

Economic Evaluation of an HIV Prevention Intervention for Seropositive Injection Drug Users

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Objective: To assess the cost-effectiveness of Intervention for HIV-Seropositive injection drug users—Research and Evaluation (INSPIRE), designed to reduce risky sexual and needle-sharing behaviors in research sites in four US cities (2001–2003).
Methods: We collected data on program and participant costs. We used a mathematical model to estimate the number of sex partners of injection drug users expected to become infected with human immunodeficiency virus (HIV) (with and without intervention), cost of treatment for sex partners who became infected, and the effect of infection on partners' quality-adjusted life expectancy. We determined the minimum effect that INSPIRE must have on condom use among participants for the intervention to be cost-saving (intervention cost less than savings from averted HIV infections) or cost-effective (net cost per quality-adjusted life year saved less than \$50,000).
Results: The intervention cost was \$870 per participant. It would be cost-saving if it led to 53 percent reduction in the proportion of participants who had any unprotected sex in 1 year and cost-effective with 17 percent reduction. If behavior change lasted 3 months, the cost-effectiveness threshold was 66 percent; if 3 years, the threshold was 6 percent.
Conclusions: Although cost-saving thresholds may not be achievable by the intervention, we anticipate that cost-effectiveness thresholds will be attained.

KEY WORDS: behavioral intervention, cost-effectiveness, HIV prevention, injection drug use, mathematical modeling

The number of human immunodeficiency virus (HIV) infected persons in the United States continues to increase. Of HIV-positive individuals, an estimated 28 percent are injection drug users (IDUs).¹ While the

risk for transmission due to drug injection practices has decreased in the past 10 years, sexual risk behaviors among IDUs have been less amenable to change^{2–4} and may be responsible for much of the transmission among IDUs in the United States.^{5,6} For example, of the 161 heterosexual male and female HIV-positive IDUs in the Seropositive Urban Drug Injectors Study (SUDIS), one fourth reported having had unprotected anal or vaginal sex in the previous year with a partner of HIV-negative or unknown HIV status.⁷

A number of studies have assessed the effectiveness of HIV prevention interventions for changing sexual behaviors of IDUs.^{3,8,9} However, economic evaluations of behavioral interventions directed primarily at HIV-positive IDUs are not available.¹⁰ Most economic

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evaluations of interventions directed at IDUs have focused on needle exchange programs.¹¹

This study was carried out to determine the cost of Intervention for Seropositive IDUs—Research and Evaluation (INSPIRE) and to determine whether the intervention is likely to be cost-effective from a societal perspective (a perspective in which all costs and benefits are included, no matter who pays or benefits). The assessment focused on HIV infections prevented through sexual risk reduction, which was the primary outcome of the study. Cost-effectiveness implications of INSPIRE's other goals (drug injection risk, utilization of medical care, and adherence to HIV medications) were not assessed.

● INSPIRE

INSPIRE was a randomized, controlled trial with longitudinal follow-up.¹² It was conducted in four cities (Baltimore, Miami, New York, and San Francisco) from 2001 to 2003 with support from the Centers for Disease Control and Prevention (CDC) and the Health Resources & Services Administration. The goals of the intervention were to prevent HIV transmission due to high-risk sexual and drug injection behaviors, to increase use of primary HIV healthcare, and to increase adherence to HIV treatments.

At each of four sites, 375 HIV-seropositive heterosexual IDUs were targeted for recruitment into the intervention, for a total of 1,500 participants. At the baseline visit, participants provided an oral fluid sample to confirm HIV status and a blood sample to measure CD4 cell counts and viral load. They completed a baseline assessment regarding sex and drug-use risk behaviors, access to and use of HIV care, and adherence to HIV medications. Approximately two thirds of those who attended the baseline visit came back for the first session and were randomly assigned to either the intervention or the comparison group (16 cohorts per site with approximately 15 individuals in each cohort were planned).

Individuals in the intervention group participated in 10 HIV prevention education sessions (seven small-group, one peer group volunteer activity, and two individual). The comparison group members participated in eight group sessions, to match the number of group sessions given to the intervention group. In one session, they received standard HIV-risk-reduction messages, and in the other sessions they watched and discussed videos covering topics such as healthy lifestyles, employment, and family. Assessments were repeated at the 3-, 6-, and 12-month postintervention visits.

● Methods

Program costs

Program costs were collected prospectively for the sixth cohort in the four sites (April–July 2002) using structured forms. This cohort was chosen because by this time in the trial site staff members were experienced in conducting the intervention and resource use was expected to have stabilized. Site staff recorded the amount of resources (personnel, transportation, facility, and material) used to recruit participants and conduct program sessions. They also reported unit costs for each resource. They excluded resources used for research activities (eg, oral HIV tests, CD4 cell counts, and viral load tests, behavioral assessments, and randomization), which would not be incurred in a nonresearch setting.

CDC researchers estimated the costs to train facilitators and to produce and procure some educational materials (eg, posters). Vehicle reimbursement rates established by the General Services Administration for 2002 were used to compute transportation costs.¹³

Costs of items expected to remain useful after completion of INSPIRE (eg, televisions, video cassette players, and educational materials such as anatomical models) were annuitized.¹⁴

Costs for the sixth cohort were multiplied by 16 (the total number of cohorts expected per site to achieve the required study sample) to calculate the total program cost. Program costs for the comparison group were not included in the calculation.

Participant costs

During the 3-month follow-up visit, participants in the fifth and sixth cohorts were asked about costs they had incurred. An interviewer-administered questionnaire asked about income loss and child and elderly care costs incurred because of participation in INSPIRE sessions and the cost of transportation to attend the sessions.

The average cost per participant was multiplied by 500 (the expected number of IDUs in the intervention group) to calculate total participant costs.

Mathematical modeling

A mathematical model was constructed to estimate the number of sex partners of IDUs expected to become infected with HIV (with and without the intervention), cost of treatment for infected individuals, and the effect of infection on partners' quality-adjusted life expectancy (in quality-adjusted life years [QALYs], a measure that combines length of life with the quality of life, rated on a scale from 0 to 1, with higher values representing better quality).

Scenarios

The model was run for two scenarios, no intervention and intervention. In the no-intervention scenario, the risk for HIV infection was analyzed for 12 categories, which were six types of sex (insertive anal and vaginal, insertive anal only, insertive vaginal only, receptive anal and vaginal, receptive anal only, and receptive vaginal only), each further categorized into exposure to or no exposure to contaminated needles.

For the intervention scenario, partners in each of 12 categories were further categorized into two: (a) no change in sexual behavior and (b) condom use during each sex act (for the duration, behavior change was expected to persist among participants).

Parameters

Model parameters used for base case and sensitivity analyses are presented in Tables 1 and 2. Base case refers

to the main analysis. Sensitivity analyses assessed the effect of changes in parameter values on study results.

All costs were updated to September 2002 US dollars according to the medical care component of the consumer price index.²⁴ As noted in Table 1, some of the behavioral parameters were derived from the SUDIS, a CDC-funded study of 161 male and female HIV-positive IDUs in San Francisco and New York. Findings of this study were used in designing INSPIRE.

Level of HIV care varies widely by geographic region in the United States; thus, for our model, we assumed that 50 percent of infected persons received low-level care and 50 percent medium-level care. Low-level care represented a low level of access to treatment for HIV; medium-level care assumed that infected individuals received recommended treatment.²³ In the base case, the undiscounted lifetime cost was \$150,181 for low-level care and \$347,078 for medium-level care. With low-level care, infected individuals' life expectancy (in

TABLE 1 • Human immunodeficiency virus (HIV) transmission—related model parameters

Parameter	Base case value	Values for sensitivity analyses	Reference
HIV transmission probability per sex act			15
Receptive anal intercourse	0.02	0.008–0.032	
Receptive vaginal intercourse	0.001	0.0005–0.0015	
Insertive anal or vaginal intercourse	0.0006	0.0003–0.0009	
HIV transmission probability per needle sharing act	0.0067	0.005–0.01	16
Condom effectiveness	0.9	0.69–0.95	15,17,18
Estimated HIV prevalence among sex partners of INSPIRE participants, %*	23.62	14.3–41	19
Estimated number of opposite-sex partners per INSPIRE participant (in each 3-mo period)			7
Male participants	2.94	1–5.88	
Female participants	2.63	1–5.26	
Sexual partner overlap, %	25	0–50	15
Estimated proportion of INSPIRE participants who practiced unprotected sex in 3-mo preintervention period, %†			‡
Insertive anal and vaginal intercourse	2		
Insertive vaginal intercourse only	16		
Receptive anal and vaginal intercourse	6		
Receptive anal intercourse only	1		
Receptive vaginal intercourse only	20		
Estimated number of unprotected sex acts (per partner) in 3-mo preintervention period per INSPIRE participant engaging in such sex acts§	6	1–12	20
Estimated proportion of INSPIRE participants who shared contaminated needles in 3-mo preintervention period, %			7
Male participants	10	...	
Female participants	16	...	
Estimated number of times (per partner) contaminated needles shared in 3-mo preintervention period per INSPIRE participant practicing such needle sharing	6.55	2.68–16.98	21
Expected duration of behavior change after participation in INSPIRE, mo	12	3–36	22

*Average of prevalence levels among injection drug users in Baltimore, Miami, New York, and San Francisco.

†None of the SUDIS participants reported practicing unprotected insertive anal intercourse only.

‡Calculated from the SUDIS data.

§For participants practicing two types of unprotected sex (ie, anal and vaginal), the acts were assumed to be equally divided between the two types.

TABLE 2 • Human immunodeficiency virus (HIV) disease–related model parameters*

Disease phase description	Parameter† (values for sensitivity analyses)					
	Quality-of-life rating‡ (range)	Low-level care§		Medium-level care		
		Duration, y	Annual medical care cost, US\$ (range)		Duration, y	Annual medical care cost, US\$ (range)
Infected; unidentified	0.94	6	...		2	...
Infected; identified; viral load monitoring; no treatment	0.91 (0.89–0.93)		1	4,127 (1,576–6,112)
Infected; identified; viral load monitoring; two-drug therapy¶	0.87 (0.82–0.92)		3	11,751 (9,200–13,736)
Infected; identified; viral load monitoring; three-drug therapy#	0.82 (0.73–0.90)		3	20,422 (17,871–22,407)
Infected; identified; CD4 cell counts 200–499/mm ³	0.76 (0.62–0.88)	3	10,242 (6,731–13,248)		4	22,529 (18,976–25,567)
Infected; identified; CD4 cell counts <200/mm ³	0.65 (0.42–0.74)	1	20,213 (11,202–28,205)		1	32,500 (23,447–40,524)
Infected; identified; clinical AIDS	0.62 (0.17–0.70)	2	49,621 (33,155–72,317)		2	61,908 (45,500–84,636)

*Adapted from Holtgrave and Pinkerton.²³

†Entries in parentheses represent values used for sensitivity analyses.

‡Higher ratings represent better health.

§Single-drug therapy (zidovudine) is given in all phases after infection is identified; viral load monitoring is not carried out in any phase.

||Viral load monitoring is carried out in all phases after infection is identified.

¶Zidovudine and lamivudine.

#Zidovudine, lamivudine, and saquinavir; three-drug therapy is continued in all subsequent phases in the medium-level care scenario.

undiscounted QALYs) was 9.81; with medium-level care, it was 12.79 QALYs (see Table 2 for details). Discounting is a method for adjusting the value of future costs and benefits to an equivalent present value; application of the method in this study is described in the “Analyses (model runs)” section.

Equations

The number of HIV infections expected among the sex partners over a 3-month period is represented by the following equation:

$$m(1-i)(1-o)[1 - \{(1-a)^{u_1}(1-v)^{u_2}\}], \quad (1)$$

in which m is the number of partners per IDU, i is the prevalence of HIV infection among partners, o is a measure of sexual partner overlap (because IDUs may share partners), a and v are the per-act HIV transmission probabilities due to unprotected anal and vaginal sex, respectively, and u_1 and u_2 represent the number (per partner) of acts of unprotected anal and vaginal sex, respectively, over the 3-month period.^{22,25–31}

Some IDUs also shared contaminated needles with their partners. The number of HIV infections expected among the partners is represented by

$$m(1-i)(1-o)[1 - \{(1-a)^{u_1}(1-v)^{u_2}(1-n)^{u_3}\}], \quad (2)$$

in which n is the per-act HIV transmission probability due to the sharing of contaminated needles and u_3 represents the number (per partner) of times contaminated needles were shared over the 3-month period.

After participating in INSPIRE, some IDUs were expected to change their behavior and use condoms during each sex act. The number of infections expected among the partners during the period such behavior change persisted is represented by

$$m(1-i)(1-o)[1 - \{(1-(1-c)a)^{p_1}(1-(1-c)v)^{p_2}\}], \quad (3)$$

in which c represents the effectiveness of condoms for preventing HIV transmission and p_1 and p_2 represent the number (per partner) of acts of condom-protected anal and vaginal sex, respectively.

For participants who continued to share contaminated needles while practicing protected sex, the number of infections expected among partners is represented by

$$m(1-i)(1-o)[1 - \{(1-(1-c)a)^{p_1}(1-(1-c)v)^{p_2}(1-n)^{u_3}\}]. \quad (4)$$

Analyses (model runs)

The estimated average age of INSPIRE participants was 42 years (based on data from the SUDIS).⁷ The average

age of their sex partners was assumed to be the same. The model was run over 3-month periods for 23 years, that is, until partners of the average age reached age 65.^{23,30,32} During each of the ninety-two 3-month periods, uninfected partners were exposed to the risk for HIV infection (as given in Equations 1–4), and costs and QALYs were calculated on the basis of the number of partners who were uninfected or infected (and in specific phases of disease). Both costs and QALYs were discounted by three percent annually. Discounted costs and QALYs were cumulated at the end of the model run. The output of the model thus consisted of two sets of cumulated and discounted costs and QALYs, one for the no-intervention scenario and the other for the intervention scenario. The difference between the two sets represented disease treatment costs averted and QALYs saved by the intervention.

Calculating cost-saving and cost-effectiveness thresholds

Analyses were conducted with the parameter values given in Tables 1 and 2 (for base case and sensitivity analyses) to estimate the thresholds (minimum reduction in unprotected sex needed for the intervention to be considered cost-saving or cost-effective). The model used to compute threshold levels of behavior change is based on the widely used cumulative probability model^{25,26} and uses estimates of HIV/AIDS treatment costs (updated for inflation) and quality-adjusted life expectancy.²³

For the intervention to be cost-saving, intervention costs must be smaller than averted disease treatment costs.³⁰ The cost-effectiveness threshold was based on a cost/QALY-saved value (\$50,000) that is usually considered cost-effective in the United States.¹⁵ Thus, for the intervention to be cost-effective, cost of the intervention must be less than the averted cost of disease treatment + (50,000 × QALYs saved).

● Results

The cost of the INSPIRE intervention was \$435,419 (Table 3). The average per-participant cost was \$870. Program personnel costs constituted a large proportion (74%) of the total cost. Nearly half of these were attributed to screening, intake, and recruitment tasks. Participant costs comprised only six percent of the total cost. Transportation costs accounted for 65 percent of cost to participants. Reported income lost because of participation in the intervention was small (average income loss \$0.89 per hour); only 11 percent of the participants reported any income loss.

Under base case assumptions, the cost-effectiveness threshold was 17 percent (Table 4). That is, if 17 percent

TABLE 3 ● Cost of INSPIRE intervention

Cost category	Units	Unit cost, US\$	Total cost, US\$
Program costs			
Personnel			
Sessions	6,380 h	19.54	124,678
Administration	1,220 h	20.62	25,156
Training and supervision	496 h	25.11	12,453
Screening, intake, and recruitment	8,784 h	18.13	159,221
Staff transportation	8,780 miles	0.37	3,205
Material	64 cohorts	527.07	33,733
Facility	74 mo	331.03	24,364
Other*	74 mo	365.62	26,909
Participant costs			
Income loss	9,000 h	0.89	8,010
Child and elderly care	9,000 h	0.11	990
Transportation	5,000 round trips	3.34	16,700
Total			435,419

*Other costs include telephone, fax, Internet, water, gas, electric, and photocopier.

of IDUs who reported having had unprotected sex before the intervention used condoms during every sex act after the intervention and this behavior persisted for a year, the intervention would be considered cost-effective. At this level of behavior change, 0.5 HIV infection would be averted and one infection would be delayed. For the intervention to be cost-saving, the corresponding level of behavior change was 53 percent (with 1.5 infections averted and three infections delayed).

Sensitivity analyses showed that the changes in many of the parameters had a modest effect on results (Table 4). The results were especially sensitive to the parameters that affect transmission (especially the number of partners and number of unprotected sex acts) and the duration of behavior change. For example, if behavior change persisted for 3 months, the cost-effectiveness threshold was 66 percent; for 6 months, 33 percent; and for 3 years, 6 percent.

Per-participant costs ranged from \$610 to \$1,120 at the four sites. Variation between sites resulted largely from differences in the number of staff hours spent in conducting the intervention and, to a smaller extent, from differences in hourly wages. The thresholds were less sensitive to variation in this parameter than to transmission parameters and the duration of behavior change.

Modeling a shorter average life span for sex partners of IDUs (55 years compared with 65 years in the base case analysis) did not affect the cost-saving threshold (53%) but increased the cost-effectiveness threshold to 35 percent. If all IDUs (infected and uninfected) were

TABLE 4 ● Results of threshold analyses: Base case and sensitivity analyses*

Parameter [†]	Threshold, % [‡]	
	Cost-effectiveness	Cost-saving
Base case	17	53
Cost of INSPIRE intervention		
\$292,221 [§]	11	36
\$572,631	22	70
Cost of treating HIV/AIDS		
Low	18	71
High	15	42
Quality rating of life with HIV/AIDS		
Low	15	53
High	18	53
Proportion of infected partners receiving low-level care		
0% [¶]	16	38
100%	17	88
HIV transmission probability per sex act		
Low	29	88
High	13	41
HIV transmission probability per needle sharing act		
0.005	17	53
0.01	17	54
Condom effectiveness		
69%	22	70
95%	16	50
HIV prevalence among injection drug users		
14.3%	15	48
41%	22	69
Expected number of opposite-sex partners per INSPIRE participant		
Low	47	#
High	8	27
Sexual partner overlap		
0%	13	40
50%	25	80
Expected number of unprotected sex acts per partner per INSPIRE participant (preintervention)		
1	73	#
12	10	34
Expected duration of behavior change after participation in INSPIRE		
3 mo	66	#
36 mo	6	18
Discount rate		
0%	11	43
7%	28	73

*HIV indicates human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome.

[†]Refer to Tables 1 and 2 for values used in sensitivity analyses for parameters for which both low and high levels consist of more than one number.

[‡]Minimum reduction needed in proportion of INSPIRE participants reporting unprotected sex (in the past 3 mo) for the intervention to be cost-effective or cost-saving. Cost-saving means that the cost of the intervention is less than the savings it generates by preventing infection. Cost-effective means that the net cost (ie, the cost of the intervention after subtracting the savings) per QALY saved is less than \$50,000.

[§]Intervention cost if the cost in all four sites equaled the cost in the least expensive site.

^{||}Intervention cost if the cost in all four sites equaled the cost in the most expensive site.

[¶]100% receive medium-level care.

#Intervention is not cost-saving even if it results in 100% reduction in unprotected sex.

assigned lower quality-of-life ratings (80% of base case values), the two thresholds were 53 percent and 20 percent, respectively.

Finally, changes in multiple parameters showed substantial changes in the thresholds. A scenario favorable to the intervention (high cost of illness, low quality-of-life ratings for HIV-positive individuals, and low cost of intervention) was associated with cost-saving and cost-effectiveness thresholds of 28 percent and 9 percent, respectively. The thresholds were 93 percent and 26 percent, respectively, in the unfavorable scenario (low cost of illness, high quality-of-life ratings for HIV-positive individuals, and high cost of intervention).

● Discussion

The results show that if the behavioral intervention provided in INSPIRE leads to modest changes in sex risk behaviors of HIV-positive IDUs, it is likely to be cost-effective.

The analysis reported here is conservative, both in the values of parameters selected for the base case calculations and in the modeling approach. Most published economic evaluations of HIV prevention behavioral interventions assume that HIV infections avoided during a brief period of behavior change (1 year or less) represent infections prevented over the individual's lifetime.^{15,30,33–36} Some of the infections avoided during the period of behavior change are not prevented, only delayed.³⁷ That is, participants or their partners escape infection while protective behaviors persist but risk becoming infected when they resume unsafe practices. In this analysis, delayed infections were included in the model and accounted for in the calculation of costs and quality-adjusted life expectancy.

It may be argued that although all infected individuals are unlikely to receive recommended care, cost-effectiveness analyses should be based, for equity reasons, on the assumption that such care is provided to everyone. Thresholds for this assumption are lower than those resulting from base case assumptions.

Published estimates of the cost per participant of multisession small-group interventions vary widely, depending chiefly on the number of sessions provided. Estimates range from approximately \$350 (in 2002 US dollars) for a 5-session intervention for urban women at high risk³³ to \$590 for a 12-session intervention for gay men.³⁴ An analysis of the cost of unmet HIV prevention needs in the United States¹⁰ assumed the per-participant cost to be \$690 for an intervention directed at HIV-positive people. Our analysis found that the average per-participant cost of the 10-session INSPIRE intervention is \$870. Although sites were asked to exclude research-related costs, as much as \$318 of the

per-participant cost was attributed to screening, intake, and recruitment activities. These costs may be lower in a nonresearch setting (in which it is less likely that public health practitioners would use strict entry criteria to enlist participants and more likely that lower-cost intake mechanisms—such as referrals from correctional facilities and drug treatment clinics—would be established).

The cost of participating in INSPIRE was found to be low; transportation accounted for a large proportion of the cost. Other studies have indicated that IDUs tend to be unemployed or to have low levels of income.^{38,39}

A limitation of our analysis is that future (secondary and tertiary) transmission of HIV is not included in the model. That is, if the intervention is successful in preventing HIV transmission to partners of INSPIRE participants, transmission by these partners to their future sex partners is also prevented. Because these successive waves of prevention are not included in the present analysis, the benefit of the INSPIRE intervention is underestimated and the reported threshold values are inflated. Similarly, potential beneficial effects of the intervention in reducing high-risk drug injection behaviors and increasing the use of primary HIV health-care and adherence to HIV treatments are not included in the analysis and the resulting threshold values are overstated.

Another limitation is that the present analysis is based on dichotomous behavioral parameters. HIV-positive IDUs are categorized by those who report any unprotected sex and those who report none. *Behavior change* is defined as a move from the first category to the second. Upon completion of INSPIRE, more detailed behavioral data would be available than are used in the present analysis, similar to the recommended dataset⁴⁰ for evaluation of HIV prevention interventions. The reduction in risk of transmission due to occasional use of condoms and a decrease in the number of partners could then be modeled, and it is likely that cost-effectiveness thresholds would be lower than those reported here.

In addition, the economic evaluation conducted at the conclusion of the INSPIRE trial will need to account for the possibility of behavioral change in the comparison group. The present analysis compared the intervention with no-intervention, a *do-nothing* scenario. In the end-of-trial evaluation, the comparison group should also be included in the analysis if participants in that group change their risk behavior.

The threshold for cost saving appears too high to be achieved by INSPIRE (especially under the assumptions used for many of the sensitivity analyses). However, it is likely that INSPIRE will produce as much behavior change as is required to achieve the cost-effectiveness thresholds reported here. INSPIRE is de-

signed to detect a 30 percent reduction in the proportion of individuals reporting unprotected sex in the past year. Therefore, if the trial were to succeed in detecting a decrease in risky-sex behaviors, it is also likely that INSPIRE would prove to be a cost-effective intervention. Interventions in the past have been successful in achieving behavioral changes of a similar magnitude.^{3,8,9,20,41}

In conclusion, this study has found that the costs of the INSPIRE intervention are similar to those described in the literature for other small group behavioral interventions for HIV prevention and that the cost to IDUs of participating in the intervention is very low. The results of mathematical modeling indicate that if the INSPIRE trial were to succeed in detecting a decrease in risky-sex behaviors among HIV-positive IDUs, the intervention would also be cost-effective. Designing cost-effective intervention for HIV-positive persons is an important way to conserve scarce HIV prevention resources and to ensure that appropriate interventions can be moved from research settings to community-based agencies serving at-need populations.

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