266 infections in infants annually at a cost of \$7,000 per life-year gained. When enhanced prenatal screening is already in place, routine screening of newborns would have a net cost of \$10,600 per life-year gained. More

TABLE 5. Cost effectiveness of enhanced prenatal screening as a function of proportion of HIV-infected mothers receiving prenatal care and incremental counseling cost^a

Percentage of HIV-infected mothers receiving prenatal care	Incremental counseling cost per women					
	\$10		\$20		\$30	
	Cost per life-year gained	Cost per infection averted	Cost per life-year gained	Cost per infection averted	Cost per life-year gained	Cost per infection averted
50	\$11,500	\$254,300	\$17,800	\$392,300	\$24,000	\$530,400
65	\$9,300	\$205,700	\$14,100	\$311,900	\$19,000	\$418,100
80	\$7,900	\$175,400	\$11,900	\$261,700	\$15,800	\$348,000
95	\$7,000	\$154,600	\$10,300	\$227,300	\$13,600	\$300,000

^a All numbers are rounded to the nearest \$100 U.S.

All numbers are measured incremental to the status quo. All amounts are given in U.S. dollars.

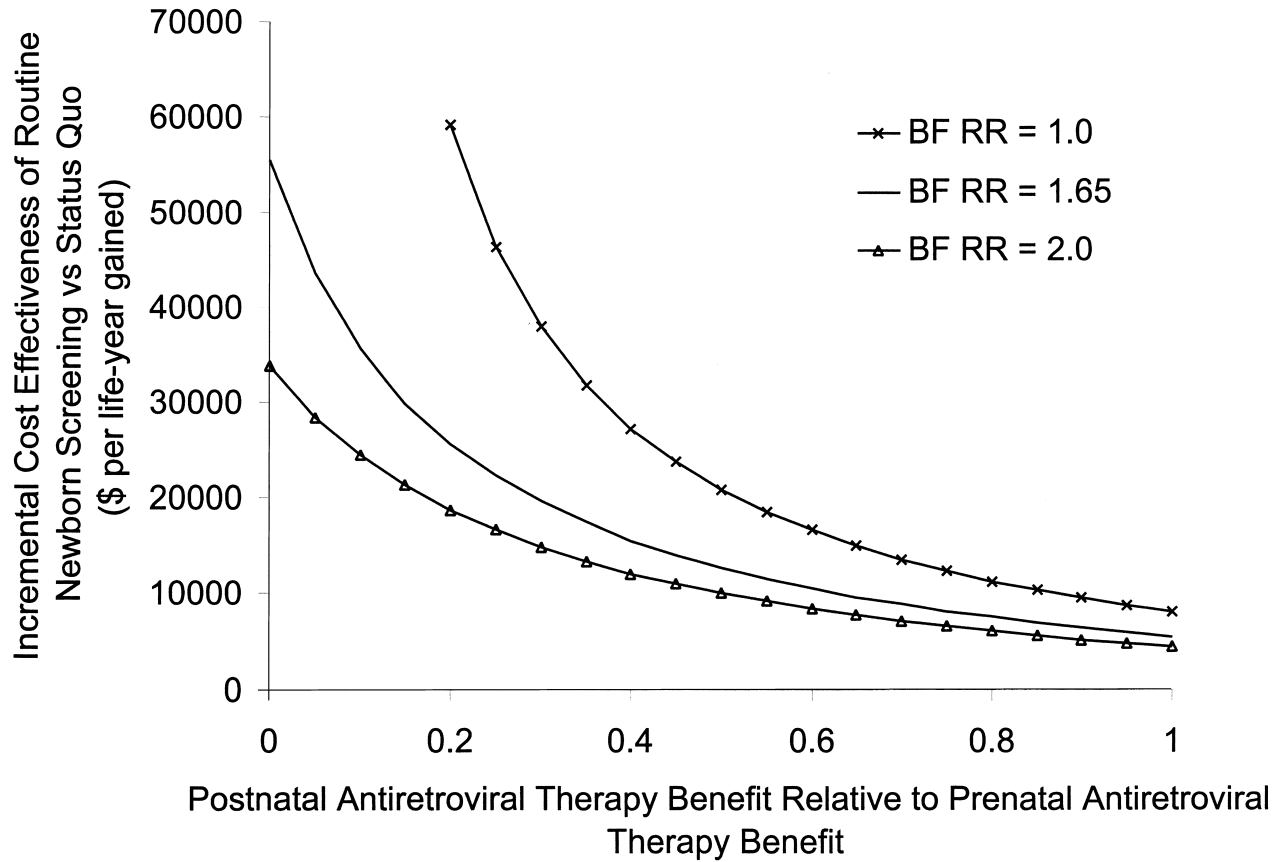


FIG. 2. Effect of the breastfeeding (BF) relative-risk ratio (RR) and the benefit of postnatal antiretroviral therapy on the cost effectiveness of routine newborn screening relative to the status quo. The benefit of postnatal antiretroviral therapy is measured relative to the benefit that could be achieved if antiretroviral drugs were initiated prenatally and continued in the postpartum period; we varied this benefit from 0% (no benefits associated with postnatal therapy) to 100% (all benefits of both prenatal and postnatal therapy achieved when therapy is initiated postnatally only); our base-case analysis assumed that postnatal therapy resulted in 0.25 of the benefit of prenatal therapy (arrow). The lines in the graph represent different breastfeeding RR levels; an RR of 1.0, corresponding to no increased risk of HIV transmission from breastfeeding; an RR of 1.66 (base-case estimate); and an RR of 2.0.

than half of the costs were incurred by the mothers, even though we assumed that health benefits accrued only to the infants. Our analysis shows newborn screening to be cost effective in part because we incorporated recent evidence that suggests that ZDV prophylaxis, begun at birth rather than during pregnancy, reduces HIV transmission from 26.6% to 9.3% (19).

Medical interventions that cost less than \$50,000 per life-year or quality-adjusted life-year (QALY) gained are commonly accepted (86). For example, the CDC recommends that acute-care hospitals and associated clinics offer voluntary screening to patients aged 15 to 54 years if HIV prevalence in the patient population is at least 1% (87). Owens et al. (88) showed that the cost per QALY gained of such a screening program is approximately \$55,000. As another example, administration of azithromycin for prophylaxis of *Mycobacterium avium* infection, a recommended intervention, has a cost-effec-

tiveness ratio of \$47,200/QALY gained (89). The cost-effectiveness ratios we calculated for the enhanced prenatal screening and newborn screening programs are significantly lower than these values. Indeed, the cost of counseling each woman as part of the enhanced prenatal screening program would have to be almost ten times as high as we assumed (\$117.52 versus \$12.35) before the cost per life-year gained by such a program reaches \$50,000.

Previous analyses have suggested that policies encouraging voluntary HIV screening of pregnant women are cost effective (90–93), but we know of no previous studies that have provided a comprehensive analysis of the cost effectiveness of routine newborn HIV screening relative to other options, including enhanced prenatal screening. One analysis examined the cost effectiveness of rapid testing of unregistered women presenting for labor and concluded that such a measure would be cost

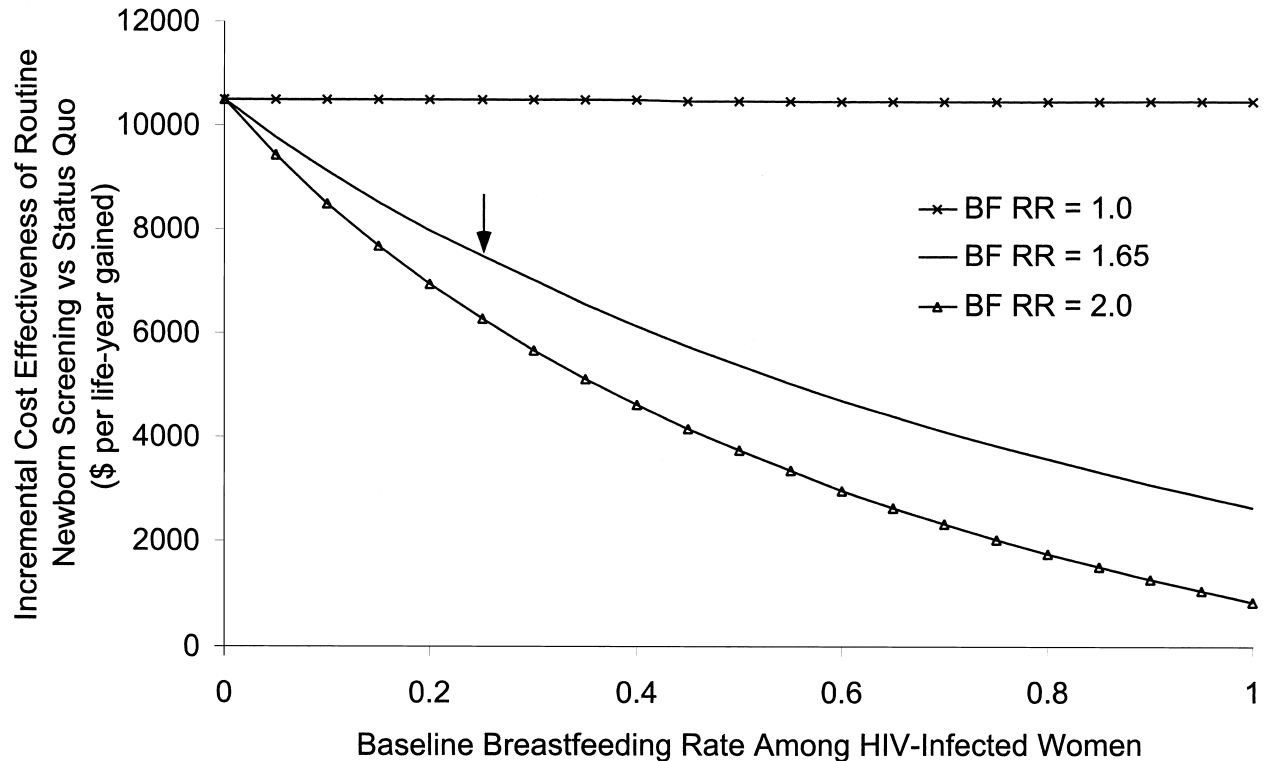


FIG. 3. Effect of the baseline breastfeeding (BF) rate and the breastfeeding relative-risk ratio (RR) on the cost effectiveness of routine newborn screening relative to the status quo. The *three lines* represent the breastfeeding RR, which are varied as shown in Figure 2. When there is no increased risk associated with breastfeeding (that is, when the RR is 1.0), then the cost effectiveness of routine newborn screening is not affected by the baseline rate of breastfeeding.

saving (94). This analysis yielded somewhat more favorable results than ours did because the authors did not include the costs associated with screening all women (only unregistered women were screened in their model) nor with treating mothers whose HIV status was identified by the testing strategy, and because they assumed a much higher prevalence of HIV in the base case (5% compared with 0.17%) than we used. Several strategies aimed at reducing vertical transmission in South Africa have also been examined and have been found to be cost effective or cost saving (95). A recent study found that mandatory prenatal screening would be cost saving relative to voluntary prenatal screening, or to no screening, but the study may have overestimated the savings associated with prevention of an HIV infection (96).

One effect of both screening programs is to inform HIV-infected mothers of their serostatus earlier than they would have been informed otherwise. The resulting costs and benefits have been ignored in some previous analyses of programs to reduce vertical transmission rates (94). An additional health benefit of the screening programs that we did not include in our analysis is reduced HIV transmission from HIV-infected mothers to people other than their newborns. Inclusion of this benefit would

increase the health benefits of the programs without changing the costs and thus make the programs appear more cost effective (32, 34). An alternative strategy that we did not consider is targeted newborn screening for women who refuse newborn screening. Such a program would be at least as cost effective as routine newborn screening when enhanced prenatal screening is already in place but would raise ethical concerns.

Our analysis has several limitations. Our analysis required assumptions about the relative risk of HIV transmission associated with breastfeeding, the reduced transmission benefits accruing from antiretroviral therapy initiated at birth, the baseline rate of breastfeeding among HIV-infected women, and the rate at which HIV-infected women receive prenatal care and accept HIV screening as part of prenatal-care programs. Current research may help to remove some of the uncertainty from our estimates. However, our sensitivity analyses revealed that, even under conservative assumptions about these factors, both routine newborn screening and enhanced prenatal screening remain cost effective. We assumed that HIV-infected and uninfected women would accept screening at the same rates. If HIV-infected women accept enhanced prenatal screening at lower rates than uninfected

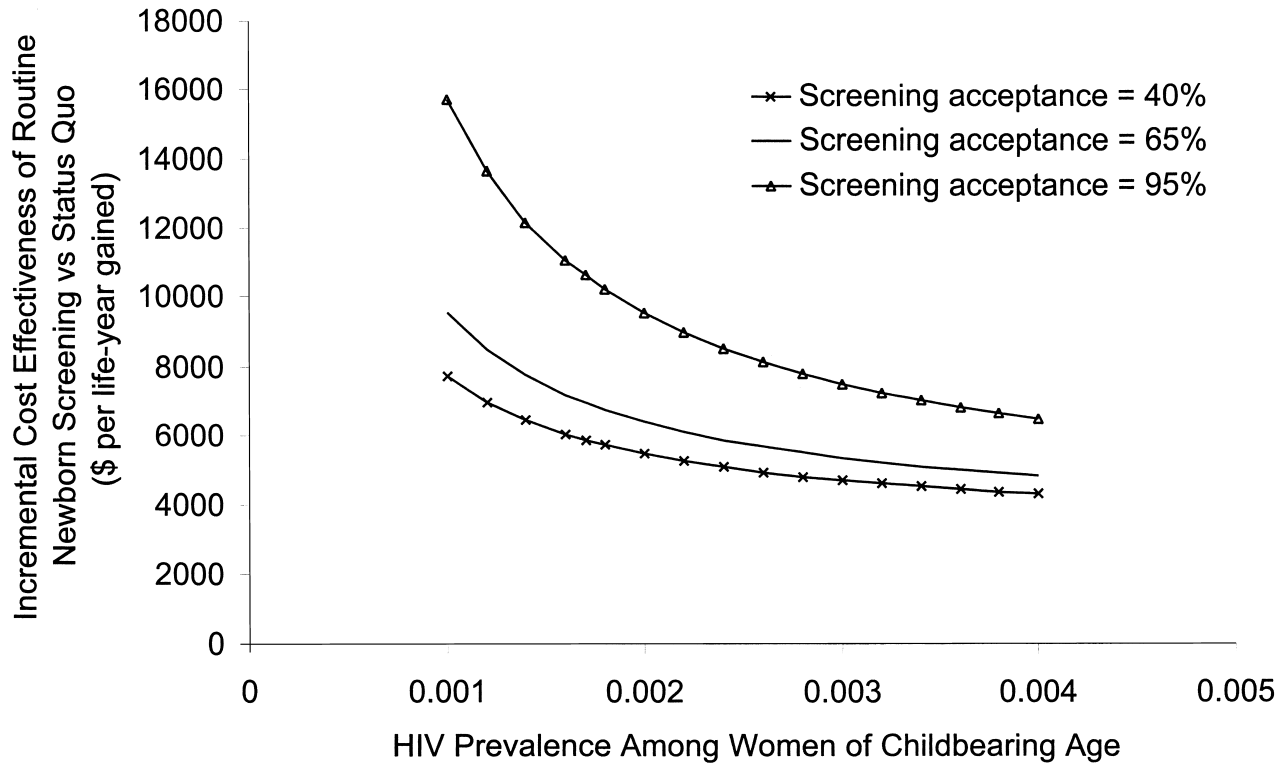


FIG. 4. Effect of the proportion of HIV-infected women who are unaware of their status and consent to HIV screening as part of prenatal care and of the prevalence of HIV among women of childbearing age on the cost effectiveness of routine newborn screening relative to the status quo. We varied HIV prevalence between 0.001 and 0.004, and we considered acceptance rates of prenatal screening of 95%, 65% (base-case estimate), and 40%.

women, voluntary prenatal screening will be less cost effective than we estimated. We did not consider the impact of cesarean section, which can reduce the rate of vertical transmission (97–99). We also did not consider the effect of other clinical and biologic factors, including viral load, which may contribute to vertical transmission (70–74,100–102).

Policy formulation necessitates consideration of not only health and economic outcomes, but also legal, political, and ethical concerns (6,103). Our analysis has not addressed the effect of a policy of routine newborn HIV screening on the civil rights of mothers or infants. Infants' advocates argue that such policies protect the health-care rights of vulnerable HIV-infected newborns who are unable to make their own treatment decisions (10). Mothers' advocates contend that such policies violate the privacy rights of women by testing for a medical condition without their consent (11). Legal decisions may favor infants who are unable to accept or refuse testing (6). This important debate is beyond the scope of our analysis here.

The question of mandating routine screening of newborns has been brought before legislators at the federal level and in many states in the United States (9,12,16).

Our analysis indicates the both newborn routine screening and enhanced prenatal screening are cost effective. A program to screen newborns would likely avert more HIV infections than a program of enhanced prenatal screening could. With prenatal screening, however, infants of HIV-infected women receive the full benefit of antiretroviral therapy in reducing HIV transmission, and the women maintain their right to determine whether they are tested for HIV. These issues deserve consideration along with the costs and benefits of alternative programs.

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REFERENCES

1. American Academy of Pediatrics. Committee on Pediatric AIDS. Surveillance of pediatric HIV infection. *Pediatrics* 1998;101:315–9.

2. Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. *N Engl J Med* 1994;331:1173–80.
3. U.S. Centers for Disease Control and Prevention. Update: perinatally acquired HIV/AIDS—United States, 1997. *MMWR Morb Mortal Wkly Rep* 1997;46:1086–92.
4. U.S. Centers for Disease Control and Prevention. Public Health Service Task Force recommendations for the use of antiretroviral drugs in pregnant women infected with HIV-1 for maternal health and for reducing perinatal HIV-1 transmission in the United States. *MMWR Morb Mortal Wkly Rep* 1998;47:1–30.
5. Sweeney PA, Fleming PL, Karon JM, et al. A minimum estimate of the number of living HIV infected persons confidentially tested in the United States [abstract No. I-16]. Presented at the Interscience Conference on Antimicrobial Agents and Chemotherapy, Toronto, Ontario, Canada, 1997.
6. Grimes RM, Richards EP, Helfgott AW, et al. Legal considerations in screening pregnant women for human immunodeficiency virus. *Am J Obstet Gynecol* 1999;180:259–64.
7. Limata C, Schoen EJ, Cohen D, et al. Compliance with voluntary prenatal HIV testing in a large health maintenance organization (HMO). *J Acquir Immune Defic Syndr Hum Retrovirol* 1997;15:126–30.
8. American Council on Obstetrics and Gynecology. HIV tests urged for all pregnant women: ob-gyns launch campaign for universal HIV screening. Available at: http://www.acog.org/from_home/publications/press_releases/nr05-23-00-2.htm. Accessed September 28, 2000.
9. Bateman DA, Cooper A, Abrams EJ. Newborn human immunodeficiency testing in New York: a legislative quandary. *Arch Pediatr Adolesc Med* 1995;149:581–2.
10. Crawford C. Protecting the weakest link: a proposal for universal, unblinded pediatric HIV testing, counselling and treatment. *J Community Health* 1995;20:125–41.
11. Dumois AO. The case against mandatory newborn screening for HIV antibodies. *J Community Health* 1995;20:143–59.
12. Fisher I. Bill would order AIDS-virus testing to protect babies. *New York Times* 1996;May 1:A1.
13. Getchell JP, Hausler WJ, Ramirez MT, et al. HIV screening of newborns. *Biochem Med Metab Biol* 1993;49:143–8.
14. Grady GF. HIV mass screening of infants and mothers: historical, technical, and practical issues. *Acta Pediatr* 1994;400(Suppl):39–42.
15. Harrigan P. Routine testing of HIV status of babies. *Lancet* 1995;345:1102.
16. Sontag D. HIV testing for newborns debated anew. *New York Times* 1997;Feb 10:A1,B8.
17. Connor E, McSherry G. Treatment of HIV infection in infancy. *Clin Perinatol* 1994;21:163–77.
18. Dunn DT, Newell ML, Ades AE, et al. Risk of human immunodeficiency virus type 1 transmission through breastfeeding. *Lancet* 1992;340:585–8.
19. Wade NA, Birkhead GS, Warren BL, et al. Abbreviated regimens of zidovudine prophylaxis and perinatal transmission of the human immunodeficiency virus. *N Engl J Med* 1998;339:1409–14.
20. Minkoff H, Willoughby A. Pediatric HIV disease, zidovudine in pregnancy, and unblinding heelstick surveys: reframing the debate on prenatal HIV testing. *JAMA* 1995;274:1165–8.
21. Wilfert CM. Prevention of perinatal transmission of human immunodeficiency virus: a progress report two years after completion of AIDS clinical trials group trial 076. *Clin Infect Dis* 1996;23:438–41.
22. American Medical Association. The Journal of the American Medical Association HIV/AIDS Information Center. AMA Ethical Opinion on HIV/AIDS Issues. 1998. Available at: <http://www.ama-assn.org/special/hiv/policy/amapol.htm>. Accessed September 28, 2000.
23. Owens DK, Holodniy M, McDonald TW, et al. A meta-analytic evaluation of the polymerase chain reaction for the diagnosis of HIV infection in infants. *JAMA* 1996;275:1342–8.
24. Gulick RM, Mellors JW, Havlir D, et al. Treatment with indinavir, zidovudine, and lamivudine in adults with human immunodeficiency virus infection and prior antiretroviral therapy. *N Engl J Med* 1997;337:734–9.
25. Dickover RE, Garratty EM, Herman SA, et al. Identification of levels of maternal HIV-1 RNA associated with risk of perinatal transmission: effect of maternal zidovudine treatment on viral load. *JAMA* 1996;275:599–605.
26. Minkoff H, Augenbraun M. Antiretroviral therapy for pregnant women. *Am J Obstet Gynecol* 1997;176:478–89.
27. *Drug Topics Red Book*. Montvale, New Jersey: Medical Economics, 1997.
28. Barnhart HX, Caldwell MB, Thomas P, et al. Natural history of human immunodeficiency virus disease in perinatally infected children: an analysis from the pediatric spectrum of disease project. *Pediatrics* 1996;97:710–6.
29. Gable CB, Tierce JC, Simison D, et al. Costs of HIV+/AIDS at CD4+ counts disease stages based on treatment protocols. *J Acquir Immune Defic Syndr Hum Retrovirol* 1996;12:413–20.
30. Havens PL, Cuene BE, Holtgrave DR. Lifetime cost of care for children with human immunodeficiency virus infection. *Pediatr Infect Dis J* 1997;16:607–10.
31. Hsia DC, Fleishman JA, East JA, et al. Pediatric human immunodeficiency virus infection: recent evidence on the utilization and costs of health services. *Arch Pediatr Adolesc Med* 1995;149:489–96.
32. Owens DK, Harris RA, Scott PM, et al. Screening surgeons for HIV infection: a cost-effectiveness analysis. *Ann Intern Med* 1995;122:641–52.
33. Holtgrave DR, Pinkerton SD. Updates of cost of illness and quality of life estimates for use in economic evaluations of HIV prevention programs. *J Acquir Immune Defic Syndr Hum Retrovirol* 1997;16:54–62.
34. Brandeau ML, Owens DK, Sox CH, et al. Screening women of childbearing age for human immunodeficiency virus: a model-based policy analysis. *Management Sci* 1993;39:72–92.
35. Cook RL, Steiner BD, Smith AC, et al. Are medical students ready to provide HIV-prevention counseling? *Acad Med* 1998;73:342–6.
36. Sorin MD, Tesoriero JM, LaChance-McCulloch ML. Correlates of acceptance of HIV testing and post-test counseling in the obstetrical setting. *AIDS Educ Prev* 1996;8:72–85.
37. *Statistical Abstract of the United States*. Washington, DC: U.S. Department of Commerce, 1997.
38. Bertolli JM, Hsu HW, Frederick T, et al. Breastfeeding among HIV-infected women, Los Angeles and Massachusetts, 1988–1993 [abstract No. We.C.3583]. Presented at the XI International Conference on AIDS, Vancouver, British Columbia, Canada, 1996.
39. Barbacci M, Repke JT, Chaison RE. Routine prenatal screening for HIV infection. *Lancet* 1991;337:709–11.
40. Elam-Evans LD, Adams MM, Gargiullo PM, et al. Trends in the percentage of women who received no prenatal care in the United States, 1980–1992: contributions of the demographic and risk effects. *Obstet Gynecol* 1996;87:575–80.
41. York R, Grant C, Gibeau A, et al. A review of problems of universal access to prenatal care. *Nursing Clin North Am* 1996;31:279–92.
42. U.S. Centers for Disease Control and Prevention. Adequacy of prenatal care utilization—California, 1989–1994. *MMWR Morb Mortal Wkly Rep* 1996;45:653–6.
43. Lewis CT, Mathews TJ, Heuser RL. Prenatal care in the United States, 1980–94. *Vital Health Stat* 1996;54:1–17.
44. Brown SS. Drawing women into prenatal care. *Family Plann Perspect* 1989;21:73–80.
45. Piper JM, Mitchel EF, Ray WA. Expanded Medicaid coverage for

- pregnant women to 100 percent of the federal poverty level. *Am J Prev Med* 1994;10:97-102.
46. Haas JS, Udvarhelyi S, Morris CN, et al. The effect of providing health coverage to poor uninsured pregnant women in Massachusetts. *JAMA* 1993;269:87-91.
 47. Carusi D, Learman LA, Posner SF. Human immunodeficiency virus test refusal in pregnancy: a challenge to voluntary testing. *Obstet Gynecol* 1998;91:540-5.
 48. Turner BJ, Markson L, Hauck W, et al. Prenatal care of HIV-infected women: analysis of a large New York state cohort. *J Acquir Immune Defic Human Retrovirol* 1995;9:371-8.
 49. Lindsay MK, Adefris W, Peterson HB, et al. Determinants of acceptance of routine human immunodeficiency virus testing in an inner city prenatal population. *Obstet Gynecol* 1991;78:678-80.
 50. Lindsay MK, Peterson HB, Feng TI, et al. Routine antepartum human immunodeficiency virus infection screening in an inner-city population. *Obstet Gynecol* 1989;74:289-94.
 51. Brent NB, Redd B, Dworetz A, et al. Breast-feeding in a low-income population. *Arch Pediatr Adolesc Med* 1995;149:798-803.
 52. Freed GL, Jones TM, Schanler RJ. Perinatal determination of demographic and attitudinal factors regarding feeding practice in an indigent population. *Am J Perinatol* 1992;9:420-4.
 53. Schwartz JB, Popkin BM, Tognetti J, et al. Does WIC participation improve breast-feeding practices? *Am J Public Health* 1995;85:729-31.
 54. Grossman LK, Harter C, Sachs L, et al. The effect of postpartum lactation counseling on the duration of breast-feeding in low-income women. *Am J Dis Child* 1990;144:471-4.
 55. Kistin N, Benton D, Rao S, et al. Breast-feeding rates among black urban low-income women: effect of prenatal education. *Pediatrics* 1990;86:741-6.
 56. Paltiel AD, Kaplan EH. The cost-effectiveness of HIV testing: accounting for differential participation rates. *Med Decision Making* 1997;17:490-5.
 57. U.S. Centers for Disease Control and Prevention. Success in implementing public health service guidelines to reduce perinatal transmission of HIV - Louisiana, Michigan, New Jersey, and South Carolina, 1993, 1995, and 1996. *MMWR Morb Mortal Wkly Rep* 1998;47:688-91.
 58. Kogan MD, Martin JA, Alexander GR, et al. The changing pattern of prenatal care utilization in the United States, 1981-1995, using different prenatal care indices. *JAMA* 1998;279:1623-8.
 59. Wortley PM, Chu SY, Diaz T, et al. HIV testing patterns: where, why, and when were persons with AIDS tested for HIV? *AIDS* 1995;9:487-92.
 60. Wiznia AA, Crane M, Lambert G, et al. Zidovudine use to reduce perinatal HIV type 1 transmission in an urban medical center. *JAMA* 1996;275:1504-6.
 61. Fiscus SA, Adimora AA, Schoenbach VJ, et al. Trends in human immunodeficiency virus (HIV) counseling, testing, and antiretroviral treatment of HIV-infected women and perinatal transmission in North Carolina. *J Infect Dis* 1999;180:99-105.
 62. Frederick T, Mascola L, Tucker D, et al. Breastfeeding and disease progression among perinatally HIV-infected children in Los Angeles County [abstract No. 720]. Presented at the IV Conference on Retroviruses and Opportunistic Infections, Washington DC, 1997.
 63. Simpson WM, Johnstone FD, Goldberg DJ, et al. Antenatal HIV testing: assessment of a routine voluntary approach. *BMJ* 1999;318:1660-1.
 64. Wilson TE, Minkoff H. Mandatory HIV testing of infants and rates of follow-up care. *Am J Public Health* 1999;89:1583.
 65. Wortley PM, Lindgren ML, Fleming PL. A four state evaluation of ZDV use to reduce perinatal HIV transmission [abstract No. 246]. Presented at the V Conference on Retroviruses and Opportunistic Infections, Chicago, 1998.
 66. Haubrich RH, Little SJ, Currier JS, et al. The value of patient-reported adherence to antiretroviral therapy in predicting virologic and immunologic response. California Collaborative Treatment Group. *AIDS* 1999;13:1099-1107.
 67. Culnane M, Fowler M, Lee SS, et al. Lack of long-term effects of in utero exposure to zidovudine among uninfected children born to HIV-infected women. Pediatric AIDS Clinical Trials Group Protocol 219/076 Teams. *JAMA* 1999;281:151-7.
 68. Sperling RS, Shapiro DE, McSherry GD, et al. Safety of the maternal-infant zidovudine regimen utilized in the Pediatric AIDS Clinical Trial Group 076 Study. *AIDS* 1998;12:1805-13.
 69. Carpenter CC, Cooper DA, Fischl MA, et al. Antiretroviral therapy in adults: updated recommendations of the International AIDS Society-USA Panel. *JAMA* 2000;283:381-90.
 70. Mofenson LM, Lambert JS, Stiehm ER, et al. Risk factors for perinatal transmission of human immunodeficiency virus type 1 in women treated with zidovudine. Pediatric AIDS Clinical Trials Group Study 185 Team. *N Engl J Med* 1999;341:385-93.
 71. Garcia PM, Kalish LA, Pitt J, et al. Maternal levels of plasma human immunodeficiency virus type 1 RNA and the risk of perinatal transmission. Women and Infants Transmission Study Group. *N Engl J Med* 1999;341:394-402.
 72. Mock PA, Shaffer N, Bhadrakom C, et al. Maternal viral load and timing of mother-to-child HIV transmission, Bangkok, Thailand. Bangkok Collaborative Perinatal HIV Transmission Study Group. *AIDS* 1999;13:407-14.
 73. Shaffer N, Roongpisuthipong A, Siriwasin W, et al. Maternal virus load and perinatal human immunodeficiency virus type 1 subtype E transmission, Thailand. Bangkok Collaborative Perinatal HIV Transmission Study Group. *J Infect Dis* 1999;179:590-9.
 74. Shapiro DE, Sperling RS, Mandelbrot L, et al. Risk factors for perinatal human immunodeficiency virus transmission in patients receiving zidovudine prophylaxis. Pediatric AIDS Clinical Trials Group protocol 076 Study Group. *Obstet Gynecol* 1999;94:897-908.
 75. Minkoff H, O'Sullivan MJ. The case for rapid HIV testing during labor. *JAMA* 1998;279:1743.
 76. Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. *N Engl J Med* 2000;342:921-9.
 77. Cao Y, Krogstad P, Korber BT, et al. Maternal HIV-1 viral load and vertical transmission of infection: the Ariel Project for the prevention of HIV transmission from mother to infant. *Nat Med* 1997;3:549-52.
 78. Burchett SK, Kornegay J, Pitt J, et al. Assessment of maternal plasma HIV viral load as a correlate of vertical transmission [abstract LB3, pp 161]. Presented at the III Conference on Retroviruses and Opportunistic Infections, Washington, DC, 1996.
 79. Mayaux MJ, Dussaix E, Isopet J, et al. Maternal virus load during pregnancy and mother-to-child transmission of human immunodeficiency virus type 1: the French perinatal cohort studies. SEROGEST Cohort Group. *J Infect Dis* 1997;175:172-5.
 80. Melvin AJ, Burchett SK, Watts DH, et al. The effect of pregnancy and zidovudine therapy on viral load in HIV-1-infected women. *J Acquir Immune Defic Syndr Hum Retrovirol* 1997;13:232-6.
 81. Thea DM, Steketee RW, Pliner V, et al. The effect of maternal viral load on the risk of perinatal transmission of HIV-1. New York City Perinatal HIV Transmission Collaborative Study Group. *AIDS* 1997;11:437-44.
 82. The European Collaborative Study. Natural history of vertically acquired human immunodeficiency virus-1 infection. *Pediatrics* 1994;94:815-9.
 83. The Italian Register for HIV Infection in Children. Human immunodeficiency virus type I infection and breast milk. *Acta Paediatr* 1994;400(Suppl):51-8.
 84. National Aeronautics and Space Administration. Parametric cost estimate reference manual: inflation calculator. 1998. Available at: <http://www.jsc.nasa.gov/bu2/inflate.html>. Accessed September 28, 2000.

85. Gold MR, Seigel JE, Russell LB, Weinstein MC, eds. *Cost-Effectiveness in Health and Medicine*. New York: Oxford University Press, 1996.
86. Owens DK. Interpretation of cost-effectiveness analyses [editorial]. *J Gen Intern Med* 1998;13:716–7.
87. U.S. Centers for Disease Control and Prevention. Recommendations for HIV testing services for inpatients and outpatients in acute-care hospital settings. Technical guidance on HIV counseling. *MMWR Morb Mortal Wkly Rep* 1993;42:1–17.
88. Owens DK, Nease RF, Harris RA. Cost-effectiveness of HIV screening in acute care settings. *Arch Intern Med* 1996;156:394–404.
89. Bayoumi AM, Redelmeier DA. Preventing Mycobacterium avium complex in patients who are using protease inhibitors: a cost-effectiveness analysis. *AIDS* 1998;12:1503–12.
90. Ecker JL. The cost-effectiveness of human immunodeficiency virus screening in pregnancy. *Am J Obstet Gynecol* 1996;174:16–21.
91. Gorsky RD, Farnham PG, Straus WL, et al. Preventing perinatal transmission of HIV—costs and effectiveness of a recommended intervention. *Public Health Rep* 1996;111:335–41.
92. Mauskopf JA, Paul JE, Wichman DS, et al. Economic impact of treatment of HIV-positive pregnant women and their newborns with zidovudine. *JAMA* 1996;132–8.
93. Postma MJ, Beck EJ, Mandalia S, et al. Universal HIV screening of pregnant women in England: cost effectiveness analysis. *BMJ* 1999;318:1656–60.
94. Stringer JS, Rouse DJ. Rapid testing and zidovudine treatment to prevent vertical transmission of human immunodeficiency virus in unregistered parturients: a cost-effectiveness analysis. *Obstet Gynecol* 1999;94:34–40.
95. Soderlun N, Zwi K, Kinghorn A, et al. Prevention of vertical transmission of HIV: analysis of cost effectiveness of options available in South Africa. *BMJ* 1999;318:1650–6.
96. Immergluck-Cheng L, Cull WL, Schwartz A, et al. Cost-effectiveness of universal compared with voluntary screening for human immunodeficiency virus among pregnant women in Chicago. *Pediatrics* 2000;105:e54. Available at: <http://www.pediatrics.org/cgi/content/full/105/4/e54>. Accessed September 28, 2000.
97. Dunn DT, Newell ML, Mayaux MJ, et al. Mode of delivery and vertical transmission of HIV-1: a review of prospective studies. Perinatal AIDS collaborative transmission studies. *J Acquir Immune Defic Syndr Hum Retrovirol* 1994;7:1064–6.
98. The International Perinatal HIV Group. The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1—a meta-analysis of 15 prospective cohort studies. *N Engl J Med* 1999;340:977–87.
99. The European Mode of Delivery Collaboration. Elective caesarean-section versus vaginal delivery in prevention of vertical HIV-1 transmission: a randomised clinical trial. *Lancet* 1999;353:1035–9.
100. Van Dyke RB, Korber BT, Popek E, et al. The Ariel Project: a prospective cohort study of maternal-child transmission of human immunodeficiency virus type 1 in the era of maternal antiretroviral therapy. *J Infect Dis* 1999;179:319–28.
101. The Italian Collaborative Study on HIV infection in pregnancy. Mother-to-child transmission of human immunodeficiency virus in Italy: temporal trends and determinants of infection. *Hum Reprod* 1999;14:242–6.
102. Simonds RJ, Steketee R, Nesheim S, et al. Impact of zidovudine use on risk and risk factors for perinatal transmission of HIV. Perinatal AIDS Collaborative Transmission Studies. *AIDS* 1998;12:301–8.
103. Bonkovksy FO. Ethical issues in perinatal HIV. *Clin Perinatol* 1994;21:15–28.
104. Gwinn M, Pappaioanou M, George JR, et al. Prevalence of HIV infection in childbearing women in the United States: surveillance using newborn blood samples. *JAMA* 1991;265:1704–8.
105. de Martino M, Balducci M, Galli L, et al. Reduction in mortality with availability of antiretroviral therapy for children with perinatal HIV-1 infection. *JAMA* 2000;284:190–7.

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