



## News Articles, Vaccine/Immunization

### Study provides more evidence for safety of immunization schedule

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A **study** published today in the *Journal of the American Medical Association (JAMA)* offers more reassuring evidence for the safety of the childhood immunization schedule.

Glanz and colleagues from the Vaccine Safety Datalink (VSD) conducted a nested case-control study of nearly half a million children to determine if exposure to multiple vaccines in early childhood was associated with an increased risk for infections that weren't targeted by the vaccines (nontargeted infections). The VSD, funded by the Centers for Disease Control and Prevention, conducts large epidemiological studies of vaccine safety using electronic health record databases.

Investigators identified about 50,000 nontargeted infections treated in emergency departments and inpatient settings from 2003-'13 in the study population. Then, they selected a random sample of 385 children who had nontargeted infections from ages 2-4 years. Upon chart review, 193 were confirmed as cases of nontargeted infections. Each case was matched with four control children having the same mean age, sex and distribution of chronic diseases.

Investigators calculated the total number of proteins and polysaccharides in each vaccine received by cases and controls from birth through age 23 months, which they termed the "mean cumulative antigen exposure." Then, they calculated the risk of nontargeted infections between 2 and 4 years old.

Results showed no statistically significant difference in the cumulative antigen exposure of cases and controls (240.6 for cases and 242.9 for controls).

"In an integrated health plan setting, cumulative vaccine antigen exposure through the first 23 months of life was not associated with an increased risk of emergency department and inpatient visits for infectious diseases not targeted by vaccines over the next 24 months," the authors concluded.

The background for this study goes back to 2002, when the Institute of Medicine (now the National Academy of Medicine) called for studies examining whether vaccines could have an effect on nontargeted infections. There are some data, primarily from the developing world, for this possibility.

Several studies have shown that children who receive a measles-containing vaccine are significantly less likely to die from infections other than measles than children who had not received the vaccine, suggesting the vaccine has a positive impact on the immune system. A few studies, however, show that whole cell pertussis vaccine - which has not been used in the U.S. since the 1990s - could increase mortality from diseases other than pertussis if given after Bacillus Calmette-Guérin vaccine, although this has yet to be confirmed.

In addition, a 2012 Institute of Medicine report called for more research into the safety of the childhood vaccination schedule in general. While the safety of individual vaccines and vaccines given in specific combinations had been studied in great detail through pre- and post-licensure studies, few studies had examined the schedule as a whole. The overall childhood immunization schedule also had evolved from eight routine vaccinations in 1994 to 14 in 2010. Furthermore, some parents were concerned that the increasing number of vaccines weakened children's immune systems, although the biologic plausibility for this premise is weak.

Thus, VSD investigators embarked on this study to answer the question of nontargeted infections.

It is difficult to overstate the value of the VSD to the U.S. immunization program. Since its creation in 1990, its



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purpose has been to study vaccine safety and strengthen public confidence in vaccines. The present study is yet another example of how the VSD successfully monitors vaccine safety.

However, studies continuing to demonstrate the safety of childhood vaccines have not translated into increased public confidence. Indeed, despite the work of the VSD, rates of vaccine refusal and vaccine delay have increased over time. It is clear that providing factual information to parents is not enough. Engaging health care providers and public health messaging regarding vaccine effectiveness and safety also are paramount in promoting the positive impact of vaccines on child health.

*Dr. O'Leary is a member of the AAP Committee on Infectious Diseases (COID), and Dr. Maldonado is vice chair of COID. They co-authored an editorial related to the study in JAMA, <https://jamanetwork.com/journals/jama/fullarticle/2673951>.*