Estimating the Effectiveness of Acellular Pertussis Vaccines

To the Editor—In the 15 June 2012 issue of Clinical Infectious Diseases, Witt et al reported that vaccine effectiveness (VE) of acellular pertussis vaccines was 41% for children aged 2–7 years, 24% for 8- to 12-year-olds, and 79% for 13- to 18-year-olds [1]. The authors conclude that their data “confirms markedly lower than expected protection afforded by the pre-school series of acellular pertussis vaccinations in the 8–12 year age group” and poor durability of protection from the vaccine. While we agree that protection wanes over time, there are important limitations to the Witt et al analysis.

VE estimates are predicated on comparing disease risk in a vaccinated group with disease risk in an unvaccinated group. When calculating VE for multiple dose vaccines, partially vaccinated persons should not be grouped with unvaccinated individuals [2, 3]. Doing so compromises the vaccine-naive comparison group and lowers VE estimates. Although the authors do not specify how undervaccinated individuals were handled in the analyses, the results presented in their Tables 1 and 2 indicate that undervaccinated and unvaccinated individuals were inappropriately categorized together, rather than excluding undervaccinated persons from the analysis. This bias explains the surprisingly low estimates in the 2 younger and combined overall age groups.

Second, Witt et al state that VE was estimated using the screening method, often used when precise attack rates cannot be calculated for vaccinated and unvaccinated individuals. However, the authors describe a cohort study and report attack rates, as well as discuss vaccination rates among cases and age-
matched controls. The methods used to assess VE are therefore unclear. If the screening method was used, further detail on how population coverage was assessed is warranted. Likewise, if attack rates were estimated, details on the denominator population are needed.

The authors categorized the 2 lower age groups (2–7 years and 8–12 years) based on low and high pertussis incidences, respectively, and not on age groups defined by the recommended immunization schedule. The definition of “fully vaccinated” therefore varies within age category, and reported VE appears to be estimates of ≥4 DTap doses for the 2- to 7-year age group, and of 5 DTap doses plus or minus a Tdap booster for the 8- to 12-year age group, further limiting interpretation of the results.

The VE in the 13- to 18-year age group is a measure of the Tdap booster. [Note: ACIP recommendations for the adolescent Tdap booster are incorrectly stated in the publication. The Tdap booster is currently recommended for adolescents at age 11 or 12 years, and for 7- to 10-year-olds who are not fully immunized against pertussis.] For the population in this study, the majority of adolescents would have received whole-cell pertussis vaccine for the first 3 doses of the series, and the estimate is not a pure measure of acellular VE.

Given the important implications for pertussis vaccine policy and clinical practice, valid methods and clear specification of the comparison group and number of doses measured by the estimates are critical in order to guide interpretation of results and allow for informed comparisons with other VE estimates reported in the literature.

Note

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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