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Impact and cost-effectiveness of a second tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine dose to prevent pertussis in the United States

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ABSTRACT

Introduction: The United States experienced a substantial increase in reported pertussis cases over the last decade. Since 2005, persons 11 years and older have been routinely recommended to receive a single dose of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine. The objective of this analysis was to evaluate the potential impact and cost-effectiveness of recommending a second dose of Tdap.

Methods: A static cohort model was used to calculate the epidemiologic and economic impact of adding a second dose of Tdap at age 16 or 21 years. Projected costs and outcomes were examined from a societal perspective over a 20-year period. Quality-adjusted Life Years (QALY) saved were calculated.

Results: Using baseline pertussis incidence from the National Notifiable Diseases Surveillance System, Tdap revaccination at either age 16 or 21 years would reduce outpatient visits by 433 (5%) and 285 (4%), and hospitalization cases by 7 (7%) and 5 (5%), respectively. The costs per QALY saved with a second dose of Tdap were approximately US $19.7 million (16 years) and $26.2 million (21 years). In sensitivity analyses, incidence most influenced the model; as incidence increased, the costs per QALY decreased. To a lesser degree, initial vaccine effectiveness and waning of effectiveness also affected cost outcomes. Multivariate sensitivity analyses showed that under a set of optimistic assumptions, the cost per QALY saved would be approximately $163,361 (16 years) and $204,556 (21 years).

Conclusion: A second dose of Tdap resulted in a slight decrease in the number of cases and other outcomes, and that trend is more apparent when revaccinating at age 16 years than at age 21 years. Both revaccination strategies had high dollar per QALY saved even under optimistic assumptions in a multivariate sensitivity analysis.

1. Introduction

Since the 1940s, pediatric diphtheria and tetanus toxoids and whole cell pertussis vaccine (DTP) was routinely recommended for children in the United States. During the 1990s, a less reactogenic pediatric acellular pertussis vaccine (diphtheria and tetanus toxoids and acellular pertussis vaccine [DTaP]) was licensed. In 1997, the Advisory Committee on Immunization Practices (ACIP) recommended infants and young children receive a 5-dose DTaP series (2, 4, 6 months; 15–18 months; 4–6 years) [1]. In 2005, ACIP recommended a single dose of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine for all adolescents aged 11–18 years (preferred at 11–12 years) and for adults aged 19–64 years who have not yet received a dose [2,3]. Currently,

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ACIP does not recommend additional doses of Tdap with the exception of pregnant women, who are recommended a dose during each pregnancy [4]. After receipt of a single dose of Tdap, a dose of Td is recommended every 10 years for protection against tetanus and diphtheria.

The United States has experienced a resurgence in pertussis over the last decade. The greatest number of reported pertussis cases in recent years was in 2012 (48,277), which has not been seen since 1955 [5]. Incidence of pertussis is highest among young infants. Rates are also high among children and adolescents, but low among adults. The true burden of disease among adults is likely to be higher than reported. Reasons for under-reporting and under-diagnosis of pertussis in adults include non-specific clinical presentation, lack of adult and provider awareness, challenges in confirming pertussis diagnosis, and limited sensitivity of the surveillance system [2].

Since 2005, vaccination coverage with Tdap among adolescents has steadily increased and was 86.0% in 2013, but uptake among adults has been poor and coverage is less than 15% [6,7]. Given the increasing burden of pertussis and that the earliest Tdap recipients would soon need a decennial tetanus booster, in February 2013 ACIP discussed the potential need for additional doses of Tdap [8]. When Tdap was first recommended in 2005, the level of vaccine effectiveness and duration of protection for pertussis were not known. Available data now suggest that initial Tdap vaccine effectiveness against pertussis is 66–78%, but duration of protection quickly wanes [9,10].

The objective of this analysis was to evaluate the impact and cost-effectiveness of adding a second dose of Tdap in a population of healthy 11 year olds who received their first dose at age 11 years compared to the current recommendation for one dose of Tdap under two separate strategies: (1) adding a second Tdap dose at age 16 years or (2) substituting decennial Td with a second Tdap at age 21 years. Because both Tdap products are currently approved by the Food and Drug Administration as a single-dose booster vaccination and have shown modest vaccine effectiveness for pertussis and short duration of protection, we chose not to model the impact and cost-effectiveness of replacing all decennial Td boosters with Tdap.

2. Methods

We constructed a static cohort model to predict the epidemiologic and economic effects of a one-time revaccination of Tdap in a healthy adolescent and adult population (Fig. 1). We examined the following strategies with respect to preventing disease and complications in a population currently recommended to receive a dose of Tdap at age 11 years: (1) revaccination of Tdap at age 16 years when a booster dose for meningococcal vaccine (MenACWY) is recommended, (2) substitution of Td with Tdap at age 21 years, and (3) no revaccination of Tdap (henceforth referred to as the base case). For each strategy, a hypothetical cohort of approximately 4.1 million healthy 11 year olds was considered (US Population Census, 2011). An analytic horizon of 20 years was chosen given that the cohort population will follow the current decennial revaccination of Td after age 30 years. For this analysis, persons not vaccinated at age 11 years were not eligible for a "catch-up" first or second dose of Tdap but were also followed until age 30. We estimated the costs and health benefits from the societal perspective and estimated cost-effectiveness ratios including cost per case averted and cost per QALY saved. When available, 95% confidence intervals (CI) are presented. All costs are presented in 2010 US dollars and discounted to present value at an annual rate of 3%. We performed the modeling in 2010 Microsoft Excel and ran simulations using @Risk for Excel (version 6.3.1 Industrial Edition).

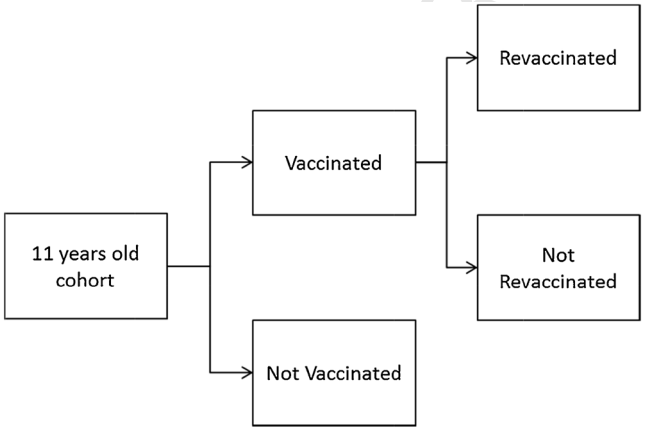

Fig. 1. Decision analytic model. Cohort population vaccinated at age 11 and revaccinated at age 16 or 21 years. Persons not vaccinated at age 11 years were not eligible for a "catch-up" first dose of Tdap or second Tdap at either age 16 or 21 years.

2.1. Population and disease parameters

Disease parameter values are list in Table 1. When available, values for parameters were broken down by age group. Incidence of pertussis and proportion of pertussis disease outcomes among the hypothetical cohort including outpatient visits, hospitalizations and deaths were based on data from the National Notifiable Diseases Surveillance System (NNDSS) from 2002 to 2011. To estimate the number of pertussis cases over the analytic horizon, 10-year average age-specific incidence for pertussis was used. Age-specific incidence for each year was estimated by dividing the number of reported pertussis cases from NNDSS (2002–2011) for each age by the age-specific U.S. population for the same years. Hospitalization probabilities used in the model varied by age. Because death due to pertussis in persons aged 11–30 years is rare, the case fatality ratio was based on the average rate of pertussis-related deaths by age group. Outpatient visits were assumed to be pertussis cases that did not report hospitalization or death (i.e., total pertussis cases reported minus hospitalized and death cases). We based the estimate of pertussis disease duration on the mean number of cough days from unpublished Emerging Infections Program Enhanced Pertussis Surveillance (EPS) data (2011–2012). Disease duration was assumed to be the same for outpatient and hospitalization-related outcomes. We also used unpublished EPS data to obtain the number of outpatient visits to healthcare providers prior to pertussis diagnosis. Age-specific mortality rates for other causes of death were incorporated into the model [11].

2.2. Vaccination program parameters

Assumptions on Tdap vaccine included vaccination coverage, cost of vaccination, initial vaccine effectiveness, and waning of effectiveness over time (Table 1). Based on Tdap vaccination coverage among adolescents aged 13–17 years during 2013, we applied 78% coverage for the first dose of Tdap [6]. For the second dose of Tdap at age 16, we assumed vaccination coverage to be 50%. Coverage for the second dose of Tdap at age 21 (64%) was based on Td vaccination coverage among adults aged 19–49 years during 2012 [7]. We assumed initial Tdap vaccine effectiveness (i.e., during the first year after receipt) to be 73%, based on a case-control study of Tdap among acellular pertussis vaccine recipients [9]. To account for waning protection after vaccination, we incorporated a 15-percentage point decrease of vaccine effectiveness each year post-vaccination, based on a Tdap vaccine effectiveness study [9]. We also assumed vaccine effectiveness and waning protection to be the same for both the first and second dose, based on the