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Modeling The Economic Burden Of Adult Vaccine-Preventable Diseases In The United States

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ABSTRACT Vaccines save thousands of lives in the United States every year, but many adults remain unvaccinated. Low rates of vaccine uptake lead to costs to individuals and society in terms of deaths and disabilities, which are avoidable, and they create economic losses from doctor visits, hospitalizations, and lost income. To identify the magnitude of this problem, we calculated the current economic burden that is attributable to vaccine-preventable diseases among US adults. We estimated the total remaining economic burden at approximately $9 billion (plausibility range: $4.7–$15.2 billion) in a single year, 2015, from vaccine-preventable diseases related to ten vaccines recommended for adults ages nineteen and older. Unvaccinated individuals are responsible for almost 80 percent, or $7.1 billion, of the financial burden. These results not only indicate the potential economic benefit of increasing adult immunization uptake but also highlight the value of vaccines. Policies should focus on minimizing the negative externalities or spillover effects from the choice not to be vaccinated, while preserving patient autonomy.

Vaccines are one of the safest and most cost-effective health interventions, with numerous social and economic benefits.[1] Despite these positive characteristics, adults in the United States are not receiving vaccinations at recommended levels. For example, the Centers for Disease Control and Prevention (CDC) estimates that approximately 42 percent of adults ages eighteen and older received the influenza vaccine in the 2015–16 flu season.[2] Low vaccine uptake means that preventable diseases result in costs to individuals and society in terms of deaths, disabilities, and economic losses from doctor visits, hospitalizations, and lost income.

The positive health impacts of vaccination, including reduced mortality and morbidity, are recognized more often than the economic burden from people not getting vaccinated. This burden includes unexpected increases in health expenditures and lost income as a result of reduced functional capacity. Estimating and considering the economic burden of adult vaccine-preventable diseases is necessary for public health spending decisions and for increasing adult uptake of vaccines in the United States.

This project was designed to estimate the economic burden that was attributable to vaccine-preventable diseases in adults ages nineteen and older in the United States for a single year. This is a more comprehensive review of the economic burden of vaccine-preventable diseases among US adults than has previously been done, as the focus to date has been on one or a few specific vaccine-preventable diseases.[1,3–6] Our approach was to estimate an age-stratified cross-section of frequency and associated economic burden of vaccine-preventable diseases among adults at a specific point in time: 2015, the year of the analysis. This approach can help inform future national immunization program planning and the allocation of health resources.

Study Data And Methods

SCOPE OF ANALYSIS This analysis focused on estimating the annual economic burden of diseases associated with ten vaccines, which protect against fourteen different pathogens, recommended by the CDC for adults. The ten vaccines protect against hepatitis A; hepatitis B; herpes zoster (shingles); human papillomavirus (HPV); influenza; measles, mumps, and rubella (MMR); meningococcal disease; pneumococcal disease; tetanus, diphtheria, and pertussis (Tdap/Td); and varicella (chicken pox). A full list of these vaccines, the pathogens, and the diseases they cover is available in online Appendix A.[7]

EPIDEMIOLOGICAL METHODOLOGY Epidemiological parameters, which are the variables that describe the percentage of population immunized, the vaccine efficacy rate, and several other boundary-defining variables mentioned below, were collected from a review of the CDC and peer-reviewed literature to develop an Excel-based cost-of-illness model. An extended bibliography with the sources for these parameters is included in Appendix B.[7] Key epidemiological variables included population data by age from the 2010 census, immunization uptake, vaccine efficacy, incidence rate, care seeking, and hospitalization rate. To fully account for potential costs averted through increased adult vaccination, incidence rates were derived for unvaccinated and vaccinated individuals based on the level of immunization uptake. These incidence rates were applied to susceptible populations in each cohort to estimate the annual number of cases and subsequently assess the number of people who received inpatient and outpatient care. An illustrative decision tree appears in Appendix C.[7]

While the majority of pathogens prevented by vaccines cause acute infections, hepatitis B, herpes zoster, HPV, meningococcal disease, and pneumococcal disease are also responsible for several delayed and chronic complications, which were included in our analysis. For hepatitis B, the outcomes included acute infection, chronic infection, cirrhosis, and liver cancer. For herpes zoster (shingles), the outcomes included herpes zoster without complications, with post-herpetic neuralgia, and with other complications. For HPV, the outcomes included genital warts, cervical cancer, vaginal cancer, vulvar cancer, anal cancer, and carcinoma in situ of the cervix. Our HPV analysis examined the impact of vaccination with Gardasil instead of the more recently licensed Gardasil 9 because of the limited evidence in the literature about Gardasil 9. Our analysis did not include the costs of preventive measures such as HPV screening. For meningococcal and pneumococcal pathogens, the outcomes included meningitis, pneumonia, and sepsis.

For pneumococcal disease, a novel methodology was devised to estimate 2015 cases that used parameters described in the published literature for all-cause pneumonia hospitalizations and subsequent changes in disease burden after the 7-valent and 13-valent pneumococcal conjugate vaccines (PCV7 and PCV13) were introduced into childhood immunization schedules.[6,8–10] This methodology first back-calculated pre-PCV7 pneumococcal hospitalized incidence and then applied the fraction of disease prevented by PCV7 and PCV13 to assess the remaining disease by incorporating serotype distribution, serotype replacement, nonhospitalized pneumonia, indirect effects, and differential disease burden by age and risk group.[11] The ratio of total pneumococcal pneumonia to inpatient pneumococcal pneumonia was applied to estimate the incidence of total (inpatient and outpatient) pneumococcal pneumonia. Similarly, the ratio of hospitalized pneumonia to hospitalized meningitis and sepsis cases was used to estimate hospitalized pneumococcal meningitis and sepsis cases.[6]

EPIDEMIOLOGICAL CONSIDERATIONS AND EXPERT REVIEW Model development for the analysis involved a series of interviews conducted with epidemiological experts regarding fourteen pathogens related to each of the ten vaccines recommended by the CDC. Twelve experts reviewed model assumptions to refine vaccine preventable disease–specific cost-of-illness models and appropriately calibrate the epidemiological parameters. Epidemiological considerations and limitations that were viewed as important to acknowledge and address were discussed and incorporated. The main topics in each interview included whether the decision tree adequately reflected the path for potential adult vaccine-preventable infections; whether parameter estimates were a reasonable reflection of adult vaccine-preventable disease epidemiology; and what is a reasonable plausibility range for each epidemiological parameter where ranges are not available from the literature.

COSTING METHODOLOGY

▸ **COST-OF-ILLNESS MODEL:** Two methods were applied to estimate the overall economic burden due to vaccine-preventable diseases in US adults. First, we used a cost-of-illness modeling approach to estimate direct costs and productivity losses due to vaccine-preventable diseases.[12,13] This method calculated a monetary cost per patient and multiplied it by the number of cases to obtain an aggregate cost of illness. This analysis measured inpatient and outpatient treatment costs, outpatient medication costs, epidemiological investigation costs for measles outbreaks,[14] and productivity losses in the form of lost wages as a result of days of work missed seeking treatment (for both inpatient and outpatient care). We took a conservative approach by including only productivity lost to care seeking and not wages lost because of disability or early loss of life. This approach is supported by the majority of burden occurring in adults older than age sixty-five, who are predominantly no longer participating in the workforce.

This study used nationwide databases and *International Classification of Diseases*, Ninth Revision (ICD-9), codes to assess the economic burden of vaccine-preventable diseases among US adults ages nineteen and older. Data were primarily obtained from the following sources, with some additional cost information extracted from literature review: the Nationwide Inpatient Sample (NIS) database from the Healthcare Cost and Utilization Project (HCUP), the largest publicly available all-payer inpatient care database in the United States, including total charges;[15] and the Medical Expenditure Panel Survey (MEPS), a national large-scale survey of families and individuals, their medical providers (doctors, hospitals, pharmacies), and employers across the United States, with data on specific health services, including costs and source of payment.[16]

The NIS database houses data for roughly eight million hospital stays annually from approximately 1,000 hospitals sampled to approximate a 20 percent stratified sample of US community hospitals. The NIS is drawn from states participating in HCUP, which included 97 percent of the US population as of 2011. We relied on 2010 and 2011 data for inpatient cost (including medications) and length-of-stay data for hospitalized adults.

The MEPS sampling frame is drawn from respondents to the National Health Interview Survey conducted by the National Center for Health Statistics. MEPS collects data from an overlapping panel design of a sample of households that are representative of the civilian noninstitutionalized population. We used this database to find outpatient costs, outpatient visits per person, and prescription drug costs, which we included in the model to calculate preventable costs from susceptible populations for each pathogen. Given the smaller sample size of approximately 30,000–35,000 people per year, we averaged ten years of data (2001–10) from this data source. Where there were gaps in epidemiological and cost parameters, we relied on published literature.

▶ **FULL INCOME MODEL:** We also used a second method, a full income model, to supplement the results derived from the cost-of-illness method.

Our study highlights the need for US adults to better appreciate the value of vaccines to prevent economic burden.

This method seeks to estimate the impact of health indicators on economic welfare, using estimates of mortality and a value-of-statistical-life approach.[17–24] In addition to capturing the monetary value of market and nonmarket production, this method also encompasses the value of lives lost, interpreted as social welfare forgone because of early death. This method uses revealed preference studies to estimate how much people already pay to prevent small life-threatening risks in labor, housing, or product markets. For example, census data are used to model wages as a function of death risk across a large population.[22] In addition, stated preference studies survey the population to elicit the amount an individual is willing to pay to avoid certain risks to life.[17] Aggregating these individual values to a societal level reflects a societal willingness to pay for a specified mortality risk reduction.

The full income model was developed using the following methodology. First, we applied the standard rules used by the Congressional Budget Office and the most recent literature from the Environmental Protection Agency (EPA), the Food and Drug Administration (FDA), and the National Highway Traffic Safety Administration (NHTSA) to determine a benchmark value and range for mortality risk reduction.[25] These values were converted into 2011 dollars using the Consumer Price Index. The value of mortality risk reduction was then multiplied by the number of deaths attributable to vaccine-preventable diseases to obtain the total economic value of immunization. Values were not calculated for diphtheria, HPV-induced genital warts, HPV-induced carcinoma in situ of the cervix, measles, mumps, and rubella, as it was assumed that these vaccine-preventable diseases do not result in death among adults. The full income and cost-of-illness model results are expected to diverge because the full income model includes the nonmarket value of living longer in better health.

LITERATURE REVIEW VALIDATION A literature review was conducted to collect unit costs and productivity loss parameters for vaccine-preventable diseases to compare and validate model inputs. Studies containing cost data in the United States for adult age groups were searched across four databases: PubMed, Scopus, EconLit, and Embase.

The search strategy used a combination of the National Library of Medicine's Medical Subject Headings (MeSH) controlled vocabulary terms and free-text terms for costs, vaccines, and vaccine-preventable diseases. We used key search terms related to the vaccines of interest and economic analyses. Articles included in the review were limited to those providing cost data for US adults since 1993. Articles that pertained solely to children or adolescents, focused on other countries, did not look at costs, were published prior to 1993, were not human studies, or contained a non-English abstract were excluded. Additional focus was given to articles reporting on cases of rare conditions among US adults, such as measles, mumps, rubella, diphtheria, tetanus, and pertussis. Publications were included in our search based on inclusion and exclusion criteria from reading the title, abstract, and full text. The full search strategy is detailed in Appendix D.[7]

SENSITIVITY ANALYSIS Sensitivity analysis was carried out through computer simulations to present uncertainty ranges around key cost-of-illness point estimates, including immunization coverage, vaccine efficacy, incidence rates, and unit costs. For each parameter, random draws were taken from specified distributions 10,000 times. Noncost values were given a beta-PERT distribution, while cost values incorporated a gamma distribution to approximate the right skew of observed costing data.[26] This analysis was implemented using the latest version of the Palisade *@RISK* software to generate uncertainty ranges for cost-of-illness results.

LIMITATIONS Our study had a number of key limitations of note. The first was regarding data abstracted from MEPS and the NIS. While the MEPS database is nationally representative of the entire US population, only a limited number of cases were recorded for some adult vaccine-preventable diseases. In addition, the NIS database provides the largest publicly available inpatient care data in the United States, but there might be pockets of inpatient services not captured by this database. We also made assumptions using published literature and summary data when vaccine preventable disease–specific data were not available from the NIS or MEPS.

Second, limited sample sizes of cases for certain vaccine-preventable diseases included in our study might limit the statistical power of our results. This was a greater limitation for rare adult conditions, such as measles, mumps, rubella, diphtheria, tetanus, and pertussis. In cases such as measles, mumps, or pertussis, the limited adult cases often occur in areas of low vaccine uptake, which are more likely in some geographic pockets and communities of certain income levels. In addition, the small sample of diphtheria cases (five in the past decade) challenges the generalizability of diphtheria results.

In addition, there might be challenges with classification of costs as a result of difficulties in comprehensively identifying ICD9 codes and linking cases by various pathogens from both the NIS and MEPS data sets. Furthermore, the MEPS data set was not accessible at the fully specified ICD9 code level, and therefore it was assumed that costs for three-digit summary codes were relevant to vaccine-preventable disease subconditions.

Study Results

Through the literature review, our initial search resulted in 25,660 articles across four databases: 5,953 in PubMed; 32 in Scopus; 91 in EconLit; and 19,584 in Embase. After we reviewed titles and abstracts, 500 of these articles were considered potentially relevant. Of these, 322 articles were excluded through full-text screening as a result of our exclusion criteria, including duplicate article and articles that did not include costs, did not pertain to the United States, or pertained solely to children or adolescents. A total of 178 articles were selected for inclusion in the final review, some of which were used as inputs in the cost-of-illness model.

UNIT COSTS The inpatient care unit costs abstracted from median values of the NIS ranged from \$5,770 for a hospitalized case of influenza to \$15,600 for a hospitalized case of invasive meningococcal disease. Abstracted from MEPS as well as the supplementary literature, the outpatient care unit costs ranged between \$108 and \$457, while medication unit costs ranged from \$0 for diseases that do not have curative drug treatment (as opposed to drugs prescribed to treat symptoms) up to \$605 for drugs used to treat tetanus. The inpatient productivity loss per person ranged from \$122 for a case of mumps to \$580 for a case of tetanus, highlighting the severity of tetanus among adults with long hospital stays. The outpatient productivity loss per person ranged from \$29 for diseases with only a single outpatient visit per case to \$154 for HPV-related cancers, which involve more follow-up visits. Exhibit 1 presents the average unit costs used in the cost-of-illness model for each cost component by pathogen.

EXHIBIT 1

Unit costs per case of vaccine-preventable disease by cost component and by pathogen used in cost-of-illness model, 2015

Pathogen	Direct costs: Inpatient unit cost	Direct costs: Outpatient unit cost	Direct costs: Medication unit cost	Productivity losses: Inpatient productivity loss per person	Productivity losses: Outpatient productivity loss per person
Hepatitis A	$ 6,590	$201	$ 0	$178	$ 58
Hepatitis B	8,940	457	223	193	23
Herpes zoster	6,160	248	40	295	54
Influenza	5,770	258	24	132	24
Measles[a]	8,690	108	0	212	29
Mumps	9,200	108	0	122	29
Rubella	6,030	108	0	176	29
Tetanus	14,400	108	605	580	29
Diphtheria	8,490	108	50	244	29
Pertussis	7,730	108	100	200	29
Varicella	7,540	112	47	273	29
Meningococcal disease	15,600	108	50	406	58
Pneumococcal disease	15,200	108	50	348	48
HPV	11,600	236	77	195	154
Source	NIS	MEPS and lit.	MEPS and lit.	NIS and DOL	MEPS and DOL

SOURCE Authors' analysis. **NOTES** HPV is human papillomavirus. NIS is Nationwide Inpatient Sample. MEPS is Medical Expenditure Panel Survey. DOL is Department of Labor. [a]The measles pathogen also included a cost component for epidemiological investigations valued at $1,470 (see Note 14 in text).

For most vaccine-preventable diseases, adults ages sixty-five and older experienced the highest unit costs, derived by dividing the total costs by cases in Appendix E.[7] Adults ages 19–49 had higher unit costs for hepatitis A, cirrhosis, meningococcal pneumonia, vaginal cancer, and vulvar cancer. Adults ages 50–64 had higher unit costs for liver cancer, mumps, meningococcemia, pneumococcal septicemia, and pneumococcal pneumonia.

ECONOMIC BURDEN

▶ **COST-OF-ILLNESS MODEL:** The total current economic burden was estimated at approximately $9 billion (plausibility range: $4.7–$15.2 billion) in 2015 from vaccine-preventable diseases relevant to ten vaccines recommended for US adults (Exhibit 2). The majority (95 percent) of this estimated burden was for direct costs, with $5.9 billion (plausibility range: $2.2–$11.6 billion) for inpatient treatment costs and $2.4 billion (plausibility range: $1.0–$4.8 billion) for outpatient treatment costs. The remaining 5 percent represents productivity losses as a result of wages lost during the course of treatment. Epidemiological investigations for measles outbreaks were estimated to cost $139,000 per year on average. Uncertainty ranges are presented in Appendix F.[7]

Sixty-five percent of the estimated annual economic burden, equivalent to $5.8 billion (plausibility range: $2.0–$11.6 billion), resulted from influenza alone—a vaccine-preventable disease that causes substantial numbers of hospitalizations and morbidity each year (Exhibit 3). An additional 21 percent ($1.9 billion) resulted from pneumococcal disease, and 9 percent ($782 million) was contributed by herpes zoster. The last 6 percent of the total economic burden was distributed among the remaining eleven pathogens, some of which are exceedingly rare in their disease presentation among US adults.

The economic burden attributable to vaccine-preventable diseases was also found to vary by age. For people ages 19–49, influenza represented the greatest remaining vaccine-preventable economic burden at 85 percent of the annual total, followed by HPV at 12 percent. For people ages 50–64, influenza contributed 67 percent of the economic burden, and herpes zoster contributed 20 percent. For adults ages 65 and older, influenza (55 percent) and pneumococcal disease (35 percent) constituted the greatest proportion of remaining economic burden. Annual cases and economic burden by pathogen and age group are presented in Appendix E.[7]

Results show that 76 percent of the current cases (14.1 million) were attributable to unvaccinated individuals. The percentage of cases attrib-

EXHIBIT 2

Total annual cases and economic burden of vaccine-preventable disease, by pathogen, 2015

Pathogen	Cases	Direct costs: Inpatient cost	Direct costs: Outpatient cost	Direct costs: Medication cost	Productivity loss: Inpatient	Productivity loss: Outpatient	Total costs
Hepatitis A	1,930	$ 2,160,000	$ 682,000	$ 0	$ 58,200	$ 98,500	$ 3,000,000
Hepatitis B	43,400	141,000,000	24,300,000	4,800,000	2,410,000	985,000	173,000,000
Herpes zoster	1,100,000	197,000,000	477,000,000	41,600,000	10,600,000	55,700,000	782,000,000
Influenza	16,600,000	3,770,000,000	1,580,000,000	175,000,000	86,100,000	178,000,000	5,790,000,000
Measles[a]	95	79,100	10,300	0	1,930	2,750	233,000
Mumps	394	72,400	42,600	0	964	11,400	127,000
Rubella	1	3,330	60	0	97	16	3,500
Tetanus	26	134,000	1,040	5,820	5,410	279	147,000
Diphtheria[b]	<1	3,900	5	23	112	13	4,100
Pertussis	4,450	1,580,000	482,000	445,000	40,900	129,000	2,680,000
Varicella	9,220	528,000	985,000	412,000	19,100	254,000	2,200,000
Meningococcal disease	303	4,750,000	65,600	16,900	102,000	17,600	5,000,000
Pneumococcal disease	283,000	1,760,000,000	27,400,000	14,000,000	49,000,000	8,220,000	1,860,000,000
HPV[c]	447,000	29,200,000	244,000,000	19,500,000	472,000	40,000,000	333,000,000
Total	18,500,000	5,910,000,000	2,360,000,000	256,000,000	149,000,000	283,000,000	8,950,000,000

SOURCE Authors' analysis. **NOTE** All estimates are rounded to three significant figures. [a]Measles total costs include $139,000 for epidemiological investigation cost. [b]Because of the rare incidence of diphtheria among adults in the United States, no more than a single case is expected; therefore, the economic burden would not exceed the per person costs. [c]Only the vaccine-preventable conditions of human papillomavirus (HPV) are included; oropharyngeal cancer, penile cancer, and recurrent respiratory papillomatosis are excluded.

utable to unvaccinated individuals also decreases with age, with adults ages 19–9, having 85 percent of vaccine-preventable diseases among the unvaccinated, compared to 81 percent for adults ages 50–64 and 56 percent for adults ages 65 and older. Eighty percent of the estimated remaining annual economic burden, equivalent to $7.1 billion (plausibility range: $3.8–$11.9 billion), resulted from these individuals, who received no direct protection from vaccination. The percentage of economic burden attributable to unvaccinated individuals ranged from 65 percent for varicella to more than 99 percent for pertussis and hepatitis A.

▸ **FULL INCOME MODEL:** The current-dollar value of statistical life calculated from each source was $5.9 billion from the FDA; $6.3 billion from the NHTSA; and $8.3 billion from the EPA.

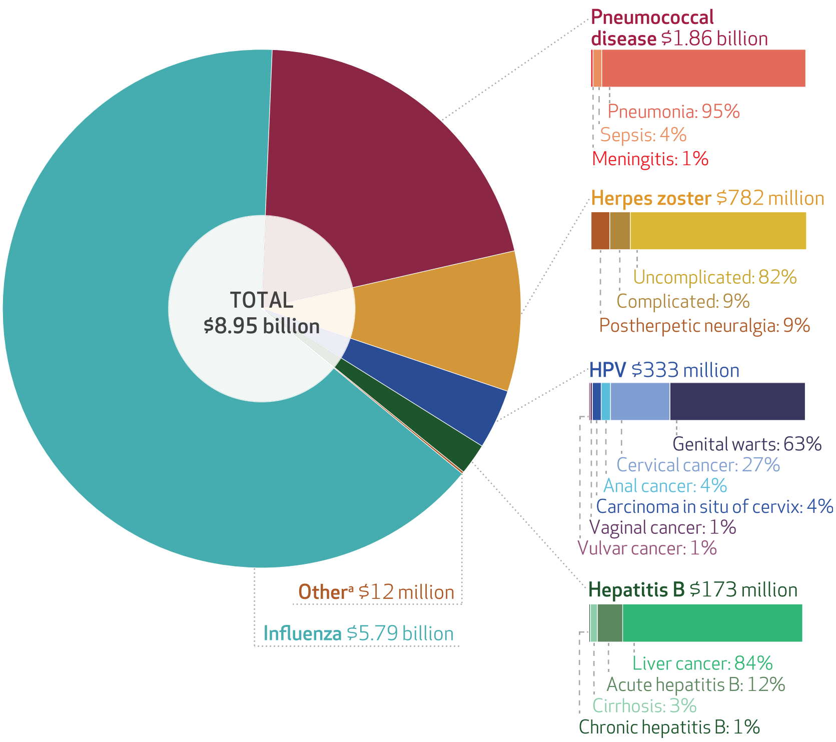
The full income value of death as a result of vaccine-preventable diseases is estimated to be $176 billion annually (plausibility range: $166 billion–$231 billion). Two-thirds (66 percent) of the full income value each year is attributable to hepatitis B alone (plausibility range: $110 billion–$152 billion), including acute and chronic infection, cirrhosis/chronic liver disease, and liver cancer. An additional 19 percent is attributable to HPV (plausibility range: $31 billion–$44 billion), and 5 percent to influenza (plausibility range: $8 billion–$11 billion). The remaining pathogens are all less than 5 percent of the overall full income value.

Discussion

Our estimation of the economic burden of vaccine-preventable diseases in adults highlights the importance of increasing adult vaccine uptake in the United States. We found that unvaccinated cases contributed a significant portion of total costs attributable to vaccine-preventable diseases. Based on current vaccination uptake rates, vaccine-preventable diseases annually cost individuals and society $9 billion (plausibility range: $4.7–$15.2 billion) through direct costs and productivity losses, $7.1 billion (plausibility range: $3.8–$11.9 billion) of which occurs among the unvaccinated. This indicates the potential impact that increased adult immunization rates might have on decreasing the annual economic burden, particularly among younger adults. It should be noted that this study examined a static annual estimate of the unvaccinated cohort, and therefore not all cases in this group are necessarily preventable by increased vaccination because of less than 100 percent vaccine efficacy as well as a target population that has aged out of the recommended age range for some of the vaccines. Furthermore, our analysis estimated current vaccine-preventable disease bur-

EXHIBIT 3

Annual economic burden of vaccine-preventable diseases, by pathogen, 2015



SOURCE Authors' analysis. **NOTES** All dollar amounts are for all US adults relevant to each vaccine-preventable disease (which target different age groups). The breakdown of results by age is presented in the online Appendix (see Note 7 in text). HPV is human papillomavirus. [a]Includes economic burden attributable to diphtheria, hepatitis A, measles, meningococcal disease, mumps, pertussis, rubella, tetanus, and varicella.

den instead of disease burden prevented as a result of vaccination or implementation of specific vaccine recommendations.

This study presents a more comprehensive analysis of the economic burden of vaccine-preventable diseases among US adults than previously conducted. The methodology of this review not only estimated the direct costs and productivity losses associated with vaccine-preventable diseases with a cost-of-illness approach but also included the value of averting death attributable to a vaccine-preventable cause using the full income model; both approaches are commonly used to estimate economic burden in the United States.[5,19,21,24]

Several other studies have sought to estimate the economic costs of various vaccine-preventable illnesses in the United States. For example, a previous CDC analysis estimated that annual influenza epidemics are estimated to cost between $1.6 billion and $25.2 billion in direct medical expenses among US adults.[3] Our study estimated direct medical costs within this range at $5.5 billion for seasonal influenza. In a different study, US adults ages 18–49 accounted for 10 percent of the total economic burden from influenza,[27] whereas our analysis estimated that young adults accounted for 31 percent. A recent analysis by John McLaughlin and colleagues looked at four of the vaccine-preventable diseases considered in the study (influenza, pneumococcal disease, herpes zoster, and pertussis) and estimated annual costs of $26.5 billion for US adults older than age fifty, compared to our conservative estimate of $6.9 billion for the same diseases and age group.[28] The higher pertussis incidence, higher base-case estimates from different sources, higher overall cost per case used, and additional indirect costs measured led to the higher costs observed by McLaughlin and colleagues.

While we found some variation between our estimates and those cited in the literature, this could be attributable to differences in methodology. As seen in Exhibit 1, among some uncomplicated acute cases such as hepatitis A and influenza, we saw similar direct costs as measured by inpatient cost per person. Overall, we saw larger outpatient care costs in the literature, which indicates that outpatient care unit costs from MEPS might be an underestimate. Because we included costs of only medication used for curative treatment, not treatment of symptoms, we did not include medication costs for diseases such as hepatitis A, for which such costs are sometimes calculated in the literature. We also saw greater variation in uncomplicated acute cases such as measles, a vaccine-preventable disease that we estimated would have an inpatient cost of $8,690 according to adult-specific NIS data, whereas other literature estimated a cost of $2,660 across all age groups.[29,30] A full comparison of inpatient care unit costs can be found in Exhibit 4.

There was also some variation in costs of cases with complications, which was not surprising considering the increased complexity and variation in the methodology used to calculate costs among these cases, particularly within disease-specific studies. Similarities and variations were additionally observed among uncomplicated versions of these cases. For example, we estimated that uncomplicated herpes zoster had inpatient costs per person of $5,280—a slightly lower figure compared to the $7,680 in the literature, but within the estimated range of $4,440–$8,890.[31]

Because of the many pathogens included in this analysis, we excluded treatment costs for sequelae (negative after-effects) for vaccine-preventable pneumococcal and meningococcal diseases from the total economic burden, as this information was not available for other pathogens. However, we examined this cost component separately. The lifetime sequelae treatment cost for meningococcal meningitis and sepsis as

EXHIBIT 4

Unit costs per case of vaccine-preventable disease with inpatient care compared to results from a literature review, 2015

Pathogen	Costs from NIS[a]	Costs from the literature[b]	Literature source
Hepatitis A	$3,970–$9,570	$2,890–$7,220	Berge et al., 2000
Hepatitis B	$5,220–$16,100	$8,600	Lee et al., 2004
Herpes zoster	$3,690–$10,400	$4,460–$8,890	Hornberger and Robertus, 2006 (Note 31 in text)
Influenza	$3,650–$9,660	$4,930–$5,680	Lin et al., 2013
Measles	$5,570–$14,200	$2,660	Miller et al., 1998 (Note 29 in text); Shim et al., 2012 (Note 30 in text)
Mumps	$6,750–$13,400	$2,660	Miller et al., 1998 (Note 29 in text); Shim et al., 2012 (Note 30 in text)
Rubella	$3,940–$9,730	$2,660	Miller et al., 1998 (Note 29 in text); Shim et al., 2012 (Note 30 in text)
Tetanus	$9,110–$48,300	$31,200	Balestra and Littenberg, 1993
Diphtheria	$7,580–$9,540	Not available	
Pertussis	$3,600–$12,600	$860–$34,500	O'Brien and Caro, 2005
Varicella	$4,830–$14,000	$6,100	Smith and Roberts, 1998
Meningococcal disease	$9,070–$34,800	$14,700–$32,400	Scott et al., 2002
Pneumococcal disease	$8,880–$27,000	$25,200–$30,100	Smith et al., 2010
HPV	$7,580–$18,700	$27,200–$55,700[c]	Chesson et al., 2012

SOURCES Authors' analysis and literature review. Complete citations, except where indicated, are in online Appendix G (see Note 7 in text). **NOTES** Costs were converted into current-year dollars. NIS is Nationwide Inpatient Sample. HPV is human papillomavirus. [a]Range from the NIS includes twenty-fifth and seventy-fifth percentiles. [b]Includes uncertainty ranges from the literature where available. [c]This is an average direct medical cost for cervical, anal, vaginal, and vulvar cancers, including screening and treatment costs beyond inpatient care, such as recurrence and terminal care. The robustness of these data differs by cancer.

well as pneumococcal meningitis were estimated at $273,000 per case.[6] For meningococcal disease, the economic burden to treat sequelae such as deafness and limb loss resulting from meningitis or sepsis are estimated to be $11.5 million over adults' lifetimes. For pneumococcal disease, the economic burden to treat sequelae resulting from pneumococcal meningitis are estimated to be approximately $57.3 million over adults' lifetimes.

The approach to estimating productivity losses in this study could also be considered very conservative, as not all productivity losses attributable to disability and death were included. This study focused only on productivity loss as a result of care seeking instead of impact on income, as significant burden was observed in adults age sixty-five or older. Productivity losses related to care seeking might underestimate the full economic burden because we did not estimate work-related productivity loss for younger ages for additional missed work for convalescence and recovery outside of direct inpatient and outpatient care. We did not specifically model parameter differences for immunocompromised populations, which might have different risks for diseases as well as higher treatment costs. This study examined a static cross-section of the adult population instead of taking a cohort-based approach.

Conclusion

The results of this study demonstrate the need for improved uptake of vaccines among adults based on a robust analysis of the societal and individual costs stemming from vaccine-preventable diseases among vaccinated and unvaccinated populations. Estimating the economic burden of vaccine-preventable diseases among adults is a first step toward understanding the benefits of increasing adult vaccine uptake in the United States. It highlights the need for US adults to better appreciate the value of vaccines to prevent economic burden. By highlighting the tremendous financial burden that unvaccinated individuals place on the economy and the health system, we hope that our estimates will spur creative policy solutions to reduce the negative externality or spillover effect, while preserving the autonomy of patients to make more informed choices. ■

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7 To access the Appendix, click on the Appendix link in the box to the right of the article online.

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