An Interactive Modeling Tool for Projecting the Health and Cost Impact of Changes in the Sexually Transmitted Diseases Prevention Program Budgets

Appendix 2: Model Details

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Overview

In this appendix, we elaborate on the calculations underlying the six steps described in the manuscript. We also provide more information on the confidence intervals, Here, our description of the SPACE Monkey 2.0 calculations of the impact of a change in sexually transmitted infection (STI) prevention funding focuses on estimates for gonorrhea incidence. Estimates of the impact of funding changes on chlamydia and syphilis were calculated in an analogous manner, using the STI-specific inputs described below and in Table 1 of the main manuscript.

Base case calculations

Time frame and scope

The time frame reflects the number of years over which the number of infections averted (or additional infections) are calculated. The direct medical costs saved (or additional medical costs) are the discounted, lifetime direct medical costs of these infections, regardless of when these costs are incurred. For example, for a 10-year time frame, infections averted (or additional infections) over the first 10 years are included. For each infection averted (or each additional infection) over the first 10 years, the discounted lifetime costs are included, even if these costs extend beyond year 10.

We assessed direct medical costs only. The direct medical costs we applied reflect the perspective of the health system, which includes all direct medical costs without regard to who incurs these costs. The lifetime direct medical cost estimates include the possibility of incurring direct medical costs of sequelae (e.g., pelvic inflammatory disease in women due to chlamydial or gonococcal infection; see the source publications referenced in Table 1 of the main manuscript for details). Other types of costs besides direct medical costs (e.g., productivity losses due to STI or HIV morbidity and mortality, the

value of a statistical life lost due to STI or HIV mortality, intangible costs of pain and suffering due to STI or HIV morbidity) were not included.

Estimating the jurisdiction's annual gonorrhea incidence rate

This corresponds to Step 2 from the manuscript.

A jurisdiction's gonorrhea incidence rate in year 0 ($Rate_0$) was calculated as the number of reported gonorrhea cases per 100,000 population, multiplied by an adjustment factor to account for all gonococcal infections, not just reported gonorrhea cases. Specifically, $Rate_0 = (Cases_0/Population_0)*100{,}000*Adjustment$, where $Cases_0$ is the number of reported gonorrhea cases in the jurisdiction in year 0, $Population_0$ is the population of the jurisdiction in year 0, and *Adjustment* is the ratio of the estimated national number of gonococcal infections in 2018 to the national number of reported gonorrhea cases in 2018. With this application of the adjustment term, we assumed that a jurisdiction's ratio of incident infections to reported cases is the same as the national-level ratio of estimated incident infections to reported cases as of 2018. For simplicity, we assumed that a jurisdiction's population was constant over time (i.e., $Population_t = Population_0$ for all years, where t denotes year). Year 0 is the final year in which the "old" funding level is in place, and year 1 is the first year in which the new funding allocation is in place. The new funding is assumed to remain constant from year 1 onward.

Estimating the percentage change in gonorrhea incidence attributable to a change in STI prevention funding

This corresponds to Step 3 from the manuscript.

SPACE Monkey 2.0 calculates the percentage change in a jurisdiction's gonorrhea incidence rate as $(1+C)^{\Delta F} - 1$, where C is the funding impact coefficient and ΔF is the jurisdiction's change in STI prevention funding per capita. The funding impact coefficient represents the estimated percentage change in gonorrhea incidence rate associated with a $1 per capita increase in funding (in 2022 dollars). The funding impact coefficient is described in Table 1 of the manuscript as "Impact of funding on incidence rate, gonorrhea." The base case value for the funding coefficient is -0.313 for gonorrhea, and thus if there is a $1 increase in per capita funding (a change of +1), then the percentage change in the STI rate is estimated as $(1 - 0.313)^1 - 1 = 0.687 - 1 = -0.313$. In this example, STI rates would decrease by 31.3 percent, which is as expected given that the funding coefficient is -0.313.

The funding impact coefficients we applied were based on Williams (2019). In the regression analysis used in the Williams (2019) study, the dependent variable (reported gonorrhea rate) and the key independent variable (STI prevention funding) were both transformed to natural logs. Thus, the results of the Williams (2019) study provide an estimate of the percentage change in STI rates associated with a percentage change in STI prevention funding. To convert the findings of the Williams (2019) study into estimates of the percentage change in STI rates associated with a $1 per capita increase in STI funding, we calculated the average estimated impact per dollar at the mean level of per-capita STI prevention funding.

Specifically, the mean level of STI funding per capita over the period of the Williams study was $0.38 in 2016 dollars, or $0.46 in 2022 dollars when updated for inflation using the "all items" component of the consumer price index (Appendix 2 Table 1). With an additional dollar of funding per capita, the funding per capita would increase from $0.46 to $1.46; the natural log of funding per capita would increase from -0.777 to 0.378, a change of 1.155. The

combined cumulative effect in year t of funding allocations in years t, t-1, and t-2 was -0.325 in the Williams (2019) study (see Table 3 of that study). As noted in the Williams (2019) study (see their technical appendix), the percentage change in STI rates as a result of a funding change can be calculated as $\exp[\beta \Delta \text{Ln(Funding)}] - 1$, where β is the sum of the funding coefficients, and ΔLn(Funding) is the change in the natural log of STI prevention funding per capita. Thus, the combined funding coefficients for gonorrhea in the base case (-0.325 in the Williams study) suggest that a $1 increase in prevention funding would reduce gonorrhea rates by 31.3%, calculated as $\exp[-0.325 \times 1.155] - 1 = -0.313$.

Example of base case calculations for gonorrhea

Here we provide an example of the SPACE Monkey 2.0 calculations for a jurisdiction of 1 million people with 1,100 gonorrhea cases reported in year 0, with annual STI prevention funding of $500,000 in year 0 and $1,000,000 in years 1 and beyond. Year 0 is the final year in which the "old" annual funding allocation of $500,000 is in place, and year 1 is the first year in which the new annual funding allocation of $1,000,000 is in place. The new annual funding allocation is assumed to remain constant from year 1 onward.

In some examples below, the results do not precisely match the described calculations because of rounding. Specifically, the results presented below were calculated without rounding, whereas the calculation steps are described using rounded numbers.

Calculation of baseline gonorrhea incidence rate

First, we calculated the gonorrhea incidence rate in year 0 as:

$$Rate_0 = (1{,}100/1{,}000{,}000)*(100{,}000)*(1{,}568{,}000/583{,}405) = 295.6437.$$

This rate per 100,000 corresponds to 2,956.4 gonococcal infections in the population of 1 million. Note that in this example, the reported gonorrhea case rate is 110 per 100,000, but the estimated incidence rate (which includes not only reported cases, but also infections that go unreported) is 296 per 100,000. The adjustment term 1,568,000/583,405 represents the estimated number of gonococcal infections in the US in 2018 (Kreisel et al., 2021) divided by the number of reported gonorrhea cases in the US in 2018 (Centers for Disease Control and Prevention, 2019).

Calculation of gonorrhea incidence rate after the change in funding

We calculated what the gonorrhea incidence rate would be after the funding change. As noted above, the percentage change in the gonorrhea rate can be estimated as $(1+C)^{\Delta F} - 1$, which in this example corresponds to $(1 - 0.313)^{0.5} - 1 = -0.1711$. The exponent 0.5 reflects the increase of 0.5 dollars per capita in STI prevention funding. Thus, in this example, gonorrhea rates are estimated to be 17.11% lower than they would have been in the absence of the funding change. A 17.11% reduction in the number of infections represents the prevention of 506.0 infections, calculated as 0.1711 x 2,956.4.

This value of 506.0 infections averted was applied for year 3 and beyond. In the Williams (2019) regression model on which our funding impact coefficients are based, reported STI rates in year t are a function of STI prevention funding in year t, year t-1, and year t-2. Thus, the full impact of a permanent change in prevention funding in year 1 will not be realized until year 3. For simplicity, we assumed that the number of infections averted in year 1 and year 2 was 1/3 and 2/3 the value for year 3, respectively. Thus, compared to the scenario in which there was no funding change, there would be an estimated 168.6 infections averted in year 1,

337.2 infections averted in year 2, and 506.0 infections averted in year 3 and in each subsequent year.

Calculation of the change in direct medical costs of gonorrhea

The direct lifetime medical costs saved by preventing gonococcal infections was calculated as the average discounted lifetime cost per infection ($190) multiplied by the annual number of gonococcal infections averted. Thus, the estimated lifetime medical costs saved each year is $32,037 for year 1 ($190 x 168.6), $64,073 for year 2 ($190 x 337.2), and $96,136 ($190 x 506.0) for year 3 and beyond. Although the lifetime medical costs were discounted to the time of infection, we did not discount these costs to year 0 or to year 1 (e.g., lifetime costs averted in year 10 were not discounted to year 1).

Calculation of the change in gonorrhea-attributable HIV infections

The annual number of gonorrhea-attributable HIV infections averted was calculated as the annual number of gonococcal infections averted multiplied by the probability of a gonorrhea-attributable HIV infection per gonococcal infection (0.00022). Thus, the number of gonorrhea-attributable HIV infections averted was 0.0371 in year 1 (0.00022 x 168.6), 0.0742 in year 2 (0.00022 x 337.2), and 0.1113 in year 3 and beyond (0.00022 x 506.0).

Calculation of the change in direct medical costs of gonorrhea-attributable HIV infections

The direct lifetime medical costs averted by preventing gonorrhea-attributable HIV infections was calculated as the average, discounted lifetime cost per HIV infection ($461,000) multiplied by the annual number of gonorrhea-attributable HIV infections averted. Thus, the estimated costs saved by averting gonorrhea-attributable HIV infections was $17,106 in year 1

($461,000 x 0.0371), $34,211 in year 2 ($461,000 x 0.0742), and $51,317 in year 3 and beyond ($461,000 x 0.1113). As with the medical costs of gonorrhea, although the lifetime medical costs of HIV were discounted to the time of infection, we did not further discount these costs to year 0 or to year 1 (e.g., discounted lifetime costs of HIV infections averted in year 10 were not further discounted to year 1).

Example of confidence interval calculations for gonorrhea

The ranges generated by SPACE Monkey 2.0 reflect approximate interquartile ranges, i.e., the approximate 25th and 75th percentiles of simulations that would be obtained when conducting probabilistic sensitivity analyses in which the parameters in Table 1 for which ranges are provided were varied.

Confidence intervals for change in number of gonococcal infections

Following the methods described above to estimate the base case number of gonococcal infections averted (or number of additional infections, in the event of a budget cut), the number of gonococcal infections averted was calculated for the lower impact scenario and the higher impact scenario. The lower impact scenario was calculated using the lower bound number of gonococcal infections nationally and using the upper bound value for the funding impact coefficient. The higher impact scenario was calculated using the upper bound number of gonococcal infections nationally and using the lower bound value for the funding impact coefficient. Funding has an inverse association with STI incidence (higher funding is expected to lead to lower STI incidence rates), so a funding impact coefficient of -0.486 reflects a greater impact than a funding coefficient of -0.081, even though the latter is a greater value (a lower negative number) than the former. Thus, Table 1 of the main manuscript presents -0.486 as the

"high impact" scenario value and -0.081 as the "low impact" scenario value, even though technically -0.486 is the lower bound of the parameter value and -0.081 is the upper bound.

To estimate the confidence interval, we assumed that the number of gonococcal infections averted (or number of additional infections) follows a lognormal distribution and that about 95% of draws from this distribution fall between the "low impact" scenario and the "high impact" scenario. The distribution parameters were calculated using the base case result (M) as the mean value, with the standard error (SE) approximated as the absolute difference between the result in the higher impact scenario and the result in the lower impact scenario, divided by (2*1.96). Specifically, the lognormal distribution parameters μ and σ were calculated as $\mu = \text{Ln}(M) - 0.5*\text{Ln}(1 + (SE^2 / M^2))$ and $\sigma^2 = \text{Ln}(1 + (SE^2 / M^2))$ (Elbasha 2010). After calculating the lognormal distribution parameters in this manner, we calculated the expected 25^{th} and 75^{th} percentiles of the distribution.

Example of calculations for confidence intervals for change in number of gonococcal infections

This example and the examples below for the calculation of the confidence intervals use the same scenario described in the examples of the base case calculations above: a jurisdiction of 1 million people with 1,100 gonorrhea cases reported in year 0, with annual STI prevention funding of $500,000 in year 0 and $1,000,000 in years 1 and beyond. The annual number of gonococcal infections averted in year 3 and beyond was calculated as 506.0 in the base case (see above example), 96.4 in the lower impact scenario, and 1,124.5 in the higher impact scenario. The percentage reduction in gonorrhea incidence was 4.1% in the lower impact scenario (calculated as $(1–0.081)^{0.5} – 1 = -0.041$) and 28.3% in the higher impact scenario (calculated as $(1–0.486)^{0.5} – 1 = -0.283$). The annual number of incident gonococcal infections in year 0 was

2,330.5 in the lower impact scenario (calculated by multiplying the reported case rate by 1,236,000/583,405) and 3,972.7 in the higher impact scenario (calculated by multiplying the reported case rate by 2,107,000/583,405).

Thus, the number of gonococcal infections averted had a base case value (M) of 506.0 with a range of 96.4 to 1,124.5. We calculated the standard error (SE) as SE = (1,124.5 – 96.4)/(2*1.96) = 262.283. We calculated the lognormal distribution parameters for the number of gonococcal infections averted as $\mu = Ln(M) - 0.5*Ln(1 + (SE^2 / M^2))$ and $\sigma^2 = Ln(1 + (SE^2 / M^2))$. Under these assumptions, $\mu = 6.108$ and $\sigma = 0.488$. Using these distribution parameters, the 25th and 75th percentiles would be 323.3 and 624.2, respectively. We used the "lognorm inverse" function in Excel for these calculations (e.g., the value of 323.3 for the 25th percentile was calculated using in Excel using "=LOGNORM.INV(0.25, 6.108, 0.488)." These results apply annually to year 3 and beyond; the 25th and 75th percentiles were assumed to be 1/3 these values in year 1 and 2/3 these values in year 2.

Confidence intervals for the change in costs of gonococcal infections

We assumed that the lifetime discounted medical cost per gonococcal infection followed a lognormal distribution, using the base case value and range presented in Table 1. As above, the lognormal distribution parameters μ and σ were calculated as $\mu = Ln(M) - 0.5*Ln(1 + (SE^2 / M^2))$ and $\sigma^2 = Ln(1 + (SE^2 / M^2))$, where M is the base case value for the lifetime cost per infection and SE is the absolute difference between the upper bound value and lower bound value for the lifetime cost per infection, divided by (2*1.96).

The total cost averted (or total additional cost) can be calculated as the number of infections averted multiplied by the lifetime cost per infection. Because both these inputs are

assumed to follow independent lognormal distributions, their product was assumed to follow a lognormal distribution as well. If the lognormal distribution parameters are $\mu 1$ and $\sigma 1$ for the number of infections averted (or additional infections) and $\mu 2$ and $\sigma 2$ for the lifetime cost per infection, then the lognormal distribution parameters for the product of these two distributions can be calculated using the following equations: $\mu = \mu 1 + \mu 2$ and $\sigma^2 = \sigma 1^2 + \sigma 2^2$ (Elie et al., 2022).

Example of calculations for confidence intervals for change in cost of gonococcal infections

Using the base case value and range presented in Table 1 for the lifetime cost per gonococcal infection, the lognormal distribution parameters are $\mu = 5.171$ and $\sigma = 0.388$. These were calculated using the formulas described above, with M being the base case value for the lifetime cost per gonococcal infection, and SE calculated as (380 – 80)/(2*1.96), where $380 and $80 are the values applied in the higher impact scenario and lower impact scenario, respectively, for the lifetime cost per infection.

The cost averted by preventing gonococcal infections is the product of the number of gonococcal infections averted and the average lifetime cost per gonococcal infection. Given that the lognormal distribution parameters (μ, σ) are 6.108 and 0.488 for the number of gonococcal infections averted and 5.172 and 0.388 for the lifetime cost per infection, then the lognormal distribution parameters for the product of these two distributions are $\mu = 6.108 + 5.172 = 11.279$, and $\sigma^2 = 0.488^2 + 0.388^2 = 0.381$ (or, $\sigma = 0.617$). The 25th and 75th percentiles of this distribution are $52,001 and $120,532, respectively. These results apply to year 3 and beyond; the 25th and 75th percentiles were assumed to be 1/3 these values in year 1 and 2/3 these values in year 2.

Confidence intervals for the change in number of gonorrhea-attributable HIV infections

We assumed that the number of gonorrhea-attributable HIV infections per gonococcal infection (which we characterize elsewhere as the "probability of a gonorrhea-attributable HIV infection per gonococcal infection") follows a lognormal distribution. We calculated parameters for this lognormal distribution using the base case value and range from Table 1, following methods described above for the lifetime cost per gonococcal infection.

Because the change in the number of gonorrhea-attributable HIV infections is the product of two factors (the change in the number of gonococcal infections and the number of gonorrhea-attributable HIV infections per gonococcal infection), and both factors are assumed to follow independent lognormal distributions, we assumed the product followed a lognormal distribution as well. The parameters for the lognormal distribution of the product of these two factors were calculated by combining their respective distribution parameters, as described above for the averted costs of gonococcal infections. Specifically, if the lognormal distribution parameters are $\mu 1$ and $\sigma 1$ for the number of gonococcal infections averted (or additional infections) and $\mu 2$ and $\sigma 2$ for the number of gonorrhea-attributable HIV infections per gonococcal infection, then the lognormal distribution parameters for the product of these two distributions are $\mu = \mu 1 + \mu 2$ and $\sigma^2 = \sigma 1^2 + \sigma 2^2$.

Example of calculations for confidence intervals for change in number of gonorrhea-attributable HIV infections

As noted above, the lognormal distribution parameters for the number of gonococcal infections averted are $\mu = 6.108$ and $\sigma = 0.488$. Using the base case value and range presented in Table 1 for the probability of an STI-attributable HIV infection per gonococcal infection, the lognormal distribution parameters are $\mu = -8.518$ and $\sigma = 0.437$. These were calculated using the formulas described above, with M being the base case value (0.00022), and SE calculated as

(0.000418-0.000022)/(2*1.96), where 0.000418 and 0.000022 are the values applied in the higher impact scenario and lower impact scenario, respectively, for the probability of a gonorrhea-attributable HIV infection, per gonococcal infection.

Given that the lognormal distribution parameters (μ, σ) are 6.108 and 0.480 for the number of gonococcal infections averted and -8.518 and 0.437 for the probability of a gonorrhea-attributable HIV infection per gonococcal infection, then the lognormal distribution parameters for the product of these two distributions are $\mu = (6.108 + -8.518) = -2.410$, and $\sigma^2 = 0.480^2 + 0.437^2 = 0.429$ (or, $\sigma = 0.655$). The 25th and 75th percentiles of this distribution are 0.058 and 0.140, respectively. These results apply to year 3 and beyond; the 25th and 75th percentiles were assumed to be 1/3 these values in year 1 and 2/3 these values in year 2.

Confidence intervals for the change in costs of gonorrhea-attributable HIV infections

We assumed that the discounted lifetime medical cost per HIV infection follows a lognormal distribution. We calculated parameters for this lognormal distribution using the base case value and range from Table 1, following methods described above for the lifetime cost per gonococcal infection.

Because the averted costs (or additional costs) of gonorrhea-attributable HIV infections averted is the product of two factors (the change in the number of gonorrhea-attributable HIV infections and the lifetime cost per HIV infection), and both factors are assumed to follow independent lognormal distributions, we assumed the product followed a lognormal distribution as well. The parameters for the lognormal distribution of the product of these two factors was calculated following the methods described above.

Example of calculations of confidence intervals for change in cost of gonorrhea-attributable HIV infections

As noted above, the lognormal distribution parameters for the change in number of gonorrhea-attributable HIV infections are $\mu = -2.410$ and $\sigma = 0.655$. Using the base case value and range presented in Table 1 for the average lifetime cost per HIV infection, the lognormal distribution parameters are $\mu = 13.036$ and $\sigma = 0.099$. These were calculated using the formulas described above, with M being the base case value ($461,000), and SE calculated as ($537,000 – $358,000)/(2*1.96), where $537,000 and $358,000 are the values applied in the higher impact scenario and lower impact scenario, respectively, for the lifetime cost per HIV infection.

Given that the lognormal distribution parameters (μ, σ) are -2.410 and 0.655 for the change in the number of gonorrhea-attributable HIV infections and 13.036 and 0.099 for the lifetime cost per HIV infection, then the lognormal distribution parameters for the product of these two distributions are $\mu = (-2.410 + 13.036) = 10.626$, and $\sigma^2 = 0.655^2 + 0.099^2 = 0.439$ (or, $\sigma = 0.662$). The 25th and 75th percentiles of this distribution are $26,352 and $64,419, respectively. These results apply to year 3 and beyond; the 25th and 75th percentiles were assumed to be 1/3 these values in year 1 and 2/3 these values in year 2.

Calculations for chlamydia and syphilis

The calculations for chlamydia and syphilis followed the same approach as described above for gonorrhea, except that STI-specific parameters from Table 1 of the manuscript were applied where applicable. As noted above, the funding impact coefficients that we applied were based on the Williams (2019) study, which provided gonorrhea-specific and chlamydia-specific estimates of the impact of funding. Because the Williams (2019) study did not examine syphilis,

we applied the same estimate of the funding impact coefficient as for gonorrhea. Given that most public health programs prioritize partner services for syphilis over that of gonorrhea and chlamydia (Golden et al., 2003), this assumption is likely conservative, as the relative impact of prevention funding on syphilis is likely more pronounced than on gonorrhea or chlamydia. In fact, an analysis of state-level syphilis elimination funding allocations found a notable impact of these funds on reported syphilis rates (Chesson et al., 2008).

Summation of results across STIs

Results across the STIs were summed to generate totals (e.g., the total number of infections averted or the total costs averted). For these totals, the confidence intervals were summed as well (e.g., the lower bound value for the number of infections averted is the sum of the lower bound values for the number of chlamydial, gonococcal, syphilitic, and STI-attributable HIV infections averted). See Appendix 2 Table 2 for an illustration of the summation of the number of STI-attributable HIV infections averted.

Comparison of program impact estimates in SPACE Monkey 2.0 vs. SPACE Monkey 1.0.

Current model version (Space Monkey 2.0)

In SPACE Monkey 2.0, we assumed that each $1 increase in per-capita STI prevention funding (2022 dollars) would reduce gonorrhea rates and syphilis rates by 31.3% (range: 8.1% to 48.6%) and would reduce chlamydia rates by 17.9% (range: 0% to 34.8%), based on the Williams (2019) analysis of state-level allocations of federal STI prevention funding from 1981 through 2016. These percentage decreases were applied in year 3 after the funding change and

in all subsequent years (Appendix 2 Figure 1, Appendix 2 Table 3). Thus, the impact of the funding change was assumed to level off after the third year. This assumption that the impact would level off in year 3 was directly based on the Williams (2019) study which reported that including lags of the funding variable beyond 2 years did not improve model performance and did not have a particularly sizeable impact on the cumulative estimated effect of prevention funding. The percentage decreases in year 1 and year 2 were assumed to be one-third and two-thirds that of the year 3 value, respectively (Appendix 2 Figure 1, Appendix 2 Table 3).

Previous model version (SPACE Monkey 1.0)

In SPACE Monkey 1.0 (Chesson 2018), each $1 increase in per-capita STI prevention funding (2022 dollars) was assumed to reduce gonorrhea rates, syphilis rates, and chlamydia rates by 13.1% (range: 7.4% to 18.9%), based on the Chesson (2005) analysis of state-level allocations of federal HIV and STI prevention funding from 1981 through 1998. These percentage decreases were applied in year 1 and were assumed to increase at a decreasing rate through year 10 (Appendix 2 Figure 1, Appendix 2 Table 3).

Comparison of model versions regarding estimated impact on gonorrhea and syphilis

The comparisons across model versions of the impact of an additional $1 in STI prevention funding (Appendix 2 Figure 1, Appendix 2 Table 3) apply to gonorrhea and syphilis for SPACE Monkey 2.0 and for gonorrhea, syphilis, and chlamydia for SPACE Monkey 1.0. The estimated impact of a $1 increase in STI prevention funding on gonorrhea and syphilis was reasonably consistent across the two versions of SPACE Monkey. The estimated annual reductions in gonorrhea and syphilis due to a $1 increase in per-capita prevention funding for the current version of the model (SPACE Monkey 2.0) were within 30% that of the previous version

of the model (SPACE Monkey 1.0) in relative terms and within 12 percentage points in absolute terms (Appendix 2 Table 3).

Comparison of model versions regarding estimated impact on chlamydia

The estimated percentage reductions in chlamydial infections due to a $1 increase in per capita funding are lower in the updated version of SPACE Monkey than in the previous version. The Williams study (2019) that informed the updated version (SPACE Monkey 2.0) included two analyses of the impact of STI prevention funding: one focusing on gonorrhea and one focusing on chlamydia. The results suggested that the impacts of prevention funding were more pronounced on gonorrhea rates than on chlamydia rates. In contrast, the previous version (SPACE Monkey 1.0) was based on Chesson (2005), which did not include chlamydia as an outcome. Thus, SPACE Monkey 1.0 assumed the impact of STI prevention funding on gonorrhea rates as estimated by Chesson (2005) could be applied to syphilis and chlamydia.

Other differences in the two model versions of SPACE Monkey

Predictions of the two model versions can vary due to other differences in the model structures and parameter values. For example, the annual number of incident gonococcal infections in the United States in the base case was 1,568,000 in SPACE Monkey 2.0 based on 2018 estimates from Kreisel et al. (2021) but was 820,000 in SPACE Monkey 1.0 based on 2008 estimates from Satterwhite et al. (2013).

These assumptions affect the incidence adjustment factor; i.e., the ratio of the number of incident infections to the number of reported cases. For SPACE Monkey 2.0, the incidence adjustment factor was 2.69 for gonorrhea as described above in the section "Calculation of baseline gonorrhea incidence rate." In contrast, for SPACE Monkey 1.0, the incidence

adjustment factor was 2.07, calculated by dividing 820,000 by 395,216, where the numerator was the annual number of gonococcal infections as estimated by Satterwhite (2013), the most recent available estimate of annual incidence at the time SPACE Monkey 1.0 was developed, and the denominator was the number of reported gonorrhea cases in 2015 (CDC 2016).

SPACE Monkey 2.0 also uses updated values for the average lifetime costs per STI and HIV infection. Additionally, the updated model inflation-adjusts to 2022 dollars.

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Appendix 2 Tables

Appendix 2 Table 1: Calculation of funding impact coefficients (estimated percent change in STI incidence rate due to $1 per capita increase in STI prevention funding) from regression coefficients in Williams (2019) analysis

Item calculated	Scenario		
	Base case	Low impact	High impact
Funding per capita calculations			
Mean funding per capita (2016 dollars) in Williams study	0.38	0.38	0.38
Mean funding per capita (2022 dollars) in Williams study	0.46	0.46	0.46
Mean funding per capita w/ $1 increase per capita (2022 dollars)	1.46	1.46	1.46
Natural log, base funding per capita (2022 dollars)	-0.777	-0.777	-0.777
Natural log, base funding per capita + $1 additional (2022 dollars)	0.378	0.378	0.378
Change in natural log of funding per capita with $1 increase per capita	1.155	1.155	1.155
Gonorrhea			
Combined funding coefficients (from Williams study)	-0.325	-0.073	-0.577
Funding impact coefficient applied in SPACE Monkey 2.0*	-0.313	-0.081	-0.486
Funding impact coefficient, expressed as a percentage	-31.3%	-8.1%	-48.6%
Chlamydia			
Combined funding coefficients (from Williams study)	-0.171	0.000	-0.370
Funding impact coefficient applied in SPACE Monkey 2.0*	-0.179	0.000	-0.348
Funding impact coefficient, expressed as a percentage	-17.9%	0.0%**	-34.8%

*The funding impact coefficient (the percentage change in STI rates as a result of a $1 increase in per-capita STI prevention funding) can be calculated as $\exp[\beta \Delta Ln(Funding)] - 1$, where β is the value of the combined funding coefficients from the Williams (2019) study and $\Delta Ln(Funding)$ is the change in the natural log of STI prevention funding per capita. In the base case the value of -31.3% was calculated as $\exp[-0.325 \times 1.155] - 1$.

**In the Williams (2019) study, the cumulative effect of STI prevention funding was significant at the $p<0.10$ level for chlamydia and at the $p<0.05$ level for gonorrhea. Accordingly, the 95% confidence interval for the cumulative impact of funding on chlamydia overlapped 0. For the low impact scenario for

chlamydia, we assumed that STI prevention funding would have no effect rather than to assume a deleterious effect; this assumption is consistent with the general findings of the Williams study.

The Williams (2019) study did not examine syphilis as an outcome. For syphilis, the percent change in incidence due to an increase of $1 in per capita funding was assumed to be the same as that of gonorrhea.

Appendix 2 Table 2: Number of STI-attributable HIV infections averted and associated medical costs saved: Example of summation of estimated impacts across STIs

Outcome and year	Number of STI-attributable HIV infections averted			Costs saved by averting STI-attributable HIV infections		
	Base case estimate	Lower bound of confidence interval	Upper bound of confidence interval	Base case estimate	Lower bound of confidence interval	Upper bound of confidence interval
Gonorrhea-attributable HIV infections averted, year 3	0.11	0.06	0.14	$51,317	$26,352	$64,419
Chlamydia-attributable HIV infections averted, year 3	0.10	0.05	0.13	$47,455	$22,366	$59,499
Syphilis-attributable HIV infections averted, year 3	1.65	0.85	2.07	$758,895	$387,988	$952,695
Total STI-attributable HIV infections averted, year 3	1.86	0.96	2.34	$857,667	$436,706	$1,076,614
Total STI-attributable HIV infections averted, year 1	0.62	0.32	0.78	$285,889	$145,569	$358,871
Total STI-attributable HIV infections averted, year 2	1.24	0.64	1.56	$571,778	$291,138	$717,742
Cumulative total, STI-attributable HIV infections averted, years 1-3	3.72	1.91	4.67	$1,715,334	$873,413	$2,153,227

This table provides examples of the calculations of SPACE Monkey for a jurisdiction of 1 million people, with 1,100 gonorrhea cases (and 2,200 chlamydia cases and 500 syphilis cases) reported in year 0, with annual STI prevention funding of $500,000 in year 0 and $1,000,000 in years 1 and beyond. Year 0 is the final year in which the old funding amount is in place, and year 1 is the first year in which the new funding allocation is in place.

This table illustrates how the base case results and confidence intervals were summed across STIs. For example, the lower bound value of the total number of STI-attributable HIV infections averted in year 3 is 0.96, which is simply the sum of the lower bound values for year 3 for gonorrhea (0.06), chlamydia (0.05), and syphilis (0.85).

Outcomes for year 1 and year 2 were assumed to be one-third and two-thirds, respectively, that of the year 3 outcomes.

Sums might not match totals of individual items due to rounding.

Appendix 2 Table 3: Percentage reduction in gonorrhea rate in years 1–10 (vs. year 0) with $1 per capita increase in funding for sexually transmitted disease prevention: Comparison of previous and current versions of SPACE Monkey

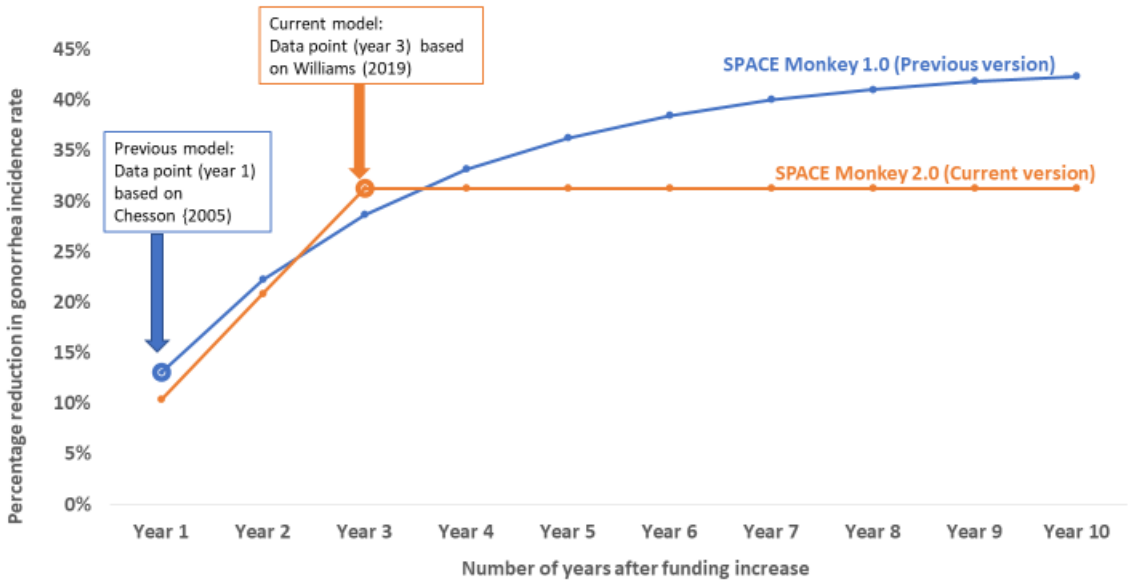
Year	Previous version (SPACE Monkey 1.0)	Current version (SPACE Monkey 2.0)	Relative difference* (current version vs. previous version)	Percentage point difference** (current version vs. previous version)
Year 1	13.1%	10.4%	-20.6%	-2.7%
Year 2	22.3%	20.9%	-6.3%	-1.4%
Year 3	28.7%	31.3%	9.1%	2.6%
Year 4	33.2%	31.3%	-5.7%	-1.9%
Year 5	36.3%	31.3%	-13.8%	-5.0%
Year 6	38.5%	31.3%	-18.7%	-7.2%
Year 7	40.1%	31.3%	-21.9%	-8.8%
Year 8	41.1%	31.3%	-23.8%	-9.8%
Year 9	41.9%	31.3%	-25.3%	-10.6%
Year 10	42.4%	31.3%	-26.2%	-11.1%

The percentage change for each year shows the reduction in gonorrhea rate vs. year 0. For example, for the current version of the model (SPACE Monkey 2.0), estimated gonorrhea rates in year 1 are 10.4% lower than that of year 0, and estimated gonorrhea rates in year 2 are 20.9% lower than that of year 0. Year 0 is the final year in which the old funding amount is in place, and year 1 is the first year in which the new funding allocation (an increase of $1 per capita compared to the old allocation) is in place.

*The relative difference is the percentage difference between the current model version and the previous version in the estimated percentage reduction in gonorrhea rates (e.g., for row 1, the value -20.6% was calculated as [10.4%–13.1%]/13.1%).

**The percentage point difference compares the estimated percentage reduction in gonorrhea rates for Version 2.0 to that of Version 1.0 (e.g., for row 1, the value -2.7% was calculated as 10.4% – 13.1%).

Appendix 2, Figure 1: Percentage reduction in gonorrhea incidence due to $1 per capita increase in STI prevention funding: Previous version (SPACE Monkey 1.0) and current version (SPACE Monkey 2.0) of model



Appendix 2 Figure 1: The estimated percentage reduction in gonorrhea rates due to a $1 increase (2022 dollars) in per-capita STI prevention funding is shown by year for the current model version (SPACE Monkey 2.0) in orange and for the previous model version (SPACE Monkey 1.0) in blue. Year 0 is the final year in which the old funding amount is in place, and year 1 is the first year in which the permanent increase of $1 per capita is in place.

For SPACE Monkey 2.0, the key data point was for year 3. Based on Williams (2019), we assumed that in year 3 and in all subsequent years there would be a reduction in gonorrhea incidence of 31.3% compared to incidence in year 0. The percentage decreases in year 1 and year 2 were assumed to be one-third and two-thirds that of the year 3 value, respectively.

For SPACE Monkey 1.0, the key data point was for year 1. Based on Chesson (2005), it was assumed that in year 1 there would be a reduction in gonorrhea incidence of 13.1% compared to incidence in year 0. The percentage reduction was assumed to increase at a decreasing rate in years 2–10 before leveling off at year 10 (Chesson 2018). The Chesson (2018) manuscript reports a 16% reduction in gonorrhea per each $1 increase in per capita spending in 2016 US dollars; the value of 13.1% applied in this figure reflects the impact of adjustment to 2022 US dollars.

This figure displays the point estimates shown in Appendix 2 Table 3.