tion between infections and coronary artery disease may be related to endothelial dysfunction, in which there is a disturbance of the dilatation capacity of the arteries. Insulin resistance lasting 1 to 3 months has been documented in subjects having ordinary bacterial or viral infections[9]; it has also been shown to be closely associated with angina pectoris without any abnormalities in coronary angiograms (syndrome X).[10] Thus, it could be possible that infections cause a reversible endothelial dysfunction.

Indeed, infection seems to be as significant a risk factor for myocardial infarction as high serum cholesterol is. We have added to the observations of earlier authors ours on the possible association between mild infections of the upper respiratory tract and myocardial infarction. Further research is needed to confirm the validity of this finding. □

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Preventing HIV/AIDS among High-Risk Urban Women: The Cost-Effectiveness of a Behavioral Group Intervention

David R. Holtgrave, PhD, and Jeffrey A. Kelly, PhD

ABSTRACT

Objectives. A human immunodeficiency virus (HIV) intervention trial for women at high risk for acquired immunodeficiency syndrome and attending an urban clinic was reported previously. The behavioral group intervention was shown to increase condom use behaviors significantly. This study retrospectively assessed the intervention's cost-effectiveness.

Methods. Standard methods of cost and cost-utility analysis were used.

Results. The intervention cost was just over $2000 for each quality-adjusted life-year saved; this is favorable compared with other life-saving programs. However, the results are sensitive to changes in some model assumptions.

Conclusions. Under most scenarios, the HIV prevention intervention was cost-effective. (*Am J Public Health.* 1996;86:1442–1445)

Introduction

Women account for a rapidly increasing percentage of cases of human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS).[1] At especially high risk are women with multiple sex partners, women with partners who inject drugs or have extrarelationship sex, and women with sexually transmitted diseases. It has been shown, however, that HIV-related risk behaviors can be modified successfully with behavioral interventions.[2–4]

A recent, randomized controlled trial evaluated a cognitive-behavioral group intervention for women at high risk for HIV infection and attending an urban primary health care clinic.[5] Among the 197 women enrolled in the study, the average age was 29 years, the average educational level was 11 years, fewer than 3% were employed, 87% were African American, and all had engaged in high-risk behaviors for HIV infection. Enrollees were randomized to one of two interventions: (1) a cognitive-behavioral HIV prevention intervention, or (2) nutritional information and skills unrelated to HIV disease and AIDS. The five-session HIV prevention intervention, which focused on skills training in condom use, problem solving, assertiveness in sexual situations, self-management, and peer support, was shown to increase condom use behaviors significantly. At 3-month follow-up, the intervention group used condoms on 56% of vaginal intercourse occasions (vs 32% for the comparison

The authors are with the Center for AIDS Intervention Research, Department of Psychiatry and Behavioral Medicine, Medical College of Wisconsin, Milwaukee.

Requests for reprints should be sent to David R. Holtgrave, PhD, Center for AIDS Intervention Research, Department of Psychiatry and Behavioral Medicine, Medical College of Wisconsin, 1249 N Franklin Pl, Milwaukee, WI 53202.

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condition) and with 66% of male sex partners (vs 48% for the comparison condition).[5]

The trial originally was designed to assess intervention efficacy, not cost-effectiveness. However, cost-effectiveness information is vitally important to policymakers, program managers, and other persons planning HIV prevention programs who must allocate limited prevention resources judiciously so as to maximize the number of HIV infections averted.[6] Here, we expand the original research agenda and present a retrospective economic evaluation that answers the following research questions:

- What is the intervention's cost per client?
- What is the cost per quality-adjusted life-year (QALY) saved, and is this at a level that is usually considered cost-effective?

We focus on this one previous intervention trial. Two other behavioral intervention trials for HIV primary prevention among women used sets of outcome measures that do not permit the full range of economic evaluation analyses described here.[7,8] Further, we present this retrospective economic evaluation as a possible model that can be adapted by other behavioral intervention researchers who seek to make their research more policy relevant.[9]

Methods

Standard methods of cost-utility analysis were used,[10,11] and a societal perspective was taken. The major analytic steps were (1) a retrospective estimation of the intervention's cost, (2) mathematical modeling to translate the observed behavioral effects into an estimate of the number of HIV infections averted and QALYs saved, and (3) an estimation of the cost per QALY saved by the intervention. Table 1 displays model parameters, base case values, and sources.

Several important methodological issues are noted for each major analytic step. Turning first to the cost analysis, all costs are in 1992 dollars (the year the intervention was implemented). The complete direct costs of intervention delivery (relative to a no-treatment, no-cost condition) were estimated. The materials costs listed in Table 1 include the cost of condoms. Indirect costs (e.g., rent, utilities, general administration, and maintenance) were estimated as a fraction of direct costs. The unknown costs of recruitment to the intervention itself (not the study) were considered to be included in indirect costs. Costs of the scientific components of the randomized trial (such as extensive survey work and study recruitment) were excluded. Clients, nearly all of

TABLE 1—Cost-Utility Analysis Model of an HIV Intervention for High-Risk Women Attending an Urban Clinic: Parameters, Base Case Values, and Sources of Information

Parameter (Symbol)	Base Case Value	Source of Value
Sex behavior and epidemiological parameters		
Sex partners' HIV seroprevalence (p)	0.03	Kelly,[a] Rosenberg[24]
Single sex act transmission probability (r_a)	.0155	Brookmeyer and Gail[25]
Single sex partner transmission probability (r_p)	.25	Blower,[16] Brookmeyer and Gail[25]
Condom effectiveness (e)	0.95	CDC[26] (low bound)
Condom use, control condition, per act (f_{ca})	0.32	Kelly et al.[5]
Condom use with intervention, per act (f_{ia})	0.56	Kelly et al.[5]
Condom use, control condition, per partner (f_{cp})	0.48	Kelly et al.[5]
Condom use with intervention, per partner (f_{ip})	0.66	Kelly et al.[5]
No. contacts with one partner (n)	31.25	Kelly et al.[5] (inferred)
No. partners per client (m)	1.5	Kelly et al.[5]
Intervention parameters		
No. clients in intervention (G)	100.0	Kelly et al.[5]
No. groups of clients	13.0	Kelly et al.[5]
No. sessions per client	5.0	Kelly et al.[5]
No. hours per session	1.5	Kelly et al.[5]
No. facilitators per session	2.0	Kelly et al.[5]
Facilitator's training, debriefing, preparation time (hours per session)	0.5	Kelly[a]
No. hours in transit per client per session	1.0	Kelly[a]
Cost-related parameters		
Facilitator's average hourly wage	$12.00	Kelly[a]
Fringe benefit rate	.27	College[b]
Materials cost per session per client	$2.00	Kelly[a]
Indirect cost rate	0.5	College[b]
Client's one-way transportation cost	$2.00	Estimate
Child care cost per hour	$5.00	Estimate
Fraction of clients needing child care	0.5	Kelly[a]
Cost of senior staff to tailor, train, and perform quality assurance	$1 625.00	Kelly[a]
Incentives per client per session	$15.00	Kelly,[a] Kelly et al.[5]
Discounted medical treatment cost (T)	$56 000.00	Guinan et al.[18]
Quality-adjusted life-years (QALYs) saved		
No. QALYs saved per prevention (Q)	7.64[c]	Holtgrave and Qualls[17] (adjusted)

Note. HIV = human immunodeficiency virus; CDC = Centers for Disease Control and Prevention.
[a]The source (or a source) of the information is Dr Jeffrey A. Kelly, the principal investigator of the original randomized intervention trial.
[b]The source of the information is the authors' home institution.
[c]Parameter Q reflects the number of discounted QALYs saved per HIV infection averted. The number of QALYs saved has been discounted at 5% to yield the value 7.64. See text and Holtgrave and Qualls[17] for further details on this calculation.

TABLE 2—Cost-Utility Analysis Model of an HIV Intervention for High-Risk Women Attending an Urban Clinic: Changes in Cost-Utility Ratios under Major Sensitivity Analyses[a]

Parameter (Symbol)	Values Used	Per-Act Model Transmission Probability[b] .0014	.0092	.0155	Per-Partner Model Transmission Probability[c] .18	.25	.28
Sex partners' HIV seroprevalence (p)	.01	$234 020	34 842	20 664	$69 002	47 638	41 752
	.03	73 140	6 749	2 024	18 135	11 014	9 052
	.05	40 964	1 131	<0	7 962	3 689	2 512
Condom use with intervention, per act (f_{ia})	.46	130 901	17 135	9 080	NA	NA	NA
	.56	73 140	6 749	2 024	NA	NA	NA
	.66	49 356	2 474	<0	NA	NA	NA
Condom use with intervention, per partner (f_{ip})	.56	NA	NA	NA	49 974	33 951	29 536
	.66	NA	NA	NA	18 135	11 014	9 052
	.76	NA	NA	NA	9 038	4 460	3 199
No. partners per client (m)	1.0	113 330	13 740	6 650	30 821	20 138	17 195
	1.5	73 140	6 749	2 024	18 135	11 014	9 052
	2.0	53 045	3 254	<0	11 793	6 452	4 980
Incentives per client per session	$30	106 776	12 634	5 935	28 780	18 681	15 899
	$15	73 140	6 749	2 024	18 135	11 014	9 052
	$0	39 504	864	<0	7 491	3 346	2 204
Indirect cost rate	1.0	94 856	10 548	4 549	25 007	15 964	13 473
	0.5	73 140	6 749	2 024	18 135	11 014	9 052
	0.2	60 111	4 469	510	14 012	8 044	6 399
No. QALYs saved per prevention (Q)	5.00	111 758	10 313	3 093	27 711	16 829	13 831
	7.64	73 140	6 749	2 024	18 135	11 014	9 052
	10.00	55 879	5 156	1 547	13 855	8 415	6 916
Discounted medical treatment costs (T)	$41 000	75 104	8 712	3 988	20 099	12 977	11 015
	$56 000	73 140	6 749	2 024	18 135	11 014	9 052
	$71 000	71 177	4 786	61	16 172	9 051	7 089

Note. HIV = human immunodeficiency virus; QALYs = quality-adjusted life-years; NA = not applicable for this model (e.g., the per-act condom use parameters are not relevant for the per-partner HIV transmission model).

[a]Cell entries are cost-utility ratios expressed as cost per QALY saved. Parameters are as defined in Table 1. Per-act transmission probabilities reflect the low end of the empirical literature (.0014), the midpoint from a relevant literature overview (.0155), and an intermediate value that mimics a per-partner transmission probability of .25 (.0092).[15,25] Per-partner transmission probabilities were chosen to reflect the range of the relevant empirical literature.[15,16,25]

[b]Under base case assumptions using the per-act model, the transmission probabilities .0014, .0092, and .0155 translate into 0.04, 0.25, and 0.38 HIV infections averted, respectively.

[c]Under base case assumptions using the per-partner model, the transmission probabilities .18, .25, and .28 translate into 0.14, 0.19, and 0.22 HIV infections averted, respectively.

whom were unemployed, were paid to attend intervention sessions. Although these costs were included as a proxy wage or valuation of client time, this assumption was subjected to sensitivity analysis. Estimated client payments for child care and transportation were included as societal costs of the intervention but were not multiplied by the indirect cost rate.

The behavioral intervention significantly increased condom use.[5] A standard cumulative probability equation[12–14] was adapted to translate these behavioral effects into an estimate of the number of HIV infections averted (A):

$$A = G\{[1-(p(1-r_a(1-ef_{ca}))^n + (1-p))^m] - [1-(p(1-r_a(1-ef_{ia}))^n + (1-p))^m]\},$$

for which all parameters are as defined in Table 1. This model (the "per-act" model) posits that each sex act poses some risk of infection. However, some researchers have found that HIV transmission is predicted as well or better by a per-partner model, which posits that each new partnership poses a risk of HIV infection.[15,16] To translate the per-act model into a per-partner model, n was set equal to 1 and r_p was substituted for r_a, f_{cp} for f_{ca}, and f_{ip} for f_{ia}. Although relevant data are lacking, it was assumed that all women were HIV seronegative at the start of the intervention and that all HIV transmission risk was from male sex partners. Behavioral effects of the intervention were estimated conservatively to last for only 3 months (the length of follow-up in the original trial). Holtgrave and Qualls[17] recently developed a method for converting an estimated HIV infection averted into a number of QALYs saved: they discounted the number of QALYs saved per infection averted at a 5% rate. Their results have been used here but adjusted for the difference in age between their study cohort and this one; this estimate of discounted QALYs saved is labeled "Q."

The following formula was used to calculate the cost-utility ratio (again, assuming a no-intervention comparison condition):

$$[I-(AT)]/[AQ],$$

where I is the total societal cost of the intervention, A and Q are as defined above, and T is the present value of treating a case of HIV disease and AIDS. Guinan et al.[18] estimated T at $56 000 in 1992 dollars using a 5% discount rate.

The time horizon of the analysis is (less than) 1 year for the costs of an intervention that yields secondary (or "downstream") benefits over 12 years for each HIV infection averted. Each uncertain model parameter was varied widely in sensitivity analyses. Cost-utility ratios that are less than zero are considered cost-saving and are simply labeled as such.[19] Those that are greater than zero but less than roughly $30 000 are associated with health service programs that are usually considered cost-effective[20–22]; programs with $30 000 to $140 000 ratios may be controversial but can be justified with numerous current examples.[22] Programs with cost-utility ratios above $140 000 are difficult to defend as cost-effective. Of course, there is no single, universally accepted cost-utility ratio for determining whether a program is cost-effective.[20–22]

Results

Under base case assumptions, the total societal cost of the intervention is $26 914, or $269 per client. The number of HIV infections averted is 0.38. The base case cost-utility ratio is $2024 per discounted QALY saved.

Table 2 displays the results of numerous sensitivity analyses. Under the per-act model (with r_a equal to .0155), none of the cost-utility ratios is too large to be easily justified as cost-effective; often the ratios are less than zero and indicate actual cost savings.

Table 2 displays other reassuring sensitivity analyses. Even if some intervention costs were inadvertently omitted from this analysis (as might be captured

by adjusting upward the indirect cost rate), the cost-utility ratio would still be at a level generally considered to be very cost-effective. Further, the various transmission models employed yield cost-utility ratios at levels generally considered to be cost-effective; the only exceptions are when the per-act transmission probability and local HIV seroprevalence approach very low levels (those well below our best estimates).

Discussion

There are some clear limitations to this analysis. First, the study is retrospective so costs are estimated rather than prospectively measured. Second, the number of infections averted is modeled rather than biologically measured. Third, these calculations do not include many start-up costs, which a brand new service provision organization would incur before being able to deliver such an intensive intervention; hence, generalizations of results should be limited to organizations currently delivering some type of behaviorally based HIV prevention programs. Fourth, such analyses by their very nature do not satisfactorily incorporate important issues of equity, access, and community support. Fifth, the short time frame of the original study's follow-up period led us to employ Occam's Razor and use simple cumulative probability equations rather than more complex, dynamic, compartmental epidemic models.[23] Hence, our model may lack some of the detailed complexity of a dynamic HIV epidemic; however, our simpler model should yield conservative estimates of HIV infections averted since it ignores secondary transmissions averted.

Even with these limitations, our analysis is cautious. It is justifiable to conclude that the intervention is cost-effective under most scenarios considered and is cost saving under some. Interventions of this type warrant careful consideration by policymakers, program managers, HIV prevention community planning group members, and other key decision makers for inclusion in portfolios of HIV prevention programs.

Finally, as the science of HIV risk reduction intervention advances and more interventions are shown to have behavioral change efficacy, it will be increasingly important to establish cost-effectiveness of these interventions as well. In this example, we have illustrated how cost-utility analysis can be applied to a single HIV prevention outcome trial. Similar analyses can be undertaken with other HIV prevention interventions, and it will be important for researchers to collect both outcome and cost data that will permit these analyses to be performed. Such analyses will better enable public health decision makers to determine the kinds of HIV prevention approaches that will produce the greatest benefits given resource constraints. □

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