HIV antibody screening among immigrants: a cost-benefit analysis

Hanna Zowall, MA; Rod D. Fraser, PhD; Norbert Gilmore, PhD, MD; Antal Deutsch, PhD; Steven Grover, MD, MPA

To assess the economic impact of HIV (human immunodeficiency virus) antibody screening among potential immigrants on Canada's health care system we estimated the costs and benefits of such screening among the 160 135 immigrants who entered Canada in 1988 using the in-hospital costs of treating AIDS (acquired immune deficiency syndrome) over the 10 years after immigration. This economic model was based on current international HIV seroprevalence data, Canadian immigration statistics and estimates of disease progression. Between 343 and 862 of the immigrants were estimated to have been HIV seropositive; with the use of the enzyme-linked immunosorbent assay and the Western blot technique 310 to 780 of them would have been correctly identified as being seropositive, and 33 to 82 would have been incorrectly classified as being seronegative. Another 16 would have been falsely classified as being seropositive. There would have been 151 to 379 cases of AIDS from 1988 to 1998 among the immigrants identified as being HIV-positive. The estimated total cost of screening would have been $3.3 to $3.4 million. The in-hospital costs of treating HIV-infected immigrants in whom AIDS developed between 1989 and 1998 would have been $5.0 to $17.1 million. Accordingly, screening would have saved $1.7 to $13.7 million over the 10 years after immigration. However, we do not advocate screening on the basis of economic analysis alone and acknowledge that any policy regarding such screening must also incorporate social, legal and ethical considerations.

Quelle serait l'incidence monétaire, sur les services de santé au Canada, de la recherche systématique des anticorps contre le virus immunodéficitaire humain (VIH) chez les candidats à l'immigration? Nous estimons les coûts et les profits d'une telle recherche si on l'avait faite chez les 160 135 immigrants entrés au Canada en 1988, vu le coût attendu du traitement hospitalier du syndrome d'immunodéficience acquise (SIDA) survenant parmi eux dans les 10 ans suivant leur arrivée. Nous prenons pour bases les données internationales sur les taux de séropositivité, les statistiques canadiennes sur l'immigration et l'évolution attendue de la maladie. Ainsi le nombre d'immigrants séropositifs serait compris entre 343 et 862, dont 310 à 780 chez qui la séropositivité aurait été démontrée par l'épreuve immuno-enzymatique et le Western blot, laissant de 33 à 82 sujets faussement séronégatifs; 16 autres sujets auraient été faussement reconnus séropositifs. Le nombre attendu de cas de SIDA survenant de 1988 à 1998 chez les

From the divisions of Clinical Epidemiology and General Internal Medicine, Montreal General Hospital, the Division of Clinical Immunology, Royal Victoria Hospital, Montreal, the Centre for Medicine, Ethics and Law, and the Department of Economics, McGill University, Montreal, and the Department of Economics, Queen's University, Kingston, Ont.

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Reprint requests to: Dr. Steven A. Grover, Division of Clinical Epidemiology, Montreal General Hospital, 1650 Cedar Ave., Montreal, PQ H3G 1A4

séropositifs serait compris entre 151 et 379. Le dépistage aurait coûté de 3,3 à 3,4 millions de dollars, le traitement hospitalier de ces sidatiques de 5,0 à 17,1 millions, soit au bout de 10 ans une économie de 1,7 à 13,7 millions du fait de ce dépistage. Mais cette économie que réaliseraient les services de santé ne motive pas seule notre recommandation d'un tel dépistage. Toute décision concernant celui-ci devra tenir compte aussi de ses incidences éthiques, sociales et juridiques.

The economic consequences of HIV (human immunodeficiency virus) infection have recently attracted much attention. Strategies to contain costs, including screening of potential immigrants for latent infection, have been widely discussed. According to Canada's Immigration Act of 1976[1] the objectives of the medical restrictions on entry into Canada are to control the spread of disease and to limit the cost of additional health care and other related public services.

To what extent newly arrived immigrants contribute to HIV transmission in Canada remains to be determined. The total number of travellers entering Canada in 1987 was 92 million, as compared with 152 000 immigrants arriving the same year.[2] Accordingly, HIV antibody screening among potential immigrants may be relatively ineffective in controlling the spread of infection. Therefore, the main rationale for implementing HIV antibody screening among all people seeking permanent residence in Canada would be to limit the health care costs incurred by those who will acquire HIV-related diseases.

To assess the economic impact of HIV antibody screening on Canada's health care system we evaluated the potential costs and benefits of such screening among immigrants entering Canada in 1988 using the expected in-hospital costs of treating HIV-infected immigrants in whom AIDS (acquired immune deficiency syndrome) would develop over the 10 years after their immigration.

Methods

Estimation of HIV seroprevalence

We calculated the HIV seroprevalence among all immigrants to Canada in 1988 from the estimated seroprevalence rates of the countries listed as the immigrants' last permanent residence. The place of residence was obtained from Employment and Immigration Canada[3] and the national seroprevalence rates from recently published reports and abstracts presented at the IVth International Conference on AIDS, held in Stockholm June 12 to 16, 1988.[4-53] We assumed that the seroprevalence rate in the immigrant population was the same as the rate in the total population of the source country, regardless of sex and age.

National seroprevalence rates were available from 30 HIV seroepidemiologic surveys in the general population and 5 studies involving blood donors and pregnant women. We calculated the low and high seroprevalence rates using 95% confidence limits based on an approximation to the binomial method for data from 31 of the 35 countries. For the remaining four countries the low and high rates were extracted from the published reports. The average sample size was 27 705, the smallest being 51 and the largest 300 000. The total sample size was 969 666 people. The source countries were grouped as follows: western Europe, eastern Europe, Africa, the Americas and Oceania, and Asia.

For western and eastern Europe the HIV seroprevalence rate for countries from which direct data were unavailable was estimated on the basis of national seroprevalence data from neighbouring countries adjusted for differences in the number of AIDS cases. The estimate was based on the ratio of available national HIV seroprevalence rates to the national rate of reported AIDS cases per population.[54]

For western Europe we used the seroprevalence data from Sweden, Italy and Switzerland[8,36,43] to calculate the HIV:AIDS ratios and to determine the national HIV seroprevalence rates. The seroprevalence rate in Czechoslovakia, estimated on the basis of 231 548 people tested,[9] was used to provide missing national rates for other countries in eastern Europe.

Few detailed seroepidemiologic studies have been conducted in the general population of Africa, the Americas and Oceania, and Asia. Again, if seroprevalence data were unavailable the data from neighbouring or representative subregional countries were used. Data from seroepidemiologic surveys were available from 27% of the countries in those regions. These surveys represented 425 179 people, the sample size being 13 287 per country on average.

HIV antibody testing

We assumed that HIV antibody screening would be done just before entry to Canada. According to the common screening strategy for HIV infection the immigrants would undergo a sequence of tests: (a) the enzyme-linked immunosorbent assay (ELISA), (b) a second ELISA if the results of the first were positive and (c) the Western blot technique if the results of the second ELISA were positive.[55]

The sensitivity of ELISA is from 98.3% to 99.6% and the specificity 99.2% to 99.8%.[56] If the false-positive rate is very low but not zero, screening a large population in which the prevalence of HIV is low will produce relatively high false-positive rates.

The Western blot technique is not a standardized commercial product, and its performance may vary substantially from laboratory to laboratory. Although it is considered to be more accurate than ELISA it is too difficult, expensive and labour-intensive if thousands of blood samples have to be processed rapidly.[57] Assuming a given HIV seroprevalence rate among immigrants and the expected sensitivities and specificities of ELISA and the Western blot technique we calculated how many HIV-infected immigrants would be identified correctly and how many would be missed by screening.

Duration of HIV infection

According to present immigration requirements all prospective immigrants have to undergo a routine medical examination. This is accompanied by serologic testing for syphilis among those over 15 years of age, chest radiography among those over 11 years and urinalysis among those over 5 years. The examination must be done within 12 months before entry to Canada.

Since all immigrants undergo a medical examination we assumed that only those who did not yet have symptoms of AIDS would be eligible for screening. Those with symptoms would be excluded before entry to Canada. Among the HIV-positive immigrants without AIDS the distribution of the duration of HIV infection would be skewed toward those more recently infected.[58]

The rate of progression from HIV infection to AIDS was estimated on the basis of the findings of the San Francisco City Clinic Cohort Study.[59] We assumed that seropositive people emigrating from endemic regions would experience a clinical course of HIV infection similar to that observed among white homosexual men.[60,61]

Seroconversion dates

Since the dates of infection among the HIV-positive immigrants were unknown we assumed that each seropositive person had an equal chance of being infected at any time between 1979 and 1988. To calculate the number of HIV-positive immigrants infected each year who were still free of AIDS on arrival in Canada, we estimated a cross-sectional distribution of duration of asymptomatic HIV infection among the 1988 immigrants using Hessol and associates' time series.[59]

To transform the time-series data into a cross-sectional distribution we divided the HIV-infected immigrants into 10 equal groups, each of which represented 1 year of infection from 1979 to 1988. According to Hessol and associates' data, collected over 10 years, 100% of the HIV-infected immigrants would remain AIDS-free during the first 3 years after seroconversion. In the fourth year 96% would be AIDS-free, and in the fifth year 91% percent would be AIDS-free. If there were initially 100 infected people in each of the 10 groups, 837 HIV-infected people could have entered Canada in 1988. Accordingly, 11.9% (100 of 837) would have been infected annually in 1988, 1987 and 1986, 11.5% (96 of 837) in 1985, 10.9% (91 of 837) in 1984 and so on. By assigning these proportions to the aggregate number of AIDS-free HIV-infected immigrants we estimated the number of AIDS-free immigrants who seroconverted in a given year between 1979 and 1988.

Progression from HIV infection to AIDS

Our analysis of the rate of progression from HIV infection to AIDS among infected immigrants was again based on the data provided by Hessol and associates.[59] The time horizon of our model was from 1979 to 1998. Since no empirical data were available for disease progression beyond 10 years we assumed that the annual progression rate would be 4% on average after the 10th year of infection, a rate similar to the actual progression rate in years 9 and 10. We multiplied the estimated number of HIV-seropositive immigrants infected in a given year by the progression rate to determine the number of AIDS cases per year.

Cost-benefit analysis

There are two major components to the cost-benefit analysis: (a) the costs of HIV antibody screening and (b), in the absence of screening, the in-hospital costs for HIV-infected immigrants in whom AIDS would develop over the 10 years after seroconversion. Accordingly, the benefits of screening were defined in terms of in-hospital costs avoided.

We assumed that the processing of blood samples would be performed in Canada to assure the quality of the results and that the related costs would be borne by the Canadian government. To estimate the costs of screening we used the Ontario Provincial Laboratory unit costs;[62] these included costs for materials, labour, professional fees and overhead for samples collected in Canada. These costs would be inflated by the additional cost of collecting and processing foreign samples but could be deflated if

some or all of these costs were passed on to potential immigrants.

The proportion of immigrants subjected to a second ELISA was determined on the basis of screening data involving US blood donors.[63] The same proportion was found among Canadian blood donors.[62]

The in-hospital costs per AIDS case were based on data extracted from the medical records of AIDS patients at the Montreal General Hospital (S.G.: unpublished data) and the Toronto General Hospital.[62] We assumed a mean survival of 1 year after the diagnosis of AIDS before the widespread use of zidovudine (AZT).[64]

All costs and benefits are in 1988 Canadian dollars. Since the hospital costs would accrue over time we discounted at 3% to arrive at the 1988 present value of hospital costs. These costs represent the size of the fund required in 1988 to pay for AIDS-related hospital expenses until 1998. In choosing a 3% discount rate we assumed that the annual rate of return on the fund would be 3%, which is the net-of-inflation long-term provincial bond rate for 1990 and thereafter.[65]

Results

HIV seroprevalence

Among the 160 135 immigrants who entered Canada in 1988 we estimated that 343 (0.2%) to 862 (0.5%) were HIV seropositive. Two major geographic areas — the Americas and Oceania, and Africa — would have accounted for over 75% of the HIV-infected immigrants but only 25% of the total 1988 immigrant population (Table 1).

HIV antibody testing

Assuming a sensitivity of 98.3% for repeated ELISA tests,[56] 337 to 847 of the HIV-infected immigrants would have been correctly identified as being seropositive (Table 2). The remaining 6 to 15 people would have been falsely identified as being seronegative and would not have undergone the Western blot technique. Given ELISA's specificity of 99.8% the number of uninfected people falsely identified as being seropositive and requiring further testing would have been 319 to 320.

Of the 319 to 320 people with initially false-positive results the Western blot technique would have identified 95% as being negative.[56] Of the 337 to 847 true-positive results the Western blot technique would have confirmed only 92%.

Overall, 310 to 780 of the HIV-infected immigrants would have been correctly identified as being seropositive by the sequence of tests, and 33 to 82 would have been falsely classified as being seronegative. Another 16 immigrants would have been falsely classified as being seropositive.

Duration of HIV infection

Using the probability of an immigrant's being

Table 2: Expected results of enzyme-linked immunosorbent assay (ELISA) and Western blot technique as screening tests for HIV infection

Test; result	Estimated limits; no. of immigrants: Low	High
Repeat ELISA*		
True positive	337	847
False positive	320	319
True negative	159 472	158 954
False negative	6	15
Western blot technique*		
True positive	310	780
False positive	16	16
True negative	304	303
False negative	27	67
Estimated no. of HIV-infected immigrants	343	862

*Sensitivity and specificity of ELISA are 98.3% and 99.8% respectively; sensitivity and specificity of Western blot technique are 92% and 95% respectively.[56]

Table 1: Low and high estimates of human immunodeficiency virus (HIV) seroprevalence among 160 135 immigrants to Canada in 1988 by region

Region	No. (and %) of immigrants	Estimated limits; no. (and %) of seropositive immigrants: Low	High
Western Europe	25 366 (15.8)	9 (2.6)	43 (5.0)
Eastern Europe	14 686 (9.2)	0 (0)	1 (0.1)
Africa	9 294 (5.8)	70 (20.4)	231 (26.8)
Americas and Oceania	30 583 (19.1)	219 (63.8)	444 (51.5)
Asia	80 206 (50.1)	45 (13.1)	143 (16.6)
Total	160 135	343	862

seropositive in a specific year and remaining AIDS-free by 1988 we calculated how many of the 310 to 780 HIV-infected immigrants identified through screening would have been infected between 1979 and 1988 (Table 3). For example, 37 to 93 of the immigrants would have been infected annually in 1988, 1987 and 1986. In a single year the number of new HIV infections would be 21 to 93.

Given the year of infection and the rate of progression to AIDS we calculated the number of AIDS cases by year. for example, of the estimated 37 to 93 immigrants infected in 1988 no one would have AIDS in the first 3 years after seroconversion. By 1991, 4% would have AIDS, and by 1992 an additional 5% would have it. By 1998, 17 to 43 cases of AIDS would be expected from immigrants infected in 1988. Additional cases of AIDS would develop from each annual cohort, resulting in a total of 151 to 379 cases of AIDS by 1998.

Cost-benefit analysis

The total cost of screening was estimated to be $3.3 to $3.4 million. Given the unit cost for ELISA of $20,[62] the initial screening would have cost $3.2 million. On the basis of the range of HIV seroprevalence the repeat ELISA screening would have cost $40 000 to $70 000. Confirmation with the Western blot technique, at $90 per test,[62] would have cost $60 000 to $110 000.

Assuming a mean survival of 1 year after the diagnosis of AIDS and annual in-patient hospital costs of $38 420 to $52 675 per AIDS case, the total in-hospital costs would be $5.8 to $20.0 million, undiscounted. Since these costs would accrue between 1989 and 1998 the discounted costs would be $5.0 to $17.1 million. The net benefits of screening would be $1.7 to $13.7 million.

Table 3: Estimated rate of progression from HIV infection to acquired immune deficiency syndrome (AIDS) by 1998

	Status; no. of immigrants	
Year of infection	AIDS-free in 1988	AIDS present in 1989–98
1988	37–93	17–43
1987	37–93	19–47
1986	37–93	20–50
1985	36–89	19–48
1984	34–85	18–45
1983	32–80	17–42
1982	29–73	14–35
1981	24–62	9–24
1980	23–58	9–23
1979	21–54	9–22
Total	310–780	151–379

Discussion

Our results depend on the accuracy of the national HIV seroprevalence estimates and on the underlying assumptions, including the sensitivities and specificities of the HIV antibody tests. For example, the manufacturers of commercially available ELISA kits have estimated the sensitivity of HIV antibody tests by calculating the percentage of positive results among AIDS patients, who are assumed to be certain carriers of HIV. The specificity was estimated by calculating the rate of negative results among random blood donors assumed to be uninfected. Thus, the specificity estimates may have been low, since some of the blood donors with positive results could actually have been infected. Also, the sensitivity estimates may have been higher than those attained in an asymptomatic but infected population. How well these estimates of sensitivity and specificity represent the tests' performance in other populations is unclear.[56,66]

False-positive results may occur because of biologic variation among people or because of specific clinical situations.[67] False-negative results may be caused by biologic factors. Some people produce lower than average levels of antibody, and some fail to produce any. Most people with a newly acquired infection will not produce detectable antibody for at least 3 to 6 weeks, some for at least a year.[68]

Because of the delay from seroconversion to the detectability of antibody through testing there are questions about the number of tests and their timing. Even if people with negative results are tested repeatedly there is no perfect screening program for prospective immigrants.

The results of our economic analysis apply only to 1988 immigrants. They exclude any AIDS-related medical costs arising after 1998. We did not include the out-of-hospital costs of treating AIDS patients, the medical costs of treating pre-AIDS patients or the opportunity costs of displacing non-AIDS patients in the health care system. Inclusion of these additional treatment costs would increase the net benefits of HIV antibody screening.

In addition, the costs of AZT and other experimental drugs used outside the hospital setting have not been included. Some reports have estimated that AZT increases the average life expectancy by 66%, but only one-third of AIDS patients can tolerate the drug.[64] The extended survival could therefore be expected to increase the overall medical costs of treating AIDS by 22%. If AZT therapy reduces the number or length of episodes of AIDS-related illness the corresponding increase in treatment costs would be less than 22%. If AZT is used, especially in the pre-AIDS stages, hospital costs may fall but outpatient costs rise. Therefore, the overall effect of AZT

on the costs of treating HIV-related illness is not easily quantifiable at this time.

Increasing HIV seroprevalence over time would increase the estimated HIV-related medical care costs. In our method of estimating the duration of HIV infection we disregarded the growth of the HIV epidemic, assuming similar numbers of potential immigrants had been infected each year since 1979. This assumption would result in the medical cost of treating AIDS patients accruing earlier and having a higher present value. Thus, the present value of hospital costs would be overestimated.

We assumed that the screening would be performed in Canada to minimize the number of false-positive and false-negative results and that the costs would be borne by the Canadian government. In 1981 the costly tests for intestinal parasites among prospective immigrants were abolished, partly because of the inability to control the quality of testing in overseas laboratories.[69] Regardless of who pays for HIV antibody screening we may have underestimated the costs of administering such a program.

We did not account for the economic losses that might result from imposing mandatory HIV antibody screening. Such screening and the exclusion of seropositive people from entering Canada might dissuade economically active members of foreign communities from immigrating. Among these would be asymptomatic HIV-infected people who could still work, people falsely identified as being seropositive and family members of seropositive people. Such losses could be avoided if those who were excluded and dissuaded could be immediately replaced by other, equally desirable and productive immigrants. Therefore, before lost income and income-related issues (consumption, savings and taxes) can be measured, the potential for replacing lost applicants would have to be determined.

Despite the limitations we have described, our analysis provides estimates of the costs and benefits of implementing an HIV antibody screening program among all prospective immigrants. It places into perspective the potential costs involved and provides input into the decision-making process for health care providers, public health officials and government leaders. As the social, legal and ethical implications were not considered in our study we do not advocate the implementation of a screening program on the basis of economic analysis alone. By defining the magnitude of the economic impact of HIV-infected immigrants on Canada's health care system we hope to open the debate to these other, equally important considerations. Only then can we formulate a policy concerning HIV-infected people that not only protects the health of our citizens and the resources of our health care system but also respects the values of our society.

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