Published in final edited form as:
Ann Intern Med. 2012 April 17; 156(8): 541–550. doi:10.1059/0003-4819-156-8-201204170-00001.

The Cost-Effectiveness of Preexposure Prophylaxis for HIV Prevention in Men Who Have Sex with Men in the United States

Jessie L. Juusola, M.S.[1], **Margaret L. Brandeau, Ph.D.**[1], **Douglas K. Owens, M.D., M.S.**[2,3], and **Eran Bendavid, M.D., M.S.**[3,4]

[1]Department of Management Science and Engineering, Stanford University, Stanford, CA

[2]Veterans Affairs Palo Alto Health Care System, Palo Alto, CA

[3]Center for Primary Care and Outcomes Research, Stanford University, Stanford, CA

[4]Division of General Internal Medicine, Stanford University Medical Center, Stanford, CA

Abstract

Background—In a recent randomized controlled trial, daily oral preexposure chemoprophylaxis (PrEP) was shown to be effective for HIV prevention in men who have sex with men (MSM). The United States Centers for Disease Control and Prevention (CDC) recently provided interim guidance for PrEP use among MSM who are at high risk for acquiring HIV. Previous studies failed to reach a consistent estimate of its cost-effectiveness.

Objective—To estimate the effectiveness and cost-effectiveness of PrEP in MSM in the United States.

Design—Dynamic model of HIV transmission and progression combined with a detailed economic analysis.

Data Sources—Published literature.

Target Population—MSM aged 13–64 in the United States.

Time Horizon—Lifetime.

Perspective—Societal.

Interventions—We evaluated PrEP for the general MSM population and for high-risk MSM. We assumed that PrEP reduces infection risk by 44%, based on clinical trial results.

Outcome Measures—New HIV infections, discounted quality-adjusted life-years (QALYs) and costs, and incremental cost-effectiveness ratios.

Results of Base-Case Analysis—If PrEP is initiated in 20% of MSM in the United States, we estimate a 13% reduction in new HIV infections and a gain of 550,166 QALYs over 20 years at a cost of $172,091/QALY gained. Initiating PrEP in a larger proportion of MSM averts more infections but at increasing cost per QALY gained ($216,480/QALY gained when 100% of MSM

Address for reprint requests: Jessie L. Juusola, Department of Management Science and Engineering, Huang Engineering Center Suite 263, 475 Via Ortega, Stanford, CA 94305.
Current mailing addresses for authors:
Jessie L. Juusola, Department of Management Science and Engineering, Huang Engineering Center Suite 263, 475 Via Ortega, Stanford, CA 94305
Margaret L. Brandeau, Department of Management Science and Engineering, Huang Engineering Center Room 262, 475 Via Ortega, Stanford, CA 94305
Douglas K. Owens, Center for Primary Care and Outcomes Research, 117 Encina Commons, Stanford, CA 94305
Eran Bendavid, Division of General Internal Medicine, 251 Campus Drive, MSOB x332, Stanford, CA 94306

receive PrEP). Using PrEP only in high-risk MSM can improve its cost-effectiveness. PrEP costs approximately $50,000/QALY gained for MSM with 5 annual partners on average. PrEP for all high-risk MSM for 20 years leads to $75 billion in healthcare-related costs incremental to the status quo and costs $600,000 per HIV infection averted, compared with incremental costs of $95 billion and $2 million per infection averted for 20% coverage of all MSM.

Results of Sensitivity Analysis—PrEP use in the general MSM population costs less than $100,000/QALY gained if the daily cost of antiretroviral drugs for PrEP is less than $15 or if PrEP efficacy is greater than 75%.

Limitation—When examining PrEP use in high-risk MSM, we did not model mixing between low- and high-risk MSM because of lack of data on mixing patterns.

Conclusion—Use of PrEP for HIV prevention in the general MSM population could prevent a substantial number of HIV infections but is expensive. PrEP use in high-risk MSM compares favorably to other interventions considered cost-effective, but could result in annual expenditures on PrEP of over $4 billion.

INTRODUCTION

Men who have sex with men (MSM) are an important group to reach with programs to prevent human immunodeficiency virus (HIV) infection. Of the estimated 48,000–56,000 annual new HIV infections in the United States, 56–61% occur among MSM (1, 2). In 2010, results from a clinical trial suggested that antiretroviral drugs (ARVs) can be effectively used as preexposure prophylaxis (PrEP) for HIV prevention among uninfected MSM (3). The Preexposure Prophylaxis Initiative (iPrEx) study showed that in MSM, daily tenofovir and emtricitabine (TDF/FTC) reduced HIV incidence by 44% overall, and by 73% among MSM who reported high adherence (3). In 2011, the Centers for Disease Control and Prevention (CDC) published interim guidance for prescribing TDF/FTC as PrEP for MSM (4). This guidance highlights the importance of regular monitoring for adverse effects from PrEP, HIV testing, and counseling to encourage adherence and risk reduction.

While PrEP has been shown to be effective at preventing HIV acquisition, its costs are considerable. Prior studies on the cost-effectiveness of PrEP in MSM in the United States have reached inconsistent conclusions (5, 6). Paltiel et al. (5) estimated that PrEP costs $298,000 per quality-adjusted life year (QALY) gained among high-risk MSM, while Desai et al. (6) estimated that a PrEP program targeting high-risk men in New York City would cost $32,000/QALY gained. We examine the effectiveness and cost-effectiveness of PrEP strategies for MSM in the United States using the newly available clinical trial data, CDC interim guidance, and an epidemic modeling framework combined with a detailed economic analysis.

METHODS

Overview and model structure

We adapted a previously published deterministic dynamic compartmental model of HIV transmission and progression to assess the effectiveness and cost-effectiveness of PrEP for HIV prevention in MSM (7). We calibrated the model to estimates of HIV incidence among MSM aged 13–64 in the United States (Appendix) (1, 2), and estimated HIV prevalence, incidence, QALYs, and healthcare costs of various PrEP strategies over a 20-year time horizon. We assumed a societal perspective and discounted costs and QALYs at 3% annually (8). Key model parameters are presented in Table 1. The Appendix provides additional model details.

We divided the population by HIV infection status, awareness of HIV status, and PrEP use. Infected individuals were additionally defined by HIV disease stage and treatment status (Appendix Figure A1). Initial HIV prevalence was 12.3% and annual incidence was 0.8%, representing an average across the United States (2, 9–12). Individuals entered the model at age 13 and were followed for 20 years or until age 65. Modeling MSM aged 13–64 is consistent with CDC recommendations for routine HIV screening (62). Mortality comprised HIV-related and non-HIV-related deaths.

HIV transmission

We modeled HIV transmission via homosexual contact based on number of male sexual partners (28, 29) and average condom use (31). We assumed proportional mixing in selecting an HIV-infected partner; that is, individuals were more likely to partner with MSM who had many partners than with those who had few partners. The probability of HIV transmission between sero-discordant partners depended on the infected individual's disease stage and antiretroviral therapy (ART) use, as well as PrEP status of the uninfected individual (25, 26).

HIV disease progression and treatment

HIV disease progression was based on the average time in each of four disease stages: acute infection, asymptomatic HIV, symptomatic HIV, and AIDS. Progression rates were based on HIV natural history and ART status (20–22, 35).

We assumed that HIV-infected individuals with a CD4 cell count of 0.350×10^9 cells/L or lower were offered ART (63). Given recent guidelines recommending ART initiation at CD4 cell counts great than 0.350×10^9 cells/L, we examined the effects of earlier ART initiation in sensitivity analysis (64). The benefits of ART and suppression of viral replication included improved quality of life and reduced disease transmission, progression, and mortality (22, 35). We assumed a 90% reduction in sexual infectivity due to ART used for treatment of HIV infection in our base case and varied this in sensitivity analysis (22, 26, 37, 38).

To be treated, HIV-infected individuals must be identified as infected. We estimated that 67% of MSM are currently screened annually using antibody tests (28, 45). Counseling accompanying HIV testing has been found to reduce risky sexual behavior (49). Accordingly, we assumed a 20% reduction in risky behavior for both infected and uninfected individuals after HIV screening (22, 35, 49).

PrEP strategies

We considered two strategies: PrEP for the general MSM population and PrEP for high-risk MSM. We chose a representative example of a high-risk population, and we varied risk levels in sensitivity analysis. We compared PrEP strategies to the status quo of no PrEP use. We assumed that MSM receiving PrEP would begin immediately and would remain on PrEP for the 20-year time horizon or until aging out of the model.

We based our PrEP protocol on the CDC interim guidance on PrEP use in uninfected MSM (4). MSM were initiated on PrEP after a negative HIV antibody test, adequate calculated creatinine clearance, and testing for sexually transmitted infections. The PrEP regimen included daily TDF/FTC and physician visits 5 times per year, or every 2–3 months, where HIV-negative status was confirmed with an antibody test and risk-reduction counseling and condoms were provided. Additionally, sexually transmitted infection testing was performed every 6 months and renal function was tested annually. Individuals who became HIV-

infected while on PrEP, once infection was detected, were provided with appropriate counseling and discontinued PrEP.

We assumed TDF/FTC reduces the probability of acquiring HIV by 44%, based on the overall reduction in incidence seen in iPrEx study subjects (3). PrEP was more effective in preventing HIV infection in iPrEx subgroups with higher adherence, and incidence reduction in study subjects who reported or exhibited pill use on at least 90% of days was 73% (3). Accordingly, we varied PrEP efficacy in sensitivity analysis. Although behavioral disinhibition is a concern with PrEP use, there is no conclusive evidence regarding the effect of PrEP on sexual risk behavior (65, 66). Hence, in our base case we assumed no change in risky behavior from counseling or risk compensation. In sensitivity analysis we examined the impact of changes in number of sexual partners and condom use as a result of PrEP.

Various studies have assessed willingness and likelihood to use PrEP in surveyed MSM populations with varying conclusions (67–70). The percentage of MSM who will ultimately use PrEP is unknown and will depend on factors such as public health campaigns and access to healthcare. We evaluated initiating 5–100% of the HIV-negative MSM population on PrEP (Appendix), but we focus results on 20%, 50%, and 100% of uninfected MSM initiating PrEP to illustrate the differences in effectiveness and cost-effectiveness as the percentage of MSM on PrEP increases.

Health outcomes and costs

We simulated the population over time and calculated discounted costs and QALYs for each PrEP use scenario. We estimated quality of life for each health state and adjusted the utilities based on the average age of the modeled population (22, 35, 71). We assumed no reduction in quality of life from PrEP, as clinical trials have shown minimal side effects from TDF/FTC (3, 72). In sensitivity analysis, we evaluated the impact of decreased quality of life while on PrEP, as study participants on PrEP were more likely than those on placebo to experience minor side effects such as nausea (3, 72).

We included costs associated with medical care in each health state, PrEP, and HIV testing, counseling, and diagnosis to calculate total health-related costs. Baseline medical costs, HIV-related healthcare costs (with costs of associated co-morbidities), cost of ART, and costs of counseling were estimated from the published literature (22, 53). Costs of ARVs for PrEP were estimated as the average monthly wholesale price of TDF/FTC adjusted to reflect rebates and retail pharmacy dispensing fees (5). Costs of non-ARV components of the PrEP protocol and the HIV testing protocol were obtained from the Centers for Medicare and Medicaid Services 2010 fee schedules (59). We also included discounted health-related costs and QALYs for the remaining lifetime of the population in the model at the end of the time horizon and for individuals who matured out of the modeled population.

Role of the funding source

The National Institute of Health and the Department of Veterans Affairs supported this study. None of the funding sources had any role in the design, conduct, or reporting of the study.

RESULTS

PrEP for the general MSM population

In the absence of PrEP use, we estimate that 491,784 new HIV infections will occur among MSM in the United States in the next 20 years (Table 2). Use of PrEP can substantially reduce this incidence. Initiating 20% of the MSM population in the United States on PrEP

will reduce the number of infections over 20 years by 62,759 (13% of the projected total) and yield 550,166 incremental QALYs (Table 2). Initiating a greater proportion of the MSM population on PrEP yields greater health benefits. With 50% of MSM using PrEP, 143,291 new infections (29%) are averted and 1.3 million QALYs are gained incremental to the status quo. If 100% of MSM use PrEP, 249,156 (51%) infections will be averted, HIV prevalence in MSM will drop to 6.4% by the end of 20 years (Appendix Figure A2a), and more than 2 million QALYs will be gained.

In the first year of PrEP use, the percentage reduction in annual HIV incidence is similar to the efficacy of PrEP scaled by the percentage of MSM using PrEP. For example, with 20% of MSM using PrEP, incidence is reduced by 10% in the first year (approximately equal to 44% efficacy multiplied by 20% on PrEP) (Appendix Figure A2b). With 50% and 100% of MSM on PrEP, incidence is reduced by 24% and 45% in the first year, respectively. However, averting secondary transmissions causes the percentage reduction in HIV incidence to increase over time. After 20 years, annual HIV incidence is reduced by 17% when 20% of MSM use PrEP, by 37% when 50% of MSM use PrEP, and by 60% when all MSM use PrEP.

PrEP is effective at preventing HIV in MSM but is an expensive intervention. Initiating PrEP in 20% of MSM has an incremental cost-effectiveness ratio of $172,091/QALY gained compared to the status quo (Table 2, Figure 1). As the percentage of MSM initiated on PrEP increases, the incremental cost-effectiveness ratio also increases because of diminishing benefits from additional PrEP. Initiating 50% of MSM on PrEP costs $188,421/QALY gained compared to the status quo, or $201,012 compared to initiating 20% on PrEP, while initiating 100% of MSM on PrEP costs $216,480/QALY gained, or $253,645 compared to initiating 50% on PrEP.

The costs associated with PrEP are substantial. PrEP use in 20% of MSM over 20 years generates an incremental $95 billion in healthcare-related costs compared to the status quo ($98 billion for PrEP minus $3 billion in savings in HIV care), or nearly $2 million per HIV infection averted (Table 2). These costs include all medical costs (HIV- and non-HIV-related) over the lifetime of the cohort. Antiretrovirals and monitoring associated with PrEP for 20% of MSM cost $98 billion over 20 years, or an average of $4.9 billion per year (Appendix Figure A3a). Costs increase as a higher percentage of MSM are initiated on PrEP. If 100% of MSM initiate PrEP for 20 years, healthcare-related costs increase by $480 billion.

PrEP use in high-risk MSM

Targeting high-risk MSM, rather than offering PrEP to the general MSM population, can improve the cost-effectiveness of PrEP. We estimated that 20% of MSM are high risk, with 5 annual partners on average, initial HIV prevalence of 20%, and initial annual incidence of 2.3%, for a representative high-risk population (28, 31, 45). PrEP use in 100% of these high-risk MSM costs $52,443/QALY gained relative to the status quo (Table 3). As with the general MSM population, there are diminishing returns associated with increasing the percentage of high-risk MSM on PrEP: if 20% of high-risk MSM use PrEP, the intervention costs $40,279/QALY gained relative to the status quo (Figure 1); with 50% access, PrEP costs $44,556/QALY gained relative to the status quo. PrEP is effective at preventing HIV infections in these scenarios, preventing 13%, 29%, and 52% of new infections in high-risk MSM with 20%, 50%, and 100% coverage, respectively (Table 3).

Use of PrEP in high-risk MSM costs less than does PrEP for all MSM. If all high-risk MSM initiate PrEP for a 20-year period, total healthcare-related costs incremental to the status quo are $75.5 billion, or approximately $600,000 per HIV infection averted. ARVs and

monitoring for PrEP cost $85.2 billion over 20 years, or an average of $4.3 billion per year, while HIV treatment and care are associated with savings of nearly $10 billion due to fewer future infections (Table 3, Appendix Figure A3b). If fewer high-risk MSM use PrEP, as would likely be the case in practice, PrEP costs are lower. With 50% of high-risk MSM initiating PrEP, the costs of PrEP over 20 years are $41.9 billion, with total healthcare-related costs incremental to the status quo of $36.4 billion. With only 20% of high-risk MSM initiating PrEP, the costs of PrEP over 20 years are $16.6 billion, or an average of $828 million per year, with total healthcare-related costs incremental to the status quo of $14.2 billion. The cost per infection averted decreases at lower coverage levels of high-risk MSM, to $460,000 per infection averted at 20% coverage of high-risk MSM.

Sensitivity analysis

In sensitivity analysis, we found that PrEP cost, efficacy, and impact on quality of life considerably affected the cost-effectiveness of PrEP. One common concern with PrEP is resulting behavioral disinhibition (65, 66), but we found that the effectiveness and cost-effectiveness of PrEP are not substantially impacted by moderate changes in number of sexual partners and/or condom use induced by PrEP use (Appendix). We also found that initiating ART at CD4 cell counts of 0.500×10^9 cells/L, as opposed to at 0.350×10^9 cells/L as in our base case, did not qualitatively change the effectiveness and cost-effectiveness of PrEP (Appendix). The daily cost of TDF/FTC and its efficacy are key drivers of the cost-effectiveness of PrEP. PrEP use in 20% of the general MSM population costs less than $100,000/QALY gained if its daily cost drops below $15 or if PrEP is more than 75% effective at reducing risk of HIV acquisition, which could possibly be attained in highly adherent patients. The daily cost would have to nearly double in order for PrEP for high-risk MSM to cost more than $100,000/QALY gained. While in our base case we assumed that PrEP had no impact on quality of life, some patients may experience side effects. We found that PrEP must reduce the quality of life by more than 8% on average for the cost of PrEP for all high-risk MSM to rise above $100,000/QALY gained.

Since risk behaviors and HIV prevalence vary across subpopulations of MSM, we examined a range of risk levels in sensitivity analysis (Appendix). In a high-risk group with 5 annual partners on average, PrEP for all high-risk MSM costs less than $100,000/QALY gained as long as initial prevalence in the group is 8% or higher. For a medium-risk group with initial prevalence of 15% and 4 annual partners on average, PrEP for 100% of the group would cost approximately $100,000/QALY gained.

Both the cost and efficacy, and thus the cost-effectiveness, of PrEP depend on patient adherence. The iPrEx finding of 44% efficacy corresponded to approximately half of the study subjects reporting or exhibiting high adherence, as defined by pill use on at least 90% of days, but average patient adherence is unknown (3). For MSM with lower adherence, the cost of PrEP will likely be lower than in our base case, which includes the costs of daily pills, since non-adherent MSM will refill their ARVs less often. If MSM on PrEP on average take their daily pills only 50% of the time and efficacy is still 44%, PrEP for high-risk MSM costs $25,165/QALY gained, as compared to $52,443/QALY gained with the full daily pill cost. If average pill use is 75%, PrEP for high-risk MSM costs $38,804/QALY gained. If all MSM are highly adherent to PrEP, such that efficacy is 73% and the full daily pill cost is realized, PrEP for high-risk MSM costs $35,080/QALY gained. Figure 2b illustrates how the cost-effectiveness of PrEP for high-risk MSM varies as a function of cost and efficacy. Since average pill use will likely be less than daily in practice, use of PrEP in high-risk MSM likely costs less than $50,000/QALY gained. Figure 2a illustrates this relationship for the general MSM population.

DISCUSSION

Our analysis demonstrates that the use of PrEP for HIV prevention in MSM could have an important impact on the HIV epidemic in the United States. We show that even if only 20% of the MSM population in the United States were to initiate PrEP, more than 60,000 new HIV infections could be prevented over the next 20 years. However, PrEP is a costly intervention, and use in high-risk MSM will be integral to producing health benefits in an economically efficient manner (73). Initiating PrEP in 20% of the overall MSM population costs $172,091/QALY gained. In contrast, targeting PrEP to all high-risk MSM, whom we estimate comprise 20% of the overall MSM population, costs approximately $50,000/QALY gained and prevents a greater number of infections. If the daily cost of ARVs for PrEP decreased to $15, PrEP could be more cost-effective in a broader population of MSM, but at current costs, use of PrEP only in high-risk MSM is attractive. While the cost per QALY gained of PrEP in high-risk MSM is comparable to other interventions considered cost-effective, initiation of PrEP in all high-risk MSM would cost more than $4 billion per year for ARVs and monitoring.

Despite the good value provided by PrEP use in high-risk MSM, the budgetary impact will be large. Affordability of PrEP is uncertain, particularly in view of other competing priorities such as providing ART to infected individuals and new prevention technologies. Other interventions for MSM also provide good value but at lower expenditures, such as symptom-based viral load testing for acute HIV infection (7). In addition, if PrEP were implemented, many practical issues remain to be resolved, such as who would prescribe and who would pay for PrEP.

Because PrEP provides the most value in reducing HIV transmission when used in high-risk MSM, efficient clinical use of PrEP will depend on clinicians' abilities to identify high-risk MSM. In MSM, number of partners and consistency of condom use are two key drivers of risk of HIV acquisition, and our results suggest that use of PrEP in MSM with multiple sexual partners can be cost-effective. To stratify patients by risk, a clinician can ask a patient how many partners he had in the past year. Additionally asking about condom use with non-primary partners could strengthen the risk assessment and inform the decision to offer PrEP to the patient. Assessing risk from these parameters is not uncommon with HIV prevention interventions (42, 62). Future studies on risk stratification of MSM could provide further guidance to clinicians in identifying high-risk MSM.

Our analysis finds that PrEP provides better value (73) when a smaller percentage of MSM initiate PrEP than when all MSM use PrEP. This phenomenon of diminishing returns is seen in other prevention programs as they are scaled up (74, 75). Secondary transmission benefits lead to substantial numbers of HIV infections averted even at low PrEP coverage. Thus, PrEP can have a clinically significant – and efficient – impact at relatively low coverage levels.

We considered daily oral PrEP. The efficacy of intermittent PrEP is currently being tested in clinical trials. If PrEP use only before high-risk behavior is shown to be effective at preventing HIV acquisition, this could substantially lower the cost of the ARVs associated with PrEP. Our examination of the cost-effectiveness of daily PrEP as a function of cost and efficacy can help estimate thresholds of cost and efficacy for intermittent PrEP to be cost-effective.

Previous studies reached different conclusions about the cost-effectiveness of PrEP in MSM. Paltiel et al. (5) found that PrEP use for MSM cost $298,000/QALY gained in a high-risk population with 1.6% annual HIV incidence, while Desai et al. (6) found that PrEP cost $32,000/QALY gained for high-risk MSM in New York City with 1.35% annual incidence.

While Paltiel et al. suggest that PrEP is only cost-effective in very high incidence subgroups, we find lower incremental cost-effectiveness ratios for PrEP for high-risk MSM under a broader set of risk assumptions. Our results differ in part because of the extent to which each model captures the full benefits from reduced transmission due to PrEP and the length of time MSM remain on PrEP. While Paltiel et al. modeled PrEP efficacy as a flat percentage reduction in incidence and kept MSM on PrEP for their entire lifetime, we captured the dynamic effects of reduced transmission on incidence and we assumed that MSM would discontinue PrEP after 20 years or at age 65. When we match Paltiel et al.'s assumptions as closely as possible given our different modeling frameworks, we arrive at a similar conclusion, that PrEP is only cost-effective for the highest-risk subgroup of MSM. With our base-case model assumptions, our findings are more similar to those of Desai et al. (6). We both find that PrEP costs less than $100,000/QALY gained for high-risk MSM with annual incidence above 1.3%. A strength of our analysis is that we capture longer-term benefits of reduced transmission and incorporate a detailed economic analysis along with the epidemic modeling.

Our analysis has several limitations. The cost-effectiveness of offering PrEP to all MSM will depend on the propensity of MSM to use PrEP by risk level. For example, if high-risk MSM are more likely than low-risk MSM to use PrEP, offering PrEP to all MSM may be cost-effective, as in practice it will be as if PrEP is targeted to high-risk MSM. If, conversely, low-risk MSM are more likely than high-risk MSM to use PrEP, perhaps because they are more risk-averse, PrEP for the general MSM population may be even less cost-effective than in our base case. Second, high-risk MSM may mix with low-risk MSM and have networks of sexual partners, which we did not model when examining PrEP for high-risk MSM because of lack of data on mixing patterns. Consequently, we cannot directly compare strategies of PrEP for all MSM with PrEP for high-risk MSM. However, we can infer that PrEP for all MSM would be even less cost-effective when compared to PrEP for high-risk MSM than when compared to the status quo. With regard to sexual networks, to the extent that PrEP could be targeted to MSM centrally located in the networks, PrEP would be even more cost-effective. Third, we did not include in our model the possibility that PrEP may facilitate the development of drug-resistant HIV, since the iPrEx study found that no resistance developed in study subjects who acquired HIV during the trial (3). In sensitivity analysis, we estimated the effects of resistance in terms of the efficacy and cost of future treatment for those who acquire HIV while taking PrEP and found that resistance did not largely affect results. Fourth, we did not include potential renal impairment associated with PrEP. Since we included monitoring for elevated creatinine levels for patients on PrEP, per CDC guidelines, and TDF/FTC was not found to create long-term renal impairment in iPrEx participants (3), we do not anticipate this exclusion to impact results. Finally, we did not model HIV risk and benefits for MSM who also have female partners or who are injection drug users.

Our analysis demonstrates that PrEP use in MSM has the potential to prevent a considerable number of new HIV infections. However, PrEP use in the general MSM population is expensive. Use of PrEP in high-risk MSM provides substantial health benefits at a lower cost, although its budgetary impact is still sizeable. PrEP use in 100% of the estimated 20% of MSM who are at high risk of acquiring HIV infection averts more than twice as many infections as does PrEP use in 20% of the general MSM population, and provides better value. These findings can help inform clinicians' decisions about whom to offer PrEP and policymakers' decisions about recommendations for the use of PrEP.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported by Grant Number R01-DA15612 from the National Institute on Drug Abuse. Dr. Owens is supported by the Department of Veterans Affairs. Dr. Bendavid is supported by the National Institute of Allergy and Infectious Diseases (K01-AI084582).

Primary Funding Source: National Institute on Drug Abuse, Department of Veterans Affairs, National Institute of Allergy and Infectious Diseases, and Stanford University.

REFERENCES

1. Centers for Disease Control and Prevention (CDC). Estimates of New HIV Infections in the United States. 2008. Accessed at http://www.cdc.gov/hiv/topics/surveillance/resources/factsheets/incidence.htm on 30 September 2009
2. Prejean J, Song R, Hernandez A, Ziebell R, Green T, Walker F, et al. Estimated HIV Incidence in the United States, 2006–2009. PLoS One. 2011; 6:e17502. [PubMed: 21826193]
3. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med. 2010; 363:2587–2599. [PubMed: 21091279]
4. Centers for Disease Control and Prevention (CDC). Interim guidance: preexposure prophylaxis for the prevention of HIV infection in men who have sex with men. MMWR Morb Mortal Wkly Rep. 2011; 60:65–68. [PubMed: 21270743]
5. Paltiel AD, Freedberg KA, Scott CA, Schackman BR, Losina E, Wang B, et al. HIV preexposure prophylaxis in the United States: impact on lifetime infection risk, clinical outcomes, and cost-effectiveness. Clin Infect Dis. 2009; 48:806–815. [PubMed: 19193111]
6. Desai K, Sansom SL, Ackers ML, Stewart SR, Hall HI, Hu DJ, et al. Modeling the impact of HIV chemoprophylaxis strategies among men who have sex with men in the United States: HIV infections prevented and cost-effectiveness. AIDS. 2008; 22:1829–1839. [PubMed: 18753932]
7. Juusola JL, Brandeau ML, Long EF, Owens DK, Bendavid E. The cost-effectiveness of symptom-based testing and routine screening for acute HIV infection in men who have sex with men in the USA. AIDS. 2011; 25:1779–1787. [PubMed: 21716076]
8. Gold, MR.; Siegel, JE.; Russell, LB.; Weinstein, MC., editors. Cost-Effectiveness in Health and Medicine. New York: Oxford University Press; 1996.
9. Centers for Disease Control and Prevention (CDC). HIV and AIDS among Gay and Bisexual Men. 2010. Accessed at http://www.cdc.gov/nchhstp/newsroom/docs/FastFacts-MSM-FINAL508COMP.pdf on 5 April 2011
10. U.S. Census Bureau PD. National Population Projections, Released 2008 (Based on Census 2000). 2008. Accessed at http://www.census.gov/population/www/projections/downloadablefiles.html on 5 April 2011
11. Centers for Disease Control and Prevention (CDC). HIV Prevalence Estimates -- United States, 2006. 2008 Accessed at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5739a2.htm on 30 September 2009.
12. Xu F, Sternberg MR, Markowitz LE. Men who have sex with men in the United States: demographic and behavioral characteristics and prevalence of HIV and HSV-2 infection: results from National Health and Nutrition Examination Survey 2001–2006. Sex Transm Dis. 2010; 37:399–405. [PubMed: 20473245]
13. Arias E. United States life tables, 2004. Natl Vital Stat Rep. 2007; 56:1–39. [PubMed: 18274319]
14. Pilcher CD, Tien HC, Eron JJ Jr, Vernazza PL, Leu SY, Stewart PW, et al. Brief but efficient: acute HIV infection and the sexual transmission of HIV. J Infect Dis. 2004; 189:1785–1792. [PubMed: 15122514]
15. Vergis EN, Mellors JW. Natural history of HIV-1 infection. Infect Dis Clin North Am. 2000; 14:809–825. v–vi. [PubMed: 11144640]
16. Hollingsworth TD, Anderson RM, Fraser C. HIV-1 transmission, by stage of infection. J Infect Dis. 2008; 198:687–693. [PubMed: 18662132]

17. Pinkerton SD. How many sexually-acquired HIV infections in the USA are due to acute-phase HIV transmission? AIDS. 2007; 21:1625–1629. [PubMed: 17630558]
18. Xiridou M, Geskus R, de Wit J, Coutinho R, Kretzschmar M. Primary HIV infection as source of HIV transmission within steady and casual partnerships among homosexual men. AIDS. 2004; 18:1311–1320. [PubMed: 15362664]
19. Long EF, Brandeau ML, Owens DK. Potential population health outcomes and expenditures of HIV vaccination strategies in the United States. Vaccine. 2009; 27:5402–5410. [PubMed: 19591796]
20. Mellors JW, Munoz A, Giorgi JV, Margolick JB, Tassoni CJ, Gupta P, et al. Plasma viral load and CD4+ lymphocytes as prognostic markers of HIV-1 infection. Ann Intern Med. 1997; 126:946–954. [PubMed: 9182471]
21. Dunn D, Woodburn P, Duong T, Peto J, Phillips A, Gibb D, et al. Current CD4 cell count and the short-term risk of AIDS and death before the availability of effective antiretroviral therapy in HIV-infected children and adults. J Infect Dis. 2008; 197:398–404. [PubMed: 18248303]
22. Long EF, Brandeau ML, Owens DK. Health outcomes and costs of expanded HIV screening and antiretroviral treatment in the United States. Ann Intern Med. 2010:153.
23. May M, Sterne JA, Sabin C, Costagliola D, Justice AC, Thiebaut R, et al. Prognosis of HIV-1-infected patients up to 5 years after initiation of HAART: collaborative analysis of prospective studies. AIDS. 2007; 21:1185–1197. [PubMed: 17502729]
24. Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies. Lancet. 2008; 372:293–299. [PubMed: 18657708]
25. Xiridou M, Geskus R, De Wit J, Coutinho R, Kretzschmar M. The contribution of steady and casual partnerships to the incidence of HIV infection among homosexual men in Amsterdam. AIDS. 2003; 17:1029–1038. [PubMed: 12700453]
26. McCormick AW, Walensky RP, Lipsitch M, Losina E, Hsu H, Weinstein MC, et al. The effect of antiretroviral therapy on secondary transmission of HIV among men who have sex with men. Clin Infect Dis. 2007; 44:1115–1122. [PubMed: 17366461]
27. Wawer MJ, Gray RH, Sewankambo NK, Serwadda D, Li X, Laeyendecker O, et al. Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. J Infect Dis. 2005; 191:1403–1409. [PubMed: 15809897]
28. Centers for Disease Control and Prevention (CDC). HIV/AIDS Surveillance Special Report, Number 5 - HIV Testing Survey, 2002. 2006. Accessed at http://www.cdc.gov/hiv/topics/surveillance/resources/reports/2004spec_no5/default.htm on 27 January 2010
29. Koblin BA, Chesney MA, Husnik MJ, Bozeman S, Celum CL, Buchbinder S, et al. High-risk behaviors among men who have sex with men in 6 US cities: baseline data from the EXPLORE Study. Am J Public Health. 2003; 93:926–932. [PubMed: 12773357]
30. Colfax GN, Buchbinder SP, Cornelisse PG, Vittinghoff E, Mayer K, Celum C. Sexual risk behaviors and implications for secondary HIV transmission during and after HIV seroconversion. AIDS. 2002; 16:1529–1535. [PubMed: 12131191]
31. Pathela P, Hajat A, Schillinger J, Blank S, Sell R, Mostashari F. Discordance between sexual behavior and self-reported sexual identity: a population-based survey of New York City men. Ann Intern Med. 2006; 145:416–425. [PubMed: 16983129]
32. Harawa NT, Greenland S, Bingham TA, Johnson DF, Cochran SD, Cunningham WE, et al. Associations of race/ethnicity with HIV prevalence and HIV-related behaviors among young men who have sex with men in 7 urban centers in the United States. J Acquir Immune Defic Syndr. 2004; 35:526–536. [PubMed: 15021318]
33. MacKellar DA, Valleroy LA, Behel S, Secura GM, Bingham T, Celentano DD, et al. Unintentional HIV exposures from young men who have sex with men who disclose being HIV-negative. AIDS. 2006; 20:1637–1644. [PubMed: 16868445]
34. Rietmeijer CA, Wolitski RJ, Fishbein M, Corby NH, Cohn DL. Sex hustling, injection drug use, and non-gay identification by men who have sex with men. Associations with high-risk sexual behaviors and condom use. Sex Transm Dis. 1998; 25:353–360. [PubMed: 9713915]

35. Sanders GD, Bayoumi AM, Sundaram V, Bilir SP, Neukermans CP, Rydzak CE, et al. Cost-effectiveness of screening for HIV in the era of highly active antiretroviral therapy. N Engl J Med. 2005; 352:570–585. [PubMed: 15703422]
36. Teshale, EH.; Kamimoto, L.; Harris, N.; Li, J.; Wang, H.; McKenna, MT. Estimated Number of HIV-infected Persons Eligible for and Receiving HIV Antiretroviral Therapy, 2003--United States (Abstract #167); 12th Conference on Retroviruses and Opportunistic Infections; 2005.
37. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011; 365:493–505. [PubMed: 21767103]
38. Wilson DP, Law MG, Grulich AE, Cooper DA, Kaldor JM. Relation between HIV viral load and infectiousness: a model-based analysis. Lancet. 2008; 372:314–320. [PubMed: 18657710]
39. Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li C, Wabwire-Mangen F, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. N Engl J Med. 2000; 342:921–929. [PubMed: 10738050]
40. Vernazza P, Hirschel B, Bernasconi E, Flepp M. HIV transmission under highly active antiretroviral therapy. Lancet. 2008; 372:1806–1807. author reply 7. [PubMed: 19027479]
41. The National Institute of Mental Health (NIMH) Multisite HIV Prevention Trial Group. The NIMH Multisite HIV Prevention Trial: reducing HIV sexual risk behavior. Science. 1998; 280:1889–1894. [PubMed: 9632382]
42. Kamb ML, Fishbein M, Douglas JM Jr, Rhodes F, Rogers J, Bolan G, et al. Efficacy of risk-reduction counseling to prevent human immunodeficiency virus and sexually transmitted diseases: a randomized controlled trial. Project RESPECT Study Group. JAMA. 1998; 280:1161–1167. [PubMed: 9777816]
43. Abbas UL, Anderson RM, Mellors JW. Potential impact of antiretroviral therapy on HIV-1 transmission and AIDS mortality in resource-limited settings. J Acquir Immune Defic Syndr. 2006; 41:632–641. [PubMed: 16652038]
44. Cohen MS, Gay C, Kashuba AD, Blower S, Paxton L. Narrative review: antiretroviral therapy to prevent the sexual transmission of HIV-1. Ann Intern Med. 2007; 146:591–601. [PubMed: 17438318]
45. Centers for Disease Control and Prevention (CDC). Human immunodeficiency virus (HIV) risk, prevention, and testing behaviors -- United States, National HIV Behavioral Surveillance System: Men who have sex with men, November 2003-April 2005. MMWR Morbid Mortal Wkly Rep. 2006; 55:1–16.
46. Manning SE, Thorpe LE, Ramaswamy C, Hajat A, Marx MA, Karpati AM, et al. Estimation of HIV prevalence, risk factors, and testing frequency among sexually active men who have sex with men, aged 18–64 years--New York City, 2002. J Urban Health. 2007; 84:212–225. [PubMed: 17295058]
47. Rose CD, Courtenay-Quirk C, Knight K, Shade SB, Vittinghoff E, Gomez C, et al. HIV intervention for providers study: a randomized controlled trial of a clinician-delivered HIV risk-reduction intervention for HIV-positive people. J Acquir Immune Defic Syndr. 2010; 55:572–581. [PubMed: 20827218]
48. Steward WT, Remien RH, Higgins JA, Dubrow R, Pinkerton SD, Sikkema KJ, et al. Behavior change following diagnosis with acute/early HIV infection-a move to serosorting with other HIV-infected individuals. The NIMH Multisite Acute HIV Infection Study: III. AIDS Behav. 2009; 13:1054–1060. [PubMed: 19504178]
49. Marks G, Crepaz N, Senterfitt JW, Janssen RS. Meta-analysis of high-risk sexual behavior in persons aware and unaware they are infected with HIV in the United States: implications for HIV prevention programs. J Acquir Immune Defic Syndr. 2005; 39:446–453. [PubMed: 16010168]
50. Schacker T, Collier AC, Hughes J, Shea T, Corey L. Clinical and epidemiologic features of primary HIV infection. Ann Intern Med. 1996; 125:257–264. [PubMed: 8678387]
51. Daar ES, Little S, Pitt J, Santangelo J, Ho P, Harawa N, et al. Diagnosis of primary HIV- 1 infection. Los Angeles County Primary HIV Infection Recruitment Network. Ann Intern Med. 2001; 134:25–29. [PubMed: 11187417]

52. Bozzette SA, Joyce G, McCaffrey DF, Leibowitz AA, Morton SC, Berry SH, et al. Expenditures for the care of HIV-infected patients in the era of highly active antiretroviral therapy. N Engl J Med. 2001; 344:817–823. [PubMed: 11248159]
53. Schackman BR, Gebo KA, Walensky RP, Losina E, Muccio T, Sax PE, et al. The lifetime cost of current human immunodeficiency virus care in the United States. Med Care. 2006; 44:990–997. [PubMed: 17063130]
54. Barnett PG, Chow A, Joyce VR, Bayoumi AM, Griffin SC, Nosyk B, et al. Determinants of the Cost of Health Services Used by Veterans With HIV. Med Care. 2011
55. Gebo KA, Chaisson RE, Folkemer JG, Bartlett JG, Moore RD. Costs of HIV medical care in the era of highly active antiretroviral therapy. AIDS. 1999; 13:963–969. [PubMed: 10371178]
56. Hutchinson AB, Farnham PG, Dean HD, Ekwueme DU, del Rio C, Kamimoto L, et al. The economic burden of HIV in the United States in the era of highly active antiretroviral therapy: evidence of continuing racial and ethnic differences. J Acquir Immune Defic Syndr. 2006; 43:451–457. [PubMed: 16980906]
57. Meara E, White C, Cutler DM. Trends in medical spending by age, 1963–2000. Health Aff (Millwood). 2004; 23:176–183. [PubMed: 15318578]
58. Thomson, PDR. Red Book: Pharmacy's Fundamental Reference. Montvale, NJ: Thomson PDR; 2010.
59. Centers for Medicare & Medicaid Services. Medicare Information for Providers, Partners and Health Care Professionals. 2010 Accessed at http://www.cms.gov/home/medicare.asp on 8 March 2011.
60. Farnham PG, Hutchinson AB, Sansom SL, Branson BM. Comparing the costs of HIV screening strategies and technologies in health-care settings. Public Health Rep. 2008; 1233(Suppl):51–62. [PubMed: 19166089]
61. Paltiel AD, Walensky RP, Schackman BR, Seage GR 3rd, Mercincavage LM, Weinstein MC, et al. Expanded HIV screening in the United States: effect on clinical outcomes, HIV transmission, and costs. Ann Intern Med. 2006; 145:797–806. [PubMed: 17146064]
62. Centers for Disease Control and Prevention (CDC). Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. MMWR Recomm Rep. 2006; 55:1–17.
63. Hammer SM, Eron JJ Jr, Reiss P, Schooley RT, Thompson MA, Walmsley S, et al. Antiretroviral treatment of adult HIV infection: 2008 recommendations of the International AIDS Society-USA panel. JAMA. 2008; 300:555–570. [PubMed: 18677028]
64. U.S. Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. 2011. Accessed at http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf on 11 May 2011
65. Myers GM, Mayer KH. Oral preexposure anti-HIV prophylaxis for high-risk U.S. populations: current considerations in light of new findings. AIDS Patient Care STDS. 2011; 25:63–71. [PubMed: 21284497]
66. Golub SA, Operario D, Gorbach PM. Pre-exposure prophylaxis state of the science: empirical analogies for research and implementation. Curr HIV/AIDS Rep. 2010; 7:201–209. [PubMed: 20809218]
67. Golub SA, Kowalczyk W, Weinberger CL, Parsons JT. Preexposure prophylaxis and predicted condom use among high-risk men who have sex with men. J Acquir Immune Defic Syndr. 2010; 54:548–555. [PubMed: 20512046]
68. Barash EA, Golden M. Awareness and use of HIV pre-exposure prophylaxis among attendees of a seattle gay pride event and sexually transmitted disease clinic. AIDS Patient Care STDS. 2010; 24:689–691. [PubMed: 20863247]
69. Mimiaga MJ, Case P, Johnson CV, Safren SA, Mayer KH. Preexposure antiretroviral prophylaxis attitudes in high-risk Boston area men who report having sex with men: limited knowledge and experience but potential for increased utilization after education. J Acquir Immune Defic Syndr. 2009; 50:77–83. [PubMed: 19295337]

70. Liu AY, Kittredge PV, Vittinghoff E, Raymond HF, Ahrens K, Matheson T, et al. Limited knowledge and use of HIV post- and pre-exposure prophylaxis among gay and bisexual men. J Acquir Immune Defic Syndr. 2008; 47:241–247. [PubMed: 18340656]
71. Honiden S, Sundaram V, Nease RF, Holodniy M, Lazzeroni LC, Zolopa A, et al. The effect of diagnosis with HIV infection on health-related quality of Life. Qual Life Res. 2006; 15:69–82. [PubMed: 16411032]
72. Centers for Disease Control and Prevention (CDC). CDC Trial and Another Major Study Find PrEP Can Reduce Risk of HIV Infection among Heterosexuals. 2011 Accessed at http://cdc.gov/nchhstp/newsroom/PrEPHeterosexuals.html on 14 July 2011.
73. Owens DK, Qaseem A, Chou R, Shekelle P. High-value, cost-conscious health care: concepts for clinicians to evaluate the benefits, harms, and costs of medical interventions. Ann Intern Med. 2011; 154:174–180. [PubMed: 21282697]
74. Alistar SS, Owens DK, Brandeau ML. Effectiveness and cost effectiveness of expanding harm reduction and antiretroviral therapy in a mixed HIV epidemic: a modeling analysis for Ukraine. PLoS Med. 2011; 8:e1000423. [PubMed: 21390264]
75. Kaplan EH. Economic analysis of needle exchange. AIDS. 1995; 9:1113–1119. [PubMed: 8519446]
76. CensusScope. United States Age Distribution. 2000. Accessed at http://www.censusscope.org/us/chart_age.html on 30 September 2009
77. Fryback DG, Dasbach EJ, Klein R, Klein BE, Dorn N, Peterson K, et al. The Beaver Dam Health Outcomes Study: initial catalog of health-state quality factors. Med Decis Making. 1993; 13:89–102. [PubMed: 8483408]
78. Bollinger RC, Brookmeyer RS, Mehendale SM, Paranjape RS, Shepherd ME, Gadkari DA, et al. Risk factors and clinical presentation of acute primary HIV infection in India. JAMA. 1997; 278:2085–2089. [PubMed: 9403423]
79. Khazeni N, Hutton DW, Garber AM, Hupert N, Owens DK. Effectiveness and cost-effectiveness of vaccination against pandemic influenza (H1N1) 2009. Ann Intern Med. 2009; 151:829–839. [PubMed: 20008759]
80. Turner DA, Wailoo AJ, Cooper NJ, Sutton AJ, Abrams KR, Nicholson KG. The cost-effectiveness of influenza vaccination of healthy adults 50–64 years of age. Vaccine. 2006; 24:1035–1043. [PubMed: 16183177]
81. O'Brien BJ, Goeree R, Blackhouse G, Smieja M, Loeb M. Oseltamivir for treatment of influenza in healthy adults: pooled trial evidence and cost-effectiveness model for Canada. Value Health. 2003; 6:116–125. [PubMed: 12641862]
82. Neuner JM, Hamel MB, Phillips RS, Bona K, Aronson MD. Diagnosis and management of adults with pharyngitis. A cost-effectiveness analysis. Ann Intern Med. 2003; 139:113–122. [PubMed: 12859161]
83. Holtgrave DR, Pinkerton SD. Updates of cost of illness and quality of life estimates for use in economic evaluations of HIV prevention programs. J Acquir Immune Defic Syndr Hum Retrovirol. 1997; 16:54–62. [PubMed: 9377126]
84. Tengs TO, Lin TH. A meta-analysis of utility estimates for HIV/AIDS. Med Decis Making. 2002; 22:475–481. [PubMed: 12458977]
85. Nyman JA, Barleen NA, Dowd BE, Russell DW, Coons SJ, Sullivan PW. Quality-of-life weights for the US population: self-reported health status and priority health conditions, by demographic characteristics. Med Care. 2007; 45:618–628. [PubMed: 17571010]
86. Sullivan PW, Ghushchyan V. Preference-Based EQ-5D index scores for chronic conditions in the United States. Med Decis Making. 2006; 26:410–420. [PubMed: 16855129]
87. Long EF, Brandeau ML, Galvin CM, Vinichenko T, Tole SP, Schwartz A, et al. Effectiveness and cost-effectiveness of strategies to expand antiretroviral therapy in St. Petersburg, Russia. AIDS. 2006; 20:2207–2215. [PubMed: 17086061]
88. Owens DK, Nease RF Jr, Harris RA. Cost-effectiveness of HIV screening in acute care settings. Arch Intern Med. 1996; 156:394–404. [PubMed: 8607724]

89. Mylonakis E, Paliou M, Lally M, Flanigan TP, Rich JD. Laboratory testing for infection with the human immunodeficiency virus: established and novel approaches. Am J Med. 2000; 109:568–576. [PubMed: 11063959]

90. Greenwald JL, Burstein GR, Pincus J, Branson B. A rapid review of rapid HIV antibody tests. Curr Infect Dis Rep. 2006; 8:125–131. [PubMed: 16524549]

91. Paltiel AD, Weinstein MC, Kimmel AD, Seage GR 3rd, Losina E, Zhang H, et al. Expanded screening for HIV in the United States--an analysis of cost-effectiveness. N Engl J Med. 2005; 352:586–595. [PubMed: 15703423]

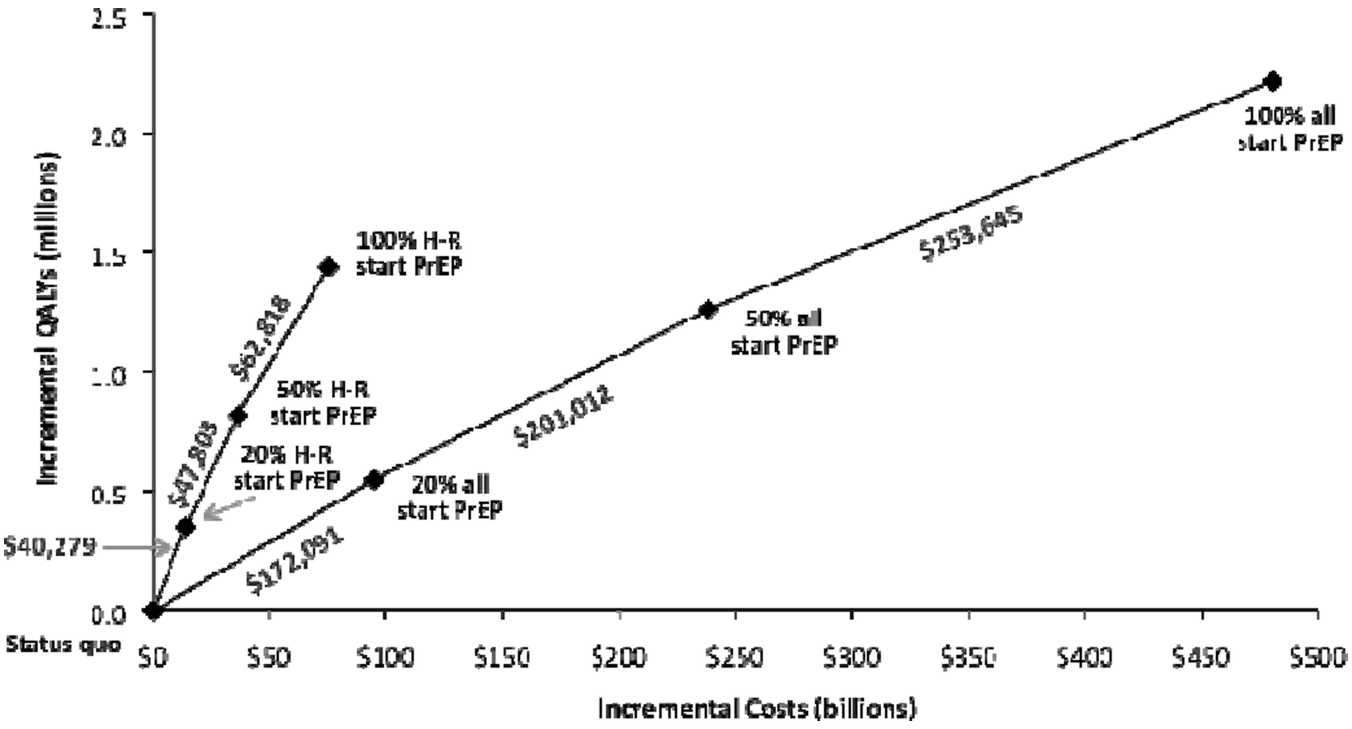

Figure 1. Cost-Effectiveness of PrEP for HIV Prevention

Incremental costs and quality-adjusted life years (QALYs) are plotted for each PrEP use scenario in the general MSM population and in high-risk MSM, with the origin corresponding to the status quo of no PrEP. The lines show the incremental cost-effectiveness ratio relative to the next lower level of PrEP use (the preceding scenario with a lower percentage of MSM starting PrEP). Under each PrEP use scenario, individuals initiate PrEP immediately and remain on PrEP for the 20-year time horizon or until they turn 65. PrEP is assumed to be 44% effective and cost $10,083 per year, inclusive of monitoring costs. Incremental costs and QALYs are calculated over a 20-year time horizon and are discounted to the present at 3% annually.

Note: H–R = high-risk, PrEP = preexposure prophylaxis, MSM = men who have sex with men.

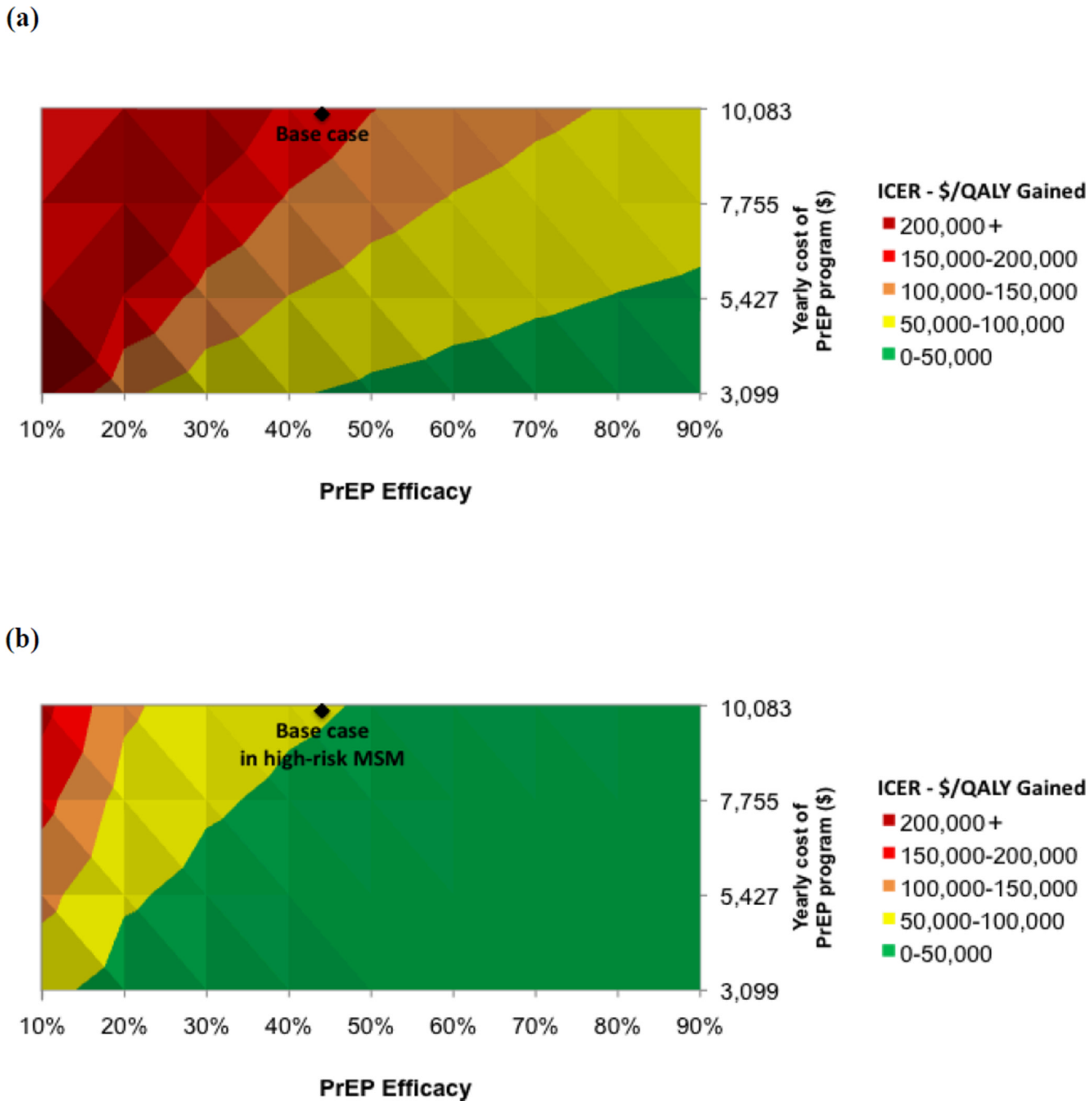

Figure 2. Cost-Effectiveness of PrEP for HIV Prevention as a Function of PrEP Efficacy and Cost

(a) This two-way sensitivity analysis shows ranges of the incremental cost-effectiveness ratio for initiating 20% of the general MSM population on PrEP as a function of PrEP efficacy and cost. Costs depicted on the vertical axis are annual and include all ARV and monitoring costs. The horizontal axis denotes PrEP efficacy, measured as the percentage reduction in the probability of an uninfected individual acquiring HIV infection from an infected individual. The color at each point signifies the incremental cost-effectiveness ratio for that PrEP efficacy and cost. For example, the incremental cost-effectiveness ratio is less than $100,000/quality-adjusted life year (QALY) gained when PrEP efficacy is greater than

75% or when efficacy is at least 40% and costs are less than $5,427 per year. Incremental costs and QALYs used to calculate the incremental cost-effectiveness ratios are calculated over a 20-year time horizon and are discounted to the present at 3% annually.
(b) This two-way sensitivity analysis shows ranges of the incremental cost-effectiveness ratio for initiating all high-risk MSM on PrEP as a function of PrEP efficacy and cost. Costs depicted on the vertical axis are annual and include all ARV and monitoring costs. The horizontal axis denotes PrEP efficacy, measured as the percentage reduction in the probability of an uninfected individual acquiring HIV infection from an infected individual. The color at each point signifies the incremental cost-effectiveness ratio for that PrEP efficacy and cost. For example, at our base-case cost, the incremental cost-effectiveness ratio is less than $100,000/QALY gained as long as PrEP efficacy is greater than 22%. Incremental costs and QALYs used to calculate the incremental cost-effectiveness ratios are calculated over a 20-year time horizon and are discounted to the present at 3% annually.
Note: PrEP = preexposure prophylaxis, MSM = men who have sex with men, ICER = incremental cost-effectiveness ratio.

Table 1

Summary of Key Model Parameters

Parameter*	Value	Range	Source
Demographic Parameters			
Total MSM population age 13–64	4,343,741	2.2–7.5 million	Calculated (9, 10)
HIV prevalence in MSM	12.3%	1–20%	Calculated (9–12)
Male mortality rate	0.0043	0.003–0.005	Calculated (13)
Disease Parameters			
Average disease duration (years)			
Acute HIV	0.25	0.08–0.40	(14–18)
Asymptomatic HIV	7	6–10	(19–22)
Symptomatic HIV	3	1–4	(19–22)
Symptomatic HIV – Treated with ART	18	12–30	(19, 22–24)
AIDS	2	1–3	(19–22)
AIDS – Treated with ART	5	2–15	(19, 22–24)
Sexual Behavior Parameters			
Annual transmission probability per MSM partnership ($M_{HIV+} \rightarrow M_{HIV-}$)			
Acute HIV	0.210	0.10–0.40	(25–27)
Asymptomatic HIV	0.039	0.02–0.08	(19, 25–27)
Symptomatic HIV	0.039	0.02–0.08	(19, 25–27)
AIDS	0.160	0.08–0.30	(1925–27)
Annual number of male partners	3.0	2.0–5.0	(1928–30)
Condom usage with male partners	40%	30–60%	(1931–34)
Treatment Parameters			
Fraction who know HIV status starting ART at CD4=0.350 × 10^9 cells/L	50%	25–75%	Estimated (19, 22, 35, 36)
Rate of initiating ART at CD4<0.350 × 10^9 cells/L	0.05	0–0.10	Estimated (19, 22, 35)
Reduction in sexual infectivity due to ART	90%	50–99%	(19, 22, 26, 35, 37–44)
Screening Parameters			
Fraction of population tested annually	67%	30–90%	(28, 45, 46)
Reduction in sexual behavior (number of male partners) due to testing and counseling	20%	0–50%	(19, 35, 47–49)
PrEP Parameters			
Reduction in risk of infection due to PrEP	44%	10–92%	(3)
Time on PrEP (years)	20	1–20	Assumed
Change in number of male partners due to PrEP	0%	−20%−20%	Assumed
Change in condom usage with male partners due to PrEP	0%	−20%−20%	Assumed
Cost Parameters (2010 US $)			
Annual HIV-related healthcare costs			
Acute HIV	30	10–500	Calculated (7, 15, 50, 51)
Asymptomatic HIV – Untreated	4,130	3,000–6,000	(19, 52–54)
Symptomatic HIV – Untreated	6,934	5,000–9,000	(19, 52–54)
Symptomatic HIV – Treated with ART (excludes ART costs)	6,181	5,000–7,000	(19, 52–54)

Parameter*	Value	Range	Source
AIDS – Untreated	21,863	15,000–26,000	(19, 52–56)
AIDS – Treated with ART (excludes ART costs)	9,950	6,000–17,000	(19, 35, 53, 54)
Annual non-HIV-related healthcare costs for uninfected and infected individuals	4,061	3,000–6,000	(57)
Annual cost of ART	15,589	12,500–19,000	(19, 35, 53, 56)
Cost of PrEP			
TDF/FTC (30 day supply)	776	300–1,118	(5, 58)
STI testing	54	25–75	(59)
Blood urea nitrogen and serum creatinine testing	23	10–40	(59)
Physician visit	100	10–200	(59)
Cost of HIV testing – Antibody test			
Uninfected	13	5–25	(59)
HIV-infected	66	50–100	(59)
Cost of counseling			
Pre-test counseling	13	0–100	(60, 61)
Post-test counseling for HIV-negative persons	7	0–50	(60, 61)
Post-test linkage/counseling for HIV-positive persons	14	0–100	(60, 61)
Cost of HIV diagnosis	491	125–1,200	(59)
Annual Discount Rate	3%	0–5%	(8)

*All rates are annual. MSM = men who have sex with men, ART = antiretroviral treatment, M_{HIV+} = HIV-positive male, M_{HIV-} = HIV-negative male, PrEP = preexposure prophylaxis, TDF/FTC = tenofovir and emtricitabine, STI = sexually transmitted infection.

Table 2

Benefits and Costs of PrEP Strategies Over 20 Years – General MSM Population

Strategy[*]	New HIV Infections[¶]	HIV Infections Prevented[†]	HIV Prevalence at 20 Years	Total Costs of PrEP (billions) [¥#]	Total Costs (billions)[¥]	Total QALYs[¥]	Incremental Costs[¥‡] (billions)	Incremental QALYs[¥‡]	ICER Relative to[§]	
									No PrEP	Next Lower Level of PrEP
100% Start PrEP	242,627	249,156 (51%)	6.4%	$495	$1,366	117,488,043	$480	2,217,732	$216,480	$253,645
50% Start PrEP	348,492	143,291 (29%)	7.9%	$247	$1,124	116,533,983	$238	1,263,673	$188,421	$201,012
20% Start PrEP	429,025	62,759 (13%)	9.0%	$98	$980	115,820,477	$95	550,166	$172,091	$172,091
Status Quo (No PrEP)	491,784		9.9%		$886	115,270,310				

[*] PrEP = preexposure prophylaxis.

[¶] New HIV infections and HIV infections prevented are undiscounted totals. Discounting infections at 3% annually reduces the number of infections averted for each strategy by approximately 22%.

[†] The values in parentheses are the fraction of total HIV infections prevented.

[¥] Costs and quality-adjusted life years (QALYs) are net present values (3% annual discount rate) over 20 years.

[#] Total costs of PrEP include the cost of antiretroviral drugs for PrEP, costs of monitoring tests and physician visits, and initiation and discontinuation costs.

[‡] Incremental costs and QALYs are relative to the status quo.

[§] ICER = Incremental cost-effectiveness ratio, relative to the status quo of no PrEP use or the next lower level of PrEP use (i.e., the PrEP use scenario in the row below, with a lower percentage of MSM starting PrEP).

Ann Intern Med. Author manuscript; available in PMC 2013 June 24.

Table 3

Benefits and Costs of PrEP Strategies Over 20 Years – High-Risk MSM

Strategy*	New HIV Infections¶	HIV Infections Prevented†	HIV Prevalence at 20 Years	Total Costs of PrEP (billions) ¥#	Total Costs (billions)¥	Total QALYs¥	Incremental Costs¥‡ (billions)	Incremental QALYs¥‡	ICER Relative to§	
									No PrEP	Next Lower Level of PrEP
100% of High-Risk Start PrEP	155,728	167,143 (52%)	17%	$85	$272	21,628,307	$75	1,439,261	$52,443	$62,818
50% of High-Risk Start PrEP	227,686	95,185 (29%)	23%	$42	$233	21,006,700	$36	817,655	$44,556	$47,803
20% of High-Risk Start PrEP	281,809	41,061 (13%)	28%	$17	$210	20,541,886	$14	352,840	$40,279	$40,279
Status Quo (No PrEP)	322,871		31%		$196	20,189,046				

*PrEP = preexposure prophylaxis. These strategies do not include any benefits to low-risk MSM, since we did not model mixing between high- and low-risk MSM in the high-risk analysis.

¶New HIV infections and HIV infections prevented are undiscounted totals. Discounting infections at 3% annually reduces the number of infections averted for each strategy by approximately 24%.

†The values in parentheses are the fraction of total HIV infections prevented.

¥Costs and quality-adjusted life years (QALYs) are net present values (3% annual discount rate) over 20 years.

#Total costs of PrEP include the cost of antiretroviral drugs for PrEP, costs of monitoring tests and physician visits, and initiation and discontinuation costs.

‡Incremental costs and QALYs are relative to the status quo.

§ICER = Incremental cost-effectiveness ratio, relative to the status quo of no PrEP use or the next lower level of PrEP use (i.e., the PrEP use scenario in the row below, with a lower percentage of MSM starting PrEP).