Evidence

Études

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Routine prenatal screening for HIV in a low-prevalence setting

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Abstract

Background: The objectives of this study were to assess the effect of British Columbia's June 1994 guidelines for prenatal HIV screening on the rate of maternal–fetal HIV transmission and to estimate the cost-effectiveness of such screening.

Methods: The authors conducted a retrospective review of pregnancy and delivery statistics, HIV screening practices, laboratory testing volume, prenatal and labour management decisions of HIV-positive women, maternal–fetal transmission rates and associated costs.

Results: Over 1995 and 1996, 135 681 women were pregnant and 92 645 carried to term. The rate of HIV testing increased from 55% to 76% of pregnancies on chart review at one hospital between November 1995 and November 1996. On the basis of seroprevalence studies, an estimated 50.2 pregnancies and 34.3 (95% confidence interval 17.6 to 51.0) live births to HIV-positive women were expected. Of 42 identified mother–infant pairs with an estimated date of delivery during 1995 or 1996, 25 were known only through screening. Of these 25 cases, there were 10 terminations, 1 spontaneous abortion and 14 cases in which the woman elected to carry the pregnancy to term with antiretroviral therapy. There was one stillbirth. One instance of maternal–fetal HIV transmission occurred among the 13 live births. The net savings attributable to prevented infections among babies carried to term were $165 586, with a saving per prevented case of $75 266.

Interpretation: A routine offer of pregnancy screening for HIV in a low-prevalence setting reduces the rate of maternal–fetal HIV transmission and may rival other widely accepted health care expenditures in terms of cost-effectiveness.

Résumé

Contexte : Cette étude visait à évaluer l'effet des lignes directrices relatives au dépistage prénatal du VIH adoptées en juin 1994 par la Colombie-Britannique sur le taux de transmission du VIH de la mère au fœtus et à évaluer l'efficacité des coûts du dépistage.

Méthodes : Les auteurs ont procédé à une étude rétrospective des statistiques sur la grossesse et l'accouchement, des pratiques de dépistage du VIH, du volume des tests de laboratoire, des décisions relatives au suivi prénatal et à la prise en charge du travail de femmes infectées par le VIH, des taux de transmission de la mère au fœtus et des coûts connexes.

Résultats : En 1995 et 1996, 135 681 femmes étaient enceintes et 92 645 ont accouché à terme. Un examen des dossiers réalisé à un hôpital entre novembre 1995 et novembre 1996 révèle que le taux des tests de dépistage du VIH est passé de 55 % à 76 % des grossesses. D'après les études de séroprévalence, on estimait attendre 50,2 grossesses et 34,3 (intervalle de confiance à 95 % de 17,6 à 51,0) naissances vivantes chez les femmes infectées par le VIH. Sur 42 paires mère–nourrisson identifiées dont la date prévue d'accouchement se situait en 1995 ou 1996, 25 cas ont été repérés par le dépistage seulement. Parmi ces 25 cas, il y a eu 10 avortements, un avortement spontané et 14 cas où la femme a

décidé de mener la grossesse à terme en suivant une thérapie antirétrovirale. Il y a eu une morti-naissance. Il y a eu un cas de transmission du VIH entre la mère et le fœtus chez les 13 naissances vivantes. L'économie nette attribuable à la prévention de l'infection chez les bébés à terme s'est établie à 165 586 $, et l'économie par cas évité, à 75 266 $.

Interprétation : Offert de routine, le test de dépistage du VIH au cours de la grossesse dans un contexte de faible prévalence réduit la transmission du VIH entre la mère et le fœtus et l'efficacité des coûts peut rivaliser avec celle d'autres dépenses de santé généralement acceptées.

Without prophylactic antiretroviral treatment, maternal–fetal HIV transmission has been reported to occur at a rate ranging from 14% to 33% in industrialized countries.[1,2] In British Columbia a rate of 21% has been reported.[3] A multicentre placebo-controlled trial of zidovudine therapy in pregnancy (ACTG 076) showed a relative risk reduction of 67%,[4] a range subsequently verified in cohort studies.[5–7]

The British Columbia Centre for Disease Control (BCCDC) recommended in June 1994 that all pregnant women be offered HIV testing as a routine part of prenatal care.[8] The recommendations included guidelines for appropriate pre- and post-test counselling, and it was advocated that informed consent be obtained before testing. Similar recommendations were published by the US Public Health Service in 1995.[9] In this paper we examine the effect of the BCCDC's recommendations on health care practice, maternal–fetal HIV transmission and costs.

Methods

Most screening and all confirmatory tests for HIV antibody in British Columbia are performed at the Provincial Laboratory. The number of tests requested during the 6 months before and after the issuing of the June 1994 guidelines was monitored. Beginning in 1994, requisitions for HIV testing requested information on whether the test was performed for prenatal screening. Enhanced non-nominal surveillance for HIV[10] was begun in 1995, whereby further information on demographic characteristics was obtained for all patients with a positive HIV test result, and physicians managing HIV-positive pregnant women were reminded of the availability and efficacy of antiretroviral therapy.

To determine changes in physician behaviour, we reviewed the charts of all women admitted to the British Columbia Women's Hospital during 1 week in November 1995 and again in November 1996. The standard antenatal record form was used. This form asks whether HIV testing has been discussed and whether it has been done.

This study focused on pregnant women with an estimated date of delivery during 1995 or 1996. Statistics for pregnancies, live births, and therapeutic and spontaneous abortions were obtained from the Information and Analysis Branch, British Columbia Ministry of Health. We estimated the prevalence of seropositivity for HIV among childbearing women from anonymous, unlinked seroprevalence surveys of pregnant women in British Columbia.[11] Expected numbers of pregnancies for HIV-positive women and their expected outcomes were calculated by muliplying the antenatal seroprevalence rate by population pregnancy statistics.

Identified pregnancies involving HIV included those that came to attention solely through screening and those for which the woman was already known to be HIV positive. Outcomes for these pregnancies were compared with those expected. We estimated the number of unidentified pregnancies involving HIV by subtracting the number of identified pregnancies from the number of expected pregnancies. Estimated outcomes for the unidentified group were based on the outcomes for the general population of pregnant women. The rate of vertical HIV transmission in the absence of intervention was assumed to be 25% on the basis of published experience.[1,2,4]

Most of the identified HIV-infected pregnant women were cared for in consultation with a multidisciplinary team at the British Columbia Women and Family HIV Centre, Vancouver. Patients were offered information and counselling regarding HIV in pregnancy, expected outcomes and options for intervention. If they chose to continue the pregnancy, they were offered prenatal care and antiretroviral therapy according to the ACTG 076 protocol,[4] with or without additional therapy. (Women were not excluded from this analysis on the basis of CD4 count or previous antiretroviral therapy.) Compliance with zidovudine therapy was estimated by the clinical care team on the basis of history and rate of medication use. Delivery management included minimizing the duration of labour after the membranes had ruptured and avoiding invasive monitoring and instrument deliveries. Women were offered induction if the length of gestation was greater than 40 weeks. Vaginal delivery was encouraged unless specific obstetric indications for cesarean section were present. Women were advised not to breast-feed.

Children born to HIV-positive women were offered the neonatal component of the ACTG 076 zidovudine

protocol. Culture for HIV and polymerase chain reaction testing were performed at monthly intervals up to 6 months of age. A child was considered to be infected if HIV infection was demonstrated by either method on 2 or more consecutive assays.

Although formal cost analysis was beyond the scope of this program review, we performed a limited analysis focusing on costs and savings attributable to mother–infant pairs identified by the screening program. We calculated the number of HIV infections prevented by subtracting the number of neonatal infections observed in the screened group from the number expected if women giving birth to live infants in that group had received no therapy. Program costs were estimated by the virology laboratory and from a literature review. We assessed costs of care using estimates from a recent Canadian study of costs associated with HIV infection in infants and children.[5] Annual costs of care for the various stages of pediatric HIV disease were applied to each year of a typical natural history[12] and were discounted at a rate of 5% per annum. We compared program costs and savings, and conducted sensitivity analyses varying discount rates, program costs, lifetime care costs for HIV-infected infants and the number of cases of maternal–infant HIV transmission prevented by the program.

We used rates and proportions to describe most findings. Univariate tests of significance (e.g., χ^2 test, Fisher's exact test) were used to compare differences in proportions.

Results

Provider practices

The results of the chart reviews are shown in Table 1. Between 1995 and 1996 the proportion of patients with whom HIV testing was discussed increased from 43% to 67% ($p < 0.001$), and the proportion in whom HIV testing was documented increased from 55% to 76% ($p < 0.001$). Family physicians performed 55% of deliveries at the hospital over this period. In 1995, 67% of family physicians included screening for HIV infection, compared with 34% of obstetricians ($p < 0.001$). The corresponding figures for 1996 were 67% and 87% ($p < 0.01$). The proportions of primiparous and multiparous women offered HIV screening were 68% and 42% respectively in 1995 ($p < 0.002$) and 77% each in 1996.

Table 1: Changes in prenatal HIV screening practices at British Columbia Women's Hospital, Vancouver, between November 1995 and November 1996

	Time; no. (and %) of women		
Practice	November 1995 *n = 145*	November 1996 *n = 121*	*p* value
HIV testing discussed			
Yes	62 (43)	81 (67)	< 0.001
No	7 (5)	4 (3)	
Not documented	76 (52)	36 (30)	
HIV testing performed			
Yes	79 (54)	92 (76)	< 0.001
No	12 (8)	10 (8)	
Not documented	54 (37)	19 (16)	

Pregnancies and laboratory screening

During the 6 months (December 1993 to May 1994) before the BCCDC's guidelines were issued, an average of 8100 tests per month for HIV antibody were submitted to the Provincial Laboratory. During the 6 months after the guidelines were issued, an average of 9171 tests per month were submitted, for an overall increase of 13.2% in testing volume.

Pregnancy and birth statistics for 1995 and 1996 are given in Table 2. Anonymous unlinked seroprevalence studies of childbearing women showed HIV seroprevalence rates of 0.27 per 1000 in 1989, 0.50 per 1000 in 1992 and 0.34 per 1000 in 1994.[11] Assuming that the seroprevalence rate among pregnant women was not significantly changed (mean 0.37 per 1000), we estimated that the expected number of pregnancies among HIV-positive women over 1995 and 1996 was 50.2, and the expected number of babies carried to term with exposure to HIV was 34.3 (95% confidence interval 17.6 to 51.0) (Table 2). With a maternal–fetal HIV transmission rate of 25%, an estimated 8.6 infants might have been infected in the absence of therapy.

Outcomes for identified mother–infant pairs

Forty-two mother–infant pairs in which the woman was HIV-positive and had a due date in 1995 or 1996 were identified as being in care, representing 84% of expected based on seroprevalence studies. Of the 37 mothers, 5 had 2 pregnancies with both estimated delivery dates during 1995 or 1996. Of the 42 identified pregnancies, 25 came to medical care because of prenatal screening (Table 2). Of these 25 cases, there were 10 terminations, 1 spontaneous abortion and 14 cases in which the woman elected to carry the pregnancy to term with antiretroviral therapy. There was one stillbirth. The mothers of all 13 live-born infants opted for some component of the ACTG 076 regimen. One child (born by spontaneous vaginal delivery) in this group was infected. The mother received oral and intravenous zidovudine therapy, and the baby received zidovudine suspension, but the woman's compliance with therapy was estimated at less than 25% of pill volume.

Two of the 13 children carried to term by women identified outside the screening program were also infected (Table

2). Neither mother received oral zidovudine therapy. One of the women received intravenous zidovudine therapy 4 hours before delivery and allowed administration of the neonatal component to her child, who was born by cesarean section 48 hours after rupture of the membranes. The other woman declined all therapy, and her child was born vaginally 20 hours after rupture of the membranes. One other infant in this group was known to have been born at term with neither the mother nor the infant receiving antiretroviral therapy, but the infant has been lost to follow-up.

Overall, among the 26 pregnancies carried to term, only 3 mothers took no zidovudine therapy for themselves, and only 2 declined it for their babies. The mean rate of compliance with oral therapy for the 19 women for whom it was recorded was 69%; 13 of the 19 used 75% or more of the pills. Invasive monitoring was known to have been used in one case, and vacuum extraction or forceps were used in one case (no associated infections). One of the 3 infected babies and 4 of the 22 uninfected babies were born by cesarean section. All but 2 of the 26 infants were born at 36 weeks of gestation or later. Both premature infants (delivered at 28 and 29 weeks) remained uninfected.

Characteristics of HIV-positive pregnant women

Of the 42 mother–infant pairs in which the mother was HIV positive, no twin pregnancies occurred but 5 of the women had 2 pregnancies with a due date in 1995 and 1996. Risk behaviours and ethnicity for the 37 women are shown in Table 3. Of the 37, 22 were found to be HIV positive through prenatal screening. Of the 15 remaining women, 10 had a positive test result predating screening, and 2 had a positive result during 1995 or 1996 but were not pregnant at the time of testing. Although 26 (70%) of the women were known to be injection drug users, use of such drugs was indicated as a risk factor on only 37% of requisitions for pregnant women with a positive test result in 1995 or 1996.

Cost

The estimated incremental cost of labour, materials and overhead associated with performing additional tests was $303 293. The estimated cost of zidovudine treatment (all 3 components of the regimen) has been estimated at $1283 per mother–infant pair.[5] With 13 screened pregnancies carried to term, the cost of treatment was $16 679, for an estimated total program cost of $319 972.

Given an expected vertical HIV transmission rate of 25%, 3.2 of the 13 infants born to HIV-infected women identified through the screening program would be expected to be infected. The observed single infection represents an estimated reduction of 2.2 infections.

The lifetime cost for care of an HIV-infected child has

Table 3: Risk behaviours and ethnicity of 37 HIV-positive women with an estimated date of delivery during 1995 or 1996 as indicated by the HIV care program

Characteristic	No. (and %) of women
Risk behaviour or factor	
Heterosexual contact	37 (100)
Injection drug use	26 (70)
Involvement in sex trade	11 (30)
Country endemic for HIV infection	4 (11)
Ethnicity	
White	14 (38)
Native	17 (46)
Black	2 (5)
East Asian	2 (5)
South Asian	2 (5)

Table 2: Expected and identified pregnancy outcomes in calendar years 1995 and 1996

Outcome	All women	HIV-positive women			
		Expected*	Identified		Estimated unidentified†
			Through screening	Previously in care	
Total no. of pregnancies	135 681	50.2	25	17	8.2
No. of pregnancies terminated	30 021	11.1	10	3	1.8
No. of spontaneous abortions or ectopic pregnancies	12 377	4.6	1	1	0.8
No. of stillbirths	638	0.2	1	0	0
No. of pregnancies carried to term	92 645	34.3	13	13	5.6
No. of HIV-infected infants	–	8.6	1	2	1.4
No. of uninfected infants	–	25.7	12	10	4.2
No. of infants lost to follow-up	–	–	0	1	–

*Estimates in this column were derived by multiplying the HIV seroprevalence rate among childbearing women by British Columbia pregnancy outcome statistics and assumed a maternal–fetal HIV transmission rate of 25% in the absence of intervention.
†The number of unidentified pregnancies was estimated by subtracting those identified from those expected. Other figures in this column assumed the same distribution of pregnancy outcomes as for the British Columbia population and a 25% vertical HIV transmission rate.

been estimated to be at least $145 000 (US$100 000).[5,13–15] When Canadian estimates identifying separate costs for each stage of infection[5] are applied to a typical natural history[12] and discounted by 5% per annum, the estimated lifetime cost of care is $220 708 (Table 4). (With discount rates of 0% and 10%, the lifetime cost would be $282 800 and $173 500 respectively.) Preventing 2.2 infections thus represents savings of $485 558.

The net program savings (savings from preventing 2.2 infections minus costs) are estimated at $165 586, with a saving per prevented case of $75 266.

Sensitivity analyses indicated that a break-even point on costs and savings of the program would occur if the lifetime cost of HIV care were reduced to $145 000, program costs over 2 years were increased to $486 000, or number of infections prevented were reduced to 1.4 over 2 years.

Interpretation

In a province with a modest prevalence of HIV infection among pregnant women, a benefit for the first 2 years of pregnancy screening is apparent. One possible explanation is a secular trend toward reduction in rates of maternal–fetal HIV transmission. However, there was no trend toward a decrease between 1993 and 1994, with rates of 20% and 30% respectively recorded in these years.[3] Furthermore, our cost analysis was limited to pregnancies identified as a result of screening. For this group of previously undiagnosed cases, there would be no biologic reason to expect a diminished rate of transmission and no likelihood of incidental antiretroviral therapy.

Notably, requisitions for prenatal screening identified a smaller proportion of HIV-positive pregnant women as injection drug users than the proportion identified during intensive HIV-specific prenatal follow-up. Targeting only known members of high-risk groups for screening may not identify most HIV-positive pregnant women and may prevent less than 25% of pediatric infections.[16,17] In the absence of a standard of universal screening, unacceptably high proportions of women and their babies fail to be identified soon enough to take advantage of therapy.[18]

Our finding that HIV screening by family physicians and obstetricians increased between 1995 and 1996 is encouraging. However, discussion of testing was not documented as frequently as HIV screening. We need to ensure that discussion takes place so that women may exercise their informed choice as to whether the test should be performed. However, if formal counselling were reimbursed in addition to the cost of prenatal care, cost benefits of pregnancy screening might no longer be apparent.[19] New models of counselling women at lower risk must be integrated into prenatal care practices.

Almost one-third of the pregnancies among HIV-positive women were terminated; for the women identified by the screening program the proportion was 40%. These figures are higher than the overall rate of 22% for British Columbia (Table 2) and may indicate a greater likelihood of termination if HIV status is known. (Three women identified by the screening program indicated to their care providers that this was a factor.) Other investigators have reported a near doubling of termination rates following diagnosis of HIV infection.[20]

Ignoring costs to the health care system estimated at $220 708 per pediatric HIV infection, we can equate the annual outlay of $319 972 for the screening program (which includes the cost of antiretroviral treatment) with $2200 per quality-adjusted life-year if applied to 2.2 infants with a 75-year life expectancy. This cost is considerably less than that of well-accepted therapeutic interventions, such as hip replacement, coronary artery bypass surgery, renal dialysis, treatment of hypertension and breast cancer screening.[21–25] Our estimates of direct costs do not account for social costs incurred by individuals and families and may be conservative.[5] Even if one used a lower cost of care ($145 000[13,14]), the savings associated with the program would approximately cover costs. Pro-

Table 4: Lifetime cost of care of an HIV-infected child

CDC clinical stage	Time spent in stage, mo[12]	Matched description for costing*	Cost per year, $[5]	Cost, $
N – no signs or symptoms	10	Indeterminate	10 922	9 065
A – mild signs or symptoms	4	Asymptomatic	25 704	8 482
B – moderate signs or symptoms	65	Asymptomatic	25 704	139 316
C – severe signs or symptoms	34	Symptomatic	44 645	126 345
Total cost				283 208
Lifetime cost per pediatric HIV infection discounted by 5% per annum				220 708

Note: CDC = US Centers for Disease Control and Prevention.
*Because Morales and colleagues[5] did not separately report Canadian costs for stages A, B and C, this calculation conservatively assumes that costs incurred during stages A and B equate with those they ascribed to asymptomatic children, and applies the annualized cost of symptomatic disease only to stage C. Similarly, because the annualized cost of indeterminate diagnosis was estimated at less than the cost of asymptomatic disease, this lower cost was applied to the first 10 months of life (stage N).

viding some infants with the opportunity for a full and healthy life is a compelling reason to continue the program, even if there were no net fiscal advantage. Diagnosing HIV infection in women also assists in reducing morbidity and costs from further sexual transmission[26] and offers women access to therapy, which confers a better chance of staying well to raise their children.

Follow-up will determine whether cost-effectiveness will be maintained over the next few years. If the prevalence of HIV infection among pregnant women rises, this screening strategy will become more cost-effective. Unfortunately, prevalence is likely to rise in British Columbia as a result of an outbreak of HIV infection among male and female intravenous drug users. Within Canada, higher rates of HIV infection among childbearing women have already been documented in Newfoundland (0.87 per 1000)[27] and among women undergoing abortion in Montreal (1.8 per 1000).[28] Seroprevalence among childbearing women in the United States is 1.7 per 1000,[29] over 3 times the rate in British Columbia. Not surprisingly, studies from the United States have documented an effect of treatment on outcome in populations[30] and concluded cost-effectiveness.[14]

Several groups have advocated strongly in favour of HIV screening during pregnancy.[8,9,31] It is now clear that, as a public health measure, prenatal screening for HIV infection in areas of low to moderate prevalence reduces the rate of maternal–fetal transmission, is widely accepted by pregnant women and compares favourably with other expenditures in preventive and acute medicine in terms of cost-effectiveness.

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