

National Vaccine Information Center (NVIC)  
Vaccine Safety Science Gap Key Points  
Summary of 2013 IOM Report on  
*The Childhood Immunization Schedule and Safety*

- “Few studies have comprehensively assessed the association between the entire immunization schedule or variations in the overall schedule and categories of health outcomes, and no study has directly examined health outcomes and stakeholder concerns in precisely the way that the committee was charged to address its statement of task;” (S-4)
- “No studies have compared the differences in health outcomes that some stakeholders questioned between entirely unimmunized populations and fully immunized children. Experts who addressed the committee pointed not to a body of evidence that had been overlooked but rather to the fact that existing research has not been designed to test the entire immunization schedule;” (S4-5)
- “The committee believes that although the available evidence is reassuring, studies designed to examine the long term effects of the cumulative number of vaccines or other aspects of the immunization schedule have not been conducted; (S-5)
- “Most vaccine-related research focuses on the outcomes of single immunizations or combinations of vaccines administered at a single visit. Although each new vaccine is evaluated in the context of the overall immunization schedule that existed at the time of review of that vaccine, elements of the schedule are not evaluated once it is adjusted to accommodate a new vaccine. Thus, key elements of the entire schedule – the number, frequency, timing, order and age at administration of vaccines – have not been systematically examined in research studies;” (S8-9)
- “The committee encountered...uncertainty over whether the scientific literature has addressed all health outcomes and safety concerns. The committee could not tell whether its list was complete or whether a more comprehensive system of surveillance might have been able to identify other outcomes of potential significance to vaccine safety. In addition, the conditions of concern to some stakeholders, such as immunologic, neurologic, and developmental problems, are illnesses and conditions for which etiologies, in general, are not well understood.” (S-9)
- “The committee found that evidence assessing outcomes in subpopulations of children who may be potentially susceptible to adverse reactions to vaccines (such as children with a family history of autoimmune disease or allergies or children born prematurely) was limited and is characterized by uncertainty about the definition of populations of interest and definitions of exposures or outcomes.” (S-9)
- “To consider whether and how to study the safety and health outcomes of the entire childhood immunization schedule, the field needs valid and accepted metrics of the entire schedule (the “exposure”) and clearer definitions of health outcomes linked to stakeholder concerns (the “outcomes”) in rigorous research that will ensure validity and generalizability;” (S-9)
- “Public testimony to the committee described the speculation that children with a family history of autoimmune disease or allergies and premature infants might be additional

subpopulations at increased risk for adverse effects from immunizations. The 2012 IOM report *Adverse Effects of Vaccines: Evidence and Causality* supports the fact that individuals with certain characteristics (such as acquired or genetic immunodeficiency) are more likely to suffer adverse effects from particular immunizations, such as MMR and the varicella vaccine;" (4-6)

- "Children with certain predispositions are more likely to suffer adverse events from vaccines than those without that risk factor, such as children with immunodeficiencies that are at increased risk for developing invasive disease from a live virus vaccine. The committee recognizes that while the CDC has identified persons with symptoms or conditions that should not be vaccinated, some stakeholders question if that list is complete. Potentially susceptible populations may have an inherited or genetic susceptibility to adverse reactions and further research in this area is ongoing." (4-9)
- "Relatively few studies have directly assessed the immunization schedule. Although health professionals have a great deal of information about individual vaccines, they have much less information about the effects of immunization with multiple vaccines at a single visit or the timing of the immunizations. Providers are encouraged to explain to parents how each new vaccine is extensively tested when it is approved for inclusion in the recommended immunization schedule. However, when providers are asked if the entire immunization schedule has been tested to determine if it is the best possible schedule, meaning that it offers the most benefits and the fewest risks, they have very few data on which to base their response;" (4-10)
- "Although the committee identified several studies that reviewed the outcomes of studies of cumulative immunizations, adjuvants and preservatives, the committee generally found a paucity of information, scientific or otherwise, that addressed the risk of adverse events in association with the complete recommended immunization schedule, even though an extensive literature base on individual vaccines and combination immunizations exists;" (4-10)
- "Research examining the association between the cumulative number of vaccines received and the timing of vaccination and asthma, atopy and allergy has been limited; but the findings from the research that has been conducted are reassuring." (5-7) - 14 studies were identified and reviewed by the IOM committee.
- "The literature that the committee found to examine the relationship between the overall immunization schedule and autoimmunity was limited." (5-9) – 4 studies were identified and reviewed by the IOM committee;
- "The evidence of an association between autism and the overall immunization schedule is limited both in quantity and in quality and does not suggest a causal association. " (5-11) – 4 studies were identified and reviewed by the IOM committee;
- "The evidence regarding an association between the overall immunization schedule and other neurodevelopmental disorders [learning disorders, communication disorders, developmental disorders, intellectual disability, attention deficit disorder, disruptive behavior disorders, tics and Tourette's syndrome] is limited in quantity and of limited usefulness because of its focus on a preservative no longer used in the United States." (S-13) – 5 studies were identified and reviewed by the IOM committee;

- “The literature associating the overall immunization schedule with seizures, febrile seizures, and epilepsy is limited and inconclusive.” (5-15) - 4 studies were identified and reviewed by the IOM committee;
- “The committee reviewed six papers on the immunization of premature infants published since 2002.....Because small numbers of infants were monitored for short periods of time, it is challenging to draw conclusions from this review.” (5-15)
- “The committee’s review confirmed that research on immunization safety has mostly developed around studies examining potential associations between individual vaccines and single outcomes. Few studies have attempted more global assessment of entire sequence of immunizations or variations in the overall immunization schedule and categories of health outcomes, and none has squarely examined the issue of health outcomes and stakeholder concerns in quite the way that the committee was asked to do its statement of task. None has compared entirely unimmunized populations with those fully immunized for the health outcomes of concern to stakeholders.” (S-15)
- “Queries of experts who addressed the committee in open session did not point toward a body of evidence that had been overlooked but, rather, pointed toward the fact that the research conducted to date has generally not been conceived with the overall immunization schedule in mind. The available evidence is reassuring but it is also fragmented and inconclusive on many issues.” (S-16)
- “A challenge to the committee in its review of the scientific literature was uncertainty whether studies published in the scientific literature have addressed all health outcomes and safety concerns. The field needs valid and accepted metrics of the entire schedule (the “exposure”) and clearer definitions of the health outcomes linked to stakeholder concerns (the “outcomes”) in research that is sufficiently funded to ensure the collection of a large quantity of high-quality data;” (S-16)
- “The committee concluded that parents and health care professionals would benefit from more comprehensive and detailed information with which to address parental concerns about the safety of the immunization schedule; (7-2)
- “The concept of the immunization “schedule” is not well developed in the scientific literature. Most vaccine research focuses on the health outcomes associated with single immunizations or combinations of vaccines administered at a single visit. Even though each new vaccine is evaluated in the context of the overall immunization schedule that existed at the time of the review, individual elements of the schedule are not evaluated once it is adjusted to accommodate a new vaccine. Key elements of the immunization schedule – for example, the number, frequency, timing, order, and age at the time of administration of vaccines – have not been systematically examined in research studies;” (7-3)
- “The committee encountered during the review of the scientific literature...uncertainty over whether the scientific literature has addressed all health outcomes and safety concerns. The committee could not determine whether its list of health outcomes was complete or whether a more comprehensive system of surveillance might identify other outcomes of potential safety significance. In addition, the conditions of concern to some stakeholders, such as immunological, neurological and developmental problems, are illnesses and conditions for

which the etiology, in general, is not well understood. Further research on these conditions may clarify their etiologies;" (7-3)

- "The committee found that evidence from assessments of health outcomes in potentially susceptible populations of children who may have an increased risk of adverse reactions to vaccines (such as children with a family history of autoimmune disease or allergies or children born prematurely) was limited and is characterized by uncertainty about the definition of populations of interest and definitions of exposures and outcomes. Most children who experience an adverse reaction to immunization have a preexisting susceptibility. Some predispositions may be detectable prior to vaccination; others, at least with current technology and practice, are not;" (7-3)