Estimates of the Lifetime Productivity Costs of Chlamydia, Gonorrhea, and Syphilis in the United States

Technical Appendix

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

Overview

This appendix provides details of the cost inputs used in the estimation of the productivity cost per infection for three sexually transmitted infections: chlamydia, gonorrhea, and syphilis. All productivity costs estimates were based on the annual productivity estimates provided by Grosse and colleagues,[1] updated to 2023 US dollars. We applied annual productivity values to quantify lost productivity of life years lost due to syphilis-attributable deaths. We applied daily productivity values to quantify lost productivity of days lost due to hospitalization (e.g., due to PID-related sequelae or long-term syphilis sequelae such as cardiovascular syphilis). The daily productivity value was calculated by dividing the annual productivity value by 365. We used hourly productivity values to quantify productivity losses due to outpatient medical visits for STI treatment, as these impose less than 1 day of productivity losses. As described below in more detail, the hourly cost was calculated as the daily cost divided by 8 (rather than by 24) because (1) even in perfect health, people are not productive for 24 hours per day and (2) we assumed that all hours lost due to seeking medical care for STIs could have been used for paid or unpaid productive activities.

Adjusting for inflation

Costs were updated to 2023 dollars using the Personal Consumption Expenditures (PCE) price index. To obtain this price index from www.bea.gov/itable/national-gdp-and-personal-income (accessed 2/13/2024), we chose (1) "Interactive Data Tables", (2) "Section 2 – Personal Income and Outlays", and (3) "Table 2.3.4 Price Indexes for Personal Consumption Expenditures by Major Type of Product." We then used the "modify" option to select the years of data needed and to obtain annual values.

Example of inflation adjustment

Annual productivity in 2016 for ages 55 to 64 years was $67,990 in 2016 dollars in the study by Grosse and colleagues (see their Table 1, final row).[1] The PCE price index (line 1 of Table 2.3.4 described above) was 98.284 for 2016 and 120.37 for 2023, as of 2/13/2024. Annual productivity was updated from 2016 to 2023 dollars by multiplying by (120.37 / 98.284), which is 1.224716. Thus, $67,990 in 2016 dollars is $83,268.45 when updated to 2023 dollars, calculated as $67,990 x (120.37 / 98.284).

Although we used the overall PCE price index to update productivity cost estimates, we used the health care component of the PCE to update the lifetime medical costs per STI to 2023 dollars. These lifetime medical costs were not used in our analysis but are reported in the discussion section to allow for a comparison of the relative magnitude of lifetime productivity costs to that of lifetime direct medical costs.

Cost inputs used in decision tree models of chlamydia and gonorrhea

The decision tree models for chlamydia and gonorrhea required the following three productivity cost estimates: productivity cost of a physician visit to receive treatment for the given STI, productivity cost per case of pelvic inflammatory disease (PID) in women, and the productivity cost per case of epididymitis in men. For convenience, Supplementary Figure 1 showing the decision tree model for chlamydia and gonorrhea is included at the end of this Technical Appendix.

Cost per outpatient medical visit for treatment of sexually transmitted infection (STI)

We included patient time costs for seeking treatment of STIs. Outpatient medical care for STIs imposes patient time costs for activities such as traveling to the point of care, waiting for care, receiving care, and picking up prescriptions if needed. Data-based estimates of the average time burden per outpatient medical visit for STIs are limited. Although we did not explicitly account for productivity losses due to STI morbidity prior to seeking treatment (such as being unable or less able to work due to STI symptoms), we assumed such impacts would be limited and could be considered to be subsumed in our estimates of patient time costs for seeking treatment.

Number of hours lost per medical visit for outpatient treatment

One of the earliest studies of the productivity cost of chlamydia treatment assumed that one day's work (e.g., 8 hours of market productivity) would be lost for treatment of acute infection in men and women, in addition to non-market productivity losses.[2] Subsequent studies using medical claims data (MarketScan) linked to employment data (Health and Productivity Management Database) found that an average of about 6 to 10 hours of work are lost per case of outpatient treatment for chlamydia or gonorrhea.[3,4] However, these claims-based estimates reflect the average number of hours of work missed among the subsample of patients with a documented work absence corresponding to the date(s)

that STI treatment was received, a subsample which might have a greater-than-average productivity loss per infection. That is, because these claims-based estimates applied only to those who missed work for their outpatient visit, they might overestimate the average time cost across all people with STIs (e.g., people who did not miss work for treatment).[4] So, although a previous study has assumed 8+ hours of lost productivity for outpatient treatment of chlamydia and gonorrhea,[2] and subsequent claims-based studies have provided some support for this assumption,[3,4] we decided to apply a lower, more conservative estimate.

In determining the base case value of the average time cost per case of outpatient STI treatment (3.7 hours), we considered three key estimates from the literature: 6–10 hours, 2.1 hours, and 3.7 hours. First, as noted previously, claims-based studies have found that an average of about 6–10 hours of work are lost per case of outpatient treatment for chlamydia or gonorrhea.[3,4] Second, the average time burden per outpatient medical visit was estimated at 2.1 hours in a study of 3,787 respondents in the American Time Use Survey data from 2005 to 2013 who reported clinic time.[5] Although not specific to clinic visits for STI treatment, this average time burden of 2.1 hours for clinic visits overall serves as a useful lower bound estimate for our study, given the large sample size. We considered 2.1 hours to be a lower bound estimate because it only includes time spent for travel to the clinic and time spent at the clinic, thereby excluding other potential time costs associated with STI treatment (such as pharmacy visits) and productivity losses due to STI morbidity prior to seeking treatment. Third, the average number of hours of productivity lost per visit for office-based testing for chlamydia among women aged 15–24 years at high risk for chlamydia has been estimated at 3.7 hours.[6] Although this estimate of 3.7 hours was based on a study of young women seeking chlamydia screening, we applied it as the base case value for both women and men for seeking STI treatment. Our rationale was that in the absence of this estimate of 3.7 hours, we likely would have applied a base case value of about 5 hours for seeking treatment of STIs, which reflects the approximate midpoint of the two other available sources of data (2.1 hours for clinic visits overall based on the American Time Use Survey and 6–10 hours for STI outpatient treatment based on claims data). Thus, the value of 3.7 was chosen because of its relevance (it was based on a study of productivity losses for an STI-related clinic visit) and because it is consistent with, but more conservative than, an estimate of 5 hours based on the average of other available data sources.

As described above, we applied 2.1 hours as the lower bound value of the time burden per STI medical care visit. We applied a value of 5.3 hours per visit as the upper bound value, so that (1) the

base case value would be at the midpoint of the lower and upper bound values and (2) the upper bound value would be lower than the 6–10 hours estimated in claims studies, given that the estimates based on claims studies might overestimate the average treatment time cost across all people treated for STIs as discussed above.

We did not stratify the analysis by the type of clinic in which STI care occurs. Our base case value of 3.7 hours per medical visit was based on the Smith (2007) study which used data a trial that included 11 community-based medical clinics in Western Pennsylvania.[6] It is possible that the duration of medical visits (time spent waiting plus time spent with the health provider) could vary by site, such as private physician offices vs. STI clinics, and could differ in other geographical settings. However, we applied a wide range of values (2.1–5.3 hours) to capture uncertainty in this estimate, including uncertainties related to the differences in time spent seeking STI treatment by health care setting.

Productivity cost per day and per hour

Given that teenagers and young adults bear a disproportionate burden of STIs, we calculated the productivity cost per day based on the average annual productivity among ages 15–34 years. Specifically, we estimated the annual productivity for ages 15–34 years as $51,960 (in 2023 dollars) as the average of the annual productivity in the 15–24 age year group and the 25–34 age year group.[1] Thus, we assumed each lost day of productivity (e.g., due to hospitalization) would impose a productivity cost of $142, calculated as $51,960 / 365.

We assumed that time spent for STI treatment would have otherwise been used for market or nonmarket productivity. So, in calculating the time cost of STI treatment visits, we applied an hourly cost of productivity of $17.75 in the base case, calculated as the daily cost of productivity ($142) divided by 8 hours. The division by 8 hours reflects our assumption of 8 hours of productivity per day when healthy.[7] The base case estimate we applied ($17.75) is consistent with but slightly lower than the $19.00 median hourly compensation of young adults in the United States in 2023, calculated as the median hourly compensation of $15.45 for ages 16–24 years in 2023 (https://www.bls.gov/cps/data.htm, accessed 2/2/2024) multiplied by 1.23 to account for fringe benefits.[1] We applied a lower bound value of $13.38 and an upper bound value of $21.66. The lower bound value reflects the approximate average minimum wage ($10.88) plus 23% for fringe benefits. The average minimum wage we applied ($10.88) in estimating the lower bound value was calculated as the

population-weighted average minimum wage across states, using state-specific minimum wage data from the US Department of Labor (https://www.dol.gov/agencies/whd/minimum-wage/state, accessed 2/2/2024) and state population data for ages 15–24 years from Atlas Plus (https://www.cdc.gov/nchhstp/atlas/index.htm, accessed 2/2/2024). [In doing so, we applied $7.25 for states without a minimum wage of at least $7.25 (the federal minimum wage), and, for states listing more than one applicable minimum wage above $7.25, we applied the lowest listed value at or above $7.25]. The upper bound value ($24.55) was calculated as the median hourly compensation of $19.96 for ages 25–34 years in 2023 (https://www.bls.gov/cps/data.htm, accessed 2/2/2024) multiplied by 1.23 to account for fringe benefits. Thus, our estimates of hourly productivity were conservative in that (1) they were based on earnings among younger people, whose productivity is on average less than those in the middle age groups, (2) the base case value we applied was less than the median hourly compensation of youth and young adults aged 16–24 years, and (3) even our upper bound values do not exceed median hourly compensation for ages 25–34 years.

As noted above, we assumed each lost day of productivity would impose a productivity cost of $142. We applied a lower and upper bound value of $107 and $196, respectively, so that the range of estimates for the daily productivity cost would be the same relative to the range of estimates for the hourly productivity cost (i.e., the lower bound was set to about 75.4% of the base case value and the upper bound was set to 138.3% of the base case value).

Multiplying the hourly cost by the number of hours lost for STI treatment

The productivity cost per clinic visit was estimated at $65.68 for the base case ($17.75 per hour x 3.7 hours), $28.10 for the lower bound ($13.38 per hour x 2.1 hours), and $130.12 for the upper bound ($24.55 per hour x 5.3 hours).

Productivity cost per case of pelvic inflammatory disease (PID)

The lifetime productivity cost per case of PID was based primarily on a study by Blandford and Gift (2006),[8] except that we applied updated estimates of the probability of long-term sequelae (chronic pelvic pain, ectopic pregnancy, and infertility) per case of PID and updated estimates of the cost per day of lost productivity. Also of note, our updated estimates of the cost per day of lost productivity included

market and non-market productivity, whereas the original Blandford and Gift study included only paid labor and thus excluded non-market productivity losses.

Calculations of the cost per case of PID

Our specific approach was to obtain estimates of the number of lost days of productivity associated with acute PID, chronic pelvic pain, ectopic pregnancy, and infertility from Blandford and Gift (2006)(Appendix Table A1),[8] which were based on an earlier study by Washington and colleagues (1986).[9] The probability of each of these outcomes per case of PID was obtained from the 2021 study by Kumar and colleagues of the direct medical cost of chlamydia, gonorrhea, and trichomoniasis.[10] Assuming a productivity cost of $142 per day, the average discounted lifetime productivity cost per case of PID, including the possibility of chronic pelvic pain, ectopic pregnancy, and infertility, was $2,173 (range: $819–$4,499).

The range was calculated as follows. Blandford and Gift (2006) suggested a range of plus or minus 50% for the number of disability days; this range, when combined with a range of $107–$196 for the productivity cost per day, yielded a range of $819–$4,499 for our average productivity cost per case of PID. That is, $819 reflects multiplication of $2,173 by 50% and 75.4% (where 50% is the adjustment for uncertainty in the number of disability days and 75.4%, or $107/$142, is the adjustment for uncertainty in the cost per disability day). Similarly, $4,499 reflects multiplication of $2,173 by 150% and 138.0% (where 150% is the adjustment for uncertainty in the number of disability days and 138.0%, or $196/$142, is the adjustment for uncertainty in the cost per disability day).

Productivity cost per case of epididymitis

As noted in the main text, to estimate the productivity cost per case of epididymitis, we multiplied the estimated number of days of lost productivity per case by the productivity cost per day. We assumed 5 lost days of productivity,[2] corresponding to a productivity cost of $710 per case. The Washington 1987 study suggested that the number of lost days of productivity could be 10 days for patients treated on an inpatient basis,[2] however, we did not include this possibility as the percentage of men with epididymitis treated on an inpatient basis has been estimated to be less than 1.2%.[11] Instead, we applied the Washington estimate of 5 days of lost productivity for all men with epididymitis.

To calculate the range ($268–$1,470 per case), we assumed the number of lost days of productivity ranged from 2.5 to 7.5, based on the relative ranges suggested by Blandford and Gift (2006) for the lost productivity days for women with PID.[8] The lower bound value of the range was calculated as the product of 2.5 and $107, and the upper bound value of the range was calculated as the product of 7.5 and $196, where $107 and $196 are the lower and upper bound values of the range of the productivity cost per day.

Cost inputs used in decision tree model of syphilis

The direct cost estimates applied in the Chesson and Peterman (2021) study of the lifetime medical costs of syphilis were based primarily on assumptions regarding the estimated resources required for the possible outcomes of syphilis, as described in their technical appendix.[12] These resources included physician visits, hospitalization days, and years of long-term care. So, to calculate productivity cost estimates of the outcomes in the syphilis decision tree model, we needed estimates of the productivity costs per medical visit for syphilis treatment, per hospitalization day, and per year of long-term care. Further, because premature death was a possibility for some of the rare outcomes of untreated syphilis, we also needed estimates of the productivity cost per year of life lost. For convenience, Supplementary Figure 2 showing the decision tree model for syphilis is included at the end of this Technical Appendix.

Productivity costs per medical visit, per hospitalization day, per year of long-term care, and per year of life lost

The productivity cost per medical visit for syphilis treatment was assumed to be the same as described above per medical visit for treatment of chlamydia and gonorrhea: $65.68 ($28.10–$130.12). The productivity cost per hospitalization day was also assumed to be the same as described above: $142 (range: $107–$196).

The productivity cost estimates per year of long-term care and per year of life lost were calculated based primarily on published estimates of the annual productivity (market productivity plus non-market productivity) of adults in the United States.[1] As stated earlier, our analysis of the productivity costs of syphilis included the possibility that untreated infection might lead to premature death or to the need for long-term care. We assumed that if these outcomes occurred, they would

occur at least 30 years after infection.[12] So, given that these outcomes would occur in older age groups if they occurred, we applied an annual productivity cost of $50,014 per year of life lost due to syphilis, calculated as the average of the annual productivity for ages 55–64 years ($83,268 in 2023 dollars), for ages 65–74 years ($47,156 in 2023 dollars) and for ages 75 years and older ($19,616 in 2023 dollars).[1] We applied a lower bound value of $37,701 and an upper bound value of $69,174, so that the relative range for the annual cost of premature death would be consistent with the relative range we applied for the hourly and daily productivity costs as described above (i.e., the lower bound was set to about 75.4% of the base case value and the upper bound was set to 138.3% of the base case value).

The assumptions regarding the resources required for each syphilis outcome are summarized in Appendix Tables A2 and A3 and described in detail in the following subsections. Except where noted, all assumptions regarding the number of medical visits, hospitalization days, years of long-term care, and years of life lost were calculated based on the resource use assumptions described in the Chesson and Peterman (2021) medical cost study (see also the technical appendix to that study for details on the resource use assumptions).[12]

For the cost of each syphilis outcome, we generated a lower and upper bound value (Table 1 of main manuscript). The lower bound value was obtained by applying the lower bound value of any applicable costs (cost per medical visit, cost per hospitalization day, cost per year of long-term care, and cost per year of life lost) and by multiplying the resulting cost estimate by 0.8 to account for uncertainty in the number of resources acquired. The upper bound value was obtained by applying the upper bound value of any applicable costs (cost per medical visit, cost per hospitalization day, cost per year of long-term care, and cost per year of life lost) and by multiplying the resulting cost estimate by 1.2 to account for uncertainty in the number of resources acquired. Parameters for the distribution of the cost of the syphilis outcomes were calculated as described elsewhere.[10] Briefly, we estimated lognormal distribution parameters by assuming the base case value reflected the mean value and that the standard deviation could be approximated based on the difference between the upper bound and lower bound values.

Productivity cost of treatment of primary and secondary (P&S) and early non-P&S syphilis

For P&S and early non-P&S syphilis, we assumed that 37.3% of patients receive follow-up treatment and have an average of 3.5 visits and the remaining 62.7% of patients without follow-up have

an average of 1.5 visits, for a weighted average of 2.25 visits. No other resource use (hospitalization, long-term care, year of life lost) was assumed.

Productivity cost of early neurosyphilis and ocular syphilis

For early neurosyphilis and ocular syphilis, we assumed that 21.3% of patients would require 12 hospitalization days and no office visits, and the remaining 78.7% would require 12 office visits and no hospitalization days, for a weighted average of 9.44 office visits and 2.56 hospitalization days. No other resource use (long-term care, year of life lost) was assumed.

Productivity cost of treatment of late syphilis

For treatment of late syphilis, we assumed that 37.3% of patients receive follow-up treatment and have an average of 6 visits and the remaining 62.7% of patients have an average of 3 visits, for a weighted average of 4.12 visits. No other resource use (hospitalization, long-term care, year of life lost) was assumed.

Productivity cost of long-term sequelae

Productivity cost of late benign syphilis

We assumed that patients diagnosed with late benign syphilis receive an average of 5 office visits. No other resource use (hospitalization, long-term care, year of life lost) was assumed.

Productivity cost of cardiovascular syphilis

For cardiovascular syphilis, we assumed that all patients have 5 office visits within the first year of diagnosis, plus 2 additional visits per year of life inclusive of the first year of diagnosis. We assumed that 73% of patients with cardiovascular syphilis die due to cardiovascular syphilis, and this death occurs 5.5 years after diagnosis, and thus these patients incur the 2 visits per year for 5.5 years, which when discounted to the time of diagnosis at 3% annually is 10.30 additional visits for a total of 15.30 visits. The remaining 27% of patients with cardiovascular syphilis do not die prematurely and instead were assumed to live 22 years after diagnosis, and thus incur the 2 visits per year for 22 years, which when

discounted to time of diagnosis is 32.83 additional visits for a total of 37.83 visits. The weighted average of office visits is 21.38 visits per patient (2 initial plus 19.38 follow-up).

We assumed half of patients with cardiovascular syphilis have cardiac surgery and incur 6 hospitalization days, for a weighted average of 3 hospitalization days per patient. Chesson and Peterman (2021)[12] reported their assumptions for the probability and cost of cardiac surgery, but did not report the number of hospitalization days for this outcome; our assumption here of 6 days of hospitalization for cardiac surgery was based on Ghanta et al. (2015).[13] The 73% of patients with cardiovascular syphilis who die due to cardiovascular syphilis are assumed to die 5.5 years post diagnosis (instead of 22 years post diagnosis) and reflect 11.26 discounted life years lost per patient who dies, or 8.22 life years lost per patient (discounted to time of diagnosis of cardiovascular syphilis).

Discounting of future streams of outcomes

For the long-term outcomes of syphilis, we needed to calculate the present value of a stream of annual outcomes in the future, such as annual physician visits, years of long-term care, and years of life lost. Here we provide an example of how the discounted number of life years lost was calculated. As noted above, we assumed that 73% of patients with cardiovascular syphilis would die due to cardiovascular syphilis, and as a result they would live 5.5 years post diagnosis rather than 22 years post diagnosis. The discounted number of years of life remaining at time of diagnosis was approximated as $(1-\beta^t)/(1-\beta)$, where t is the number of life years remaining at time of diagnosis and $\beta = 1/(1+r)$, where r is the annual discount rate. A person living for 5.5 additional years post diagnosis would accrue 5.152 discounted life years, calculated as $(1-\beta^{5.5})/(1-\beta)$, while a person living 22 additional years post diagnosis would accrue 16.415 discounted life years. Thus, the number of life years lost due to cardiovascular syphilis death after 5.5 years, discounted to time of diagnosis, was calculated as 16.415 minus 5.152, or 11.263. The average number of life years lost per patient with cardiovascular syphilis (including those that die of cardiovascular syphilis and those that do not) was calculated as 0.73 x 11.263 = 8.222, where the value 0.73 reflects the assumption that 73% of patients with cardiovascular syphilis would die due to cardiovascular syphilis.

Productivity cost of tabes dorsalis

For tabes dorsalis, we assumed that all patients have 2 office visits within the first year of diagnosis, plus 2 additional visits per year of life inclusive of the first year of diagnosis. We assumed that

73% of patients with tabes dorsalis die due to tabes dorsalis, and this death occurs 5.5 years after diagnosis, and thus these patients incur the 2 visits per year for 5.5 years, which when discounted to present value is 10.30 additional visits for a total of 12.30 visits. The remaining 27% of patients with tabes dorsalis do not die prematurely and instead were assumed to live 22 years after diagnosis, and thus incur the 2 visits per year for 22 years, which when discounted to present value is 32.83 additional visits for a total of 34.83 visits. The weighted average of office visits is 18.39 visits per patient. The 73% of patients with tabes dorsalis who die due to tabes dorsalis are assumed to die 5.5 years post diagnosis (instead of 22 years post diagnosis) and reflect 11.26 discounted life years lost per patient who dies, or 8.22 life years lost per patient (discounted to time of diagnosis of tabes dorsalis). These assumptions were obtained from Chesson and Peterman (2021), except that our assumption of 2 visits per year post-diagnosis was not specified in that study.[12] We assumed 2 visits per year to be consistent with their cardiovascular syphilis assumptions.

Productivity cost of meningovascular syphilis

For meningovascular syphilis, we assumed all patients have 1 office visit and 10 days of hospitalization. In addition, we assumed that 75% of patients with meningovascular syphilis have a stroke due to meningovascular syphilis and incur an additional 6.9 days of hospitalization, which would occur in the first year after diagnosis. Thus, the weighted average number of days of hospitalization was 15.18 across all patients with meningovascular syphilis. Among patients with meningovascular syphilis who have a stroke, we assumed 17% would require long-term care on a level consistent with that of dementia patients. This long-term care was assumed to be for 5.5 years for the 73% of patients with meningovascular syphilis with death attributable to meningovascular syphilis, and 22 years for the 27% of patients with meningovascular syphilis whose death was not attributable to meningovascular syphilis. Thus, the weighted average number of years of long-term care required was 1.04 across all patients with meningovascular syphilis, which is discounted to the time of diagnosis of meningovascular syphilis. The 73% of patients with meningovascular syphilis who die due to meningovascular syphilis are assumed to die 5.5 years post diagnosis (instead of 22 years post diagnosis) and reflect 11.26 discounted life years lost per patient who dies, or 8.22 life years lost per patient (discounted to time of diagnosis of meningovascular syphilis). These assumptions were obtained from Chesson and Peterman (2021), except that our assumption of 6.9 days of hospitalization for stroke was not specified in that study.[12] We assumed 6.9 days of hospitalization for stroke based on a study by Khan and colleagues (2021) using the National Inpatient Sample database.[14]

Productivity cost of general paresis

For general paresis, we assumed all patients had 3 office visits and 10 hospitalization days. We assumed that 73% of patients with general paresis live for 2 years after diagnosis, all of which are in long term care, and thus when compared to 22 years of life expectancy in the absence of general paresis, these patients incur 1.97 years of long-term care and 14.45 years of life lost, discounted to time of diagnosis of general paresis. We assumed that 27% of patients with general paresis live for 8 years after diagnosis, all of which are in long term care, and thus when compared to 22 years of life expectancy in the absence of general paresis, these patients incur 7.23 years of long-term care and 9.19 years of life lost, discounted to time of diagnosis of general paresis. The weighted average is 13.03 years of life lost and 3.39 years of long-term care across all patients with general paresis. These assumptions were obtained from Chesson and Peterman (2021), except that the life expectancy of 22 years in the absence of general paresis was not explicitly stated in that study, but instead is consistent with the assumptions explicitly stated for the other long-term sequelae such as cardiovascular syphilis and meningovascular syphilis.[12]

Accounting for discounting of future syphilis outcomes

The costs shown in Table 1 of the main manuscript and in Appendix Table A3 are discounted to the time of diagnosis and onset of treatment. Appendix Table A4 shows how these costs were discounted to the time of infection. Appendix Table A5 lists all the possible outcomes of the syphilis decision tree and shows the cost per outcome, discounted to the time of infection.

Probabilities applied in the decision tree models

All probabilities for the chlamydia and gonorrhea decision trees were obtained directly from the Kumar et al. (2021) medical cost study[10] and are listed in Appendix Table A6. The distribution assumptions for these probabilities that we applied in the probabilistic sensitivity analyses were obtained directly from the Kumar et al. (2021) medical cost study[10] as well and are listed in Appendix Table A7. These probabilities were obtained by Kumar et. al (2021) from epidemiologic models of chlamydia and gonorrhea incidence and prevalence.[15,16] All probabilities for the syphilis decision tree

were obtained directly from the Chesson and Peterman (2021)[12] medical cost study and are listed in Appendix Table A8. We did not make any changes to these probabilities, ranges, or distributions.

Additional results and data

The complete results from the one-way sensitivity analyses are provided in Appendix Table A9 for chlamydia and gonorrhea and in Appendix Table A10 for syphilis. Appendix Table A11 provides unrounded values for the syphilis cost inputs for those who want to replicate our calculations more precisely.

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Appendix Table A1. Estimated productivity cost per case of pelvic inflammatory disease (PID): number of disability days, cost, probability, and timing assumptions for acute PID, chronic pelvic pain, ectopic pregnancy, and infertility

Outcome	Number of days of productivity lost*	Productivity cost, not discounted	Number of years from infection to outcome	Productivity cost, discounted to time of infection	Probability of outcome, per case of PID	Contribution to total discounted lifetime productivity cost per case of PID
Acute pelvic inflammatory disease (PID)	11.2	$1,590	0	$1,590	1	$1,590
Chronic pelvic pain	10.6	$1,505	2	$1,419	0.18	$255
Ectopic pregnancy	28	$3,976	5	$3,430	0.076	$261
Infertility	14	$1,988	10	$1,479	0.045	$67
Total						$2,173

*The number of days of productivity loss per outcome was obtained from Blandford and Gift (2006). The values shown for acute PID and chronic pelvic pain reflect the assumption of 10 lost days per case treated on an outpatient basis and 21 lost days per case treated on an inpatient basis along with the assumption that the probability of outpatient treatment is 89.5% for acute PID and 94.4% for chronic pelvic pain.

The productivity cost per day of productivity lost was $142 (range: $107–$196) and includes market (paid) and non-market (non-paid) productivity among teenagers and young adults.[1]

The number of years from infection to outcome and the probability of each outcome per case of PID were both obtained from Kumar and colleagues (2021); the value shown for the probability of productivity losses for infertility given PID reflects the product of a 10% probability of infertility and a 45% probability of seeking treatment given infertility.

Costs were discounted using a 3% annual discount rate as is common in US health economic studies.[17]

The total average cost per case was $2,173. Blandford and Gift (2006) suggested a range of plus or minus 50% for the number of disability days; this range, when combined with a range of $107–$196 for the productivity cost per day, yields a range of $819–$4,499 for our average productivity cost per case of PID. That is, $819 reflects multiplication of $2,173 by 50% and 75.4% (where 50% is the adjustment for number of

disability days and 75.4%, or $107/$142, is the adjustment for the cost per disability day). Similarly, $4,499 reflects multiplication of $2,173 by 150% and 138.0% (where 150% is the adjustment for number of disability days and 138.0%, or $196/$142, is the adjustment for the cost per disability day).

Appendix Table A2. Number of visits to clinic or other outpatient settings, number of hospital days, number of long-term care years, and number of life years lost for outcomes of syphilis, per infection

Outcome	Number of clinic visits	Number of hospital days	Number of long-term care years	Number of years of life lost
Treated for P&S or early non-P&S syphilis	2.25	0	0	0
Treated for early neurosyphilis/ocular syphilis	9.44	2.56	0	0
Treated for late syphilis or syphilis of unknown duration	4.12	0	0	0
Treated for late benign syphilis	5	0	0	0
Treated for cardiovascular syphilis	21.39	3	0	8.22
Treated for tabes dorsalis	18.39	10	0	8.22
Treated for meningovascular syphilis	1	15.18	1.04	8.22
Treated for general paresis	3	10	3.39	13.03

The numbers of outcomes have been discounted to the time of onset of diagnosis and treatment. For example, the average patient diagnosed with general paresis (bottom row) will lose an estimated 13.03 discounted years of life (discounted to the time of diagnosis and treatment of general paresis).

Assumptions regarding the number of medical visits, hospitalization days, years of long-term care, and years of life lost were calculated based primarily on the resource use assumptions described in the Chesson and Peterman (2021) medical cost study (see also the technical appendix to that study for details on the resource use assumptions).[12]

Appendix Table A3. Productivity cost of visits to clinic or other outpatient settings, hospital days, long-term care years, years of life lost, and average cost per outcome of syphilis: Illustration of calculation of base-case values

Outcome	Cost of clinic visits	Cost of hospital days	Cost of long-term care years	Cost of years of life lost	Total cost per outcome
Treated for P&S or early non-P&S syphilis	$148	$0	$0	$0	$148
Treated for early neurosyphilis/ocular syphilis	$620	$364	$0	$0	$984
Treated for late syphilis or syphilis of unknown duration	$271	$0	$0	$0	$271
Treated for late benign syphilis	$328	$0	$0	$0	$328
Treated for cardiovascular syphilis	$1,405	$426	$0	$411,115	$412,946
Treated for tabes dorsalis	$1,208	$1,420	$0	$411,115	$413,743
Treated for meningovascular syphilis	$66	$2,156	$52,015	$411,115	$465,351
Treated for general paresis	$197	$1,420	$169,547	$651,682	$822,847

Costs are in 2023 US dollars. See Appendix Table A11 for unrounded results. The costs in this table have been discounted to the time of onset of diagnosis and treatment.

Appendix Table A4. Productivity cost of syphilis outcomes, discounted to time of treatment and discounted to time of infection

Outcome	Cost of outcome, discounted to time of treatment	Number of years from infection to initiation of treatment	Cost of outcome, discounted to time of infection
Treated for P&S or early non-P&S syphilis	$148	0	$148
Treated for early neurosyphilis/ocular syphilis	$984	1	$955
Treated for late syphilis or syphilis of unknown duration	$271	1	$263
Treated for late benign syphilis	$328	30	$135
Treated for cardiovascular syphilis	$412,945	30	$170,128
Treated for tabes dorsalis	$413,742	30	$170,456
Treated for meningovascular syphilis	$465,351	30	$191,718
Treated for general paresis	$822,847	30	$339,002

Costs are in 2023 US dollars.

Appendix Table A5. Productivity cost per occurrence of outcomes in the syphilis decision tree model

Outcome	Cost of outcome, discounted to time of infection	Notes*
Treated for P&S or early non-P&S syphilis, no early neurosyphilis/ocular syphilis	$148	
Treated for P&S or early non-P&S syphilis, and early neurosyphilis/ocular syphilis	$1,103	Calculated as $148 + $955
Treated for late syphilis/unknown duration, no early neurosyphilis/ocular syphilis	$263	
Treated for late syphilis/unknown duration, and early neurosyphilis/ocular syphilis	$1,218	Calculated as $263 + $955
Treated for syphilis but not reported as a case	$190	Calculated as (0.63 x $148) + (0.37 x $263)
Treated inadvertently, or unrelated death within 30 years, or both	$0	
Latent syphilis, no adverse outcomes, no treatment costs	$0	
Treated for late benign syphilis	$135	
Treated for cardiovascular syphilis	$170,128	
Treated for tabes dorsalis	$170,456	
Treated for meningovascular syphilis	$191,718	
Treated for general paresis	$339,002	

*See Appendix Table A4 for additional information, including a description of the value $955 applied for early neurosyphilis/ocular syphilis. This table contains similar information to Table A4, except that it is formatted to show the cost of outcomes in the syphilis decision tree model as presented in Table 3 of the manuscript. The calculations presented in the "Notes" column are described in more detail in Chesson and Peterman (2021).[12]

Costs are in 2023 US dollars.

Appendix Table A6. Probabilities used in decision tree analysis of the lifetime medical cost of chlamydia and gonorrhea in men and women, per infection: Base case value (range)

Model input	Chlamydia		Gonorrhea	
	Men	**Women**	**Men**	**Women**
Probabilities*				
Probability that infection is symptomatic	0.158	0.254	0.589	0.314
	(0.082–0.262)	(0.177–0.344)	(0.314–0.830)	(0.155–0.510)
Probability of treatment, symptomatic infection	0.936	0.894	0.744	0.750
	(0.893–0.967)	(0.855–0.931)	(0.621–0.846)	(0.631–0.846)
Probability of treatment, asymptomatic infection	0.137	0.241	0.020	0.068
	(0.092–0.213)	(0.208–0.276)	(0.012–0.034)	(0.043–0.111)
Probability of sequelae, treated symptomatic infection†	0.00	0.00	0.00	0.00
Probability of sequelae, treated asymptomatic infection	0.00	0.06	0.00	0.06
		(0.01–0.12)		(0.01–0.12)
Probability of sequelae, untreated infection	0.02	0.12	0.02	0.12
	(0.01–0.04)	(0.02–0.24)	(0.01–0.04)	(0.02–0.24)

*These probabilities were taken directly from Kumar et al. (2021)[10] who obtained them from epidemiologic models of chlamydia and gonorrhea incidence and prevalence.[15,16] For each input, the lower bound, base case, and upper bound values we applied corresponded to the 2.5th percentile, median, and 97.5th percentile, respectively, from the source study.

As in Kumar et al. (2021),[10] for gonorrhea and chlamydia the probability of sequelae following treatment of symptomatic infections was 0, under the reasoning that these infections are likely treated promptly; and the probability of epididymitis was 0 for treated infections (asymptomatic and symptomatic.

Appendix Table A7: Distributions used for probabilities in probabilistic sensitivity analyses of the productivity costs of chlamydia and gonorrhea

Parameter	Chlamydia		Gonorrhea	
	Males	**Females**	**Males**	**Females**
Probability that infection is symptomatic	Beta	Beta	Beta	Beta
	(9.81, 52.28)	(26.26, 77.14)	(7.64, 5.33)	(7.93, 17.33)
Probability of treatment, symptomatic infection	Beta	Beta	Beta	Beta
	(156.40, 10.69)	(224.49, 26.62)	(42.27, 14.54)	(46.00, 15.33)
Probability of treatment, asymptomatic infection	Beta	Beta	Beta	Beta
	(16.86, 106.23)	(146.26, 460.62)	(12.43, 608.85)	(14.25, 195.36)
Probability of sequelae, treated asymptomatic infection	not varied	Beta	not varied	Beta
	(always 0)	(4.24, 66.39)	(always 0)	(4.24, 66.39)
Probability of sequelae, untreated infection	Beta	Beta	Beta	Beta
	(6.67, 326.97)	(3.90, 28.62)	(6.67, 326.97)	(3.90, 28.62)

These values were obtained directly from Kumar and colleagues (2021) as described in their manuscript appendix.[10] The values in parentheses for the Beta distributions are the α and β shape parameters.

Appendix Table A8. Probabilities applied in syphilis decision tree: Base case value, lower bound, upper bound, and distribution assumptions

Outcome	Base case value	Lower bound value	Upper bound value	Distribution used in probabilistic sensitivity analysis
Probability that infection is reported as a case	0.800	0.650	0.950	Beta (21.05, 5.26)
Probability of treatment for P&S or early non-P&S syphilis, among those with reported syphilis	0.630	0.460	0.810	Beta (17.79, 10.45)
Probability of early symptomatic neurosyphilis or ocular syphilis, among those with reported syphilis	0.032	0.004	0.078	Beta (2.75, 83.17)
Probability of remaining alive and still infected 30 years after acquisition, among those not reported as cases ("probability of incurring long-term sequelae costs")	0.033	0.016	0.091	Beta (2.84, 83.33)
Among those not reported as a case and who do not remain alive and still infected 30 years after acquisition, the proportion treated for syphilis	0.750	0.250	1	Beta (3.09, 1.03)
Probability of latent syphilis in those still infected after 30 years	0.680	0.480	0.880	Beta (13.53, 6.37)
Probability of late benign syphilis in those still infected after 30 years*	0.160	NA	NA	NA
Probability of cardiovascular syphilis in those still infected after 30 years*	0.090	NA	NA	NA
Probability of tabes dorsalis in those still infected after 30 years*	0.020	NA	NA	NA
Probability of meningovascular syphilis in those still infected after 30 years*	0.030	NA	NA	NA
Probability of general paresis in those still infected after 30 years*	0.020	NA	NA	NA

NA: Not applicable.

These values were obtained directly from Chesson and Peterman (2021).[12] The values in parentheses for the Beta distributions are the α and β shape parameters.

*The probabilities of late benign syphilis, cardiovascular syphilis, tabes dorsalis, meningovascular syphilis, and general paresis were not varied directly in the sensitivity analyses but instead were varied indirectly when the probability of latent syphilis (P_{latent} = 0.68 in the base case) was varied. In all sensitivity analyses, the probabilities of late benign syphilis, cardiovascular syphilis, tabes dorsalis, meningovascular syphilis, and general paresis calculated so that they (1) summed to 1 - P_{latent} and (2) maintained their same relative proportion to one another as in the base case (e.g., the probability of late benign syphilis was always 8 times the probability of tabes dorsalis).

Appendix Table A9: Complete results of one-way sensitivity analysis of productivity costs of chlamydia and gonorrhea: Estimated productivity cost when varying one model parameter value at a time, holding all other parameters at their base case values.

Parameter varied	Estimated productivity cost per infection			
	Men		Women	
	Lower value applied	Higher value applied	Lower value applied	Higher value applied
Chlamydia				
Probability that infection is symptomatic	$25	$32	$217	$191
Probability of treatment, symptomatic infection	$27	$28	$207	$203
Probability of treatment, asymptomatic infection	$26	$31	$206	$203
Probability of sequelae, treated asymptomatic infection	$28	$28	$185	$228
Probability of sequelae, untreated infection	$23	$38	$76	$359
Productivity cost of treatment of infection	$18	$45	$190	$231
Productivity cost of sequelae	$21	$39	$94	$395
Gonorrhea				
Probability that infection is symptomatic	$27	$46	$234	$184
Probability of treatment, symptomatic infection	$33	$40	$219	$206
Probability of treatment, asymptomatic infection	$37	$37	$213	$210
Probability of sequelae, treated asymptomatic infection	$37	$37	$207	$218
Probability of sequelae, untreated infection	$33	$45	$56	$399
Productivity cost of treatment of infection	$20	$66	$201	$230
Productivity cost of sequelae	$32	$46	$91	$419

Costs are in 2023 US dollars.

Appendix Table A10: Complete results of one-way sensitivity analysis of productivity costs of syphilis: Estimated productivity cost when varying one model parameter value at a time, holding all other parameters at their base case values

Parameter varied	Productivity cost	
	Lower value applied	Higher value applied
Probability that infection is eventually reported as a case	$553	$268
Of cases reported, probability of treatment in P&S stage or early non-P&S stage	$429	$391
Among those with reported syphilis, probability of early symptomatic neurosyphilis or ocular syphilis	$389	$446
Probability of incurring long-term sequelae*	$305	$772
Among those not reported as a case and who do not remain untreated for 30+ years, the proportion treated for syphilis	$392	$420
Probability of latent syphilis, full life, no complications in those untreated for 30+ years after infection	$540	$282
Productivity cost of treating P&S syphilis or early non-P&S syphilis	$353	$532
Productivity cost of treating syphilis of unknown duration or late syphilis	$350	$537
Productivity cost per case of early neurosyphilis and ocular syphilis	$397	$438
Productivity cost per case of late benign syphilis	$411	$411
Productivity cost per case of cardiovascular syphilis	$370	$478
Productivity cost per case of tabes dorsalis	$402	$426
Productivity cost per case of meningovascular syphilis	$396	$436
Productivity cost per case of general paresis	$393	$440
Number of years of discounting	$581	$315

P&S: primary & secondary.

*This probability is described as "the probability of remaining alive and still infected 30 years after acquisition, among those not reported as cases" in the Chesson and Peterman study (2021)[12] and corresponds to the value of 0.033 near the bottom center of Supplemental Figure 2.

Costs are in 2023 US dollars.

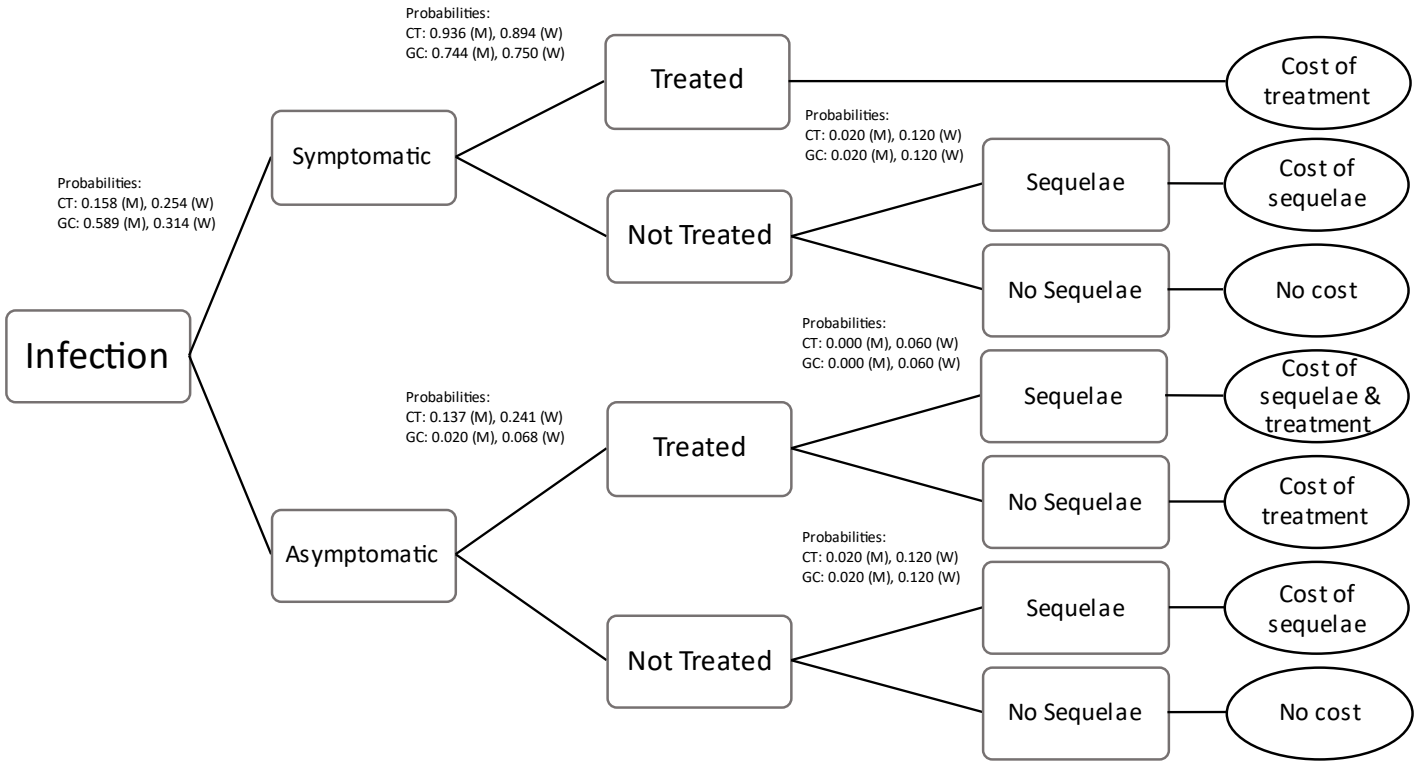
Appendix Table A11. Unrounded productivity costs of syphilis outcomes

Outcome	Base case	Lower bound value	Upper bound value
Treated for P&S or early non-P&S syphilis	$147.78	$50.58	$351.32
Treated for early neurosyphilis/ocular syphilis	$983.54	$431.35	$2,076.11
Treated for late syphilis or syphilis of unknown duration	$270.60	$92.62	$643.31
Treated for late benign syphilis	$328.40	$112.40	$780.72
Treated for cardiovascular syphilis	$412,945.32	$248,659.20	$686,376.29
Treated for tabes dorsalis	$413,742.28	$249,190.96	$687,554.26
Treated for meningovascular syphilis	$465,350.88	$280,610.90	$772,387.97
Treated for general paresis	$822,846.92	$496,163.78	$1,365,824.93

The costs in this table have been discounted to the time of onset of treatment. These unrounded estimates are provided for readers who want to replicate the calculations in the manuscript more precisely. The base case values shown here in the first column correspond to the rounded results in Appendix Table A3. The lower bound values were obtained by applying the lower bound value of any applicable cost input (cost per medical visit, cost per hospitalization day, cost per year of long-term care, and cost per year of life lost) and by multiplying the resulting cost estimate by 0.8 to account for uncertainty in the number of resources acquired. The upper bound value was obtained by applying the upper bound value of any applicable cost input (cost per medical visit, cost per hospitalization day, cost per year of long-term care, and cost per year of life lost) and by multiplying the resulting cost estimate by 1.2 to account for uncertainty in the number of resources acquired.

Costs are in 2023 US dollars.

Supplemental Figure 1: Decision tree model used to estimate productivity cost of chlamydia and gonorrhea

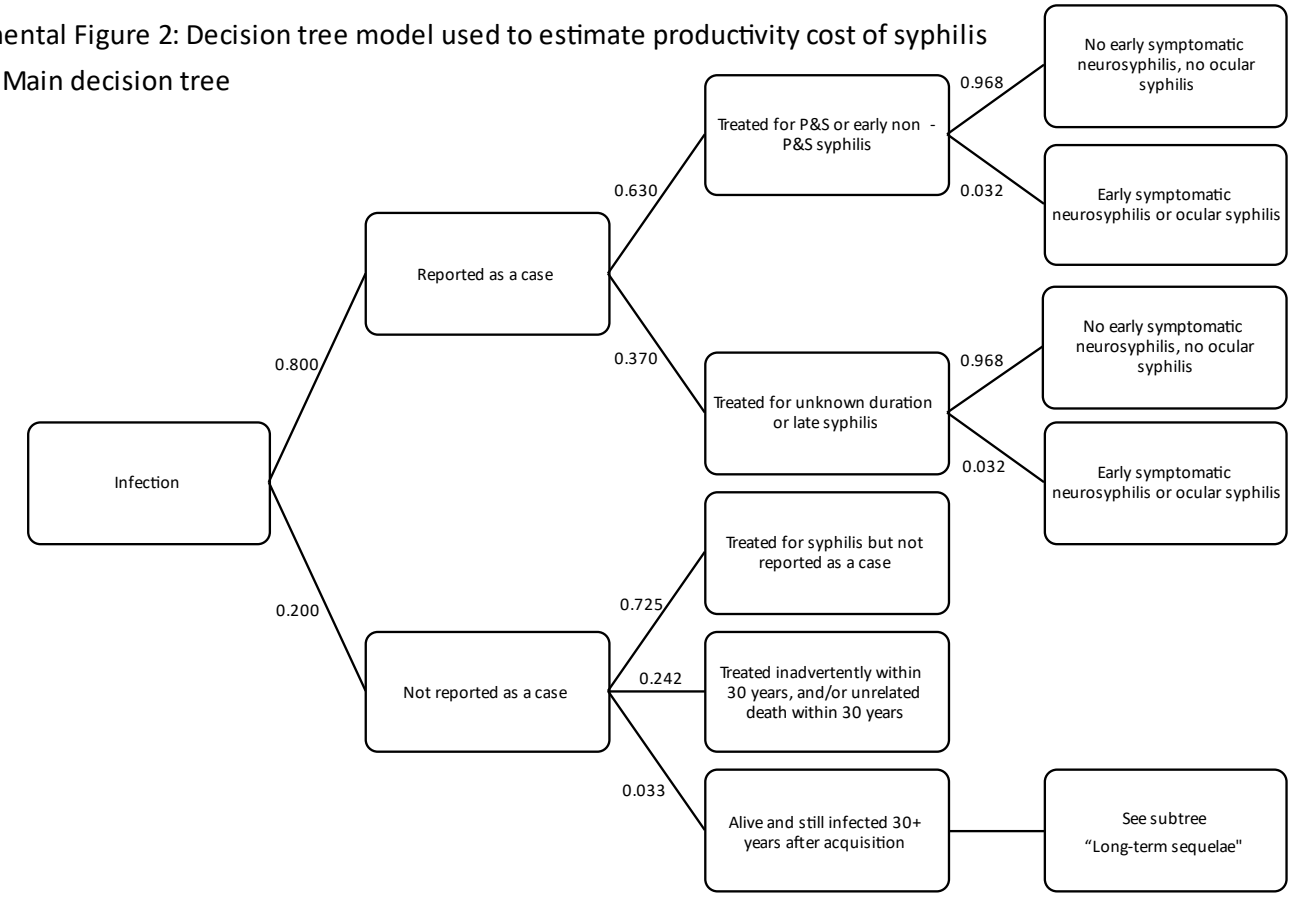


Supplemental Figure 1: This decision tree model of the possible outcomes of infection was obtained directly from Kumar et al. (2021), except that we added the base case probabilities of the outcomes. Following the approach used in that study we included the possibility of sequelae in men (epididymitis) and women (pelvic inflammatory disease, which included the possibility of chronic pelvic pain, ectopic pregnancy, and infertility). For each outcome, the base case probabilities are shown for both STIs, by sex. For example, for symptomatic chlamydial infections, the probability of receiving treatment is 0.936 for men and 0.894 for women; the probability of not receiving treatment (not shown) is 1 - 0.936 for men and 1 - 0.894 for women. Abbreviations: CT: Chlamydia; GC: gonorrhea; M: men; W: women

Reference: Kumar S, Chesson HW, Spicknall IH, Kreisel KM, Gift TL. The Estimated Lifetime Medical Cost of Chlamydia, Gonorrhea, and Trichomoniasis in the United States, 2018. Sex Transm Dis. 2021;48(4):238-46.

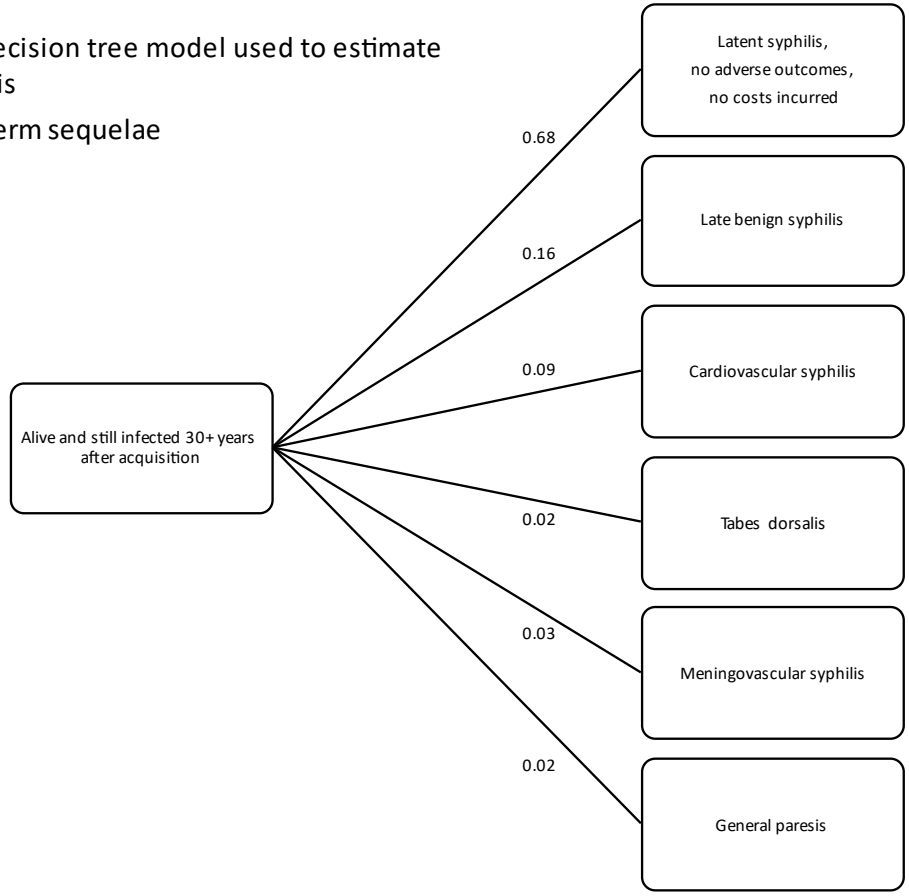
Supplemental Figure 2: Decision tree model used to estimate productivity cost of syphilis

Panel A: Main decision tree



Supplemental Figure 2: Decision tree model used to estimate productivity cost of syphilis

Panel B: Subtree of long-term sequelae



Supplemental Figure 2: This decision tree model of the possible outcomes of infection was obtained directly from Chesson and Peterman (2021). The outcome "Not reported as a case" refers to those who are not reported as a case within 30 years of infection; people in this group include those who are treated for syphilis but not reported as a case, those treated inadvertently through receipt of antibiotics for purposes other than syphilis treatment, those with an unrelated death prior to long-term sequelae, and those who are still alive and infected 30 years after acquiring infection. For simplicity, the probability of remaining alive and still infected 30 years after acquisition, among those not reported as a case, is referred to in the sensitivity analysis as "the probability of incurring long-term sequelae costs." The numbers shown are the base case probabilities applied in the analysis. For example, of all infections, we assumed 80% would be reported as a case, of which 63% would be treated in the primary and secondary (P&S) or early non-P&S stage and the remaining 37% would be treated in the unknown duration or late syphilis stage.

Abbreviations: P&S: primary and secondary

Reference: Chesson HW, Peterman TA. The Estimated Lifetime Medical Cost of Syphilis in the United States. Sex Transm Dis. 2021;48(4):253-59.