PERTUSSIS

# Comment on "The impact of past vaccination coverage and immunity on pertussis resurgence"

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**Limitations in the data used for a recent modeling study of pertussis resurgence in the US may explain why the results were not consistent with several observational studies demonstrating a shorter duration of protection after acellular pertussis vaccine administration.**

In this Technical Comment, we present concerns regarding some of the conclusions drawn from a recent publication by Domenech de Cellès *et al.* (*1*) in *Science Translational Medicine*. In this study, the authors find no evidence that the transition from a whole-cell vaccine against pertussis (DTwP) to an acellular vaccine (DTaP), which occurred in the United States in the 1990s, was a driver in the resurgence of pertussis (*1*). However, we believe that limitations in the data used by Domenech de Cellès *et al.* for the modeling in this study led to an inaccurate depiction of pertussis resurgence in the United States.

The study population of reported pertussis cases in Massachusetts from 1990 to 2005, which was the dataset analyzed by Domenech de Cellès *et al.* (*1*), included only a small proportion of individuals who were born in 1997 or later. This is the cohort that only received the acellular vaccine (*2*) and that has a greater lifelong risk of pertussis infection *(3, 4)*. The effects of more rapid waning of immunity after immunization with the acellular vaccine, particularly for the priming doses, can only be assessed several years after the last dose of vaccine has been administered. However, the few members of the cohort receiving only the acellular vaccine analyzed in the study of Domenech de Cellès *et al.* (*1*) were no more than 8 years of age and would have received their last dose of acellular vaccine at 4 to 6 years of age. This would limit the ability to assess the shorter duration of vaccine-induced immunity from the acellular pertussis vaccine compared to the whole-cell pertussis vaccine. It is this shorter duration of protection that is thought to be driving the resurgence of reported pertussis cases in the United States among the cohort receiving the acellular pertussis vaccine (*5*).

We also disagree that the findings of the study of Domenech de Cellès *et al.* (*1*) are consistent with a number of observational studies evaluating vaccine effectiveness and duration of protection among cohorts receiving the DTaP acellular vaccine (*6*–*8*). Domenech de Cellès *et al.* used their best-fitting waning model for the 1990–2005 time period to simulate pertussis incidence during 2006 to 2015. They then compared their predicted relative change in age-specific odds of disease to findings from three observational studies (*6*–*8*). However, Domenech de Cellès *et al.* did not account for the addition of the adolescent acellular pertussis vaccine booster (called Tdap) as a universal recommendation for 11 to 12 year olds in 2006 in the empirical data. Furthermore, the three empirical vaccine effectiveness studies only included data through 2010 (*7*, *8*) or 2011 (*6*), so the authors did not compare their model-forecasted pertussis incidence with the current pertussis trends being observed in the United States, including the marked increase in incidence among high school–aged students in 2014 (*9*), which is consistent with aging of the cohort receiving exclusively the acellular vaccine.

Last, Domenech de Cellès *et al.* make the assumption that immunity mediated by pertussis infection is lifelong. However, a review of the published data on duration of immunity estimated that infection-acquired immunity against pertussis wanes after 4 to 20 years (*10*). In addition, pertussis antibody has been found to persist at higher concentrations among DTwP-vaccinated adults compared to vaccine-naïve adults with exposure to natural disease (*11*). The assumption of lifelong immunity would have an artificial impact on vaccine effectiveness when introducing vaccine into a highly immune population and calls into question the "honeymoon effect" described by Domenech de Cellès *et al.* (*1*).

The Domenech de Cellès *et al.* study provides an interesting hypothesis regarding the resurgence of pertussis reported before 2005 in the United States. However, we feel that conclusions derived from their model about the long-term effectiveness of the DTaP acellular pertussis vaccine versus the whole-cell pertussis vaccine are limited. Much is still unknown about pertussis, and further research is needed to fully understand the causes of its changing epidemiology in the United States.

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