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Lana Childs Date

Estimating the number of pertussis-susceptible children aged 0-23 months in the United States

Using the National Immunization Survey (NIS) 2013

By

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Master of Public Health

Global Epidemiology

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Oregon State University
2013

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Abstract

Estimating the number of pertussis-susceptible children aged 0-23 months in the United States

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By Lana Childs

Despite high coverage with pertussis-containing vaccines in the United States (US), children who are unvaccinated or not fully vaccinated remain susceptible to pertussis. Over multiple birth cohorts, the number of children who are not immune to pertussis will accumulate due to factors such as the child's age and age-specific vaccination status and vaccine dose-specific vaccine effectiveness. The total number of pertussis-susceptible children aged 0-23 months in the US is unknown. By using age-specific data on receipt of pertussis-containing vaccine by children evaluated in the 2013 National Immunization Survey, and accounting for vaccine effectiveness, maternal transfer of anti-pertussis antibodies, and vaccination disparities by poverty status, we estimated the number of pertussis-susceptible children aged 0-23 months. Of 7,905,672 children aged 0-23 months in the US, we estimate that approximately 22% (1,726,113) are susceptible to pertussis. Children aged 0-23 months living below poverty are more susceptible to pertussis than children living at or above poverty (below 23% susceptible compared to 20% for at or above). In sensitivity analysis, a sustained decrease to 95% of current vaccination levels would increase the proportion of children susceptible to pertussis to 26%. Age was a large factor in susceptibility with 76% of children aged 0-2 months not immune to pertussis compared to 7% of children aged 21-23 months. These estimates underscore the need to monitor age-specific pertussis vaccine coverage and to increase childhood pertussis vaccine coverage, to maintain population level immunity and to prevent the spread of pertussis among young children.

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Introduction

In recent years, pertussis morbidity in the United States (US) has reached levels not seen since the introduction of a pertussis-containing vaccine during the 1940s. In 2014, there were 32,971 cases reported, a 15% increase over the previous year (1). Most pertussis cases occur in children who are too young to be fully vaccinated and pre-adolescents who experience waning immunity from childhood vaccination (1-3). In the US, childhood vaccine coverage measured at 19-35 months of age is high overall, however coverage for 4-dose series of diphtheria, tetanus, and acellular pertussis (DTaP) vaccine (84.2% in 2014) remains lower than coverage for other childhood vaccinations (e.g. coverage greater than 90% for measles, mumps, rubella vaccine; poliovirus vaccine; and hepatitis B vaccine, in 2014) (4). Due to variations in vaccine coverage by sociodemographic characteristics, the risk of pertussis among certain populations is increased. In 2014, childhood coverage with 4 or more DTaP doses was lower among children living below poverty (79.1%) compared to children living at or above poverty (87.4%) (4).

Various factors may explain the recent resurgence of pertussis. In the 1990s, whole cell pertussis vaccine was replaced by acellular pertussis vaccine due to concerns with safety, however recent evidence demonstrates acellular pertussis vaccine wanes more rapidly (6-10). The waning immunity of acellular pertussis vaccine results in vaccinated populations who may be susceptible to pertussis despite vaccination. Vaccine hesitancy, which may cluster geographically (5), may also be contributing to an increase in the morbidity of pertussis due to populations that are unvaccinated or only partially

vaccinated. Risk of pertussis is not only high among these populations, but it also poses a risk to surrounding populations who may be too young to vaccinate or unable to vaccinate for medical reasons.

While the National Immunization Survey (NIS) provides estimates of vaccine uptake by ages 19 to 35 months, it does not provide an estimate of the cumulative number of children who are susceptible to disease across multiple cohorts born into the population. The Advisory Committee on Immunization Practices (ACIP) recommends a primary series of DTaP vaccine at 2, 4, 6, 15-18 months with a booster given before entrance to school (11). Because vaccine hesitancy may result in parents delaying or spacing out vaccinations, or not vaccinating their children at all (12-14), children may remain unvaccinated or partially vaccinated for longer intervals. As new birth cohorts are successively incompletely vaccinated, there will be an accumulation of children who are not fully immunized. Even children who receive the vaccines according to schedule may be susceptible since (a) they are not fully protected until completing the 4^{th} dose at 15 to 18 months of age and (b) dose-specific vaccine effectiveness is not 100%, so some vaccinated children may not be fully immune to pertussis. Additionally, vaccine coverage estimates do not account for children who are too young to vaccinate, but who contribute to the pool of susceptible children, and children who may have protection from transplacentally transferred maternal antibodies following maternal tetanus, diphtheria, and acellular pertussis (Tdap) vaccination. Recently, the ACIP made recommendations that pregnant women receive one dose of Tdap vaccine during each pregnancy to provide protection to infants too young to vaccinate (15, 16). This transfer of maternal

antipertussis antibodies has shown to provide infants with some level of protection against pertussis during the first few months of life (17).

To our knowledge, the total number of pertussis-susceptible children aged 0-23 months who have accumulated in the US population is unknown, nor do we have estimates of the total number of pertussis-susceptible children aged 0-23 months by poverty status. Generating estimates of pertussis-susceptible children by poverty status will aid in evidence-based planning to reduce health disparities and target vulnerable populations. We have computed estimates of accumulated pertussis-susceptible children, overall and by poverty status, in the US, and compared these estimates to herd immunity threshold for pertussis (93%) (18). These findings can provide supportive evidence for policies to increase childhood protection from pertussis.

Methods

Analytic dataset

The analysis was conducted using publically available data from the 2013 National Immunization Survey (NIS). The NIS is an annual survey sponsored by the Centers for Disease Control and Prevention (CDC) to monitor national childhood immunization coverage. Data are collected through a representative sample of household surveys of parents of children between the ages of 19-35 months and through provider verification of vaccination information. Past history of receipt of a pertussis-containing vaccine and age in months of each dose of pertussis-containing vaccine are collected through the household questionnaire and verified with the child's healthcare providers. For the purpose of this analysis, only provider verified vaccine receipt was utilized.

Variable estimates from baseline model

The analysis was conducted using the PROC SURVEYFREQ procedure in SAS v.9.4 (The SAS Institute, Cary NC) with the provider-phase sampling weight. We identified the age at receipt of the first four doses of pertussis vaccine for children from birth through age 23 months. We only considered the first four doses of pertussis vaccine because the Advisory Committee on Immunization Practices (ACIP) recommendation for the fifth pertussis vaccine indicates vaccination prior to entrance into school (ages 4-6 years), which is outside the age range of the NIS data (0-36 months) (11). We generated estimates for children aged 0-23 months due to sparseness in the data for age-specific pertussis vaccine receipt after 23 months. In the 2013 NIS, children aged 0-23 months were born between February 2011 and June 2012. We obtained the birth cohort sizes for 2011 and 2012 from CDC's National Vital Statistics System (19, 20). To obtain the most conservative estimates, we used the smaller yearly birth cohort (2012; N=3,952,841) to approximate the monthly birth cohort size (329,403 births/month). The monthly birth cohort size was used to generate all estimates of the total number of children susceptible to pertussis aged 0-23 months.

We estimated the proportion of children vaccinated within each monthly birth cohort through the provider verified data on age in months at receipt of pertussis-containing vaccine. We were able to generate monthly estimates of the number of children vaccinated for pertussis within each monthly birth cohort spanning across 24 months. From the provider verified variables on age at receipt of each dose of pertussis-containing vaccine, we factored in children who may not have received the vaccine according to the ACIP recommended schedule (2, 4, 6, and 15-18 months) (11). For

example, according to the NIS 2013 data approximately 87% of children received their first dose of pertussis-containing vaccine by 2 months of age while the remaining children received the vaccine at various other times over the 24-month period (Table 1). Therefore, within the 2-month old birth cohort, 87% have at least one dose protection while 13% remain completely unprotected. Further, we estimated conditional probabilities of age-specific vaccine dose receipt. For example, of the children identified as having received their first vaccine dose at two months of age, we estimated the proportion that received their second vaccine dose at each successive month, and repeated this process for each vaccine dose.

Once we estimated the number and proportion of children who received specific doses of pertussis-containing vaccine within each monthly birth cohort, we determined the number and proportion that received at least one, only one, two, three, or all four doses of vaccine by each age, in months. Through this method, we were able to compare susceptibility among successive monthly birth cohorts and among all children 0-23 months. A 23-month old birth cohort, for example, would have had up to 23 months to receive four doses of pertussis-containing vaccine while a 7-month old birth cohort would have had up to 7 months to receive three doses of pertussis-containing vaccine. Monthly age-specific vaccine uptake estimates were generated for 24 months to account for children aged 0-23 months. By considering vaccine uptake within each monthly birth cohort, we were able to obtain an overall estimate of the number of children aged 0-23 months fully or partially vaccinated against pertussis.

Vaccine effectiveness

We accounted for DTaP vaccine effectiveness using data from two studies that evaluated dose-specific vaccine effectiveness (53.7% after one dose, 75.3% after two doses, 83.5% after three doses (21); 68.0% after one dose, 91.8% after two doses, 99.8% after three doses, 98.6% after four doses) (22). For our base model, we used the average of these estimates (60.9% after one dose, 83.6% after two doses, 91.7% after three doses, 98.6% after four doses) to determine, among the children who were vaccinated, the number and proportion of children who were protected after vaccination based on the number of vaccines received and the vaccine effectiveness of each dose.

Variable estimates from poverty status models

We also considered the impact of poverty status on children's vaccination status, and therefore, susceptibility to pertussis. We dichotomized the NIS 2013 poverty status variable (based on the 2012 Census poverty threshold) into "at or above" and "below" poverty. After dichotomizing the poverty status variable, approximately 71% were considered at or above poverty while 25% were below so we adjusted the monthly birth cohort size based on these percentages. Then we estimated the proportion of children vaccinated within each monthly birth cohort by poverty level. The estimates were generated in the same manner as previously stated above.

Infant protection from maternal Tdap-induced antibodies

We used a recent national estimate of Tdap vaccination coverage during pregnancy (9.8%) (23) and assumed infant protection among those born to Tdap-vaccinated mothers was 100% for children aged 0 month and 50% for children aged 1 month (17, 24). To adjust for Tdap vaccination coverage during pregnancy by poverty status, we used Tdap coverage estimates based on insurance coverage during pregnancy

(7.2% for private insurance and 12.5% for Medicaid) and use of WIC during pregnancy (13% Tdap coverage among WIC mothers and 7.5% Tdap coverage among non-WIC mothers) (23).

Sensitivity analysis - overview

We conducted multiple sensitivity analyses to estimate the changes based on variability in estimates for vaccine coverage, vaccine effectiveness, maternal antipertussis antibody protection, and waning DTaP immunity among all children and children living at or above and below poverty. Detailed sensitivity analysis inputs are presented below, and summarized in Table 2. Utilizing all of these estimates and assumptions, we calculated the number and proportion of children who were immune and not immune to pertussis across all monthly birth cohorts up to 23 months of age. Immunity levels were compared with the pertussis herd immunity threshold of 93% (18). This was repeated for all sensitivity analyses.

Sensitivity analysis – DTaP vaccine coverage

We estimated the relative change in the number of children susceptible to pertussis as vaccine coverage increases and decreases. We applied a relative increase in coverage of 1%, 2%, 3% and a relative decrease in coverage of 1%, 2%, 3%, 4%, and 5% to the base model. All changes in vaccine coverage relative to baseline were considered to be constant over the 24 birth cohorts used to model children aged 0 to 23 months of age.

Sensitivity analysis – vaccine effectiveness

As described above, the baseline model utilized the average vaccine effectiveness estimates from two studies (21, 22). In sensitivity analysis, we evaluated these two dose-

specific vaccine effectiveness estimates (53.7% after one dose, 75.3% after two doses, 83.5% after three doses (21); 68.0% after one dose, 91.8% after two doses, 99.8% after three doses, 98.6% after four doses (22) individually.

Sensitivity analysis – maternal antipertussis antibody protection

We evaluated the impact of maternal antipertussis antibody protection lasting to 2 months of age. Sensitivity analysis was based on higher coverage found in a recent study (41.7%) (25) with 70% vaccine effectiveness used as the level of protection afforded to infants born to vaccinated mothers, assuming protection dropping to 50% of baseline at one month of age and 0% of baseline at two months of age. We also applied different levels of maternal Tdap coverage (10%, 25%, 40%, 55%, and 70%) to the base model to determine the impact of increasing maternal Tdap coverage on pertussis susceptibility.

Sensitivity analysis – waning DTaP immunity

Because acellular pertussis vaccine may not offer long-term immunity to pertussis (26, 27), we used estimates of waning immunity 6 months after the fourth DTaP dose. We assumed a reduction to 75% of baseline immunity levels 6 months after the fourth DTaP dose, and applied this to the age-specific vaccine coverage data.

Ethics Review

This analysis utilized publically available data without any personal identifiers and was considered non-human subjects research by Emory University and did not require institutional review board approval.

Results

Base models

Of 7,905,672 children born over 24 cumulative monthly birth cohorts, we estimate that 1,726,113 (22%) children are not immune to pertussis (Figure 1). Susceptibility to pertussis was largely impacted by age with 76% (771,074 of 988,209 children) of children age 0-2 months susceptible to pertussis compared to 7% (71,998 of 988,209) of children age 21-23 months.

Models based on poverty status

Accounting for poverty, we estimate that among children 0-23 months of age living at or above the poverty line, 20% (1,106,447 of 5,606,712) are not immune to pertussis, compared to 23% (450,751 of 1,940,040) of children living below the poverty line (Figure 2). There was no significant change in the proportion of children immune to pertussis as we changed Tdap coverage estimates based on private or Medicaid insurance during pregnancy compared to use of WIC during pregnancy.

Sensitivity analysis – vaccine effectiveness

Varying the vaccine effectiveness after each dose of DTaP changed the overall susceptibility in children aged 0-23 months (Figure 1). From the base model, overall susceptibility to pertussis was 22% compared to a higher susceptibility found in the model with an overall lower vaccine effectiveness (27%) (21) and a lower susceptibility in the model with an overall higher vaccine effectiveness (17%) (22).

Sensitivity analysis – relative increases and decreases in vaccination coverage

The number of susceptible children was impacted by vaccination coverage (Figure 3). With a sustained 3% relative increase in coverage, immunity to pertussis increased from 78% to 80%. With a sustained 5% relative decrease in coverage, the proportion of children immune to pertussis decreased from 78% to 74%

Sensitivity analysis – maternal antipertussis antibody protection

Maternal Tdap coverage and transfer of maternal antipertussis antibodies made an impact in susceptibility among children 0-2 months. Of 988,209 children aged 0-2 months 751,072 (76%) are not immune to pertussis. If maternal Tdap coverage increased to 41.7% (25), the proportion of susceptible children aged 0-2 months would decrease to 65% (751,072 to 640,738 children). Steady increases in maternal Tdap coverage also increased the number of immune children. With 10% coverage, we estimate 24% of children aged 0-2 months are immune to pertussis while 45% would be immune with maternal Tdap coverage increased to 70% (Figure 4). Overall immunity among children aged 0-23 months also increased from 78% with 10% maternal Tdap coverage to 81% with 70% maternal Tdap coverage.

Sensitivity analysis – waning immunity

Waning immunity had a large impact on the long-term immunity of children who received 4 doses of DTaP. In the base model, 122,743 of 1,647,015 (7%) of children aged 19-23 months are not immune to pertussis. However, when we factored in waning immunity 6 months after receipt of the fourth dose of DTaP, 261,098 of 1,647,015 (16%) of children in the same age group are susceptible to pertussis (Figure 5).

Discussion

To our knowledge, this is the first assessment of the cumulative number of pertussis-susceptible children aged 0-23 months in the US, accounting for age-specific vaccination coverage, vaccine effectiveness, maternal vaccination, waning immunity, and poverty-related differences in vaccine uptake. From the base models, our findings

indicate the overall immunity levels of children by 23 months are close or higher than the estimated herd immunity threshold for pertussis (93%) (18). However, in sensitivity analysis models at the lower end of documented vaccine effectiveness, the overall immunity levels in that model did not reach the herd immunity threshold (Figure 1) (18). Because DTaP vaccine effectiveness after 4 doses (80-85%) (2) is much lower than for other childhood vaccines like measles, mumps, rubella (MMR) (97% after 2 doses) (28) or inactivated polio vaccine (IPV) (99% after 3 doses) (29), a larger proportion of children need to be vaccinated to reach and maintain herd immunity thresholds.

We estimated approximately 1.7 million children aged 0-23 months are susceptible to pertussis. Young children are at the highest risk for complications from pertussis infection, (2, 30-32) and we estimate that between 76% children under 2 months of age are susceptible to pertussis. This highlights the need for higher Tdap vaccine utilization during pregnancy to provide maternal pertussis antibodies transplacentally for protection in the first months of life. Maternal Tdap vaccination coverage during pregnancy remains low (9.8% in 2011) (23). Because maternal antibodies may only protect infants through the first 2-months of life (17), timely DTaP vaccination according to the ACIP recommended immunization schedule is key to prevent infant pertussis, especially considering 13% of children did not receive the first dose of DTaP by 2 months of age (Table 1).

Waning immunity is important to consider given the possible higher risk of pertussis in fully vaccinated children in the years following receipt of the last dose of DTaP (26, 27). Populations of fully vaccinated children becoming susceptible over time is particularly concerning given the herd immunity threshold was not reached once we

factored in waning immunity. Older children are also important risk factors for pertussis transmission in younger infants (32-34), and maintaining high coverage of pertussis-containing vaccines, especially the fifth dose recommended at 4-6 years of age and adolescent Tdap vaccination is important for sustaining sufficient levels of immunity in the population to prevent pertussis outbreaks.

From our estimates, we found children living below poverty are more susceptible to pertussis than those living at or above poverty. Lower vaccination coverage among children living below poverty is likely the main factor for the difference in susceptibility between the two populations (4). The Vaccines For Children (VFC) program aims at reducing racial/ethnic and income-related disparities in vaccine uptake, and since the start of the program, in 1994, major strides have been made in reducing these disparities (35). Despite the availability of vaccines through VFC, income-related disparities persist. The best estimates of maternal Tdap coverage by poverty level was based on use of WIC and insurance status during pregnancy. In this case, women living below poverty had higher maternal Tdap coverage, which may negate some of the 0-23 month population estimates of immunity among children living below poverty. More research aimed at understanding other barriers to vaccination among children living below poverty is needed in order to reduce this disparity. Targeted efforts to reduce health disparities and increase vaccination coverage are vital to reduce the susceptibility to pertussis among children living below poverty.

Our estimates for susceptibility to pertussis are based on national-level data. However, there may be geographic areas with a greater number of pertussis-susceptible children due to clustering of populations who are vaccine hesitant (36) or differences in

DTaP coverage by state (4). Omer and colleagues found significant overlap between clusters of nonmedical vaccine exemptions and cluster of pertussis cases (5). Given the distribution of age-specific vaccine coverage, we were unable to further stratify these estimates by state. Future studies should evaluate the impact of these differences in vaccine coverage and pertussis-susceptibility by geographic area, to aid in implementing vaccination activities to prevent potential future pertussis outbreaks.

Our sensitivity analysis accounting for relative increases and decreases in vaccination coverage provide the means to assess changes in overall immunity and susceptibility levels among children aged 0-23 months, and highlight how small, sustained drops in coverage can reduce pertussis immunity below the herd immunity threshold. Generally, there are small fluctuations in coverage each year, however in 2012, the year with the highest incidence of pertussis since the development of the vaccine (1), there was a 2% decrease in coverage from the previous year (2011: 84.6%; 2012: 82.5%) (37, 38). Conversely, small-sustained increases in vaccination coverage can improve our ability to prevent pertussis outbreaks, particularly in children aged 0 to 23 months. It is critical to maintain and increase current DTaP coverage to levels seen in other childhood vaccines in order to ensure herd immunity and reduce the potential for pertussis outbreaks. Our findings highlight the importance of assessing pertussis susceptibility by age rather than only focusing on cumulative vaccine coverage at a later age. This is particularly important given concerns about delays in vaccine receipt relative to the ACIP-recommended vaccine schedule (12, 39, 40).

This study has some limitations. First, we only considered children aged 0-23 months and the first four doses of DTaP. We decided to focus on two annual birth cohorts

(0-23 months) due to sparseness of the pertussis-containing vaccine data after 23 months in the National Immunization Survey, which does not include the ages at which the fifth DTaP dose is administered. Currently, there is no national survey that estimates vaccine coverage for children between 4 and 12 years of age, so we were unable to consider receipt of the fifth dose of pertussis since this dose is recommended between 4-6 years of age (11). Future studies should include a larger age range of children and include data on receipt of the fifth doses of pertussis and possibly receipt of a Tdap in pre-adolescence or adolescence. This analysis would give an overall estimate of pertussis-susceptibility in all children and adolescents in the US.

Second, estimates of the vaccine effectiveness after each dose of DTaP are limited, and vary greatly. We based our analysis on the average vaccine effectiveness found in two available studies (21, 22). The two studies found different vaccine effectiveness after each dose, which resulted in variations in our estimates. Different formulations of DTaP vaccine exist, which may explain the differences in their estimates. More research is needed to better understand the vaccine effectiveness of DTaP after each dose.

Third, while we were able to factor in waning immunity following the fourth dose, we did not take into account any waning immunity that may have occurred among children who only received one, two, or three doses of DTaP. We also did not consider waning immunity that may occur between receipt of the third dose at 6 months and the fourth dose between 15-18 months. If there is appreciable waning of pertussis immunity in these periods, our estimates of susceptibility may be underestimates. Future modeling

activities with more refined estimates of waning pertussis vaccine effectiveness in childhood are needed to clarify this issue.

Finally, we factored in maternal antipertussis antibody protection in our sensitivity analysis, however there is some uncertainty on the duration of protection provided to infants from maternal antibodies through Tdap vaccination. We assumed any level of protection decayed fully by 2 months of age (17). We also assumed that, of children whose mothers received Tdap, 100% of children aged 0 month and 50% of children aged 1 month would be fully protected through maternal antipertussis antibodies. Additional research is needed to fully understand the duration and level of protection from maternal transfer of antipertussis antibodies.

In conclusion, the overall immunity level to pertussis for children aged 0 to 23 months is close or above than the herd immunity level needed for pertussis. However, this level of immunity was not reached until at least 9 months of age. There are a substantial number of children aged 0-23 months in the US who are susceptible to pertussis with higher numbers found in children living below poverty. Susceptibility was particularly high among the young birth cohorts who are too young to vaccinate and at the highest risk for complications from pertussis so herd immunity levels need to be maintained in order to protect this vulnerable population. Relative decreases in coverage and waning immunity of DTaP can exacerbate the proportion of children who are susceptible. The estimates emphasize the need for public health professionals to continue efforts to increase DTaP vaccine coverage, plan for potential outbreaks, and maintain immunity levels needed to prevent the spread of pertussis.

Disclaimer: The National Immunization Survey 2013 is available from the Centers for Disease Control and Prevention (U.S. Department of Health and Human Services (DHHS). National Center for Health Statistics. The 2014 National Immunization Survey. Hyattsville, MD: Centers for Disease Control and Prevention, 2014. http://www.cdc.gov/nchs/nis/data_files.htm). All analyses, interpretations, or conclusions reached are attributable to the authors and not to the National Center for Health Statistics (NCHS), which is responsible only for the initial data.

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Table 1. Age in months at receipt of 4-dose series of diphtheria, tetanus, and acellular pertussis vaccine, estimates from the 2013 National Immunization Survey

Age, months	Dose 1 DTaP (%)	Dose 2 DTaP (%)	Dose 3 DTaP (%)	Dose 4 DTaP (%)
Missing	2.62	4.11	6.28	20.36
0	0.05	-	-	-
1	13.99	0.03	-	-
2	72.84	0.81	0.03	-
3	4.75	8.19	0.42	0.01
4	2.10	68.83	0.48	0.03
5	0.86	7.63	4.37	0.04
6	0.82	4.18	63.52	0.25
7	0.30	1.83	9.97	0.16
8	0.26	0.92	3.14	0.12
9	0.25	0.72	3.50	0.09
10	0.21	0.31	1.65	0.14
11	0.17	0.23	1.08	0.07
12	0.12	0.57	1.26	4.14
13	0.04	0.27	0.56	1.75
14	0.05	0.22	0.53	2.73
15	0.09	0.12	0.97	31.17
16	0.17	0.13	0.33	7.76
17	0.10	0.04	0.41	4.80
18	0.07	0.24	0.43	15.18
19	0.03	0.14	0.28	5.47
20	0.01	0.11	0.20	2.51
21	0.03	0.25	0.20	1.47
22	0.06	0.07	0.19	1.11
23	0.03	0.07	0.18	0.68

Source: CDC, NCRID and NCHS (2014), 2013 National Immunization Survey.

Table 2a. Summary of the methods used to generate estimates for the sensitivity analysis, NIS 2013

Input category	Model 1 (Baseline)	Model 2 (Sensitivity analysis for different vaccine effectiveness)			Model 3 (Sensitivity analysis for relative changes in DTaP coverage)
Vaccine coverage	As estimated from 2013 NIS	As estimated from 2013 NIS			Relative decrease of 1%, 2%, 3%, 4% and 5% Relative increase of 1%, 2% and 3%
Vaccine effectiveness	Dose 1: 60.9% Dose 2: 83.6% Dose 3: 91.7% Dose 4: 98.6%	Dose 1: 60.9% Dose 2: 83.6% Dose 3: 91.7% Dose 4: 98.6%	Dose 1: 53.7% Dose 2: 75.3% Dose 3: 83.5% Dose 4: 98.6%	Dose 1: 68.0% Dose 2: 91.8% Dose 3: 99.8% Dose 4: 98.6%	Dose 1: 60.9% Dose 2: 83.6% Dose 3: 91.7% Dose 4: 98.6%
Maternal Tdap vaccine coverage during pregnancy	9.8%	9.8%			9.8%
Maternal Tdap vaccine effectiveness	70%	70%			70%
Children living at/above and below poverty	At/above: 71% Below: 25%	-			-

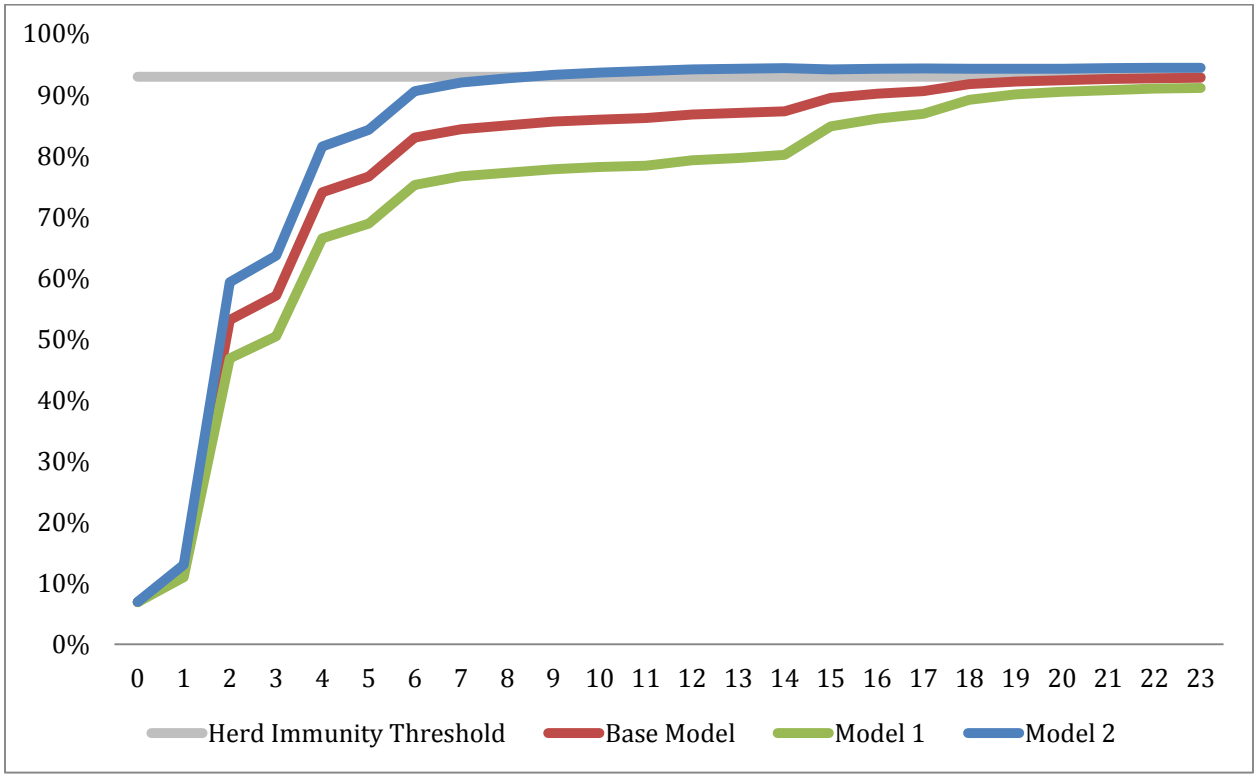
Source: CDC, NCRID and NCHS (2014), 2013 National Immunization Survey.

Table 2b. Summary of the methods used to generate estimates for the sensitivity analysis, NIS 2013

Input category	Model 4 (Sensitivity analysis for changes in maternal TDaP coverage)	Model 5 (Sensitivity analysis for accounting for waning immunity)
Vaccine coverage	As estimated from 2013 NIS	As estimated from 2013 NIS with a reduction to 75% of baseline immunity levels 6 months
Vaccine effectiveness	Dose 1: 60.9% Dose 2: 83.6% Dose 3: 91.7% Dose 4: 98.6%	Dose 1: 60.9% Dose 2: 83.6% Dose 3: 91.7% Dose 4: 98.6%
Maternal Tdap vaccine coverage during pregnancy	Model 1: 41.7% Model 2: 10% Model 3: 25% Model 4: 40% Model 5: 55% Model 5: 70%	9.8%
Maternal Tdap vaccine effectiveness	70%	70%
Children living at/above and below poverty	-	-

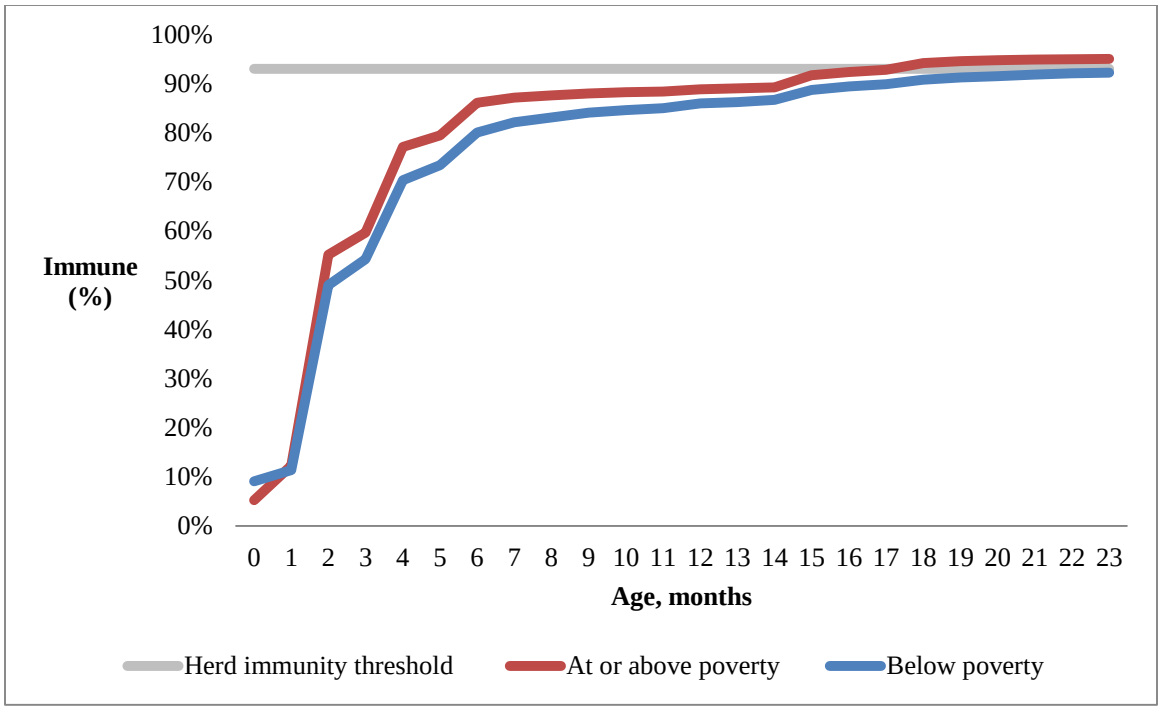
Source: CDC, NCRID and NCHS (2014), 2013 National Immunization Survey.

Figure 1. Age-specific pertussis susceptibility in the United States, estimated using National Immunization Survey 2013 data. (A) Base model assuming an average vaccine effectiveness of 60.9%, 83.6%, 91.7%, and 98.6% for dose 1-4 of DTaP (B) Model 2 assuming a vaccine effectiveness of 53.7%, 75.3%, 83.5%, and 98.6% for dose 1-4 of DTaP (18,19). (C) Model 3 assuming a vaccine effectiveness of 68%, 91.8%, 99.8%, and 98.6% for dose 1-4 of DTaP (19). (D) Using a 93% herd immunity threshold (15).



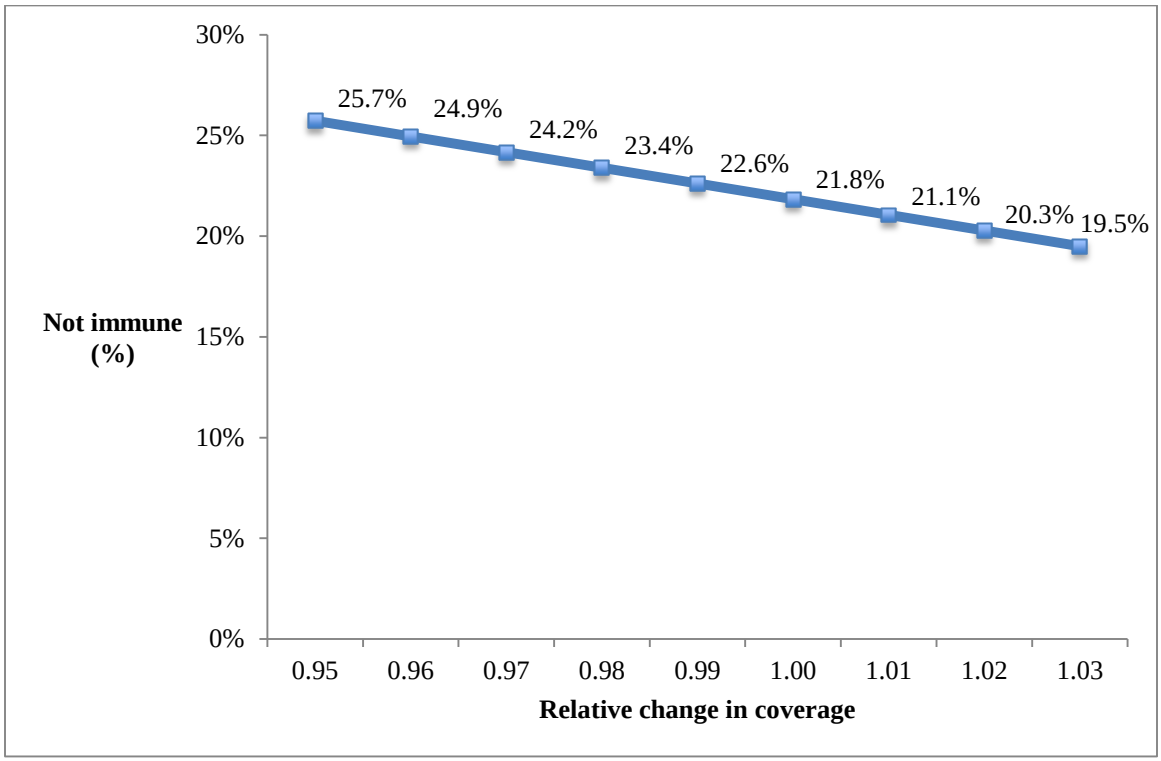
Source: CDC, NCRID and NCHS (2014), 2013 National Immunization Survey.

Figure 2. Age-specific pertussis susceptibility by poverty level in the United States, estimated using National Immunization Survey 2013 data. (A) At or above poverty level maternal TDaP coverages (7.5%) (23) estimates based on "No" for use of WIC during pregnancy. (B) Below poverty maternal TDaP coverage (13.0%) (23) estimates based on "Yes for use of WIC during pregnancy.



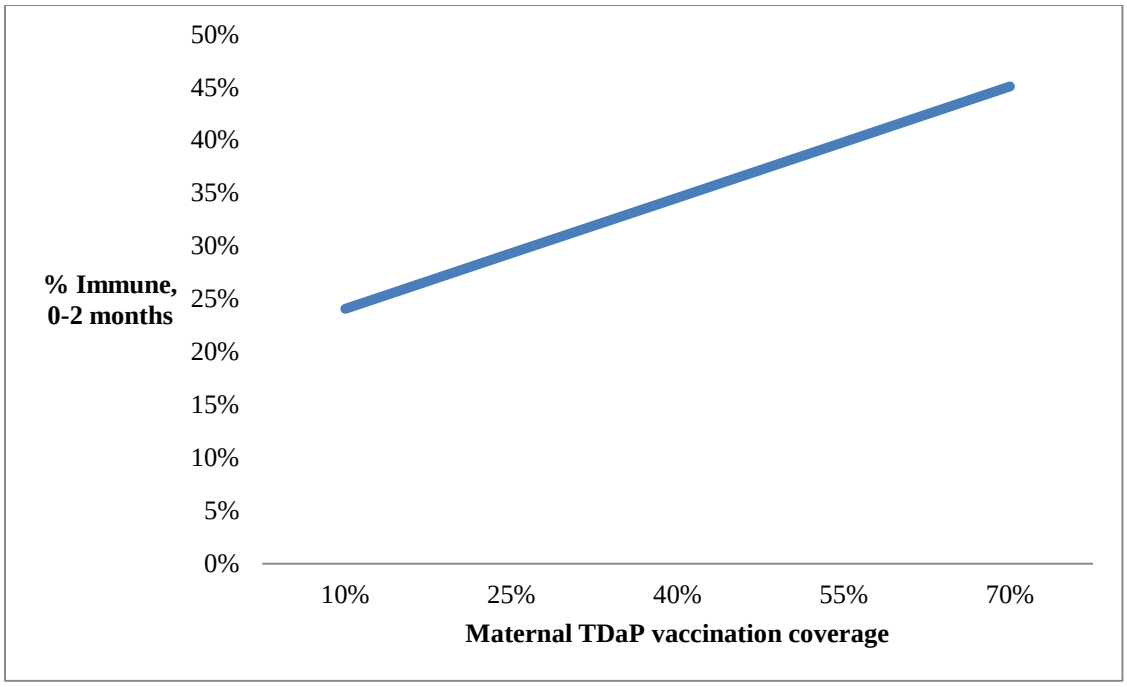
Source: CDC, NCRID and NCHS (2014), 2013 National Immunization Survey.

Figure 3. Projected proportion of susceptible children aged 0-23 months with 1%, 2%, 3% increases and 1%, 2%, 3%, 4%, and 5% decreases in childhood pertussis-containing vaccine uptake relative to the pertussis-containing vaccine coverage in the 2013 National Immunization Survey.



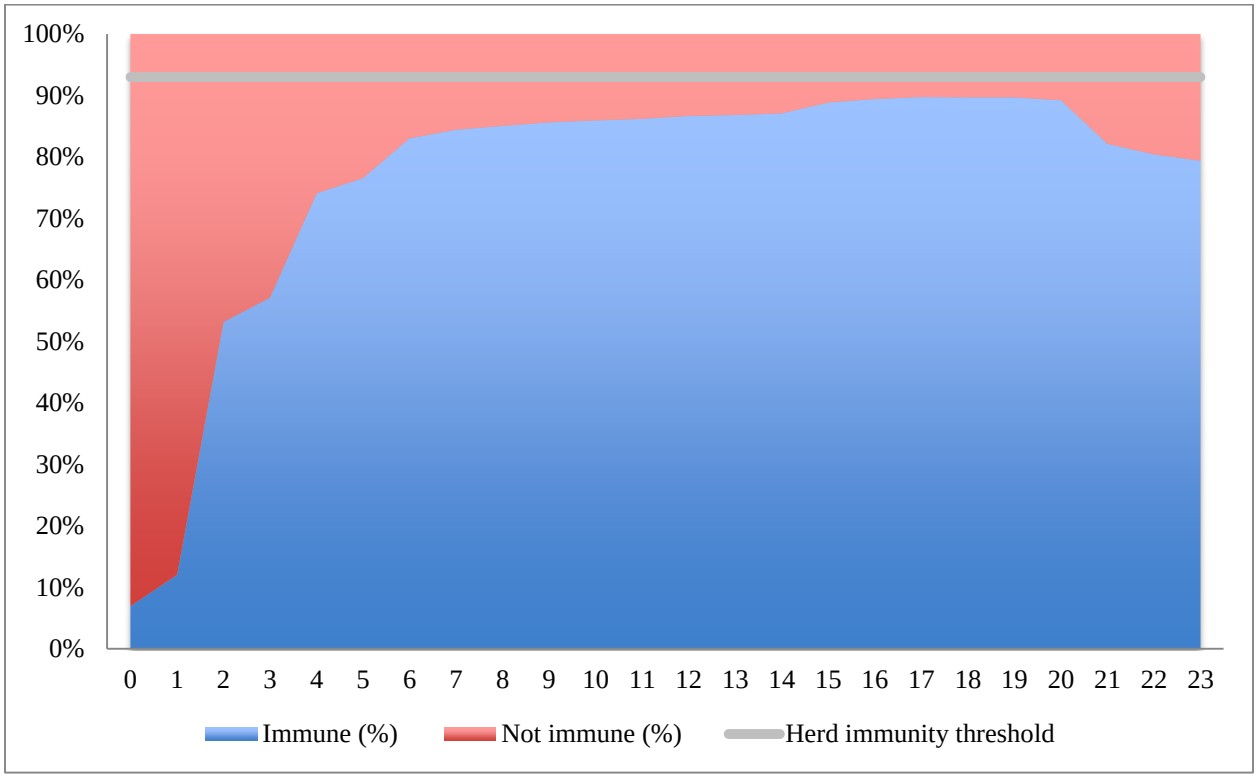
Source: CDC, NCRID and NCHS (2014), 2013 National Immunization Survey.

Figure 4. Projected proportion of children aged 0-2 months immune to pertussis due to maternal antipertussis antibody protection and diphtheria, aceullular pertussis, and tetanus vaccination with variations of 10%, 25%, 40%, 55%, and 70% in maternal tetantus, dipetheria, and acellular pertussis vaccination during pregnancy using 2013 National Immunization Survey.



Source: CDC, NCRID and NCHS (2014), 2013 National Immunization Survey.

Figure 5. Age-specific pertussis susceptibility in the United States factoring in waning immunity 6-months after receipt of the fourth dose of dipetheria, acellular pertussis, and tetantus vaccine. (A) Model assuming an average vaccine effectiveness of 60.9%, 83.6%, 91.7%, and 98.6% for dose 1-4 of DTaP. (B) Assuming a reduction to 75% of baseline immunity levels 6 months after receipt of the fourth dose of vaccine applied to age-specific vaccination data from the 2013 National Immunization Survey



Source: CDC, NCRID and NCHS (2014), 2013 National Immunization Survey.