Waning Tdap Effectiveness in Adolescents

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abstract

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 litle protection remained 2-3 years after vaccination.

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Dr Klein led the design of the study, oversaw the data collection, interpreted the data, drafted the initial manuscript, and was the lead author of the manuscript; Ms Bartlett collected the data, conducted the analysis, and contributed to critical revision of the manuscript for important intellectual content; Mr Fireman contributed to study design, assisted with the analysis, and contributed to critical revision of the manuscript for important intellectual content; Dr Baxter assisted with the study design and contributed to its critical revision for important intellectual content; and all authors approved the final manuscript as submitted.

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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) vaccinefor 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.

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The United States switched from whole cell pertussis to 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 States[2] and other countries[3–7] have experienced increased pertussis disease in the years after the switch to DTaP.

In 2010, California experienced the largest pertussis epidemic since 1958[2] 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 children[8–12] 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 age[8] 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 vaccines[17];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 later[13] 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 receivedTdap and then moved across

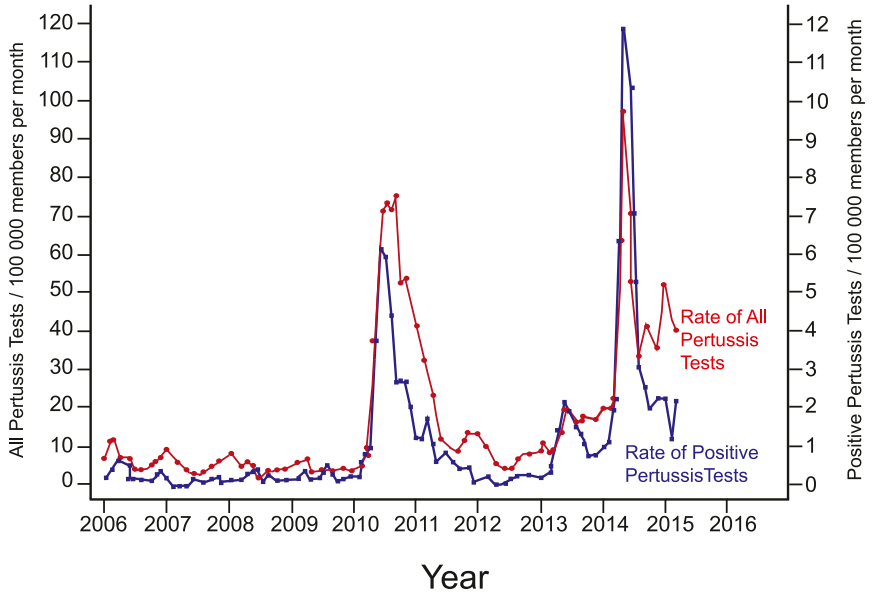

FIGURE 1

Monthly rates of pertussis PCR tests and positive pertussis PCR results in the KPNC population from January 2006 through March 2015, including 2 pertussis outbreaks. Red line represents all PCR tests performed per 100 000 members per month. Blue line represents positive pertussis PCR results per 100 000 members per month.

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[8,13] 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%

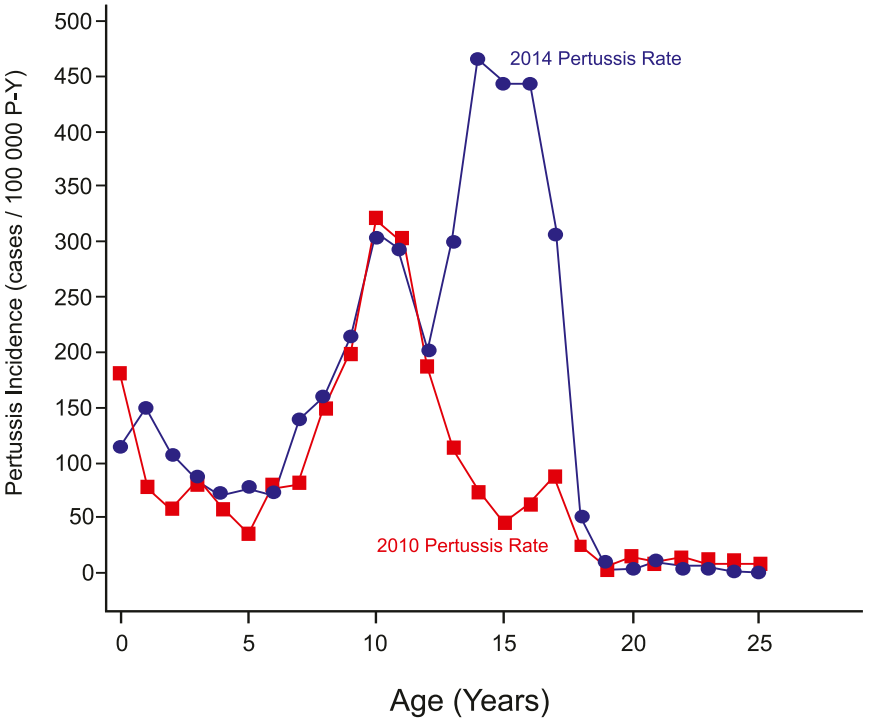

FIGURE 2
Annual rate of PCR-confirmed pertussis by age in the KPNC population in the 2010 and 2014 outbreaks. The outbreak periods were defined as the 12 consecutive months with the highest pertussis rates. Red line represents pertussis rates during the 2010 outbreak (May 2010–April 2011). Blue line represents pertussis rates during the 2014 outbreak (April 2014–March 2015).

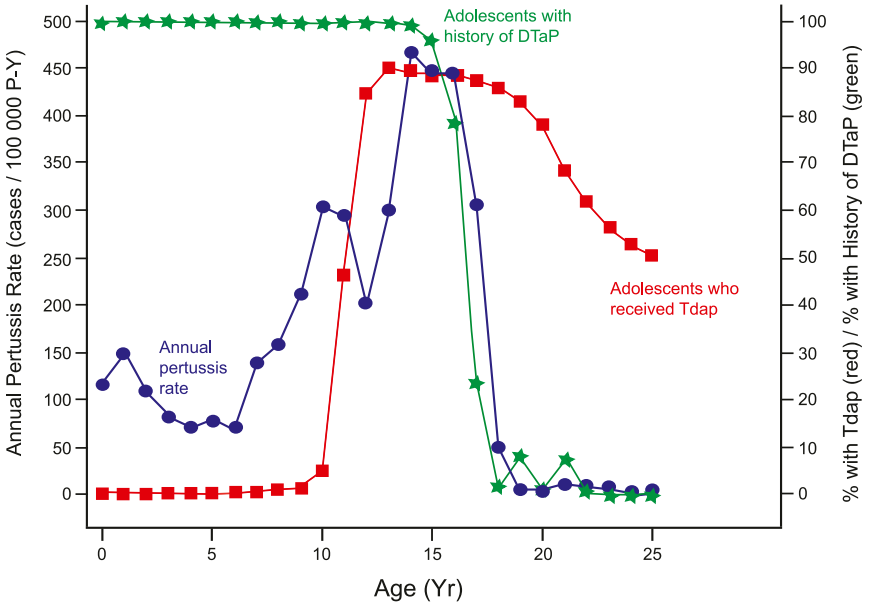

FIGURE 3
Annual pertussis incidence, Tdap vaccination rate, and DTaP history in the KPNC population, by age, during the pertussis outbreak from April 2014 to March 2015. Blue line represents the annual rate of pertussis during the outbreak. Red line represents the percentage of members who had received Tdap as of June 25, 2014 (the median diagnosis date of cases during the outbreak). Green line represents the percentage of members who were likely as of June 25, 2014 to have received all DTaP vaccines in early childhood.

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

	Number Vaccinated With Tdap (%) Total = 175 094	Tdap Vaccination Rate per 100 P-Y (95% CI)	Average P-Y Follow-up per Vaccine (10th–90th Range)	Unvaccinated P-Y of Follow-up
Gender				
Female	86 199 (49.2)	47.2 (46.8–47.5)	2.4 (0.4–4.5)	182 785
Male	88 895 (50.8)	46.5 (46.2–46.8)	2.4 (0.4–4.5)	191 038
Age group, y				
10	20 423 (11.7)	8.7 (8.5–8.8)	2.7 (0.6–4.5)	235 995
11	117 019 (66.8)	107.4 (106.8–108)	2.3 (0.4–4.5)	108 994
12	33 162 (18.9)	160.1 (158.4–161.8)	2.4 (0.6–4.3)	20 718
13	3823 (2.2)	75.3 (73.0–77.8)	3.1 (0.7–4.3)	5075
14	577 (0.3)	29.6 (27.3–32.1)	2.6 (0.6–3.9)	1950
15–19	90 (0.1)	8.2 (6.7–10.1)	1.0 (0.2–2.1)	1092
Birth year				
1996	320 (0.2)	34.1 (30.6–38.1)	5.1 (2.5–7.2)	937
1997	7284 (4.2)	38.2 (37.4–39.1)	4.7 (1.9–6.5)	19 057
1998	13 202 (7.5)	42.6 (41.9–43.4)	4.1 (1.9–5.6)	30 976
1999	31 734 (18.1)	49.3 (48.8–49.9)	3.5 (1.4–4.7)	64 345
2000	33 717 (19.3)	58.0 (57.4–58.7)	2.9 (1.2–4.0)	58 103
2001	33 156 (18.9)	57.0 (56.4–57.6)	2.0 (0.9–3.0)	58 146
2002	32 242 (18.4)	55.3 (54.7–55.9)	1.2 (0.6–1.9)	58 292
2003	21 011 (12.0)	38.8 (38.3–39.4)	0.5 (0.1–1.0)	54 099
2004	2386 (1.4)	8.3 (8.0–8.7)	0.3 (0.0–0.8)	28 655
2005	42 (0.0)	3.5 (2.6–4.7)	0.1 (0.0–0.2)	1212
Race/ethnicity				
White	62 042 (35.4)	46 (45.6–46.3)	2.5 (0.5–4.6)	134 996
Asian or Pacific Islander	36 057 (20.6)	52.1 (51.6–52.7)	2.4 (0.4–4.5)	69 182
Hispanic (regardless of race)	52 775 (30.1)	49.3 (48.8–49.7)	2.3 (0.4–4.4)	107 129
Black or African American	15 839 (9.0)	46.2 (45.5–46.9)	2.5 (0.5–4.6)	34 307
American Indian or Alaskan Native	1123 (0.6)	47.2 (44.5–50.0)	2.5 (0.4–4.6)	2380
Multiracial	2 (0.0)	86.0 (21.5–343.9)	2.5 (0.2–4.8)	2
Imputed	7256 (4.1)	28.1 (27.5–28.8)	1.9 (0.3–3.9)	25 826

per year on averageaftervaccination. 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.

We[8,13] and others[9–11] 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 2 Incidence of Pertussis by Age Group and Tdap Vaccination Status in the Study Population

Age, y	Unvaccinated			Vaccinated[a]			IRR (95% CI)
	Pertussis cases, *n*	Unvaccinated P-Y	Incidence Rate/100 000 P-Y (95% CI)	Pertussis Cases, *n*	Vaccinated P-Y	Incidence Rate/100 000 P-Y (95% CI)	
All ages (10–19)	582	373 823	155.7 (143.3–168.9)	613	415 251	147.6 (136.2–159.8)	0.95 (0.85–1.06)
10	303	235 995	128.4 (114.3–143.7)	8	8680	92.2 (39.8–181.6)	0.72 (0.33–1.38)
11	218	108 994	200 (174.3–228.4)	32	75 175	42.6 (29.1–60.1)	0.21 (0.14–0.31)
12	39	20 718	188.2 (133.9–257.3)	91	117 911	77.2 (62.1–94.8)	0.41 (0.28–0.60)
13	11	5075	216.8 (108.2–387.8)	117	94 894	123.3 (102.0–147.8)	0.57 (0.32–1.11)
14	7	1950	359 (144.3–739.7)	166	64 244	258.4 (220.6–300.8)	0.72 (0.36–1.67)
15–19	4	1092	366.2 (99.8–937.6)	199	54 345	366.2 (317.1–420.7)	1.00 (0.41–3.18)

IRR, incidence rate ratio.

[a] Vaccinated time began 8 d after receipt of Tdap.

TABLE 3 Tdap VE by Year After Tdap Vaccination

Year After Tdap (Time Since Tdap)	HR (95% CI)	Tdap VE(95% CI)
Year 1 (8 d to <1 y)	0.31 (0.24 to 0.40)	68.8 (59.7 to 75.9)
Year 2 (1 to <2 y)	0.43 (0.32 to 0.59)	56.9 (41.3 to 68.4)
Year 3 (2 to <3 y)	0.75 (0.54 to 1.04)	25.2 (−4.3 to 46.4)
Year 4+ (≥3 y)	0.91 (0.64 to 1.31)	8.9 (−30.6 to 36.4)

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.[20] 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.[21] 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.

Immunizing women with Tdap during pregnancy is effective at protecting infants against pertussis.[22,23] A recent study found that siblings (median age 8 years) are now the most common source of pertussis infection in infants[24]; however, it is not clear whether adolescent Tdap boosters are important for protecting infants.[25] 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.[26]

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[27]; 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.[23] 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

(Sanofi Pasteur), whereas among the study participants for whom we had complete DTaP vaccine data, 75% of DTaP doses were from GlaxoSmithKline. In addition, because nearly all of the study population had received Tdap by age 13 years and >85% were vaccinated at age 11 or 12, there were small differences in age distribution by Tdap vaccination status: unvaccinated (92% of P-Y was contributed by persons aged 10–11 years), vaccinated 8 days to <1 year (86% of P-Y was contributed by persons aged 11–12 years), vaccinated 1 year to <2 years (85% of P-Y was contributed by persons aged 12–13 years), vaccinated 2 years to <3 years (83% of P-Y was contributed by persons aged 13–14 years), and vaccinated ≥3 years (89% of P-Y was contributed by persons aged 14–16 years). Finally, recent reports have suggested that pertactin-deficient pertussis strains may be contributing to ongoing outbreaks[28,29] and the degree to which pertactin-deficient pertussis strains may have contributed to our results is not known.

Waning immunity is seen for other vaccines, yet disease control can often 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.[30] 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.[31–36] 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

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POTENTIAL 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 potential conflicts of interest to disclose.

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