The cost-effectiveness of screening men who have sex with men for rectal chlamydial and gonococcal infection to prevent human immunodeficiency virus (HIV) infection: Supplemental appendix

1. The model

The population is divided into four groups, S, $\hat{S}$, I, and $\hat{I}$, where S denotes those susceptible to rectal CT/GC infection and I denotes those with rectal CT/GC infection and the hat (^) indicates those with HIV:

S = Number of people with no rectal CT/GC infection, without HIV,

$\hat{S}$ = Number of people with no rectal CT/GC infection, with HIV,

I = Number of people with rectal CT/GC infection, without HIV,

$\hat{I}$ = Number of people with rectal CT/GC infection, with HIV.

Transition from one group to another is calculated using the following difference equations:

$$S_{t+1} = S_t - S_t\lambda_{HIV}\Omega_{HIV} - S_t\lambda_{STD}\Omega_{STD} + I_t r,$$

$$I_{t+1} = I_t - I_t r - I_t\theta\lambda_{HIV}\Omega_{HIV} + S_t\lambda_{STD}\Omega_{STD,}$$

$$\hat{S}_{t+1} = \hat{S}_t - \hat{S}_t\hat{\lambda}_{STD}\Omega_{STD} + S_t\lambda_{HIV}\Omega_{HIV} + \hat{I}_t\hat{r},$$

$$\hat{I}_{t+1} = \hat{I}_t - \hat{I}_t\hat{r} + I_t\theta\lambda_{HIV}\Omega_{HIV} + \hat{S}_t\hat{\lambda}_{STD}\Omega_{STD,}$$

where λ_{HIV} denotes HIV incidence in those without rectal CT/GC infection; λ_{STD} and $\hat{\lambda}_{STD}$ denote rectal STD incidence rates among those without and with HIV, respectively; Ω_{HIV} and Ω_{STD} are adjustment factors to account for dynamic changes in HIV and CT/GC prevalence over time; θ represents the increased rate of HIV incidence among those with rectal CT/GC; and r and $\hat{r}$ represent the clearance rate of rectal CT/GC among those without and with HIV, respectively. More details are provided below.

Closed population

In all of the results we present in the manuscript, there was no entry or exit from the model over the 10-year period (a closed population). In exploratory analyses, we found that the cost-effectiveness of screening was slightly more favorable when we allowed entry and exit, although the difference was limited.

Weekly calculations

Time cycles were one week in length, and the impact of rectal CT/GC screening was modeled over 10 years (520 cycles). Weeks are denoted by t; thus the equations above describe how the distribution across the four infection classes changes from one week to the next. Annual rates presented in the text were converted to weekly rates as shown in Appendix Table 1. The incidence rate of rectal CT/GC infection is $\lambda_{STD}\Omega_{STD}$ and $\hat{\lambda}_{STD}\Omega_{STD}$ among those without and with HIV, respectively, where λ_{STD} and $\hat{\lambda}_{STD}$ are the incidence rates of rectal CT/GC infection at the onset of the screening program among those without and with HIV, respectively, and Ω_{STD} is an adjustment factor to account for changes in the prevalence of CT/GC in sex partners over time as a result of the screening program. The clearance rate (r) of rectal CT/GC infection is a function of two factors: duration of infection and screening rates. The HIV incidence rate among those without rectal CT/GC infection is $\lambda_{HIV}\Omega_{HIV}$, where λ_{HIV} is the HIV incidence at the onset of the screening program and Ω_{HIV} is an adjustment factor to account for changes in the prevalence of HIV in sex partners over time. The rate of HIV incidence among those with rectal CT/GC infection was assumed to be θ times that of those without rectal CT/GC infection.

The adjustment factors (Ω_{STD} and Ω_{HIV})

Our model inputs reflect averages for all MSM, stratified only by HIV status and rectal CT/GC status. We used average HIV incidence rates and average rectal CT/GC incidence rates so that we did not have to classify men according to their sexual practices (e.g., receptive only, insertive only, both, or neither) or their number of sex partners. However, in the dynamic version of the model, we implicitly assumed that treating any given man (Man X) for rectal CT/GC could interrupt transmission of CT/GC from Man X to insertive partners of Man X, but not from Man X to receptive partners of Man X. Thus, treatment of rectal CT/GC could lead to reductions in genital CT/GC among the sex partners of those treated, which in turn could lead to

reductions in rectal CT/GC among the partners' partners, and so on. To incorporate these transmission dynamics in our model without distinguishing between insertive and receptive sex partners, the rate of acquisition of rectal CT/GC was multiplied by an adjustment factor (Ω_{STD}) to account for changes in the prevalence of genital CT/GC in the population over time. The reduction in prevalence of genital CT/GC as a result of rectal CT/GC screening was a function of the reduction in prevalence of rectal CT/GC. Specifically, the adjustment factor in week t+1 was calculated as $(STD\_Prev\_Screen_t/STD\_Prev\_NoScreen_t)^{\alpha}$, where $STD\_Prev\_Screen_t$ is rectal CT/GC prevalence at week t in the scenario of rectal screening and $STD\_Prev\_NoScreen_t$ is rectal CT/GC prevalence at week t in the scenario of no rectal screening. This ratio was raised to the power of α ($\alpha = 0.5$), because rectal CT/GC screening was assumed to have less of an impact on genital CT/GC prevalence than on rectal CT/GC prevalence. That is, rectal CT/GC screening would likely have more of an impact on rectal CT/GC among those screened than on genital CT/GC among the partners of those screened, just as female-only STD screening might have less of an impact on male STD prevalence than on female STD prevalence.

The clearance rate (r)

The clearance rate of rectal CT/GC infection (denoted by r for those without HIV and by $\hat{r}$ among those with HIV) was a function of two factors: duration of infection and screening rates. Specifically, we set the clearance rate equal to $(1/d) + \sigma$, where d is duration of infection and σ is the annual screening rate in those without HIV ($\hat{\sigma}$ for those with HIV). The screening rate was 0 in the scenario of no rectal CT/GC screening. In the scenario of rectal CT/GC screening, the screening rate was 0.37 among MSM without HIV and 0.58 among MSM with HIV (see the section "Estimated screening rates and numbers of MSM screened" for more details). By incorporating screening in this manner, we implicitly assumed that all rectal CT/GC infections detected through screening would be treated successfully, immediately upon infection.

Dynamic and static versions of model

We estimated two model versions; a static version and a dynamic version. The static version included benefits of rectal CT/GC screening only to those who are screened, whereas the dynamic version included benefits of rectal CT/GC screening to those who are screened, their

partners, their partners' partners, and so on. In the dynamic version, the adjustment factors (Ω_{STD} and Ω_{HIV}) were used to account for changes in the prevalence of CT/GC and HIV, respectively, in sex partners over time as a result of rectal CT/GC screening. In the static version of the model, these adjustment terms were set to 1.

Dynamic version of model: an example

For example, in week 52 of the dynamic model, rectal CT/GC prevalence was 3.26%. The model suggested that in the absence of screening, rectal CT/GC prevalence would have been 4.54% in week 52. The term ($STD\_Prev\_Screen_t/STD\_Prev\_NoScreen_t$) was calculated as 3.26/4.54 = 0.7187, suggesting that because of screening, rectal CT/GC prevalence with the screening program is 0.7187 times what it would have been in the absence of screening. Given that the prevalence of rectal CT/GC infection decreases as a result of screening, we would expect that the prevalence of genital CT/GC would decrease among sex partners of MSM at risk for rectal CT/GC infection. To estimate the reduction of genital CT/GC prevalence as a result of the screening program for rectal CT/GC infection, the term 0.7187 described above was raised to the power of 0.5, which yielded 0.8478. Thus, in week 52 in the model, the incidence of rectal CT/GC infection was multiplied by 0.8478 to reflect the reduction in CT/GC in sex partners of MSM at risk for rectal CT/GC infection. So, in other words, prevalence of rectal CT/GC was reduced by about 28% in week 52 of the screening program (from 4.54% to 3.26%). The reduction in prevalence of genital CT/GC was estimated to be about 15%, or 1-0.8478. Thus the incidence of rectal CT/GC infection was reduced in week 53 by about 15% to account for the reduction in genital CT/GC in the population.

2. Details of model parameters

HIV incidence among those with and without rectal CT/GC infection

HIV incidence among MSM without rectal CT/GC infection was based on HIV incidence rates reported by the San Francisco Department of Public Health (SFDPH), as follows. As described later, rectal CT/GC prevalence among MSM without HIV was 3.1% in the base case. HIV incidence among MSM with rectal CT/GC infection was assumed to be 2.36%, calculated as the average HIV incidence among men with 0, 1, and 2 prior rectal infections in the previous 2 years [Bernstein 2010]. That is, among men with rectal CT/GC, HIV incidence was 1.80 among

the 445 men with no prior rectal infections, 3.41 among 83 men with 1 prior rectal infection, and 15.00 among the 13 men with 2 prior rectal infections. We applied the weighted average of 2.36% rather than the overall average of 2.25% for two main reasons. First, the overall average of 2.25 seroconversions per person-year reported by Bernstein and colleagues was based on the total number of seroconversions and the total number of person-years at risk. The average number of person-years at risk was lower for the higher risk men, and the 2.36% weighted average risk we applied is an approximation of the average number of seroconversions per person year that might have been observed in the Bernstein 2010 study if the average time of follow-up (number of person-years observed per study participant) were more consistent across men with 0, 1 and 2 prior infections. Second, we did not directly model the number of prior rectal infections, and applying the weighted average HIV incidence rate across men with 0, 1, and 2 prior infections allowed us to account for the potential impact of prior rectal infections.

HIV incidence overall was 1.27% according to the SFDPH surveillance report. HIV incidence among those without rectal GC was calculated as [0.0127 - (0.031*0.0236)]/(1-0.031) = 0.0124. This estimate (1.24%) for HIV incidence among MSM without rectal CT/GC infection is consistent with unpublished SFDPH data on HIV incidence among MSM without rectal CT/GC infection.

The relative risk of acquiring HIV among those with rectal CT/GC infection was 1.9 (0.0236/0.0124) in the base case, with a lower bound of 1.2 (0.0149/0.0124) and an upper bound of 2.6 (0.0326/0.0124). That is, for the base case, the relative risk was calculated as the HIV incidence among MSM with rectal CT/GC infection (2.36%) divided by the HIV incidence among those without rectal CT/GC infection (1.24%). For the lower and upper bounds, the numerators (0.0149 and 0.0326) are from the 95% confidence interval of HIV incidence among those with rectal CT/GC infection from the 2010 Bernstein paper.

Calculation of incidence of rectal CT/GC infection

Incidence rates were approximated as prevalence rates divided by duration. Prevalence rates of 3.1% and 9.7% were estimated for MSM without and with HIV, based on 462 and 676 cases of rectal CT/GC infection detected (SFDPH, unpublished data), respectively, among about

15,131 and 6,984 men screened, respectively (see below for screening assumptions). These estimated case numbers for rectal CT/GC infection reflect the assumption that rectal CT/GC cases for which HIV status was unknown were distributed in the same proportion as the known cases (SFDPH, unpublished data).

Lower and upper bound values of the number of rectal CT/GC cases detected among MSM without HIV were calculated assuming that 0% and 100%, respectively, of the cases of rectal CT/GC for which HIV status was unknown occurred among MSM without HIV. Lower and upper bound values of the number of rectal CT/GC cases detected among MSM with HIV were calculated in an analogous manner. The resulting prevalence rates from these lower and upper bound values were used to calculate the lower and upper bound incidence rates of rectal CT/GC.

Estimated screening rates and numbers of MSM screened

The estimated numbers of MSM screened reflect the assumption that 31% of MSM without HIV and 44% of MSM with HIV are screened each year. This assumption is based on STOP AIDS Behavioral Risk Assessments, San Francisco 2010 (personal communication, Jennifer Hecht to Kyle Bernstein, February 15, 2012) in which 31% of MSM without HIV and 44% of MSM with HIV report having been screened in the past six months. Although the survey assessed self-reported screening in the past six months, we assumed these responses would more accurately reflect annual screening participation because self-reported preventive screening rates can substantially exceed actual screening rates [Insinga 2004], and because misconceptions about STD testing (such as the belief that STD testing was included in a health care encounter when it was not) [Royer 2012, Ogbechie 2012] can lead to over-estimation of one's utilization of STD testing. Because of this uncertainty in screening rates, screening rates (and the incidence rates of rectal CT/GC, which are calculated based on screening rates as described above) were varied in the sensitivity analyses. These annual probabilities of screening of 31% and 44% for MSM without and with HIV correspond to annual rates of screening of 0.37 and 0.58.

Costs

For the discounted, lifetime cost per case of HIV, we applied the average of two estimates: $236,000 [Hutchinson et al. (2006), updated to 2011 dollars] and $391,000 [Schackman et al.

(2006), updated to 2011 dollars]. Of note, the Schackman estimate we applied was the lifetime cost discounted to time of infection, not the lifetime cost discounted to time of onset of treatment.

Screening costs were calculated as the cost of the screening visit plus the cost of the test. The cost of a screening visit was estimated at $9.66 (low) and $40.98 (high) in 2011 dollars, based on Begley et al. (1989) as described in Appendix Table 2. We applied a test cost of $15.45 in 2011 dollars (Steece 2008), which includes our addition of courier costs of about $2 per test. For the total cost per screen, we calculated a baseline estimate of $40.77 (range $25.11 - $56.43). This range was obtained by adding the $15.45 test cost to the low and high screening visit costs ($9.66 and $40.98, respectively). The baseline estimate was taken as the midpoint of the range. The screening costs we applied are appropriate for a societal or health care system analysis. A payer-perspective analysis would need to account for the possibility of higher testing costs. In the analysis, we applied rounded estimate of $41 (range: $25 - $56).

Treatment costs were calculated as the cost of the treatment visit plus the cost of the drugs. The treatment visit costs ranged from a low of $3.81 (pharmacist cost only) to $34.46 (treatment visit + contact letter + pharmacist cost). The drug costs were $15.43 for chlamydia and $31.79 for dual treatment of chlamydia and gonorrhea (Thompson Healthcare 2008). For chlamydia, we added the drug cost to the low and high treatment visit costs estimates for a total treatment cost of $19.24 to $49.89 (midpoint: $34.57). For dual treatment of chlamydia and gonorrhea, we added the drug cost of $31.79 to the high treatment visit cost of $34.46 for a total cost of $66.25. The cost of treatment we applied in our analysis was the average of the chlamydia treatment cost and the dual treatment cost: $50 (range: $43 - $58).

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Appendix Table 1: Summary of model parameters

Parameter	Symbol	Annual value	Weekly value	Source
Incidence of rectal CT/GC among those without HIV	λ_{STD}	0.041	0.000788	See text*
Incidence of rectal CT/GC among those with HIV	$\hat{\lambda}_{STD}$	0.129	0.002481	See text*
Duration of infection	d	0.75 years	39 weeks	Althaus 2012, Althaus 2010
Rate of screening (MSM without HIV)	σ	0.37	0.007115	Assumed
Rate of screening (MSM with HIV)	$\hat{\sigma}$	0.58	0.011154	
Incidence of HIV among those without rectal CT/GC	λ_{HIV}	0.0124	0.000238	SFDPH
Rate of recovery from rectal CT/GC infection	r			
Scenario of rectal CT/GC screening (men without HIV)		1.703333333	0.032756	Calculated**
Scenario of rectal CT/GC screening (men with HIV)		1.913333333	0.036795	Calculated**
Scenario of no rectal CT/GC screening (all men)		1.333333333	0.025641	Calculated**
Relative risk of acquiring HIV in MSM with rectal CT/GC (vs. MSM without rectal CT/GC)	θ	1.9	1.9	Bernstein 2010 SFDPH***

SFDPH: San Francisco Department of Public Health

*See the appendix section "Calculation of incidence of rectal CT/GC" for details; this information is also summarized in the footnotes of Table 1 of the main manuscript. **See the appendix section "The clearance rate (r)" for details.

*** See the appendix section "HIV incidence among those with and without rectal CT/GC" for details.

Appendix Table 2: Calculation of screening visit costs

Item estimated	Cost Estimate (1987 dollars)	Source/Notes
Screening visit costs, low scenario		
Family planning lab costs	$2,158.20	Begley Table 2
Family planning screening visits	327	Begley Table 4
Family planning lab cost per screening visit	$6.60	Calculated as lab costs divided by screening visits
Total cost of family planning screening visit	$9.74	Begley Table 4
Non-lab cost of family planning screening visit	$3.14	Calculated as total cost minus lab cost
Screening visit costs, high scenario		
Lab costs of drop-in diagnostic visit	$244.20	Begley Table 2
Number of drop-in diagnostic visits	37	Begley Table 4
Lab cost per drop-in diagnostic visit	$6.60	Calculated as lab costs divided by screening visits
Total cost of drop-in diagnostic visit	$19.92	Begley Table 4
Non-lab cost of drop-in diagnostic visit	$13.32	Calculated as total cost minus lab cost

In order to describe how these costs were obtained from the Begley paper, these costs are shown as they appear in the Begley paper without adjustment for inflation. For use in the analysis, these costs were updated to 2011 dollars, under the assumption that the Begley costs were in 1987 dollars (the year of the data collection in the Begley study). That is, the $3.14 and $13.32 estimates shown above in 1987 dollars were adjusted to $9.66 and $40.98 in 2011 dollars.