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# The Estimated Direct Lifetime Medical Costs of Sexually Transmitted Infections Acquired in the United States in 2018

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## Abstract

**Background:** We estimated the lifetime medical costs attributable to STIs acquired in 2018, including sexually acquired HIV.

**Methods:** We estimated the lifetime medical costs of infections acquired in 2018 in the United States for eight STIs: chlamydia, gonorrhea, trichomoniasis, syphilis, genital herpes, human papillomavirus (HPV), hepatitis B, and HIV. We limited our analysis to lifetime medical costs incurred for treatment of STIs and for treatment of related sequelae; we did not include other costs such as STI prevention. For each STI except HPV, we calculated the lifetime medical cost by multiplying the estimated number of incident infections in 2018 by the estimated lifetime cost per infection. For HPV, we calculated the lifetime cost based on the projected lifetime incidence of health outcomes attributed to HPV infections acquired in 2018. Future costs were discounted at 3% annually.

**Results:** Incident STIs in 2018 imposed an estimated $15.9 billion ($25^{th}$–$75^{th}$ percentile: $14.9–16.9 billion) in discounted, lifetime direct medical costs (2019 U.S. dollars). Most of this cost was

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due to sexually acquired HIV ($13.7 billion) and HPV ($0.8 billion). STIs in women accounted for about one-fourth of the cost of incident STIs when including HIV, but about three-fourths when excluding HIV. STIs among 15–24-year-olds accounted for $4.2 billion (26%) of the cost of incident STIs.

**Conclusions:** Incident STIs continue to impose a considerable lifetime medical cost burden in the United States. These results can inform health economic analyses to promote the use of cost-effective STI prevention interventions to reduce this burden.

## Short Summary

In the United States in 2018, incident sexually transmitted infections (including sexually acquired HIV) imposed an estimated $15.9 billion ($25^{th}$–$75^{th}$ percentile: $14.9–16.9 billion) in lifetime direct medical costs.

### Keywords

sexually transmitted infections; cost; burden of disease

## Introduction

Estimates of the direct medical cost of sexually transmitted infections (STIs) are important to the field of STI prevention. Cost estimates can help quantify the burden of STIs in the United States, illustrate the scope of need and provide justification for public health interventions to prevent and control STIs, and inform a wide range of health economic studies, such as cost-effectiveness analyses of STI prevention interventions. Medical costs of STIs include not only the costs associated with treatment of infection, but also the costs of treatment of sequelae. Examples of costly sequelae include pelvic inflammatory disease (PID) caused by chlamydia and gonorrhea, cervical and other cancers caused by human papillomavirus (HPV), opportunistic infections caused by human immunodeficiency virus (HIV), and liver cirrhosis caused by hepatitis B.

Estimates of the lifetime medical cost of incident STIs in the United States have been updated several times over the past 25 years, most recently for 2008.[1–4] Over time, estimates of the annual medical cost of STIs can become outdated due to changes in the annual number of incident infections and the average lifetime medical cost per infection. For example, HPV vaccination was introduced in the United States in 2006 and has had a notable impact on HPV prevalence and disease associated with the HPV types targeted by the vaccine.[5] Similarly, changes in health care technology and service delivery can affect the cost of treating STIs and related sequelae.[4,6,7] Further, STI prevention activities such as screening and treatment can reduce not only the number of new infections over time,[8] but also the average lifetime cost per infection by reducing the probability of costly sequelae.

Given the availability of STI incidence estimates for 2018[9] and updated estimates of the average lifetime medical cost per infection,[10–13] our goal was to provide updated estimates of the medical cost burden of STIs. Specifically, we estimated the expected lifetime direct medical costs of STIs acquired in 2018 in the United States, including sexually acquired HIV.

## Overview of Methods and Data Sources Used

We estimated the lifetime medical costs attributable to infections acquired in the United States in 2018 through sexual contact for eight STIs: *Chlamydia trachomatis* (chlamydia), *Neisseria gonorrhoeae* (gonorrhea), *Trichomonas vaginalis* (trichomoniasis), *Treponema pallidum* (syphilis), genital herpes (due to herpes simplex virus type 2, HSV-2), HPV, hepatitis B virus (HBV), and HIV. For HBV and HIV, we included only infections attributed to sexual transmission. Specifically, the HIV incidence estimates we applied included infections in the "male-to-male sexual contact" and "heterosexual contact" transmission categories but excluded those in the "injection drug use" and "male-to-male sexual contact and injection drug use" categories.

### Focus on direct medical costs of STIs

We limited our analysis to lifetime medical costs incurred for treatment of STIs acquired in 2018 and for treatment of sequelae of STIs acquired in 2018. However, we did not include medical costs associated with maternal transmission (e.g., congenital syphilis, neonatal herpes). We also did not include costs of STI prevention (e.g., surveillance, contact tracing), lost productivity, and other non-medical costs of STIs. Because STI prevention costs were excluded, we did not include STI screening costs. However, we did include some diagnostic testing costs incurred by persons with STIs, which could include the cost of a screening test that yielded a positive result and/or subsequent diagnostic tests necessitated by the positive result, as was done in previous analyses.[2,4] The cost papers in this Special Issue provide more precise descriptions of the costs included for specific STIs.

### Multiplying the number of infections by the lifetime cost per infection

For each STI except HPV, we calculated the lifetime medical cost of incident infections by multiplying the estimated number of incident infections in 2018 by the estimated lifetime cost per infection. Estimates of the number of incident infections in 2018 were obtained from the study by Kreisel and colleagues[9] in this Special Issue (Table 1). Estimates of the lifetime cost per infection were obtained from cost studies that follow in this Special Issue for chlamydia,[10] gonorrhea,[10] trichomoniasis,[10] syphilis,[11] genital herpes,[12] and HIV[13] (Tables 1 and 2). The inclusion of these cost studies in this Special Issue allows for a detailed description of the methods used to arrive at the estimated lifetime cost per infection for each of these STIs, along with extensive documentation of data sources and assumptions. For HBV, we obtained estimates of the lifetime cost per infection from studies published elsewhere;[4,14] there is no separate cost study of HBV in this Special Issue. For HPV, we did not apply an estimate of the lifetime cost per infection. Instead, we used the estimated total cost of HPV infections acquired in 2018, which we obtained from a study in this Special Issue that estimated the lifetime number and cost of diagnosed cases of disease attributable to HPV infections acquired in 2018.[15]

### Discounting future costs

All costs are expressed in 2019 US dollars unless otherwise noted. The lifetime cost estimates we applied represented the average lifetime medical cost per infection, discounted

at an annual rate of 3% to the time of infection. Discounting is a standard practice in health economic studies and allows for future costs to be expressed in terms of present value.[16]

### Point estimates and uncertainty intervals

In estimating the lifetime medical costs of STIs acquired in 2018, we first calculated a base case cost estimate (a single point estimate) and then calculated uncertainty intervals using the 25$^{th}$ and 75$^{th}$ percentiles (described below). For HPV, the base case estimate of the lifetime cost of infections acquired in 2018 was obtained directly from the HPV cost study.[15] For each STI other than HPV, the base case estimate was calculated by multiplying the median incidence estimate of the given STI as described in the Kreisel study[9] by the base case estimate of the lifetime cost per infection for the given STI.

Our general approach for calculating uncertainty intervals, for each STI other than HPV, was to perform 10,000 Monte Carlo simulations of the lifetime medical costs of incident infections in 2018, each time drawing a random value for the estimated number of incident infections (following methods described elsewhere[9]) which we multiplied by a random value for the estimated lifetime cost per infection obtained as described in Table 2. This process resulted in 10,000 estimates of the lifetime cost of incident infections in 2018 for each STI (other than HPV), and we calculated the uncertainty intervals as the 25$^{th}$ and 75$^{th}$ percentiles of these estimates. For HPV, we obtained 10,000 estimates of the lifetime cost of diseases attributable to infections acquired in 2018 from the probabilistic sensitivity analyses reported in the HPV cost manuscript.[15] To calculate uncertainty intervals for the total estimated cost of all STIs acquired in 2018, we obtained 10,000 simulations of the total cost by combining the sets of 10,000 results for each STI.[9]

### Chlamydia, gonorrhea, and trichomoniasis

The base case values for the estimated lifetime cost per infection for men and women, respectively, were $46 and $262 for chlamydia, $78 and $254 for gonorrhea, and $5 and $36 for trichomoniasis (Table 1).[10] The decision tree models for these three STIs incorporated probability and cost data from recent studies. Values for the probability that the infection is symptomatic, the probability of treatment for symptomatic infections, and the probability of treatment for asymptomatic infections were obtained for chlamydia, gonorrhea, and trichomoniasis from the respective models of these STIs described in this Special Issue.[17,18] Estimates of the medical cost of treatment of infection for chlamydia, gonorrhea, and trichomoniasis were obtained from recent analyses of medical claims data.[7,19] For chlamydia and gonorrhea, the decision trees also included the possibility of epididymitis in men and PID in women.

### Syphilis

The base case value for the estimated lifetime cost per infection was $1,190 for men and women (Table 1).[11] The decision tree model allowed for numerous possible outcomes of infection, including treatment at various stages, inadvertent treatment through receipt of antibiotics for a condition other than syphilis, unrelated death prior to onset of sequelae, and late syphilis outcomes in those who are alive and still infected 30 years after infection. The probabilities assigned in the decision tree were selected to yield outcomes consistent with

two main national sources of data: STI surveillance data (regarding the number of reported cases of syphilis by stage) and mortality data (regarding the number of deaths attributable to syphilis each year). All cost estimates applied in the decision tree were updated using data from published studies.

### Genital Herpes

For genital herpes (attributed to HSV-2), the base case values for the estimated lifetime medical cost per infection for men and women were $156 and $169 respectively (Table 1).[12] A key assumption behind these estimates was that 17% of people with genital herpes would incur medical costs as a result of their infection;[20] the remaining 83% would incur no medical costs. For those incurring medical costs, the average lifetime cost per diagnosed case of genital herpes was $920 for men and $996 for women,[12] based on medical claims data for a cohort of commercially insured individuals continuously enrolled for at least 4 years during 2010–2018.

The medical claims data yielded estimates of: (1) the cost of an initial clinical visit (stratified by inpatient and outpatient status), (2) the probability that the initial visit was inpatient (vs. outpatient); (3) the number and cost of follow-up clinical visits for each of the three years following an initial visit; (4) the cost of drugs for the treatment of genital herpes for each of the three years following an initial visit; and (5) trends in resource use in the three years following an initial visit, for use in projecting lifetime costs beyond the first three years.

### Human Papillomavirus (HPV)

Our approach for HPV differed from that of all other STIs. Rather than multiplying the estimated number of HPV infections in 2018 by the estimated lifetime cost per infection, the HPV cost study estimated the lifetime number of diagnosed cases of disease (genital warts; cervical intraepithelial neoplasia; and cervical, vulvar, vaginal, penile, anal, and oropharyngeal cancers) that would result from HPV infections acquired in 2018.[15] The HPV-ADVISE model[21] applied in the HPV cost study is a dynamic, individual-based model of HPV infection and disease that has been calibrated to a wide range of U.S. data (e.g., sexual behavior, cervical cancer screening behavior, HPV prevalence, and cancer incidence). Cost estimates were informed by a 2019 review of medical care cost estimates for HPV-associated cancer,[22] and included data from several cost studies published in 2017 or later.[23–27]

### Hepatitis B (HBV)

The estimated discounted lifetime cost per HBV infection was calculated as the average value from two published studies. From Owusu-Edusei et al. (2013),[4] we obtained a base case estimate of $3,040 (range: $2,470–3,330). From Hoerger et al. (2014),[14] we obtained a base case estimate of $8,020 (range: $6,010–10,020). The average of these two base case estimates was $5,530. Health economics guidelines suggest using a broad range of possible values in sensitivity analyses when there is little information available on a parameter.[16,28] To ensure that we used the broadest range of values suggested by these studies, we applied the lower bound value from the Owusu-Edusei study and the upper bound value from the Hoerger study.

The distribution parameters we applied for the lognormal distribution (Table 2) were calculated such that the average value from this distribution would be consistent with the base case value of $5,530 and about 95% of random draws from this distribution would fall between the lower bound value of $2,470 and the upper bound value of $10,020.[29] Existing guidelines for model parameter estimation suggest that it is reasonable for the 95% confidence interval of the distribution to reflect the lower and upper bound values of the range.[28]

### Human Immunodeficiency Virus (HIV)

The base case values for the estimated lifetime medical cost per infection for men and women was $420,285.[13] The HIV cost study used an updated version of PATH 3.0 (Progression and Transmission of HIV), an agent-based model that allows for the analysis of individual-level disease progression and transmission, to estimate the lifetime treatment cost of persons with HIV (PWH). The model, which represents a cross section of PWH in the United States, was calibrated using 2006–2015 surveillance data.

The model was stratified by age, sex, and transmission risk group. The model allowed for persons with HIV to be at any one of the following stages of the HIV care continuum: acutely infected, but not aware; non-acutely infected and unaware; aware, but not in care; in care, but not virally suppressed; and in care and virally suppressed. The PATH model analyzed a cohort of PWH infected in 2015, simulated the cohort until all persons had died, and estimated average lifetime treatment costs discounted to the time of infection. Costs estimates applied in the PATH model were based on published studies.

## STI-attributable HIV costs

For illustrative purposes only, we included an assessment of the number and cost of STI-attributable HIV infections. These estimates, however, had no effect on our estimate of the total lifetime cost of STIs acquired in 2018. Because our total cost estimate included the cost of sexually acquired HIV infections, of which STI-attributable HIV infections are a subset, the cost of STI-attributable HIV infections would have been double-counted had they been included as a separate component of the total cost estimate in addition to the costs of all sexually acquired HIV infections.

We obtained estimates of the number and cost of HIV infections attributable to other STIs from multiple modeling studies, as compiled and calculated elsewhere in this Special Issue.[30] An estimated 2,489 HIV infections in 2018 among MSM could be attributed to gonorrhea and chlamydia, at an estimated lifetime cost of $1.05 billion.[30] The 2,489 result was calculated as 24,400 multiplied by 10.2%, where 24,400 is the estimated number of HIV infections acquired in 2018 through male-to-male sexual contact[31] and 10.2% is the estimated percent of HIV infections among MSM attributable to the facilitative effects of chlamydia and gonorrhea on HIV transmission and acquisition.[32] Using another modeling approach, an estimated 2,349 HIV infections in the general population (including MSM) could be attributed to chlamydia, gonorrhea, syphilis, and trichomoniasis acquired in 2018, at an estimated lifetime cost of $0.99 billion.

## Overall Estimate of STI Costs

Across all age groups, the estimated total lifetime cost of incident STIs acquired in 2018 through sexual contact was $15.9 billion ($25^{th}$–$75^{th}$ percentile: $14.9–16.9 billion), of which about $13.7 billion was for HIV, $0.8 billion was for HPV, and $1.0 billion was for chlamydia and gonorrhea combined (Table 3). When excluding HIV, the lifetime cost of incident STIs was $2.2 billion, of which about $1.6 billion was attributable to STIs in women. For persons aged 15–24 years, the total cost of incident STIs was $4.2 billion ($25^{th}$–$75^{th}$ percentile: $3.9–4.5 billion), of which about $3.0 billion was for HIV, $0.6 billion was for chlamydia and gonorrhea combined, and $0.4 billion was for HPV (Table 3).

## Discussion

We estimated the lifetime medical cost of STIs acquired through sexual contact in 2018 to be $15.9 billion in the United States, including sexually acquired HIV. STIs in women accounted for about one-fourth of this cost burden when including HIV, but about three-fourths of the cost burden when excluding HIV. The $15.9 billion estimate can be interpreted as the lifetime medical costs incurred for treatment of STIs that were acquired in 2018 plus the lifetime medical costs incurred for treating sequelae of STIs that were acquired in 2018, exclusive of costs associated with maternal transmission (e.g., congenital syphilis, neonatal herpes).

Our lifetime medical cost estimates are specific to the context of existing STI prevention activities (including HIV prevention) and screening programs for HPV-associated cancers in the United States. In the absence of STI prevention programs, the number of incident infections in 2018 would likely be substantially higher than the estimates we applied.[33] Examples include the impact of HPV vaccination on the incidence and prevalence of HPV types targeted by the vaccine[5,9] and the impact of chlamydia screening on chlamydia incidence and prevalence.[8] Further, in the absence of STI prevention efforts, the average lifetime medical cost per infection could be notably higher than the estimates we applied. For example, screening women for chlamydia and gonorrhea can reduce the risk of PID, which could in turn reduce the average lifetime medical cost of these infections in women.[7,34] Although estimating the annual cost of STI prevention activities was beyond the scope of this study, evidence suggests that reductions in current investments for STI prevention would result in subsequent increases in lifetime medical costs that could exceed the reductions in investments in prevention.[35–37] Thus, all else equal, we would expect that the cost of incident STIs in future years would be notably higher in the absence of STI prevention efforts than would be expected if current prevention efforts were continued or enhanced. Similarly, all else equal, we would expect the cost of incident STIs in future years to increase under scenarios of population-level changes in sexual behavior, such as decreases in condom usage or increases in the number of sex partners.

Medical costs of treating STIs and related sequalae represent only one component of the economic burden of STIs. As noted, we did not include the costs of STI prevention, without which the lifetime medical cost burden would be even greater than we estimated. We also excluded costs associated with congenital syphilis, neonatal herpes, and other adverse health

outcomes associated with maternal transmission of STIs. Other notable types of costs that we excluded from this analysis were: (1) medical treatment costs that are not attributable to an STI, such as presumptive treatment of a patient who is not actually infected;[38] (2) productivity costs associated with STI morbidity and mortality;[7,39] and (3) intangible costs associated with STI health effects (e.g., pain and suffering), interpersonal effects of STIs (e.g., for couples of discordant genital herpes status);[40] and behavioral effects of STIs (e.g., perceived loss in pleasure associated with condom usage).[41] These types of costs can be difficult or virtually impossible to quantify reliably, but likely far exceed the direct medical costs.

The lifetime medical cost of incident STIs in the United States has been estimated several times, most recently for 2008 and 2000.[1,2,4] Each iteration has followed the general approach of the previous study, while also making notable methodological improvements and incorporating better and more recent data. Because of changes in methods and data sources from one study to the next, these studies are not well-suited for assessing trends in the cost of incident STIs.

Our study of the cost of incident STIs in 2018 made three key improvements over the study of the cost of incident STIs in 2008. First, the estimates of STI incidence that we used for 2018 were based on modeling approaches that are more robust, comprehensive, and transparent than in the previous study, as described in more detail in the source studies.[17,18,42–45] Second, for all STIs examined, with the exception of HBV, we obtained lifetime cost estimates from studies published in this Special Issue.[10–13,15] Because full manuscripts were devoted to estimating the lifetime cost of a single STI or a group of related STIs, the methods, assumptions, and data sources have been described and documented in far more detail than previously. These STI-specific manuscripts also allow for discussion of key STI-specific issues, such as the effect of HIV pre-exposure prophylaxis (PrEP) on the proportion of HIV infections attributable to STIs,[30] declines in the burden of HPV in the HPV vaccination era,[15,43] and potential increases in gonorrhea costs in the future due to increases in antimicrobial resistance.[10,30] Third, we accounted for uncertainty not only in the estimated cost per infection but also in the estimated number of incident infections.

Our approach would be expected to yield a precise, accurate calculation of the lifetime medical costs of STIs acquired in 2018 if we knew (1) the exact number of incident infections of each STI in 2018 and (2) the exact average lifetime medical cost per infection for each STI. Thus, the main limitation of our study is that there are considerable uncertainties in these two key inputs needed for our calculations. Limitations associated with the models that provided the incidence estimates we used include a scarcity of data to inform the model parameters.[17,18,42–45] Similarly, estimates we applied of the lifetime medical cost per infection are limited by uncertainties regarding the cost of treatment, the probability of treatment or uptake of therapy, the probability and cost of sequelae, and other factors, as described in more details in the source manuscripts.[10–13,15] We addressed these unavoidable limitations by calculating ranges for the estimated lifetime cost of STIs acquired in 2018, using an approach specifically designed to reflect the likely impact and magnitude of the effect of the uncertainty in the studies that informed our analysis.

Another difficulty in determining a precise estimate of the lifetime medical cost per infection is that the lifetime cost can vary by age at infection. Given data limitations, we did not apply age-specific lifetime cost estimates. However, the studies from which we obtained our lifetime cost estimates attempted to address this limitation where possible by calculating cost estimates that reflect the age distribution or median age at which infections are acquired, and by applying parameter values to the STI models that reflect the average population values across all relevant age groups.

It is important to note that the base case estimates and ranges we applied for the lifetime cost per infection for each STI were calculated using a 3% annual discount rate for future costs. Applying a lower discount rate would increase the estimated cost burden and applying a higher discount rate would reduce the estimated cost burden. The selection of the discount rate can have a notable effect on lifetime cost estimates for STIs such as HIV and HPV with substantial long-term costs. For example, the base case cost per HIV infection we applied ($420,285, using a 3% discount rate) would have instead been $1,079,999 if future costs were not discounted.[13]

Previous estimates of the medical cost burden of STIs have been used in studies of cost-effectiveness and return on investment of a wide range of STI prevention interventions.[46–49] These previous estimates have also been incorporated in spreadsheet-based tools that allow STI program personnel to estimate the health and economic impact of their program activities.[36,50] Our study, along with the other studies in this Special Issue, can inform updates of these existing tools. Further, we hope that this Special Issue can help to spur the development of new tools that would allow for state and local STI program personnel to estimate the cost burden of STIs in their jurisdictions and the cost-effectiveness of their activities.

Our study is one of few studies estimating the lifetime cost of incident STIs in the United States over the past two decades and is the first that accounts for uncertainty in the estimated number of infections and the estimated lifetime medical cost per infection. Despite limitations, our study provides a useful update of the medical cost burden of STIs in the United States. We hope the extensive documentation of the methods and assumptions provided here and in the source studies will inform future health economic studies, including future endeavors to update and improve upon our estimates of the cost burden of STIs.

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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.

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**Table 1.**

Estimates of the Number of Incident STIs in 2018 and the Average Lifetime Medical Cost per Incident STI in the United States

| STI | Number of incident infections in 2018* | | Discounted lifetime cost per incident infection† | |
|---|---|---|---|---|
| | Men | Women | Men | Women |
| Chlamydia | 1,621,000 | 2,354,000 | $46 | $262 |
| Gonorrhea | 697,000 | 853,000 | $78 | $254 |
| Trichomoniasis | 3,278,000 | 3,536,000 | $5 | $36 |
| Syphilis | 121,000 | 25,000 | $1,190 | $1,190 |
| Genital herpes‡ | 300,000 | 260,000 | $156 | $169 |
| HPV | NC§ | NC§ | NC§ | NC§ |
| HBV¶ | NC# | NC# | $5,530 | $5,530 |
| HIV¶ | 26,900 | 5,700 | $420,285 | $420,285 |

STI=sexually transmitted infection; HPV=human papillomavirus; HBV=hepatitis B virus; NC=not calculated; HIV=human immunodeficiency virus.

*The point estimates of the number of incident infections in 2018 were obtained from the median values reported by Kreisel et al. (2021) in this Special Issue.[9] See that study for details on how these numbers were estimated and how they should be interpreted. The ages for which these incident estimates were calculated varied by STI: chlamydia: 15–39 years; gonorrhea: 15–39 years; syphilis: 14–49 years; trichomoniasis: 15–59 years; genital herpes: 15–49 years; HPV: 15–59 years; HBV ≥15 years; HIV: ≥13 years.

†The discounted lifetime cost per infection reflects the average lifetime cost and includes the possibility of incurring treatment costs and/or sequelae costs; future costs were discounted at an annual rate of 3%. For example, the $5 cost for trichomoniasis in men resulted from the decision tree model prediction that 3.3% of infected men would be treated, that treated men would incur a cost of $151 (3.3% × $151 = $5), and that no men would incur sequelae costs. Estimates of the average lifetime cost per infection were obtained from cost studies included in this Special Issue for chlamydia,[10] gonorrhea,[10] trichomoniasis,[10] syphilis,[11] genital herpes,[12] and HIV.[13] The cost per HBV infection was obtained from other published sources[4,14] as described in the text. Costs are in 2019 US dollars. Methods for updating for inflation varied across the studies that informed our cost estimates. Medical cost estimates we obtained from other sources that were not already expressed in 2019 US dollars were updated to 2019 US dollars using the using the personal consumption expenditures price index for health care (https://www.bea.gov/).

‡The estimated lifetime cost per genital herpes infection was not specific to herpes simplex virus (HSV) type 2 or HSV-1. However, the number of incident infections we applied for genital herpes included HSV-2 only, as described in the Kreisel study.[9] Thus, costs of genital herpes attributable to HSV-1 were not included in our estimated cost of genital herpes infections acquired in 2018.

§The cost of incident HPV infections in 2018 was not calculated as the product of the number of incident infections and the average cost per infection. Instead, these costs were calculated using model-based estimates of the lifetime number of diagnosed cases of disease (e.g., genital warts, cervical cancer) attributable to HPV infections acquired in 2018.[15]

¶Incidence estimates for HBV and HIV exclude infections acquired by routes other than sexual contact.

#Incidence estimates for HBV could not be stratified by sex and age group. The median estimated incidence of sexually-acquired HBV infections among persons aged 15 years and older was 8,300.

**Table 2.**

Summary of data sources used to calculate point estimates and ranges of the lifetime medical costs of sexually transmitted infections acquired in 2018

| STI | Source for cost estimates: Lead author* | Model used in source study | Source for cost estimates used in probabilistic sensitivity analysis (PSA)† |
|---|---|---|---|
| Chlamydia, gonorrhea, and trichomoniasis | Kumar[10] | Decision tree model | PSA used in Kumar study[10] |
| Syphilis | Chesson[11] | Decision tree model | PSA used in Chesson study[11] |
| Genital herpes | Eppink[12] | Medical claims cohort | PSA used in Eppink study[12] |
| HPV | Chesson[15] | Individual-level, transmission-dynamic, type-specific model (HPV-ADVISE)‡ | PSA used in Chesson study[15] |
| HBV | Various§ | Decision tree models and Markov models | Lognormal distribution (8.561, 0.338) ¶# |
| HIV | Bingham[13] | Individual-level disease progression model (PATH 3.0) | Lognormal distribution (12.944, 0.099) ¶** |

STI=sexually transmitted infection; PSA=probabilistic sensitivity analysis; HPV=human papillomavirus; HBV=hepatitis B virus; HIV=human immunodeficiency virus; HPV-ADVISE=HPV Agent-based Dynamic model for Vaccination and Screening Evaluation; PATH=Progression and Transmission of HIV.

*For each STI except HPV, the base case estimate of the lifetime medical cost of infections acquired in 2018 was calculated as the number of incident infections multiplied by the average lifetime medical cost per infection. The source for estimated number of infections in 2018 was the Kreisel study[9] in this Special Issue. The source of the estimate for the cost per infection was the study listed in the first column of data. The cost of incident HPV infections acquired in 2018 was calculated using model-based estimates of the lifetime number of diagnosed cases of disease attributable to HPV infections acquired in 2018 as described in the HPV cost study in this Special Issue.[15]

†To generate uncertainty intervals (specifically, 25$^{th}$ and 75$^{th}$ percentiles), we performed a probabilistic sensitivity analysis (PSA) which consisted of 10,000 simulations of the cost of STIs acquired in 2018. For each STI except HPV, 10,000 random values for the estimated number of incident infections were obtained as described in the Kreisel study.[9] For the estimated lifetime cost per case, 10,000 random values were obtained as noted in the final column of the table, from either (1) the PSA used in the source study or (2) a lognormal distribution with STI-specific parameters as described below. For HPV, we did not apply 10,000 estimates of the lifetime cost per infection in the PSA; instead we obtained 10,000 estimates of the total lifetime cost of diseases attributable to HPV infections acquired in 2018 from the PSA described in the HPV cost manuscript.[15] To calculate uncertainty intervals for the total estimated cost of infections acquired in 2018 across all 8 STIs, we combined these 8 sets of 10,000 results following the same approach as described in the Kreisel study[9] (i.e., one column for each STI and 10,000 rows for each estimate of the lifetime cost of incident infections in 2018). Each row was then summed, representing the total cost of incident infections in 2018 across all eight STIs in that row. To clarify, in each of the 10,000 simulations, the total cost of all 8 STIs was calculated as $\Sigma_{i=1}^{i=7} C_i N_i + COSTHPV$, where the subscript i denotes the seven STIs other than HPV (chlamydia, gonorrhea, trichomoniasis, syphilis, genital herpes, HBV, and HIV), C denotes the lifetime cost per infection, N denotes the number of infections in 2018, and COSTHPV denotes the lifetime cost of diseases attributable to HPV infections acquired in 2018. We calculated the uncertainty interval as the 25$^{th}$ and 75$^{th}$ percentiles of these summations.

‡Details of the HPV-ADVISE model are available at https://marc-brisson.net/HPVadvise-US.pdf.

§There is no HBV cost paper in this Special Issue. Instead, we obtained lifetime cost estimates for HBV from Owusu-Edusei et al. (2013)[4] and Hoerger et al. (2014),[14] who reported HBV costs based on cost-effectiveness studies of HBV vaccination that used decision tree models and Markov models.

[¶]The values in parentheses are the lognormal distribution mean and standard deviation parameters μ and σ. We calculated μ as $\ln(b) - 0.5 * \ln(1 + [SE^2/b^2])$, where b is the base case value, SE is the standard error, and ln denotes the natural log.[29] SE was approximated as the difference between the lower and upper bounds of the range, divided by 3.92.[29,51] We calculated σ as the square root of $\ln(1 + [SE^2/b^2])$.[29]

[#]For HBV, the distribution parameters we applied were calculated as described above such that the average value from this distribution would be consistent with the base case value of $5,530 and about 95% of random draws from this distribution would fall between the lower bound of $2,470 and the upper bound of $10,020.[29]

[**]To inform the lognormal distribution for the lifetime cost per HIV infection, we applied a lower bound of $326,411 and an upper bound of $490,045, which reflects the lifetime cost estimate from a least-favorable scenario (a 5% dropout rate, 5-year median diagnosis delay) and a most-favorable scenario (1% dropout rate, a 1-year median diagnosis delay) examined in the HIV cost study.[13] The distribution parameters we applied were calculated as described above such that the average value from this distribution would be consistent with the base case value ($420,285) and about 95% of random draws from this distribution would fall between the lower bound value of $326,411 and the upper bound value of $490,045.

**Table 3.**

Estimated Lifetime Cost of Sexually Transmitted Infections Acquired in 2018 in the United States, by Age Group ($ millions)

| Sexually transmitted infection (STI) | Men Point estimate (25th–75th percentile) | Women Point estimate (25th–75th percentile) | Total (Men and Women) Point Estimate (25th–75th percentile) |
|---|---|---|---|
| All ages* | | | |
| Chlamydia | 74.57 (62.23–85.93) | 616.75 (455.97–736.88) | 691.31 (530.17–814.53) |
| Gonorrhea | 54.37 (39.83–68.53) | 216.66 (144.80–275.17) | 271.03 (200.09–333.96) |
| Trichomoniasis | 16.39 (7.85–21.61) | 127.30 (94.70–153.81) | 143.69 (109.94–171.11) |
| Syphilis | 143.99 (111.33–174.28) | 29.75 (24.49–34.79) | 173.74 (137.77–207.33) |
| Genital herpes (HSV-2) | 46.80 (29.73–61.20) | 43.94 (28.62–57.92) | 90.74 (68.88–113.65) |
| HPV† | 204.57 (154.61–250.44) | 543.46 (342.54–750.52) | 755.32 (535.95–990.74) |
| HBV‡ | NC§ | NC§ | 45.90 (34.52–54.37) |
| HIV‡ | 11,305.67 (10,472.73–12,071.26) | 2,395.62 (2,184.95–2,575.61) | 13,701.29 (12,707.45–14,600.43) |
| Total, excluding HIV¶ | 540.68 (481.92–618.92) | 1,577.86 (1,338.18–1,847.18) | 2,171.73 (1,922.26–2,486.89) |
| Total, including HIV | 11,846.35 (11,036.18–12,629.87) | 3,973.48 (3,675.63–4,306.04) | 15,873.02 (14,880.74–16,877.30) |
| Ages 15–24 years# | | | |
| Chlamydia | 41.86 (34.81–48.45) | 452.74 (333.61–542.98) | 494.60 (375.26–585.65) |
| Gonorrhea | 21.61 (15.69–28.21) | 127.51 (84.12–166.18) | 149.11 (106.74–189.51) |
| Trichomoniasis | 2.84 (1.25–3.99) | 18.72 (12.87–23.82) | 21.56 (15.70–27.21) |
| Syphilis | 28.56 (21.81–35.93) | 9.52 (7.43–11.21) | 38.08 (30.14–46.46) |
| Genital herpes (HSV-2) | 13.88 (9.16–17.88) | 25.69 (17.25–32.39) | 39.57 (29.94–48.20) |
| HPV† | 76.43 (59.45–93.72) | 326.56 (195.06–444.14) | 404.24 (269.33–535.10) |
| HBV‡ | NC§ | NC§ | NC§ |
| HIV‡ | 2,647.80 (2,409.70–2,865.11) | 378.26 (322.56–426.14) | 3,026.05 (2,762.25–3,263.29) |
| Total, excluding HIV | 185.18 (167.64–213.86) | 960.73 (798.19–1,139.55) | 1,147.16 (986.08–1,346.86) |
| Total, including HIV | 2,832.98 (2,603.24–3,061.85) | 1,338.99 (1,165.86–1,526.11) | 4,173.21 (3,885.10–4,502.55) |

Costs are in millions (2019 US dollars) and represent the estimated discounted lifetime costs of STIs acquired in 2018 (future costs were discounted at 3% annually). Cost estimates have been rounded to the nearest hundredth.

HSV-2=herpes simplex virus type 2; HPV=human papillomavirus; HBV=hepatitis B virus; NC=not calculated; HIV=human immunodeficiency virus.

[*] The age groups included in the “all-ages” cost calculations varied by STI: chlamydia: 15–39 years; gonorrhea: 15–39 years; syphilis: 14–49 years; trichomoniasis: 15–59 years; genital herpes: 15–49 years; HPV: 15–59 years; HBV ≥15 years; HIV: ≥13 years.

[†] For HPV, the total (male + female) cost was higher than the sum of the costs for males and females because the total also includes the cost of adult-onset recurrent respiratory papillomatosis (RRP), which was not included in the sex-specific estimates. For this reason, the total (male + female) cost across STIs (in the bottom two rows) was higher than the sum of the costs for males and females. Although costs of juvenile-onset RRP and adult-onset RRP were included in the separate HPV cost study in this Special Issue,[15] we did not include costs of juvenile-onset RRP in the calculations shown in this table because our analysis excluded costs associated with maternal transmission across all STIs (e.g., congenital syphilis, neonatal herpes, juvenile-onset RRP).

[‡] For HBV and HIV, costs include only those of sexually acquired infections and exclude costs of infections acquired by other transmission routes such as injection drug use.

[§] Incidence estimates for HBV could not be stratified by sex and age group.

[¶] The total cost (for men and women, all ages) when including STI-attributable HIV but excluding all other HIV was $3.2 billion ($25^{th}$–$75^{th}$ percentile: $2.9–3.6 billion).

[#] The estimates for HIV for the “Ages 15–24 years” category included ages 13–24 years.