Screening Blood Donors for Human Immunodeficiency Virus Antibody: Cost-Benefit Analysis

RICHARD S. EISENSTAEDT, MD, AND THOMAS E. GETZEN, PHD

Abstract: The costs and benefits of screening blood donors for antibody to human immunodeficiency virus (HIV) are assessed. Total costs, including testing, discarding processed blood, marginal donor recruiting, notifying and evaluating positive donors, are $36,234,000 annually for 10 million donors in 1986. Screening these donors will prevent 292 cases of transfusion-transmitted acquired immune deficiency syndrome (TT-AIDS), saving the costs of therapy and loss of earnings for total benefits of $43,490,480, a benefit:cost ratio of 1.2:1. Net economic benefits of $0.73 per donor will arise from the program. Calculated benefits will rise as increased numbers of infected recipients are diagnosed with longer follow-up or as partially effective therapy increases the cost of caring for patients with AIDS. Changes in test sensitivity, follow-up procedures, estimated value of life, and testing costs will also alter these projections, but none as dramatically as a change in the overall specificity of the screening process. The cost per case of TT-AIDS prevented, $124,089, and cost per year of life extended, $10,885, are comparable to costs of other screening programs. (*Am J Public Health* 1988; 78:450–454.)

Introduction

Acquired immunodeficiency syndrome (AIDS) may affect the general medical public receiving blood products,[1] although the magnitude of risk remains small compared to the total number of patients transfused.[2] Two measures introduced by the blood bank industry have improved transfusion safety: discouraging individuals in high-risk groups from donating, and screening donors for antibody to human immunodeficiency virus (HIV-Ab). An enzyme-linked immunoassay (EIA) screening test for donor HIV-Ab was routinely incorporated by blood processing centers in mid-1985. More technically complex, expensive, but specific methodology to detect virus antibody using Western blot (WB) techniques was simultaneously developed. Much has been written about the scientific basis of these tests,[3] their sensitivity and specificity in certain defined populations,[4] and the moral, ethical, and legal ramifications inherent in screening healthy donors and notifying them of their test results.[5,6] This report examines the economic impact of HIV-Ab screening during 1986 from a cost-benefit approach.

Methods

Test Sensitivity

Two types of false negative HIV-Ab tests may occur. A *technical* false negative occurs when the EIA fails to detect antibody which is clearly present. Mosely found one such false negative in 13,463 specimens tested[7]; a *biological* false negative occurs in individuals who harbor live transmissible virus, but have not yet formed detectable antibody. Although most individuals form EIA detectable antibody within several months of virus infection, a small but as yet unknown per cent fail to produce antibody or have much more prolonged intervals before overt seroconversion.[8–11] The manufacturers of EIA test kits in applying for licensure have estimated sensitivity at approximately 98 per cent. This estimate, to be employed in this analysis, may seem overly optimistic when compared to data from Ranki, *et al,* who found either free HIV antigen or low titer antibodies to recombinant viral proteins 6–14 months before EIA test positivity in all nine seroconverters in their cohort study.

Test Specificity

The specificity of HIV-Ab testing is impossible to predict without an ideal gold standard for comparison. Epidemiological data suggest that most tests positive by EIA and negative by Western blot are false positives. Screening data from American Red Cross blood centers revealed initially positive EIA tests in about 1 per cent of donors, persistently positive repeat EIA tests in 0.33 per cent, and WB positive in 0.031 per cent.[13,14] Of those whose EIA were repeatedly positive by EIA but only weakly or moderately reactive compared to controls, only 1 per cent were WB positive and 1.9 per cent were culture positive. These same blood donors did not fit into age-sex patterns typical of those with AIDS and were extremely unlikely to admit to a risk factor for AIDS. Conversely, donors whose EIA was strongly reactive were almost always men and often disclosed additional risk factors; 84 per cent of those strongly reactive donors were WB positive and 51 per cent culture positive.

Initial EIA test specificity will be computed at 99 per cent. Repeat EIA testing in duplicate of an initially positive specimen will be somewhat less specific. WB positivity of a specimen repeatedly positive by EIA will be interpreted as optimally, 100 per cent, specific.

Prevalence of HIV-Ab

By December 1986, almost 30,000 cases of AIDS had been reported in the United States, but some public health officials fear that as many as one million more Americans may have been exposed to the virus and remain potentially infectious. HIV prevalence in the population at large, however, may not reflect that of blood donors, as individuals at high risk for AIDS are actively discouraged from donating.

Using American Red Cross screening data and interpreting all donors confirmed by WB as true positive, the estimated prevalence of detectable HIV-Ab is 31/100,000 donors.[13] If initial screening is only 98 per cent sensitive, an additional 0.6 donors who are infected with transmissible HIV will be missed as false negatives, but they will contribute neither to additional testing costs nor to benefits of TT-AIDS prevented.

Incidence of TT-AIDS

The benefits of testing are most dependent on TT-AIDS prevented. From December 1985, to December 1986, 298 cases of TT-AIDS were reported, occurring about 2.6 years

From the Department of Medicine, Temple University School of Medicine, and the Department of Health Administration, Temple University School of Business. Address reprint requests to Dr. Richard S. Eisenstaedt, Temple University Hospital, Broad and Ontario Streets, Philadelphia, PA 19140. This article, submitted to the Journal April 21, 1987, was revised and accepted for publication December 11, 1987.

following transfusion.[1,15] This period undoubtedly underestimates the true latency of TT-AIDS since cases with longer incubation periods have not yet been diagnosed. Lui, *et al,* used mathematical models to correct for this underestimation bias and concluded that the mean incubation period will be 4.5 years.[16]

To estimate the annual number of donations and patients transfused, two sources were utilized: the American Blood Commission (ABC) 1979 survey of 213 regional and community blood centers and over 6,000 hospitals,[17] and the American Association of Blood Banks (AABB) 1985 annual report.[18] Both agreed that approximately 14 million components are transfused annually. One per cent of donations (140,000) come from individual plateletpheresis or granulocyte donors who did *not* simultaneously donate red cells, but between 9.3 (AABB) and 10.8 (ABC) million units were whole blood donations from which the remaining plasma, platelet, and cryoprecipitate components were produced. Averaging the two whole blood donation estimates and adding the single donor platelet and granulocyte products suggests about 10 million blood donations annually. Assuming that: a) all donated units are transfused, b) plasma, platelet and granulocytes are virtually never administered to patients not receiving RBC transfusion as well, and c) ABC estimates that 3.3 red cell units are transfused per patient remain valid, one concludes that the 10 million blood donations were received by approximately 3 million patients. Holding these data constant through 1986, the incidence of TT-AIDS would be $[298 \div 3.0 \times 10^6] \times 100{,}000 = 9.9$ per 100,000 recipients or $[298 \div 10 \times 10^6] \times 100{,}000 = 3.0$ per 100,000 donors. Of note, the incidence of TT-AIDS for 1986 is one-tenth the prevalence of donor HIV-Ab positivity screened during the same period. This disparity is explained, in part, by an infectivity rate less than 100 per cent and by the fact that some infected recipients die of other causes before developing AIDS, but is mainly due to lengthy latency from virus exposure to disease expression and by the growing prevalence of virus exposure in the donor pool in the years prior to screening implementation. Benefits here will be calculated using 1986 TT-AIDS incidence data.

Benefits

Benefits are calculated by combining direct costs of medical treatment with indirect costs of lost earnings.

Costs of Medical Treatment—Hardy and colleagues examined medical care costs for the first 10,000 patients with AIDS reported to the Centers for Disease Control and they calculated that each patient would spend an estimated 168 days hospitalized at an average cost per day of $878. Average cost for treatment from diagnosis to death was $147,000.[19] Since that time, treatment patterns have changed, tending toward shorter lengths of stay and more extensive outpatient support. More recently, Seage and collegues report an average cost of $50,380,[20] while Scitovsky and colleagues compute costs of $27,571 inpatient and $3,621 outpatient in caring for predominantly middle-class gay men in Boston and San Francisco.[21] These costs must be discounted for the time lag between transfusion and treatment. Our estimate of $40,776 is obtained by taking the average of the recent Seage and Scitovsky estimates, adjusted upwards by 14.2 per cent for the 1984–86 increase in the Medical Care Price Index,[22] and adjusted downwards by 14.22 per cent to discount (at 3 per cent annually) for the 4.5 year lag between transfusion and disease onset. Note, however, that treatment costs will continue to change, particularly if even partially effective therapy is identified. For example, Zidovudine (AZT), thought to prolong life in AIDS patients with pneumocystis carinii pneumonia,[23] is the most expensive drug ever marketed, costing $10,000 per patient per year for the drug alone,[24] and commonly causes side effects which in turn may be costly to treat. Additional therapeutic advances may cause treatment costs to climb sharply making estimates relying on hospice-like supportive care obsolete.

Earnings Foregone—To calcualte the indirect costs of future earnings lost by patients with TT-AIDS as compared to a transfusion receiving cohort who are not infected, the following assumptions were made:

1) present value of future lifetime earnings and household labor by age and sex for *healthy* individuals is that reported by Scitovsky and Rice[25] expressed in 1986 dollars;

2) transfused patients will have shortened life expectancy and chronic morbidity by virtue of the underlying illness necessitating transfusion in the first place, even if they avoid TT-AIDS;

3) in the absence of data to quantitate the impact of such shortened survival and morbidity, future lifetime earnings of uninfected transfusion recipients will be calculated as *one-half* that projected for age-sex matched healthy people;

4) the age distribution of TT-AIDS is presumed similar to that reported by Peterman, *et al,* in 1985[26] after reviewing the first 194 cases, and the sex distribution (6 male:4 female) also remains consistent;

5) patients with TT-AIDS are assumed to be equally healthy as uninfected transfusions recipients during their 4.5 year latent HIV infection and totally disabled following their diagnosis with AIDS. Although neither premise in this latter assumption is, in reality, apt to occur, their impact on lost earnings in a more detailed analysis would be counterbalancing;

6) the effect of the 4.5 year lag between transfusion and disease onset is calculated by assuming that the earnings stream is evenly divided over the remaining years of life expectancy with a real rate of discount of 3 per cent. For example, a one-year-old male transfusee with a 35-year life expectancy loses the discounted value of his last 30.5 years of earnings;

7) morbidity costs, requiring a number of additional estimates for which hard data are lacking and which, in other analyses[25] accounted for less than 8 per cent of lost earnings following death, will be omitted.

In Table 1, the age-sex distribution of TT-AIDS is listed along with the adjusted present value of lifetime earnings for uninfected transfused patients. Adding together the earnings lost per case at each age-sex bracket, multiplied by the per cent with TT-AIDS within that bracket, gives an average earnings lost for the population as a whole of $108,164. Performing similar calculations for life expectancy gives an average survival for the group of transfusion recipients of 16.9 years. Assuming a latency of 4.5 years and a mean survival of one year following TT-AIDS diagnosis, these patients will, on average, lose 11.4 years of life.

Costs

Costs of HIV-Ab screening may be divided into five categories: 1) the cost of testing, per se, including materials, equipment, personnel, administration and record keeping; 2) the cost of processing ultimately discarded blood; 3) the marginal recruitment cost to compensate for lost donor units; 4) the cost of donor test result notification; 5) the costs of donor medical evaluation.

TABLE 1—Age-Sex Adjusted Life Expectancy and Discounted Future Earnings

AGE	Per cent at each age with TT-AIDS[a]		Life expectancy (years)[b]		Adjustment for 4.5 year latency[c]		Present value of lifetime earnings loss (adjusted)[d]	
	Male	Female	Male	Female	Male	Female	Male	Female
0–1	6.2%	4.1%	35.0	38.8	0.81	0.82	212,150	177,309
1–5	0.0%	0.0%	35.0	38.7	0.81	0.82	223,426	186,586
6–10	0.9%	0.6%	33.1	36.8	0.80	0.81	242,311	202,601
11–20	1.5%	1.0%	29.4	33.1	0.79	0.80	274,499	228,347
21–40	9.3%	6.2%	22.5	25.8	0.74	0.77	269,413	200,338
41–50	8.0%	5.4%	15.7	18.7	0.66	0.71	160,484	114,357
51–60	15.5%	10.3%	11.5	14.2	0.57	0.64	70,204	57,573
61–65	10.2%	6.8%	8.7	11.1	0.45	0.55	19,855	24,126
66–70	5.6%	3.7%	7.1	9.2	0.34	0.47	5,418	11,229
70+	1.8%	1.9%	4.4	5.8	0.00	0.20	0	1,454
Age-sex weighted mean			**16.9 years**				**$108,164**	

[a]From Peterman, et al, estimates for the first 194 cases of TT-AIDS.[26]
[b]Assuming life-expectancy is equal to one-half that predicted for a healthy age-matched population.[27]
[c]The 4.5 year latency adjustment factor (LAF) is computed by determining [predicted value of annuity for total life expectancy—predicted value of annuity for the next 4.5 years], the difference divided by predicted value of annuity for total life expectancy.
[d]Assuming uninfected transfusion recipients have future lifetime earnings and household productivity one-half that estimated by Scitovsky and Rice for healthy individuals,[25] increased by 5.3% for wage increases from 1984–1986 and multiplied by the 4.5 year LAF.

TABLE 2—Cost-Benefit of HIV-Ab Testing

COSTS			
Donors	10,000,000	EIA @ $3	30,000,000
+Screen	119,000	EIA × 2 @ $6	714,000
+Repeat (0.33%)	33,000	WB @ $50	1,650,000
		Blood Wastage @ $75	2,475,000
+WB (0.031%)	3,100	Followup @ $450	1,395,000
Total Costs			$36,234,000
BENEFITS			
Recipients	3,000,000		
TT-AIDS Expected:	298		
TT-AIDS Prevented:	292	Medical Care @ $40,776/case	11,906,592
		Lost Earnings @ 108,164/case	31,583,888
Total Benefits			**$43,490,480**
	Benefit:Cost	1.2:1	
	Net Benefit/Donor	$0.73	
	Cost/Case Prevented	$124,089	
	Cost/Year of Life Extended	$10,885	

The average cost of HIV-Ab testing performed at three large, geographically dispersed procurement centers is $3/test. Each initially positive test will be repeated in duplicate, and a consisently positive EIA test will be confirmed by WB technique costing, itself, $50. Processing costs of $75/unit including a marginal recruitment cost of $6/donor are estimated.[28]

All donor units repeatedly positive by EIA will be discarded, but only donors whose confirmatory WB is abnormal will be notified of their test result. Donor notification is followed by medical evaluation including a comprehensive physical exam, two follow-up visits, and the screening laboratory studies; an average of three household contacts per donor will also have HIV-Ab screening. Total costs will be $450.

Sensitivity Analysis

Alternative estimates may be employed for much of the data used in calculating this cost-benefit analysis. Calculations will be repeated varying the primary data as follows: a) the incidence of TT-AIDS will be computed at rates varying from one-tenth to 100 times baseline; b) expected benefits will be computed altering earnings estimates to range from 25–75 per cent of healthy age-sex matched controls; c) benefits will also be calculated using Lui's upper (9.0 years) and lower (2.6 years) bounds for predicted latency[16] and varying incidence, accordingly. The elasticity of each variable, defined as the per cent change in cost-benefit ratio per each 1 per cent change in the variable, will also be illustrated.

Results

Ten million donors will undergo initial EIA screening; 119,000 donors initially testing positive will have two additional EIA tests and the 33,000 donors who are repeatedly test positive will have confirmatory WB testing. These donor units will be discarded. The 3,100 confirmed positive by WB will be notified and further evaluated, generating total costs of $36,234,000—83 per cent of which arise from the initial EIA test (Table 2).

On average, 3.3 units of red cells are required per transfusion recipient. The ten million donors will, therefore, transfuse 3 million patients. Ninety-eight per cent of the expected 298 cases of TT-AIDS will be prevented, generating benefits of $148,940 per case prevented or $43,490,480 in total

TABLE 3—Impact of Variation in Donor HIV-Ab Prevalence and TT-AIDS Incidence on Screening Cost and Benefit

Incidence TT-AIDS	Prevalence HIV-Ab	Cases Prevented	B:C Ratio	Net Benefit/Donor
Baseline (3.0)	Baseline (31)	2.92	1.2:1	$ 0.73
× 1/10	× 1/10	.292	.13:1	−$3.03
× 10	Baseline	29.2	12:1	$ 40.00
× 100	× 100	292.0	20:1	$414.00

Incidence, prevalence, cases prevented are expressed per 100,000 donors

TABLE 4—Impact of Change in Earnings Estimate on Screening Cost:Benefit

Present Value of Lifetime Earnings for Uninfected Transfusion Recipient	Earnings/Case	Benefit: Cost Ratio	Net Benefit/Donor
Baseline (50% healthy age-sex matched control)	$108,164	1.2:1	$ 0.73
Low (25%)	$ 54,082	0.8:1	$−0.85
High (75%)	$162,246	1.6:1	$ 2.30

benefits. The benefit cost ratio is 1.2:1 and the net benefits per donor $0.73. The cost per case prevented is $124,089. TT-AIDS will result in a loss of 11.4 years in expected lifespan. Thus, the cost per year of life extended is $10,885.

The effect of a change in the incidence of TT-AIDS and prevalence of HIV-Ab positive donors is presented in Table 3. In a community where donor exposure to HIV is one-tenth baseline, TT-AIDS is presumed to fall by a similar rate. The costs of testing will decline minimally (<5 per cent) based on fewer true positive donors requiring repeat EIA, WB, and follow-up and fewer true positive units being discarded, while testing benefits fall 90 per cent. Costs will exceed benefits, creating a net cost per donor of about $3. If one maintains baseline estimates for donor HIV-Ab prevalence, but assumes that each WB positive donor will infect a recipient so that the TT-AIDS incidence without testing is 10× original projections, the benefit cost ratio increases to 12:1 and net benefits of $40 per donor are generated. This scenario may more accurately describe TT-AIDS incidence just prior to donor screening in April 1985, since the estimate of a 4.5 year latency between transfusion and symptomatic illness implies that most recipients of infected blood are not yet diagnosed. In communities where as high as 3 per cent of the donor pool are infected, HIV-Ab prevalence, TT-AIDS incidence, and opportunity for prevention increase 100-fold. The six-fold increase in testing costs is small compared to 100× increase in benefits from TT-AIDS prevention and net benefits of $414 per donor accrue.

If transfusion recipients who escape HIV infection are healthier than initially assumed with projected earnings 75 per cent of an age-sex matched control not requiring transfusion, benefits will be 1.6 times costs. Conversely, if these transfusion recipients are assumed to have underlying illness such as cancer or heart diseases that, even without concomitant HIV infection, limit their projected earnings to 25 per cent of a healthy counterpart, costs will exceed benefit, resulting in a net cost of $0.85/donor (Table 4).

In Table 5, alternate assumptions regarding incidence and latency, using upper and lower limits predicted by mathematical models, are analyzed. Testing benefits decrease with longer, presumed healthy intervals between transfusions and TT-AIDS, but this decrease will be more

TABLE 5—Effect of Change in Latency from Transfusion to Disease Manifestation on Blood Donor Screening Benefit:Cost

Latency	Incidence	Benefit:Cost Ratio	Net Benefit/Donor
4.5 yrs	Baseline	1.2:1	$0.73
4.5 yrs	2× Baseline	2.4:1	$5.06
2.6 yrs	Baseline	1.4:1	$1.33
9.0 yrs	4× Baseline	3.3:1	$8.53

TABLE 6—Elasticity* of the Estimated Benefit:Cost Ratio

	Current Value	% Change in B:C Ratio Due to 1% Change
INCIDENCE TT-AIDS	9.9/100,000 recipients	1.0
Prevalence HIV-Ab	31/100,000 donors	0.95
Sensitivity:EIA	98%	0.95
Specificity:EIA	99%	13.96
Lag to Onset	4.5 years	−0.32
COST		
EIA	$3	−0.84
Western Blot	$50	−0.05
Follow-up	$450	−0.04
BENEFIT		
Medical Care	$40,776	0.27
Earnings	$108,164	0.73

*"Elasticity" is measured as the percentage change in the benefit:cost ratio per 1% change in each independent variable.

than offset by the higher TT-AIDS incidence that will undoubtedly evolve.

The relative impact of a small change in estimates for a variety of variables on cost-benefit ratio is shown in Table 6. The elasticity is measured as the percentage change in benefit:cost per 1 per cent change in independent variable. As shown, net benefits are most dependent on a change in the overall specificity of testing, with a 1 per cent change in overall false positive rate producing a 14 per cent change in benefit:cost ratio. Changes in TT-AIDS incidence, HIV-Ab prevalence, or EIA sensitivity will have proportionate impact on net benefits, while changes in such factors as medical care costs of TT-AIDS victims or follow-up costs of WB positive donors have a considerably reduced impact.

Discussion

This analysis suggests that the current testing procedures generate net economic benefits in aggregate even using a fairly conservative methodology. The net savings from HIV-Ab screening of $0.73/donor is likely to understate screening benefits for several reasons. First, TT-AIDS cases occurring yearly will peak higher than the 298 reported in 1986 before the beneficial impact of donor screening is recognized. In addition, cost of caring for AIDS patients may climb considerably as partially effective treatment emerges. This analysis has not considered additional benefits in preventing the secondary spread of HIV infection from transfusion recipients to their sexual partners and offspring. Finally, the analysis has not considered psychological costs and benefits.[29] The willingness of individuals to pay for added health protection usually exceeds their expected loss measured purely by health care expense and lost earnings.

The absolute costs, net costs and benefit:cost ratio can be compared to analogous figures in other screening programs. McNeil and Eddy analyzed screening asbestos workers with a relative risk for colon cancer of 1.6 and computed screening costs at $420/year of increased life expectancy if

testing began at age 35.[30] Similar analyses estimated cost/increased year of life expectancy to range from $19–38,000 for hypertension screening and therapy[31] or $20,000 to screen cholesterol levels in 10-year-olds.[32] These costs are all expressed as 1986 dollars for comparison to the computed costs of HIV-Ab screening per year of life extended, $10,885.

Although donor HIV-Ab screening can be compared with other programs in terms such as benefit:cost ratio, cost per life saved, or year of life extended, there are unique aspects of the former to be considered. Most screening programs are chosen by the individual to be screened or his/her competent parent for the express purpose of learning the screening test result. For blood donors, the HIV-Ab screening test clearly is not a major or minor motivation behind their decision to volunteer. It may even act as a deterrent. The screening test result is of greatest value to the blood recipient, not the donor undergoing the testing. One could argue that knowledge of HIV-Ab positivity would also benefit the informed donor in helping to prevent subsequent virus transmission to, for example, sexual contacts, but clearly this benefit is secondary.

Perhaps most analogous to donor HIV-Ab screening is donor alanine aminotransferase testing in an effort to reduce post-transfusion non-A, non-B hepatitis. Hornbrook, *et al,* described costs, converted to 1986 dollars, of transaminase screening ranging from $353,540 to $449,140 per 100,000 donors and benefits of hepatitis avoided as $100,755 to $3,548,000.[27] The costs of such screening compare closely with those of HIV-Ab screening; the wide range in calculated benefits reflect uncertainty about the natural history of post-transfusion non-A, non-B hepatitis and its propensity to progress to cirrhosis and liver failure. Yet even assuming low estimated benefits and high estimated costs, the benefit:cost ratio for transaminase screening approaches that for HIV-Ab testing in most United States communities where AIDS incidence is low. Issues of economic costs and benefits alone are, thus, unlikely to explain the rapid implementation and acceptance of HIV-Ab screening while blood centers argued the merits and, until recently, avoided the use of surrogate tests for non-A, non-B hepatitis transmission, despite demonstrated association of positive donors with post-transfusion hepatitis.[33]

It is clear that issues dealing with AIDS are viewed by the public with passion exceeding numerical estimates of incidence and fear surpassing the likelihood of HIV transmission outside high-risk groups. One might, therefore, question whether the hard numerical data of cost-benefit analysis appropriately reflects the public willingness to pay for added protection.

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