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SUBSTANTIVE REVIEW

Selecting Evidence-Based HIV Prevention Behavioral Interventions for HIV-Negative Persons for National Dissemination

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Abstract
This paper describes the development of a formula to determine which evidence-based behavioral interventions (EBIs) targeting HIV-negative persons would be cost-saving in comparison to the lifetime cost of HIV treatment and the process by which this formula was used to prioritize those with greatest potential impact for continued dissemination. We developed a prevention benefit index (PBI) to rank risk-reduction EBIs for HIV-negative persons based on their estimated cost for achieving the behavior change per one would-be incident infection of HIV. Inputs for calculating the PBI included the mean estimated cost-per-client served, EBI effect size for the behavior change, and the HIV incidence per 100,000 persons in the target population. EBIs for which the PBI was ≤ $402,000, the estimated lifetime cost of HIV care, were considered cost-saving. We were able to calculate a PBI for 35 EBI and target population combinations. Ten EBIs were cost-saving having a PBI below $402,000. One EBI did not move forward for dissemination due to high start-up dissemination costs. DHAP now supports the dissemination of 9 unique EBIs targeting 13 populations of HIV-negative persons. The application of a process, such as the PBI, may assist other health-field policymakers when making decisions about how to select and fund implementation of EBIs.

Keywords HIV · Cost-saving · Incidence · Evidence-based · Prevention

Introduction

Over the past three decades, researchers, scientists, and practitioners have grown the evidence base for HIV prevention interventions [1–3]. This process has been consistent with a greater value placed on evidence-based practice across a variety of health domains, including mental health [4, 5], public health [6, 7], and medicine [8–10]. Since 2000, the Centers for Disease Control and Prevention's (CDC) Division of HIV/AIDS Prevention (DHAP) has promoted the use of risk-reduction evidence-based behavioral interventions (EBIs), grounded in the belief that HIV-prevention practice should be informed by science [2, 3, 11–13], and DHAP's research-to-practice model has provided the backbone for HIV prevention planning and EBI implementation for more than a decade [14]. Historically, DHAP has principally focused on the identification and dissemination of EBIs targeting sex or drug risk behaviors that prevent HIV acquisition among HIV-negative individuals or HIV transmission from HIV-positive individuals [2, 11, 15]. As of March 2018, DHAP's *Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention* (http://www.cdc.gov/hiv/prevention/research/compendium/index.html) has identified 61 risk-reduction EBIs, 29 of which have been packaged or disseminated for HIV-negative persons. In more recent years, 3 additional chapters have been added to the Compendium; (1) interventions for adherence to HIV medications, (2) interventions for linkage to, retention in, or re-engagement in care, and (3) structural interventions. In addition, there has been increased emphasis on biomedical interventions such as pre-exposure prophylaxis.

The DHAP research-to-practice model has focused considerable resources on primary prevention through

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risk-reduction EBIs. However, emerging research demonstrated the high efficacy and cost-effectiveness of antiretroviral therapy in preventing HIV [16]. In addition, HIV pre-exposure prophylaxis was shown highly efficacious in preventing HIV acquisition among uninfected individuals. [17] The efficacy of these new biomedical approaches called for an assessment of the relative cost-effectiveness among behavioral EBIs supported by DHAP resources, in particular those targeting HIV-negative individuals in small groups which were relatively costly to implement and difficult to scale. This report does not make a comparison between the behavioral EBIs and biomedical interventions with proven prevention benefits such as anti-retroviral treatment (ART) or pre-exposure prophylaxis (PrEP).

Given that there were many efficacious behavioral EBIs for HIV-negative persons from which to choose, DHAP developed a high-impact HIV prevention (HIP) strategy to assist with prioritization of EBIs [18, 19]. The intent of the HIP strategy was to maximize the impact of HIV prevention efforts by prioritizing those EBIs that are most cost-effective and targeting them to populations where benefit would be greatest [18]. Weighing available HIV prevention strategies against one another, through cost-effectiveness studies or resource allocation modelling, in order to determine the optimal mix of EBIs for a given context is central to the effective implementation of a HIP strategy. While resource allocation has been important in deciding how broad types of prevention strategies (e.g., HIV testing, EBIs for HIV-negative persons) should be funded relative to one another, it had not yet been used to prioritize specific EBIs within a particularly strategy. Because 29 risk-reduction EBIs for at-risk persons have been identified and disseminated by DHAP, it was necessary to consider which of these EBIs would have the greatest impact on preventing HIV infections and should, therefore, be promoted for continued use by state and local HIV prevention partners. This report describes a two-step process to determine which risk-reduction EBIs for HIV-negative persons were likely to have higher impact and be selected to receive continued support by DHAP.

Methods

Our first step was to construct a prevention benefit index (PBI). This allowed us to estimate the relative potential for achieving the behavior change associated with reducing HIV incidence for HIV-negative persons. The PBI was calculated based on three standard inputs: the mean yearly programmatic costs-per-client served, annual HIV incidence rate for each target population, and the EBI effect size of the most relevant biologic or behavioral outcome available, assuming a one-year duration of effect. A separate PBI was calculated for each behavioral EBI related to each specific at-risk population for which the EBI was evaluated or implemented.

The PBI was calculated using the following formula:

$$Prevention\ Benefit Index(PBI) = \frac{Cost per\ Client\ \times\ 100,000}{HIV incidence\ per 100,000\ \times\ (1 - Effect\ Size[OR])}$$

The PBI increases as costs-per-client increase, or as incidence of target population or EBI effect size decreases. And, visa versa, the PBI decreases as cost-per-client decreases, or as incidence of EBI effect size increases. As a result, those EBIs with the lowest costs-per-client and greatest efficacy that target populations with the highest incidence rate, or the lowest PBI, provide the greatest prevention potential per dollar spent.

PBI threshold used for EBI selection. The PBI was compared against the standard lifetime cost of HIV treatment, approximately $402,000 in 2011 US dollars [20] to determine whether the cost of the prevention benefit conferred by an EBI was at least less expensive than the lifetime costs of treatment. The PBI is estimating a cost associated with behavior changes that are associated with HIV incidence, and not directly estimating a cost for preventing an incidence infection of HIV. In this sense the estimated PBI underestimates the costs needed for averting a new infection. This threshold, however, was chosen as an objective, a priori cut-off to help identify EBIs more likely to be more cost-saving than other EBIs. The lower the PBI implies a more cost-effective EBI in reducing important HIV risk behaviors that reduces the likelihood of new infections.

Cost per client. To account for the fact that EBI delivery costs tend to be affected by local considerations, a 2012 sample of community-based organizations (CBOs) (N = 132) delivering a range of EBI-based prevention programs (N = 176) for HIV-negative persons was used to generate cost estimates. CBOs funded by DHAP submitted separate budgets for each EBI they delivered and client service data estimating the number of persons reached by each community-level EBI and the number of persons that complete the EBI for individual-level and group-level EBIs. For some EBIs, cost data could not be obtained from CBOs and were provided from either demonstration sites or the original researchers. Because a CBO may not fully know the exact costs of an EBI until delivering the EBI for some time, cost data were obtained from CBOs in their third year of funding and implementation, thus ensuring more accurate estimates of expenditures. Estimates of the number of clients who completed an EBI were obtained from the second year of funding to ensure that the typical 6-month start-up time for an EBI was not included in the analysis. Costs-per-client served were then calculated by dividing the total projected annual cost of an EBI in the third year of funding by the total number of clients who completed an EBI during

the second year of funding. The projected annual cost of an EBI included both fixed and variable costs. The total number of clients who completed an EBI was not available for community-level EBIs, which use peer volunteers to deliver prevention messages. Rather, CBOs reported the number of peer volunteers recruited for program implementation. We estimated that each peer volunteer would reach 8 individuals in the community with targeted risk-reduction messages each year, which is a conservative estimate of contacts for peer-based programs [21, 22]. Finally, to account for the fact that not all CBOs operate with the same level of efficiency, the EBI programs that were one standard deviation above the mean for costs-per-client-served for each individual EBI were dropped from the analysis. After these outliers were removed, clients and costs were aggregated across each specific EBI and the mean cost-per-client for delivery was calculated.

Incidence. The 2010 HIV incidence rates specific to each targeted population were obtained from published DHAP incidence rate reports when available [23]. When incidence rates were not available for certain at-risk populations, data were derived from other published reports and specialized studies [16, 24, 25]. In some cases, incidence rates were estimated using unpublished DHAP data and 2010 U.S. Census population denominator estimates. We were unable to obtain incidence rates for specific risk groups corresponding to three EBIs implemented with or delivered to sexually transmitted infection (STI) clinic patients *(Focus on the Future, Safe in the City*) and high-risk heterosexual STI clinic patients (*RESPECT*). Neither the CDC's National HIV Surveillance report [23] nor National STD Surveillance report [26] provide HIV incidence of STD clinic populations. Various publications have reported some data on HIV infection among STD clinic populations but the data is clinic specific and often not stratified by risk population, in particular HIV infections for heterosexual men as compared to MSM. We were also unable to obtain incidence rates for specific risk groups corresponding to three EBIs implemented with or delivered to high-risk adolescents (*Community PROMISE),* homeless and runaway adolescents (*Street Smart*), and male prisoners (*START*). Instead, we used estimates from slightly broader, less specific population groups to approximate incidence rates for these risk groups. To account for the fact that actual incidence rates for these more specific risk groups would likely be greater than that in the more general population groups, we conducted sensitivity analyses to estimate the potential PBI if incidence rates were two, four, and eight times as great as that of the more general population groups (data not shown). The initial PBI calculations, and those from the sensitivity analyses, were then compared to the PBI threshold. If the calculated PBI fell below the cost-saving threshold based on the sensitivity analyses that would suggest a potential to be cost-saving and need for better incidence estimates in the future. We also calculated the estimated incidence rate that would be required to achieve a cost-saving prevention benefit for each included EBI, with cost and EBI effect remaining fixed, to compare to estimates used in the PBI calculations and consider if targeting higher risk populations could result in cost-saving efforts.

EBI effect size. EBI effect sizes for the HIV risk reduction were obtained either from published meta-analyses [1, 27, 28] or from the original EBI studies and were expressed as odds ratios. For studies reporting multiple outcomes, we established a hierarchical criterion to select the most relevant HIV risk outcome as follows: (1) HIV incidence rate, (2) STI incidence rate, (3) condomless sex, consistent condom use, or drug-injection risk behaviors, or (4) number of sex partners. However, no EBI studies evaluated changes in HIV incidence rate. For studies reporting multiple assessment time points, EBI effects for all time points ≤ 12 months post-intervention were pooled to estimate the average effect over the course of a year. If all EBI follow-ups were < 12 months, we assumed that the duration of effect was 1 year. For studies in which the EBI effect was not expressed as an odds ratio, we used raw proportions to calculate an odds ratio or, for continuous outcomes, we calculated standardized mean differences, which were subsequently converted to odds ratios. Although some effect estimates were expressed as increased odds of engaging in a protective behavior, we used standard methods (i.e., by calculating the natural logarithm of the odds ratio and its variance) to align the referent group so that all effect sizes represented reductions in HIV-related risk. Baseline adjusted outcomes were selected when available or calculated if baseline levels of the outcome were reported.

A PBI was calculated for risk-reduction EBIs for HIV-negative individuals that were previously identified as efficacious by DHAP and were either being disseminated by DHAP or packaged but not disseminated. An EBI package typically contains an implementation manual, training materials, and other guides for implementation with fidelity to the original research protocols. Some of the included EBIs were tested with multiple at-risk populations or were subsequently implemented with additional risk groups. We calculated a separate PBI for each EBI and target population combination. For example, four different PBIs were calculated for *Community PROMISE* [29], which was tested with three distinct populations and implemented with a fourth. No school-based EBIs were included, but EBIs for high-risk youth delivered in non-school venues were included.

Our second step was to weigh the results of the PBI calculations alongside three considerations to narrow the candidate EBIs to a final list that represented the most cost-effective and comprehensive selection of EBIs that DHAP would continue to support for national dissemination. One consideration was EBI startup costs. After an EBI

is packaged for dissemination, a series of startup activities takes place. These include piloting the EBI training curriculum, developing train-the-trainer materials for the EBI, conducting train-the-trainer sessions to develop a cohort of national trainers for the EBI, and preparing a cohort of technical assistance providers to assist with implementation in the field. These startup activities have considerable costs ($485,000–$985,615) and, therefore, EBIs that have been packaged but had not moved into the startup phase were considered alongside the costs of alternative EBIs where the startup costs had already been incurred. Second, we considered the potential benefit of using cost-saving alternatives for some EBIs. A cost-saving alternative would be an EBI with a lower PBI that reached the same target population, focused on similar risk-reduction outcomes, and had similar implementation strategies and venues. Finally, we considered the availability of new research findings regarding the efficacy of EBIs. Subsequent research on an EBI could inform the process of whether that EBI warranted increased dissemination efforts or possible discontinuation if negative findings were reported.

Results

The CBOs in the sample (N = 132) were funded to implement a range of EBI programs (N = 176) for HIV-negative persons. The sample of EBI programs was reduced (N = 169) because 7 CBOs reported the number of clients recruited into EBIs but failed to report the number of clients who actually completed the EBI. After removing those EBI programs that reported costs-per-client-served that were one standard deviation greater than the mean for that particular EBI (N = 19), the final sample (N = 150) of EBI programs was used to calculate a mean cost-per-client served for each EBI.

Table 1 summarizes the characteristics of the 29 unique risk-reduction EBIs for HIV-negative persons that were reviewed through this process. We were able to calculate a PBI for 35 EBI and target population combinations considered; a total of 13, representing 10 unique EBIs, had a PBI below the selected threshold of $402,000. The 10 EBIs with greatest prevention potential, based on the PBIs, included *Many Men, Many Voices* [30], *Community PROMISE* [29], *d-up: Defend Yourself! (d-up!)* [31], *Focus on the Future* [32], *Mpowerment* [33], *Personalized Cognitive Counseling* [34], *Popular Opinion Leader* [21], *Safe in the City* [35], *Sister to Sister* [36], and *Sin Buscar Excusas* [37].

Generally, EBIs with a very high cost-per-client served could not meet the threshold, even when targeting a high-incidence rate population and with a large EBI effect. For example, 3 EBIs targeted persons who inject drugs—*Modelo de Intervencion Psycomedica* [38], *Safety Counts* [39], *Self-Help in Eliminating Life-threatening Diseases (SHIELD)* [40]—yet did not pass the PBI threshold due to high costs-per-client served. Two EBIs' implementation costs exceeded $7000 per client served: *Future is Ours* [41] and *Modelo de Intervencion Psicomédica* [38]. Neither of these EBIs had a PBI below the threshold, despite the fact that *Modelo de Intervencion Psicomédica* targets a high-risk population, Latino persons who inject drugs.

As displayed in Table 1, except for *RESPECT* [42], all of the EBIs designed for or implemented with men who have sex with men (MSM), whose target populations' HIV incidence rates ranged from 655 to 1897 infections per 100,000 persons, fell below the PBI threshold, while none of the EBIs targeting the lowest risk populations (i.e., incidence rate ranges from 3 to 19 infections per 100,000 persons) did. These lowest risk populations included African American and Latino youth and adult heterosexual men and women. Generally speaking, EBIs designed for HIV low-incidence rate target populations (i.e., 24/100,000 for high-risk youth) could obtain a PBI score below the threshold, but only with a very low cost of delivery (i.e., < $36 per client served for *Community PROMISE*).

All of the EBIs examined had already been identified by DHAP as efficacious. For EBIs that fell above the PBI threshold (Table 1) the effect size range was 0.21–0.099 and the mean effect size was 0.61, whereas for the supported EBIs the effect size range was 0.29–0.91 and the mean effect size was 0.61, the same as for the non-supported EBIs. Thus, effect size was less of a determining factor for the PBI than was HIV incidence rate for the EBI target population and the costs of intervention delivery. Sensitivity analysis was conducted by recalculating the PBI for all EBIs that had failed to score below the threshold replacing the effect size expressed as an odds ratio (OR 0.21) for the most highly efficacious intervention, *Sisters Informing Healing Living and Empowering (SIHLE)* [43], into each calculation. All but one of the EBIs that failed to score below the PBI threshold also failed to fall below the threshold even when a more robust effect size was used in the calculations. *VOICES/VOCES* when delivered to African American heterosexual men and women fell below the PBI threshold when the *VOICES/VOCES* effect size (OR 0.78) was replaced by the *SIHLE* effect size (OR 0.21). There were a few instances, however, when EBI effect size appeared to play a role in the PBI estimate and this was especially true of EBIs falling just above and below the threshold. For example, an EBI effect size just 0.02 points more effective (i.e., an OR 0.77) would have put *RESPECT* for MSM, which had mid-range costs and targeted a high-incidence rate population, just below the PBI threshold. Conversely, a slightly less effective effect size (OR 0.60) would have prevented *Sister to Sister*, a low-cost EBI delivered to a low-incidence population (i.e., African American women), from meeting the PBI threshold. The

Table 1 Prioritization of risk reduction evidence-based interventions for HIV-negative persons

EBI	Population	# Sessions (unit of delivery)—implementation description	Cost per client	Effect size (OR)	Incidence per 100,000 [24, 25, 52, 53]	Prevention benefit index (PBI)	Incidence required to achieve cost-saving prevention benefit	Decision to support dissemination
Behavioral EBIs for HIV-negative persons that met the PBI criteria								
3MV: many men, many voices [30]	AA MSM	6 (GLI)	$1733	0.77	1897	$397,218	1874	✓
Community PROMISE [29]	AA women[a]	CLI	$36[b]	0.54	38	$205,993	19	✓
	High-risk youth	CLI	$36[b]	0.54	24	$326,155	19	✓
	PWID and their sex partners	CLI	$36[b]	0.54	515	$15,188	19	✓
	MSM	CLI	$36[b]	0.54	655	$11,951	19	✓
d-up: defend yourself! [31]	AA MSM	CLI	$393[b]	0.66	1897	$60,952	288	✓
Focus on the future [32]	Heterosexual AA men with an STI	1 (ILI)—in STI clinics	$34	0.32	≥ 19[c]	≤ $265,111	12	X
Mpowerment [33]	YMSM	CLI	$167[b]	0.59	713	$57,084	101	✓
Personalized Cognitive Counseling [34]	MSM	1 (ILI)—coupled with testing	$145	0.29	655	$31,261	51	✓
Popular Opinion Leader [21, 22]	MSM	CLI	$265[b]	0.66	655	$119,195	194	✓
Safe in the City [35]	STI clinic patients	1 (GLI)—video in STI clinic waiting rooms	$0.24	0.91	≥ 19[c]	≤ $14,109	1	✓
Sister to sister [36]	AA women	1 (ILI)	$62	0.43	38	$285,491	27	✓
Sin buscar Excusas [37]	Latino MSM	1 (GLI)	$198	0.78	655	$137,543	224	✓
Behavioral EBIs for HIV-negative persons that did not meet the PBI criteria								
Adult identity mentoring [50]	AA youth (pre- and post-risk)	12 (GLI)	$175	0.58	3	$14,367,816	104	X
CONNECT [46, 47]	AA and Hispanic/Latino heterosexual couples	6 (1 ILI and 5 couples)	$2528	0.92	15	$209,842,297	7861	✓, for HIV-discordant couples
Cuidate [51]	Hispanic/Latino youth	6 (GLI)	$150	0.52	8	$3,858,025	78	X
FIO (future is ours) [41]	Multicultural women	9 (GLI)—8 core and 1 booster	$7029	0.66	7	$283,199,033	5143	X
Focus on youth + IMPACT [54]	AA youth (pre-risk)	9 (GLI)—8 adol. and 1 parent	$1172	0.57	3	$93,982,358	678	X
Healthy love [55]	AA women	1 (GLI)	$124	0.72	38	$1,162,355	110	X

Table 1 (continued)

EBI	Population	# Sessions (unit of delivery)—implementation description	Cost per client	Effect size (OR)	Incidence per 100,000 [24, 25, 52, 53]	Prevention benefit index (PBI)	Incidence required to achieve cost-saving prevention benefit	Decision to support dissemination
INSIGHTS [56]	Multicultural women (sample predominately white)	2 (ILI)—magazine delivery	$871	0.54	7	$25,938,058	471	X
Modelo de intervencion Psicomedica [38]	PWID	7 (ILI)	$7331	0.55	515	$3,160,997	4053	X
	Latino IDUs	7 (ILI)	$7331	0.55	762	$2,137,748	4053	X
NIA [57]	Heterosexual AA men	5 (GLI)	$968	0.97	19	$171,129,374	8029	X
Real AIDS prevention project [58]	Sexually-active, low-income AA women in high prevalence areas	CLI	$128	0.99	38	$33,498,360	3175	X
RESPECT [42]	MSM	2(ILI)	$601	0.79	655	$437,048	711	X
	Heterosexuals in STI clinics	2 (ILI)	$601	0.79	> 19[c]	$15,062,656	711	X
Safety counts [39]	Active IDUs and crack smokers	7 (5 ILI + 2 GLI)	$2632	0.89	515	$4,642,343	5952	X
Salud Educacion Prevencion Autocuidado (SEPA) [59]	Latina women	6 (GLI)	$840	0.63	8	$28,378,378	565	X
Self-help in eliminating life-threatening diseases (SHIELD) [40]	Networks of PWID (predominately AA)	CLI	$1975	0.31[d]	515	$555,480	712	X
Sisters informing healing living and empowering (SIHLE) [43]	Sexually active AA adolescent females	4 (GLI)	$1204	0.21	38	$4,000,963	379	X
Sisters informing sisters about topics on AIDS (SISTA) [60]	AA women	5 (GLI)	$1155	0.48	38	$5,827,377	552	X
START [48]	Soon-to-be released male prisoners	6 (ILI)—2 in prison and 4 out of prison	$3154	0.45	≥ 31[c]	≤ $18,679,420	1427	✓, for HIV-positive soon-to-be released prisoners
Street smart [49]	Homeless and runaway adolescents who use drugs	8 (GLI)	$2491	0.55	24[c]	$23,064,814	1377	X

Table 1 (continued)

EBI	Population	# Sessions (unit of delivery)—implementation description	Cost per client	Effect size (OR)	Incidence per 100,000 [24, 25, 52, 53]	Prevention benefit index (PBI)	Incidence required to achieve cost-saving prevention benefit	Decision to support dissemination
VOICES/VOCES [61]	AA heterosexual men and women	1 (GLI)	$198	0.78	69	$1,307,560	244	X
	Latino heterosexual men and women	1 (GLI)	$198	0.78	28	$3,276,033	224	X

[a]Reflects real-world implementation with a target population not included or reached in the original efficacy trial(s)

[b]Cost-per-client was provided as cost per opinion leader or peer advocate. For these CLIs, the cost was calculated assuming a reach of 8 for each opinion leader or peer advocate trained

[c]Incidence rates were not ascertained for individuals visiting an STI clinic (*Safe in the City*, *Focus on the Future*, *RESPECT for heterosexuals in STD clinics*), runaway and homeless adolescents (*Street Smart*) and men newly released from prisons or jails (*START*). The PBI for interventions implemented in STI clinics was calculated using the population incidence rate for all people in the U.S. or for the entire target population (e.g., AA men, multicultural women). Because incidence is presumed to be higher among men in STI clinics the PBI for these interventions would be less than or equal to the PBI if implemented with the general population

[d]Effect size is from the continued injection drug use outcome. Sharing needles was also reported, but only for the subgroup of those who continued to inject drugs; the effect for this outcome was slightly larger in magnitude, but substituting it into the PBI calculations didn't change the overall outcome

same is true for *Community PROMISE* targeting African American women or high-risk youth.

As a second step, in which the results of the PBI calculations were weighed alongside three other considerations, we decided that 9 of the 10 risk-reduction EBIs meeting the PBI threshold would receive continued support. *Focus on the Future*, an EBI for African American men diagnosed with an STI [32], met the PBI threshold, but it was not supported for future funding because it was already packaged but not yet disseminated and dissemination would require startup costs. In addition, there was a cost-saving alternative EBI—*Safe in the City*—that could be implemented with African American men in STI clinics. This EBI was already being disseminated so saving the required startup costs.

Among all EBIs that met the PBI threshold, we compared the cost-saving potential for those EBIs targeting similar populations as part of the decision making process. *D-up: Defend Yourself!* was considered as a cost-saving alternative to *Many Men, Many Voices* for African American MSM. However, *d-up: Defend Yourself!* focused on consistent use of the male condom for anal intercourse whereas *Many Men, Many Voices* not only focused on consistent use of the male condom but taught sexual negotiation skills and encouraged knowledge of one's HIV status and HIV antibody testing. Therefore, both EBIs are being supported for African American MSM. In addition, *Personalized Cognitive Counseling* was considered as a cost-saving alternative to *Popular Opinion Leader*, but *Personalized Cognitive Counseling* is an EBI for MSM repeat HIV testers and is linked to HIV testing, whereas the *Popular Opinion Leader* is a community-level EBI and can be implemented in a broad range of community settings, not just the HIV testing encounter. Therefore, both EBIs are being supported for MSM. For HIV prevention with African American women, *Community PROMISE* was considered as a cost-saving alternative to *Sister to Sister*. However, *Sister to Sister* is delivered to African American women in primary care settings by nurses and the credibility of nurses as prevention providers led us to retain both EBIs for African American women.

Additional published research evaluating these EBIs was also considered. Research on *RESPECT*, specifically when integrated with HIV rapid testing, found that the risk of STIs significantly increased among MSM who received the intervention [44]. The PBI for *RESPECT* was greater than the cost-saving threshold, although very close to the threshold for MSM. Due to the negative findings, however, the decision was made to no longer disseminate *RESPECT*. In addition, research on the *Popular Opinion Leader* in international settings where intervention effects were not detected were considered. However, we also considered subsequent publications discussing the reasons intervention effects were not detected, including potentially inadequate implementation, and determined to retain the *Popular Opinion Leader*

among those EBIs that DHAP would continue to support [45].

Many EBIs did not meet the PBI criteria with targeting populations based on the original research (Table 1). However, focusing on more specific risk groups within the existing target populations could improve their PBI substantially and result in greater potential impact. Two EBIs were of particular interest for continued dissemination efforts because of the relatively easy transition to more focused, higher risk subgroups. *CONNECT* fell outside the PBI threshold but continued to receive support for dissemination by adapting *CONNECT* to be delivered to HIV discordant couples [46, 47]. Narrowing the target population for *CONNECT* to HIV discordant couples would presumably reduce the PBI substantially, for at least two reasons. HIV incidence is much higher among HIV discordant couples than all heterosexual couples in general; and, the intervention effect on reducing HIV risk could arguably be stronger among discordant couples where the risk is much more relevant than among concordant HIV-negative or HIV-positive couples. *START* [48] was also adapted to be delivered to HIV positive soon-to-be released male prisoners and thus the decision was made to continue dissemination efforts to prevention programs targeting HIV-positive soon-to-be released male prisoners focusing on linkage to HIV prevention and care services, particularly treatment and viral suppression.

The sensitivity analyses related to the five EBIs where incidence rates for the specific risk groups were unavailable did not affect any decisions. Two of these EBIs—*Focus on the Future* and *Safe in the City*—met the PBI threshold with these lower estimates and were already discussed previously. For three of these EBIs—*RESPECT* for heterosexual STI clinic patients, *START* [48] for soon-to-be-released incarcerated men, and *Street Smart* [49] for drug-using, homeless adolescents—the HIV incidence rate required to achieve a cost-saving prevention benefit was unrealistically high, and the decision was made to no longer support them. As related above, *START* for HIV positive soon-to-be released male prisoners was selected for continuing support.

In summary, DHAP supported the dissemination of 9 unique risk-reduction EBIs targeted to thirteen groups of HIV-negative persons: adult MSM (n = 6), young MSM (n = 1), persons who inject drugs and their sex partners (n = 1), African American women (n = 2), high-risk youth (n = 1), and STI clinic patients (n = 1). The original *Community PROMISE* [27] study included four risk groups, one of which was a combined target population of PWID and their sex partners, all of which are supported, so thirteen total groups of HIV-negative persons are represented in the nine EBIs supported by DHAP. In addition, DHAP supported the dissemination of two risk-reduction EBIs that did not meet the PBI threshold but adapted to reach high risk HIV-positive populations—*CONNECT* was adapted to address HIV-discordant couples and *START* was adapted to address HIV-positive soon-to-be released male prisoners.

Discussion

Using a PBI, we identified 10 EBIs that could be implemented with 13 HIV-negative target populations that had the lowest costs per prevention potential. These EBIs were the most cost-effective in reducing important HIV risk behaviors that, in turn, reduces the likelihood of new infections. Because cost-effectiveness should not be the sole criterion for making policy decisions, DHAP reviewed these results alongside other key considerations. These considerations included dissemination start-up costs, cost-saving alternative EBIs, and subsequent research indicating that the EBI failed to demonstrate efficacy in subsequent trials [44]. One of the 10 EBIs noted above (*Focus on the Future*) did not move forward for dissemination due to high start-up dissemination costs. This resulted in identifying 9 unique HIP interventions as having the greatest potential impact on HIV prevention among a wide range of high risk HIV-negative populations.

Two interventions that did not meet the PBI criteria, and thus were not supported for dissemination with original target populations, were supported for HIV-discordant couples [46, 47] and HIV-positive soon-to-be released male prisoners [48]. These are included within the large portfolio of supported HIP interventions for HIV-positive persons (effectiveinterventions.cdc.gov)

HIV incidence rate in the target population was one of the most important inputs in our analysis. Our findings suggest that there is substantial benefit gained by targeting EBIs to the highest-incidence rate risk groups, in particular MSM. Conversely, targeted youth EBIs, including those focused on racial and ethnic minority youth, did not meet the PBI criteria. Even when these EBIs were implemented at a low cost, very low HIV incidence rates in adolescent populations (with the exception of MSM adolescents, to whom few behavioral EBIs are targeted) precluded their ability to achieve a low enough cost for the prevention benefit.

Because this analysis would have policy and programmatic impact, the authors considered the implications for this type of modelled decision-making about resource allocations. HIV prevention for youth offers an example of resource allocation modeling for policy decisions but also the need to keep policy options open should there be additional information. We considered whether other divisions of the CDC or other federal agencies would disseminate the EBIs for adolescents that DHAP would no longer support. CDC's Divisions of Adolescent and School Health (DASH) and Reproductive Health support three adolescent-focused interventions that were previously part of the EBI portfolio.

These include *Adult Identify Mentoring* (AIM) [50], SIHLE [43], and *Cuidate* [51].

Since the PBI is sensitive to HIV incidence, increases in incidence among adolescents would indicate that increased resources may be allocated to adolescent prevention programs. For the *Street Smart* [49] intervention we used the CDC's estimated HIV incidence among adults and adolescents in the United States, 2007–2010 which was 24/100,000 for adolescents/young adults [23] but to consider new information on HIV incidence among this population and reconsider dissemination of *Street Smart* should the incidence data indicate the need. Development of intervention implementation materials is a resource intensive task and all the materials developed by DHAP to support evidence-based interventions for adolescents remains accessible through various websites including effectiveinterventions.org. We see cost and resource allocation analyses as a first step, not a last step, and this is an important part of communicating what results like these mean. Models are meant to guide decisions, not dictate them.

Cost of delivery was also central to determining whether an EBI fell below the PBI threshold: all but one (*Many Men, Many Voices* [30]) of the EBIs with the lowest cost per prevention benefit–cost–less than $500 per-client to deliver. In general, as evidenced in Table 1, EBIs that met the PBI threshold were single-session or delivered at the community-level, as these formats tended to have the lowest associated costs. EBIs with high delivery costs, even when targeted to high-incidence rate populations, did not meet the PBI threshold. In general, EBIs targeted to low-incidence rate populations only met the PBI criteria if they had an extremely low cost-per-client-served. As a result, EBIs for youth and heterosexual women and men, with few exceptions, did not meet our criteria for dissemination and support.

Four EBIs for PWID were included in our analysis and *Community PROMISE* was retained for continued support by DHAP. However, the CDC has expanded prevention programs for PWID beyond the original four EBIs. Congress has permitted the use of federal funds for syringe services programs (SSPs), and CDC has been the agency that reviews and approves applications by jurisdictions to use federal funds for this purposes. To date, CDC has approved of 39 states (https://www.cdc.gov/hiv/risk/ssps-jurisdictions.html) to use funds for SSPs, which often include behavioral elements similar to some of the EBIs described above.

There are a number of important limitations to this study. First, the PBI is used to make these EBIs more comparable by approximating their cost per unit of prevention potential, based on the amount of behavioral change associated with implementing the EBI. This relates to a specific risk-reduction benefit, and is not the same as infections averted, as would be the case if HIV incidence were the outcome measured. In this paper, the PBI did not extend the calculations from behavior change to infections averted. As a result, the absolute dollar amounts estimated may underestimate the actual costs needed for averting a new infection. However, this prevention benefit is associated with the likelihood of preventing a new HIV infection, because the risk behaviors used in the calculations are associated with HIV incidence. Despite this limitation, the relative costs or benefit when comparing between EBIs are likely to be accurate.

A further sensitivity approach was conducted that did not use the $402,000 lifetime HIV treatment costs as the cutoff for selection. Instead, the EBIs were put into rank order based on their PBI scores (lowest to highest). Then, we began identifying interventions designed for HIV risk populations starting with the lowest PBI score, and selected interventions until all high priority risk populations were addressed. An intervention was skipped for support consideration if another intervention addressed the same risk population. Using this selection method, nine interventions were selected for continued DHAP support as compared to twelve interventions when the threshold was lifetime costs of HIV care. *Popular Opinion Leader* and *Many Men Many Voices* would be dropped since *Community PROMISE*, *Personalized Cognitive Counseling*, *Mpowerment*, and *d-up: Defend Yourself* all addressed various sub-populations of MSM. *Sister to Sister* would be dropped since *Community PROMISE* has demonstrated applicability to African American women.

Second, this approach used a simplified cost-saving model. Our model reflects the perspective of the CDC's DHAP and its CBO prevention providers but does not include a societal perspective that would include the costs to clients, their families, and their communities when an individual receives HIV prevention services. A case can be made that single-session interventions, waiting room video-based interventions, and community level interventions would have a lower personal and societal burden that multi-session interventions. The evidence-based behavioral interventions used in our study had risk reduction outcomes rather than direct cases of HIV averted. Thus longevity effects and health-related quality-of-life effects were not included in our analysis. These are limitations of the current study. However, all 134 CBOs used the same 424A budget template that standardized intervention costs across interventions and increased comparability.

Third, the odds ratios used to measure the effects of each EBI may not be equivalent. Since the behavioral effects measured in the RCTs for these EBIs differed from one another (e.g., condom use, condomless sex events, condomless sex by casual versus main partner, and number of partners), we were not able to standardize to one specific behavioral outcome for exact comparisons across EBIs. Given that the cost-per-client served and the incidence rate in the target population had a much greater impact on the resulting PBI estimate than the effect size,

it appears that adjusting the effect sizes to one standard metric would not have affected our conclusions.

Fourth, whereas the PBI establishes selection criteria for behavioral EBIs, it does not address the levels of implementation and fidelity necessary for population-level impact. Fifth, the use of real-world program costs data in this analysis produced results that were more realistic for planning and cost allocation purposes, but within-group differences in costs-per-client served were very broad for some EBIs such as *Community PROMISE* [29], *START* [48], and *Safety Counts* [39].

Sixth, many of the efficacy trials included looked at behavior change outcomes at the 3-, 6-, or 9-month periods after EBI delivery. We assumed a one-year prevention benefit effect, which may be overly optimistic. Seventh, this paper made a comparison among behavioral EBIs and not a comparison between behavioral EBIs and biomedical strategies with proven prevention benefits. Finally, the PBI was designed to identify those EBIs that may be cost-saving, and as such does not take into account the community and political dynamics that often play a role in public health decision-making. Thus DHAP ensured that behavioral interventions for all primary risk populations remained in the menu of prevention options to address community concerns and to support behavioral risk reduction for groups most affected by HIV. In addition, prevention materials on discontinued EBIs remained available for programs that may wish to implement these EBIs with funds from other federal and state agencies or foundations. To address these community dynamics further DHAP began funding CBOs to provide both HIV antibody testing and linkage to medical care so that the important role of community in HIV prevention was reinforced.

Conclusions

Our aim in developing the PBI was to a create a decision-making tool that would be easy to use and would provide objective criteria to select those HIP interventions from the numerous risk-reduction EBIs for HIV-negative persons that were part of the DHAP portfolio that would have the greatest potential for impact at the lowest cost moving forward. Although the PBI formula was not designed to determine how much funding to allocate to specific EBIs nationally, it proved useful to DHAP when trying to determine which EBIs for HIV-negative persons to continue to disseminate and support. The PBI along with local resource allocation data may help other funders and policymakers when making decisions about how to select and subsequently fund HIP interventions for HIV-negative persons.

Disclaimer The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflicts of interest.

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