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# Vaccine effectiveness of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine during a pertussis outbreak in Maine

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ABSTRACT

*Background:* Multiple school-associated pertussis outbreaks were reported in Maine from 2010 to 2011. These outbreaks were associated with an overall increase in pertussis cases statewide. Waning of protection in students recently vaccinated with tetanus, diphtheria, and acellular pertussis (Tdap) has been implicated in the increase in reported rates of pertussis nationally.
*Methods:* We conducted a retrospective cohort study to evaluate Tdap vaccine effectiveness (VE) among students aged 11–19 years in two schools reporting outbreaks in 2011. All pertussis cases reported from August through November, 2011 at the two schools were included. Vaccination history was verified using provider information, state vaccine registry data, and parental verification. Attack rates (AR) were calculated. VE and duration of protection was calculated as $VE = 1 - (AR_{vaccinated}/AR_{unvaccinated}) \times 100\%$ using a log binomial regression model.
*Results:* Of 416 students enrolled, 314 were included in the analyses. Twenty-nine cases collectively in Schools A and B. Tdap coverage was 65% at School A and 42% at School B before the start of the outbreak. Among students enrolled in the study, attack rates were 11.9% and 7.7% at Schools A and B, respectively. Overall VE was 68.5% (95% confidence interval (CI) 37.7–86.2). VE was 70.4% (95% CI 17.5–89.4) for School A and 65.2% (95% CI −19.2 to 89.9) for School B. VE <2 years versus ≥2 years from outbreak onset was not significantly different.
*Conclusions:* Tdap was moderately effective in preventing disease among vaccinated students. Vaccine coverage of 65% or less was suboptimal and might contribute to outbreaks. Waning VE was not demonstrated. Increased vaccination coverage rates as well as further evaluation of the role of acellular vaccine on VE is needed.

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## 1. Background

In 2014, there were 28,660 cases of pertussis reported in the US – the most since 1960 [1]. Although infants continue to have the highest reported rates (150.9/100,000 persons/year), rates in adolescents have risen over the past several years. From 2009 to 2014, the annual rate of pertussis in adolescents age 11–19 increased from 10.3 cases per 100,000 persons/year to 25.1 cases per 100,000 persons/year, accounting for 33% of all cases reported [1]. Recommendations for an adolescent booster dose of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine at age 11 have been in place since 2006 to control disease in this age group [5]. However, despite high national vaccine coverage of 86% in adolescents 13–17 years of age in 2013, reported rates of pertussis disease continues to be high [2]. While morbidity and mortality in adolescents and adults is low, they represent important sources of infection for infants, who are at highest risk for severe disease and death [3,4].

Vaccination in infancy with a primary series of diphtheria, tetanus and acellular pertussis vaccine (DTaP) followed by a booster with Tdap for all adolescents and adults is recommended to prevent pertussis [25]. Though based on a small number of cases, a pre-licensure clinical trial measured the effectiveness of

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reduced acellular pertussis vaccine (aP) to be 92% [8]. Pre-licensure immunologic studies of Tdap predicted 85–89% efficacy based on bridging to infant DTaP efficacy trials [6,7]. Several post-licensure studies evaluating Tdap effectiveness in adolescents following priming in infancy with DTaP have been performed. One study of 167 cases in an Australian high school reported vaccine effectiveness (VE) of 78% using the screening method [9]. Another small retrospective cohort study of 51 adolescent cases in St. Croix, U.S. Virgin Islands reported VE of 66% [10].

As reported rates of pertussis have increased and large outbreaks of pertussis have emerged in recent years, the durability of immunity conferred by DTaP and Tdap has been questioned. A large case–control study in California demonstrated waning VE in the primary DTaP series from 98% to 72% over 5 years [21]. Waning immunity in adolescents following Tdap was observed during pertussis epidemics in Washington State and Wisconsin as well. In Washington, Tdap VE among adolescents who received DTaP as infants was 73% at 1 year and 34% at 2–4 years post-vaccination. This decline in effectiveness is thought to be a major contributing factor for high disease rates among adolescents [11,12].

Since 2010, numerous states have reported outbreaks in schools, with a large proportion of cases in adolescents (CDC, unpublished data, 2013). Maine reported a 260% increase in pertussis cases (737 cases versus 205 cases) in 2012 compared to 2011 [13,14]. Many of these cases were among adolescents during school outbreaks. The objectives of this study were: (1) to characterize a school based outbreak of pertussis in rural Maine and (2) to conduct a Tdap vaccine effectiveness study in the context of this outbreak.

## 2. Methods

### 2.1. Site description

The number and reported rate of pertussis cases for the state of Maine and Penobscot County was collected through the state notifiable disease reporting system. Two schools serving rural communities in Penobscot County, Maine (pop. 153,364) reporting pertussis outbreaks were included in the study. The selection of schools was based on their relatively high attack rates. School A is a small private school with a student population of approximately 230 students enrolled in kindergarten through 12th grade. School B is a public school with approximately 700 students enrolled in kindergarten through 8th grade. The outbreak period was defined as the cough onset date of the first case through the cough onset date of the last case at both schools and lasted from August 15 through November 26, 2011.

### 2.2. Case ascertainment

A confirmed case was defined as any acute cough illness with isolation of *Bordetella pertussis* from a clinical specimen or a cough illness lasting ≥2 weeks with one of the following: paroxysms, inspiratory whoop, post-tussive vomiting, or apnea; and a polymerase chain reaction (PCR) positive for pertussis or contact with another confirmed case. A probable case was defined as a cough illness lasting ≥2 weeks with one of the following: paroxysms, inspiratory whoop, post-tussive vomiting, or apnea; and an absence of laboratory confirmation and no linkage to a confirmed case [15]. We also included a suspect case definition defined as an acute cough illness of any duration with a positive *B. pertussis* PCR test.

All cases reported from the two schools during the outbreak period were included. Cough onset date, symptoms, cough duration, and laboratory results were collected for each case. Laboratory confirmation for *B. pertussis* by PCR or culture was performed at a private laboratory (Affiliated Laboratories Inc.) or the Maine Department of Health's Health and Environmental Testing Laboratories (HETL) using modified CDC protocols [16].

### 2.3. Study design

We conducted a retrospective cohort study to evaluate Tdap VE in the two outbreak schools. All students aged 11 through 19 years enrolled in either school at the beginning of the outbreak period were included in the study. Health records for all students in grades 5–12 at School A and 5–8 at School B were reviewed. Demographic information and pertussis-specific vaccination history, including type, brand and lot number were recorded. Vaccination records were verified using the Maine state immunization registry (ImmPact), school health records, parent interviews, and provider records.

### 2.4. Vaccine history ascertainment

All records were assessed for completeness. Vaccination history was considered complete if the student received four (if the 4th dose was administered after their 4th birthday) or five doses of DTaP or diphtheria, tetanus, whole-cell pertussis vaccine (DTP) during childhood, and one dose of Tdap on or after their 11th birthday and at least 2 weeks before the start of the outbreak period. Students vaccinated within 2 weeks of the start of the outbreak or during the outbreak were considered unvaccinated. Vaccination history was initially ascertained using school health records and ImmPact. If a student had no or only partial documentation of the DTaP/DTP series or Tdap dose, further verification of vaccination status was conducted through follow up with providers and parent interviews. Parents were also asked if students received vaccinations at a site other than their primary care physician; these sites were contacted for further verification. Students' Tdap vaccination status was verified as unvaccinated if non-receipt was confirmed by the parents; if parents confirmed the student received no care other than with their PCP and the PCP had no record of Tdap receipt; if the student had documentation of an adolescent encounter and was given other adolescent vaccines such as MCV4 or HPV, but had no record of Tdap; or if a personal belief or medical exemption was on file with the PCP. Incomplete records that could not be verified were excluded from the final analysis. For the primary analysis, students with an incomplete or unverifiable primary DTaP series were excluded.

### 2.5. Data analysis

Descriptive epidemiology, attack rates by school and Tdap VE were calculated using SAS and MS Excel. Proportions were compared using $\chi^2$ or Fisher's exact tests. VE was calculated as $VE = 1 - (\text{Attack rate}_{\text{vaccinated}}/\text{Attack rate}_{\text{unvaccinated}}) \times 100\%$ using a log binomial regression model and adjusted for school [17]. VE was calculated for School A at different time intervals since vaccination, <2 years and ≥2 years from the beginning of the outbreak, to assess duration of protection. School B was excluded from duration of protection analysis because no student was vaccinated more than 2 years before the outbreak. Primary analyses were restricted to students with verified Tdap vaccination histories and completed childhood DTaP/DTP series. Secondary analyses were performed including: (1) all students with verified Tdap status regardless of childhood DTaP vaccination history; and (2) in which students with unverified Tdap vaccination histories were designated as unvaccinated.

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