Waning Tdap Effectiveness in Adolescents
Nicola P. Klein, MD, PhD, Joan Bartlett, MPH, MPP, Bruce Fireman, MA, Roger Baxter, MD

BACKGROUND AND OBJECTIVE: Because the effectiveness of diphtheria-tetanus-acellular pertussis (DTaP) vaccine wanes substantially after the fifth dose at ages 4 to 6 years, there is a growing cohort of adolescents who rely on tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) for protection against pertussis. Yet despite high Tdap vaccine coverage among adolescents, California experienced large pertussis outbreaks in 2010 and 2014. We investigated Tdap vaccine effectiveness (VE) and waning within Kaiser Permanente Northern California among adolescents exclusively vaccinated with DTaP vaccines.

METHODS: We modeled pertussis risk in relation to Tdap vaccination status among adolescents beginning on their 10th birthday. We estimated the hazard ratio (HR) for each subsequent year after Tdap compared with unvaccinated adolescents by using Cox regression, adjusting for calendar time, age, gender, race, and facility. We calculated VE as $1 - HR$. We also treated time since Tdap vaccination as a continuous variable and estimated the change in the HR per 1-year increase since vaccination.

RESULTS: On the basis of 1207 pertussis cases, Tdap VE during the first year after vaccination was 68.8% (95% confidence interval [CI] 59.7% to 75.9%), decreasing to 8.9% (95% CI –30.6% to 36.4%) by ≥4 years after vaccination. Adolescents who were more remote from Tdap were significantly more likely to test positive for pertussis than were those vaccinated more recently (HR per year 1.35, 95% CI 1.22 to 1.50).

CONCLUSIONS: Routine Tdap did not prevent pertussis outbreaks. Among adolescents who have only received DTaP vaccines in childhood, Tdap provided moderate protection against pertussis during the first year and then waned rapidly so that little protection remained 2-3 years after vaccination.

WHAT’S KNOWN ON THIS SUBJECT: Diphtheria, tetanus toxoids, acellular pertussis (DTaP) vaccine effectiveness wanes after the fifth dose, and adolescents who have only received DTaP vaccines rely on reduced antigen content acellular pertussis (Tdap) vaccine for protection against pertussis. Despite high Tdap vaccine coverage among adolescents, California experienced large pertussis outbreaks in 2010 and 2014.

WHAT THIS STUDY ADDS: Routine Tdap vaccination did not prevent pertussis outbreaks in adolescents. Among adolescents previously vaccinated only with DTaP, Tdap provided moderate protection during the first year and then waned rapidly so that little protection remained 2-3 years after vaccination.
The United States switched from whole cell pertussis to an acellular pertussis vaccines during the 1990s and now uses diphtheria-tetanus-acellular pertussis (DTaP) vaccine for all 5 childhood doses at ages 2, 4, 6, 12 to 18 months, and 4 to 6 years. In 2006, a booster tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis(Tdap) vaccine, was recommended by the Advisory Committee on Immunization Practices for all adolescents.1 Despite high levels of vaccine coverage, the United States2 and other countries3–7 have experienced increased pertussis disease in the years after the switch to DTaP.

In 2010, California experienced the largest pertussis epidemic since 19582 as the first cohort of children to receive all DTaP vaccines (without any doses of a whole cell pertussis vaccine) were starting to reach 10 to 12 years of age. This 2010 outbreak was associated with 10 infant deaths. We and others subsequently demonstrated that the effectiveness of DTaP vaccines wanes substantially in school age and younger children8–12 and that DTaP provides reduced long-term protection against pertussis when compared with whole cell pertussis vaccines.13–15 We estimated that DTaP protection wanes 42% per year on average after the fifth dose at 4 to 6 years of age8 and predicted that there would be larger pertussis outbreaks as the cohort of children vaccinated exclusively with DTaP vaccines expanded and became older and more distant from their fifth DTaP dose.8,16

This growing cohort of adolescents who have only received DTaP vaccines therefore relies on the booster dose of Tdap for protection against pertussis. We previously demonstrated using data from the 2010 epidemic that Tdap provided moderate protection against pertussis in adolescents who had only received acellular pertussis vaccines17; however, we did not assess Tdap waning because most of the adolescents who had received Tdap had received it recently (few adolescents who had only received DTaP vaccines and who also received Tdap were older than 12 years in the 2010 epidemic).

In July 2011, the state of California mandated that all adolescents receive a dose of Tdap vaccine before entering seventh grade.18 Despite this requirement, California again experienced another pertussis epidemic in 2014, with an incidence rate surpassing that of the 2010 epidemic.19

Tdap's effectiveness during 2 successive pertussis outbreaks has not been assessed, nor is it well understood whether Tdap prevents new outbreaks in an exclusively DTaP-vaccinated population. In this study, we examined Tdap vaccine effectiveness (VE) among adolescents previously vaccinated only with DTaPin Kaiser Permanente Northern California (KPNC) after both the 2010 and 2014 outbreaks. Our aims were to evaluate Tdap VE during the first year after vaccination and then during each of the next several years and to estimate the average annual percentage decrease in Tdap VE among adolescents previously vaccinated only with DTaP.

**METHODS**

**Setting**

KPNC is an integrated health care delivery system that provides medical care to ~3.5 million members, and operates 55 medical clinics and 20 hospitals and its own pharmacies and laboratories. KPNC databases capture vaccinations, laboratory tests, and inpatient, emergency department (ED), and outpatient diagnoses. KPNC performs all pertussis testing in a single, centralized laboratory by using real-time polymerase chain reaction (PCR).8,13

**Study Population**

This study followed all KPNC members starting at age 10 years who had exclusively received DTaP vaccines in infancy and childhood. We limited the study population to individuals who were born in 1999 or later13 or who were born in 1996–1998 and received 3 infant doses of DTaP at KPNC. We excluded individuals who received Tdap vaccine or who were positive for pertussis before age 10 years. We defined a case as testing PCR positive for pertussis.

KPNC has used both available Tdap vaccines, Boostrix (GlaxoSmithKline) and Adacel (Sanofi Pasteur), but predominantly Adacel. KPNC has administered DTaP vaccines from various manufacturers but has mostly used those from GlaxoSmithKline. This study included all acellular pertussis vaccines regardless of manufacturer.

KPNC's Institutional Review Board approved this study.

**Statistical Analyses**

We modeled risk of pertussis in relation to Tdap vaccination status starting from the 10th birthday until the first occurrence of a PCR-positive test for pertussis, receipt of a second Tdap, disenrollment from KPNC, or end of follow-up (March 31, 2015). Tdap vaccination status was specified as a set of time-varying variables that indicated whether a person was unvaccinated, too-recently-vaccinated-to-benefit (within 1–7 days), or vaccinated in the previous 8 days to <1 year (“year 1”), 1 to <2 years (“year 2”), 2 to <3 years (“year 3”), or ≥3 years (“year 4+”). VE was assessed for each of the 4 ranges of vaccinated person-time beginning 8 days after receipt of Tdap. Adolescents were considered unvaccinated until they received Tdap and then moved across
the year-since-vaccination indicator variables with each additional year of follow-up (individuals contributed unvaccinated person-time until their date of Tdap vaccination, and then contributed vaccinated person-time). We used a Cox regression model to estimate the hazard ratio (HR) of pertussis for each Tdap time interval compared with the unvaccinated reference period. For example, the HR for the 1 to <2 years since vaccination variable estimates the risk of pertussis in an adolescent who received Tdap 1 to <2 years ago divided by the risk in an otherwise similar unvaccinated adolescent. The Cox regression was on the calendar timeline and stratified by birth year and included covariates that adjusted for gender, race, and facility. We compared the Tdap status of each pertussis case with the Tdap status of all persons born the same year who were at risk on the same day the case was identified. We calculated VE as 1 – HR.

We evaluated the HR for several subsequent years after Tdap vaccination and found that the waning of Tdap effectiveness was approximately linear on the log-odds scale. We then treated Tdap vaccination as a continuous variable and estimated the HR per 365 days since Tdap vaccination by using a Cox regression model similar to that described earlier. This (single) HR indicates the average percent increase in the odds of acquiring pertussis per year of additional time since Tdap vaccination.

We used SAS software, version 9.2 (SAS Institute, Cary, NC) for all analyses.

RESULTS

Incidence of pertussis for the entire health plan population varied by year, peaking sharply during the 2010 and 2014 California outbreaks (Fig 1). Pertussis incidence also varied by age during each of the outbreaks (Fig 2). Age-specific incidence peaked at ages 10 to 11 in each outbreak (at ~300 cases per 100 000 person-years [P-Y]) during 2010 and 2014 (Fig 2). Pertussis incidence in the 2010 outbreak sharply declined after this peak and stayed low at older ages (Fig 2), a decline that we have previously demonstrated to be associated with the receipt of whole cell instead of acellular pertussis vaccines in infancy and childhood as well as with Tdap receipt. Pertussis incidence in the 2014 outbreak declined similarly among 12-year-olds to 205 cases per 100 000 P-Y. In contrast to 2010, disease rose again sharply among 14- to 16-year-olds, with incidence rate reaching its highest level at 14 years of age (465 cases per 100 000 P-Y), despite Tdap coverage rates close to 90% (Fig 3). The high rate of pertussis at 14 to 16 years of age decreased beginning at ages 18 to 19 years (Fig 2), which corresponds to the ages of persons who had received whole cell pertussis vaccines as young children (Fig 3).

To analyze Tdap VE, the study population included 1207 pertussis cases among 279 493 persons contributing 792 418 P-Y from January 2006 to March 2015. Almost 85% of all P-Y were contributed by persons aged 10 to 13 years, 15% by those aged 14 to 16 years, and 0.5% by those aged 17 to 19 years. Within the study population, 175 094 persons received Tdap and were followed for an average of 2.4 years (10th–90th, range 0.4–4.5 years) after Tdap, totaling 418 595 vaccinated P-Y (Table 1). The unadjusted pertussis incidence rates per 100 000 P-Y for all ages combined were similar in unvaccinated versus vaccinated adolescents (incidence rate ratio 0.95, 95% confidence interval [CI] 0.85–1.06; Table 2). In the Cox regression analyses, Tdap VE steadily decreased each additional year after vaccination, starting at 68.8% (95% CI 59.7% to 75.9%) during year 1, declining to 56.9% (95% CI 41.3% to 68.4%) during year 2, further declining to 25.2% (95% CI –4.3% to 46.4%) during year 3, and to 8.9% (95% CI –30.6% to 36.4%) during the 4+ years after...
vaccination (Table 3). The estimated increase in the HR per year since Tdap vaccination was 1.35 (95% CI 1.22 to 1.50), indicating that during recent pertussis outbreaks the risk of pertussis in Tdap vaccinees was higher by 35% per year after vaccination in the vaccinees who were more remote from Tdap vaccination.

Pertussis cases were mild or moderate in severity regardless of Tdap status. Within 5 days before or after the positive PCR test, 1185 per 1207 cases (98.2%) had a health care visit; 1041 (86.2%) received a diagnosis of pertussis, cough, or exposure to pertussis; and 138 (11.4%) received a “pertussis-related” diagnosis (upper respiratory infection, viral syndrome, asthma/wheezing/bronchospasm, bronchitis, allergic rhinitis, nasal congestion, vomiting, croup, pneumonia, shortness of breath, or sinusitis); 1164 (96.4%) received a prescription for azithromycin, except for 1 erythromycin. We identified 44 (3.6%) cases with 50 total ED visits for pertussis care. The diagnoses received, percent who received antibiotic treatment, and percent who sought ED care did not vary according to Tdap vaccination status. There were no pertussis-related hospitalizations or deaths in the study population.

DISCUSSION

This study investigated the effectiveness of Tdap against pertussis in a highly vaccinated population during 2 successive epidemics. We demonstrate that among a cohort of teenagers who have exclusively received acellular pertussis vaccines, Tdap provides moderate protection 1 year after vaccination and then protection wanes rapidly. Tdap VE was 69% during the first year after vaccination, declining to <9% by ≥4 years after vaccination. This amounted to a waning of Tdap protection of 35%...
per year on average after vaccination. In this study, 96.5% of adolescents had received Tdap by their 14th birthday because California mandates it before beginning seventh grade. Widespread Tdap vaccination seen in Fig 3 although associated with a transient decrease in pertussis incidence, did not prevent outbreaks among this population of teenagers who have only ever received acellular pertussis vaccines.

This study demonstrates that despite high rates of Tdap vaccination, the growing cohort of adolescents who have only received acellular pertussis vaccines continue to be at high risk of contracting pertussis and sustaining epidemics. In 2010, children aged 10 to 12 were the first cohort to have exclusively received DTaP vaccines and they were the population at highest risk of disease. The strategy of routinely vaccinating adolescents to prevent future disease did not prevent the 2014 epidemic, arguably because the protection afforded by a dose of Tdap was too short-lived.

We8,13 and others9–11 have previously shown that the effectiveness of DTaP vaccines wanes substantially, even among fully vaccinated children. An important consideration in this current study is that Tdap waning estimates may reflect both ongoing...

### TABLE 1 Tdap Vaccination Rates and Follow-Up Time by Age, Gender, Birth Year, and Race/Ethnicity in the Study Population

<table>
<thead>
<tr>
<th>Gender</th>
<th>Number Vaccinated With Tdap (%) Total = 175 094</th>
<th>Tdap Vaccination Rate per 100 P-Y (95% CI)</th>
<th>Average P-Y Follow-up per Vaccine (10th–90th Range)</th>
<th>Unvaccinated P-Y of Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>86 189 (49.2)</td>
<td>47.2 (46.8–47.5)</td>
<td>2.4 (0.4–4.5)</td>
<td>182 785</td>
</tr>
<tr>
<td>Male</td>
<td>88 885 (50.8)</td>
<td>46.5 (46.2–46.8)</td>
<td>2.4 (0.4–4.5)</td>
<td>191 038</td>
</tr>
<tr>
<td>Age group, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>20 423 (11.7)</td>
<td>8.7 (8.5–8.8)</td>
<td>2.7 (0.6–4.5)</td>
<td>235 995</td>
</tr>
<tr>
<td>11</td>
<td>117 019 (66.8)</td>
<td>107.4 (106.8–108)</td>
<td>2.3 (0.4–4.5)</td>
<td>108 994</td>
</tr>
<tr>
<td>12</td>
<td>33 162 (18.9)</td>
<td>160.1 (158.4–161.8)</td>
<td>2.4 (0.6–4.3)</td>
<td>20 718</td>
</tr>
<tr>
<td>13</td>
<td>3823 (2.2)</td>
<td>75.3 (73.0–77.8)</td>
<td>3.1 (0.7–4.3)</td>
<td>5075</td>
</tr>
<tr>
<td>14</td>
<td>577 (0.3)</td>
<td>29.6 (27.3–32.1)</td>
<td>2.6 (0.6–3.9)</td>
<td>1950</td>
</tr>
<tr>
<td>15–19</td>
<td>90 (0.1)</td>
<td>8.2 (6.7–10.1)</td>
<td>1.0 (0.2–2.1)</td>
<td>1092</td>
</tr>
<tr>
<td>Birth year</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1996</td>
<td>320 (0.2)</td>
<td>34.1 (30.6–38.1)</td>
<td>5.1 (2.5–7.2)</td>
<td>937</td>
</tr>
<tr>
<td>1997</td>
<td>7264 (4.2)</td>
<td>38.2 (37.4–39.1)</td>
<td>4.7 (1.9–6.5)</td>
<td>19 057</td>
</tr>
<tr>
<td>1998</td>
<td>13 202 (7.5)</td>
<td>42.6 (41.9–43.4)</td>
<td>4.1 (1.3–5.8)</td>
<td>30 976</td>
</tr>
<tr>
<td>1999</td>
<td>31 734 (18.1)</td>
<td>49.3 (48.4–49.9)</td>
<td>3.5 (1.4–4.7)</td>
<td>64 345</td>
</tr>
<tr>
<td>2000</td>
<td>33 711 (19.3)</td>
<td>58.0 (57.4–58.7)</td>
<td>2.9 (1.2–4.0)</td>
<td>58 103</td>
</tr>
<tr>
<td>2001</td>
<td>33 186 (18.9)</td>
<td>57.0 (56.4–57.6)</td>
<td>2.0 (0.9–3.0)</td>
<td>58 146</td>
</tr>
<tr>
<td>2002</td>
<td>32 242 (18.4)</td>
<td>55.3 (54.7–55.9)</td>
<td>1.2 (0.6–1.9)</td>
<td>58 292</td>
</tr>
<tr>
<td>2003</td>
<td>21 011 (12.0)</td>
<td>38.8 (38.3–38.9)</td>
<td>0.5 (0.1–1.0)</td>
<td>54 089</td>
</tr>
<tr>
<td>2004</td>
<td>2366 (1.4)</td>
<td>8.3 (8.0–8.7)</td>
<td>0.3 (0.0–0.8)</td>
<td>28 655</td>
</tr>
<tr>
<td>2005</td>
<td>42 (0.0)</td>
<td>3.5 (2.6–4.7)</td>
<td>0.1 (0.0–0.2)</td>
<td>1212</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>62 042 (35.4)</td>
<td>46 (45.6–46.3)</td>
<td>2.5 (0.5–4.6)</td>
<td>134 996</td>
</tr>
<tr>
<td>Asian or Pacific Islander</td>
<td>36 057 (20.6)</td>
<td>52.1 (51.6–52.7)</td>
<td>2.4 (0.4–4.5)</td>
<td>69 192</td>
</tr>
<tr>
<td>Hispanic (regardless of race)</td>
<td>52 775 (30.1)</td>
<td>49.3 (48.8–49.7)</td>
<td>2.3 (0.4–4.4)</td>
<td>107 129</td>
</tr>
<tr>
<td>Black or African American</td>
<td>15 839 (9.0)</td>
<td>46.2 (45.5–46.9)</td>
<td>2.5 (0.5–4.6)</td>
<td>34 307</td>
</tr>
<tr>
<td>American Indian or Alaskan Native</td>
<td>1123 (0.6)</td>
<td>47.2 (44.5–50.0)</td>
<td>2.5 (0.4–6.4)</td>
<td>2380</td>
</tr>
<tr>
<td>Multiracial</td>
<td>2 (0.0)</td>
<td>80.0 (21.5–343.9)</td>
<td>2.5 (0.2–4.8)</td>
<td>2</td>
</tr>
<tr>
<td>Imputed</td>
<td>7256 (4.1)</td>
<td>28.1 (27.5–28.8)</td>
<td>1.9 (0.3–3.9)</td>
<td>25 826</td>
</tr>
</tbody>
</table>

### TABLE 2 Incidence of Pertussis by Age Group and Tdap Vaccination Status in the Study Population

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Unvaccinated</th>
<th>Vaccinated</th>
<th>IRR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pertussis Cases, n</td>
<td>582</td>
<td>373 823</td>
<td>155.7 (143.3–168.9)</td>
</tr>
<tr>
<td>Incidence Rate/100 000 Y (95% CI)</td>
<td>10</td>
<td>9488</td>
<td>128.4 (114.5–137.3)</td>
</tr>
<tr>
<td>Pertussis Cases, n</td>
<td>11</td>
<td>709</td>
<td>108.94</td>
</tr>
<tr>
<td>Incidence Rate/100 000 Y (95% CI)</td>
<td>12</td>
<td>75</td>
<td>108.3</td>
</tr>
<tr>
<td>Pertussis Cases, n</td>
<td>13</td>
<td>11</td>
<td>5075</td>
</tr>
<tr>
<td>Incidence Rate/100 000 Y (95% CI)</td>
<td>14</td>
<td>7</td>
<td>1950</td>
</tr>
<tr>
<td>Pertussis Cases, n</td>
<td>15–19</td>
<td>4</td>
<td>1092</td>
</tr>
</tbody>
</table>

IRR, incidence rate ratio.

a Vaccinated time began 8 d after receipt of Tdap.
DTaP waning as well as Tdap waning because as vaccinees become an additional year more remote from Tdap, they simultaneously become 1 year more remote from their last DTaP dose. This study was unable to disentangle the waning of Tdap effectiveness from the ongoing waning of previous doses of DTaP because the years since vaccination for Tdap and the fifth DTaP dose are closely correlated.

Our estimate of Tdap waning is consistent with previous observations but provides additional data including 2 separate pertussis epidemics. Koepke et al evaluated Tdap waning during a 2012 pertussis outbreak in Wisconsin and found that Tdap VE was 75% for those vaccinated in 2012, and much lower at ∼12% for those vaccinated 3 to 4 years earlier in 2008–2009. Our results are also consistent with a case-control study that investigated Tdap VE during a 2012 pertussis outbreak in Washington State. This study estimated that among adolescents with an exclusive acellular pertussis vaccine history, VE was 73% within 1 year of vaccination and declined to 34% by 2 to 4 years after Tdap. Taken together with the current study, these results all indicate that Tdap provides little protection against pertussis beyond the first 2 to 3 years after vaccination.

TABLE 3 Tdap VE by Year After Tdap Vaccination

<table>
<thead>
<tr>
<th>Year After Tdap (Time Since Tdap)</th>
<th>HR (95% CI)</th>
<th>Tdap VE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1 (8 d to &lt;1 y)</td>
<td>0.31 (0.24 to 0.40)</td>
<td>68.8 (59.7 to 75.9)</td>
</tr>
<tr>
<td>Year 2 (1 to &lt;2 y)</td>
<td>0.45 (0.32 to 0.60)</td>
<td>56.9 (41.3 to 68.4)</td>
</tr>
<tr>
<td>Year 3 (2 to &lt;3 y)</td>
<td>0.75 (0.54 to 1.04)</td>
<td>25.2 (4.3 to 46.4)</td>
</tr>
<tr>
<td>Year 4+ (≥3 y)</td>
<td>0.91 (0.64 to 1.31)</td>
<td>8.9 (30.6 to 36.4)</td>
</tr>
</tbody>
</table>

Importantly for protecting infants, Tdap vaccination of pregnant women is likely to have a larger impact on pertussis in infants. Protection by Tdap during pregnancy is thought to be due to the passage of antibodies across the placenta. Therefore, the half-life of immunoglobulin G and when Tdap is given in pregnancy relative to delivery largely determines the level of antibodies transferred to the neonate rather than Tdap duration of protection. As yet, most women currently receiving Tdap during pregnancy received whole cell pertussis vaccines during infancy and childhood; however, as the current adolescent population ages into adulthood, an increasing proportion of pregnant women will have only ever had DTaP vaccines. It is not known whether Tdap vaccination of these pregnant women will result in transfer of antibodies that are comparable in quantity and quality and that will similarly protect infants. In the meantime, because Tdap’s protection is short-lived, it is important to continue current Advisory Committee on Immunization Practices policy of vaccinating all pregnant women with Tdap during every pregnancy.

A significant strength of this study was our ability to follow a large study population over a long period of time that included 2 pertussis outbreaks. We followed all KPNC members who only received DTaP vaccines starting at age 10 years and continuing until the occurrence of pertussis, a censoring event, or the end of the study in March 31, 2015. The large study population allowed us to stratify the analyses by birth year to control for age-related confounding. Our study calculated Tdap effectiveness using data that spanned over 9 years and 2 separate pertussis epidemics. We used calendar time as the timeline in the Cox regression model so that cases were compared only with other persons at risk on the same date. Careful adjustment for calendar time is important because risk of pertussis exposure changes rapidly during an outbreak.

It has been suggested that recent increases in pertussis incidence are mostly due to greater test sensitivity, awareness, or testing utilization; however, it is unlikely that our findings were related solely or even primarily to those reasons. In particular, KPNC has used the same PCR test for pertussis since 2006, and thus greater test sensitivity did not play a role. Furthermore, while the 2010 California outbreak received substantial media attention at the time, the outbreak in 2014 received less coverage and was less visible to the general public. Finally, the age-specific incidence patterns during the 2 epidemics had distinct peaks that coincided with the aging of the cohort exclusively vaccinated with DTaP and the timing of Tdap receipt. It is not plausible that the shift in peak incidence to an older age over the 2 epidemics is mainly related to selective testing utilization within the adolescent population.

Our study was not designed to directly compare the 2 brands of Tdap vaccine and had limited ability to detect differences in duration of protection between the brands. We observed substantial waning after both Tdap vaccines and found no evidence that waning was greater after one or the other. We were also not able to compare individuals who received all acellular pertussis vaccines from 1 manufacturer versus individuals who received vaccines from both manufacturers. Most of the teenagers in this study received pertussis vaccines from both manufacturers. Almost 80% of Tdap doses were from 1 manufacturer.

Immunizing women with Tdap during pregnancy is effective at protecting infants against pertussis. A recent study found that siblings (median age 8 years) are now the most common source of pertussis infection in infants; however, it is not clear whether adolescent Tdap boosters are
Waning immunity is seen for other vaccines, yet disease control can be maintained in a population provided vaccine coverage is high enough in the right age groups. This is not the case for pertussis. Mathematical models have found that pertussis transmission is affected by both variations in VE and pertussis transmission rates. Additional modeling may be helpful in further determining factors important for future interventions on a population basis.

**CONCLUSIONS**

Among teenagers who have only ever received acellular pertussis vaccines, Tdap provides moderate protection against pertussis during the first year after vaccination, and then protection wanes to <9% at ≥4 years after vaccination. Routine immunization with Tdap did not prevent pertussis outbreaks among this highly vaccinated population. We expect future pertussis epidemics to be larger as the cohort that has only received acellular pertussis vaccines ages. The results in this study raise serious questions regarding the benefits of routinely administering a single dose of Tdap to every adolescent aged 11 or 12 years. Because Tdap provides reasonable short-term protection against pertussis, Tdap may more effectively contain pertussis if it is administered to adolescents in anticipation of a local pertussis outbreak rather than on a routine basis. For other vaccines, some countries have successfully implemented national or regional immunization campaigns in the face of an epidemic. While awaiting development of new vaccines that will provide long-lasting protection against pertussis, we should consider alternate Tdap immunization strategies for adolescents.

**ABBREVIATIONS**

- CI: confidence interval
- DTaP: diphtheria-tetanus-acellular pertussis
- ED: emergency department
- KPNC: Kaiser Permanente Northern California
- HR: hazard ratio
- PCR: polymerase chain reaction
- P-Y: person-years
- Tdap: tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis, adsorbed
- VE: vaccine effectiveness

**FINANCIAL DISCLOSURE:** Dr Klein reports research support from GlaxoSmithKline for a separate pertussis vaccine effectiveness study. Drs Klein and Baxter report additional research support from GlaxoSmithKline, Sanofi-Pasteur, Pfizer, Merck & Co., Novartis, Protein Science, Nuron Biotech, and MedImmune. Drs Bartlett and Fireman have indicated they have no financial relationships relevant to this article to disclose.

**FUNDING:** This study was funded by Kaiser Permanente.

**POSSIBLE CONFLICT OF INTEREST:** Drs Klein and Baxter report potential conflicts of interest relevant to this article. The pertussis vaccines purchased by Kaiser Permanente Northern California that are the focus of this study were manufactured by GlaxoSmithKline and Sanofi Pasteur. Ms Bartlett and Mr. Fireman have indicated they have no financial relationships relevant to this article to disclose.

**REFERENCES**


12. Quinn HE, Snelling TL, Macartney KK, McIntyre PB. Duration of protection after first dose of acellular pertussis vaccine in infants. *Pediatrics.* 2014;133(5). Available at: www.pediatrics.org/cgi/content/full/133/5/e513


25. Auger KA, Patrick SW, Davis MM. Infant hospitalizations for pertussis before and after Tdap recommendations for adolescents. *Pediatrics.* 2013;132(5). Available at: www.pediatrics.org/cgi/content/132/5/e1149


Waning Tdap Effectiveness in Adolescents
Nicola P. Klein, Joan Bartlett, Bruce Fireman and Roger Baxter

Pediatrics originally published online February 5, 2016;

Updated Information & Services
including high resolution figures, can be found at:
http://pediatrics.aappublications.org/content/early/2016/02/03/peds.2015-3326

References
This article cites 34 articles, 9 of which you can access for free at:
http://pediatrics.aappublications.org/content/early/2016/02/03/peds.2015-3326.full#ref-list-1

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
Infectious Disease
http://classic.pediatrics.aappublications.org/cgi/collection/infectious_diseases_sub

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
https://shop.aap.org/licensing-permissions/

Reprints
Information about ordering reprints can be found online:
http://classic.pediatrics.aappublications.org/content/reprints
Waning Tdap Effectiveness in Adolescents
Nicola P. Klein, Joan Bartlett, Bruce Fireman and Roger Baxter
Pediatrics originally published online February 5, 2016;

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/early/2016/02/03/peds.2015-3326