Impact of Tetanus, Diphtheria, and Acellular Pertussis (Tdap) Vaccine Use in Wound Management on Health Care Costs and Pertussis Cases

Sandra E. Talbird, MSPH; Jonathan Graham, BS; Josephine Mauskopf, PhD;
Cristina Masseria, PhD; and Girishanthy Krishnarajah, MPH, MBA/MS, PhD

ABSTRACT

BACKGROUND: The Advisory Committee on Immunization Practices (ACIP) recommends the use of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine for routine wound management in adolescents and adults who require a tetanus toxoid-containing vaccine who were vaccinated ≥5 years earlier with tetanus toxoid, reduced diphtheria toxoid (Td) vaccine, and who have not previously received Tdap.

OBJECTIVE: To estimate the overall budget and health impact of vaccinating individuals presenting for wound management with Tdap instead of Td vaccine, the current standard of care in practices that do not use Tdap for purposes of wound management.

METHODS: A decision-analytic economic model was developed to estimate the expected increase in direct medical costs and the expected number of cases of pertussis avoided associated with the use of Tdap instead of Td vaccine in the wound management setting. Patients eligible for Tdap were aged 10+ years and required a tetanus-containing vaccine. Age-specific wound incidence data and Td and Tdap vaccination rates were taken from the National Health Interview Survey and the National Immunization Survey for the most recent available year. Age-specific pertussis incidence used in this analysis (151 per 100,000 for adolescents, 366 per 100,000 for those aged 20-64 years, and 176 per 100,000 for those aged 65+ years) used reported incidence rates adjusted by a factor of 10 for adolescents and by a factor of 100 for adults, based on assumptions previously made by ACIP to account for underreporting. Vaccine wholesale acquisition costs without federal excise tax were assumed in the base case. Efficacy of vaccination with Tdap in preventing pertussis was based on clinical trial data. Possible herd immunity effects of vaccination were not included in the model. Costs associated with vaccination and treatment of pertussis cases were reported as total annual costs and per-member-per-month (PMPM) costs for hypothetical health plans and for the U.S. population. Aggregate and incremental costs and pertussis cases avoided were presented undiscounted (as recommended for budget-impact analyses) annually and cumulatively over a 3-year time horizon in 2012 U.S. dollars. Scenario analyses were conducted on key parameters, including wound incidence, pertussis incidence, vaccine efficacy and waning protection against pertussis, uptake rates for Tdap, and vaccine prices using alternative data sources or alternative clinically relevant assumptions.

RESULTS: For a health plan with 1 million covered lives aged < 65 years, vaccination with Tdap instead of Td was estimated to cost an additional $132,364 ($0.01 PMPM) in the first year and an additional $368,640 ($0.01 PMPM) cumulatively over 3 years. For a health plan with 1 million covered lives aged 65+ years, vaccination with Tdap instead of Td was estimated to cost an additional $201,165 ($0.02 PMPM) in the first year and an additional $549,568 ($0.02 PMPM) cumulatively over 3 years. For the U.S. population aged 10+ years, vaccination with Tdap instead of Td was estimated to result in protection against pertussis for an additional 2.7 million patients with wounds annually and was estimated to cost an additional $121,101,671 to avoid 42,104 cases of pertussis over the 3-year time horizon. Results were sensitive to input parameter values, particularly parameters associated with the number of patients with wounds vaccinated with Tdap (range 2.7 to 5.1 million patients). However, for all of the alternative scenarios tested, the expected increase in PMPM costs ranged from < $0.01 to $0.03.

CONCLUSIONS: Vaccination of adolescents and adults with Tdap for wound management may result in an increase in PMPM costs for health plans of < $0.01 to $0.03. Given the potential reduction in pertussis cases at the population level, vaccination with Tdap for routine wound management could be considered as another strategy to help address the pertussis public health concern in the United States.

J Manag Care Pharm. 2015;21(1):88-99

What is already known about this subject

- The Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices currently recommends the use of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine in routine wound management for adolescents and all adults who require a tetanus toxoid-containing vaccine who were vaccinated ≥ 5 years earlier with tetanus toxoid, reduced diphtheria toxoid (Td) vaccine, and who have not previously received Tdap.
- Coverage rates for Tdap vaccination remain below 80% among adolescents (78.2% in 2011) and adults aged < 65 years (12.5% in 2011) and are negligible among adults aged 65+ years (coverage rate was not reported in 2011 because Tdap has only been recommended for use in this age group since July 2011).
- Several studies have shown that vaccination against pertussis in the form of a Tdap vaccine for adolescents, adults, and the elderly is cost-effective compared with no vaccination.

What this study adds

- This study estimates the budget impact of vaccinating individuals presenting to the health system for wound management with Tdap instead of Td, as well as the likely clinical outcomes from a health plan or U.S. population perspective.
- Our base-case findings provide evidence that vaccination of adolescents and adults with Tdap instead of Td for wound management results in an annual budget impact ranging from $113,793 to $201,165 ($0.01-$0.02 per member per month) for health plans with 1 million members.
- This study estimated that a Tdap vaccination strategy targeting patients with wounds requiring a tetanus-containing vaccine would impact between 2.7 and 5.1 million people each year in the United States.

Pertussis is an acute respiratory infection caused by a gram-negative bacterium that typically results in spasmodic paroxysmal coughing bouts ending with an inspiratory whoop sometimes followed with vomiting. For the very young, the elderly, and adults with conditions that put them at risk of complications from any respiratory infection, pertussis can be a serious illness, requiring hospitalization and even resulting in death.[1] Even for those not experiencing severe complications, prolonged periods with paroxysmal coughing bouts may result in multiple visits to a health provider and extended absences from school or work.[1-3]

A combined diphtheria, tetanus, and whole pertussis vaccine was introduced into routine vaccination schedules for infants and young children in the late 1940s, and subsequently, a vaccine containing combined diphtheria, tetanus, and acellular pertussis (DTaP) was introduced in the late 1990s.[1] These vaccination strategies resulted in significant reductions in the annual incidence of pertussis and deaths due to pertussis in the United States, from approximately 200,000 cases per year in the prevaccine era to a low of 1,010 cases reported in 1976.[1] However, there have been subsequent increases in the number of cases (up to 48,277 in 2012[4]), most commonly in adolescents and adults.[1,5]

A combined tetanus toxoid, reduced-antigen content diphtheria toxoid, and acellular pertussis (Tdap) vaccine was first licensed for single use in adolescents in May 2005, in adults aged 19 to 64 years in June 2005, and in adults aged 65+ years in July 2011.[6] Recommendations by the Centers for Disease Control and Prevention (CDC) for the use of these vaccines in adolescents and adults followed after the license dates.[1] The CDC currently recommends a single dose of Tdap in adolescents and in adults of all ages.[7] In addition, the current CDC recommendations state that "Tdap is preferred to Td vaccination for adults who require a tetanus toxoid-containing vaccine as part of wound management, who have received a Td ≥5 years previously, and who have not previously received Tdap."[7]

Despite the CDC recommendations and a safety profile comparable to that of tetanus toxoid, reduced diphtheria toxoid (Td) vaccinations,[8,9] the coverage rate for Tdap vaccination remains below 80% among adolescents (78.2% in 2011[10]) and adults aged <65 years (12.5% in 2011[11]) and are negligible among adults aged 65+ years (coverage rate was not reported in 2011 because Tdap has only been recommended for use in this age group since July 2011). These differences in coverage rates by age are driven primarily by school entry vaccination requirements that ensure high coverage rates among adolescents. Additionally, Tdap coverage rates among adults may have been historically low as a result of lack of insurance coverage for the vaccine or low reimbursement rates prior to implementation of the Affordable Care Act.[12]

Individuals present to the health system for wound management with an estimated annual incidence rate between 0.028 per 100,000 (aged 65+ years) and 0.053 per 100,000 (aged 15-24 years).[13] Thus, the CDC recommendation for the use of Tdap in routine wound management could help to increase the coverage rates for pertussis revaccination in the adolescent and adult populations in the United States.

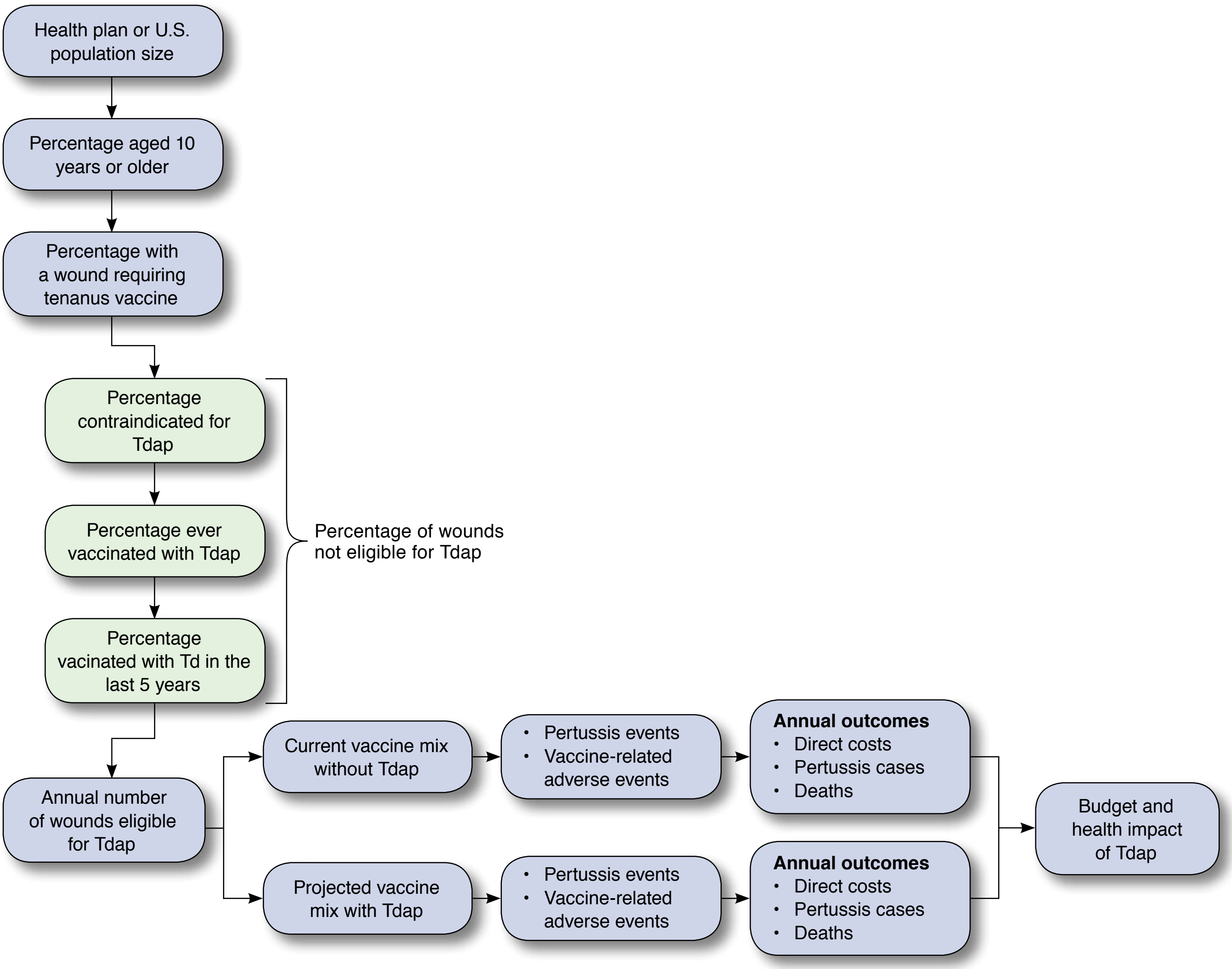
Vaccination of adolescents, adults, and the elderly against pertussis with a Tdap vaccine has been shown to be cost-effective (incremental cost per quality-adjusted life-year gained of <$50,000), compared with no vaccination, in U.S. published studies[14-17] and in presentations to the Advisory Committee on Immunization Practices (ACIP) at the CDC.[18,19] The cost-effectiveness analyses took a societal perspective that included both direct and indirect costs. In addition to evaluating the cost-effectiveness of introducing Tdap for routine wound management, it is important to understand the potential impact of the new recommendations on the health care expenditures for those responsible for its implementation. In this study, a decision-analytic model was developed to estimate the budget impact and reduction in pertussis cases expected from vaccinating individuals with Tdap instead of Td for routine wound management from the perspective of a health plan and the U.S. population.

Methods

Model Structure

A decision-analytic model was developed in Microsoft Excel (Microsoft Corporation, Redmond, WA) to estimate the budget impact of substituting Td vaccination with Tdap for individuals presenting for wound management (see Figure 1). The model was designed to estimate the budget impact and pertussis cases avoided for 2 types of hypothetical health plans: (1) a health plan with 1 million members that includes only individuals aged <65 years and (2) a health plan with 1 million members that includes only individuals aged 65+ years. The model was also designed to estimate the budget impact and pertussis cases avoided for the U.S. population aged 10+ years.

FIGURE 1 Budget-Impact Model Structure



Td = tetanus toxoid and reduced diphtheria toxoid; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

The time horizon for the budget-impact analysis was 3 years, with each annual cohort representing individuals presenting with first-time or previous wounds. Each annual cohort was monitored for pertussis cases for the entire time period of the model. In other words, those presenting in the first year were tracked during the year of vaccination and the following 2 years; those presenting in the second year were tracked during the year of vaccination and the following year; and those presenting in the third year were tracked only in the year of vaccination. This approach captures all costs relating to vaccination and pertussis disease for the 2 base-case scenarios for the model time horizon but does not capture the pertussis disease costs for the 3 vaccinated cohorts that persisted beyond the 3-year model time horizon.

The model captured only the direct effects of pertussis vaccination efficacy on those vaccinated and did not estimate herd immunity effects on unvaccinated contacts. Waning of vaccine efficacy and protection against pertussis during the first 3 years was included in the model, and alternative values for the level of waning (i.e., drop in efficacy) were tested in a scenario analysis using new data for adolescents vaccinated with acellular pertussis vaccination as part of their primary vaccine

TABLE 1 Estimated Annual Number of Patients with Wounds Eligible for Tdap Vaccine[a]

	Aged 10-64 Years	Aged 65+ Years
U.S. population		
Open wounds only	2,212,332	519,075
Open and other[b] wounds	4,267,706	814,004
Health plans		
Open wounds only	8,240	12,891
Open and other[b] wounds	15,896	20,215

[a]Values were estimated by multiplying the age-specific population in 2010 (from U.S. Census Bureau data[21]) by the age-specific data for the percentage of patients with "open" wounds or "open" and "other" wounds (from the National Health Interview Survey[13]). This total number of wounds presumed to require a tetanus-containing vaccination was then multiplied by the percentage of the population eligible for Tdap vaccination (from the National Immunization Survey-Teen[10] and National Health Interview Survey[11]).

[b]Other wounds include fire-, burn-, or scald-related episodes; animal or insect bites; machinery accidents; and other but not specified episodes.

Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

series.[20] Exclusion of herd immunity and inclusion of vaccine waning were conservative assumptions for estimating the budget impact of Tdap in reducing the estimated health care costs associated with the estimated avoided cases of pertussis.

Eligible Population for Tdap Vaccine (Number of Wounds)

The annual number of wounds eligible for Tdap was derived using annual wound incidence data from the 2007 U.S. National Health Interview Survey,[13] and self-reported data on vaccination with Td or Tdap from the 2011 National Immunization Survey among adolescents[10] and the 2011 National Health Interview Survey among adults.[11]

To estimate the annual number of patients with open wounds eligible for Tdap, a series of filters were applied on the population of a hypothetical health plan or on the total U.S. population as follows (see Appendices [available in online article] for detailed description of data and calculations used to estimate percentage of patients with open wounds eligible for Tdap):

- *Step 1.* The modeled population was divided into 3 age groups—10 to 19, 20 to 64, and 65+ years—in order to use age-specific pertussis incidence and wound incidence data, both of which are highly age-dependent. The age distribution within the United States for 2010 was used for the U.S. population analysis.[21] The U.S. age distribution for 2010 for those under 65 years also was applied to health plans with individuals aged <65 years to calculate the percentage of individuals who were aged 10 to 19 years and 20 to 64 years.
- *Step 2.* The number of patients with a wound requiring tetanus-containing vaccination (including first-time or recurrent wounds) was estimated using age-specific annual wound incidence data to fit the age groups in the model.[13] Wounds requiring tetanus vaccine were those reported as "open" wounds. Wounds reported as "other"—including fire-, burn-, or scald-related episodes; animal or insect bites; machinery accidents; and other but not specified episodes where a tetanus booster vaccination might be considered—were included in the scenario analyses.
- *Step 3.* The number of people who either had not received a Td vaccine within the last 5 years or had never been vaccinated with a Tdap vaccine was estimated among individuals with wounds using national survey data of vaccination rates among adolescents (National Immunization Survey–Teen[10]) and adults (National Health Interview Survey[11]; see Appendices A, B, and C, available in online article). Although the vaccination survey data were among the general U.S. population, Td and Tdap vaccination rates among those with wounds were assumed to be similar to those among the general U.S. population.
- *Step 4.* The number of patients with open wounds eligible for vaccination with a Tdap vaccine was calculated and aggregated across age groups (see Table 1 and Appendix D, available in online article).

All patients with wounds eligible for vaccination with Tdap were assumed to accept vaccination with either Td or Tdap. Two base-case scenarios were compared: Scenario 1, all individuals were vaccinated with Td, and Scenario 2, all individuals were vaccinated with Tdap.

Although a vaccination uptake rate of 100% and market share assumptions of either 100% Td and 0% Tdap or vice versa is unlikely to reflect the real-world situation, vaccination acceptance rates for wound management are largely unknown, and this methodology allows for the estimation of the upper bound of the budget impact and pertussis cases avoided when comparing vaccination with Tdap instead of Td.

Pertussis Cases

Pertussis cases were estimated according to disease severity to accurately estimate pertussis-related mortality and costs. Based on data available in the literature and definitions used by previous models, the following definitions were used for mild, moderate, and severe cases:

- *Mild:* cases without paroxysmal cough; reported cases require 1 physician visit in an outpatient setting and no treatment.
- *Moderate:* cases with paroxysmal cough with or without other complications (including cyanosis, vomiting, urinary incontinence) requiring medical care and treatment in an outpatient setting (but not requiring hospitalization).
- *Severe:* cases with paroxysmal cough and other serious complications (including pneumonia) requiring hospitalization.

In a review by Cortese et al (2007),[2] the true incidence of disease in the United States was estimated from population-based active surveillance studies showing estimates ranging

TABLE 2 Model Input Parameters

Parameter	Value	Reference
U.S. population size and distribution by age		
Aged 10-19 years	13.8%	U.S. Census Bureau, 2011[21]
Aged 20-64 years	60.0%	
Aged 65+ years	13.0%	
Annual percentage of people with first-time or recurrent wounds (open wounds only)		
Aged 10-19 years	2.50%	2007 National Health Interview Survey[13]; estimated from Table 1A and Table 7 to fit model age groups[a,b]
Aged 20-64 years	1.76%	
Aged 65+ years	1.77%	
Annual percentage of people with first-time or recurrent wounds (open and other wounds)		
Aged 10-19 years	5.35%	2007 National Health Interview Survey[13]; estimated from Table 1A and Table 7 to fit model age groups[a,b]
Aged 20-64 years	3.36%	
Aged 65+ years	2.78%	
Percentage of population eligible for Tdap vaccination		
Aged 10-19 years	18.96%	Estimated from the 2011 National Immunization Survey–Teen[10] and from the 2011 National Health Interview Survey[11,b]
Aged 20-64 years	61.60%	
Aged 65+ years	72.80%	
Percentage of population contraindicated for vaccine		
All age groups	0.0%	Assumption
Adjusted pertussis incidence (per 100,000)[c]		
Aged 10-19 years	15.07%	U.S. Census Bureau, 2011[21]; CDC, 2012[22]; Acosta, 2012[18]
Aged 20-64 years	3.66%	
Aged 65+ years	1.76%	
Distribution of pertussis cases by severity		
Aged 10-19 years		
Mild	24.3%	Lee et al., 2004[3]; Caro et al., 2005[15]
Moderate	73.6%	
Severe	2.1%	
Aged 20-64 years		
Mild	11.0%	Cortese et al., 2007[2]
Moderate	86.0%	
Severe	3.0%	
Aged 65+ years		
Mild	14.0%	Cortese et al., 2007[2]
Moderate	74.0%	
Severe	12.0%	
Among severe cases of pertussis, probability of death		
Aged 10-19 years	0.0%	Derived from Caro et al., 2005[15,d]
Aged 20-64 years	0.86%	
Aged 65+ years	0.86%	
Vaccine efficacy against pertussis, years 1, 2, and 3		
Tdap (all age groups)	89.0%, 79.0%, 69.0%	Year 1: BOOSTRIX PI, 2012[8]; Years 2 and 3: assumption
Td (all age groups)	0.0%	Assumption
Vaccine-related costs		
Tdap (children aged ≤ 19 years)	$35.30	RED BOOK, 2012[25,e]
Tdap (adults ≥ 20 years)	$35.30	
Td (children aged ≤ 19 years)	$17.21	
Td (adults ≥ 20 years)	$17.99	
Cost per treated case of pertussis (100% of cases treated)		
Mild	$70.46	*The Essential RBRVS*, 2012[31,f]
Moderate	$239.28	Acosta, 2012[18]
Severe	$7,748.42	O'Brien and Caro, 2005[27]
Incidence of vaccine-related adverse events (incremental Tdap vs. Td)		
Local reaction	2.0%	Lee et al., 2007[14]
Systemic reaction	1.0%	
Anaphylaxis	0.0001%	

TABLE 2 Model Input Parameters *(continued)*

Parameter	Value	Reference
Cost per case of vaccine-related adverse event		
Local reaction	$1.41	Lee et al., 2007[14,g]
Systemic reaction	$1.41	
Anaphylaxis	$2,662.26	

[a]The values for individuals aged 10 to 19 years were estimated using the survey values for individuals aged 15 to 24 years; the values for individuals aged 20 to 64 years were estimated using the survey values for individuals aged 25 to 64 years.
[b]See Appendices in online article for more details.
[c]Incidence for individuals aged 10 to 19 years was calculated as a population weighted average of the individuals aged 5 to 14 years and 15 to 24 years and then multiplied by an adjustment factor of 10; incidence for individuals aged 20 to 64 years was calculated as the population weighted average of the individuals aged 15 to 24, 25 to 39, and 40 to 64 years and then multiplied by an adjustment factor of 100; incidence for individuals aged 65+ was multiplied by an adjustment factor of 100.
[d]Using the hospitalization rate as a proxy for the percentage of cases that were severe and the case fatality rate among all cases, the case fatality rate among severe (i.e., hospitalized) cases was derived from Caro et al., 2005.[15] In that study, adults were defined as aged ≥ 18 years; thus, the same value was used for individuals aged 20 to 64 and 65+ years.
[e]Tdap and Td prices reflect the wholesale acquisition cost minus federal excise tax for BOOSTRIX and for generic Td (NDC 00006-4133-41).
[f]Assumption; cost of 1 physician visit (CPT code 99213).
[g]Based on assumption that only 2% of the local reaction and systemic reaction adverse events require a physician visit at a cost of $50 per visit.
CDC = Centers for Disease Control and Prevention; CPT = Current Procedural Terminology; NDC = National Drug Code; PI = prescribing information; RBRVS = Resource-Based Relative Value Scale; Td = tetanus toxoid, reduced diphtheria toxoid; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

from 97 to 699 cases per 100,000 person-years, or approximately 10 to 77 times higher than the incidence of disease reported by passive surveillance data (8.97 cases per 100,000 person-years).[22] Therefore, to estimate the number of cases of pertussis and to account for underreporting of pertussis cases in the United States, the most recent data on reported incidence of pertussis by age from the CDC were adjusted by a factor of 10 for adolescents and by a factor of 100 for adults in the base-case analysis based on assumptions previously made by the CDC ACIP (Table 2).[18,22] Higher adjustment factors were tested in a scenario analysis, resulting in incidence values ranging from 151 (base case) to 753 per 100,000 for adolescents, 366 (base case) to 731 per 100,000 for those aged 20-64 years, and 176 (base case) to 352 per 100,000 for those aged 65+ years. When disease incidence is adjusted upward in the model to account for underreporting of passive surveillance data, we assumed that all levels of severity of disease are equally underreported. This assumption is consistent with data seen in prospective surveillance studies (using the definitions outlined previously).[23]

For each base-case scenario, the number of patients with wounds vaccinated (by age) was multiplied by pertussis incidence (by age) and by vaccine efficacy against pertussis (0% for Td; 89% for Tdap).[8] Waning of vaccine efficacy was included, assuming protection against pertussis lasted for 8 years and declined exponentially each year, such that efficacy dropped from 89% in the first year to 79% in the second year and 69% in the third year for the 3-year model time horizon (Table 2). In scenario analyses, lower baseline efficacy and a larger decrease in efficacy was tested based on recent data from the CDC: 75%, 56%, and 39% efficacy in the first, second, and third year, respectively.[20]

Deaths

The model accounted for mortality due to pertussis as well as all-cause mortality. Pertussis-related death was included for severe cases of disease only. Case fatality rates for the 3 age groups were derived from data used by a previous model (Table 2).[15] All-cause mortality was estimated using age-specific U.S. mortality rates.[24]

Costs

Costs were estimated for vaccine acquisition, vaccine-related adverse events, and treatment of pertussis (Table 2). In the base-case analysis, vaccine wholesale acquisition costs minus federal excise tax were used, using values for BOOSTRIX and generic Td as representative of Tdap and Td vaccines generally.[25] In a scenario analysis, the lower vaccine costs were tested using contracted public prices ($14.51 for Td and $28.16 for Tdap for children; $11.88 for Td and $22.71 for Tdap for adults) based on the CDC vaccine price list.[26] A 10% higher price for Tdap also was tested. Costs for treating vaccine-related adverse events were estimated for the Td and the Tdap vaccines, based on the incidence rates and costs for treating these events used in a previous cost-effectiveness analysis of pertussis vaccine.[14] Vaccine administration costs were not included.

Costs for treatment of mild, moderate, or severe cases of pertussis were consistent with the definitions presented previously for incidence of reported pertussis cases by severity type. The cost for treating a mild case of pertussis was assumed to be equivalent to the cost of 1 physician visit; the cost for treating a moderate case of pertussis was based on average costs for outpatient cases used by the CDC ACIP[18]; the cost for treating a severe case of pertussis was based on the cost of hospitalized cases (Table 2).[27] Costs by age were explored, but there was

TABLE 3 Budget-Impact Results for a Health Plan by Age over a 3-Year Time Horizon (2012 U.S. Dollars)

Outcomes by Year	Scenario 1: 100% Td, 0% Tdap		Scenario 2: 0% Td, 100% Tdap		Budget Impact (Scenario 2 Minus Scenario 1)[a]	
Health plan with 1 million covered lives aged < 65 years (8,240 patients with open wounds eligible for Tdap vaccine)						
Year 1 annual medical costs (PMPM)	$160,277	($0.01)	$292,641	($0.02)	$132,364	($0.01)
Year 2 annual medical costs (PMPM)	$172,857	($0.01)	$295,340	($0.02)	$122,484	($0.01)
Year 3 annual medical costs (PMPM)	$185,396	($0.02)	$299,188	($0.02)	$113,793	($0.01)
Cumulative over 3 years: medical costs	$518,529		$887,169		$368,640	
Cumulative over 3 years: pertussis cases	171		30		-141	
Health plan with 1 million covered lives aged 65+ years (12,891 patients with open wounds eligible for Tdap vaccine)						
Year 1 annual medical costs (PMPM)	$257,236	($0.02)	$458,401	($0.04)	$201,165	($0.02)
Year 2 annual medical costs (PMPM)	$281,399	($0.02)	$463,586	($0.04)	$182,187	($0.02)
Year 3 annual medical costs (PMPM)	$304,442	($0.03)	$470,657	($0.04)	$166,215	($0.01)
Cumulative over 3 years: direct medical costs	$843,077		$1,392,645		$549,568	
Cumulative over 3 years: pertussis cases	132		23		-109	

[a]*This column may not equal the difference in Scenario 1 and Scenario 2 due to rounding.*
PMPM = per member per month; Td = tetanus toxoid, reduced diphtheria toxoid; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

a lack of data in the published literature on differential costs by age, particularly for mild and moderate cases of pertussis. Thus, costs differed by severity of disease but not by age.

The costs of treating long-term complications of pertussis, including neurological sequelae, were excluded because of the short time horizon. Excluding these costs was conservative because inclusion would lead to greater cost savings per case of pertussis avoided with protection from Tdap and a lower budget impact. All costs related to wound management, including vaccine administration costs, were not included because they are equal for both vaccines and were considered beyond the scope of this analysis.

When necessary, all costs were inflated to 2012 U.S. dollars using the medical care component of the Consumer Price Index.[28]

Model Outcomes

For each base-case scenario, the number of patients with wounds who were vaccinated, number of cases of pertussis, cost of treating pertussis cases, vaccine costs, and vaccine-related adverse event costs were calculated on an annual basis and calculated cumulatively over the 3-year time horizon. The aggregate and incremental undiscounted health outcomes and cost outcomes are shown annually and cumulatively for 2 types of health plans (those with people aged < 65 years and those with people aged 65+ years) and for the U.S. population aged 10+ years. Costs are reported as total annual costs and per-member-per-month (PMPM) costs because PMPM costs represent the impact vaccination has on the insurance premiums for the health plans. Outcomes are undiscounted, as recommended for budget-impact analyses.[29]

Sensitivity Analyses

A series of scenario analyses were conducted to test how changing specific input parameter values or model assumptions would affect results. All of the input parameters in the model were varied using alternative data sources or alternative clinically relevant assumptions. Scenarios with the largest (positive or negative) impact on either total medical costs or cases of pertussis cases avoided are presented. Alternative scenarios are presented for the following key parameters: annual number of patients with wounds eligible for vaccination with Tdap, uptake rates for Tdap, annual pertussis incidence, waning of Tdap efficacy (i.e., protection against pertussis), and prices for Td and Tdap vaccines.

For each of the scenario analyses, the number of pertussis cases avoided and the increase in total medical costs are shown cumulatively over the 3-year time horizon for the 2 types of health plans and for the U.S. population.

Results

For a health plan with 1 million members aged <65 years, an estimated 8,240 patients with open wounds were eligible for Tdap vaccination each year (Table 1). Vaccination with Tdap instead of Td for wound management was estimated to increase annual medical costs (additional costs due to vaccination minus reduced costs for treating pertussis) in year 1 from $160,227 to $292,641 for a total increase of $132,364 or an increase in PMPM costs of $0.01 (Table 3). The estimated increase in medical costs was slightly lower in year 2 ($122,484) and year 3 ($113,793), with an estimated increase in PMPM costs of $0.01. Over the 3-year time horizon, an estimated 141 cases of pertussis were avoided if people presenting with wounds were vaccinated with Tdap instead of Td.

For a health plan with 1 million members aged 65+ years, an estimated 12,891 patients with open wounds were eligible for Tdap vaccination each year (Table 1). Vaccination with Tdap instead of Td was estimated to increase annual medical costs in year 1 from $257,236 to $458,401 for a total increase of $201,165 or an increase in PMPM costs of $0.02 (Table 3). The estimated increase in medical costs was lower in subsequent

TABLE 4 U.S. Annual Population Costs and Clinical Outcomes over a 3-Year Time Horizon (2012 U.S. Dollars)

Year/Parameter	Scenario 1: 100% Td, 0% Tdap	Scenario 2: 0% Td, 100% Tdap	Incremental (Scenario 2 Minus Scenario 1)[a]
U.S. population (2,731,407 patients with open wounds eligible for Tdap vaccine each year)			
Year 1			
Number of people vaccinated in year 1	2,731,407	2,731,407	0
Pertussis cases in those vaccinated in year 1	8,574	943	-7,630
Vaccine acquisition costs	$48,980,087	$96,418,682	$47,438,595
Vaccine-related adverse event costs (incremental)	N/A	$122,745	$122,745
Pertussis-related costs	$4,408,947	$484,984	-$3,923,963
Total medical costs	**$53,389,034**	**$97,026,411**	**$43,637,377**
Year 2			
Number of people vaccinated in years 1 or 2 and still alive	5,431,862	5,431,865	3
Pertussis cases in those vaccinated in years 1 or 2	17,080	2,768	-14,311
Vaccine acquisition costs	$48,980,087	$96,418,682	$47,438,595
Vaccine-related adverse event costs (incremental)	N/A	$122,745	$122,745
Pertussis-related costs	$8,759,448	$1,418,506	-$7,340,942
Total medical costs	**$57,739,534**	**$97,959,932**	**$40,220,398**
Year 3			
Number of people vaccinated in years 1, 2, or 3 and still alive	8,102,500	8,102,507	7
Pertussis cases in those vaccinated in years 1, 2, or 3	25,520	5,359	-20,162
Vaccine acquisition costs	$48,980,087	$96,418,682	$47,438,595
Vaccine-related adverse event costs (incremental)	N/A	$122,745	$122,745
Pertussis-related costs	$13,053,726	$2,736,282	-$10,317,444
Total medical costs	**$62,033,813**	**$99,277,709**	**$37,243,896**
Cumulative over 3 years			
Number of eligible patients with wounds vaccinated	8,194,222	8,194,222	0
Pertussis cases in those vaccinated	51,174	9,070	-42,104
Vaccine acquisition costs	$146,940,260	$289,256,046	$142,315,786
Vaccine-related adverse event costs (incremental)	N/A	$368,234	$368,234
Pertussis-related costs	$26,222,121	$4,639,772	-$21,582,349
Total medical costs	**$173,162,381**	**$294,264,052**	**$121,101,671**

[a]This column may not equal the difference in Scenario 1 and Scenario 2 due to rounding.
N/A = not available; Td = tetanus toxoid, reduced diphtheria toxoid; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

years. Over the 3-year time horizon, an estimated 109 cases of pertussis were avoided.

For the U.S. population aged 10+ years, an estimated 2,731,407 patients with open wounds were eligible for Tdap vaccination each year (Table 1). Vaccination with Tdap instead of Td was estimated to increase annual medical costs by $43,637,377 in year 1, $40,220,398 in year 2, and $37,243,896 in year 3 (Table 4). Over the 3-year time horizon, the expected number of pertussis cases avoided among people aged 10+ years in the United States was 42,104, with an estimated additional expenditure of $121,101,671 or approximately $2,876 per case avoided.

Scenario analyses showed that the results (i.e., cumulative direct medical costs or cases avoided over the 3-year time horizon) were sensitive to the number of patients with wounds vaccinated with Tdap, the adjustment factor to account for underreporting of pertussis, and the incremental price difference between Td and Tdap vaccines. The parameters to which the results were most sensitive were similar for the 2 types of health plans and the U.S. population: more wounds eligible for Tdap by including both open wounds and other wounds led to the largest increase in cumulative direct medical costs (ranging from 57% to 93% higher than the base case); lower uptake rates for Tdap led to the largest decrease in cumulative direct medical costs (ranging from 48% to 49% lower than the base case); and higher pertussis incidence also reduced the cumulative direct medical costs (ranging from 18% to 22% lower than the base case; Table 5).

For all of the scenarios tested, the increase in PMPM costs ranged from < $0.01 to $0.02 for health plans for ages < 65 years and ranged from < $0.01 to $0.03 for health plans for ages 65+ years. For the U.S. analysis, the cumulative increase in direct medical costs over the 3-year time horizon ranged from $62.1 million to $226.0 million, and the cumulative number of pertussis cases avoided ranged from 17,919 to 88,724 (Table 5).

TABLE 5 Scenario Analyses for Cumulative 3-Year Incremental Budget and Health Outcomes (2012 U.S. Dollars)

Scenario	Alternative Assumption/Value	Health Plan (Aged < 65 Years)		Health Plan (Aged 65+ Years)		U.S. Population	
		Pertussis Cases Avoided (% Change)	Increased Total Costs (% Change)	Pertussis Cases Avoided (% Change)	Increased Total Costs (% Change)	Pertussis Cases Avoided (% Change)	Increased Total Costs (% Change)
Base case[a]		141	$368,640	109	$549,568	42,104	$121,101,671
More wounds eligible for Tdap[b]	Open and other wounds combined	269 (90.8%)	$712,351 (93.2%)	171 (56.9%)	$861,822 (56.8%)	79,188 (88.1%)	$225,954,110 (86.6%)
Fewer wounds eligible for Tdap[c]	Patients with wounds previously vaccinated with Td in the past 10 years excluded	83 (-41.1%)	$221,286 (-40.0%)	68 (-37.6%)	$344,235 (-37.4%)	24,901 (-40.9%)	$73,271,878 (-39.5%)
Lower Tdap uptake	25%, 50%, 75% in year 1, year 2, year 3, respectively	60 (-57.4%)	$188,963 (-48.7%)	47 (-56.9%)	$283,521 (-48.4%)	17,919 (-57.4%)	$62,149,206 (-48.7%)
Higher pertussis incidence[d]	50 times reported cases for aged 10-19 years, 200 times reported cases for aged 20+ years	298 (111.3%)	$300,499 (-18.5%)	218 (100.0%)	$427,993 (-22.1%)	88,724 (110.7%)	$97,911,542 (-19.1%)
Lower Tdap efficacy[e]	75%, 56%, 39% in years 1, 2, 3, respectively	107 (-24.1%)	$383,414 (4.0%)	83 (-23.9%)	$578,088 (5.2%)	32,109 (-23.7%)	$126,216,567 (4.2%)
Lower Td and Tdap price[f]	Td children: $14.51 Tdap children: $28.16 Td adults: $11.88 Tdap adults: $22.71	141 (0.0%)	$213,148 (-42.2%)	109 (0.0%)	$299,131 (-45.6%)	42,104 (0.0%)	$69,270,801 (-42.8%)
Higher Tdap price	10% higher price: $38.83	141 (0.0%)	$455,905 (23.7%)	109 (0.0%)	$686,078 (24.8%)	42,104 (0.0%)	$150,027,275 (23.9%)

[a]*Base-case assumptions/values: annual number of patients with wounds eligible for Tdap is based on "open" wounds (i.e., 8,240 patients with wounds for health plan patients aged < 65 years, 12,891 patients with wounds for health plan patients aged 65+ years, 2,731,407 patients with wounds per year for the U.S. population); patients with wounds previously vaccinated with Td in the past 5 years were excluded as not eligible for Tdap; 100% Tdap uptake in years 1, 2, and 3; reported pertussis incidence adjusted by 10 times for patients aged 10 to 19 years, adjusted by 100 times for patients aged 20+ years; Tdap efficacy equal to 89%, 79%, 69% in years 1, 2, and 3, respectively; Tdap price of $35.30 (i.e., wholesale acquisition cost for BOOSTRIX) and Td price of $17.99 (adults) and $17.21 (children; wholesale acquisition cost for generic NDC 00006-4133-41).*

[b]*Annual number of patients with wounds eligible for Tdap used in the base-case and scenario analysis are shown in Table 1.*

[c]*The alternative percentages of individuals eligible for Tdap were 14.70%, 35.70%, and 45.60% instead of 18.96%, 61.60%, and 72.80% (shown in Table 2) for individuals aged 10 to 19 years, 20 to 64 years, and 65+ years, respectively.[10,11] This resulted in 4,923 patients with wounds for health plan patients aged < 65 years, 8,074 patients with wounds for health plan patients aged 65+ years, and 1,646,921 patients with wounds per year for the U.S. population.*

[d]*Alternative assumptions for the adjustment factor for pertussis incidence were based on previously made assumptions by the Advisory Committee on Immunization Practices.[18]*

[e]*Alternative vaccine efficacy data were based on recent CDC data.[20]*

[f]*Alternative vaccine prices were from the CDC vaccine price list.[26]*

CDC = Centers for Disease Control and Prevention; NDC = National Drug Code; Td = tetanus toxoid, reduced diphtheria toxoid; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

Discussion

Vaccination with Tdap instead of Td for patients presenting to the health system with a wound requiring tetanus vaccine and who are eligible for Tdap is estimated to lead to an increase of < $0.01 to $0.03 in health plan PMPM costs for the health plan with all members aged < 65 years and for the health plan with all members aged 65+ years. Direct medical costs are expected to increase each year, but the increase in costs (i.e., budget impact) is expected to be lower in year 2 and year 3 as compared with year 1. This is because the number of avoided cases of pertussis and the associated offsetting cost savings in medical costs are expected to increase each year due to the increase in the cumulative number of people vaccinated and protected against pertussis. Over 3 years, vaccination with Tdap was estimated to cost an additional $368,640 ($0.01 PMPM), with 141 pertussis cases avoided per 1 million health plan members aged < 65 years. Tdap was estimated to cost an additional $549,568 ($0.01 to $0.02 PMPM), with 109 pertussis cases avoided per 1 million health plan members aged 65+ years. Results for the analysis of the U.S. population aged 10+ years showed that over the 3-year time horizon the estimated expected number of pertussis cases avoided was 42,104, at a cost of approximately $2,876 per case avoided.

This cost per case avoided, which is based on an assumed pertussis incidence of 151, 366, and 176 cases per 100,000 people aged 10-19, 20-64, and 65+ years, respectively, is similar to cost-effectiveness ratios found by other studies using similar ranges for pertussis incidence (ranging from $830 to $2,220 per case avoided among adolescents and from $538 to $1,966 per case avoided among people aged 65+ for pertussis incidence values between 100 and 200 cases per 100,000).[3,17] However, these cost-effectiveness ratios are not directly comparable because our budget-impact analysis used undiscounted direct medical costs over a short (3-year) time horizon, whereas cost-effectiveness analyses typically include direct and indirect costs discounted over a long (i.e., lifetime) time horizon to estimate the economic efficiency of a new intervention from a societal perspective.

The estimated total costs and incremental costs are greater for health plans with individuals aged 65+ years than costs for those with individuals aged <65 years because of the number of unvaccinated people in the older age group and subsequently the greater number of patients with wounds who are vaccinated (12,891 vs. 8,240 patients with wounds per year). Although people aged 65+ years have a higher likelihood of developing a severe case of pertussis and thus an overall higher cost of treatment, pertussis costs in this age group are lower because the estimated number of cases of pertussis avoided is lower for health plans including individuals aged 65+ years (109 vs. 141 avoided cases), despite the higher number of vaccinated individuals. This finding can be explained by the lower incidence of pertussis among individuals aged 65+ years when compared with younger individuals.

For people aged 65+ years, Tdap is typically covered under Medicare Part D instead of under Medicare Part B. A recent survey of U.S. physicians found that financial barriers, such as lack of reimbursement for a vaccine, low reimbursement rates for a vaccine, or coverage under Medicare Part D (which typically includes high out-of-pocket costs), were the most commonly reported reasons for low vaccination rates among adults.[12] Because of low vaccination rates, ACIP recommends physicians vaccinate persons aged 65+ years with either Tdap vaccine they have available so as not to "miss an opportunity to vaccinate."[7] Although the Affordable Care Act mandated that private health plans cover all vaccines recommended by ACIP without requiring a copayment, eliminating the financial barrier for individuals with private insurance, this law does not impact Medicare coverage policies. Since the burden of pertussis remains a concern and vaccine coverage rates remain suboptimal in this age group, coverage of Tdap vaccine for routine wound management by Medicare Part B and vaccination with either Tdap vaccine for patients with wounds could be considered as strategies for increasing pertussis vaccine coverage among people aged 65+ years.

Results of this study were sensitive to input parameter values, particularly parameters associated with the number of patients with wounds vaccinated with Tdap. This study estimated that a Tdap vaccination strategy targeting patients with wounds requiring a tetanus-containing vaccine would impact between 2.7 and 5.1 million people in the United States, which is similar to or substantially smaller than other target populations for Tdap vaccination.[16] The estimated increases in annual medical costs and cases of pertussis avoided are both a function of the number of patients with wounds eligible for and vaccinated with Tdap (i.e., as the number of patients with wounds vaccinated with Tdap increases, annual medical costs and cases of pertussis avoided increase). Therefore, it is not surprising that the results were most sensitive to parameters that directly impacted the number of patients with wounds vaccinated with Tdap: the annual incidence of wounds (or specifically whether wounds categorized as "other" were included in addition to open wounds) and the uptake rate for Tdap. Lower vaccine efficacy and greater waning of efficacy over time were tested in scenario analyses using recent real-world effectiveness data[20]; however, results were more sensitive to other input parameters previously discussed.

Despite the wide range of our results, they likely overestimate the expected increase in medical costs and underestimate the benefits of Tdap for 2 reasons. First, assuming that Tdap provides protection against pertussis for more than 3 years, the impact on pertussis cases prevented each year will increase each year as long as those in the first vaccinated cohort maintain their protection. Once that protection is lost, a steady-state number of pertussis cases avoided may be reached. Second, the analysis of the benefits of the vaccine program for routine wound management does not include the possible herd immunity benefits for reduced cases of pertussis in people who have contact with those who receive Tdap for wound management and who do not have active protection against pertussis.

The strength of the current analysis is that it is the first to provide estimates of the expected financial cost (i.e., affordability) and the expected number of pertussis cases avoided from a vaccination strategy using the Tdap vaccine in routine wound management. Such estimates are valuable to health care decision makers who are responsible for health plan or national budgets. To assist with this, the results have been presented from the health plan and the U.S. population perspectives.

Limitations

This analysis has several limitations, particularly with respect to the input data used to populate the model. The National Health Interview Survey is a self-reported survey on the incidence of wounds, which introduces reporting bias. However, the strength of this source is that it captures all patients with wounds who received health care (i.e., incurred some sort of direct medical cost). Other approaches, such as using claims databases to identify patients with wounds by the *International Classification of Diseases, Ninth Revision, Clinical Modification* codes, would require piecing together multiple databases to account for patients with wounds presenting in various health settings (e.g., outpatient setting, inpatient setting, emergency department, urgent care facility), which could lead to double counting or an overestimate. Given the uncertainty in the number of patients with wounds requiring tetanus vaccination each year and the sensitivity of our study's results to this parameter, future analyses using alternative methods for estimating wound incidence may be warranted to improve the precision around our study's estimates.

Another limitation in the model is the considerable uncertainty about 2 input values that make the most difference to the budget impact of Tdap. First, the budget impact of Tdap decreases when the annual incidence of pertussis is higher. There is considerable uncertainty in the annual pertussis incidence data, especially in the proportion of cases that are correctly diagnosed and/or reported. Incidence rates ranging from 151 to 753 per 100,000 for adolescents and ranging from 176 to 731 per 100,000 for adults were explored. Second, the budget impact of Tdap increases when the total number of patients with wounds for which a tetanus booster may be considered is higher. Age-specific annual wound incidence data are reported in 2 categories: open wounds—management of which would almost certainly include the recommendation for a tetanus booster vaccination in patients without a recent booster vaccination (3.0 million)—and other wounds—including fire-, burn-, or scald-related episodes; animal or insect bites; machinery accidents; and other but not specified episodes (2.6 million)—where a tetanus booster vaccination might be considered (see Appendix E, available in online article). Thus, there is considerable uncertainty about the total number of patients with wounds each year for which a tetanus booster vaccination might be recommended.

Long-term complications of pertussis, including encephalopathy, were not included in the model. Not including the costs of treating long-term pertussis-related disabilities leads to an underestimate in the savings from Tdap vaccination and subsequently an overestimate in the budget impact. However, because of the extremely low incidence of long-term disabilities requiring treatment (estimated as 0.02%-0.07% of pertussis cases[15,30]) and because of the short time frame of this analysis, these cost savings are assumed to be negligible.

It should be noted that costs and efficacy values used in this analysis were specific to BOOSTRIX for Tdap. In the United States, there are multiple generics for Td and 2 Tdap brands (BOOSTRIX and Adacel); using different prices for each of these inputs would affect the results. However, findings were consistent in a scenario analysis that used costs and efficacy associated with Adacel instead of BOOSTRIX (not reported here), indicating that results from the current study may be applicable to Tdap vaccines in general.

The use of a simple Microsoft Excel model to estimate the budget impact did not allow us to include possible herd immunity effects that are a result of substituting Tdap for Td in patients eligible for Tdap when presenting for management of a wound. Thus, the impact of increasing vaccine coverage rates on pertussis cases is likely underestimated.

Conclusions

The current study estimated that vaccination of the U.S. population aged 10+ years with Tdap instead of Td for routine wound management would impact between 2.7 and 5.1 million people with wounds annually. Over a 3-year time horizon, this vaccination strategy is expected to result in 42,104 cases of pertussis avoided at a cost of approximately $2,876 per case avoided. For hypothetical health plans, this translates to an additional cost of $368,640 per 1 million members aged < 65 years and an additional cost of $549,568 per 1 million members aged 65+ years (< $0.01 to $0.03 PMPM). Results were sensitive to input parameter values, particularly parameters associated with the number of patients with wounds vaccinated with Tdap. Vaccination with Tdap for routine wound management could be considered as another strategy to help address the pertussis public health concern in the United States. Future analyses using alternative methods for estimating wound incidence could improve the precision around the estimated budget and health impact of this vaccination strategy to confirm its affordability.

Authors

SANDRA E. TALBIRD, MSPH, is Director, Health Economics; JONATHAN GRAHAM, BS, is Associate Director, Health Economics; and JOSEPHINE MAUSKOPF, PhD, is Vice President, Health Economics, RTI Health Solutions, Research Triangle Park, North Carolina. CRISTINA MASSERIA, PhD, is Health Outcomes Manager, NAVD Health Outcomes, and GIRISHANTHY KRISHNARAJAH, MPH, MBA/MS, PhD, is Therapy Area Head, NAVD Health Outcomes, GlaxoSmithKline, King of Prussia, Pennsylvania.

AUTHOR CORRESPONDENCE: Sandra E. Talbird, MSPH, Director, Health Economics, RTI Health Solutions, 200 Park Offices Dr., Research Triangle Park, NC 27709. Tel.: 919.541.7258; Fax: 919.541.7222; E-mail: stalbird@rti.org.

DISCLOSURES

Talbird, Graham, and Mauskopf (and/or their institutions) received research funding from GlaxoSmithKline to develop the budget-impact estimates and for other research studies. Masseria and Krishnarajah are employees of and hold stock options in the GlaxoSmithKline group of companies.

GlaxoSmithKline Biologicals SA funded this study/research and was involved in all stages of study conduct, including analysis of the data. GlaxoSmithKline Biologicals SA also undertook all costs associated with the development and publication of this manuscript.

Talbird, Graham, and Mauskopf were primarily responsible for the design and programming of the economic model, identification and final selection of the input parameter values, interpretation of the study results, and preparation of the study report. Masseria and Krishnarajah contributed to model design, input parameter estimation, interpretation of the results, and review of and revisions to the study report. All authors had access to the data, participated in the development of this manuscript, and gave final approval before submission. All authors have agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ACKNOWLEDGMENTS

We thank Julia Donnelly (freelance Publication Manager on behalf of GlaxoSmithKline group of companies) for her valuable editorial assistance.

REFERENCES

1. Kretsinger K, Broder KR, Cortese MM, et al.; Centers for Disease Control and Prevention; Advisory Committee on Immunization Practices; Healthcare Infection Control Practices Advisory Committee. Preventing tetanus, diphtheria, and pertussis among adults: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine recommendations of the Advisory Committee on Immunization Practices (ACIP) and recommendation of ACIP, supported by the Healthcare Infection Control Practices Advisory Committee (HICPAC), for use of Tdap among health-care personnel. *MMWR Recomm Rep.* 2006;55(RR-17):1-37. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5517a1.htm. Accessed November 6, 2014.

2. Cortese MM, Baughman AL, Brown K, Srivastava S. A "new age" in pertussis prevention: new opportunities through adult vaccination. *Am J Prev Med*. 2007;32(3):177-85.

3. Lee GM, Murphy TV, Lett S, et al. Societal costs and morbidity of pertussis in adolescents and adults. *Clin Infect Dis.* 2004;39(11):1572-80.

4. Centers for Disease Control and Prevention. About pertussis outbreaks. August 28, 2013. Available at: http://www.cdc.gov/pertussis/outbreaks/about.html. Accessed November 6, 2014.

5. Güris D, Strebel PM, Bardenheier B, et al. Changing epidemiology of pertussis in the United States: increasing reported incidence among adolescents and adults, 1990-1996. *Clin Infect Dis.* 1999;28(6):1230-37.

6. Immunization Action Coalition. Historic dates and events related to vaccines and immunization. Available at: http://www.immunize.org/timeline/. Accessed November 6, 2014.

7. Centers for Disease Control and Prevention. Updated recommendations for use of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine in adults aged 65 years and older—Advisory Committee on Immunization Practices (ACIP), 2012. *MMWR Morb Mortal Wkly Rep.* 2012;61(25):468-70. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6125a4.htm. Accessed November 6, 2014.

8. BOOSTRIX (tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine, adsorbed). Prescribing information. GlaxoSmithKline Biologicals. Revised November 2013. Available at: http://us.gsk.com/products/assets/us_boostrix.pdf. Accessed November 6, 2014.

9. Tseng HF, Sy LS, Qian L, et al. Safety of a tetanus-diphtheria-acellular pertussis vaccine when used off-label in an elderly population. *Clin Infect Dis.* 2013;56(3):315-21.

10. Centers for Disease Control and Prevention. National Immunization Survey–Teen. 2011. Available at: http://www.cdc.gov/vaccines/imz-managers/coverage/nis/teen/tables/11/tab01_iap_2011.pdf. Accessed November 6, 2014.

11. Centers for Disease Control and Prevention. Noninfluenza vaccination coverage among adults—United States, 2011. *MMWR Morb Mortal Wkly Rep.* 2013;62(4):468-70. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6204a2.htm. Accessed November 6, 2014.

12. Hurley LP, Bridges CB, Harpaz R, et al. U.S. physicians' perspective of adult vaccine delivery. *Ann Intern Med.* 2014;160(3):161.

13. Chen LH, Warner M, Fingerhut L, Makuc D. Injury episodes and circumstances: National Health Interview Survey, 1997-2007. *Vital Health Stat 10.* 2009;10(241):1-55.

14. Lee GM, Murphy TV, Lett S, et al. Cost effectiveness of pertussis vaccination in adults. *Am J Prev Med.* 2007;32(3):186-93.

15. Caro JJ, Getsios D, El-Hadi W, Payne K, O'Brien JA. Pertussis immunization of adolescents in the United States: an economic evaluation. *Pediatr Infect Dis J.* 2005;24(5 Suppl):S75-S82.

16. Hay JW, Ward JI. Economic considerations for pertussis booster vaccination in adolescents. *Pediatr Infect Dis J.* 2005;24(6 Suppl):S127-S33.

17. McGarry LJ, Krishnarajah G, Hill G, et al. Cost-effectiveness analysis of Tdap in the prevention of pertussis in the elderly. *PLoS One.* 2013;8(9):e67260.

18. Acosta A. Cost-effectiveness of pertussis vaccine substitution for tetanus booster in prevention of pertussis in adults 65 years and older. Presentation to the Advisory Committee on Immunization Practices (ACIP). February 22, 2012. Atlanta, GA: US Department of Health and Human Services, CDC; 2012.

19. Krishnarajah G. Cost-effectiveness analysis of Boostrix (tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine, adsorbed) among individuals ≥65 years of age in prevention of pertussis. Presentation to the Advisory Committee on Immunization Practices (ACIP). February 22, 2012. Atlanta, GA: US Department of Health and Human Services, CDC; 2012.

20. Liang J. Considerations for a second Tdap for the general population. Pertussis Vaccines Work Group. Centers for Disease Control and Prevention. June 19, 2013.

21. Howden LM, Meyer JA. Age and sex composition: 2010. U.S. Census Bureau. 2010 Census Briefs. May 2011. Available at: http://www.census.gov/prod/cen2010/briefs/c2010br-03.pdf. Accessed November 6, 2014.

22. Centers for Disease Control and Prevention. Summary of notifiable diseases—United States, 2010. *MMWR Morb Mortal Wkly Rep.* 2012;59(53):1-111. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5953a1.htm. Accessed November 6, 2014.

23. Strebel P, Nordin J, Edwards K, et al. Population-based incidence of pertussis among adolescents and adults, Minnesota, 1995-1996. *J Infect Dis.* 2001;183(9):1353-59. Available at: http://jid.oxfordjournals.org/content/183/9/1353.long. Accessed November 6, 2014.

24. Miniño AM, Murphy SL, Xu J, Kochanek KD. Deaths: final data for 2008. *Natl Vital Stat Rep.* 2011;59(10):1-126. Available at: http://www.cdc.gov/nchs/data/nvsr/nvsr59/nvsr59_10.pdf. Accessed November 6, 2014.

25. RED BOOK Online 2.0 (2012). Available at: http://micromedex.com/redbook. Accessed December 4, 2014.

26. Centers for Disease Control and Prevention. CDC vaccine price list. August 1, 2014. Available at: http://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/index.html. Accessed November 6, 2014.

27. O'Brien JA, Caro JJ. Hospitalization for pertussis: profiles and case costs by age. *BMC Infect Dis.* 2005;5:57. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1184075/. Accessed November 6, 2014.

28. U.S. Bureau of Labor Statistics. Consumer Price Index—all urban consumers. U.S. medical care, 1982-84 (CUUR0000SAM). [Not seasonally adjusted; value for March 2012 used]. Available at: http://data.bls.gov/cgi-bin/surveymost?cu. Accessed November 6, 2014.

29. Sullivan SD, Mauskopf JA, Augustovski F, et al. Budget impact analysis—principles of good practice: report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force. *Value Health*. 2014;17(1):5-14.

30. Centers for Disease Control and Prevention. Pertussis: United States, 1997-2000. *MMWR Morb Mortal Wkly Rep.* 2002;51(4):73-76. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5104a1.htm. Accessed November 6, 2014.

31. Ingenix. *The Essential RBRVS: A Comprehensive Listing of RBRVS Values for CPT and HCPCS Codes.* Salt Lake City, UT: Ingenix, Inc; 2012.

The following appendices provide additional details on the tetanus toxoid and reduced diphtheria toxoid (Td) and the tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccination rates as reported by 2 nationally representative U.S. surveys: the National Immunization Survey–Teen (NIS–Teen) and the National Health Interview Survey (NHIS). Appendix A presents the vaccination rates for Td and Tdap for adolescents as reported by NIS–Teen. Appendix B presents the vaccination rates for Td and Tdap for adults as reported by the NHIS. Appendix C presents the Tdap vaccination rates among adults aged 19 to 64 years who received a tetanus vaccination. Appendix D describes the calculations and assumption we made to estimate the annual percentage of patients with wounds who were eligible for Tdap vaccination for the 3 age groups in our model (10 to 19 years, 20 to 64 years, and 65+ years) and summarizes the values used in the base-case and sensitivity analyses.

APPENDIX A Self-Reported Td and Tdap Vaccination Rates from the Teen National Immunization Survey for Adolescents Aged 13 to 17 Years, 2006-2011

Parameter	2011	2010	2009	2008	2007	2006
Percentage vaccinated ≥ 1 Td or Tdap since aged 10 years	85.3%	81.2%	76.2%	72.2%	72.3%	60.1%
95% CI	84.5%-86.1%	80.2%-82.2%	75.1%-77.2%	70.8%-73.4%	70.3%-74.3%	57.8%-62.4%
Percentage vaccinated ≥ 1 Tdap since aged 10 years	78.2%	68.7%	55.6%	40.8%	30.4%	10.8%
95% CI	77.3%-79.1%	67.5%-69.8%	54.3%-56.8%	39.3%-42.2%	28.2%-32.7%	9.4%-12.3%
Percentage vaccinated with ≥ 1 Td (not Tdap) since aged 10 years[a]	7.1%	12.5%	20.6%	31.4%	41.9%	49.3%

[a]*Calculated by the authors of this article.*

CI = confidence interval; Td = tetanus toxoid and reduced diphtheria toxoid; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

APPENDIX B Self-Reported Td and Tdap Vaccination Rates Among Adults in the United States, National Health Interview Survey, 2007-2011

Parameter	2011	2010	2009	2008	2007
Percentage receiving tetanus vaccination (Td or Tdap) in the past 10 years					
Aged 19-24 years	N/A	N/A	66.4%	69.7%	N/A
n			2,353	1,759	
Aged 25-49 years	N/A	N/A	62.3%	62.2%	N/A
n			12,025	9,395	
Aged 19-49 years	64.5%	64.0%	N/A	63.6%[a]	57.2%[b]
n	16,483	13,946	N/A	11,154	1,738
Aged 50-64 years	63.9%	63.4%	62.8%	62.4%	57.2%
n	7,822	6,349	6,540	5,003	1,957
Aged 19-64 years	64.3%[c]	63.8%[c]	62.9%[c]	63.2%[c]	57.2%
n	24,305	20,295	20,918	16,157	3,695
Aged 65-74 years	N/A	N/A	58.3%	56.0%	N/A
n			2,765	2,140	
Aged 75+ years	N/A	N/A	46.0%	47.1%	N/A
n			2,367	1,969	
Aged 65+ years	54.4%	53.4%	52.6%[c]	51.7%[a]	44.1%
n	6,471	5,069	5,132	4,109	2,802
	Past 6 Years (2005-2011)	**Past 5 Years (2005-2010)**	**Past 4 Years (2005-2009)**	**Past 3 Years (2005-2008)**	**Past 2 Years (2005-2007)**
Percentage receiving tetanus vaccination, including pertussis vaccine (i.e., percentage ever receiving Tdap during time period)					
Aged 19-64 years	12.5%	8.2%	6.6%	5.7%	2.1%
n	17,480	14,824[d]	15,722	12,682	3,525
Percentage-point increase from previous year	4.3%	1.6%	0.9%	3.6%[c]	N/A
P value	< 0.05	< 0.05	0.02	N/A	N/A

[a]*Values were taken from the 2008 National Health Interview Survey and do not match precisely the calculated weighted average from the 2009 National Health Interview Survey, which reports data from the 2008 survey in more detail (i.e., broken down by more age groups). This discrepancy was assumed by the authors of this article to be based on differences in weighting and sample size. Therefore, the 2008 weighted data calculated by the Centers for Disease Control and Prevention were assumed to be correct.*

[b]*Age group was for ages 18 to 49 years.*

[c]*Calculated by the authors of this article.*

[d]*This value was taken from the 2010 National Health Interview Survey. The footnotes in the survey refer to a value of 14,582, but the tabular value was assumed to be correct.*

N/A = not applicable; Td = tetanus toxoid and reduced diphtheria toxoid; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

APPENDIX C Self-Reported Tdap Vaccination Rates Among Adults Aged 19 to 64 Years Who Received a Tetanus Vaccination, National Health Interview Survey, 2007-2011

Parameter	Past 6 Years (2005-2011)	Past 5 Years (2005-2010)	Past 4 Years (2005-2009)	Past 3 Years (2005-2008)	Past 2 Years (2005-2007)
Proportion of total tetanus vaccinations that were Tdap[a]	61.1%	52.3%	50.8%	51.5%	20.7%[b]
n	3,422	2,198	1,998	1,312	324

[a]*The Centers for Disease Control and Prevention report that this was calculated by dividing number of respondents who reported receiving Tdap by the sum of those who reported receiving Tdap and those who reported receiving other tetanus vaccination; respondents who reported that the doctor did not inform them of the vaccine type they received and those who could not recall the vaccine type were excluded.*
[b]*Age group was for ages 18 to 49 years.*
Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

APPENDIX D Estimated Percentage of Patients, by Age Group, Eligible for Tdap Vaccination for Wound Management (Used in Model)

Model Age Group	Not Eligible for Tdap (Range, %)	Eligible for Tdap (Range Used in Model, %)
Aged 10-19 years	81.04-85.30	14.70-18.96[a]
Aged 20-64 years	38.40-64.30	35.70-61.60[a]
Aged 65+ years	27.20-54.40	45.60-72.80[a]

[a]*Base-case value.*
Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

Calculations and Assumptions to Estimate the Percentages of Patients Eligible for Tdap Vaccination for Wound Management

We used the vaccination rate data for the most recent year available (2011) presented in Appendix A and Appendix B to estimate the percentage of patients eligible for Tdap vaccination for the age groups in our model (10 to 19 years, 20 to 64 years, 65+ years). The calculations and assumptions used for each age group are described in the following subsections.

Percentage of 10 to 19 Year Olds Eligible for Tdap Vaccination (Appendix A)

- Approach 1:
  = 1 – percentage receiving Tdap since aged 10 years – percentage receiving Td within the past 5 years
  = 1 – 0.782 – 0.0284 = 0.1896
- Approach 2:
  = 1 – percentage receiving Td or Tdap since aged 10 years
  = 1 – 0.853 = 0.1470

In Approach 1, we first excluded patients who reported receiving Tdap since aged 10 years (78.2%). Next, we assumed that among the patients aged 13 to 17 years who reported receiving a tetanus-containing vaccine but not Tdap since aged 10 years (7.1% [85.3% – 78.2% = 7.1%]), approximately two-fifths would have been 16 or 17 years old. Making a further assumption that all 16 and 17 year olds received Td more than 5 years ago, we estimated that 2.84% would not be eligible for Tdap and that the remaining three-fifths (4.26%) would be eligible for Tdap. This approach yielded 18.96% of patients eligible for Tdap, which was a slight overestimate because there were likely some 16 or 17 year olds who received Td less than 5 years ago and who therefore would not be eligible for Tdap.

In Approach 2, we simply excluded all patients who reported receiving Td or Tdap since aged 10 years (85.3%). This approach yielded 14.7% of patients eligible for Tdap, which was a slight underestimate because it excluded 16 or 17 year olds who could have received Td vaccine 6 or 7 years ago and therefore technically would be eligible for Tdap.

Approach 1 was used in the base-case analysis, and Approach 2 was used in sensitivity analysis.

Percentage of 20 to 64 Year Olds Eligible for Tdap Vaccination (Appendix B)

- Approach 1:
  = 1 – percentage receiving Tdap – percentage receiving Td within the past 5 years
  = 1 – 0.125 – [(0.643 – 0.125) / 10 × 5] = 0.6160
- Approach 2:
  = 1 – percentage receiving Tdap – percentage receiving Td within the past 10 years
  = 1 – 0.125 – (0.643 – 0.125) = 0.3570

In Approach 1, we first excluded patients who reported receiving Tdap in the past 6 years (2005-2011): 12.5%. Next, we calculated the weighted average among patients aged 19 to 64 years who reported receiving Td or Tdap in the past 10 years (64.3% in 2011) and assumed that 51.8% (64.3% – 12.5% = 51.8%) had received Td vaccine in the past 10 years. Finally, we assumed that patients were vaccinated with Td uniformly over the 10-year reporting time period, i.e., 5.18% per year. Thus, 25.9% of patients received Td within the past 5 years and were not eligible for Tdap. This approach yielded 61.6% of patients aged 19 to 64 years eligible for Tdap.

In Approach 2, we simply excluded all patients who reported receiving Td or Tdap in the past 10 years. This approach yielded 35.7% of patients eligible for Tdap, which was an underestimate because it excluded patients who could have received Td vaccine 5 to 10 years ago and who technically would be eligible for Tdap.

Approach 1 was used in the base-case analysis, and Approach 2 was used in sensitivity analysis.

Percentage of 65+ Year-Olds Eligible for Tdap Vaccination (Appendix B):

- Approach 1:
  = *1 – percentage receiving Tdap – percentage receiving Td within past 5 years*
  = *1 – 0.0 – (0.544 / 10 × 5) = 0.7280*
- Approach 2:
  = *1 – percentage receiving Tdap – percentage receiving Td within past 10 years*
  = *1 – 0.0 – 0.544 = 0.4560*

First, we assumed that no one aged 65+ years (i.e., 0.0%) received Tdap because it was not indicated or recommended in this population until 2012, which is the year of our analysis. Next, we assumed that patients who reported receiving Td were vaccinated uniformly over the 10-year time period. Given that 54.4% of patients aged 65+ years reported receiving Td in the past 10 years, we assumed each year there was a uniform percentage of patients (i.e., 5.44% of patients) vaccinated with Td each year. Thus, 27.2% of patients were vaccinated with Td within the past 5 years and not eligible for Tdap. This approach yielded 72.8% of patients aged 65+ years eligible for Tdap in Approach 1. In Approach 2, we simply excluded all patients who reported receiving Td in the past 10 years. Approach 1 was used in the base-case analysis, and Approach 2 was used in sensitivity analysis.

Underlying Assumptions to Estimate the Percentage Eligible for Tdap Vaccination for Wound Management

For all age groups, we made the underlying assumption that the percentage of patients who reported receiving Td or Tdap vaccine from the general population was equivalent to the percentage of patients among the wound population. This was a simplifying assumption that was necessary in the absence of data specifically among patients with wounds.

APPENDIX E Wound Descriptive Statistics and Pertussis Incidence, by Age Group

Parameter/Age Group	Data Point	Reference
Annualized number of injury episodes (in thousands)[a]		2007 National Health Interview Survey, Table 1[a,13]
Under 15 years	6,827	
15-24 years	6,304	
25-44 years	9,699	
45-64 years	6,861	
65-74 years	2,205	
75+ years	2,451	
All ages	34,347	
Percentage of injury episodes resulting in open wounds or other wounds[a]		2007 National Health Interview Survey, Table 7[13]
Under 15 years	23.7%, 15.9%	
15-24 years	15.1%, 17.2%	
25-64 years	15.2%, 13.8%	
65+ years	13.2%, 7.5%	
All ages	16.4%, 13.8%	
Percentage of the population with open wounds only, and with open and other wounds combined		Calculated values
Under 15 years	2.74%, 4.59%	
15-24 years	2.50%, 5.35%	
25-64 years	1.76%, 3.36%	
65+ years	1.77%, 2.78%	
All ages	2.08%, 3.83%	
Pertussis incidence		CDC, 2012[22]
5-14 years	24.78 per 100,000	
15-24 years	5.97 per 100,000	
25-39 years	3.78 per 100,000	
40-64 years	3.10 per 100,000	
65+ years	1.76 per 100,000	
All ages	8.97 per 100,000	

[a]*Not all patients with injuries require a tetanus-containing vaccine. Only patients with open wounds and burns (captured as part of the "other" category) likely require vaccination.*
CDC = Centers for Disease Control and Prevention.