Proposed ACCV Workgroup

Vaccinated vs Unvaccinated Epidemiological Health Outcomes Assessment Workgroup

Karen Kain, ACCV Commissioner
Presented March 3, 2022

Does the proposed workgroup fall under ACCV statutory obligations?

Workgroup Formation Process

- ACCV Charter – Subcommittees composed of members of the parent committee, may be established with the approval of the Secretary or designee to perform specific functions within the ACCV's jurisdiction. Subcommittees must report back to the ACCV.
- ACCV must - "(j) Provide the opportunity for reasonable participation by the public in advisory committee activities, subject to §102–3.140 and the agency's guidelines."
- Sister federal advisory committees - The National Vaccine Advisory Committee and Advisory Committee on Immunization Practices form workgroups/subcommittees with outside public participants under these same guidelines.

Key ACCV Functions

42 U.S.C. §§ 300aa-19(f)

Advise Secretary on Implementation of

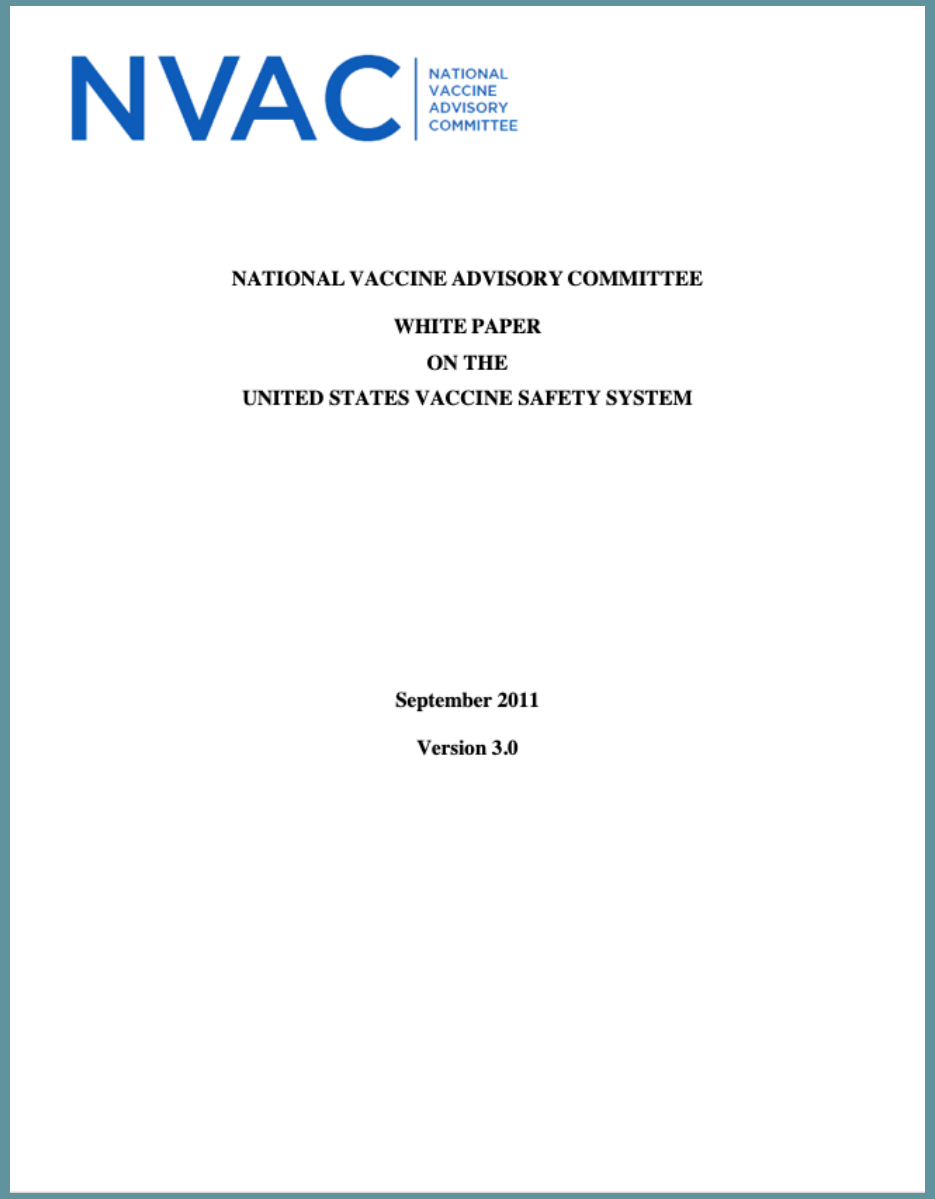
- the Vaccine Injury Compensation Program – VICP;
- the responsibility to promote the development and refining of childhood vaccines resulting in fewer and less serious adverse reactions (42 U.S.C. §§ 300aa-27).

ACCV also makes research recommendations to the Director of the National Vaccine Program.

Does the proposed workgroup fall under ACCV statutory obligations?

YES

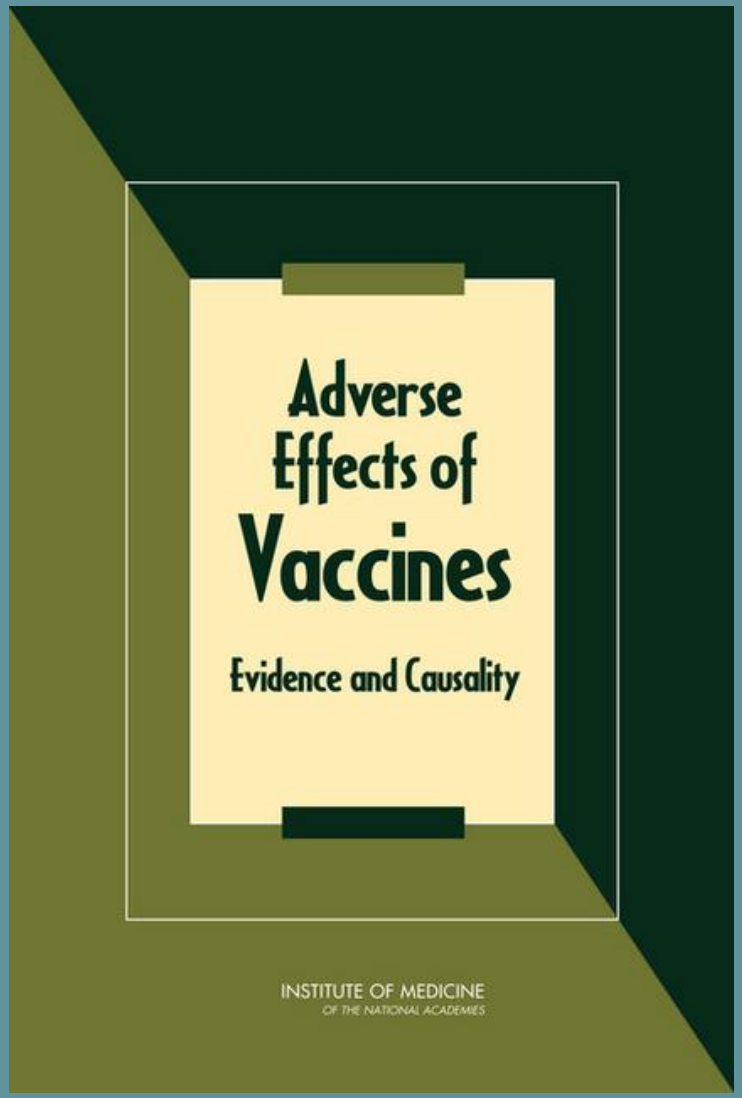
Do vaccine safety research gaps exist that require ACCV attention to better advise on implementation of VICP and the Secretary's research responsibilities?



2011 - National Vaccine Advisory Committee White Paper

Vaccine Safety Research Gaps Acknowledged

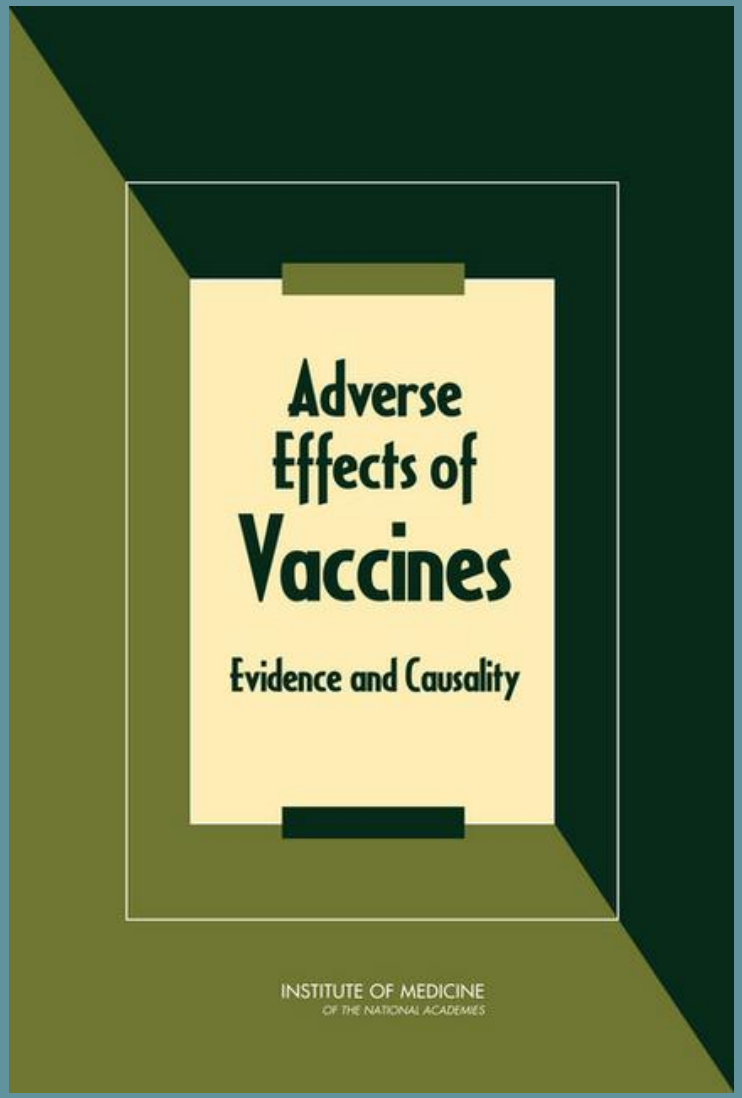
- IOM was initially charged by Congress in 1986 Act to review the evidence for causality assessments.
- NVAC reported that the IOM completed 11 reviews and that all were *"hindered by an inadequate understanding of potential biologic effects elicited by immunization."*
- ***"Because 60% of the IOM causality assessments have found "inadequate evidence to make a determination, further research into this area may lead to more definitive causality assessments."***



National Academies of Science

Institute of Medicine (IOM) definition of "inadequate" evidence = lack of quality research and/or absence of quality research.

"The evidence is not reasonably convincing either in support of or against causality; ***evidence that is sparse, conflicting, of weak quality,*** *or merely suggestive—whether toward or away from causality—falls into this category.*[8] ***Where there is no evidence meeting the standards described above****, the committee also uses this causal conclusion."*



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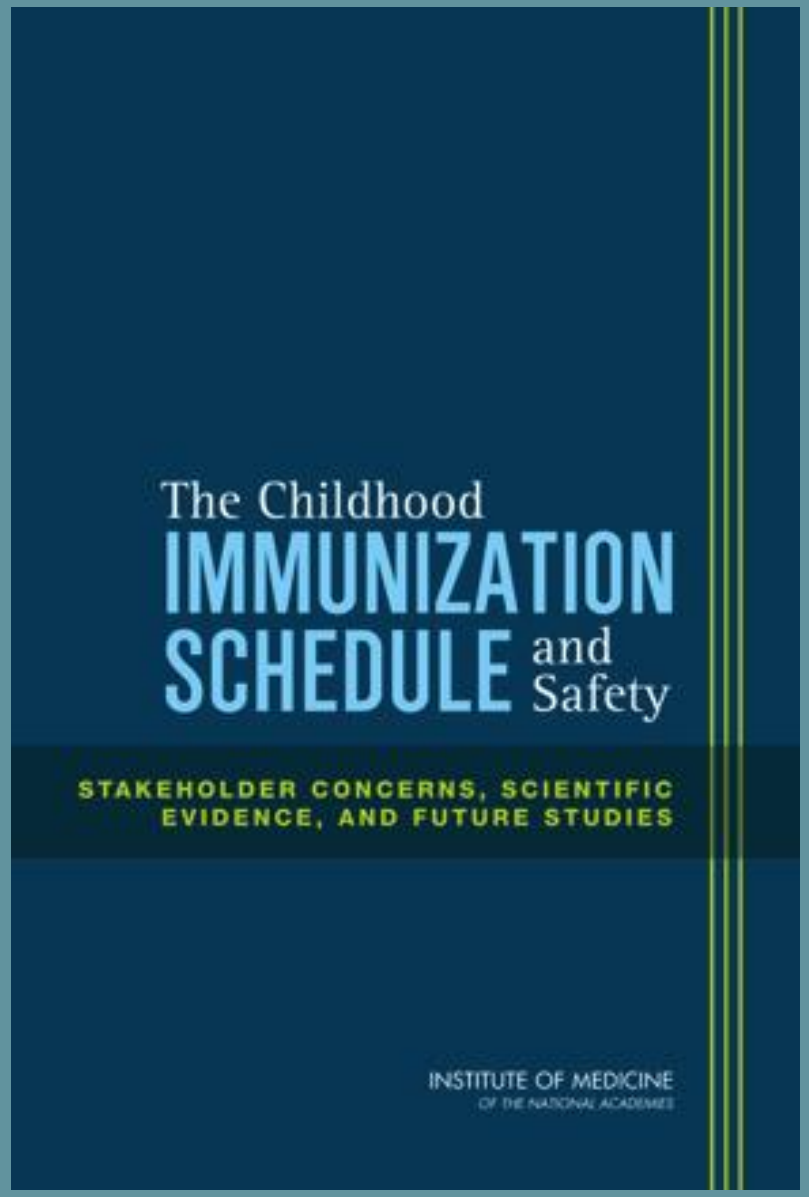
2012 - To date, the largest IOM report on adverse effects of vaccines published.

- Reviewed research for 158 of the most commonly reported vaccine adverse events for 8 routine childhood vaccines;
- For 85%, or 135 events, the IOM was again prevented from making causality statement due to “inadequate” evidence.
- Research gaps impact over 100 serious brain and immune system problems.



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2013 - Public requested IOM to review the scientific studies comparing health outcomes among fully vaccinated, partially vaccinated, and unvaccinated children and found:

- *"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."*
- ***"None [no study] has compared entirely unimmunized populations with those fully immunized for the health outcomes of concern to stakeholders."***
- ***"VSD is currently the best available system for studying the safety of the immunization schedule in the United States."***

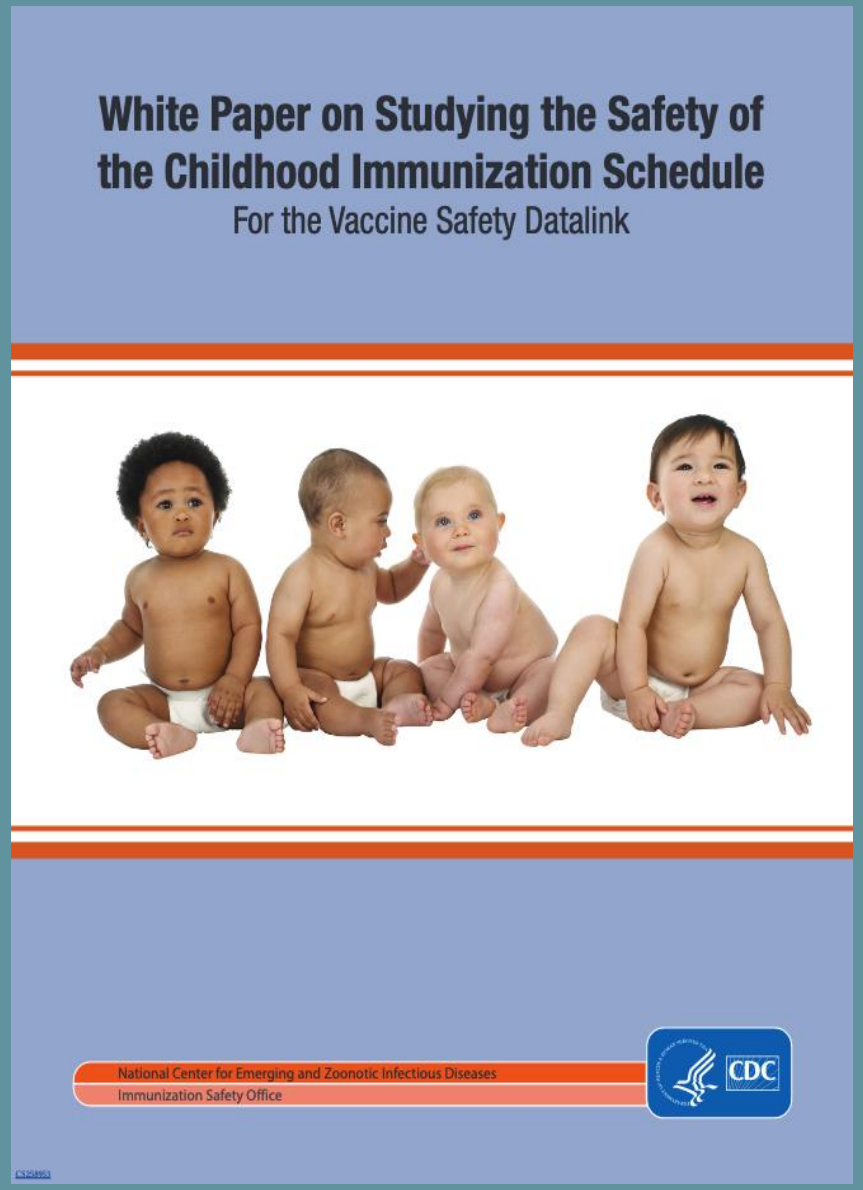
ACCV Guiding Principles - Research

- Adopted 2006 for the purpose of making recommendations for additions to the federal vaccine injury table (VIT);
- Acknowledged role of the Institute of Medicine (National Academy of Medicine - NAM) in providing causality statements to the ACCV for VIT change recommendations to the Secretary;
- ACCV is to assess the strength of other research sources, potential bias, etc. and request assistance from HRSA and other program members to conduct assessment;
- Guidelines include many research types and sources - including VSD data;
- When considering changes to the VIT, ACCV should tend toward adding or retaining the proposed injuries.

Do vaccine safety research gaps exist that require ACCV attention to better advise on implementation of VICP and the Secretary's research responsibilities?

YES

Is high quality data comparing the health outcomes of children vaccinated according to the federally recommended schedule to health outcomes of unvaccinated children available?



Centers for Disease Control

2016 - Use of VSD to study the safety of the entire childhood immunization schedule.

- Confirmed feasibility of VSD to study the safety of the recommended childhood immunization schedule as a whole;
- Confirmed IOM statement - ***"VSD is currently the best available system for studying the safety of the immunization schedule in the United States."***
- The VSD has been previously used to identify the undervaccinated, inclusive of zero vaccinated, for research purposes;
- Outlined a 4 stage approach with 20 prioritized health outcomes in response to IOM recommendations;

Is high quality data comparing the health outcomes of children vaccinated according to the federally recommended schedule to health outcomes of unvaccinated children available?

YES

Has this study been conducted using VSD data and replicated by independent external researchers?

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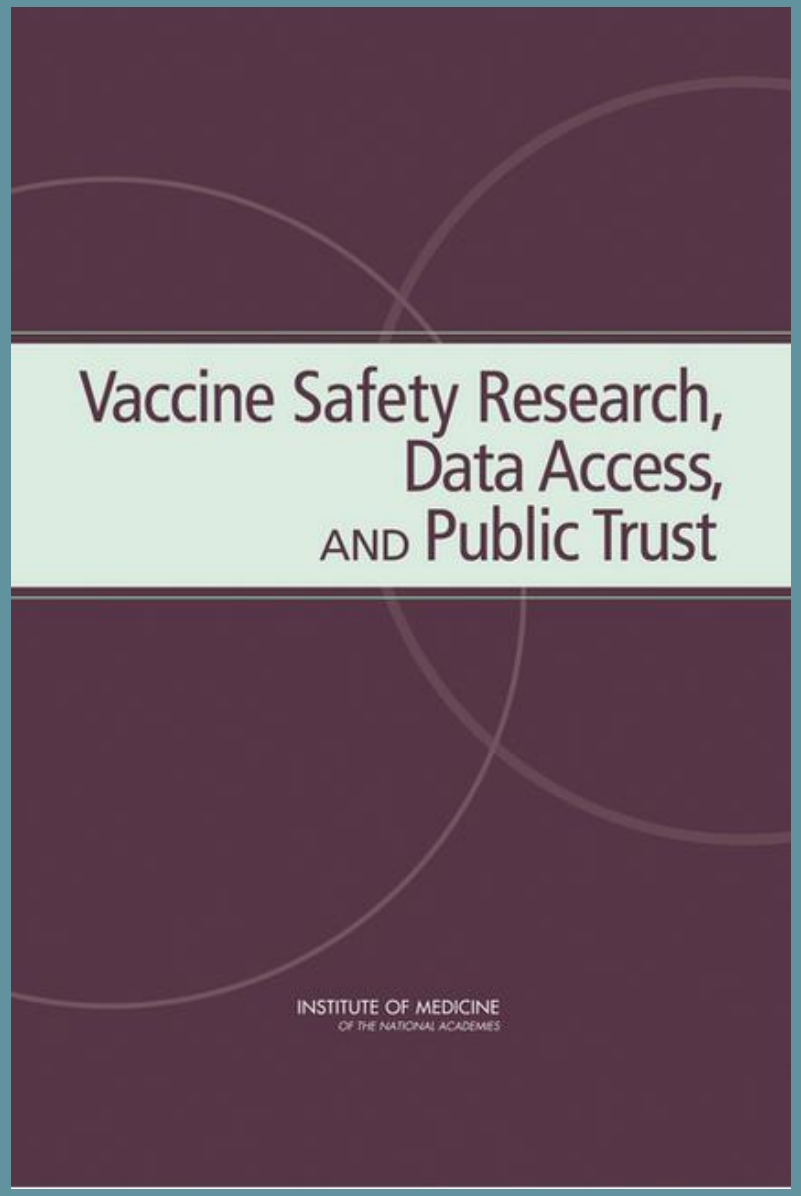
1991 IOM – Replication, a gold standard

"The scientific process depends in no small part on the ability of independent observers to repeat and confirm one another's findings. In this context, replication is not only legitimate but essential, providing "proof positive" of otherwise uncertain research findings and lending confidence to conclusions drawn from them. Replication also serves to overthrow false hypotheses: if an experiment is repeated and does not confirm the original results, the alternative hypothesis must be seriously considered."



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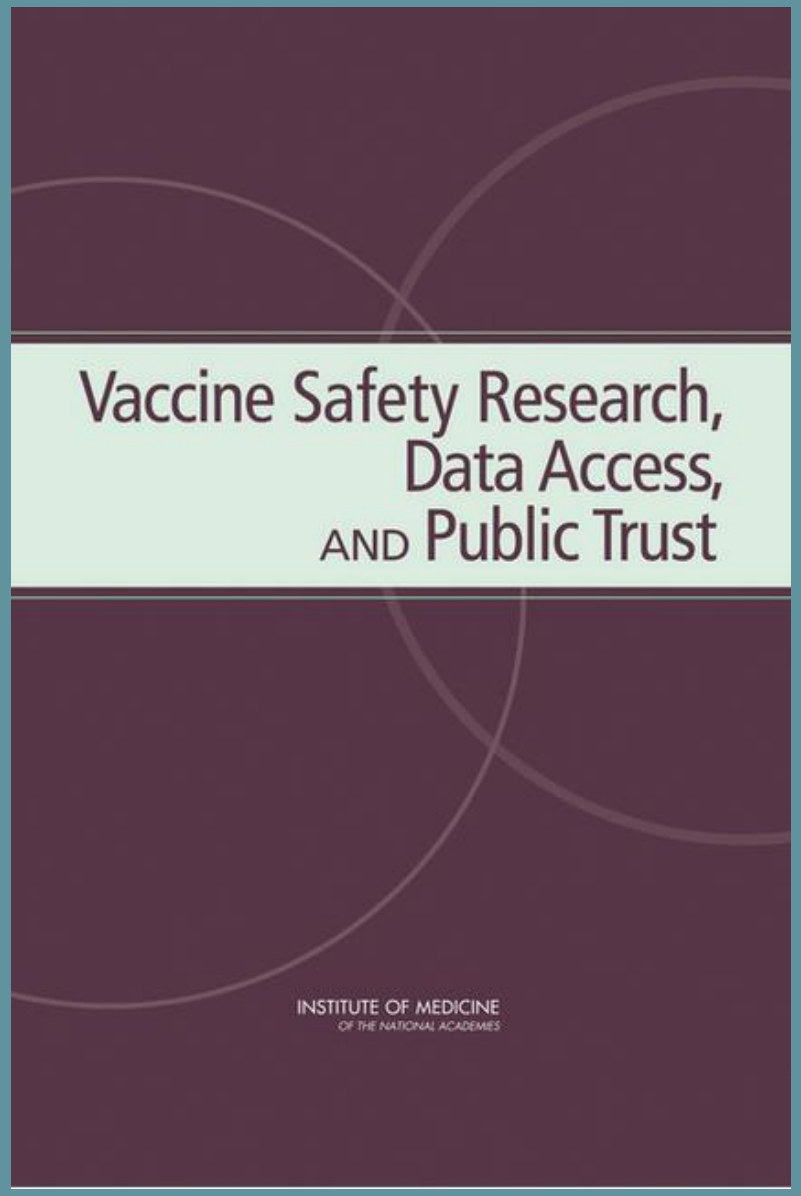
2005 – Review VSD design and assess compliance of VSD Data Sharing Program with data sharing standards of practice:

Overarching Principles

- **Independence** – Minimize biases and conflicts of interest;
- **Transparency – Development of processes, practices and policies are clear and in spirit of openness;**
- **Fairness – All processes, practices and policies are implemented** fairly;
- **Protection** – Design and implementation protects individually identifiable information.



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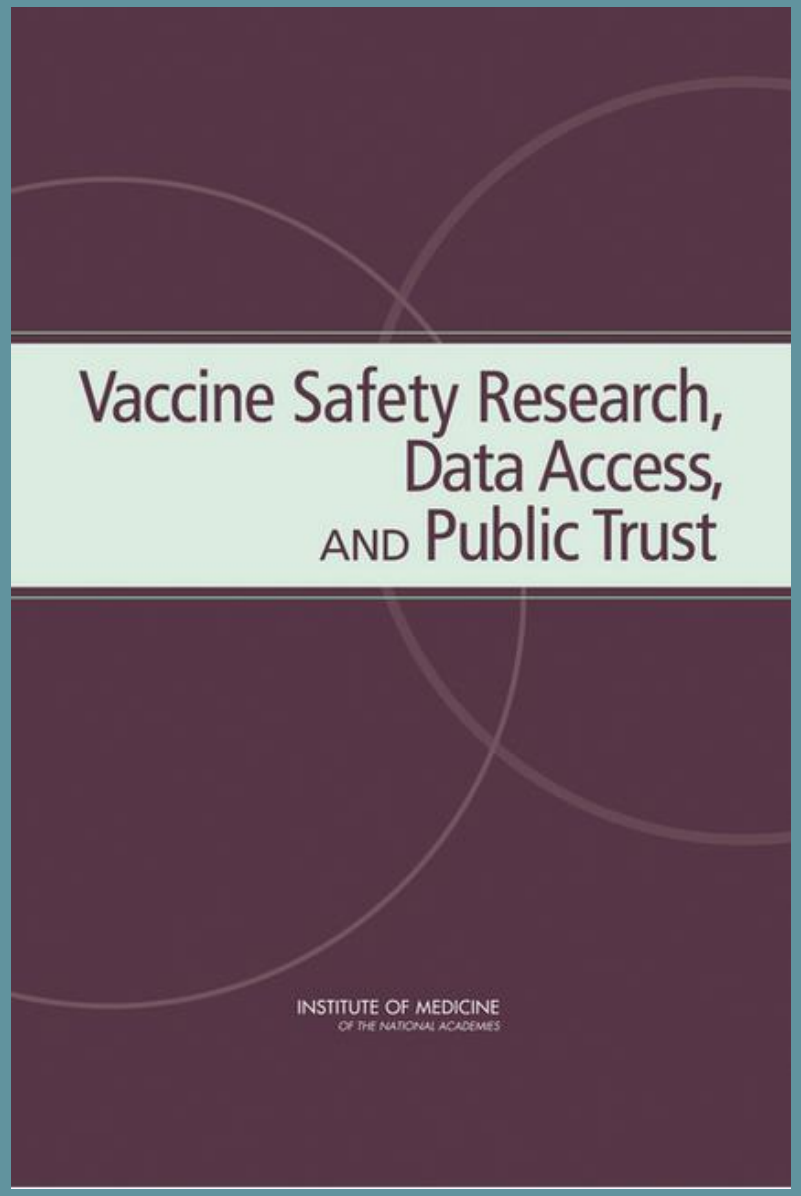
IOM found legitimate reasons for public concern about VSD data-sharing program and transparency. IOM recommended federal agencies seek legal advice on applicability of federal laws to VSD data and the public's access to the data.

- **Shelby Amendment (1999)** – requires public access to *"research data relating to published research findings produced under an award that were used by the Federal Government in developing an agency action that has the force and effect of law"*
- **Information Quality Act (IQA – 2000)** – Guidelines to ensure the objectivity, utility and integrity of information (including statistical information) disseminated to the public by federal agencies.



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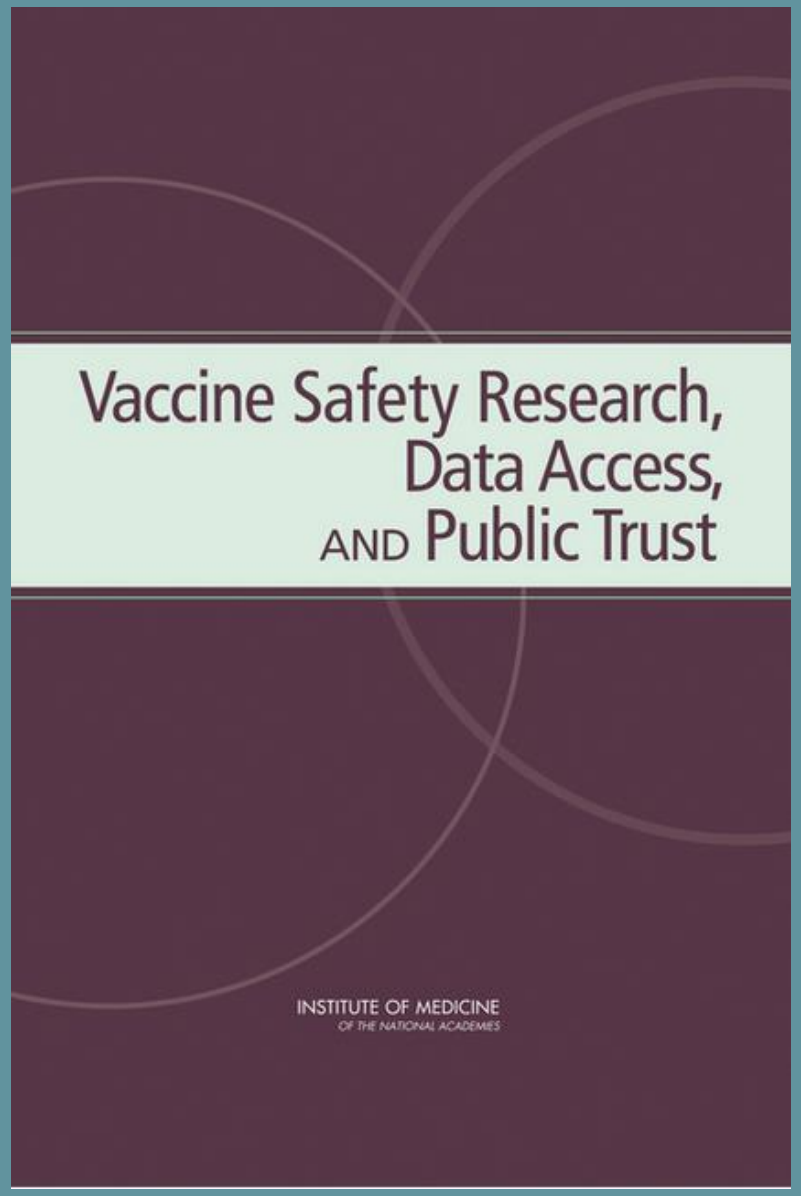
IOM found that the VSD data-sharing program did not align with traditional data-sharing and recommended formation of independent review committee with minimal biases and conflicts to address:

- Review independent external researchers' proposals to use VSD data;
- Review internal research proposals and provide oversight of research protocols for VSD studies; and
- Provide advice on making preliminary VSD findings public.



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Additional recommendations:

- Streamlining of IRB process and clarification of data limitations;
- Allow independent researchers access to datasets that allow for formulation of alternative hypotheses and analyses;
- Provide a list of recommended competencies to assist independent external researchers in VSD data analysis.

Has this study been conducted using VSD data and replicated by independent external researchers?

UNKNOWN

Summary

- The establishment of a workgroup to assess studies of health outcomes in a vaccinated vs unvaccinated study and/or make research recommendations that such a study be conducted are well within the ACCV's statutory functions and responsibilities;
- IOM has stated such a study has not been conducted;
- Utilization of the VSD to determine the safety of the childhood schedule as whole has been recommended by the IOM;
- CDC confirmed the IOM's findings that the VSD was the best resource to study the safety of the childhood schedule and that such a study was feasible;
- IOM has transparency, and independent replication of findings are necessary to the scientific process, and the maintaining of the publics trust and recommended independent external researchers have access to core VSD data to form alternate hypotheses and analyses;

Summary

- It is unknown what legal advice has been obtained by federal agencies on the applicability of the Shelby Amendment and Information Quality Act relating to the VSD and what improvements have been to the VSD data-sharing program;
- It is unknown what access to date independent external researchers have been given in context with IOM data sharing recommendations;

Closing thought…

"Trust can be enhanced only if the public has confidence in the independence and fairness of the decision-making process for VSD research priorities and approval of VSD data sharing proposals."

Institute of Medicine - 2005
Vaccine Safety Research, Data Access, and Public Trust

Proposed Workgroup Charge

Vaccinated vs Unvaccinated Epidemiological Health Outcomes Assessment Workgroup

- Assess epidemiological studies conducted since the IOM"s 2013 report on the safety of the childhood schedule that compare the short and long-term health outcomes of vaccinated and unvaccinated children, inclusive of the VSD;
- Report findings and make recommendations for the ACCV's consideration.

Discussion & Questions