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HIV Pre-exposure Prophylaxis (PrEP) in the United States: Impact on Lifetime Infection Risk, Clinical Outcomes, and Cost-effectiveness

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Abstract

Background—The combination of tenofovir and emtricitabine (TDF/FTC) shows promise as HIV pre-exposure prophylaxis (PrEP). We sought to forecast clinical, epidemiologic, and economic outcomes of PrEP, taking into account uncertainties regarding efficacy, risk of resistance and toxicity, behavioral disinhibition, and drug costs.

Methods—We adapted a computer simulation of HIV acquisition, detection, and care to model PrEP in high-risk (1.6% average annual HIV incidence) men who have sex with men (MSM) in the United States. Base case assumptions included: 50% PrEP efficacy and $753 monthly TDF/FTC costs. We used sensitivity analyses to examine the stability of results and to identify critical input parameters.

Results—In a cohort with mean age 34 years, PrEP reduced lifetime HIV infection risk from 44% to 25% and increased average life expectancy from 39.9 to 40.7 years (21.7 to 22.2 discounted, quality-adjusted life-years or QALYs). Discounted mean lifetime treatment costs increased from $81,100 to $232,700 per person, indicating an incremental cost-effectiveness ratio (ICER) of $298,000 per QALY gained. Markedly larger reductions in lifetime infection risk (from 43.5% to 5.8%) were observed assuming greater (90%) PrEP efficacy. More favorable ICERs were obtained by targeting younger, higher-incidence populations and with improvements in the efficacy and cost of PrEP.

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Potential conflicts of interest

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Conclusions—PrEP could substantially reduce HIV transmission in high-risk populations in the United States. Although it is unlikely to confer sufficient benefits to justify current TDF/FTC costs, price reductions and/or increases in efficacy could make PrEP a cost-effective option in younger or higher-risk populations. Given recent disappointments in HIV prevention and vaccine development, further study of PrEP-based HIV prevention is warranted.

INTRODUCTION

Dramatic advances in HIV treatment in the United States over the last decade [1] contrast with the persistent frustrations surrounding HIV prevention efforts over the same period [2]. Recent setbacks include the halting of major microbicide and vaccine trials [3–6], discouraging results regarding the efficacy of female-initiated barrier methods in preventing heterosexual transmission [7,8] and equivocal findings on the impact of male circumcision on HIV risk in MSM [9–12]. In the face of these disappointments, the combination of tenofovir and emtricitabine (TDF/FTC) shows promise as pre-exposure prophylaxis (PrEP) for persons at high risk of HIV infection [13–19].

Trials of TDF/FTC-based chemoprophylaxis in macaques report nearly 8-fold reductions in the risk of HIV infection [20]. In humans, recent observations in high-risk women suggest an efficacy estimate of 65% [21]. However, the long-term impact of PrEP on transmission, behavior, clinical outcomes, and cost has not been studied. Based on its current annual price of US$8,700 per person (when used for treatment), some observers conclude that TDF/FTC could not be cost-effective when used for PrEP, except in populations at highest HIV risk [22]. Others have noted that PrEP poses risks for additional drug toxicity, viral resistance, and behavioral disinhibition [23]. Our objective was to weigh these considerations and to provide practical guidance – to practitioners, payers and designers of upcoming clinical trials [24] – regarding the clinical, epidemiological, and economic circumstances under which PrEP might serve as a viable and appropriate use of prevention resources.

METHODS

Study design

We used a widely published computer simulation of HIV acquisition, detection and care [1, 25–27] to forecast outcomes of TDF/FTC-based PrEP delivered to a population of high-risk MSM (1.6% average annual HIV incidence) in the US. Outcomes included lifetime infection risk, life expectancy, quality-adjusted life expectancy and cost. Conforming with the recommendations of the US Panel on Cost-Effectiveness in Health and Medicine [28], we measured comparative value in 2006 US dollars per quality-adjusted life-year (QALY) gained, reporting all economic evaluation outcomes from the societal perspective using a 3% annual discount rate.

Disease model

The Cost-Effectiveness of Preventing AIDS Complications (CEPAC) Model (the Disease Model) – is a state-transition, Monte Carlo simulation of the natural history, clinical management, outcomes, and costs of HIV disease [25–27]. Natural history of illness in a patient is represented by a sequence of monthly transitions between “health states” describing current health (i.e., CD4 cell count, HIV RNA level, relevant history, quality of life, and resource use) and predicting further disease progression (i.e., immune system deterioration, opportunistic infections (OIs), therapeutic response, and medication resistance/toxicity). The model permits users to define both patient attributes (i.e., age, sex, CD4 count, HIV RNA, and other demographic/clinical attributes) and therapeutic alternatives (i.e., number, sequencing, and efficacy of antiretroviral therapy (ART) regimens). Treated patients receive up to six sequential

regimens, with progressively diminishing HIV RNA suppressive efficacy (Table 1). ART failure is defined by either an observed increase in HIV RNA level or a decrease of 50% from peak CD4. Each patient's clinical course is tracked from entry into the simulation until death. Large numbers of individual simulations are then aggregated to estimate survival, quality-adjusted survival, and costs for alternative PrEP strategies.

Population model

Entry into the Disease Model is regulated by a population-level simulation that captures the incidence of HIV infection and the mechanics of HIV counseling, testing, and referral [26, 27]. Users can specify variables governing the provision, performance, and cost of pre- and post-test counseling services and PrEP. The Population Model has the flexibility to capture a range of program intensities, from no intervention, to basic risk counseling, to more elaborate behavioral and chemoprophylactic prevention. For patients receiving PrEP, the model tracks changes in risk-taking behavior, toxicity, occurrence of drug resistance in individuals who become HIV-infected and are subsequently treated with ART, quality of life, and cost of HIV-related care.

The Population Model also captures clinical and economic outcomes associated with HIV transmission, detection, and referral activities. Using methods described elsewhere [26,27], the model estimates lifetime infection risk under alternative PrEP scenarios. The Population Model conveys information to the Disease Model on HIV infection status, whether and when HIV detection, follow-up, and linkage to care occur, and whether an infected person previously received TDF/FTC-based PrEP. The Disease Model then combines this information with its own output on the timing of AIDS-defining complications to establish whether, when, and how an individual case of HIV infection will be treated.

Input data: Target populations

We defined a high-risk target population, using age and annual HIV incidence data obtained from men who have sex with men (MSM) in the HIVNET Vaccine Preparedness Study (Table 1) [29]. The base case population had mean age 34 years (SD = 9.4 years), reflecting the expected enrollment of a US prevention trial amongst high-risk MSM [29,40,41]. We used HIVNET data to produce age-specific HIV incidence estimates (Table 1). In sensitivity analysis, we considered mean ages as low as 20 years (SD = 2) and population average annual HIV incidences ranging from 0.1% to 3.1%.

In the absence of published data on HIV screening activities in the target population, we assumed that individuals receive annual HIV tests. Given reports suggesting average infection-to-detection times greater than five years [42], this assumption introduced a deliberately conservative analytic bias against PrEP. In sensitivity analysis, we considered average frequencies ranging from monthly to every 3 years to never. We varied these frequencies depending on whether the individual was receiving PrEP.

Input data: Impact of PrEP

PrEP efficacy—We modeled PrEP efficacy as a percent reduction in HIV incidence. Our baseline efficacy assumption (50%) corresponds to the value used by Desai [31], reflects observed rates of protection in macaque-based studies of TDF/FTC-based chemoprophylaxis [20], and matches the efficacy for which current human trials are powered [24]. It is conservative compared with the 65% point estimate reported by the only study in humans to date [21]. Recognizing the uncertainty surrounding this estimate, the possibility that newer agents might exhibit greater preventive properties, and the potential offsetting influence of imperfect adherence and other behavioral factors, we examined efficacy values ranging from 10% to 90% in sensitivity analysis.

Resistance—Resistance to emtricitabine via the M184V mutation occurs rapidly in patients with detectable HIV RNA on this drug; tenofovir resistance with the K65R mutation is less common [32,43,44]. Although data are not yet available on resistance to either drug after PrEP failure, limited evidence from animal studies suggest that substantial rates of resistance are possible [16,45]. We modeled PrEP-related resistance conservatively: First, we assumed resistance in all HIV-infected patients with a PrEP history. Second, we assumed that clinicians would eliminate the initial efavirenz-based regimen for patients with a history of PrEP, because of the low resistance threshold of efavirenz (especially when combined with potential NRTI resistance). Third, because these are generally used in the first line of therapy [46], we assumed an absolute 5% decrease in rates of virologic suppression for all lines of ART in patients infected after PrEP. Finally, we examined a wide range of alternative assumptions in sensitivity analyses, varying the decrease in suppression on all lines of therapy from 0% to 15%.

Toxicity—The incidence of adverse effects with TDF/FTC when used in HIV-infected patients is low [23,47] but it is not zero [48,49]. Studies addressing long-term safety in HIV-negative subjects are emerging [21,50]. We conducted extensive sensitivity analysis on toxicity-related reductions in both quality of life and survival. Specifically, we considered scenarios ranging from no TDF-related toxicity to the case where 10% of all patients initiating PrEP suffer chronic renal disease resulting in a permanent decrement of 10% in quality of life and where an additional 1% of patients suffer a TDF-toxicity-related death shortly following PrEP initiation. This “extreme toxicity scenario” greatly exceeds the morbidity and mortality effects implied by recent reports of TDF toxicity [51].

Behavioral disinhibition—HIV risk reduction creates the potential for behavioral disinhibition [52]. However, there is little evidence linking HIV prevention to increased risk-taking and even less evidence to suggest that the magnitude of any risk compensation is sufficient to offset the preventive effect [53]. Recognizing that the issue remains to be resolved empirically for the particular case of PrEP, we considered a broad range of behavioral assumptions. In sensitivity analysis, the potential effects of disinhibition were modeled as a percent reduction in PrEP efficacy. Thus, the “PrEP efficacy” parameter described above should be understood as a “net” value that includes synergistic effects (e.g., increased condom use; adoption of adult male circumcision), unfavorable behavioral offsets (e.g., reduced condom use; increased partnerships), and imperfect adherence and take-up.

Cost—In the base case, we used the $724 current average monthly wholesale price of TDF/FTC (300/200 mg per day), adjusted to reflect rebates to Medicaid programs and retail pharmacy dispensing fees [37]. This value reflects the conservative assumption that prescriptions will be filled and costs incurred, even if pills are not consumed. We considered costs as low as 10% of this baseline value ($72) in sensitivity analysis. This permitted us to capture emerging evidence on the favorable outcomes and possible cost reductions associated with less frequent or lower dosing of TDF/FTC [16,54,55]. We further assumed that individuals receiving PrEP received quarterly laboratory monitoring (complete blood counts, comprehensive metabolic panels, and chemistry panels), semi-annual physical examinations, and annual full lipid panels; these added $28 to the monthly cost of PrEP (Table 1). Greater detail on cost data used in the analysis is provided elsewhere [27,56].

RESULTS

Base case

In a high-risk population with mean age 34 years and an average annual HIV incidence of 1.6%, current practices of HIV prevention and care produced a lifetime HIV infection risk of 44% and survival of 39.9 years. Discounted survival for the entire population totaled 21.7

QALYs, at an average discounted lifetime cost of $81,100 (Table 2). Introduction of TDF/FTC-based PrEP with 50% efficacy reduced lifetime infection risk to 25% and increased survival to 40.7 years. Discounted quality-adjusted survival rose to 22.2 QALYs and discounted lifetime costs increased to $232,700 per person, suggesting an incremental cost-effectiveness ratio (ICER) of $298,000 per QALY gained.

Sensitivity analysis

Table 2 presents results from alternative illustrative scenarios. Lifetime infection risk decreased and the cost-effectiveness of PrEP improved when we assumed greater PrEP efficacy. We obtained more favorable ICERs by assuming either a younger or a riskier target population, reduced PrEP costs, and reduced rates of HIV case identification for persons not receiving PrEP. For example, when we assumed that PrEP prevented 90% of new HIV infections, lifetime infection risk fell to 6%, survival increased to 42.5 years, and the ICER improved to $107,000/QALY. Less favorable ICERs resulted when PrEP reduced the number of available ART regimens or increased adverse events (result not shown).

One-way sensitivity analyses (Figure 1) highlighted six parameters whose uncertainty over plausible ranges of variation produced sizeable changes in cost-effectiveness. Five of these parameters – PrEP efficacy, HIV incidence in the target population, cost of PrEP, rate of HIV case detection in persons not receiving PrEP, and age of the target population – could adopt values that materially improved the ICER. For example, reducing the rate of HIV screening among persons not receiving PrEP from “annual” to “never” reduced the ICER to $109,000/QALY. Assumptions regarding lost ART efficacy and the risk of TDF resistance in breakthrough HIV infections had little impact.

Guidance for the prospective evaluation of PrEP

Figure 2 depicts the cost-effectiveness of PrEP as a function of four influential parameters identified via the one-way sensitivity analyses: PrEP efficacy, PrEP cost, and the age and HIV incidence in the target population. In the base case (50% PrEP efficacy, $9,000 annual cost, target population 34 years and 1.6% average annual HIV incidence, ♣), the intervention is deemed cost-effective only if society’s willingness to purchase an additional QALY of health for its citizens (i.e., the cost-effectiveness threshold) exceeds $200,000 [57,58]. ICERs in the $100,00–$200,000/QALY range for PrEP can be achieved via any one of the following changes: increase efficacy above 70% (♠); target a population with annual incidence greater than 2.4% (♦); reduce price to $4,700/year (♥); or target a population with average age 20 years (▲). Simultaneous changes in these parameters could produce even lower ICERs. For example, a 60%-effective program costing $4,700/year and targeted to a 20-year-old population with annual HIV incidence 1.5% would have an ICER of $50,000/QALY (▼). Further reduction in the price of the same intervention to $2,500/year would be cost-saving (+).

DISCUSSION

This analysis suggests that TDF/FTC-based PrEP could substantially reduce the lifetime risk of HIV infection in persons at high risk in the United States. Given the persistent disappointments of HIV prevention interventions over the last decade [2–8], this finding alone justifies continued study of PrEP-based approaches. While there is no consensus defining acceptable value for money, ICERs are often placed in context by comparisons with interventions that are widely recommended and generally viewed as non-controversial, such as colorectal cancer screening, home dialysis, and cholesterol-lowering drugs for men with cardiovascular risk factors [59,60]. Based on the current treatment cost of TDF/FTC and conservative estimates of efficacy, we estimate that PrEP has an ICER of $298,000/QALY

gained, making it an unattractive intervention, from a US-based cost-effectiveness perspective, compared to most (but not all) observers' thresholds [57,58].

This assessment hinges on several key parameter assumptions that, taken collectively, have important policy relevance. The PrEP efficacy parameter establishes a quantitative benchmark by which to judge newer ART agents that may exhibit HIV prevention properties. It suggests that small improvements in efficacy over that which has already been observed in preliminary studies would significantly improve the attractiveness of TDF/FTC-based PrEP but would not be sufficient to meet most standards of cost-effectiveness in the US [57]. It also provides a framework by which to weigh the transmission benefits of PrEP-based prevention and the additional, synergistic benefits of other HIV prevention strategies (e.g., increased condom use and and adoption of adult male circumcision) against the potential offsetting impact of behavioral disinhibition. The cost parameter indicates the potential of price reductions to greatly improve the attractiveness of PrEP. These reductions might be achieved either via lower pricing of ART when used for preventive purposes or if clinical evidence suggests a lower effective dose to achieve adequate HIV prevention. The age and HIV incidence parameters indicate that the attractiveness of PrEP would increase if it were targeted to populations at even greater risk (e.g., younger, HIV-discordant MSM). The final parameter – frequency of HIV testing in persons not receiving PrEP (Figure 1) – highlights the strong interdependence of HIV prevention and care. PrEP-based prevention is most attractive where there is poor identification and linkage of infected persons to lifesaving care. High rates of HIV testing in the principal target population groups may reduce the attractiveness of PrEP. At a minimum, they serve as a reminder that while prevention and treatment activities may not be substitutes, the costs and benefits of one can only be evaluated in the context of the other.

Although we adopted highly pessimistic base case assumptions, our findings do not identify resistance in breakthrough infections to be a critical driver of the attractiveness of PrEP. The expanding array of increasingly effective ART options dampens the potential harm to patients with resistant infection caused by the loss of an entire line of therapy and potential reduction in the efficacy of the remaining regimens. When risks and benefits are measured using a common metric (i.e., their impact on quality-adjusted survival) across the entire at-risk population, the preventive benefits of PrEP outweigh the risk of resistance.

This analysis has several limitations. First, we rely on data obtained from preliminary studies. Our intent is to suggest standards of evidence for further data collection. Until confirmatory trials can verify the plausibility of the critical input value assumptions (notably PrEP efficacy and required dosage), our policy conclusions should be interpreted with caution. Second, the usual parameters by which cost-effectiveness is judged may be different in persons at the very highest risk of infection, whose willingness to pay may differ from society's. Anecdotal evidence suggests that TDF/FTC is already being used off-label by high-risk HIV-uninfected MSM [61,62]. Third, by ignoring the secondary transmissions averted when a primary case of HIV infection is prevented, we understated the transmission benefits of PrEP. This might be an important omission in identifiable, small networks of sexually active MSM, given the possible adverse impact of transmitted resistance from failed PrEP subjects to their partners before being on suppressive ART [63,64]. Fourth, we do not consider the possibility of optimizing the time on PrEP as a function of patient age and risk behavior. Here again, we may have overstated the costs of PrEP by pursuing an expensive strategy of HIV prophylaxis in patients who are at lower risk as they age. We do not tackle the challenges of using TDF/FTC in patients potentially requiring this treatment intervention for hepatitis B co-infection. Positive testing for hepatitis B surface antibody (acquired either through natural immunity or vaccination) might be an appropriate eligibility criterion for PrEP use. We have not addressed important ethical and financial considerations of priority setting. Even if the cost-effectiveness of PrEP can be established, questions of who should receive PrEP and who should pay for it

– over what duration and at what frequency – remain to be addressed. Finally, our analysis focuses on the United States, ignoring the potential impact of PrEP globally. With an estimated 2.5 million people newly infected with HIV in 2007 [65], chemoprophylaxis with antiretroviral agents represents a promising new approach to containing the epidemic.

Current approaches to HIV chemoprophylaxis can substantially reduce the lifetime risk of HIV infection in the US. With improvements in efficacy, targeting, or pricing, such approaches may also be cost-effective by current US standards. The significance of this analysis lies not only in its relevance to TDF/FTC-based PrEP but also in the establishment of performance benchmarks for future generations of antiretroviral agents, many of which are likely to display chemoprophylactic properties. Given the many disappointments of HIV prevention efforts in recent years, greater focus on PrEP-based approaches is warranted.

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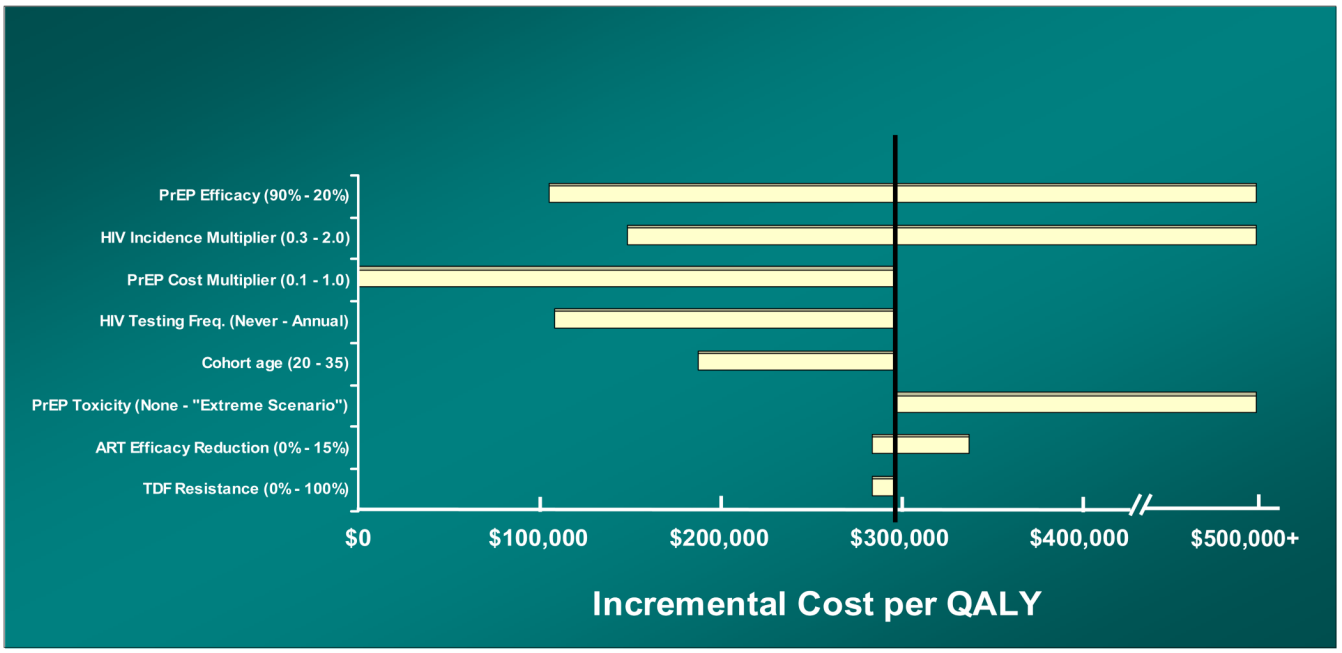

FIGURE 1. One-Way Sensitivity Analyses

A "tornado diagram" summarizes the results of a series of 1-way sensitivity analyses on the incremental cost-effectiveness of PrEP. Each horizontal bar represents the full range of costeffectiveness ratios produced by varying a given model parameter across its entire plausible range, as described in the Methods section. The bar denoting the "HIV testing frequency" variable, for example, summarizes the results we obtained using all of the following frequencies: never; once every 10 years; once every 5 years; once every 3 years; once every 2 years; and annually. The vertical line denotes the base case incremental cost-effectiveness estimate ($298,000/QALY). Note: The horizontal axis should be understood to extend beyond $500,000/QALY and to include instances where the PrEP intervention is dominated (i.e., it costs more and confers fewer QALYs than its comparator). PrEP = pre-exposure prophylaxis; QALY = quality-adjusted life-year; ART = antiretroviral therapy; TDF = tenofovir.

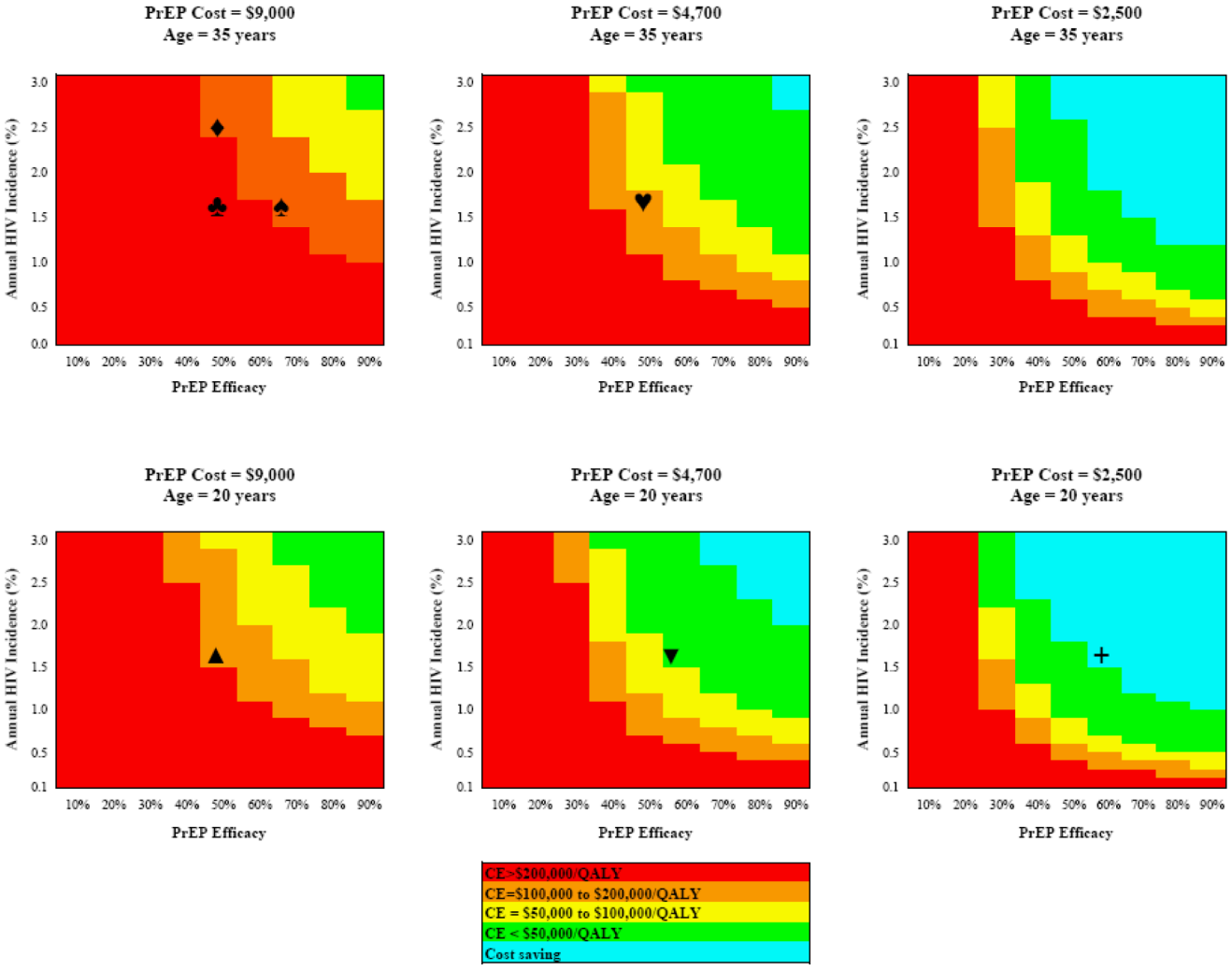

FIGURE 2. Multi-Way Sensitivity Analyses

The figure reports ranges of incremental cost-effectiveness for PrEP as a function of the four influential parameters identified via the one-way sensitivity analyses in Figure 1: PrEP efficacy, PrEP cost, and the age and HIV incidence in the target population. In each of the six panels, the horizontal axis denotes PrEP efficacy (measured as a % reduction in infections) and the vertical axis denotes the average annual HIV incidence in the target population. The top three panels consider a target population with mean age 34 years; the lower three panels consider a younger target cohort (mean age = 20 years). Moving from left to right, the three columns of panels consider decreasing annual PrEP costs, ranging from $9,000 to $2,000. The shading denotes the resultant ICER, ranging from >$200,000/QALY through cost-saving.

Table 1

Input Data Values for Analysis of PrEP

Variable	Baseline Value	Range Evaluated	Source
Initial cohort			
Mean age (SD)	34 (9.4)	20 – 34	[40]
% male	100	---	Assumption
Average HIV incidence (per 100 person-years)	1.6	0.1 – 3.1	[29]
Incidence distribution by age (per 100 PY)			[29]
< 18 years	2.1	0.1 – 4.1	
18 – 25 years	2.1	0.1 – 4.1	
26 – 30 years	1.9	0.1 – 3.8	
31 – 35 years	1.8	0.1 – 3.6	
36 – 40 years	1.1	0.07 – 2.1	
41 – 45 years	0.8	0.05 – 1.7	
> 45 years	1.5	0.09 – 2.9	
Viral load distribution if infected (%)			[30]
> 30,000 copies/ml	25.73	---	
10,001 – 30,000 copies/ml	25.02	---	
3,001 – 10,000 copies/ml	25.21	---	
500 – 3,000 copies/ml	16.33	---	
< 500 copies/ml	7.71		
PrEP efficacy[a] (%)	50	10 – 90	[31]

Efficacy of antiretroviral therapy without history of PrEP: % HIV RNA suppressed to <400 copies/ml (increase in CD4 cells/μl)[b]

	% HIV RNA suppressed to <400 copies/ml[c]	Increase in CD4 cells/μl [c]	Source
1. TDF/FTC + EFV	81	190	[32]
2. ATV/r + 2NRTIs	70	110	[33]
3. LPV/r + 2NRTIs	58	121	[33]
4. RAL + OBR	65 (24 weeks)	102 (24 weeks)	[34]
5. 50% ENF + OBR; 50% MVC + OBR +/− ENF[d]	40 (24 weeks)	117 (24 weeks)	[35,36]
6. OBR	12	45	[35]

Monthly Costs (2006 US$)	**Baseline Value**	**Range evaluated**	**Source**
Antiretroviral therapy			[37]
TDF/FTC + EFV	1,139	---	
ATV/r + 2NRTIs	1,741	---	
LPV/r + 2NRTIs	1,748	---	
RAL + OBR	2,209	---	
50% ENF + OBR; 50% MVC + OBR +/− ENF	3,338	---	
OBR	1,549	---	

Efficacy of antiretroviral therapy without history of PrEP: % HIV RNA suppressed to <400 copies/ml (increase in CD4 cells/μl)[b]			
	% HIV RNA suppressed to <400 copies/ml[c]	**Increase in CD4 cells/μl [c]**	**Source**
PrEP (TDF/FTC)	753	101 – 753	[37–39]

PrEP = pre-exposure prophylaxis; SD = standard deviation; TDF = tenofovir; FTC = emtricitabine; EFV = efavirenz; ATV/r = ritonavir-boosted atazanavir; LPV/r = ritonavir-boosted lopinavir; RAL = raltegravir; OBR = optimized background regimen; ENF = enfuvirtide; MVC = maraviroc

[a] PrEP efficacy is modeled as a net percent reduction in the monthly incidence of HIV infection, accounting for both the chemoprophylactic effect of PrEP and the potential offset of behavioral disinhibition.

[b] Values reported in the table reflect values found in the original source papers. In some instances, results reported by authors on an "intention-to-treat" basis were adjusted to reflect an "as-treated" basis before being used in the model.

[c] Values are reported at 48 weeks unless otherwise specified.

[d] Values reported for this regimen are weighted averages of the values found in the two original source papers.

Table 2

Base Case Results and Selected Scenario Analyses

	Undiscounted Results		Discounted Results		
	Lifetime Infection Risk (%)	Life-Years	Cost ($)	QALYs	$/QALY
Base case					
no PrEP	44	39.9	81,100	21.7	
PrEP	25	40.7	232,700	22.2	298,000
PrEP efficacy[a] increased to 90%					
no PrEP	44	39.9	81,100	21.7	
PrEP	6	42.5	215,400	23.0	107,000
Base HIV incidence increased to 3.1%					
no PrEP	66	37.8	136,700	20.7	
PrEP	44	38.9	250,800	21.4	150,000
PrEP cost reduced 50%					
no PrEP	44	39.9	81,100	21.7	
PrEP	25	40.7	139,300	22.2	114,000
No routine HIV screening in the "no PrEP" scenario					
no PrEP	44	35.4	16,800	20.2	
PrEP	25	40.7	232,700	22.2	109,000
ART after PrEP including EFV					
no PrEP	44	39.9	81,100	21.7	
PrEP	25	41.2	231,500	22.4	234,000
PrEP extreme toxicity scenario [b]					
no PrEP	44	39.9	81,100	21.7	
PrEP	25	40.7	232,700	21.8	1,546,000 [c]
Mean target population age decreased to 20 years (SD = 2)					
no PrEP	55	49.5	116,900	24.1	
PrEP	25	51.2	270,600	24.9	189,000

QALY = quality-adjusted life-year; $/QALY = incremental cost-effectiveness ratio measured in 2006 US dollars per quality-adjusted life-year gained; ART = antiretroviral therapy; EFV = efavirenz.

[a] PrEP efficacy is modeled as a net percent reduction in the monthly incidence of HIV infection, accounting for both the chemoprophylactic effect of PrEP and the potential offset of behavioral disinhibition.

[b] The "extreme toxicity scenario" assumes that 10% of all patients initiatiating PrEP suffer chronic renal disease resulting in a permanent decrement of 10% in their quality of life and where an additional 1% of patients suffer a TDF-toxicity-related death shortly following PrEP initiation.

[c] A dominated strategy has a higher cost and an equal or lower quality-adjusted life expectancy than some combination of other strategies.