Evidence-based guidelines for universal counselling and offering of HIV testing in pregnancy in Canada

Evidence

Études

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Abstract

Objective: To provide Canadian health care workers with evidence-based guidelines for universal counselling about HIV testing and the offering of such testing to all pregnant women.

Options: Universal counselling and offering of HIV testing to all pregnant women versus targeted testing of only pregnant women at high risk for HIV infection. Antiretroviral treatment protocols for HIV-positive mothers and their infants are discussed as the intervention to reduce mother-to-child transmission rates.

Outcomes: Main outcomes are mother-to-child HIV transmission rates and consequences of HIV testing on the mother and infant.

Evidence: Articles published from January 1985 to March 1997 identified through a MEDLINE search; articles published in pertinent medical journals in 1996 and 1997 identified through a manual search; and abstracts presented at international HIV/AIDS conferences.

Benefits, harms and costs: Early diagnosis of HIV infection in a pregnant woman optimizes her medical and psychosocial care, decreases the incidence of mother-to-child transmission and decreases the risk of horizontal transmission to sexual partners. New, third-generation HIV tests have reduced false-positive rates and thus diminished the harm of screening.

Recommendations: A screening strategy consisting of universal counselling and offering of HIV testing is recommended for all pregnant women in Canada (grade B recommendation). Targeted testing of only pregnant women at high risk for HIV infection fails to identify a substantial proportion of HIV-positive pregnant women and is therefore not recommended (grade D recommendation). Women who identify themselves as being at high risk and whose initial HIV test result is negative should be counselled about the reduction of high-risk behaviours and retested in 6 months (grade B recommendation). Treatment of seropositive women and infants with zidovudine to prevent mother-to-child transmission is recommended (grade A or B recommendation depending on gestational age and CD4 count).

Validation: These guidelines are endorsed by the Canadian Pediatric AIDS Research Group and are in agreement with the recommendations of the Canadian Paediatric Society and the US Public Health Service Task Force.

Résumé

Objectif : Fournir aux travailleurs de la santé du Canada des lignes directrices fondées sur des données probantes qui portent sur le counselling universel au sujet des tests de dépistage du VIH et sur la possibilité d'offrir ces tests à toutes les femmes enceintes.

Options : Counselling universel et offre de tests de dépistage du VIH à toutes les femmes enceintes par rapport aux tests visant uniquement les femmes enceintes à risque élevé d'infection par le VIH. Les auteurs discutent de protocoles de traitement antirétrovirus administré aux mères infectées par le VIH et à leur nou-

veau-né, ainsi que de l'intervention nécessaire pour réduire les taux de transmission de la mère à l'enfant.

Résultats : Les principaux résultats sont les taux de transmission du VIH de la mère à l'enfant et les conséquences des tests de dépistage du VIH sur la mère et le nouveau-né.

Preuves : Articles publiés de janvier 1985 à mars 1997 trouvés à la suite d'une recherche dans MEDLINE; articles publiés dans des journaux médicaux pertinents en 1996 et 1997 trouvés à la suite d'une recherche manuelle; résumés présentés au cours de conférences internationales sur le VIH et le sida.

Avantages, préjudices et coûts : Le diagnostic précoce d'une infection par le VIH chez une femme enceinte optimise les soins médicaux et psychosociaux qui lui sont donnés, réduit l'incidence de la transmission de la mère à l'enfant et réduit le risque de transmission horizontale à des partenaires sexuels. De nouveaux tests de troisième génération de dépistage du VIH ont réduit les taux de résultats faussement positifs et, par conséquent, le préjudice découlant des tests de dépistage.

Recommandations : Une stratégie de dépistage constituée de counselling universel et d'offre de tests de dépistage du VIH est recommandée dans le cas de toutes les femmes enceintes au Canada (recommandation de niveau B). Soumettre à des tests ciblés seulement les femmes enceintes à risque élevé d'infection par le VIH omet de repérer un pourcentage important de femmes enceintes infectées par le VIH et ce n'est donc pas recommandé (recommandation de niveau D). On devrait conseiller aux femmes qui se déclarent à risque élevé et dont le test initial de dépistage du VIH donne un résultat négatif de modifier leur comportement et les soumettre à un autre test de dépistage dans les six mois (recommandation de niveau B). On recommande d'administrer aux femmes séropositives et aux nouveau-nés de la zidovudine pour prévenir la transmission de la mère à l'enfant (recommandation de niveau A ou B selon l'âge gestationnel et la numération CD4).

Validation : Ces lignes directrices ont l'appui du Canadian Pediatric AIDS Research Group et sont conformes aux recommandations de la Société canadienne de pédiatrie et du Public Health Service Task Force des États-Unis.

In Canada the incidence of pediatric HIV infection from perinatal transmission is increasing rapidly, with conservative estimates of 120 infants born to HIV-positive women each year.[1] HIV infection rates, although declining in some populations, continue to increase among Canadian women of child-bearing age.[2]

The issues surrounding HIV antibody testing in pregnant women have been debated in the medical and lay literature since the beginning of the HIV/AIDS epidemic. Initial arguments against routine screening focused on the ramifications of unacceptably high false-positive rates in low-risk populations, the lack of available interventions to prevent mother-to-child transmission and the fact that no therapy was available for asymptomatic infection. Since then, progress has been made in all of these areas. Newer generations of HIV antibody tests have essentially removed the likelihood of false-positive results while maintaining very high sensitivity. In 1994 a randomized controlled trial demonstrated significant reductions in mother-to-child transmission rates with the use of the antiretroviral agent zidovudine (ZDV, AZT).[3] Finally, recent advancements in our understanding of the pathogenesis of HIV infection have warranted the adoption of early aggressive treatment strategies even in asymptomatic individuals.

For these reasons, we felt that it was time to define a national strategy for universal antenatal counselling and the offering of HIV testing to all pregnant women and subsequent management of patients with positive results. These guidelines are intended for use by all Canadian health care workers caring for pregnant women. High values were placed on maternal rights and the reduction of neonatal HIV infection rates.

Review methods

MEDLINE was searched for articles published from January 1985 to March 1997. The search strategy included "exp HIV infections," "exp HIV," "HIV infections/dt," "antiviral agents/tu," "counseling," "HIV seropositivity" and the text words "women," "antenatal," "perinatal" and "pregnancy."

Also searched were the abstracts presented at the third

and fourth Conference on Retroviruses and Opportunistic Infections, held in 1996 and 1997 respectively, and the XI International Conference on AIDS, held in 1996. The bibliographies of pertinent articles were reviewed, and relevant HIV/AIDS and infectious diseases journals published in 1996 and 1997 were searched manually.

Two reviewers independently evaluated the retrieved studies using the grades of evidence of the Canadian Task Force on the Periodic Health Examination.[4] Group discussion was used to reach consensus following iteration of the summarized evidence. No disagreements regarding the recommendations occurred.

Burden of illness

The annual incidence of AIDS among females over the age of 15 in Canada in 1995 was 1.3 per 100 000.[5] Women of child-bearing age accounted for 63.3% of all AIDS cases in Canadian females. In this age group, women who were infected through heterosexual contact or who were classified as having had no identifiable risk factors accounted for 70.2% of the cases, whereas intravenous drug users and transfusion recipients accounted for only 29.7%.

Mother-to-child transmission is the most common route of HIV infection among Canadian children, accounting for 77% of all reported pediatric AIDS cases.[5] In 1995 the annual incidence of pediatric AIDS was 0.5 per 100 000 children aged 15 years or less.[5] Several Canadian studies measuring HIV seroprevalence rates among pregnant women have now been completed. Cohort studies performed by public health units across Canada have used anonymous unlinked methods to test samples of maternal blood obtained during routine prenatal care, cord blood at the time of delivery or blood from infant heel picks.[6-8] Each method, designed to determine maternal rather than infant HIV infection rates, captured a slightly different population. Seroprevalence rates ranged from 0.0 to 16.6 per 10 000 pregnant women. The highest rates were seen in Vancouver, Edmonton, Winnipeg, Toronto, Ottawa and Montreal; the lowest were in the Yukon and Northwest Territories, Nova Scotia and Newfoundland.

Manoeuvres

The 2 components of antenatal screening are counselling and HIV antibody testing. Throughout this article "screening" will be used to describe the entire process. The goals of antenatal screening are to identify women who are HIV positive so that they may receive optimal medical and psychosocial care for themselves, to decrease the incidence of mother-to-child HIV transmission and to decrease the risk of horizontal transmission to sexual partners.

Cohort and case–control studies have shown that targeted testing of only pregnant women with identifiable risk factors will identify only 8%–58% of those who are HIV positive.[9-17] Coplan and colleagues,[18] in a population-based retrospective study, compared the number of children exposed perinatally to HIV who were followed in regional pediatric HIV clinics with the maternal seroprevalence rates determined through blinded newborn studies. Only 56% of the seropositive infants born during the study period had presented for follow-up of their HIV status; of these, only 28% had been evaluated within the first 3 months of life. This demonstrates a problem with identifying HIV-exposed infants and a delay in the start of appropriate infant care. Optimal care during the neonatal period is important regardless of the infant's ultimate HIV status.

Counselling

General counselling guidelines for HIV testing have been published by the Canadian Medical Association[19] and include recommendations for both pre- and post-test counselling. The pretest interview includes an assessment of risk factors, determination of the existence of a seroconversion window (the time during early infection when the host immune system has not yet developed antibodies to the virus), provision of information regarding HIV infection, discussion of testing options, confidentiality issues and the implications of test results. Specific attention is given to prenatal testing procedures. An inception evaluation of the content and face validity of the guidelines revealed that they are generally well received by primary care physicians.[20]

Case–control studies have shown that the length of time spent counselling and the individual counsellor involved are the strongest predictors of who will accept testing.[21,22] Rates of acceptance of voluntary prenatal HIV testing have been increasing in recent years. In large cohort studies they have varied from 44% in British community-based clinics,[9,23] to over 95% in an American population[16,24] and to more than 99% in France and Sweden.[25,26] In France 69% of pregnant women surveyed supported mandatory antenatal HIV screening;[25] those women who were aware of the possibility of mother-to-child transmission were significantly more likely than the other women to support mandatory testing. Pretest counselling of pregnant women has led to higher acceptance rates of testing, increased knowledge regarding HIV transmission and higher rates of contraceptive and condom use.[25,27]

Given HIV seroprevalence rates of 1.0 and 10.0 per 10 000 pregnant women and a 95% testing acceptance rate, about 10 000 and 1000 pregnant women respectively

would need to be counselled to detect 1 woman who is HIV positive.

HIV testing

The first step in HIV testing in adults is a screening antibody detection test using the enzyme-linked immunosorbent assay (EIA). The newer, third-generation EIA kits have sensitivities of 99.4%–100% and specificities of 99%–100%.[28–33]

For blood samples that test positive the EIA test is repeated twice. If both repeat tests give negative results, the sample is reported as negative. False-negative results are possible if blood is taken during the seroconversion window. It has been determined that seroconversion will occur within 3 months in more than 97% of infected individuals and in most cases within 2–8 weeks.[34] Testing and mathematical models using the third-generation EIA tests have found the seroconversion window to be on average 20.3 (95% confidence interval [CI] 8–32.5) to 25 (95% CI 9–41) days.[35,36] The US Centers for Disease Control and Prevention, however, reported a case in which a patient had culture-positive results indicating HIV infection but repeatedly negative EIA results over a 4-year period.[37] Health Canada recommends that people seeking HIV testing who have self-reported high-risk behaviours and whose initial EIA result is negative should have repeat serological testing performed after 6 months.[34]

To increase the specificity of the testing procedure all samples that are repeatedly found to be positive on the EIA are subject to a confirmatory Western blot test. Cohort studies have shown that false-positive results with the Western blot test are extremely rare. No false-positive result was detected in over 290 000 blood donors,[28] and only one was detected in 135 187 military recruits.[38] Both of these studies were conducted before 1990 and thus used earlier, less specific, generations of tests.

The sensitivity and specificity of the combined EIA and Western blot testing protocol are at least 99% and 99.99% respectively. False-positive rates are extremely unlikely, and the false-negative rate is 0 to 6.0 per 100 000 people tested.[38,39] Incorrect results occur mainly because of specimen handling and laboratory errors.[40]

Consequences of HIV seropositivity

The consequences of a positive prenatal HIV test result have been studied using descriptive methodologies. Lester and colleagues[41] demonstrated both qualitative and quantitative differences between pregnant women who tested positive and matched HIV-negative control subjects in episodes of discrimination, decreased satisfaction with primary sexual partners, changes in childbearing plans and increased anxiety. Lindsay and associates[42] found that more HIV-positive women chose tubal sterilization after their pregnancy and were less likely to have a subsequent pregnancy than pregnant women who were HIV negative. A cohort study involving pregnant intravenous drug users revealed no statistically significant differences regarding pregnancy termination between HIV-positive and HIV-negative women.[43] Mandatory premarital testing in Illinois resulted in fewer marriage licenses being issued and more people leaving the state to get married.[44,45] Such practices would lead to underreporting of HIV seroprevalence rates.

Treatment

A multinational randomized double-blind placebo-controlled trial (ACTG [AIDS Clinical Trials Group] trial 076) evaluated the efficacy of the reverse transcriptase inhibitor ZDV (AZT) in reducing the rate of mother-to-child transmission.[3] The treatment arm involved oral ZDV administration to the mother antenatally, intrapartum administration of ZDV intravenously and oral ZDV administration to the newborn for 6 weeks. The mother-to-child transmission rates were 25.5% in the placebo group and 8.3% in the treatment group, with a relative risk reduction of 67.5% (95% CI 40.7%–82.1%). The number needed to treat (NNT) to decrease the infant infection rate by 1 was 5.9. Adverse effects to both the mother and the fetus were minimal and reversible. The study infants have continued to be followed, and no adverse effects were reported at 2 years.[46] The limitation of this study is that its results are not generalizable to pregnant HIV-positive women who do not meet the ACTG 076 inclusion criteria.

Three subsequent cohort studies have been published that evaluated ZDV efficacy outside of the ACTG 076 protocol.[47–49] A retrospective observational cohort study involving 321 women evaluated the efficacy of maternal ZDV treatment only.[49] The primary outcome measure was the mother-to-child transmission rate. The rate was significantly lower among women with varied CD4 counts who took ZDV antenatally at any time during the pregnancy than among those who did not take ZDV ante-natally (14% v. 23%, $p = 0.002$; adjusted odds ratio 0.36 [95% CI 0.14–0.92]). Potential confounding variables were analysed in a logistic regression model and did not significantly alter the odds ratio. There were no differences in adverse events between the 2 groups.

Dickover and colleagues[48] conducted a nonrandomized prospective cohort analysis of 92 HIV-positive pregnant women. Their secondary objective was to examine the effectiveness of ZDV in reducing the mother-to-child transmission rate. The methods of ZDV assignment varied. The transmission rate was 29.6% among

women not given ZDV and 9.3% among those who used ZDV at any time during pregnancy, for a relative risk reduction of 68.6%. There was no difference in the transmission rates between infants given ZDV and those who were not.

A statewide reduction in the mother-to-child transmission rate in North Carolina was reported by Fiscus and associates[47] following the recommendation for antenatal maternal use of ZDV. The authors, who matched anonymous HIV seroprevalence rates with the number of pregnant women receiving antenatal HIV care, demonstrated a significant increase in the number of treated women after 1994. The mother-to-child transmission rate was 21% among those not given ZDV and 8.5% among those who were.

Three further studies evaluating either different antiretroviral regimens or different patient populations were found in abstract form.[50–52] A prospective nonrandomized cohort study explored the possibility of decreasing the length of maternal antenatal treatment: 80 pregnant women were offered ZDV therapy commencing at 24 weeks' gestation; the mother-to-child transmission rate was 4.5% among those who took ZDV, as compared with 30.5% among those who did not.[52] A multicentre cohort analysis comparing ZDV use and transmission rates before and after publication of the ACTG 076 trial data revealed an overall reduction in the mother-to-child transmission rate from 19% to 8% and an increase in the use of ZDV from 22% to 89%.[50]

Benefits of screening

Identification of asymptomatic HIV-positive pregnant infected women allows for the early initiation of HIV therapy for the woman herself and counselling regarding methods of infant feeding. These 2 areas warrant detailed comments that are beyond the scope of this article.

Antiretroviral therapy in asymptomatic patients has demonstrated proven sustained benefits.[53–62] Recent advances in our knowledge of the dynamics of plasma viral load has led to new treatment strategies that focus on early aggressive antiretroviral therapy.[63–66] The safety and efficacy of commencing combination antiretroviral therapies during pregnancy requires investigation.

Recommendations

The recommendations are summarized in Table 1, and the strategy for universal HIV screening among pregnant women in Canada is presented in Fig. 1.

All pregnant women should be counselled about HIV infection and offered HIV testing (grade B recommendation).

It has been shown that universal screening is socially acceptable and identifies a greater proportion of HIV-positive pregnant women. The quality of pre- and post-test counselling has been shown to correlate with test acceptance rates and levels of satisfaction. The CMA's counselling guidelines for HIV testing should be made readily available to practising physicians who care for pregnant women. Although seroprevalence rates among pregnant women vary across Canada and are higher in urban centres, they are on the rise everywhere. The increased specificity of current testing techniques has essentially removed the problems of false labelling. During the counselling session, all women must be made aware of their right to refuse any medical test or procedure and give consent for testing to be done.[67]

Targeted testing of pregnant women who report high-risk behaviours is not recommended (grade D recommendation).

High-risk behaviours are classified as intravenous drug use, sex with multiple partners, and sex with a partner who is from an HIV-endemic area, is known to be HIV positive or has known high-risk behaviours. Targeted testing fails to identify a significant proportion of HIV-positive women. This is either because of unknown risk factors or an unwillingness to be identified as having a risk factor.

Pregnant women who report high-risk behaviours and whose initial test result is negative should be counselled about the reduction of high-risk behaviours and offered repeat testing in 6 months (grade B recommendation).

Although the sensitivity of EIA screening tests and confirmatory Western blot tests is high, a very low false-negative rate persists because of the seroconversion window. The persistent false-negative rate and the likely ongoing HIV exposure support the recommendation for counselling to reduce high-risk behaviours and offering of repeat testing in 6 months.

ZDV therapy, at least, should be offered to HIV-positive pregnant women and subsequently to their infants (grade A or B recommendation depending on gestational age and CD4 count).

Recommendations regarding antiretroviral therapy are made for previously undiagnosed, asymptomatic women. There is good evidence from the ACTG 076 trial[3] to support a grade A recommendation that ZDV therapy be offered to women who meet the trial's inclusion criteria (no clinical indications for antiretroviral therapy, gestational age between 14 and 34 weeks and CD4 count of more than 0.2×10^9/L) and subsequently to their infants. This level I evidence reveals a risk reduction in the mother-to-child transmission rate of 67.5%. For HIV-positive pregnant women who do not meet the

above inclusion criteria, cohort studies provide level II-2 and II-3 evidence to support a grade B recommendation that ZDV therapy be offered to these women and subsequently to their infants.

Validation

These guidelines have been reviewed by experts in the areas of HIV therapy, epidemiology of HIV infection and clinical epidemiology and are endorsed by the Canadian Pediatric AIDS Research Group. The guidelines are in agreement with those published in 1994 by the Canadian Paediatric Society (CPS), which recommended voluntary testing of all pregnant women and appropriate counselling and suggested that ZDV therapy be offered to HIV-positive women.[68] The CPS guidelines also suggested that mother–infant pairs who receive ZDV therapy be enrolled in the International Antiretroviral Pregnancy Registry. Given the national focus of our recommendations and the fact that provincial guidelines are in various stages of development the provincial guidelines have not been included here.

Although statements from other countries are not directly applicable to Canada's situation because of differences in health care delivery and seroprevalence rates, several published recommendations are worth noting. Recommendations from the US Public Health Service Task Force on the use of ZDV to reduce perinatal HIV transmission were published in 1994.[40] The task force recommended following the ACTG 076 guidelines if the woman meets the entrance criteria and went further to suggest regimens of ZDV therapy if she does not. In 1994 the task force published recommendations stating that all pregnant women be counselled and encouraged to undergo HIV testing and that the testing be voluntary.[40] It urged that counselling and testing be performed as early as possible in the pregnancy and that pregnant women found to be HIV negative but who have high-risk behav-

Table 1: Summary of manoeuvres, effectiveness, levels of evidence and recommendations for universal HIV screening and treatment among pregnant women

Manoeuvre	Effectiveness	Level of evidence*	Recommendation*
Screening			
General population			
Counsel all pregnant women about HIV infection and recommend HIV testing†	Increased proportions of HIV-positive women identified prenatally with universal screening	Cohort and case–control studies (II-2, II-3)[2,16,21–26,33–36,38,39]	Fair evidence to include manoeuvre in clinical practice (B)
Women at high risk‡			
Counsel and recommend HIV testing only to pregnant women with high-risk behaviours (targeted testing)	Significant proportions of HIV-positive women not identified prenatally with targeted testing	Cohort and case–control studies (II-2, II-3)[9–17]	Fair evidence *against* targeted testing (D)
Counsel about reducing high-risk behaviour and recommend retesting after 6 months if initial test result is negative	Detection of recently infected HIV-positive women later in the pregnancy will enable earlier treatment of the woman and proactive management of the exposed infant	Cohort studies (II-2, II-3)[33–36,38,39]	Fair evidence to include manoeuvre in clinical practice (B)
Intervention			
Offer at least ZDV therapy to HIV-positive pregnant women who meet ACTG 076 trial inclusion criteria§	Risk reduction of 67.5% in mother-to-child transmission rate with antenatal and perinatal therapy	Double-blind randomized placebo-controlled trial (I)[3]	Good evidence to offer intervention (A)
Offer at least ZDV therapy to HIV-positive pregnant women who do not meet ACTG 076 trial inclusion criteria	Significant reduction in mother-to-child transmission rate with antenatal and perinatal therapy in women with varying CD4 counts	Cohort studies (II-2, II-3)[47–52]‖	Fair evidence to offer intervention (B)

Note: ZDV = zidovudine.
*Levels of evidence and classification of recommendations are those of the Canadian Task Force on the Periodic Health Examination.[4]
†Informed consent must be obtained at time of counselling.
‡Includes sex-industry workers, women with multiple sexual partners and intravenous drug users.
§ACTG (AIDS Clinical Trials Group) 076 trial inclusion criteria: no clinical indications for antiretroviral therapy, gestational age between 14 and 34 weeks and CD4 count of more than 0.2×10^9/L.
‖References 50–52 are non-peer-reviewed abstracts from international HIV/AIDS conferences.

iours be encouraged to avoid further exposure and be retested in the third trimester.

Research questions

The guidelines in this article are based on critical analysis and grading of published studies. The literature on HIV pathogenesis and therapy is rapidly changing, and therefore guidelines such as these should be reviewed regularly. Questions that need to be addressed through further research include the following.

- *What is the best mechanism for implementing these guidelines?* Provincial and national committees should be established to ensure that the rights of women being counselled and tested are preserved, that test results are provided to the women in a caring and confidential matter and that those who are found to be HIV positive are able to have immediate access to medical and psychosocial support.
- *What are the long-term effects of ZDV monotherapy on the development of viral resistance?* The recommendation of offering ZDV monotherapy to pregnant women, although considered aggressive in 1994, is now contentious. The long-term effect of this short course of monotherapy on the development of viral resistance to ZDV must be addressed to determine the safest treatment for HIV-positive women and their infants.
- *Are combination antiretroviral drug regimens safe and effective during pregnancy?* Several HIV experts recommend that combination antiretroviral therapy be offered in pregnancy and that the combination be decided on an individual basis according to the medical needs and wishes of each woman. Prospective data must be collected to understand fully the safety and efficacy of these combination regimens. Among women already receiving combination therapy at the time of conception, the efficacy of the regimen in reducing

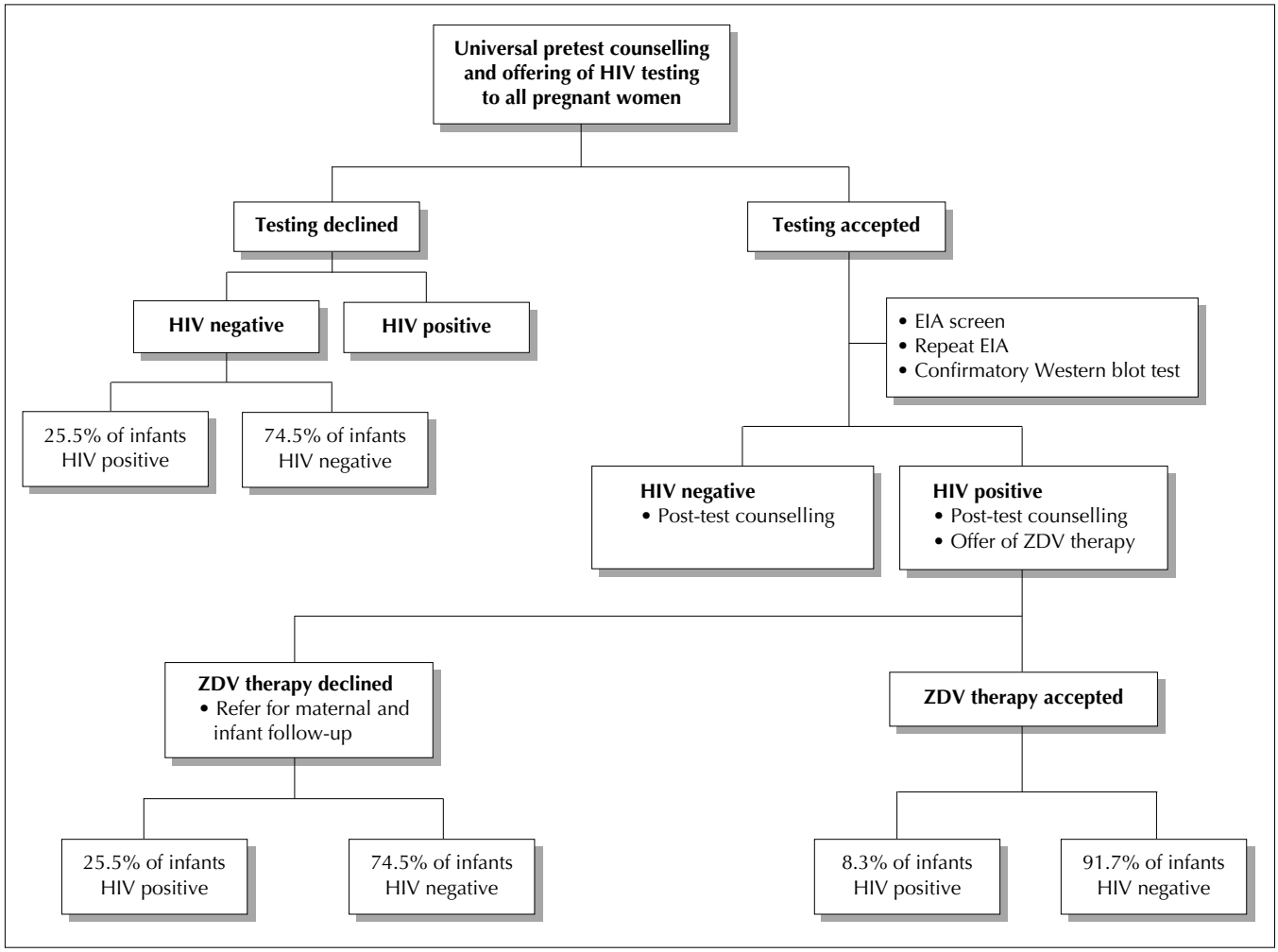

Fig. 1: Recommended strategy for universal HIV screening among pregnant women in Canada. Outcomes have been estimated from results of the Pediatric AIDS Clinical Trials Group protocol 076 trial.[3] EIA = enzyme-linked immunosorbent assay, ZDV = zidovudine.

the risk of transmission and the long-term effects on the developing fetus need to be documented. Among women who have not previously received antiretroviral therapy, the added benefit of immediate combination therapy (including the potential prevention of ZDV resistance) needs to be assessed.

- *What are the long-term effects of exposure to antiretroviral therapy on the developing fetus?* A compulsory, standardized system of follow-up should be initiated on a national level to determine such long-term effects in all infants exposed to ZDV or other antiretroviral agents either in utero or post partum, regardless of their ultimate HIV status. Although a US-based international registry exists, the compliance rates with enrolment remain low. A Canadian registry is being set up for this purpose.
- *What other interventions are possible to reduce the mother-to-child transmission rate further?* A mother-to-child transmission rate of 8% remains despite the use of ZDV. Research efforts should continue to focus on the pathogenesis of HIV transmission and other strategies to reduce these rates further. As well, strategies should be developed that can be feasibly implemented in developing countries where costly antiretroviral drugs are not generally affordable.
- *Is routine HIV screening among Canadian pregnant women cost-effective?* A cost-effectiveness study should be performed at a national level using Canadian seroprevalence and financial data.

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