Would Universal Antenatal Screening for HIV Infection Be Cost-Effective in a Setting of Very Low Prevalence? Modelling the Data for Australia

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Background. The economics of universal antenatal human immunodeficiency virus (HIV) screening should be explored if mother-to-child transmission of HIV occurs, the health-service infrastructure for universal screening exists, and optimal risk-reducing treatments can be supplied.

Methods. We evaluated a hypothetical cohort of the antenatal population of Australia during 2001–2002, to examine whether universal antenatal HIV screening is cost-effective in this setting. A quasi-societal perspective was adopted, secondary data sources were used, and sensitivity analyses were undertaken. Costs and benefits incurred in the future were discounted to their present value.

Results. The intervention would be cost-effective if the prevalence of undiagnosed HIV in the currently unscreened Australian antenatal population was \( \geq 0.004372\% \). We predict 6.95 new diagnoses of HIV, 1.73 infections avoided, and 46.97 discounted-life-years gained. Applying favorable and unfavorable values for key variables suggests that the prevalence at which the intervention would be cost-effective is \( 0.0016\%–0.0106\% \).

Conclusions. Universal antenatal HIV screening would be cost-effective at a very low prevalence and would generate net benefits under many scenarios; accurate statistics on the true prevalence of HIV in the currently unscreened antenatal population are required.

Previous studies of the cost-effectiveness of universal antenatal HIV screening in high-income countries have reported or assumed a prevalence of disease of \( \geq 0.01\% \) (1 case/10,000 population) in the target population [1–5]. All have supported a policy of universal screening. The economics of universal antenatal HIV screening have not yet been evaluated in high-income settings, where the prevalence is perceived to be very low but where cases of mother-to-child transmission still occur. Australia is a good example.

In 1991, Garland and Kliman [6] argued that universal screening was not appropriate, because of small numbers of cases of HIV in the antenatal population. However, information published in 2003 [7] indicates that 71 cases of mother-to-child transmission of HIV occurred between 1982 and 2002, primarily among women whose HIV infection was diagnosed postnatally [7]. Also, very effective interventions are now available to reduce the risk of mother-to-child transmission for women whose HIV infection was diagnosed antenatally [8–11]. In Australia, the use of interventions in women whose HIV infection was diagnosed antenatally has been associated with a substantially lower risk of HIV transmission, compared with women whose HIV infection was diagnosed postnatally [9].

Although current antenatal HIV screening practice varies across the states and territories in Australia, the national policy is that HIV testing should be conducted if requested by the woman or if an increased risk is identified [12], although what constitutes this risk is undefined. Of those women currently screened, 89 with perinatally exposed children were newly diagnosed with HIV infection in Australia between 1998 and 2002.
Incremental benefits. The values for variables used in the model reflect the preferences of individuals in the community [16].

Health-care sector and a valuation of a life-year gained that is perceived to be very low, and develop a model of the incremental cost-effectiveness of universal screening of the antenatal population of Australia, compared with the current practice.

**METHODS**

*Overview of the model.* The predicted incremental costs of universal screening are estimated and compared with the predicted incremental benefits. We adopt a quasi-societal perspective by including costs and benefits to the state-funded health-care sector and a valuation of a life-year gained that reflects the preferences of individuals in the community [16]. We assume that the intervention is cost-effective if the incremental cost is less than or equal to the monetary valuation of incremental benefits. The values for variables used in the model are included in table 1. The model is evaluated for a hypothetical 12-month cohort of pregnant women and includes all future costs and benefits, which are discounted in-line with recent debate and recommendations [38–43]. Uncertainty is assessed by univariate sensitivity analyses. All values for cost variables are reported in Australian dollars and reflect 2001–2002 prices. The average exchange rates for Aus$1 during this time period were US$0.54, £0.60, 50.37, and NZ$1.25 [44].

Estimation of incremental screening and treatment costs. We assume that antenatal HIV screening would be universally recommended and conducted, with informed consent, by midwives, obstetricians, and general practitioners. To achieve high uptake and informed consent, we envisage the need to invest in the continuing professional education of these health-care professionals [45]. We assume that a proportion of women are already subject to HIV testing and, therefore, exclude the screening and treatment costs for this group.

At the first contact with a health-care professional, every pregnant woman would be supplied with an information packet about the risks of HIV infection and the advantages and disadvantages of the proposed universal screening program. They would also have an opportunity to discuss any concerns with the relevant health-care professional. An HIV antibody test would be performed for all those who consent, and the sample would be processed by 1 of the 52 authorized and publicly funded laboratories in Australia [46]. On the basis of an assumption that all the additional testing is shared evenly between these laboratories, workload would increase by 55 tests/week/laboratory. This does not suggest the need to invest in extra capital or labor. The unit cost of an ELISA that we include in the baseline model reflects this assumption.

Women with a positive result at screening would need 2 further antibody tests and a Western blot test, for confirmation of HIV infection, and women with true-positive results would require additional posttest counseling. A proportion of women with confirmed HIV infection would choose to terminate the pregnancy. Those who continue would be offered antiretroviral therapy under the guidance of their physician. We assume that the women would attend regular outpatient appointments and that the 076 treatment strategy would be followed but would be modified to include combivir and nelfinavir for 12 weeks, in-line with Australian guidelines for optimal treatment [47].

All women would be offered antiretroviral therapy during labor, and some proportion would deliver by elective caesarean delivery. During the first 6 weeks after delivery, the infant would receive antiretroviral therapy and would attend outpatient appointments. At 6 weeks, pneumocystis prophylaxis would commence and continue until at least 2 negative polymerase chain reaction results were obtained, but the outpatient appointments and associated diagnostic tests would continue for 12 months. The costs of the antiretroviral therapy and other health-care
Table 1. Values used for variables included in cost-effectiveness model.

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<thead>
<tr>
<th>Variable</th>
<th>Baseline values (unfavorable; favorable)</th>
<th>Source</th>
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<tbody>
<tr>
<td>To determine epidemiological parameters</td>
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<td></td>
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<tr>
<td>Antenatal population currently tested (without universal screening program), %</td>
<td>33 (36; 30)</td>
<td>[13]</td>
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<tr>
<td>Proportion of unscreened antenatal population who accept universal screening, %</td>
<td>96 (70; 100)</td>
<td>[59, 66–72, 75]</td>
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<td>False-positive rate, %</td>
<td>0.10 (0.05; 0.2)</td>
<td>E. Dax, personal communication</td>
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<td>Termination-of-pregnancy rate after new diagnoses identified by screening, %</td>
<td>4 (10; 0)</td>
<td>P. Tookey, personal communication</td>
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<tr>
<td>HIV-positive women who deliver by caesarean section, %</td>
<td>40 (21; 50)</td>
<td>[9]</td>
</tr>
<tr>
<td>Incidence of transmission without treatment, %</td>
<td>28 (21.1; 34.3)</td>
<td>[8, 57]</td>
</tr>
<tr>
<td>Incidence of transmission with treatment, %</td>
<td>2 (4; 0)</td>
<td>[8, 11, 17–21]</td>
</tr>
<tr>
<td>No. of live births per year</td>
<td>249,595 (244,603; 254,587)</td>
<td>[22]</td>
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<tr>
<td>Gain in life-years (discounted for an avoided case of HIV, years)</td>
<td>22.99 (12.19; 29.99)</td>
<td>[1, 35, 36]</td>
</tr>
<tr>
<td>Gain in life years due to early treatment (discounted) for newborns, years</td>
<td>1.27 (0.35; 3.70)</td>
<td>[1]</td>
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<tr>
<td>Gain in life years due to early treatment (discounted) for pregnant women, years</td>
<td>1 (0; 1.97)</td>
<td>[5]</td>
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<tr>
<td>To determine cost and benefit parameters</td>
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<td>Pretest counseling, min</td>
<td>7.5 (40; 1)</td>
<td>[73, 74, 23]</td>
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<tr>
<td>Posttest counselling for true-positive result, min</td>
<td>30 (60; 10)</td>
<td>J. Murray, personal communication</td>
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<tr>
<td>Time to first true-negative result, min</td>
<td>2 (3;1)</td>
<td>J. Murray, personal communication</td>
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<tr>
<td>No. of obstetricians</td>
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<td>[24]</td>
</tr>
<tr>
<td>No. of practicing midwives</td>
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<td>[25]</td>
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<tr>
<td>No. of general practitioners</td>
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<td>[24]</td>
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<td>Lifetime costs for HIV-positive infant, Au$</td>
<td>55,511 (41,633; 69,389)</td>
<td>[26, 64]</td>
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<td>Investment in education for each HCP that may perform screening, Au$</td>
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<td>Gorton C. 2003, personal communication; Lambert S. 2002, personal communication</td>
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<td>Unit cost, Au$</td>
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<td>HIV antibody test</td>
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<td>[27], P Robertson, personal communication</td>
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<td>Western blot confirmation</td>
<td>110 (132; 88)</td>
<td>[28]</td>
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<td>Outpatient consultation with doctor, per h</td>
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<td>Nelfinavir tablet</td>
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<td>Combivir tablet</td>
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<td>T cell test</td>
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<td>[28]</td>
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<td>CMV antibody test</td>
<td>18 (21; 14)</td>
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<td>Termination of pregnancy</td>
<td>2565 (3078; 2052)</td>
<td>[31]</td>
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<td>Virus load determination</td>
<td>176 (211; 141)</td>
<td>[28]</td>
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<td>Caesarean delivery procedure</td>
<td>7454 (8945; 5963)</td>
<td>[31]</td>
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<td>Full blood count</td>
<td>10 (12; 8)</td>
<td>[28]</td>
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<td>Antenatal care given, per h</td>
<td>24.72 (29.67; 19.78)</td>
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<td>Annual incremental treatment costs for all perinatally exposed infants, Au$</td>
<td>11,181 (13,417; 8945)</td>
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<tr>
<td>Incremental treatment costs of HIV-pregnant women due to early diagnosis, Au$</td>
<td>18,222 (24,138; 12,306)</td>
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<td>Twice the median per capita annual income, Au$</td>
<td>39,000</td>
<td>[16, 48]</td>
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<td>Discount rates used</td>
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<td></td>
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<td>Costs, %</td>
<td>3 (2; 5)</td>
<td>[32, 33]</td>
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<tr>
<td>Benefits, %</td>
<td>3 (5; 0)</td>
<td>[1, 2, 41, 32, 34]</td>
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**NOTE.** CMV, cytomegalovirus; HCP, health-care professional (includes all midwives, general practitioners, and obstetricians).

* Indicates a caesarean delivery rate of 21%; however, currently unpublished data by the National Centre in HIV Epidemiology and Clinical Research indicate a rate of 40%.

Assuming for baseline (HIV negative, 79 years; HIV positive, 10 years), unfavorable (HIV negative, 71 years; HIV positive, 26 years), and favorable (HIV negative, 87 years; HIV positive, 6 years) values.

The original data were published in 1996 and have been adjusted to 2002 prices by use of data produced by the Australian Bureau of Statistics.

For baseline, we assume that an educational CD-ROM developed by the Australasian Society for HIV Medicine and a brochure including policies and guidelines is sent to every HCP involved in screening. For the favorable value, we assume zero investment; for the unfavorable value, we assume baseline values and that every HCP attends a 2-day course on HIV and screening practice.
services supplied to the mother would be counted up to a point at which they would have been diagnosed through voluntary testing in other settings, regardless of the universal screening program. To obtain the net cost of universal screening, the cost savings from an avoided case of HIV infection—the lifetime costs of treatment for a child born with HIV—are deducted from the screening and treatment costs.

**Estimation of incremental benefits.** We assume that only a proportion of all currently unscreened pregnant women would consent. To predict the number of true- and false-positive results, a range of values for HIV prevalence (0%-0.02%) and a rate of false-positive results were applied. The frequency of HIV infection avoided among the children born to the women diagnosed by universal screening was estimated by comparing the rate of HIV transmission with treatment with the rate of HIV transmission without treatment. The total life-years gained reflect the increased life expectancy for the infants in whom HIV infection was avoided, because of the earlier onset of treatment, the gain in life expectancy for the infants who still contract HIV despite optimal interventions, and the gain in life expectancy for HIV-positive mothers. Each life-year gained was assigned a value of twice the median per capita annual income [48] (AUS$39,000), a figure shown in a theoretical model to result in efficient allocation of resources [16]. We therefore assume that the intervention is cost-effective if the cost per life-year gained (CPLYG) is ≤AUS$39,000. This approach was preferred to the often arbitrary financial valuations of an incremental life-year that appear throughout the literature [16]. It was also assumed that treatment with antiretroviral drugs causes no adverse effects to the health of uninfected infants [49–52].

**Data sources and assumptions.** All values used for the variables included in the model are included in table 1. The favorable and unfavorable values included for each variable allow the model to be evaluated for alternate scenarios.

**RESULTS**

The results of costs and benefits for a range of prevalences are included in table 2. The relationship between the true prevalence of HIV in the currently unscreened antenatal population and the CPLYG from a universal screening program is illustrated in figure 1.

In the base case, the intervention would be cost-effective if the prevalence of HIV among the currently unscreened antenatal population was ≥0.004372% (1 case/22,872 population). Under this scenario, 6.95 new diagnoses/year would be made, with a gain of 46.97 discounted-life-years. Valuing each life-year gained at AUS$39,000 suggests incremental benefits of AUS$1,831,963 are achieved for an identical change in cost.

At this prevalence, the incremental costs of the program comprise $1,408,000 (73%) for pretest counselling and ELISA, $357,000 (18%) for training health-care professionals, $16,000 (1%) for sending information to women, and $147,000 (8%) for treatments for women and infants. These costs are offset by savings of $96,000 due to avoided HIV treatments, which represent 5% of the incremental costs.

The prevalence of 0.004372% is, therefore, the switching point for cost-effectiveness. Universal screening would not be cost-effective at lower prevalences, and net benefits would accrue at any prevalence >0.004372%.

**Sensitivity analysis.** The CPLYG changed by >5% if favorable or unfavorable values were applied to 10 of the 35 variables included in the model; the results of this are included in table 3. These results illustrate the minimum prevalence among the currently unscreened antenatal population at which universal screening would be cost-effective if the favorable or unfavorable values were applied. For example, if the unfavorable value for the proportion of women who accept screening is applied to the model, then the minimum prevalence at which the intervention is cost-effective increases from 0.004372% to 0.006%. Also, when benefits are discounted at all rates between and including 0% and 5%, the minimum prevalence for cost-effectiveness is 0.0015% at discount rate 0%, 0.0023% at discount rate 1%, 0.0032% at discount rate 2%, 0.0044% at discount rate 3%, 0.0057% at discount rate 4%, and 0.0071% at discount rate 5%.

**DISCUSSION**

With baseline values for all variables, we find a policy of cost-effectiveness of universal screening if the prevalence among the currently unscreened antenatal population is ≥0.004372% (1 case/22,872 population). Net benefits accrue at higher prevalences. We modelled a number of scenarios where favorable and unfavorable values were applied to the most-influential variables in the model. The minimum prevalence at which universal screening was cost-effective, for the best-case scenario, was 0.0016% (1 case/62,500 population) and, for the worst-case scenario, was 0.0106% (1 case/9434 population). We, therefore, have demonstrated that universal screening is cost-effective in a setting of very low prevalence.

There was uncertainty with regard to the values for the epidemiological and economic parameters. Data on the prevalence of HIV infection among the antenatal population of Aus-
are set to baseline values. Although those currently tested and, therefore, 0.023% (1 case/4348 population) among pregnant women in Australia [13]. Although those currently tested and, therefore, included in this survey may be considered a high-risk population, the reported prevalence of 0.023% (1 case/4348 population) easily exceeds the threshold for cost-effectiveness that we have identified.

By mapping these data on figure 1, we see that the estimates of Chew et al. [54] and Spencer et al. [13] imply a particularly low CPLYG. The higher of the 2 estimates (i.e., that from Law et al. [55]) illustrates a CPLYG of <Au$39,000, but the lower estimate, for the period of 1983–1985, implies the opposite.

We assumed the rate of mother-to-child transmission of HIV, without treatment, to be 28%. This was derived from an assumption that the Australian population will breast-feed for at least 6 months [56] and from the findings of a randomized trial undertaken in Kenya [57] that reported a transmission rate of 28% at 6 months, among women enrolled in the breast-feeding arm of the study. Although we might expect the Kenyan population to be quite different from that of a more developed country, the transmission rate in the non-breast-feeding arm of the Kenyan study was 20.5% and very close to the 20% transmission rate reported for a non-breast-feeding group of women in the United States [58]. We assumed a 2% rate of transmission.

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</tbody>
</table>

NOTE. IA, infection avoided; LYG, life-years gained; ND, new diagnosis.

a Prevalence of undiagnosed HIV in the currently unscreened antenatal population.

b In the baseline analysis, all life-years are discounted to a present value by use of a 3% rate.

c Incremental benefits associated with universal screening are based on the decision rule that a life-year gained is valued at twice the median per capita annual income [16].

d Incremental costs associated with universal screening.

e Incremental benefit minus incremental cost equals the incremental net benefits associated with universal screening.

Lowest prevalence at which the intervention is cost-effective (the break-even point at which incremental benefits equal incremental costs), if all variables are set to baseline values.
when interventions were used, which, we suggest, may be a conservative estimate. The interventions we advocate in this model may well achieve a lower rate, such as 1.2% (reported by Cooper et al. [58]). In fact, there were zero transmissions in 103 babies delivered to women in Australia who were aware of their HIV status before birth, between 1998 and 2002 [7].

We assumed that 4% of pregnant women with confirmed HIV infection would terminate the pregnancy. Although the literature suggests that the figure might be as high as 20% [59], this finding was derived from data obtained between 1990 and 1995, a time before the effectiveness of antiretroviral therapies had been fully realized and when the risks of vertical transmission were still considerable. The value that we used was obtained from data obtained in 1999 and, we argue, is a more accurate reflection of current practice.

There is debate among economists and policy makers over whether the same or different discount rates should be applied to costs and benefits that arise in the future [38–43]. In the baseline analysis, we chose to discount future costs and benefits at the same rate, and we evaluated scenarios where benefits were not discounted at all. Of course, the less aggressively that future benefits are discounted, the lower the prevalence at which universal screening is cost-effective.

The estimated marginal cost of Au$4.50 (US$2.40)/screening test exceeds estimates reported for the United Kingdom [1]. By pooling serum samples, English researchers found that costs could be reduced to £0.60 (Au$1.60; US $0.86)/test, without prejudicing test sensitivity or specificity.

There is great uncertainty with regard to the gain in life expectancy due to either an avoided case of HIV or the early diagnosis of the mother and for the subsequent lifetime costs of treating a child with HIV infection. For this analysis, we used the best available sources and included scenarios that reflect a wide range of values. Because treatments are evolving rapidly, the likely survival and cost of achieving that survival are difficult to predict. We recommend that further research that determines values for this important variable be undertaken.

The present study has illustrated that universal antenatal screening for HIV infection is cost-effective in a setting of very low prevalence. Furthermore, there is some evidence that the true prevalence in the currently unscreened antenatal population of Australia would exceed the minimum required for this intervention to be considered cost-effective.

The other published cost-effectiveness studies were conducted in the United Kingdom [1, 5], where 75% of 300 births to women with HIV are undetected each year [60]; the United States [3], where the prevalence of undiagnosed HIV infection in the general population is estimated to be at least 1% [61]; New Zealand [2], where the prevalence of HIV infection in antenatal women is estimated to be 0.02%–0.04%; and Canada, where the prevalence of HIV infection in antenatal women is estimated to be 0.037% [4].
One of the cost-effectiveness studies in the United Kingdom [1] assumed a value of £10,000 (US$15,000)/life-year gained; the authors recommended that universal screening be adopted under most scenarios within London and outside London if uptake was >90% and if the cost of an HIV antibody test was Au$1.60 (US$0.86). The study of pregnant women in Chicago [3] valued a life-year gained at US$50,000 and concluded that universal antenatal HIV screening was cost-effective. The authors of the New Zealand study [2] also concluded that universal antenatal HIV screening should be adopted if policy makers are willing to pay NZ$17,000 (US$8400)/life-year gained. The research conducted in Canada estimated that the net savings attributable to prevented infections among babies carried to term were Can$166,000 (US$121,000), with a savings per prevented case of Can$75,300 (US$55,000) [4].

The results of our research suggest that a policy of universal screening remains cost-effective at much lower prevalences than those assumed or reported for the United States, United Kingdom, Canada, and New Zealand. Universal screening should therefore be considered in countries with the following characteristics: very low prevalence, a relatively high per capita income, an established infrastructure for prenatal care, and a health-care system already delivering optimal risk-reducing therapies and treatments.

Comparisons can also be drawn with other screening programs in Australia. The authors of a review of the effectiveness of mammographic screening of women in Australia aged 40–49 concluded the CPLYG to lie between Au$24,000 and Au$65,000 [62] (US$13,000–35,000). Also, an analysis of the decisions made by the Australian Pharmaceutical Licensing Authorities between 1991 and 1996 [63] indicated that policy makers were unlikely to recommend a drug if the CPLYG was >Au$86,000 (US$46,000) but most often endorsed a drug if the CPLYG was <Au$48,000 (US$26,000); these costs are reported in 2002 prices [64]. Clearly, the threshold of Au$39,000 (US $21,000)/life-year that we have used here compares favorably. Also, investing the additional Au$1.8 million (US$0.9 million) in universal screening would increase annual expenditures on health care by just 0.003% [65].

As illustrated by the data in table 3, we found the results to be highly sensitive to whether investments were made in the continuing professional education of the health-care professionals who would counsel the women and offer the screening. However, for all scenarios, we assumed that the uptake of screening would remain at 95% and that informed consent would be obtained in an ethical manner. The literature [45, 59, 66–75] suggests that high compliance and ethical screening is determined by careful and sensitive pretest counselling, the level of training for each health-care professional, a need to take particular care when English is not the first language (in countries where English is the most commonly spoken language), and the age, attitudes, and experience of the health-care professionals. On the basis of this, we recommend that appropriate investments be made in continuing professional education. Note that universal screening was found to be acceptable to pregnant women in New Zealand [76], Sweden [66], and Scotland [45] and that women with HIV who are unaware of their status are more likely to accept screening if it is presented to them as “routine,” rather than as something that they have been “selected” for [71]. Also, after a change in the testing policy at a London genito-urinary medicine clinic, where detailed verbal counselling was replaced with a shorter written explanation, a substantial increase of the proportion of clients who accepted HIV screening was observed [77].

The results presented here reflect an average for the whole of Australia. There may well be variation in the prevalence of HIV infection and the intensity of the current screening activities across the states and territories of Australia, and this will have

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**Table 3. Results of sensitivity analysis—the lowest prevalence of HIV infection among the currently unscreened antenatal population of Australia at which universal screening is cost-effective.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unfavorable</th>
<th>Favorable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients who accept screening</td>
<td>0.0060 (1/16,667)</td>
<td>0.0042 (1/23,810)</td>
</tr>
<tr>
<td>Termination of pregnancy rates in HIV-positive women</td>
<td>0.0047 (1/21,277)</td>
<td>0.0043 (1/23,256)</td>
</tr>
<tr>
<td>Incidence of transmission without treatment</td>
<td>0.0058 (1/17,241)</td>
<td>0.0036 (1/27,778)</td>
</tr>
<tr>
<td>Incidence of transmission with treatment</td>
<td>0.0047 (1/21,277)</td>
<td>0.0041 (1/24,390)</td>
</tr>
<tr>
<td>Gain in life expectancy for case avoided</td>
<td>0.0075 (1/13,333)</td>
<td>0.0038 (1/26,316)</td>
</tr>
<tr>
<td>Gain in life expectancy due to early treatment for mother</td>
<td>0.0052 (1/19,231)</td>
<td>0.0039 (1/25,641)</td>
</tr>
<tr>
<td>Hours of pretest counselling</td>
<td>0.0099 (1/10,101)</td>
<td>0.0033 (1/30,303)</td>
</tr>
<tr>
<td>Discount rate for benefits</td>
<td>0.0071 (1/14,085)</td>
<td>0.0016 (1/62,500)</td>
</tr>
<tr>
<td>Unit cost of HIV antibody test</td>
<td>0.0079 (1/12,658)</td>
<td>0.0038 (1/26,316)</td>
</tr>
<tr>
<td>Investment in education for each HCP that may perform screening</td>
<td>0.0106 (1/9434)</td>
<td>0.0035 (1/28,571)</td>
</tr>
</tbody>
</table>

**NOTE.** Data are percentage (no. of cases/population). HCP, health-care professional (includes all midwives, general practitioners, and obstetricians).

a With all other variables at baseline values.
implications for cost-effectiveness. The results would be made
prevalence of unrecognized HIV among pregnant women in
Australia, universal antenatal screening for HIV would be a
cost-effective use of resources.

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