The Development of Federal Vaccine Recommendations:
An Examination of The Advisory Committee on Immunization Practices (ACIP)

by

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# Table of Contents

**Introduction** .................................................................................................................. 5

**Chapter 1: Structure of the ACIP** .................................................................................. 18  
  A Brief Overview of the ACIP ......................................................................................... 19  
  Harmonization .................................................................................................................. 21  
  Post-Licensure Safety Surveillance .................................................................................. 26  
  Economic Considerations ............................................................................................... 31  
  GRADE Approach ........................................................................................................... 35

**Chapter 2: Conflicts of Interest and ACIP Membership** .................................................. 41  
  Membership Process ........................................................................................................ 43  
  A Case Study: The Committee on Government Reform .................................................. 51

**Chapter 3: Implications of the ACIP’s Recommendations** ................................................. 60  
  Federal versus State Role in Immunization Activities ..................................................... 63  
  Economic Implications of ACIP Recommendations ...................................................... 71

**Chapter 4: A Case Study of the HPV Vaccine Recommendation** .................................... 85  
  Setting the Scene ............................................................................................................ 91  
  The ACIP’s Initial Recommendation .............................................................................. 99  
  The Early Years: Merck’s Mistake ................................................................................. 110  
  The Role of Social Factors ............................................................................................ 119

**Conclusion** .................................................................................................................... 132

**Appendices** ................................................................................................................... 138

**Bibliography** .................................................................................................................. 147
“History shows us clearly that science does not provide certainty. It does not provide proof. It only provides the consensus of experts, based on the organized accumulation and scrutiny of evidence.”

I stood awkwardly outside the doctor’s office waiting for the nurse to tell me that it was OK to go in. I smoothed down my slacks and fiddled with my blouse to make sure I wasn’t showing signs of sweat from my morning commute in the hot August air. Once I received the green light from the nurse, I entered the office. The scene was usually the same: a patient, somewhere between the ages of the nine to eighteen, sitting on the bench, their parent or guardian anxiously hovering to their side. Sometimes there were also siblings in the room, young children with boundless energy wreaking havoc in the office.

Timing was everything in my short visits. I had to catch the patient in the brief moment between the nurse’s patient workup (standard blood work, height, weight, etc.), and the physician’s check-in. I introduced myself and explained my purpose: “I am here representing the Vaccine Education Center at the Children’s Hospital of Philadelphia. Would you be interested in participating in a brief educational study about the Human Papillomavirus Vaccine?”

Many parents were caught off guard, requiring assurance that no, they would not be required to give their child the vaccine if they participated in the study. Some parents refused to participate. Of the one’s that agreed to participate, most would reluctantly shrug, or grunt a perfunctory word of consent. I would then pull out an iPad and show them a short informational video about the vaccine in which a middle-aged adult with a slow cadence and
sympathetic demeanor, described the Human Papillomavirus (HPV) and explained the vaccine's risks and benefits.

HPV is the most common sexually transmitted infection (STI) in the United States. Persistent HPV infection can cause cervical cancer, anal cancer, oropharyngeal cancers, or genital warts. Today, it is recommended that the HPV vaccine be routinely administered to all children at the age of eleven or twelve before teens become sexually active. The vaccine can only act as a prophylactic against HPV; it cannot treat HPV strains that have already been contracted.

The actor on the screen gently explained all of this to parents watching the video. When it was finished I then asked the parents a series of questions about whether they intended to get their children vaccinated against HPV. The reactions were varied. Some parents were receptive, expressing interest in the vaccine and appreciation for the information provided in the video. Others were frustrated that I had wasted their time. Some believed the vaccine was dangerous and the video did nothing to alleviate their fears. Others were steadfast in their belief that their children did not need the vaccine because they were not yet sexually active. Others gave no explanation for their resistance to the vaccine.

When I left at the end of the day I could not stop thinking about these parent's responses. The “educational video” was supposed to inform parents and give them the knowledge to make responsible choices about their children's health but it clearly wasn’t enough, as many parents seemed unimpressed by the information presented. The video tried to persuade parents by appealing to the
authority of science, using *scientific evidence* as a weapon to combat the
hesitancy, confusion and misinformation surrounding vaccination.

Public health officials have relied on their scientific authority as the
reason the public should trust vaccine recommendations. However, the sterility
of a peer-reviewed, well-cited journal article will never be as poignant as the
emotional appeal of a fear-mongering tale, even if it is not based in fact.

Though once universally exalted, the public perception of vaccination has
shifted radically to be more hostile than celebratory. This negative trajectory has
been catalyzed by fraudulent scientists, egotistical celebrities, and concerned
parents airing their grievances and pontificating about the dangers of
vaccination. The rise of online journalism and blogging has allowed anyone to
front as a public health expert. Parents who go online to research a vaccine-
related question will find themselves inundated with horror stories about the
dangers of vaccines, heart-wrenching tales of adverse events related to vaccines,
and stories that inevitably plant a seed of doubt. The Internet is a Pandora’s box
of anti-vaccine rhetoric, traumatic first-hand accounts, and blogs purporting to
be authoritative sources of information about the dangers of vaccinations.

In part, the skepticism about vaccinations results from public mistrust of
the pharmaceutical industry and the perception that vaccines have been
developed and promoted only to benefit big pharma. This skepticism is not
unfounded as it is certainly true that the industry has not always put the
interests of the public ahead of its own.
However, it is not just the pharmaceutical industry encouraging us; virtually all of the scientific and medical communities have been speaking in a unified voice and beseeching us to get vaccinated. While the pharmaceutical industry is primarily responsible for research and development of vaccines, the guidance to get vaccinated is coming from all sides of the healthcare industry, including providers, public health officials, public and private researchers, and government employees. This advice has become the consensus of the medical and scientific communities. But citing this consensus has not always proven to be an effective tool for communicating to parents why they should get their children vaccinated. ‘Consensus’ is an amorphous entity; what does that really mean? Who are these public health and medical experts that are making the decisions for our children, and how do they go about making these decisions?

These were the questions that ultimately led me to this thesis. It seemed to me that the only way to reassure parents that they should vaccinate their children was by articulating the inner workings of this system. This was how I arrived at my examination of the Advisory Committee on Immunization Practices (ACIP).

The ACIP is a group of medical and public health officials who are responsible for developing recommendations on the appropriate use of vaccines to control infectious disease in the US. The committee was established in 1964 by the Surgeon General of the US Public Health Service, charged with the job of providing expert external advice and guidance to the Director of the Center for
Disease Control and Prevention (CDC) and the Secretary of the United States Department of Health and Human Services (DHHS).  

I looked everywhere for an in-depth summary of the ACIP that would explain how its vaccine recommendations were produced but I could not find one. Most of the information about the committee was on the CDC’s website, limited mostly to the committee’s charter, its structure, and its meeting minutes, which are all available online. There were a few journal articles. Overall, there was not a substantial body of literature about the committee.

And so I set off on my journey to produce a comprehensive investigation of the ACIP. This started as purely a technical summary of the committee: its structure, mechanism, and function. However, this evolved over time to become a critical analysis of the committee, an examination of its strengths and weaknesses, and an analysis of the historical events that shaped it.

Conceptual Framework: The “ACIP Home” and The Biopolitical Paradigm

Before I begin unpacking the black box of the ACIP, I would like to present two conceptual lenses for understanding my thesis argument. The first is a metaphor; the second, a sociological framework.

Visualize the ACIP as a new house. It is advertised as a high quality, sturdy home, built from four foundational materials. For the sake of this metaphor, let’s call these materials (1) wood, (2) steel, (3) concrete, and (4) stone.

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After centuries of trial and error, it has been demonstrated that these are the strongest materials currently available for building homes, though better materials may appear someday as a result of further research and innovation.

In the case of the “ACIP home”, the four foundational materials are the ethical tenets of the committee: (1) evidence-based science, (2) transparency, (3) nonpartisanship, and (4) evaluation of risks versus benefits. These tenets are foundational to every element of the committee, from the people that constitute it to the way that evidence is produced and presented to the committee. The tenets are not arbitrary. They have been shown to be the strongest available tools for producing recommendations based on our body of scientific/medical knowledge.

Figure 1. Visualizing the metaphor: The “ACIP House: For Sale”

While built to be strong, our metaphorical home is also built to be attractive and functional in order to appeal to many potential buyers. However,
not everyone has the same taste nor does everyone have the same expectations for what a home will contain, so many people may still not like this house.

The architectural style of our home can be equated to the ACIP’s structure and presentation: its procedures for selecting members, mechanisms for producing harmonized recommendations with other professional organizations, formulas for standardizing presentation and evaluation of data, etc. The ACIP is specifically structured to promote public confidence in its recommendations and to satisfy the expectations of as many stakeholders as possible. Going back to our metaphor, the ACIP's structure and presentation are akin to stylistic and construction choices that are made to convince people to purchase the home.

There are many reasons that potential homebuyers may not like this home. This might be addressed by remodeling one or more of the home's features without compromising its overall integrity. However, if potential buyers simply do not believe in the value of the home’s foundational materials, it will be hard to convince the critic to purchase it.

Critics of the ACIP are those individuals who are skeptical of vaccine recommendations. This could include members of the general public or even state or local government officials. In some cases, their concerns can be addressed by minor changes to the committee, such as the addition of new procedures or regulations. They could also perhaps be addressed by a straightforward explanation of the evidence that the committee’s structure is the highest standard available. However, when people do not believe in the ethical integrity of the committee or that the decision-making procedures are based on
lessons from centuries of policy-making and the best research and safety procedures in current existence, it is very challenging to convince them to accept the committee’s recommendations. In other words, when there is a lack of trust in ACIP’s fundamental tenets, the recommendations will face cynicism and disbelief.

The critics of our home are not entirely irrational. Even given all of the work and consideration that went into the construction of this home, no structure is perfect. It will not exist in a vacuum. It will inevitably be influenced by external factors. To build a strong home, one must consider all possible factors to ensure that it will not crumble when exposed to external forces. It should be continually examined and updated if it is to remain strong.

Similarly, there are external factors acting on the ACIP. These include the influence of the pharmaceutical industry, external biases, social factors, policy changes, and social movements. These external considerations have played a fundamental role in shaping the ACIP. However, in some cases the committee may not have mechanisms in place for coping with an external factor and may demonstrate a weakness or limitation in its structure. Just as no home exists in a vacuum, the ACIP also will never be immune (no pun intended) to external factors. Although at this moment the ACIP is considered to be the strongest system for producing vaccine recommendations, this could change over time as we gain more policy experience and greater scientific understanding. Even though the current structure works well for the ACIP now, it may no longer be
considered adequate in the future and should be modified accordingly to ensure the committee remains strong.

It is for this reason that we must continue to critically evaluate the ACIP. Although the committee is built on high quality evidence, this does not mean that it cannot be improved with new understanding. Also, the consensus of the field may shift over time (due to, for example, social dynamics and changing priorities of the medical and political field) and make it so the committee’s structure may no longer be the most effective way to generate public confidence in its recommendations. Or to return to our metaphor, as styles change, it gets harder to convince people to buy an out of date house, no matter how sturdy or well-built.

Stepping back from our house metaphor for a moment, I would like to present a second conceptual framework for understanding the ACIP. I would like to view it through Steven Epstein’s notion of the “biopolitical paradigm.”

Epstein builds upon Peter Hall’s concept of the ‘policy paradigm’ and Michel Foucault’s ‘biopolitics.’ The term biopolitical paradigm defines the framework of the field of scientific policy-making, which integrates the disciplines of biomedicine and state policy. It is challenging to define the boundaries of the biopolitical paradigm; it is more than simply a framework of guidelines, but rather it encompasses the “ideas, standards, formal procedures, and unarticulated understandings” that determine how health, medicine, and the

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3 Stephanie Thomas, "Advisory Committee on Immunization Practices Application for Membership," Centers for Disease Control and Prevention, Atlanta, Georgia, 2016, 6.
body are integrated into state policy. The paradigm encompasses the ideas and standards that guide state policy and biomedicine, our understanding of science and the human body, the language that we use in both the scientific and political spheres, the tools that we have available to use for investigation, and the dynamic relationship between policy and science. The scope of the biopolitical paradigm is amorphous, socially determined, and highly contextual, constantly adapting with continual scientific investigation and political experience.

The biopolitical paradigm can be situated within our house metaphor, but it is not featured in our image of the home in Figure 1; it is much broader than that. The biopolitical paradigm could be considered the neighborhood, the standards of the architectural community, the real-estate agents who are selling the home, and the expectations of the general public; all of the abstract entities, ideas, and sources of knowledge that have shaped our understanding of what constitutes a strong home.

With these two conceptual frameworks I would like to articulate a framework for understanding the ACIP. Together, they help us to understand the relationship between the foundational tenets, structure, and public perception of the committee, as well the external factors at play and how the committee was born out of the integration of two disciplines to incorporate priorities and concepts from both.

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With these frameworks in mind, the question I would like to answer is: How does the ACIP make its recommendations as strong as possible, and what are the limitations of this system?

A Preview Into the Chapters Ahead

In coming chapters, I will explore how the ACIP has developed from these four principle tenets [(1) evidence-based science, (2) transparency, (3) nonpartisanship, and (4) evaluation of risks versus benefits]. I will historically situate all of these structures or mechanisms by examining the events, movements, or general social/political atmospheres that catalyzed their development. One of my fundamental goals with this thesis is to map a topography of ACIP’s evolution over time so as to understand how these tenets have become the focal point of the committee’s process. I will also demonstrate how external factors have shaped the committee by changing its priorities, expanding or limiting the parameters it can work within, and defining the scope of its influence. I hope that through a critical examination of these factors I will be able to (1) demonstrate the strength of the committee’s recommendations based on our current scientific capacities and the more abstract public expectations of the committee, and (2) the limitations of the committee and the issues that it struggles to address when remaining strictly within these tenets.

In the first chapter, I will be examining several structural components of the ACIP, specifically the process of harmonization of recommendations with other professional organizations, the safety surveillance of vaccines, the
presentation of economic evaluations, and the current framework for evaluating quality of evidence and strength of recommendations. I would like to demonstrate how all of these structural components have changed or been implemented over time to strengthen the committee’s recommendation process.

In the second chapter, I will be examining the mechanisms in place to control for conflicts of interest and bias amongst the ACIP’s members. I would like to consider the role of scientific expertise and deconstruct the notion of the “unbiased expert.” I will use a case study of a specific moment in history when the public questioned the altruism and honesty of the committee’s members.

In the third chapter, I will consider the implications of the ACIP’s recommendations. While this may seem to diverge slightly from my abstraction of the structure and strategy of the ACIP, I believe that a chapter of this nature is essential for properly understanding the committee. This chapter will include a brief history of how the state and federal governments have compartmentalized their roles in terms of immunization activities in the United States. This chapter will also include an explanation of the financial implications of the ACIP’s regulations. Together I hope to illuminate the ramifications of the ACIP’s recommendations and show how they have been shaped by the unique priorities of the United States’ political construction.

The final chapter of this book will use a case study of the HPV vaccine to examine the ACIP’s structure in the face of external factors, including anti-vaccine rhetoric, external political events, and social dynamics that complicate its recommendation process. Specifically I would like to contextualize the
complications, shortcomings, and strengths of the ACIP’s recommendation process when dealing with external factors within its limited framework.
Chapter 1
Structure of the ACIP: Contextualizing the Canons of the Committee

Vaccination is a central facet of the United States’ public health infrastructure and is integral to the control of infectious disease in the general population. Vaccines have demonstrated their ability to save innumerable lives and even to completely eradicate infectious diseases. However, vaccines are also, one of, if not the most controversial health interventions of all time.

Vaccines are unlike most other health interventions. There are several main qualities that set vaccines apart. First and foremost, they are unique because they are the only health interventions to be mandated for school attendance throughout the US. Second, instead of treating sick patients to cure disease, vaccines are provided to healthy people to prevent the incidence of disease altogether. Third, vaccines are a community-based health intervention. In order to maximize the benefits of a vaccination campaign the vaccine must be administered to a large enough segment of the population to confer *herd immunity*. This will allow the entire community to feel the protection of the vaccine even if they have not received it.

While the implementation of school mandates for vaccination, the administration of vaccines to healthy populations, and herd immunity, are what make vaccines such an effective public health interventions, these factors have also augmented the public’s skepticism of vaccines. Therefore, the ACIP works

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hard to promote public confidence in its recommendations by grounding them in the highest quality evidence available and by structuring itself so as to facilitate nonpartisanship and transparency throughout its process.

The ACIP has adapted over time to implement structural mechanisms that fulfill current standards of the field, and address vaccine-related issues as they arise. Specific components of the committee that have emerged include (1) harmonization of vaccine recommendation with other professional organizations, (2) post-licensure safety surveillance, (3) standardized guidelines for presentation of economic consideration, and (4) the GRADE approach.

The evolution of the committee can be explicitly mapped onto the events that have transpired since its inception. Examining the events, changing priorities of the fields, and public attitudes that have impacted the formation of the committee illuminate why these structures have emerged. Together, they also demonstrate how the committee has adapted over time to promote public trust in vaccines.

A Brief Overview of the ACIP

Before jumping into the specific structural mechanisms of the ACIP, it is important to provide a broad overview of the committee: its structure, its mechanisms for producing recommendations, and its role.

The ACIP is a group of scientific, medical, and public health experts responsible for advising the US government on the most appropriate use of vaccines and related agents to control vaccine-preventable diseases. The
committee is composed of fifteen voting members from a variety of clinical or scientific specialties and public health backgrounds, eight *ex officio* members from government agencies, and twenty-six liaison representatives from health-related organizations. The committee meets three times a year at the Centers For Disease Control and Prevention (CDC) headquarters in Atlanta, Georgia.⁶

The ACIP is responsible for producing recommendations on the proper populations or specific circumstances under which a vaccine should be used; the route, dose, and frequency in which a vaccine should be delivered; and potential contraindications or adverse events related to vaccines. The committee releases annual recommended immunization schedules for infants, children, adolescents and adults that address all of these factors (See Appendix 1 and 2).⁷,⁸

ACIP work groups (WGs) are formed as a resource for collecting, analyzing, and presenting data to the committee on particular topics (i.e. specific vaccines or vaccine-related topics). There are currently four permanent ACIP WGs: the Adult Immunization Schedule, Influenza, General Recommendations, and Harmonized Schedule for Children and Adolescents. There are also temporary WGs that arise for each new vaccine or vaccine-related issue addressed by the committee. WGs must include at least two voting members of the ACIP and an expert from the CDC.⁹

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⁶ Smith, "The Structure, Role, and Procedures of the U.S. Advisory Committee on Immunization Practices (ACIP)." A68.
⁷ Ibid., A71.
⁸ "Birth 18 Years and 'Catch Up' Immunization Schedules" CDC, last updated March, 29, 2016.
WG's will collect data on disease epidemiology (including morbidity, mortality, and specific risk groups), vaccine efficacy and safety, potential programmatic barriers, and economic data and then are responsible for developing options for policy recommendations that can be presented to the ACIP voting members. Most recommendations take years of discussion before they are ever put to a vote and in that time the WG will continue to collect new data to present to the committee. After several years of extensive scrutiny from the committee, a recommendation is developed and voted on by the ACIP voting members. There must be a majority vote in order for a recommendation to be approved by the committee.\textsuperscript{10}

Once recommendations have been voted-in by the ACIP, they are forwarded to the Director of the CDC, who has the authority to adopt immunization policy on behalf of the Department of Health and Human Services (DHHS). Since the ACIP is purely an advisory body to the federal government, the CDC Director or the Secretary of DHHS has the prerogative to modify or reject the committee's recommendations. Once the recommendations have been finalized, they are published in the CDC's \textit{Morbidity and Mortality Weekly Report}, at which point they are considered official CDC recommendations.\textsuperscript{11}

\textbf{Harmonization: Promoting a Unified Voice}

Prior to the ACIP there were no formalized mechanisms in place for providing guidance on the proper use of immunizations in the US. Immunization

\textsuperscript{10} Ibid.
\textsuperscript{11} Ibid., A70.
was dealt with by each locality at its own discretion, with no central source of
guidance on the most effective and proper way of using vaccines. There was no
national immunization program nor was there a formalized committee for
providing advice on appropriate use of vaccines.\textsuperscript{15}

Before the ACIP recommendations for the use of vaccines were made by
professional societies such as the American Academy of Pediatrics (AAP), and
the American Public Health Association (APHA), or by \textit{ad hoc} advisory groups
convened by the federal government to address individual issues such as they
arose.\textsuperscript{16} The AAP was particularly notable for spearheading the formalization of
the recommendation process—in 1936 it established the Committee on
Immunization Procedures and two years later published its first report titled,
\textit{Report of the Committee on Immunization Procedures of the American Academy of
Pediatrics}, a provider's handbook detailing the proper prevention techniques for
pediatricians in the control of infectious disease.\textsuperscript{17}

As the frequency and complexity of vaccine-related issues increased and
the number of vaccines on the market rose, it was determined that these
disparate mechanisms and \textit{ad hoc} committees were no longer sustainable, and
another strategy had to be developed.\textsuperscript{18} Thus the United States Surgeon General
formed the Advisory Committee on Immunization Practices (ACIP) in the spring

\begin{footnotesize}
\begin{enumerate}
\item[	extsuperscript{15}] J. C. Smith, D. E. Snider, and L. K. Pickering, "Immunization Policy Development in the United
States: The Role of the Advisory Committee on Immunization Practices," \textit{Ann Intern Med} 150, no. 1
\item[	extsuperscript{16}] Ibid.
\item[	extsuperscript{17}] L. K. Pickering, G. Peter, and S. T. Shulman, "The Red Book through the Ages," \textit{Pediatrics} 132,
no. 5 (2013): 900.
\item[	extsuperscript{18}] Smith, Snider, Pickering, "'Immunization Policy Development in the United States: The Role of
the Advisory Committee on Immunization Practices," 408.
\end{enumerate}
\end{footnotesize}
of 1964, charged with the mission of providing informed, evidence-based, and consistent advice about how to most effectively implement immunizations for the control of infectious disease. Dr. James L. Goddard, the chief of the CDC at the time, chaired the committee.

Even after the creation of the ACIP, the AAP was still producing independent vaccine recommendations. Initially, the ACIP and AAP had different target audiences; the ACIP focused on public health departments and the AAP focused on physicians. Informal efforts for coordination were achieved by having a liaison representative from each group sit on both committees, but these efforts were minimal. At first, these disparate recommendations did not seem to present an issue, but it was not soon before the inconsistencies began to cause problems. Ultimately, it was the recommendation of the second dose of the measles vaccine, which catalyzed the decision to harmonize the committee's immunization recommendations.

At first, evidence seemed to suggest the complete success of the one-dose measles immunization program. Within five years of the development of the vaccine in 1963, the incidence of measles had fallen to 5% of the pre-vaccine levels. The option of delivering a second dose of the vaccine was considered but

19 Ibid.
22 Walton, Orenstein, Pickering," The History of the United States Advisory Committee on Immunization Practices (ACIP)," 408.
ultimately deemed extraneous because 95 to 98% of children were demonstrating immunity after a single dose.\textsuperscript{23,24}

However, much to the dismay of public health officials, there were several major measles outbreaks in the 1970s and 80s that demonstrated flaws in the measles vaccination campaign.\textsuperscript{25} These outbreaks prompted a rapid federal response, including President Carter’s 1977 National Childhood Immunization Initiative (CII), which aimed to increase coverage rates, implement legislative mandates, and allocate funding for measles surveillance.\textsuperscript{26} CDC epidemiologists launched an investigation into the source of outbreaks and identified two major population which appeared to be the source: the first were unvaccinated children that had not yet entered school, the second were school-aged children who had been vaccinated but had not sufficiently launched an immune response after the single dose of the measles vaccine.\textsuperscript{27}

Based on this evidence, both the ACIP and AAP updated their measles vaccination recommendation to incorporate a second dose of the vaccine. The ACIP recommended a second dose at the ages of four to six while the AAP recommended a second dose at ages eleven to twelve. Each recommendation had its own strategic advantage. The ACIP’s approach utilized the existing healthcare infrastructure, streamlining the vaccine delivery process to the pre-
school physician visit. The AAP’s approach was backed by epidemiological data demonstrating that most outbreaks were taking place in middle and high schools and would protect teens as they transitioned into a particular vulnerable period. In spite of the benefits of both strategies, the contradictory recommendations were grounds for concern because they were likely to cause confusion amongst healthcare personnel and could cause them to delay or skip the second dose of the vaccine, leaving the general population susceptible to outbreak.

This eventually led the CDC to hold a summit in 1994 with representatives from the ACIP, AAP, the American Academy of Family Physicians (AAFP), the Food and Drug Administration (FDA) and the National Institutes of Health (NIH). At that conference, it was decided that in order to facilitate ease-of-use in vaccine schedules, it would be best that the ACIP and other professional organizations should publish a systemically coordinated schedule. The first harmonized schedule of this nature was published in 1995.

Harmonization of recommendations is now one of the top priorities of the ACIP. Today, the AAP, the AAFP, the American College of Gynecologists and Obstetricians (ACOG), and the American College of Physicians (ACP) issue recommendations for routine use of vaccines jointly.

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28 Ibid., 408-9.
30 Ibid.
Disjointed recommendations may negatively interfere with vaccine campaigns by raising public concern that there is unreliable or contradictory evidence founding the committee’s recommendations or cause confusion amongst providers. Harmonization is essential for ensuring public confidence in the recommendations produced by the ACIP because it demonstrates to the general public a consensus amongst relevant scientific and medical experts.

Post-licensure Safety Surveillance

Vaccination more than any other health intervention is constantly under the microscope of the public gaze. Promoted by the fear mongering of the media and the Internet, the public is constantly on guard for vaccine-related adverse events. Vaccines are unique because the success of a vaccination campaign is defined by the absence of disease altogether. Paradoxically, the absence of disease makes their side effects far more conspicuous and therefore makes vaccine-related adverse events far more likely to raise public alarm.\(^32\), \(^33\)

Vaccines save an innumerable number of lives every years, but they are not completely risk-free. Side effects are usually mild, such as a low fever or localized injection reactions, but in some rare cases there are serious adverse events such as anaphylaxis. Vaccination campaigns are fundamentally based upon an evaluation of risks versus benefits. While it is not unlikely that individuals receiving the vaccines may have some minor adverse reactions, the


evidence indicates that in most cases the life-saving benefits of vaccines will outweigh the risks. In order to minimize risks, vaccines undergo extensive pre-licensure testing to determine their safety. However, these tests may not detect everything and there must be mechanisms for continuing safety surveillance after licensure.

Clinical trials are restricted in their ability to detect all safety concerns because of the limitations on the number of patients they can enroll, and the fact that can generally only enroll healthy patients. Post-licensure surveillance systems increase the likelihood of identifying events that may only be noticeable once hundreds of thousands of people have received the vaccine. Also, post-licensure surveillance may reveal contraindications of the vaccine that are specific to new populations that were not tested in the clinical trials.34

The need for surveillance mechanisms became clear after several majorly publicized adverse events. This included the infamous “Cutter incident” in 1955, in which some of the Salk polio vaccine was not fully inactivated and resulted in 260 cases of polio.35 Also, the swine flu immunization program of 1976, in which there was mass campaign initiated to vaccinate the US population against an influenza pandemic that never happened. The vaccine in question was linked to cases of Guillain-Barré syndrome, a life-threatening disorder in which the body’s

immune system attacks part of the peripheral nervous system.\textsuperscript{36} These scandals prompted the establishment of a preliminary system for monitoring adverse events following immunization by the CDC, which was expanded in 1978 to become The Monitoring System for Adverse Events Following Immunization (MSAEFI). This was a passive monitoring system (as in it does not actively seek out reports of adverse events from patients) to receive reports of adverse events from the public sector. It began on a pilot basis in several states and was expanded to all fifty states by the end of the year.\textsuperscript{37}

The National Childhood Vaccine Injury Act (NCVIA) of 1986 formalized the CDC's system for conducting post-licensure surveillance of vaccinations; systems that are still the primary mechanisms for detecting safety concerns to this day. The Act required by law that all vaccine administrators must report certain adverse events following vaccination. This program also provided compensation to people who may have been injured by vaccines, and worked to counteract factors that may destabilize immunization programs, such as liability concerns of providers or vaccine shortages.\textsuperscript{38}

This Act included the establishment of a passive surveillance system called the Vaccine Adverse Events Reporting System (VAERS), one of the most fundamental post-licensure surveillance mechanisms. VAERS is a passive surveillance system, which means it is an open-source system for reporting

\textsuperscript{36} "Vaccines for Children Program (VFC)," Centers for Disease Control and Prevention, http://www.cdc.gov/vaccines/programs/vfc/about/..

\textsuperscript{37} Salmon, Moulton, and Halsey, "Enhancing Public Confidence in Vaccines through Independent Oversight of Postlicensure Vaccine Safety," 948.

\textsuperscript{38} Ibid.
vaccine-related adverse events and is dependent on public reports for its data collection. Unlike clinical trials, VAERS has no limit on the number of patients it can collect data points from (assuming that people routinely report) and can therefore detect much rarer adverse events. While passive surveillance systems cannot prove a link of causality between adverse events and vaccines, they function as hypothesis generating systems, indicating the need for further clinical trials and investigation.39

The NCVIA also created the Vaccine Safety Datalink (VSD), a network of eight large medical-care organizations that track all medical encounters in approximately nine million patients. Unlike VAERS, the VSD is an active surveillance system and can be used for conducting research about vaccine safety questions.40 In concert, VSD and VAERS provide systems for detecting safety signals and investigating these potential linkages.

The CDC and the FDA are responsible for conducting the post-licensure safety surveillance independently from the pharmaceutical industry. The goal of this dichotomy is to ensure that the public feels confident that vaccine safety surveillance is being conducted by qualified professionals whose principle responsibility is verifying the safety of vaccines and are not driven by financial gain, public imagine, or program goals.41 The ACIP is responsible for continually

40 Ibid., 2.
41 Shimabukuro et al., "Safety Monitoring in the Vaccine Adverse Event Reporting System (Vaers)," 4398.
examining this surveillance data and making well-informed and explicit judgments about the safety of the vaccine when making recommendations.

These systems were put to the test in the late 1990s with the introduction of the Rotavirus vaccine, RotaShield, developed by Wyeth pharmaceuticals. Prior the vaccine’s licensure in 1997, there had been data presented to the committee about a possible connection between RotaShield and intussusception (bowel obstruction) but no formal connection was established between the two.42 The vaccine with licensed by the FDA in 1998 and the ACIP’s recommendation was finalized and published in March 1999, with no further discussion of the potential risks of intussusception. The vaccine gained in popularity following its release. However, at the same time, more and more cases of intussusception were being reported to VAERS, over ten cases by June 1999. Finally, concerns reached the Director of the CDC, Dr. Jeffrey Koplan, and he decided to temporarily suspend the vaccine while they conducted an investigation. By July 15, eighty-three additional cases of intussusception were reported to VAERS. Mere months later, after clear evidence from controlled trials demonstrated a relationship between the vaccine and intussusception, the decision to withdraw the RotaShield vaccine was announced by the ACIP at the October 1999 meeting.43

As was demonstrated by the committee’s response to this case, the ACIP is dedicated to continual surveillance of the safety of vaccinations. If at any time

43 Ibid.
causal-linkages are indicated then the ACIP has the prerogative to withdraw its recommendation.

Economic Considerations

The ACIP routinely considers cost as a factor when making recommendations for a vaccine. However, the consideration of cost is in no way straightforward. There are two conflicting factors at play when the ACIP evaluates economic data in its committee deliberations: first, the necessity that cost play a role because of the immense financial implications of the committee’s recommendations; second, the ethical issues that arise with cost considerations because of the inherent arbitrary judgments that are being made about how much is worth spending on human life.

While vaccines have demonstrated themselves to be one of the most effective health interventions of all time, *efficacy is not equivalent to cost-effectiveness*. A vaccine may be very effective at preventing disease, but its market value (the amount of money that must be spent to demonstrate its benefit) may not be minimal. The early vaccines were highly cost-effective, because they targeted ubiquitous childhood infections that had both high incidence and high mortality, such as measles or smallpox. However, as vaccines have begun to target less common diseases that have high mortality but lower incidence, the cost-effectiveness estimates have become less favorable. For example, Meningococcal disease has a low incidence in the US of about 0.3 per 100,000 people, a high mortality rate of about 8%, and its vaccine demonstrates
an unfavorably high cost-estimate of about $633,000 per case prevented.\textsuperscript{44, 45, 46}

Although the vaccines targeting low incidence/high mortality diseases can be very effective live-saving tools for the few who would contract the infection without the vaccine, this protection comes at a high price.

Cost of the vaccination has not always been a standard component of the ACIP’s deliberations. However, the issue of cost became a formal consideration after the addition of the pneumococcal conjugate vaccine to the childhood immunization schedule in 2000. The high price of the vaccine almost doubled the total cost of recommended vaccinations and the initial cost-benefit analysis of this vaccine projected an estimate of $80,000 per life year saved.\textsuperscript{47} These were shocking figures for public health officials evaluating the vaccine, and they elicited a conversation about cost-benefits of the vaccine. Since then, cost has been integral to the ACIP’s deliberations.\textsuperscript{48}

The issue of making judgments about the cost-effectiveness of a vaccine is very complicated as there are ethical issues that arise with the assignment of monetary value to human life. The standard measure of cost-effectiveness by the ACIP is usually a cost-utility analysis measure known as the Quality-Adjusted Life Year (QALY). Essentially the QALY gives an estimate of much it would cost to give an individual (or population, depending on the scale of measure) a year of

\textsuperscript{48} Ibid.
life in perfect health. An option for using the QALY estimates is the implementation of a cost threshold above which all vaccines are dismissed (for example a cut-off of $50,000 per QALY). However this can be problematic because using cost estimates as “gating criteria” can be relatively arbitrary and does not take into account the lives that could be saved or improved with access to the vaccine. It could also have the unintended consequence of discouraging manufacturers from developing vaccines that may be particularly expensive. Overall, the cost threshold is considered unethical because it prioritizes cost cutting over human life.

A study piloted in 2008 tried to articulate the role of cost-benefit estimates in the decision-making process of the ACIP by interviewing current members. Of the fifteen voting members on the committee, only four members reported that they had any experience with economic analyses before starting with the ACIP. All of the voting members interviewed expressed that even if the cost-benefit analysis indicated that the price of a vaccine would be exorbitantly high, it would not immediately disqualify the vaccine for use. They conveyed that while economic data is important, it should not be a dominant factor in the decision. They explained that each vaccine’s cost was considered on a case-by-case basis.

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46 Ibid.
49 Dempsey et al., “The Role of Economic Information in Decision-Making by the Advisory Committee on Immunization Practices.”
case basis and there were no discrete standards for making recommendations based on cost.  

While there is no consensus on the proper use of cost-benefit analyses in the ACIP’s deliberations, there have been standards set for the proper presentation of economic data. This ensures that all members can interpret the estimates regardless of their background in economics. In 2008, the ACIP inaugurated these guidelines, prepared by the ad hoc Work Group of Economic Analyses. The precedent for implementing these standards was the decision by major scientific journals such as the British Medical Journal and Vaccine to adopt standards for analyzing the quality of economic analyses used in their journal articles.

The ACIP’s economic guidelines explicitly outline what information needs to be included in economic analysis and dictates how data should be presented to the committee. The guidelines mandate that an analysis must be submitted no later than eight weeks before the meeting at which it is going to be presented (although an appeal can be made to submit later in extenuating circumstances). A peer reviewer from the National Center for Immunization and Respiratory Disease (NCIRD) will anonymously review the analysis and return it with follow-up questions to the presenter. If necessary, these questions and responses should be included in the final presentation of the economic analyses to promote

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53 Ibid.
59 Black, ”The Role of Health Economic Analyses in Vaccine Decision Making.”
60 Ibid.
transparency.\textsuperscript{61} This process controls for major gaps or bias in the economic analyses presented at the committee.

A central facet of these economic guidelines is the standard that any economic expert with adequate time, expertise, and interest, could independently replicate the results of an economic analysis presented to the committee.\textsuperscript{62} Reproducibility is critical because it assures that the analyses have been conducted correctly and using the best available data and models.

The goal of these guidelines is to ensure that voting members are well prepared and unbiased in their discussions of vaccine-related costs. Especially without the implementation of a cost threshold or any discrete procedures for making decisions about cost, it is essential that all members have the technical understanding to consider the data presented.

The GRADE Approach

In October 2010 the ACIP unanimously voted in a new framework for developing evidence-based recommendations, called the GRADE approach, which stands for Grades of Recommendation, Assessment, Development and Evaluation.\textsuperscript{65} This approach was adopted in an effort to increase transparency in the ACIP recommendation process to warrant the trust of ACIP stakeholders.\textsuperscript{66}

The GRADE system has three central components: (1) the evaluation of quality of evidence (high, moderate, low, very low), (2) a judgment about harms

\textsuperscript{61} Martin I. Meltzer Tracy Lieu, Mark L. Messonnier, "Guidance for Health Economics Studies Presented to the Advisory Committee on Immunization Practices (ACIP)," ed. Center For Disease Control (2007), 3.
\textsuperscript{62} Ibid., 7.
\textsuperscript{66} Ibid.
and benefits of vaccine, and (3) a rating of the strength of a recommendation (strong, weak).\textsuperscript{68}

The GRADE approach systematically looks at evidence produced by clinical trials and ranks its quality. This includes explaining why the evidence received the rating it did, and discussing the strengths and weaknesses of the trial’s design. All clinical trials are not created equal and may have major limitations or bias skewing the quality of evidence. The goal with the GRADE approach is to transparently address the limitations and bias of each trial using a standardized and accessible approach.\textsuperscript{70}

According to the GRADE approach there are many factors that may interfere with the quality of a clinical trial. A common problem is the inappropriate selection of experimental or control populations, which could produce inaccurate or misleading results. Another frequent issues is the use of imprecise estimates or wide confidence intervals, which can be ambiguous and provide little information of value. Also there may be the risk of publication bias due to selective presentation of data by researchers.\textsuperscript{71}

A limitation observed in past vaccine clinical trials is the indirectness of evidence, meaning that the trials were conducted in populations other than the target population for the vaccine. This limitation is frequently observed in vaccine trials because of the ethical issues related to measuring certain

\textsuperscript{70} Guyatt et al., "Grade: An Emerging Consensus on Rating Quality of Evidence and Strength of Recommendations," 926.
\textsuperscript{71} F. Ahmed et al., "Methods for Developing Evidence-Based Recommendations by the Advisory Committee on Immunization Practices (ACIP) of the U.S. Centers for Disease Control and Prevention (Cdc)," \textit{Vaccine} 29, no. 49 (2011): 9173.
preventable disease endpoints in clinical trials or conducting trials in particular populations. For example, clinical trials measuring the efficacy of the HPV vaccine deemed it unethical to actually measure cervical cancer as a primary disease endpoint in trials because it would take decades to reach that outcome and because of the ethical necessity to treat all pre-cancerous lesions in the patients enrolled in the trial as early as they were identified.

When using the GRADE system, presenters will thoroughly examine each trial and identify the shortcomings of its design. The evidence from that trial is then grouped into one of four ranked categories reflecting the confidence in the evidence (1 = high quality evidence, 2 = moderate, 3 = low, 4 = very low). The standards for each category are as follows:

1- Randomized controlled trials or overwhelming evidence from observational studies
2- Randomized controlled trials with important limitations, or really strong evidence from observational studies
3- Observational studies or RCTs with limitations
4- Clinical experience and observations, observational studies with important limitations, or randomized controlled trials with several major limitations

This provides an easy mechanism for voting members to determine the weight that should be given to a particular piece of evidence in their decision-making process. Evidence given a rating of 1 is said to have such a strong design that continued research or modification of trials would be unlikely to change the

72 Meeting of the Advisory Committee of Immunization Practices (ACIP), Summary Report, June 29-30, 2007, Atlanta, GA, Centers for Disease Control and Prevention, Online.
75 Ahmed et al., "Methods for Developing Evidence-Based Recommendations by the Advisory Committee on Immunization Practices (ACIP) of the U.S. Centers for Disease Control and Prevention (CDC)," 9174.
committee’s confidence in the estimate. In contrast, a lower ranking of three would indicate that the evaluators feel that further research is likely to have a significant impact on the evidence and change the estimate.76

There is an obvious shortcoming to this hierarchical approach, which is that quality of evidence is a continuum, and any attempt to discretely categorize is subject to some degree of arbitrariness. However the committee has decided that the benefit of having a straightforward approach for transparently addressing the shortcomings of evidence outweighs the risks of using discrete categorization.77

The separate evaluation of strength of evidence and strength of recommendation is a fundamental principle of the GRADE approach. Both are independently evaluated every time that an ACIP recommendation is made and those judgments are included in the final recommendation. The dichotomy between evaluation of strength of evidence and recommendation is based on the belief that strong evidence does not inevitably indicate strong recommendations, nor does weak evidence exclude the possibility of a strong recommendation.78

There are many factors that must be considered when evaluating the strength of a recommendation. As identified by the GRADE approach, these include the balance of desirable and undesirable effects, quality of evidence,

76 MMWR 61(8), ”New Framework (Grade) for Development of Evidence-Based Recommendations by the Advisory Committee on Immunization Practices,” *MMWR Morb Mortal Wkly Rep* 61, no. 18 (2012): 327.
77 Guyatt et al., ”Grade: An Emerging Consensus on Rating Quality of Evidence and Strength of Recommendations,” 926.
78 Ibid., 925.
uncertainties about particular values or preferences, and costs. After all of these factors have been considered, a recommendation can be rated either “strong” or “weak”.

The use of the GRADE approach is a strategy for furthering transparency, accessibility, and simplicity in the ACIP's recommendations. It is a way to explicitly address the reality that scientific evidence is vulnerable to bias and is often skewed based on the design of clinical trials, the aspirations of the scientist, or a plethora of other factors. In the end, it is a strategy for making sure both that all representatives at the committee understand the strengths and weaknesses of the evidence provided and for helping state governments and providers interpret the ACIP's recommendations.

**Recommendation Strength and Public Trust**

All of the structures implemented by the ACIP demonstrate a concerted effort to build vaccine recommendations that are as strong as possible using evidence-based science and a clear evaluation of risks versus benefits. The ACIP's structure has also been founded with the explicit goal of encouraging public confidence in its recommendations by promoting transparency. This gives all ACIP stakeholders the tools for critically considering vaccine recommendations and understanding the rationale of the committee's process.

Situating these structures in their history is also essential for helping the public understand the committee's process. As can be observed by the trajectory

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79 Ibid.
of the structures mapped above, the ACIP has evolved since its inception to address the emergence of new vaccines, the incidence of vaccine-related events, and the changing consensus of the scientific field. With time, it is likely that the committee will continue to adapt to address new issues that emerge.
Chapter 2
Conflicts of Interest and ACIP Membership

“Well, I guess the point I’m trying to make, and the question I’m trying to make is that, I have a grandchild. One of them almost died from a vaccine, the other one is now autistic, we believe, from vaccines. And I think that I, like most people who have children or grandchildren that are having these things put into these bodies, need to be assured that they’ve been thoroughly tested and that the people who are making the decisions on whether or not those should have been mandated, mandated by law, don’t have a conflict of interest”
--Dan Burton,
Committee on Government Reform, House of Representatives, June 15, 2000

At the turn of the century, House Representative Dan Burton organized a hearing in front of the Committee on Government Reform to address the concerns about conflicts of interest amongst ACIP members. The hearing was dramatically titled, “Conflicts of Interest and Vaccine Development- Preserving the Integrity of the Process.” Mr. Burton was not secretive about his personal stake in the issue: his firm belief that his grandchildren had been injured by vaccinations. While he may not have been justified in his opinions, his voice was an important one to be heard, as it reflected the voices of many parents and consumers who questioned the safety of vaccines and feared the people producing vaccine recommendations.

Burton’s hearing spurred an investigation of how the ACIP manages potential conflicts of interest in its structure and throughout its membership process. The fundamental question at the forefront of Burton’s investigation was whether the ACIP’s process was corrupted by the pharmaceutical industry. The answer to this question was of great consequence because it could undermine
the integrity of all of the recommendations produced by the committee. Even to this day, unpacking the answer to this question is integral to promoting public confidence in the committee and defending the strength of the committee’s recommendations.

After the ACIP was chartered in 1964, the first federal statute that specifically addressed the committee’s membership practices was the Federal Advisory Committee Act (FACA) of 1972. This designated the ACIP as a Federal Advisory Committee and its member’s as Special Government Employee’s (SGE’s).\(^82\) FACA was enacted with the goal of ensuring the objectivity and accessibility of federal advisory committees. The Act implemented a formalized system for establishing, managing, and terminating advisory bodies.\(^83\) This included making all committee meetings and minutes open to the public, implementing standards and guidelines for selecting committee members, instating four year term limits for voting members, and restricting financial compensation for membership.\(^84\) The mechanisms instituted by FACA are a few of many strategies utilized by the ACIP to manage its membership process, promote high quality recommendations, and instill public confidence in the recommendation process.

Ultimately, the goal of the membership process is to ensure that the advice of the committee is not inappropriately influenced by external factors,

\(^82\) Walton, Orenstein, and Pickering, "The History of the United States Advisory Committee on Immunization Practices (ACIP)."

\(^83\) "Federal Advisory Committee Act (Faca) Management Overview," General Services Administration (GSA), http://www.gsa.gov/portal/content/104514.

\(^84\) Ibid.
and is the result of the committee’s nonpartisan judgment based on the available evidence.\(^8^5\) There are three main ways that the committee models its membership process in order to promote nonpartisanship and produce high quality recommendations. These strategies are (1) diversity of representation on the committee, (2) prioritization of expertise in members, and (3) accountability and disclosure of conflicts of interest.

**Membership Process**

*Diversity of Representation*

One of the most important tools that the ACIP uses for producing high quality recommendations is the cultivation of a diverse range of representation at its meetings. Seating the committee with a heterogeneous group of scientific, medical, public health, and policy experts ensures that the recommendations are based off of well-rounded evidence and are not driven by the partisan goals of one individual or group. Having the broadest range of representation at meetings also helps to present the committee’s recommendations as the consensus of the scientific/medical community.

The ACIP has adapted since its inception to accommodate the growing number of vaccines available and the complexity of vaccine-related issues. In part, the ACIP has addressed these new issues by expanding the committee to provide a range of expertise and working to ensure that all parties with a vested interest in vaccine-related issues are able to have a voice in the recommendation

\(^8^5\) Dixie E. Snider, "Testimony on Vaccine Advisory Committee;S," ed. Committee on Government Reform U.S. House of Representatives (Department of Health and Human Services, 2000).
process. When the ACIP began, it was very small, consisting of only the chair of the committee, two federal government employees, and seven non-governmental health experts in the field of immunization.\(^86\) The committee grown to now consist of fifteen voting members, twenty-nine non-voting liaison representatives from relevant professional organizations, and eight non-voting \textit{ex officio} members representing federal agencies involved in immunization (See Appendix 3).\(^87\)

The ACIP works to promote diversity in the committee as a whole entity, as well as specifically within its voting members. As an entire entity, the ACIP accomplishes a diversity of representation by including non-voting members from a range of professional organizations (liaison and \textit{ex officio} members) and by having committee meetings that are open to the public (as stipulated by FACA). This ensures a wide variety of perspectives and knowledge at the disposal of the voting members producing the recommendation. Liaison and \textit{ex officio} members are specifically invited to ACIP meetings to share the standpoint of the organizations that they represent; expected to voice the needs of their organization and share relevant experience that has not already been shared.\(^88\) Public access to committee meetings also creates a mechanism for any


\(^87\) Smith, "The Structure, Role, and Procedures of the U.S. Advisory Committee on Immunization Practices (ACIP)."

individuals with relevant experience or concerns to have a voice in the process and promotes transparency in the ACIP’s process.

The second way that the ACIP encourages diversity of representation is through the constitution of its voting cohort. At any given time the committee is comprised of 15 voting members who are ultimately responsible for deciding on vaccine recommendations. Fourteen of the members are representatives from clinical medical fields or public health professionals. However, the final member is always a consumer representative who is knowledgeable about consumer perspectives and/or social and community aspects of immunization programs.\(^89\)

These members are limited to a four-year term to ensure continual turnover of representation and to prevent from monopolization of voting rights.\(^90\)

Diversity of voting members is accomplished by bringing in individuals with a range of professional backgrounds, scientific/medical expertise, and specialized areas of interest. Professional backgrounds include the medical field, academia, economics, public health or vaccine safety. Scientific/medical expertise represented by committee members includes pediatrics, family, nursing, vaccine research, infectious disease, immunology, and consumer needs. Specialized areas of interest could be in topics such as particular vaccine-preventable diseases, health economics, influenza control, etc. The ACIP also takes into account regional backgrounds, gender distribution, and inclusion of racial and ethnic minority groups when trying to build a well-rounded

\(^89\) Thomas, "Advisory Committee on Immunization Practices Application for Membership," 94.
\(^90\) Snider, "Testimony on Vaccine Advisory Committee;S."
committee.\textsuperscript{91}

Each time a new vaccine comes to the market, there is a novel disease and potentially a new population that the ACIP must have the technical skills and expertise to consider in its deliberations. Thus, as the market has expanded, the ACIP has worked to incorporate a wider range of expertise amongst its members. For example, historically most clinical experts on the committee had focused on pediatrics and family medicine, but with the rising number of adult and adolescent vaccines, Dr. Laura Riley was added to the committee in 2014 as the first expert on maternal health to sit on the committee.\textsuperscript{92}

The result of this structure is an informal system of checks and balances in the recommendation process. By working to include a diverse range of voices and perspectives and opening the committee to the public, the ACIP has tried to ensure that all considerations are voiced in its deliberations.

\textit{Prioritization of expertise amongst voting members}

Along with the diversity of representation, when selecting members for the ACIP’s voting cohort the committee has worked to build a committee comprised of leading experts in the relevant scientific/medical fields. The voting members are “acknowledged experts” in their disciplines, with exceptional records of achievement and strong backgrounds that will enable them to

\textsuperscript{92}CDC, "ACIP Members July 1, 2015- June 30, 2016," ed. Centers for Disease Control and Prevention (Atlanta, Georgia: CDC, 2016).}
interpret relevant data in the recommendation process. Nominees for membership are reviewed by the ACIP Steering Committee and approved by the Secretary of the Department of Health and Human Services. Applicants are selected based on their qualifications and their unique abilities to contribute to the committee.

Candidates for membership are vigorously screened for potential conflicts of interest before their names are submitted for final consideration. This includes actual conflicts of interest that may impact the integrity of the voting member’s decision-making, and perceived conflicts that could raise alarm from the general public. The public perception of the committee is a serious issue as its can impact the uptake of vaccinations.

It is essential that voting members of the committee be experts in relevant scientific/medical fields for multiple reasons. First, members must have the technical expertise to understand data presented at meetings. This ensures that members have the technical expertise to make well-informed decisions, and to recognize the shortcomings and bias in clinical data (which are explicitly outlined using the GRADE approach). Also, experts in the field are more likely to provide additional relevant expertise beyond what may be selectively presented at a meeting, such as the newest breakthroughs in the field or unpublished work. This can facilitate diversity of perspectives and avoid the exclusion of relevant scientific/medical fields.

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94 "Faca: Conflicts of Interest and Vaccine Development- Preserving the Integrity of the Process.."
96 Smith, "The Structure, Role, and Procedures of the U.S. Advisory Committee on Immunization Practices (ACIP)."
information from a discussion.97

The issue with selecting members based on their expertise in fields related to immunization/vaccinology is that these members are more likely to have potential conflicts of interest with the pharmaceutical industry, given the close relationship of the fields. The paradox is that the very same experiences that have given these qualified individuals the technical expertise to sit on the committee are the ones that may be viewed as a conflict of interest.98 However, the ACIP has come to prioritize relevant expertise when selecting committee members and has tried to cope with this issue by instituting mechanisms for transparently evaluating the risks presented by a potential conflict.

Potential conflicts of interest must be considered even past the membership selection process and regularly addressed throughout a voting member's tenure on the committee. Every member must be continually evaluated to see whether new or old conflicts of interest could interfere with the integrity of ACIP's discussions at the moment. The US Code of Federal Regulations, and general guidelines produced by the Office of Government Ethics in 1996 outline the standards for this process.99, 100 The guidelines dictate that an advisory committee member may not participate in an official capacity in deliberations which he has a financial interest if it is likely to have an effect on his decision-making. However, this is not an ultimatum; appointing officers may

97 Snider, "Testimony on Vaccine Advisory Committee;S."
98 Ibid.
100 Ibid., 95.
issue limited waivers if it is determined that the financial interest is remote, or is determined to be unlikely to impact the member’s decision-making process. The member may also be granted a limited waiver to participate in the deliberations if the committee feels that the value of the member’s expertise outweighs the risk of his potential conflict of interest.101

This system is built upon an evaluation of risks versus benefits: the “[balance of] the possibility of bias caused by a conflict with the need for vaccine and immunization expertise.”102 While the waiver system is not the most straightforward approach for limiting bias (compared to absolute restriction of all potential conflicts) and may not always be looked upon favorably by the general public, it is born out of a prioritization of highly knowledgeable voting members and is fundamental to the ACIP’s membership process.

Transparency

The limitation of the ACIP’s prioritization of relevant expertise is that by deliberately seeking out experts in the field, they are targeting individuals that inherently have a level of bias as a result of their backgrounds. This could be a direct connection such as past employment, stock ownership, or receipt of honoraria from the vaccine research industry. It could also be an indirect connection, such engagement with research conducted by an academic institution that has received funding from a vaccine manufacturer. Even a

101 Ibid., 94.
102 Smith, “The Structure, Role, and Procedures of the U.S. Advisory Committee on Immunization Practices (ACIP).”
private physician with a specialty in preventative medicine or pediatric care could be linked to the vaccine industry— they could have worked for a managed care organization that is involved in clinical trials for a vaccine manufacturer or presented at a scientific meeting that could have been sponsored by a pharmaceutical company.\textsuperscript{103} It is very challenging to completely eliminate all connections to the industry when specifically targeting experts in the field.

The committee manages this issue by prioritizing transparency in its process, both in its membership procedures and throughout its deliberations. At the beginning of each meeting and each time the committee takes a vote, members are mandated to declare any potential conflicts of interest, relevant business interests, or leadership positions that may impact their ability to vote impartially. Also they are required file an annual Confidential Financial Disclosure Report, which will be comprehensively reviewed by the ACIP Secretariat, the Federal Advisory Committee Management Branch (FACMB) and the Office of General Counsel for sources of conflict. If a conflict is identified members will be asked to not to participate in relevant discussions or abstain from votes regarding specific vaccines. In some circumstances, a member may be asked to leave the committee if the conflict is deemed to be significant enough.\textsuperscript{104}

The limited financial compensation to members of the committee is another strategy for promoting transparency. Non-voting members are offered no financial compensation for their time on the committee, with the exception of

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\textsuperscript{103} "Faca: Conflicts of Interest and Vaccine Development- Preserving the Integrity of the Process."
\textsuperscript{104} Thomas, "Advisory Committee on Immunization Practices Application for Membership."
\end{flushleft}
coverage for any incidental costs incurred at the meeting such as travel, food and lodging. Voting members receive an honorarium of up to $250 for every day they serve on the committee as well as coverage for incidental costs. Committee membership requires a relatively large time commitment over the course of a member's tenure, includes three meetings annually, each of which lasts three days, and participation with at least two ACIP Work Groups that generally meet monthly. Offering minimal financial compensation sends a clear message to the public that committee members are not being incentivized to sit on the committee to fulfill a particular agenda—the committee’s only goal is to produce high quality recommendations based off of the available evidence.

A Case Study: The Committee on Government Reform

Undeniably, the ACIP is in not a perfect system in spite of the many safeguards that have been put in place to optimize recommendations. Not all people agree with the techniques used by the ACIP to minimize bias and evaluate conflicts of interest. This was addressed head on when Chairman Dan Burton brought the ACIP in front of the Committee on Government Reform at the House of Representatives in 2000.

In a conversation about bias and conflicts of interest, it is essential to consider the background of all parties involved. Mr. Burton was a Republican

105 Smith, "The Structure, Role, and Procedures of the U.S. Advisory Committee on Immunization Practices (ACIP)," A70.
Congressman from Indiana. During his tenure on the House of Representatives, Burton reportedly held over 20 hearings to promote the belief that the mercury-derivative in vaccines was the cause of autism (this theory had been almost unanimously rejected by the scientific community). More recently, he has been an active lobbyist for the Church of Scientology, a religious group that is notorious for their anti-vaccine stance. He was also present when the Church of Scientology opened its national office in Washington D.C. in 2012, and was has openly supported the Church’s work. He has loudly voiced his belief that grandchild’s autism was an adverse event to a vaccine and openly questions the benevolence and reliability of the ACIP. It is clear, based on Mr. Burton’s actions and political/religious affiliations, what his stance towards vaccines was even before he arrived at the hearing.

Mr. Burton argument was that the pharmaceutical industry had too much influence over the decision-making of the ACIP. His intentions in some ways were laudable: the goal of ensuring confidence in the fact that the ACIP’s recommendations had not been skewed by the influence of big pharma. On the other hand, Mr. Burton’s personal biases were apparent throughout the deliberations.

Mr. Burton was not explicitly suggesting a conspiracy amongst ACIP members. Nor was he suggesting that pharmaceutical companies were directly buying off members in exchange for their votes. Rather he alluded to the fact that

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“close and remunerative collaboration with a company naturally creates goodwill on the part of the researchers and the hope that the largesse will continue. This attitude can subtly influence scientific judgment.”

Fundamentally, the arguments raised by Mr. Burton were important and valid. He emphasized that it was important to maintain the highest level of integrity throughout the entire vaccine policy process. It was the responsibility of the DHHS, he said, to elect committee members without conflicts of interest. However, the issue at hand was not nearly as clear-cut as Mr. Burton made it seem.

The topic that Mr. Burton specifically addressed in his June 2000 hearing was the Rotashield Scandal of the late 1990s, (which was mentioned in Chapter One as an example of the ACIP’s use of the VAERS system). The vaccine had been recommended by the ACIP in February 1999, in spite of data presented to the committee about the potential connection between the vaccine and intussusception. But just months later the ACIP withdrew its recommendations after an investigation established a causal connection between the two, and the vaccine was removed from the market.

Mr. Burton argued that the decision not to investigate the connection after the initial presentation of the possible connection to intussusception was an intentional oversight by members of the ACIP who had financial ties to the

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111 “Faca: Conflicts of Interest and Vaccine Development- Preserving the Integrity of the Process."
vaccine but were granted waivers which allowed them to vote in favor of a vaccine they knew to be unreliable. According to Mr. Burton, these members had significant financial conflicts of interest and therefore should not have been allowed to participate in the voting process.\textsuperscript{113}

The fundamental disagreement between Mr. Burton and the representatives from the ACIP was whether it was necessary or appropriate to let experts with indirect or insignificant connections to the pharmaceutical industry sit on the committee or participate in its deliberations. While the ACIP prioritized these members’ expertise, Mr. Burton argued that having members with \textit{any} degree of connection to big pharma is a violation of the public’s trust and indicates partisanship in the ACIP’s process. Burton felt that the transparency of disclosing financial records and conflicts of interest did not sufficiently address these potential sources of bias. Representatives from the ACIP disagreed; they felt that ensuring expertise should be prioritized over the elimination of any and all potential connections to the industry.\textsuperscript{114}

Mr. Burton found this defense to be inadequate. He struggled to accept the argument that there were not enough qualified experts in the field to serve on the committee that had no direct or indirect connections to the vaccine industry. He poignantly called it the “old boys network” of the vaccine industry: “How can we be confident in a system when the agency seems to feel that the

\begin{footnotesize}
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\item \textsuperscript{113} Dan Burton in Committee of Government Reform, “Faca: Conflicts of Interest and Vaccine Development- Preserving the Integrity of the Process.”
\item \textsuperscript{114} Dixie Snider in ibid.
\end{itemize}
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numbers of experts is so few around the country that everyone appears to have a conflict of interest and thus waivers must be granted?"\textsuperscript{115}

The ACIP representatives responded with the argument that based on the committee's experience it is very difficult to find qualified experts in vaccinology and immunology, or public health that have no connections to the vaccine industry, given the interrelatedness of the fields.

Mr. Burton cited several examples of members with perceived conflicts to the pharmaceutical industry that were deemed indirect conflicts and therefore granted waivers. This included Dr. Chinh Le, a member of the ACIP Working Group. Dr. Le was employed Kaiser Permanante, one of the largest health care providers in the country. When Dr. Le was on the committee Kaiser was participating in vaccine studies with Merck, Wyeth, and SmithKline, three very large pharmaceutical companies. According to Burton, this was identified as a conflict of interest and was a reason that Dr. Le should have been excluded from committee membership. However, the ACIP had judged that this connection was remote enough that it was unlikely to skew Dr. Le's objectivity in the proceedings.\textsuperscript{116}

Mr. Burton also cited the example of the chair of the RotaShield WG, Dr. John Modlin, a Pediatric Infectious Disease Specialist from Duke University School of Medicine. Dr. Modlin had served on the committee for four years and was the chair of the ACIP during the RotaShield scandal. Dr. Modlin owned about

\textsuperscript{115} "Federal Advisory Committee Act (Faca) Management Overview".
\textsuperscript{116} "Faca: Conflicts of Interest and Vaccine Development- Preserving the Integrity of the Process."
600 shares of stock in Merck, worth about $26,000, an investment that Mr. Burton argued should have excluded Dr. Modlin from the committee. The debate that followed raised a wide range of controversial issues. It is indicated the confusing and fluid line between expertise and conflict of interest in ACIP membership based on the waiver system.

While Burton did raise some legitimate points, much of the evidence he shared was inaccurate or a conflation of issues. One major gap in Mr. Burton’s argument was that Dr. Modlin was favorable towards the vaccine because of his financial connection to Merck. However, the rotavirus vaccine that was removed from the market was not manufactured by Merck, but rather by Wyeth pharmaceuticals. Merck actually did have a Rotavirus vaccine under development at the time, but Modlin denied knowing that Merck was an affected party during the ACIP's deliberations over RotaShield. However, even if Dr. Modlin had known that Merck was developing a competitor vaccine, it seems more likely that his bias in this case would lead him to oppose the Wyeth vaccine because it could pose a threat to the success of Merck's vaccine.

There are no explicit guidelines that committee members are not allowed to hold stock in pharmaceutical companies developing vaccines; it is simply required that they disclose these financial holdings in order to determine whether the holdings may pose a potential conflict of interest. FACA specifically states that a committee member is considered to have a direct financial interest if there is a “direct and predictable effect between the action that the [group

117 Ibid.
member] will take and the expected effect on his/her financial interest." In this case, Dr. Modlin’s financial interest did not seem to directly impact his preference for the vaccine, since he supported a vaccine manufactured by Wyeth that would actually be detrimental to his financial investment in their competitor Merck.

The underlying question at hand was whether the risk of Dr. Modlin’s financial conflict of interest outweighed the benefits of having his knowledge at the disposal of the committee. For Mr. Burton, the answer to this question was an absolute yes. But the ACIP disagreed. Dr. Modlin was a leading expert in the field of vaccinology. He was the medical director of the Clinical Virology Laboratory of the Mary Hitchcock Memorial Hospital in Lebanon, NH; he had sat on several editorial boards and acted as a reviewer for more than twenty medical journals; he had attended several conferences and workshops on a variety of vaccine-related issues. He was clearly knowledgeable about the topics at hand.

The argument that Dr. Modlin would support a particular vaccine because of his relatively minimal stake in the company was flimsy. While he did hold 600 shares of stock in Merck, the chances of a single vaccine dramatically impacting the value of his stock was minimal. Vaccines are generally not large blockbuster drugs for pharmaceutical companies given that they are only administered once throughout the lifetime (i.e. one completion of a vaccine series), unlike many drugs that treat mental or chronic illnesses that must be

118 "Federal Advisory Committee Act (Faca) Management Overview".
119 "Faca: Conflicts of Interest and Vaccine Development- Preserving the Integrity of the Process."
taken indefinitely. Also, more than 50% of vaccines are provided by the federal government and are therefore purchased from the pharmaceutical company at a negotiated discount price. For the pharmaceutical company in general, barely over 1% of their revenues actually come from vaccines, a pretty insignificant quantity when one considers the scale of a large pharmaceutical company.\textsuperscript{120}

Mr. Burton also argued that it was a violation of the public’s trust that the financial records of the ACIP’s members were confidential. Mr. Burton argued that this lack of public disclosure meant that these members were not necessarily being held to the highest level of scrutiny. This too is a contestable issue. Ms. Marilyn Glynn, a general Counsel Woman of the Office of Government Ethics responded that public financial disclosures are usually reserved for higher-level government employees or people with political appointments. Congress has determined that SGE’s such as ACIP members are not in positions which require public financial disclosure.\textsuperscript{121} This concession is a compromise to ensure that there aren’t too many barriers in place of recruiting qualified members. Members are required to spend a significant amount of time over the course of the year participating in the committee, without any financial compensation for these activities. They are also meant to be top experts in the field) and have no financial conflicts of interest. According to Glynn, asking potential candidates to publically disclose their financial records annually is just

\textsuperscript{120} Ibid.
\textsuperscript{121} Ibid.
another hindrance to finding committee members that fulfill these qualifications.\textsuperscript{122}

As demonstrated by this hearing, the issue of minimizing bias in the recommendation process is very complex and often the source of public skepticism. Although the ACIP’s tools for addressing potential conflicts of interest have been strategically implemented to promote nonpartisanship and to produce the highest quality recommendations, the ACIP’s complicated approach does not necessarily instill confidence in the general public. In contrast, Mr. Burton’s absolutist approach for addressing conflicts of interests in membership is much more direct and can be more appealing and persuasive to the concerned parent.

\textsuperscript{122} Ibid.
Chapter 3
Implications of the ACIP Recommendations

On May 1, 2015, Republican Congresswoman Frederica Wilson introduced the Vaccinate All Children Act of 2015 to Congress. This bill proposed legislation that would harmonize the disparate state vaccination laws throughout the United States to ensure that all children, regardless of where they live, would receive vaccinations in accordance with the recommendations made by the ACIP. It would enforce this requirement by withholding federal public health funding from states that refused to create appropriate school mandates, and limit immunization exemptions nationwide to cases of extenuating medical circumstances, restricting all philosophical or religious exemptions. If this bill had passed, it would have meant a dramatic decrease in the number of unvaccinated children throughout the US and be a huge victory for public health officials who worked to increase vaccine coverage. However, unsurprisingly, this bill failed to pass.

The fact that Ms. Wilson’s law did not make it through Congress reflects the prevailing influence of states’ rights advocates who believe that the federal government should have limited authority to set standards for the states except where these rights are clearly articulated in the Constitution. From this perspective, if this bill had passed, it would have meant that the federal

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124 Ibid., 195.
government was overstepping its Constitutional bounds and violating this underlying principle.

The role of governmental powers in immunization policy has been clearly shaped by this dichotomy between federal and state power. Historically, the federal government’s role in immunization-related activities has been compartmentalized to only guidance and funding of immunization programs, and sponsorship of vaccine research. Only the states are able to enact policies mandating compulsory vaccination for their respective populations.

The first compulsory state law dates back to 1809 in Massachusetts, when the state mandated that the population be vaccinated against smallpox. Today, all states have implemented laws requiring children to be vaccinated as a prerequisite for school attendance, although these requirements vary across the states. While states do look to the ACIP for guidance, most do not currently require all of the immunizations on the committee’s recommended schedule. For example, only three states have requirements for the human papillomavirus (HPV) and influenza vaccine, although they are both indicated on the ACIP schedule. Even for vaccines that are universally recommended, such as the measles, mumps, rubella (MMR) vaccine, the actual requirements can vary by state (See Appendix 4). Some states choose to follow the ACIP

127 Ibid.
recommendations precisely but many diverge by mandating a different number of doses of a vaccine or a different target age range than recommended by ACIP.

States are also responsible for laws regarding immunization exemptions, which could allow individuals to opt-out of vaccine mandates for medical, religious, and philosophical reasons. All states have medical exemption laws but there is variability in state legislation on religious and philosophical exemptions. In 2016, all but three states allowed for religious exemptions (Mississippi, West Virginia, and California), while less than half allowed for philosophical exemptions. Each state can make these discretionary choices and the federal government has no power to enforce the ACIP’s recommendations.

As a federal committee, the ACIP has no direct authority to create vaccine mandates by law. In spite of this limitation, the ACIP’s recommendations still have immense implications. The committee’s two primary spheres of influence are (1) guiding state legislation, and (2) dictating federal, state, and private spending. In order to fully understand the implications of the ACIP’s recommendations it is important to begin by articulating its role as a federal advisory committee. Examining the history of immunization activity in the US can illuminate this role: a history muddled by fear of socialist institutions, the

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129 CDC, "State School and Childcare Vaccination Laws".
130 Ibid.
vehement defense of state’s rights, and the resistance to federal interference in healthcare.\textsuperscript{131}

\textbf{Federal versus State Role in Immunization Activities}

\textit{The legal precedent for federal vs. state roles}

The dichotomy between the federal and state government’s rights are written into the US Constitution, entrenching ideas from one of the first political parties in the US, the Federalists. The central principle of federalism is the division of national and state government powers. Any power that is not specifically allocated to the federal government under the Constitution is presumed to be left for the states. This includes the “police powers” of the state: the power to regulate and enforce authority within state boundaries to promote the health, safety, and general welfare of the people under the state’s sovereignty.\textsuperscript{132} The federal government’s role in vaccine policy is the “quintessential example of a persisting Federalist system.”\textsuperscript{133}

In the last century, there have been two seminal Supreme Court cases upholding the state’s constitutional rights over vaccination policy in the United States. The first was \textit{Jacobson v Commonwealth of Massachusetts}, in 1905, which upheld the state’s right to mandate compulsory immunization in the event of an

\textsuperscript{131} Bylander, "The United States' Piecemeal Approach to Vaccine Policy."
\textsuperscript{132} Mariner, Annas, and Glantz, "Jacobson V Massachusetts: It’s Not Your Great-Great-Grandfather’s Public Health Law."
\textsuperscript{133} Bylander, "The United States' Piecemeal Approach to Vaccine Policy," 196.
outbreak of a vaccine-preventable disease. Three years earlier, there had been an outbreak of smallpox in the city of Cambridge, MA. In response, the state had granted the city’s Board of Health the right to issue an order that all adults get vaccinated, with a $5 fee for those who did not comply. One resident had refused vaccination and sued the city. The Court determined that the mandate fell under the umbrella of the state’s “police powers,” as it had the intention of preserving the health of its residents.

The second case came two decades later, in 1922, Zucht v King. In this case the Court upheld a city ordinance that prohibited anyone from attending a public or private school without a certificate of smallpox vaccination. Unlike Jacobson, this case did not specify whether there needed to be immediate danger of outbreak for a state to implement vaccine mandates. Zucht simply upheld the state’s right to accord cities the general authority to choose when to implement health regulations. In concert, these cases solidified the legal precedent for the current vaccine policy system in the US.

Articulating the federal role

Along with the defense of states’ rights, the limited role of the federal

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135 Ibid., 582.
136 Henning Jacobson V. Commonwealth of Massachusetts., February 20 1905.
government in immunization activities has been influenced by historical events and political trends. Two specific movements in history that shaped the federal government’s role were the polio politics of the second half of the twentieth century, and the fear of communism and socialist institutions during the Cold War.

In the early twentieth century, although there was legal precedent for establishing state immunization policy, there was limited public health infrastructure for supporting these activities at the state level. Few states had active public health programs and therefore most public health activities were carried out at the local level. Some cities distributed free or discounted immunizations to the public, but these programs were minimal. 140

Primarily the issue of payment for vaccines was an individual responsibility. Along with the limited infrastructure, public health initiatives such as free vaccine programs were stifled by the political climate in the 1920s. The close proximity to the ‘Red Scare’ of 1919 spurred antagonism towards any potential infiltrations of communism into the United States. 141 Libertarian and anti-government civic organizations were lobbying fiercely against developments that they thought to be approaching socialist territory; turf that public health programs seemed to be encroaching upon. Even during the Great Depression in 1929, Franklin Roosevelt’s multitude of federal programs to alleviate economic distress in the US did not include programs for increasing

141 Ibid., 251.
healthcare coverage or infrastructure.\textsuperscript{142}

This began to slowly shift leading into the second half of the century. An important moment was President Roosevelt’s Public Health Service Act of 1944. Its goal was to broaden the scope of the federal Public Health Service (PHS) to control the spread of communicable disease. The Act increased the funding available to the PHS to distribute to state health departments for controlling disease and training public health personnel. This act explicitly included the federal right to implement quarantine and isolation measures to control disease outbreak, but it did not extend this authority to include the ability to mandate vaccination programs during a public health emergency.\textsuperscript{143,144} The Public Health Service Act sent a clear message: while it was the federal prerogative to promote the health of citizens by giving money to states to build healthcare infrastructure, the right to mandate vaccinations remained only under the jurisdiction of the states.

Given the limited public health infrastructure and the resistance to public provision of vaccines, up until the 1960s immunization-related funding was generally a private, individual, or local issue. For example, in 1938, President Roosevelt, spurred by his own experience with polio, founded the private non-profit organization called the National Foundation for Infantile Paralysis (NFIP--now known as the March of Dimes), which played a leading role in raising money

\textsuperscript{142} Ibid.
for the research and development of the polio vaccine.\textsuperscript{145} The NFIP hired Dr. Jonas Salk to spearhead this research.\textsuperscript{146}

Much of the current federal policy related to vaccine activities grew out of the public response to the polio infection. 1955 saw the worst ever recorded polio epidemic in US history in which almost fifty-eight thousand cases were reported. This outbreak put pressure on the expedited development of the polio vaccine, which was successfully discovered by Salk and licensed in April 1955. After the vaccine was developed the NFIP raised $9 million for publically distributing the vaccine. However, this funding was not enough to cover everyone and NFIP began to put pressure on the federal government to step in.\textsuperscript{147}

As a moderate conservative, President Eisenhower was uninterested in increasing the federal influence in healthcare but with pressure from the Democratic Party he signed in the 1955 Polio Vaccination Assistance Act (PVAA). This act allowed Congress to appropriate funds to what was then known as the Communicable Diseases Center (now the Center for Disease control or CDC) to help states afford to buy the polio vaccine for their populations. This act gave the federal government the ability to cover the costs of planning and conducting

\textsuperscript{145} Colgrove, "Immunity for the People: The Challenge of Achieving High Vaccine Coverage in American History."


\textsuperscript{147} Elena Conis, "Vaccine Nation: America’s Changing Relationship with Immunization," Health Affairs 33 (2014). 23.
vaccination programs.\textsuperscript{148} A total of $53.6 million were appropriated to states from 1956 to 1957 as a result of this Act.\textsuperscript{149}

Although PVAA allowed the federal government to decide how much money to grant to states for the provision of the polio vaccine, it left it up to the states and only the states to decide how they wanted to use these funds. Eisenhower’s cabinet was careful to distance itself from anything that could appear to be socialized medicine.\textsuperscript{150} This made sense, as the Act was signed in during the early years of the Cold War, a period in US history fraught with fear and resistance to anything that resembled communism.\textsuperscript{151}

Even with PVAA, most people were not taking advantage of the vaccines that were available to them (diphtheria, pertussis, tetanus, polio). When President John F. Kennedy took office in 1961 about two-thirds of children weren’t immunized, nor were 80% of adults.\textsuperscript{152} Kennedy’s administration was far more receptive to federal involvement with immunization activities than Eisenhower’s had been.\textsuperscript{153} In 1962, President Kennedy signed in the Vaccination Assistance Act (VAA). This Act added a new Section 317 to the previously established Public Health Service Act. The central goal of VAA was to allow the CDC to support the establishment of mass, intensive vaccination campaigns,\

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\textsuperscript{148} Ibid., 22.
\textsuperscript{150} Conis, "Vaccine Nation: America’s Changing Relationship with Immunization." 22,
\textsuperscript{151} Colgrove, "Immunity for the People: The Challenge of Achieving High Vaccine Coverage in American History."
\textsuperscript{152} Conis, "Vaccine Nation: America’s Changing Relationship with Immunization."
\end{flushright}
especially targeted at preschool children.\textsuperscript{154} It gave the CDC the ability to allocate funds to the states to support the cost of vaccination programs, although it still did not dictate how the states should use those funds. It also established a mechanism for providing ongoing financial support to state or local health departments and allowed the federal government to provide vaccinations as well as CDC Public Health Advisors to assist in the management of local health programs.\textsuperscript{155}

At first, the VAA was not well received by the general public, as many still did not feel it was the responsibility of the federal government to provide healthcare for the poor. However, the 1960s brought the Golden Age of vaccine development, with the development oral polio (1961), measles (1963), mumps (1967), and rubella (1969) vaccines in quick succession.\textsuperscript{156} This dramatic increase in the number of vaccines spurred a shift in the public perception of the acceptability of federal involvement in the distribution of vaccines. Also, President Kennedy carefully marketed VAA so as to encourage public approval. He noted that almost 40\% of the nation’s population were under twenty (now known as the ‘baby boomer’ generation), and argued that risks of communicable disease were a public security threat because they could cause disability in

\textsuperscript{154} Hinman, Orenstein, and Schuchat, "Vaccine-Preventable Diseases, Immunizations, and Mmwr-1961-2011," 49.
\textsuperscript{155} Ibid.
\textsuperscript{156} Colgrove, "Immunity for the People: The Challenge of Achieving High Vaccine Coverage in American History."
youths, weakening the nation’s ability to respond to an attack. This was a particularly convincing argument in the midst of the Cold War.¹⁵⁷

With this infrastructure in place there began to be an increased focus on supporting immunization initiatives. Following soon after Kennedy's VAA was the enactment of Medicaid in 1965 and a Medicaid benefit program known as the Early, and Periodic Screening, Diagnosis and Treatment Program, which focused on providing preventative care for low-income children.¹⁵⁸ The CDC also launched an effort in 1967 to unify the “hodgepodge” of state and local vaccine recommendations (many of which were left over from early smallpox vaccination in the 1800s) to make these laws more “uniform and extensive.”¹⁵⁹

From 1968 to 1974 the number of states requiring all or most vaccines before school entry increased from twenty-five to forty, and by 1981 all fifty states had mandates.¹⁶⁰

These events and laws shaped the contemporary system for distributing, overseeing, funding, and mandating vaccinations in the United States. They are indicative of how the strict divide between the federal and state role in immunization policy was defined. Also they demonstrate how the federal government has become an integral player in ensuring equitable access to healthcare for those who cannot afford it as well as providing funds to states to implement vaccination activities. The ACIP is integral to this process because, as

¹⁵⁷ Conis, "Vaccine Nation: America’s Changing Relationship with Immunization."
¹⁵⁸ Colgrove, "Immunity for the People: The Challenge of Achieving High Vaccine Coverage in American History."
¹⁵⁹ Conis, "Vaccine Nation: America’s Changing Relationship with Immunization."
¹⁶⁰ Colgrove, "Immunity for the People: The Challenge of Achieving High Vaccine Coverage in American History."
the advisory committee to the federal government, the committee provides direct advice and expertise on how to properly use available funds.

Economic Implications of ACIP Recommendations

President Kennedy’s VAA was a pivotal moment for the immunization program in the US. The early 1960s was a brief time of collective faith in the vaccine industry born out of the Golden Age of vaccine discovery and a general amicability towards the expertise of scientists.\textsuperscript{161} This attitude has shifted dramatically since the mid-1960s, but the foundation set by Kennedy’s VAA solidified the precedent for vaccination as a \textit{right} of US citizens. It clearly demarcated the federal government’s commitment to providing equal access to vaccinations for all people.

The public health infrastructure and public/private funding for vaccines has expanded dramatically over the past half-century. There has been a clear commitment to trying to ensure that all citizens have access to vaccinations, either through their private insurance coverage or through the public sector. Although there are still some gaps, the expanded infrastructure has allowed over 80\% of infants nineteen to thirty-five months old to get vaccinated (percent varies by vaccine, although some of this these differences can be due to state mandates or exemption laws, not due to cost or access issues). The ACIP’s recommendations guide decisions about public/private provision of vaccines

\textsuperscript{161} Conis, "Vaccine Nation: America's Changing Relationship with Immunization."
and therefore the committee’s recommendations have immense implications for federal, state, and private spending.

These implications have grown over the past few decades with the dramatic spike in the cost of newer vaccines coming on to the market. From 1988 to 1997 the cumulative cost of all recommended vaccine doses for a child through age six doubled from $100 to $200 (under the federally negotiated contract prices). The price skyrocketed again in 2001 to $395 with the addition of the pneumococcal conjugate vaccine (PCV) to the childhood immunization schedule (See Appendix 5). This demonstrated the dramatic impact that the ACIP recommendations could have on the national expenditures for vaccines. According to a study piloted in 2002, on average, in the years in which there was a vaccine recommendation by the ACIP the cost of vaccination increased 35% in that year (See Appendix 6).

It is important to clarify that the ACIP is purely an advisory body and in order for its recommendations to have any real power they must be approved by Director of the CDC and the Secretary of HHS and published in the MMWR, at which point they are official federal recommendations. The ACIP has direct influence over federal spending, which means that they play a direct advisory role to those who allocate federal funds, but not a direct role in actually allocating funds. The committee can also have an indirect advisory role over funding for immunizations, specifically for the state. These are indirect because

163 Ibid., 1984.
each state is able to look to recommendations made by the ACIP and then make discretionary decisions about which vaccines they are willing to cover. Many states will not directly follow the guidelines set by the ACIP precisely. The ACIP is also gaining increasing direct control over private spending, as federal policy such as President Obama’s 2010 Affordable Care Act (ACA) expand the committee’s scope of influence.164

Vaccinations in the United States are funded by a combination of federal, state, and private sources. The primary sources of funding for vaccinations in the US are from the Vaccines For Children (VFC) Program, Section 317 funds, Medicaid, Medicare, private insurance, or state funds. Depending on the source of funding, the ACIP’s recommendations may have a direct or indirect influence over spending. However, there has been increasing pressure from the federal government to ensure that these funding sources follow the recommendations of the ACIP. The federal government has also expanded the federal money available to fill in the cracks for individuals that may not have access to vaccination. Each of these sources covers different populations, has varying eligibility requirements and sources of funding; and is impacted differently by the ACIP’s recommendations (See Appendix 7). Articulating each of these programs illuminates the immense impact of the ACIP’s recommendations on national expenditure for immunization activity.

**Vaccines For Children (VFC) Program**

Over half of the vaccines that are distributed through the public sector in the United States are through the VFC Program. This program was established in 1993 as an amendment to the Social Security Act of 1935. VFC provides free vaccines to children age eighteen and under who are Medicaid-eligible uninsured, or Native American/Alaska natives. VFC also covers underinsured children (children who have health insurance that does not provide coverage for all recommended vaccines) who receive vaccines at Federally Qualified Centers (FQCs). Except for the underinsured, VFC program allows eligible patients to receive immunizations in their own medical home at no cost.  

VFC guidelines may not exactly follow the general immunizations produced by the ACIP. Each time the ACIP recommends a vaccine it takes a separate vote about whether the vaccine should be added to the VFC entitlement. If the ACIP’s recommendation are accepted and published in the MMWR, then the CDC will negotiate a discounted contract price with the vaccine manufacturer for the federal purchase of vaccines. States are then allocated a “credit balance” based on their estimated number of recipients and are able to use those funds to purchase the vaccine from the manufacturer at the discounted prices. The states are responsible for creating a stockpile of the vaccine as well. 

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as providing them to registered providers to deliver to VFC-eligible children.\textsuperscript{166}

Regardless of whether or not a state chooses to require the vaccine in question in their legislation, the VFC program will still allocate funds to provide eligible children with all recommended vaccines, free of charge. The ACIP has direct influence over the federal spending on the VFC-entitlement, and this spending is not dependent on the discretion of the individual states. While the state is not required to mandate all ACIP-recommended vaccines through school-entry laws, VFC-eligible children will still have access to all vaccines.\textsuperscript{167}

The result of the VFC program has been the large transfer of financial responsibility for vaccines from the states to the federal government. The federal funding for the VFC has meant that states are no longer under any obligation to purchase childhood vaccines with their own Medicaid budgets.\textsuperscript{168} Many states have allowed VFC funding to replace or crowd out state funds that previously met the state's vaccine needs for providing children vaccines for the needy.\textsuperscript{169}

Since more than 50\% of vaccines are provided through the public sector, primarily through the VFC program, each vaccine that is added to the VFC entitlement has significant financial implications for federal spending.

\textit{Section 317 Funding}

The Section 317 program was established as a part of President Kennedy's VAA, also known as Section 317 of the Public Health Service Act. The

\textsuperscript{166} Ibid., 67.
\textsuperscript{167} "Vaccines for Children Program (VFC)".
\textsuperscript{169} Ibid., 45.
Section 317 funds are the backbone of the national immunization program and have played an integral role in helping achieve national immunization goals, including filling gaps in vaccine coverage, and planning and developing a national vaccination infrastructure.\textsuperscript{170} The greatest strength of Section 317 is its ability to adapt to the current needs of the states based on the development of new vaccines and the risks of disease outbreak. At first, the program was only established to promote public funding of polio, diphtheria, tetanus, and smallpox vaccines, but it has evolved with the addition of new vaccines. Each fiscal year, a new budget for 317 funds is determined and funds are allocated to each state based on their needs at the given time.\textsuperscript{171}

The Section 317 funds help support almost every element of the national immunization program, including granting awards to sixty-four immunization programs (all fifty states, the District of Columbia, five large cities, five US territories, and three Pacific-associated states) to support the region’s healthcare workforce and mechanisms for providing immunizations to these region’s citizens. It also plays a role in funding educational techniques, promoting public awareness, addressing vaccine shortages, and responding to potential outbreaks.\textsuperscript{172}

A majority of Section 317 funds are used on infrastructure activities. The rest of the funds, about 34%, are used to fill in the gaps for individuals that do not have access to public vaccines and for rapidly responding to potential

\textsuperscript{170} “Protecting the Public’s Health: Critical Functions of the Section 317 Immunization Program—a Report of the National Vaccine Advisory Committee,” \textit{Public Health Rep} 128, no. 2 (2013).
\textsuperscript{171} Ibid.
\textsuperscript{172} Ibid.
outbreaks of vaccine-preventable diseases. Specifically the populations that the Section 317 funds work to address are uninsured or underinsured adults. Adults are a particularly vulnerable population when comes to immunization coverage because they are not VFC-eligible, may not have total immunization coverage on their private insurance plan, and also may not qualify for their state Medicaid health coverage. The Section 317 funds are used to address this unmet need and to ensure that adults have adequate access to vaccinations.\(^\text{173}\)

The Section 317 funds for vaccine purchase are directly influenced by the recommendations of ACIP, as the advisory body of the CDC. According to the Federal Code of Regulations, the CDC has authority and responsibility over all 317 funds.\(^\text{174}\)

\textit{Private Insurance}

Many people receive vaccines through their private health insurance plans. Until recently, there were no standards about which vaccines needed to be covered by private insurance plans. This was a major problem because it meant that individuals with health insurance still did not have adequate access to vaccines. This was addressed by President Obama’s ACA.\(^\text{175}\) The ACA mandates that starting on September 23, 2010, all private insurers that were not grandfathered-in were required to cover all immunizations recommended by the

\(^{173}\) Ibid.
\(^{174}\) Ibid.
\(^{175}\) Orriel L. Richardson Alexandra M. Stewart, Marisa A. Cox, Katherine Hayes, Sara Rosenbaum, "The Affordable Care Act: U.S. Vaccine Policy and Practice," Health Policy (The George Washington University Medical Center School of Public Health and Health Services, 2010), 1.
ACIP without cost sharing or deductibles. “Grandfathered plans” include state regulated health insurance coverage that were already being sold in individual or group markets when the ACA was signed, although a plan may lose its grandfathered status if it makes significant changes to its coverage plan.176

As stipulated by the ACA, private insurers are required to provide the recommended vaccines to their enrollees within one year of a new vaccine’s recommendation by the ACIP. These vaccines should be available to patients for free through their medical home. The caveat to this is that a provider is not required to cover an immunization that is provided for an enrollee by an out-of-network provider.177 This Act has significantly increased the private insurance market’s expenditures on vaccinations in the United States.

The federal government does not have direct control over vaccine coverage provided through private insurers. However, as more and more plans lose their grandfathered-status, the scope of the ACIP’s influence over private insurance plans will continue to increase.

**Medicaid**

Many low-income individuals throughout the nation receive health insurance through their state’s Medicaid Programs. All US citizens below the federal poverty line (FPL) are eligible to enroll in Medicaid. However, in many states there are coverage gaps in populations that are not below the FPL and cannot afford private insurance or receive insurance though their provider. The

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176 Ibid., 5.
177 Ibid., 6.
ACA worked to address this by implementing the optional state expansion of the Medicaid program for all persons with family incomes under 133% of the FPL. This expansion would include coverage of immunization services for children and adults with no cost sharing or deductibles.¹⁷⁸

However, states are not required to opt-in to this expansion. The 2012 Supreme Court case, *National Federation of Independent Business v Sebelius*, declared the unconstitutionality of mandatory Medicaid expansion for the states. This limited the federal government’s ability to enforce Medicaid expansion and allowed states to make the choice to abstain without losing all of their federal Medicaid funding.¹⁷⁹

Medicaid funds for the provisions of vaccinations are used exclusively for adults ages nineteen and older (children covered through Medicaid receive vaccines through the VFC entitlement). The eligibility requirements for Medicaid will vary by state depending on whether the state has chosen to opt-in to the Medicaid expansion program. States are also able to make their own discretionary decisions about which vaccinations to cover through their Medicaid programs. While most states have at least partial coverage through Medicaid, they may not choose to cover all ACIP-recommended vaccines.¹⁸⁰

¹⁷⁸ Tan, "Impact of the Affordable Care Act (Aca) on Immunizations- Opportunities and Challenges".


Medicaid is funded through a mix of state and federal money. The amount of federal dollars allocated to each state for Medicaid expansion is calculated using the Federal Medical Assistance Percentage (FMAP). Since the federal government is not allowed to enforce Medicaid expansion, the ACA enacted an FMAP incentive to encourage states to opt-in, which would increase the allocation of federal dollars to that state significantly. The states that accept this incentive have to expand their Medicaid programs to cover all adult beneficiaries on all ACIP-recommended vaccines without cost sharing.\textsuperscript{181}

Prior to the ACA the public sector didn't really play an important role in administering adult immunization nor were there any financial incentives to health care personnel for providing the vaccines. Since adult vaccinations are often quite expensive, these barriers often discouraged providers from administering adult vaccinations. The expansion of Medicaid is an effort by the federal government to address the barriers to adult vaccination. The ACA also includes increased funding of immunization programs through the Public Health Service Act, and the expansion of Community Health Centers to increase access to immunizations for medically underserved adults at low cost.\textsuperscript{182}

\textit{Medicare Part B and Part D}

The ACA also expands coverage of immunization activities for older adults through Medicare. To be eligible for Medicare you must be a US citizen ages sixty-five or older. The expansion of Medicare benefits under the ACA

\textsuperscript{182} Ibid., 31.
stipulates the addition of preventive benefits to Medicare Part B, including full coverage of some immunizations that are administered at outpatient departments. The vaccines covered by Medicare Part B include pneumococcal, influenza and Hepatitis B vaccines. Beneficiaries of Medicare Part D can receive coverage for all immunizations. However, both Medicare Part B and Part D require monthly premium payments from the beneficiaries and therefore may not be accessible for all elderly adults.\textsuperscript{183} The ACIP has limited influence over these funds. However, this may change if the number of adult vaccines increase.

\textit{State Funds}

Instead of being purely reliant on Section 317 funds, states may choose to supplement their immunization programs with their own funds. The ACA encouraged the use of state funding by authorizing states to purchase adult vaccines at CDC-negotiated discount rates from vaccine manufacturers.\textsuperscript{184} States are not required to use their own funds for covering vaccine coverage. This is a discretionary choice by the state. However, as the number of adult vaccines increase there is a push towards supporting infrastructure for providing vaccines.

\textit{Manufacturer Assistance Programs}

Some vaccine manufacturers may choose to supplement adult immunization gaps by providing free vaccines through Manufacturer Assistance Programs.

\textsuperscript{183} Ibid., 16.
\textsuperscript{184} Ibid., 23.
Programs. Pharmaceutical companies with large manufacturer assistance programs include Merck, Pfizer, and GlaskoSmithKline. These programs are indirectly led by ACIP recommendations as they are privately funded and ultimately at the discretion of the manufacturer.185

**ACIP decision-making**

ACIP’s recommendations have extensive financial implications on state, federal, and private spending and therefore it is essential that the committee consider a vaccine’s cost in its deliberations. As was outlined in chapter one, the ACIP has standardized procedures for the presentation of economic data in its deliberations.186 However, in spite of the immense implications of the ACIP’s recommendations on national expenditure, cost of vaccination has so far not been used as a gating technique for recommending vaccine recommendations.187

It has been suggested in the past that the ACIP does not necessarily have the most effective process for considering cost in its recommendation process, given the potential financial impact. An investigation conducted by the Committee on the Evaluation of Vaccine Purchase Financing in the United States of the Institute of Medicine (IOM) outlined some of the limitations of the ACIP’s system in 2004.

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185 "RxAssist," http://www.rxassist.org/.
186 Tracy Lieu, "Guidance for Health Economics Studies Presented to the Advisory Committee on Immunization Practices (ACIP)," 2.
187 Dempsey et al., "The Role of Economic Information in Decision-Making by the Advisory Committee on Immunization Practices."
One major flaw identified by the IOM was that the ACIP’s recommendation process happens before the government purchase price has been negotiated with the manufacturer, but Medicaid and VFC providers are expected to provide the vaccine to beneficiaries within ninety days of vaccine licensure. Federal dollars cannot be provided until this price has been negotiated and sometimes state funding may not cover the entire price of the vaccine. This may mean that providers end up privately purchasing the vaccine at full price. Most states will reimburse clinicians for vaccines provided to Medicaid patients, but most will not for VFC patients. This can mean that providers are not properly reimbursed after the discounted price has been negotiated.\footnote{188} As vaccine prices rise, shouldering this cost can become a huge financial liability for providers.

Another problem is that the ACIP makes cost evaluations before knowing what the federally-negotiated price of the vaccine will be. Although economic experts can estimate this, the lack of this knowledge is just another barrier to producing accurate cost estimates.\footnote{189}

The IOM’s evaluation postulated that the ACIP’s influence had extended far further than was originally intended, “[wielding] power beyond its mission, design, or authority.”\footnote{190} The committee now does much more than just making vaccine recommendations. It also plays a pivotal role in determining vaccine markets, affecting vaccine prices through consideration of cost-benefit thresholds, and influencing federal, state, and private expenditure. This

\footnote{188 Frank Sloan, \textit{Financing Vaccines in the 21st Century: Assuring Access and Availability}, 59.}
\footnote{189 Ibid.}
\footnote{190 Ibid.}
investigation suggested that the committee’s current practices for evaluating cost in the recommendation process were not adequate given the immense implications.\textsuperscript{191} However, this conclusion is complicated by the federal government’s commitment to providing access to vaccines for all, a role that has been articulated through years of immunization policy in the US.

The ACIP’s role in determining national expenditure, as well its ability to guide state policy, is critical to understanding the scope of the committee’s influence. These immense implications reinforce the necessity of the ACIP’s commitment to transparency, evidence-based science, and nonpartisanship in order to produce the strongest possible recommendations. The important implications of ACIP’s recommendations highlight the necessity of continual surveillance and scrutiny of its process.

\textsuperscript{191} Frank Sloan, \textit{Financing Vaccines in the 21st Century: Assuring Access and Availability.}
Imagine a hypothetical situation: You are a parent of an eleven-year-old girl. She is the light of your life. She loves singing and reading sci-fi novels. She wears the same dirty sneakers no matter how many times you plead with her to let you buy her new ones. She is still a picky eater and will never eat the dinners you make her and instead asks for Annie's Mac and Cheese. She can now walk to her friends' houses alone and she never wants you to walk with her. Even though she sometimes acts like a preteen, she giggles whenever you tickle her and she still crawls into your lap occasionally when she is scared or tired. You can't believe how fast she's growing.

You go to her annual physician check-up and the doctor tells you that the next time she comes he recommends that she receive the Gardasil vaccine. He explains that the Gardasil vaccine protects against four different strains of the human papillomavirus (HPV), a very common sexually transmitted infection (STI). If it is not naturally cleared by the immune system, HPV can persist and become cervical cancer, anal cancer, oropharyngeal cancer, or genital warts. He tells you it is important that your daughter receives the vaccine before she becomes sexually active so that she doesn't have the opportunity to contract the infection. He gives you a Vaccine Information Statement (VIS) for you to read later. It is up to you whether or not you want your daughter to receive the
vaccine, he says. Your state’s laws do not mandate it for school-entry. But he highly recommends that you do so.

Later that night you go home and empty your purse onto your nightstand. You find the VIS statement that you had unceremoniously shoved into one of the pockets. In the back of your head you remember a Facebook status posted by one of your coworkers. You scroll back through her page and find the status. It’s a link to an article on herbs-info.com, stating that the one of the lead developers of the Gardasil Vaccine was now warning parents about the dangerous link between the vaccine and serious adverse events. Your coworker laments:

“Just read this and saw venous thrombosis as one of top risks – [my older daughter’s] blood clot was a venous thrombosis and she received the HPV vaccine. I think we’ll be skipping it for [my younger daughter]! Thought I should share this.”

You click on the link and skim the article. You are getting a little nervous at this point. Did this really cause her daughter to get a blood clot? You go on Google to find out more. What you find shocks and terrifies you: an onslaught of horror stories about the vaccine; articles and blogs claiming its dangers: seizures, extreme fatigue, stomach pain, even death. Each site you click on seems to give you conflicting information. Some assure the vaccine’s safety and efficacy, while others profess its menace. You start to panic. Are you really going to let your daughter receive this vaccine? If you do, are you putting her at extreme risk?

What would you do?
The Internet is inundated by anti-vaccine horror stories such as these: links on Facebook, YouTube videos, blogs, and sites posing as legitimate sources of medical information (such as the National Vaccine Information Center). On the Internet it is challenging to distinguish between a medical expert and a layperson with no experience. Every source on the web is given equal legitimacy- anyone from the radical anti-vaxxer, the conspiracy theorist, to the moderate critic. Parents trying to educate themselves about the risks and benefits of a vaccination for their children must try to differentiate the legitimate from the illegitimate often based on nothing more than their own perception of quality of evidence and gut instinct.

Sources on the Internet that promote the safety of vaccines (such as medical journals, the CDC, the FDA, and professional organizations), ground their defense in the legitimacy of scientific evidence, well-designed clinical trials, and continual safety surveillance data. But these defenses are sterile, unsexy, and forgettable in contrast to the traumatic tales of adverse reactions to vaccines. Even the most rational and well-educated parent may squirm after reading horror stories online. When it comes to your child’s safety, even the most well defended scientific source will never alleviate the fears triggered by a tale of tragedy.

The ACIP’s focus on evidence-based science struggles to overwhelm the persuasive anti-vaccine rhetoric, even from the most discredited, fraudulent, or unreliable source. The healthcare industry and the ACIP have struggled to
completely overcome these voices and convince parents of the safety and efficacy of vaccinations.

There is no single reason for the pervasive anti-vaccine rhetoric: opponents raise a complex amalgam of issues, including skepticism of the pharmaceutical industry and the government; a fear of putting “unnatural” substances into our bodies; and uncertainty about the urgency of vaccination given the low incidence of many vaccine-preventable infectious diseases. Unfortunately, the powerful sway of skepticism and fear will always be a fierce competitor of the scientific voice.

The ACIP, as the committee in charge of producing the recommendations that are regularly cited by public health and medical officials, recognize that its recommendations must withstand the public’s critical eye. In spite of the ACIP’s structural mechanisms to appeal to transparency, non-partisanship, and evidence-based science, these canons are not always enough to convince the public of the veracity of its decision-making.

The HPV vaccine has been particularly fraught with controversy since its initial licensure in 2006. HPV is the most common STI in the US, accountable for an estimated 6.2 million new infections each year at the time of the vaccine’s licensure.\(^{192}\) HPV refers to a group of 150 related viruses, which can be transmitted through skin-to-skin contact, or vaginal, anal or oral sex with someone who already has the virus.\(^{193}\) Most HPV infections are transient and


asymptomatic, quickly cleared by the immune system. However, the ones that persist are responsible for a variety of deleterious health effects. Most notoriously, infection with HPV is associated with cervical cancer, which infects about 12,000 women in the United States a year and kills almost 5,000.194

From the outset, it was clear that an HPV vaccine would present a unique set of challenges when being distributed to the public because it protects against an STI. Providing the vaccine meant acknowledging its connections to sex and sexuality. While it was strategically framed as an anti-cancer vaccine, carefully avoiding its linkage to the STI, the issue of sexuality was impossible to entirely circumvent. In addition, the extent of other the social complications that the vaccine would face were immediately not obvious. The HPV vaccine’s connection to sex, sexual orientation, and socio-economic status, to name a few (all topics that have been minimized if not completely silenced in society) further complicated the issue.

While the ACIP continued to make its recommendations framed by clinical trial and other quantitative data, its course was made more challenging by the actions of Merck, the public perception of the vaccine, and the complex social issues surrounding HPV. The HPV vaccine’s progress is indicative of a critical shortcoming of the ACIP’s structure. While the committee’s careful commitment to evidence-based science effectively allows it to present its recommendations as non-partisan, this strategy may have its limitations when faced with complex social issues. The intricacies of social dynamics are much

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194 Ibid.
more challenging to navigate when working within the confines of quantitative scientific data and an evaluation of risks versus benefits.

Contextualizing the complications and shortcoming of the ACIP’s recommendation process through a case study of the HPV vaccine illuminates the relationship between complex social factors and success of the ACIP. It elucidates the dynamic interplay between the committee and the social world; the way that the social context has shaped the priorities of the committee, and has both encouraged and impeded its progress, and the way that the committee has worked to navigate social factors within its restrictive framework.

This case study will be broken down into four sections. The first will be an examination of the events that led up to the vaccine’s development, including both the women’s health movement and the anti-vaccine rhetoric at the end of the twenty-first century.

The second is an examination of the ACIP’s recommendation process for the vaccine. This will be mostly an examination of the committee meetings that were involved in the decision-making as well as the judgments of risks versus benefits made by the committee.

The third section will be a description of the events that transpired soon after the vaccine’s licensure, specifically the actions of Merck (the developer of the Gardasil vaccine) and the public response to the company’s vaccination campaign. This will include a consideration of how Merck’s efforts to promote the vaccine ultimately were detrimental to the vaccine’s success.
The final section will be a critical analysis of the social factors that were at play throughout the ACIP’s deliberations over the vaccine. This illuminates both how external factors have guided the committee’s recommendation process and how the committee has navigated these factors.

Overall this case study demonstrates the ACIP’s structure in practice. It will never be sufficient to only consider this committee as a singular entity, or even to contextualize it in the historical events that influenced its emergence. The use of a case study gives a new dimension to understanding how the ACIP makes vaccine recommendations; it illuminates why it is so important that its structure is built upon its fundamental tenets; it demonstrates the influence of external factors on the success of vaccine uptake; and demonstrates the limitations of the committee’s structure.

Setting the Scene: Women’s Health and Anti-Vaccine Rhetoric

In 1997 The Washington Post reported, "Wall Street investors, the pharmaceutical and hospital industries and Madison Avenue marketers all agree: Women’s health care has become one of the hottest fields in medicine and marketing." In an abrupt shift at the turn of the century, women’s health went from clandestine to a top priority of the research industry. Women’s healthcare, a field that even as early as the mid-1980s was limited to essentially just reproductive care, had exploded to become an expansive field including menopause, bone deterioration, and diseases that primarily affect women.

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“Women's health is a big business,” said Florence Haseltine, a NIH researcher and co-founder of the Washington-based Society for the Advancement of Women’s Health Research, “I think it’s fabulous. These issues need to be taken seriously and the market will make sure they are.”

The whole healthcare field was beginning to hop on board the women’s health train, as it promised an untapped potential market. Large pharmaceutical companies, such as Pfizer Inc. and Eli Lilly & Co. began to focus on women’s medicine and formed women’s health care divisions in their offices; Procter & Gamble Co. donated $1 million to Columbia University to study heart problems and osteoporosis in women; Federal agencies, such as the DHHS, the NIH, the FDA, and the CDC all established offices on women’s health, working to concentrate federal money on the subject. While the motivation for this upsurge was primarily financial, driven by pharmaceutical companies and private investors identifying a huge emerging market, it did not mean that there were not going to be positive effects for those on the receiving end. For example, federal funding for breast cancer research rose from $75 million in 1989 to over $550 million in 1996. By 1999, the New York Times reported that pharmaceutical companies had devoted about a fifth of their total budget in the previous year ($12 billion) to products for women’s health.

During the 1980s and 90s, significant progress was made in women’s health at the federal policy level. The first formal federal action was in 1983,

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196 Ibid.
197 Ibid.
198 Ibid.
with the creation of the Public Health Service Task Force on Women’s Health Issues by the U.S. Public Health Service (USPHS).\textsuperscript{200} The Task Force’s first report, in 1985, issued the recommendation that women’s health issues be assigned an independent office within the DHHS.\textsuperscript{201} In 1986, in response to the DHHS Task Force, the NIH issued guidelines that, for the first time, recommended the inclusion of women in research studies funded by the NIH. However, this recommendation lacked real clout, as it instituted no mechanisms for following up on or reinforcing these guidelines.

In response to these toothless guidelines, female leaders in 1989 expressed their dissatisfaction to the Congressional Caucus for Women’s Issues. This prompted the General Accounting Office (GAO), Congress’s investigative agency, to launch an investigation into the reception of the NIH’s recommendation. Unsurprisingly, the investigation found that the effort had been a perfunctory attempt at increasing attention to women in clinical trials.\textsuperscript{202} The NIH policy had been poorly communicated, and impossible to implement.

The GAO report was a turning point in the women’s health movement.\textsuperscript{203} Released strategically to attract maximum attention from the public and media, it caused a dramatic shift in the focus of pharmaceutical companies in the next decade.\textsuperscript{204} The investigative report also triggered a fusillade of legislative action around women’s health. In 1990, the Office of Research on Women's Health

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\textsuperscript{201} Epstein, \textit{Inclusion: The Politics of Difference in Medical Research}, 75.
\textsuperscript{202} Nichols, "History of the Women’s Health Movement in the 20th Century," 59.
\textsuperscript{203} Epstein, \textit{Inclusion: The Politics of Difference in Medical Research}, 77.
\textsuperscript{204} Ibid.
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(ORWH) was established within NIH and charged with the mission of ensuring adequate inclusion of women in clinical research; this included a $625 million long-term Women’s Health Initiative study.\textsuperscript{205}

Other federal agencies were soon to follow with notable policy changes in the arena of women’s health. Congress allocated over $50 million to the CDC for women’s health program such as STI screening, Pap smears and mammography screening. In 1994 both the CDC and FDA created their own Offices of Women’s Health (OWH). The CDC’s OWH was charged with the role of leading and coordinating policies and programs related to women’s health, while the FDA’s was responsible for addressing gender disparities in drug research and administration policies.\textsuperscript{206,207} Finally, in 1993 the FDA eliminated the 1977 law that formally excluded ‘women of childbearing potential’ from many drug trials, which had been enacted to avoid harming a fetus if the women became pregnant while enrolled in the clinical trial, but had all but eliminated the option of including women in research because they were either too young or ‘at-risk’ of getting pregnant.\textsuperscript{208}

With this foundation in place, the focus on women’s health in clinical research gained ground at an unprecedented pace. From 1990 to 1994, Congress enacted over twenty-five pieces of legislation involving women’s health, many regarding education and management of women’s health issues.\textsuperscript{209}

\textsuperscript{205} Nichols, ”History of the Women’s Health Movement in the 20th Century,” 59.
\textsuperscript{206} Londa Schiebinger, ”Women’s Health and Clinical Trials,” \textit{Journal of Clinical Investigation} 112, no. 7 (2003).
\textsuperscript{207} Nichols, ”History of the Women’s Health Movement in the 20th Century,” 59.
\textsuperscript{208} Epstein, \textit{Inclusion: The Politics of Difference in Medical Research}, 45.
\textsuperscript{209} Schiebinger, ”Women’s Health and Clinical Trials.”
notable of these legislative pieces were the NIH Revitalization Act of 1993 and the publication of the *NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research*. Both worked to mandate requirements and set standards for adequate representation of females and minority groups in clinical trials.\(^{210}\)

With these major federal gains, the stage had been set for a dramatic spike in women’s health research and development. Sparked by the outcries of concerned activists and augmented by the pharmaceutical industry salivating over a huge emerging market, the women’s health industry boomed. According to a survey published by the Pharmaceutical Research and Manufacturers of America (PhRMA), there was a 75% increase in research on women’s health from 1991 to 1999.\(^{211}\)

Whether the motivations for the upswing were purely capitalistic or truly the result of a benevolent shift in the healthcare research field’s priorities, the consequence was an undeniable victory for the women’s health movement. As noted by a health care analyst in 1997, “Companies may tout themselves as being out to achieve the goal of helping women when, in fact, they are out to increase profits in an increasingly older population. The two are not incompatible, and in fact go hand in hand. Welcome to America.”\(^{212}\)

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\(^{210}\) Ibid., 975.
\(^{212}\) Day, “In a Fever over Her Health Care: Purchasing Power Drives This Medical Trend.”
This movement coincided with a shift in the medical rhetoric of the time, with the introduction of a new conception of group difference and the paradoxical relationship between the individual and group body. This is what Steven Epstein calls, the inclusion-and-difference paradigm; this new paradigm prioritized the inclusion of members of minority groups that had been historically underrepresented in clinical trials and the simultaneous study and measurement of the differences across (but not within) groups. This paradigm emphasized the individualization and generalization of the biological understanding of the body in terms of social, ethnic, and gender groups. It worked both to accommodate the idiosyncrasies of these group’s healthcare needs while also focusing on the generalization of biological processes within groups. This marked a notable shift from ‘one-size-fits-all’ medicine to a focus on the medically distinct bodily subtype, a practice that Epstein calls niche standardization: the rejection of the idea of a universal body in favor of a subgroup standardized body.

This shift established a new focus for the ACIP: the prioritization of group designation in the recommendation process. Previously all recommendations by the ACIP had universally targeted individuals within the recommended age group and had not focused on specific risk-group subpopulations (gender, race, behavior, etc.), but this movement allowed (if not encouraged) the subgroup recommendation.

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214 Ibid., 3.
Primed by this shift, the women’s health activism, and new legislation in the late 1990s, the HPV vaccine was poised for success. The HPV infection does not exclusively affect women, although it does biologically manifest differently between genders. The choice to do clinical trials exclusively on women was a strategic choice by Merck, quietly encouraged by the women’s health movement. Cervical cancer became the centerpiece of this movement not because it was the only malady related to HPV, but because of its gender-based risk.

Intuitively, it seems that the HPV vaccine would then be braced to succeed. The first anti-cancer vaccine to come onto the market, a women’s health tool at the peak of the women’s health movement, and primed by a new understanding of group difference—how could it fail? However, these were not the only factors at play when the HPV vaccine came on the scene.

The rise of the women’s health movement catalyzed the development of the HPV vaccine and charged it as a women’s health issue but it also coincided with changing public attitudes towards immunization. In the 1950s and 60s, vaccines were glorified – seen as saviors at the time – the most effective public health measure to come on the scene since antibiotics. But this lionization began to shift at the end of the century.

Three driving factors encouraged this change of attitude: public skepticism of the pharmaceutical industry, a number of well-publicized adverse reactions to vaccinations, and the Internet as an incubator for misinformation. Adverse events connected to vaccination gained huge media attention. The "Cutter Incident" of 1955, the influenza scandal in 1976, and the RotaShield
scandal were all a huge blow to the vaccine movement.\textsuperscript{215} All of these adverse events promoted public fear and mistrust of vaccinations and some people began to fear that the risks of vaccines might outweigh the benefits.

There were also many well-publicized cases of fraudulent scientific data being used to make extreme claims about the dangers of vaccination that terrified and riled up the public. Several allegations of the neurodevelopmental risks of the diphtheria-tetanus-pertussis (DTP) vaccine led to a series of lawsuits directed against vaccine manufacturers. The suggestion that the MMR vaccine was the cause of autism spectrum disorder gained significant traction among anti-vaxxers. There was also a huge amount of public skepticism about the safety of thimerosal, a mercury-derivative used as a preservative in many vaccines.\textsuperscript{216} Although these claims were continually disproven by extensive clinical trials, once the ideas were in circulation it was challenging to stop the spiral of misinformation and fear.

Skepticism of the pharmaceutical industry (particularly of the Gardasil developer, Merck) was also at a high point at the beginning of the twenty-first century because of the Vioxx Scandal of 2004. Merck withdrew its arthritis drug Vioxx from the market after studies began to indicate that it was linked to increased risks of cardiovascular problems. The FDA approved the vaccine in 1999 and by the time it was withdrawn in 2004 more than eighty-four million people worldwide had used the drug. There had been evidence indicating the possible link between Vioxx and heart problems as early as 2000, but Merck

\textsuperscript{216} Ibid., 286.
failed to follow-up on this disturbing evidence until four years later.\textsuperscript{217} Public health officials accused Merck of holding off on these clinical trials for fear of what they might find. Vioxx was one of Merck’s biggest blockbuster drugs and its loss would be a huge blow.\textsuperscript{218} This scandal perpetuated the public mistrust of the pharmaceutical industry and the perception of the industry as interested in financial gain, even at the expense of the public.

These discordant events preceded the HPV vaccine’s entrance into the market. The events that followed can all be understood more clearly with an understanding of the vaccine’s historical context. The successes and failures of the HPV vaccine campaign were all foreshadowed by the events that led up to the vaccine’s licensure.

**The ACIP’s Initial Recommendation**

Given the complicated environment in which the HPV vaccine was introduced, it was important that the ACIP instill public confidence in the vaccine through its recommendation process. As such, the committee’s deliberations over the vaccine were extensive, thorough, and carefully grounded in evidence of the safety and efficacy of the vaccine. Although there were undoubtedly social considerations involved in the ACIP’s recommendation of the vaccine (i.e. connection to STI), these factors were framed through a quantitative lens. The recommendation was strategically formed so that medical professionals, and the


\textsuperscript{218} Ibid.
public, could feel confident that it was based on expert consensus and strong scientific evidence.

The initial meeting of the HPV Vaccine Work Group was February 2004, two years prior to the licensure of the first HPV vaccine. The Work Group was chaired by Dr. Lauri Markowitz from the National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention (NCHSTP), and contained six other members, all from specialties related to cancer prevention and infectious disease control. The Work Group met regularly for a year before presenting at an ACIP meeting in June 2005.

There were two vaccine candidates under consideration at that first meeting. The first was Gardasil, developed by Merck & Co. The second was Cervarix, under development by British pharmaceutical company GlaskoSmithKline (GSK). While the vaccines were initially pushed as anti-cancer vaccines to prevent the acquisition of cervical cancer, their differences were notable. The GSK vaccine was a bivalent prophylactic vaccine, developed against the two most carcinogenic strains of HPV, types 16 and 18. These are considered high-risk strains, able to cause low-grade cervical cell abnormalities that are cancer precursors. The quadrivalent Merck vaccine contained 16 and 18, but

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also contained protection against HPV 6 and 11. The two additional strains are responsible for about 90% of genital warts.\(^{221}\)

Merck explained its choice to include these two additional strains at the first ACIP meeting. They explained that genital warts, while not fatal, could be very physically uncomfortable, psychologically damaging, and expensive.\(^{222}\) Beyond that, 6 and 11 can cause cervical intraepithelial neoplasia grade 1 (CIN-1) lesions that appear to be precancerous and can therefore be misconstrued as dangerous and incur extraneous costs in screening programs. The prevention of genital warts is also an important incentive for adolescent and young adult populations. Merck hoped that by reaching the larger population they would be able to accomplish an overall reduction in the risk of cervical cancer; CINs grade 1, 2, or 3; genital warts; and other vulvovaginal HPV-related lesions, and intraepithelial neoplasia (IN), whether anal (AIN), vulval (VIN) or vaginal (VaiN).\(^{223}\)

While the compositions of the vaccines were dissimilar, the market they were trying to fill was the same. The target populations for both vaccines were preteens and teens, ages nine to eighteen. As a prophylactic vaccine for an STI, both pharmaceutical companies recognized the necessity that the vaccination be administered before individuals become sexually active. The vaccine can only serve as a preventive measure, providing protection against future HPV

\(^{221}\) "Meeting of the Advisory Committee of Immunization Practices (ACIP), Summary Report, June 29-30, 2006," Atlanta, GA, Centers for Disease Control and Protection, Online. 65.


\(^{223}\) Ibid.
infection. It cannot function as a treatment for current infections. HPV is ubiquitous sexually transmitted infection, and is often contracted rapidly upon becoming sexual active. A study of college-aged students estimated that within 24 months after first intercourse, more than 39% of individuals were infected with HPV, and greater than 50% by 48 months. Most of these infections are transient, about 70% will clear within a year, but some may persist into precancerous lesions. Only by ensuring that the vaccine is administered prior to first sexual contact can full protection from the vaccine be guaranteed.

In the early 2000s, when the HPV vaccine was introduced, cervical cancer was the second most common cancer among women worldwide. Before the introduction of Papanicolaou testing (colloquially known as the Pap smear), invasive cervical cancer was the leading cause of cancer-related deaths in the United States. This dropped dramatically after 1955, when the Pap smear, which is able to detect precancerous lesions of the cervix, was introduced. Between 1955 and 1992, the rates of deaths associated with cervical cancer dropped 74%.

However, the Pap smear has its limitations. In 2007, a half-century after its inception, there were an estimated 11,100 new cases of cervical cancer and approximately 3,700 women would die from the disease in the United States.

While the Pap test is able to detect the presence of carcinogenic HPV-DNA types

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224 "Ibid.
226 Ibid.
227 L. Markowitz, et al., "Quadrivalent Human Papillomavirus Vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP)."
in the cervix, it does not indicate concrete evidence of consequent progression to cervical cancer. Also, the screenings must be conducted regularly to ensure efficacy and this requires regular access to medical care.

Even with the introduction of screening methods, cervical cancer and other HPV-related infection was still a major issue. The CDC’s National Cancer for Health Statistics measured approximately 10,500 cervical cancer cases and 4,000 deaths in 2002.\footnote{228} Also, cervical cancer screening had the unfortunate result of exacerbating the social and economic disparities of HPV-related disease. While survival is very high (nearly 100%) among women detected with early stage HPV-related disease before it becomes invasive, not all women have equal access to regular cervical cancer screening.\footnote{229}

The success of Pap smears in the prevention of cervical cancer is inherently correlated to socioeconomic status, thus making it dependent on adequate access to health care. Cervical cancer disproportionately affects the underserved, uninsured, under-screened and racial and ethnic minorities.\footnote{230} Data charted by the CDC’s National Health Interview Study (NHIS) from 2000 showed differences in Pap smear screening directly related to socioeconomic status. While the results indicated that 82% of all US women had a Pap test in the last three years, group differences emerged when it came to insurance

\footnote{228}{Dr. Herschel Lawson at, "Meeting of the Advisory Committee of Immunization Practices (ACIP), Summary Report, June 29-30, 2005," Atlanta, GA, Centers for Disease Control and Protection, Online. 66.}
\footnote{229}{Ibid., 66.}
\footnote{230}{"Meeting of the Advisory Committee of Immunization Practices (ACIP), Summary Report, February 21-22, 2006," Atlanta, GA, Centers for Disease Control and Protection, Online. 33.}
status; 85% of insured women were screened, versus only 62% of uninsured.\textsuperscript{231} The study also demonstrated the disparities within racial groups that seemed to be directly related to Pap access, with higher incidence and mortality in black and Hispanic women.\textsuperscript{232} The HPV vaccine advertised itself as a way to overcome this socioeconomic barrier. Given the large quantity of federal, state, and private funding that is channeled into supplementing immunizations, vaccinations could be a pathway to minimizing the stratification of cervical cancer prevention.

At the February 2006 ACIP meeting, Dr. Carolyn Runowicz, President of the American Cancer Society expressed her strong support for the ACIP’s approval of the HPV vaccine, noting that “not only is it historic as the first cancer vaccine, but it can help address cancer’s disparity.”\textsuperscript{233} The Director of Women’s Health at the Balm in Gilead (BIG) noted that African American woman have the highest burden of disease from cervical cancer and therefore urged the most comprehensive possible indications for the use of the vaccine, to ensure everyone would have equal access. The American Social Health Association (ASHA) urged the ACIP to make a recommendation for as broad an age group as possible and to encourage national outreach for vaccination and screening to ensure that underserved women would have access.\textsuperscript{234}

Merck’s clinical trials were conducted on over 20,000 women worldwide. The average age of the women tested was twenty and the average sexual debut

\textsuperscript{231} Dr. Herschel Lawson at, "Meeting of the Advisory Committee of Immunization Practices (ACIP), Summary Report, June 29-30, 2005,"
\textsuperscript{232} Ibid.
\textsuperscript{233} "Meeting of the Advisory Committee on Immunization Practices, February 21-22, 2006." 33.
was age seventeen. 75% of the women tested were naïve to all four HPV strains contained in the vaccine when the trials began. The endpoints used in these clinical trials were persistent infection, CIN, and external genital lesions due to one of the four strains of HPV in the vaccine. Cervical cancer was not used as an endpoint due to the ethical complications of using cancer as an endpoint and the amount of time that it would take to complete those trials since it takes many years for HPV to progress into cancer.\textsuperscript{235} Vaccine efficacy was 100% in women who did not contract HPV during the trials against HPV-related infection for the four strains in the vaccine. For women who did contract any of the four HPV strains during the trial, the vaccine efficacy was 95%.\textsuperscript{236} The safety profile of the vaccine was also favorable. The incidence of injection site reactions and low grade fevers were higher in the Gardasil group than the placebo group in clinical trials, but no concerning adverse events were identified.\textsuperscript{237}

In February 2006, the Phase III trials were terminated early for the HPV vaccine. The FDA had granted a priority review to Merck’s December 2005 application for licensure of the vaccine because of the overwhelming efficacy and safety demonstrated by the vaccine.\textsuperscript{238} The Data Safety and Monitoring Board (DSMB) determined that it was no longer ethical to withhold the vaccine from the placebo group in the clinical trials, and it was therefore mandated that they

\textsuperscript{236} Ibid., 15.
\textsuperscript{237} Dr. Eliav Barr, Merck &Co. at, "Meeting of the Advisory Commitee on Immunization Practices, June 29-30, 2006."
\textsuperscript{238} Ibid., 15.
receive the accelerated vaccine. There were still questions that remained at the termination of the clinical trials, but it was determined that the safety and efficacy of the vaccine seemed to outweigh the ambiguities that remained.

The major unanswered question at the termination of the trials was how long the vaccine-induced immunity would last. The clinical data to date had demonstrated that the antibody levels from the vaccine declined slightly from its peak after administration, plateauing to a level similar to antibody levels in women who have naturally cleared the infection. In 48 months of clinical trials, there were no documented cases of anti-HPV antibody levels declining to a point that individuals lost their immunity. However, if antibody levels continued to decline with time, there was still the possibility that individuals could be susceptible to infection again if they did not receive a second dose of the vaccine. This left the question unanswered of whether a future booster dose of the vaccine would be necessary to add to the schedule later.

During the public comment section of the ACIP's meetings, several public representatives came forward to express their approval for the vaccine. This included Ms. Amelia Toper, a survivor of cervical cancer who urged the ACIP to make a general recommendation for the vaccine, with no age restrictions. She explained how she had regularly received her cervical cancer screenings yet she was still diagnosed with cervical cancer. Her voice was one of many that

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240 Ibid.
241 Ibid.
expressed the urgency of the HPV vaccine, as a life-saving tool for women, men and children.242

This was not the universal opinion of the general public towards the HPV vaccine. There were still many who questioned the evidence presented by Merck about the safety and efficacy of the vaccine. One of these questions was whether Merck’s clinical trial techniques for measuring vaccine efficacy in their target age group were accurate and adequate. Merck’s huge international clinical trials were conducted in women ages nine to sixteen, an age group that was older than their target age group (i.e. pre-adolescents). Merck conducted trials in the older age group because of the challenges associated with demonstrating efficacy of the vaccine in the younger age group (before their ‘sexual debut’ and therefore before they are going to be exposed to the virus).

Merck used a strategy in their pre-licensure clinical trials to demonstrate efficacy in the younger population, called “immunobridging.” This technique looks at the immune response of the two different age groups by measuring their anti-HPV antibody concentrations. If the immune response in both age groups were the same (aka “non-inferior”) then it is determined that the efficacy of the vaccine would be the same in both age groups.243 Merck used this immunobridging strategy to demonstrate the efficacy of the immune response in girls nine to sixteen extrapolated from efficacy results in an older age group.244

The only alternative to immunobridging clinical trials in this context would be very-long-term efficacy data. It was decided that since the vaccine induced higher anti-HPV responses in children than adults, there seemed to be adequate evidence to bridge adult vaccine efficacy data to the younger population. However, the public perception of immunobridging was mixed. Although the scientific evidence seemed to conclusively indicate that the vaccine would be effective in both populations, many were still skeptical due to the fact that the clinical trials had not been conducted in the target population.

At the June 2006 meeting, the ACIP made their recommendations for the Gardasil Vaccine. They looked at data from Merck’s clinical trials and from economic modeling conducted by Merck researchers as well as economists independent of Merck. The ACIP chose to recommend the vaccine to females eleven to twelve years of age, with three doses of the vaccine. However, the vaccine series could be started in girls as young as nine at the discretion of the medical provider. There was also a catch up recommendation made for girls thirteen to twenty-six who hadn’t yet been vaccinated. Individuals in this age group may not get the full benefit of the vaccine because they may have already contracted one of the strains of HPV in the vaccine and, if so, the vaccine would confer no further protection nor would it have any therapeutic benefit.

The ACIP’s recommendation of the HPV vaccine was based on evidence from five years worth of clinical trials conducted by Merck and a thorough

247 Ibid., 17.
evaluation by the ACIP. The ultimate recommendation sent a clear message that, based on the evidence available, the benefits of administering the vaccine to preteen girls seemed to outweigh the risks presented by the unknowns at the end of the clinical trial. Although there were limitations in the evidence, the committee agreed that the evidence adequately supported the administration of the vaccine.

The recommendation cannot be entirely extricated from the goals of Merck and the pharmaceutical industry. Undeniably, the HPV vaccine’s development and gender-specific recommendation was driven by the lucrative women’s health market. The double-edged sword of the having a privatized pharmaceutical industry is that companies have incentive to develop drugs that will benefit them financially. This is exacerbated by the prioritization of evidence-based recommendations. Production of high quality evidence to meet the standards of scientific and medical consensus requires large-scale clinical trials, which are very expensive to conduct. The capitalist goals of the pharmaceutical industry can thus become the agenda behind the production of evidence that is used to make guidelines.\[^{248}\]

However, this does not counteract the potential benefits of the vaccine. While the evidence guiding the recommendations may have been catalyzed by the goals of the pharmaceutical industry, the people evaluating the evidence are an independent entity. The committee’s expert consensus about the HPV vaccine was that the evidence from Merck’s trials indicated the use of the vaccine.

The Early Years: Merck’s Mistake

The advertisement opens with the image of a teenage girl - her hair is matted into dreadlocks, and she is wearing a broad rim hat. She is rebellious, unconventional, and independent. She looks seriously into the camera and warns the viewer, “Each year in the US, thousands of women learn they have cervical cancer. I could be one less.” She lifts her skateboard to display the words “One Less” splayed across it and then makes her way down the skateboarding ramp. The ad continues with an eclectic crew of empowered young women: a soccer player, a basketball player, a drummer, a step team, representing a range of ages, and races. Also featured were the concerned mothers of these women. Together, these images were powerful; “strong representations of girls that seem to challenge dominant media representations and [the] appeal to mother’s protective instincts and to teen girl’s desire for rebellion.” All of these women promoting the message that they were taking control of their health and their bodies to ensure that they would not get cervical cancer by receiving the Gardasil Vaccine (See Appendix 8).

By 2007 one could not turn on a television or go to the theater without seeing advertisements for Gardasil. It wasn’t long before Merck’s campaign became iconic. With the dramatic tagline “One Less Girl,” the marketing

251 “Gardasil Commercial”
campaign was soon ubiquitous. Merck’s campaign was unique and ingenious. The girls and mothers represented in Merck’s advertisements were diverse, powerful, self-assured, while also being traditionally feminine.252 Merck’s strategy in their campaign was to instill the suggestion that young women are empowered with a "mastery over their bodies;" they are able to make the active choice to get vaccinated and to protect themselves from cervical cancer.253 This was coupled with the concerned and compassionate mothers who calmly describe the risks and benefits of the vaccine, subtly suggesting a maternal obligation associated with the vaccination.

The advertisements also strategically circumvented the vaccine’s connection to an STI, instead skillfully framing the vaccine as an anti-cancer vaccine. Merck knew from the outset that the vaccine would present a unique set of challenges; providing the vaccine meant that providers would be engaging preteens in conversations about sex and forcing parents to acknowledge the inevitability of their child’s sexual activity. Merck worked to strategically overcome this barrier by reframing the vaccine. Overall, the advertisements were a brilliant example of medical marketing.

The Gardasil vaccine came on the scene at what felt like lightning speed to many. The licensure of the vaccine was accelerated as a demonstration of the FDA’s commitment to making safe and effective vaccines available as quickly as possible, according the Director of the FDA’s Center for Biologics Evaluation and

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253 Branson, "I Want to Be One Less": The Rhetoric of Choice in Gardasil Ads," 148.
Research at the time.\textsuperscript{254} However, coinciding with the Merck’s aggressive lobbying and advertising campaign, many people felt that the vaccine’s expeditious entrance into the public was too fast.

The HPV vaccine has been particularly fraught with controversy since its initial licensure in 2006. Millions of girls had received the vaccine within years of the vaccine’s licensure. This left many people with the feeling uneasy about the sharp transition from “newly minted injection to must-have injection.” While Merck accredited the rapid uptake to its successful “education” campaign, some people felt that it was simply due to successful marketing.\textsuperscript{255}

After the HPV vaccine’s recommendation, there quickly arose the question of whether states should establish school mandates for the use of the vaccine. This would ensure rapid uptake of the vaccine among school-aged children and had the strategic advantage of utilizing an already established infrastructure for promoting vaccination. However, there was no clear consensus on whether this would be an appropriate strategy for the HPV vaccine.

ACIP voting member Dr. Rick Zimmerman argued that he could not support mandates for HPV vaccine in schools in the same way that he supports mandates for the measles or pertussis vaccine. The latter vaccines are highly contagious infections that can be transmitted through the air as well as through

\textsuperscript{254} Zawisza, "Fda Licenses New Vaccine for Prevention of Cervical Cancer and Other Diseases in Females Caused by Human Papillomavirus: Rapid Approval Marks Major Advancement in Public Health".

direct contact, posing immediate risk to all children in the classroom in the case of an outbreak. In contrast, HPV is an STI that can only be transmitted through intimate skin-to-skin contact that could hypothetically be prevented through behavioral choices and thus poses a less "urgent" risk. On the other hand, the goal of school mandates is not only to reduce transmission within schools. These laws also function as a safety net, “catching children who might slip through the cracks.” This could be particularly beneficial for the HPV vaccine because of the clear evidence that HPV-related disease primarily affects individuals of low socioeconomic status.

Although there was no consensus amongst medical and public health professionals about the propriety of school mandates for HPV, Merck had launched a massive lobbying campaign for HPV vaccine mandates even before the vaccine’s licensure. In 2005, Merck redeployed 1,500 of their sales representatives to marketing the vaccine and dramatically increased their donations to a variety of political campaigns as well as different women’s health interest groups. Merck’s HPV campaign began full force in 2006 with a huge nationwide lobbying campaign working towards implementing legislation in each state that would mandate vaccination for pre-teen girls. Merck also started their iconic “One Less Girl” advertising campaign. Initially, Merck’s campaign

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257 Dr. Julia Morita at, Ibid., 83.
seemed to be succeeding. Within a few months of the vaccine’s licensure Merck had sold about $80 million worth of the vaccine.\textsuperscript{259}

Merck’s campaign was met with praise from the pharmaceutical industry, providers, and public health officials, etc. Merck was awarded the title of ‘Brand of the Year’ from \textit{Pharmaceutical Executive}, a publication that follows current events in the pharmaceutical industry. The magazine praised Merck for their “[combination of] innovative science, strategic commercialization and savvy disease education” in the name of eliminating cervical cancer.\textsuperscript{260} The company was praised for skillfully turning a medical breakthrough into a campaign focusing on female empowerment.

Merck worked hard to convince state legislatures and policymakers to add Gardasil to the compulsory vaccine schedule in their states. One group that Merck lobbied particularly hard to influence was Women in Government (WIG), a nonpartisan political group that works to mobilize and empower female legislators.\textsuperscript{261} Members of WIG spoke at the ACIP in June 2006 and encouraged the ACIP to recommend the vaccine for the largest possible age group.\textsuperscript{262} WIG has a broad national influence and described how their “Challenge to Eliminate Cervical Cancer Campaign” had resulted in state legislatures introducing bills in forty-five states related to reducing cervical cancer (mostly bills regarding education or Pap smear access, as the HPV vaccine had not yet been licensed).\textsuperscript{263}

\textsuperscript{259} Ibid.
\textsuperscript{261} Fernandez Branson, "‘I Want to Be One Less’: The Rhetoric of Choice in Gardasil Ads," 153.
\textsuperscript{262} "Meeting of the Advisory Commitee on Immunization Practices, June 29-30, 2006," 15.
\textsuperscript{263} Gloria Lawlah at, Ibid.
However, in spite of Merck's efforts, not everyone was on board with mandating the vaccine. Conservatives and parent’s rights groups were nervous that mandating the vaccine would condone premarital sex and encourage sexual promiscuity in teens. Also, many people were skeptical of the vaccine because of its high price, $360 for the complete series, which at the time was the most expensive vaccine in history. Mandating the vaccine would consume an unprecedented amount of limited state and federal funds. Some people questioned whether Merck had enough clinical data to defend mandatory vaccination. There was skepticism about Merck’s immunobridging technique since it meant that only about 5% of the almost 25,000 patients tested were actually a part of their target age group. Also, some people felt that it was too soon after the vaccine’s licensure to implement state mandates. Traditionally vaccines had been in use for a longer period of time before they became compulsory.264

From 2006 to 2007, twenty-seven states and Washington DC considered legislation to mandate the vaccine, but none signed the mandate into law. In a controversial move, on February 3, 2007, Governor Rick Perry of Texas bypassed the legislature and signed an executive order mandating the vaccine. This made Texas the first state to implement compulsory HPV vaccination.265 The public was outraged and mystified by Gov. Perry’s actions. The mandate caught Perry’s constituents off guard, considering that historically his platform had focused on

264 “Flogging Gardasil.” 261.
The decision to mandate a vaccine that prevented an STI seemed shockingly out of character.\textsuperscript{266}

The greatest outrage however, came from Perry's ties to Merck. He had received $6,000 from Merck's political action committee during his previous election campaign. Perry's Former Chief of Staff, Mike Toomey, was a lobbyist for Merck. Even beyond that, his current Chief of Staff's mother, Texas Republican State Representative Dianne White Delisi, was the state director for WIG.\textsuperscript{267} The general public was livid with Perry's actions and Merck's blatant cooption of political representatives for their financial gain. Perry's financial and personal linkages to Merck demonstrated a fissure in the system, a clear demonstration of bias in the immunization system. In a social climate already poised to find examples of partiality in the system, this was an easy event to grasp onto as a reason to resist the HPV vaccine.

While the ACIP only briefly discussed Perry's actions in its deliberations, this was ultimately a moment of great consequence and a massive hindrance to the HPV vaccination campaign. Along with the general public's outrage at the executive order, the scandal also resulted in Merck's suspension of all of their lobbying activities. Merck representative, Dr. Rick Haupt, made a statement at the February 2007 ACIP meeting indirectly addressing the incident and the public response to the issue:

Merck's goal has been to have the broadest potential impact and use of this vaccine in the appropriate populations, especially underserved and poor populations, those missed in screening. As such, Merck supported

\textsuperscript{266} Ibid.
\textsuperscript{267} Fernandez Branson, "I Want to Be One Less": The Rhetoric of Choice in Gardasil Ads." 154.
school requirements initially at the state level, which increased funding and access to the vaccine. However, based on ongoing discussions with many different stakeholders and the perception this may be a distraction from getting women vaccinated, Merck is suspending its lobbying efforts for school requirements at this time. It will continue to provide information about HPV and the vaccines and advocate for public health programs that provide education about cervical cancer as well as screening and funding for vaccines at the state level.²⁶⁸

It seemed to be the general consensus that Merck and Perry had crossed a line and had created an uncomfortable and unreliable atmosphere surrounding the HPV vaccine, in spite of its benefits for public health. State Senator Janey Howell, who was actually a supporter of the bill noted that "she is comfortable with the public health benefits of mandating Gardasil. But she agreed that Merck's lobbying role complicated efforts to make that case."²⁶⁹

Although historically school mandates had been a successful strategy for increasing uptake of immunizations, Merck had not allowed for what the Association of Immunization Managers (AIM) call the “implementation period”: the time between licensure of the vaccine and the introduction of legislation. This period is critical because it ensures that the necessary infrastructure is in place to support a school requirement. This includes adequate insurance coverage for the vaccine in all private insurance plans, funding for physicians to purchase the vaccine; provider and general public acceptance and support; stable and adequate supply of the vaccine; and significant uptake of the vaccine in the recommended population in order to minimize the “compliance burden” on the school system (i.e. the potential challenges faced by school districts with

state mandates that must get many of their students vaccinated before they can let them attend school). By aggressively lobbying and expediting the legislative process, Merck circumvented this traditional implementation system, a detour that did not encourage confidence in the vaccine from the general public. As an editorial published in 2007 in *Nature’s Biotechnical Journal*, “in its rush to market its HPV vaccine, Merck forgot to make a strong and compelling case for compulsory immunization.”

The result of Merck’s aggressive marketing was the deterioration of the ACIP’s message that the recommendations were grounded in scientific evidence. Merck’s campaign sent the contradictory message that the HPV vaccine was being distributed purely for the financial benefit of the greedy pharmaceutical industry. The decision to mandate the immunization for school-entry, and even the recommendation by providers, was tainted by the huge media scandal. The public’s skepticism of the vaccine was reflected in the poor rates of coverage.

A year after the vaccine’s approval at least one dose had been administered to about one-quarter of US girls thirteen to seventeen. This coverage rate seemed encouraging, as it was similar to the coverage rates of other adolescent vaccines in their first year, such as the meningococcal conjugate or Tdap vaccines. However, unlike other adolescent vaccines, the coverage rates of HPV vaccine remained relatively stagnant over time. By 2012, only 53.8% of girls thirteen to seventeen had received at least one dose of the vaccine and only 33.4% had received all three doses. This is a notably low rate of

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271 "Flogging Gardasil," 261.
coverage compared to other adolescent vaccines that have achieved about 80% coverage rates within years of their recommendation.\textsuperscript{272}

These stunted coverage rates were also a problem unique to the US. Data from the United Kingdom showed that the country had achieved approximately 80\% coverage of the HPV vaccine by 2009.\textsuperscript{273} Clearly, something about the strategies for distributing the vaccine, and the public perception of the vaccine had fallen short in the US.

\textbf{The Role of Social Factors}

The legacy of the HPV vaccine is as much a story about what \textit{is not} talked about in the vaccine recommendation process as what \textit{is} talked about. The HPV vaccine was specifically marketed as an anti-cancer vaccine targeting cervical cancer. While it was not a secret that the vaccine was connected to an STI, this was never the focal point of the conversation. In some ways this made sense: ultimately the role of the vaccine was to prevent cancer and the other deleterious effects of HPV infection. But still, the marketing choices were more than a decision to try to avoid a conversation about the STI. The campaign was a strategic decision to avoid conversations about sex, sexual orientation, and sexual behavior.

Throughout this thesis I have worked to paint a picture of how the ACIP strategically structures the committee and its recommendations so as to

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\textsuperscript{272} Keith Wailoo et al., \textit{Three Shots at Prevention: The HPV Vaccine and the Politics of Medicine's Simple Solutions} (JHU Press, 2010).
\end{flushright}
encourage public confidence in vaccines. I have also tried to show how the historical and social context has shaped the strategies and priorities of the committee. Just as important to this conversation, however, is the consideration of what was not discussed or prioritized by the committee and the pharmaceutical industry. The language used to discuss the vaccine, the data available for review from clinical trials, and the conversations that did and did not happen in the committee meetings, were all dictated by social factors.

As a society, we struggle to openly talk about issues related to sex and sexuality; these conversations are minimized and stigmatized, and this discomfort was clearly demonstrated in the ACIP’s deliberations about the vaccine. The strategic marketing of the vaccine as an anti-cancer vaccine and even the vocabulary used by the ACIP did everything possible to minimize the sexualization of the vaccine. When discussing the concerns of parents that administering the vaccine would increase sexual activity, the term used by the representative from the Division of STD Prevention from the CDC was the possible "behavioral disinhibition" of teens as a result of the HPV vaccine.274 Instead of explicitly addressing the sexual activity of teens, these issues were tiptoed around, and strategically avoided using framing techniques such as careful word choices and marketing.

There was also the challenge presented by conversations about risk-based recommendations for the vaccine. Over time, the ACIP began to expand the recommended population to receive the vaccine, catalyzed by the expansion

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of clinical trials by Merck and GlaskoSmithKline in new populations. The first population under consideration was young adult females, ages twenty-six and above (the age group that would not be reached by the catch-up vaccination). It was rationalized by the GSK representative that most adult women were unlikely to have already contracted all the strains of HPV contained in the vaccine. While the peak incidence of HPV infection is ages fifteen to twenty-five, there are still emergent HPV infections in women of all ages. GSK argued that adult women are a population of unmet medical need and would likely benefit from the administration of the vaccine.

This begged the question of what the most effective strategy for implementing the vaccine to adult women would be. The option of universally recommending the vaccine did not demonstrate cost-efficacy because many adult women may not be at risk of contracting the infection and the vaccine is very expensive, $360 for a complete series. However the remaining options would be a risk-based recommendation (a recommendation for women with specific risk factors for contracting HPV) or a permissive recommendation (a recommendation that would functionally endorse the vaccine and allow providers to make discretionary decisions about who would benefit from the vaccine). The benefit of a permissive recommendation would be that it would allow the vaccine to be administered to adult women who may benefit from it, but the downside was that it would likely not be covered by insurance.

companies and may therefore not be available to women of low socioeconomic status who have the greatest need for vaccination.276

The risk-based approach would recommend the vaccine for adult women who have risk factors for HPV infection; namely sexual behavior, marital status, and socioeconomic status. Epidemiological data presented by the Division of STD Prevention at the CDC in February 2010 suggested that sexual behaviors are risks for infection with HPV. For example, based on studies of adult women over twenty-five, adult women engaging in online dating were more likely to have HPV. There was also a relationship demonstrated between incident infection associated with increasing lifetime sex partners, and marital status.277 The WG considered a variety of different targeted risk-based options, but ultimately decided that “it would be a major disservice to the use of this vaccine in the adolescent population if it became stigmatized to be used for certain risk-based socioeconomic.”278 However, this rationalization glazed over the full extent of the issues related to using a risk-based recommendation.

Using a risk-based approach would require targeting women for their sexual behavior, a complicated approach that would face a variety of issues. In another example of using language to avoid the sexual connotations of a topic, the WG described these barriers as “programmatic issues,” since it is challenging to identify women with particular sexual behaviors in a clinical settings.279 However the underlying reason that this cannot be used as a recommendation

276 Ibid.
277 Ibid., 20.
279 Ibid.
approach for the vaccine is far more complicated. Targeting women for their sexual behavior is a point of contention because of a long history in the United States of regulation of female bodies including stigma surrounding female sex workers, forced sterilization and contraception, and federal regulation of abortion, to name a few. Choosing to target women for their sexual behaviors would just contribute to the laundry list of moments in history when the government has overstepped its rights when it comes to regulation and control of female sexual bodies and behavior.

Ultimately, it was decided that there should be a permissive recommendation made for adult women, given the high cost of the vaccine and the minimal additional benefit of providing vaccine to adults. This recommendation was indicative of the limitations of evidence-based decision-making. In the quantitative evaluation of risks versus benefits, the risk-based recommendation was the most utilitarian strategy for providing the vaccine. This approach would ensure adequate insurance coverage of the vaccine and that the adult women who would benefit the most from the vaccine could have appropriate access. But the social considerations, the implications of making policy decisions based on sexual behavior, made this approach impossible. This consideration could not really be addressed in an evidence-based framework. The ACIP never openly addressed these issues in its deliberations, instead dutifully framing its recommendation in cost-benefit analysis and the defense of “programmatic issues.”
However, the greatest limitation of evidence-based recommendations is the necessity for high quality evidence, given that the pharmaceutical companies conducting the clinical trials dictate the production of this evidence. A recommendation cannot be made for a population that has not had extensive studies of safety and efficacy of the vaccine in that cohort. This was explicitly demonstrated by the trajectory of the HPV vaccine; the recommendations of the committee were blatantly driven by the choices made by Merck and GSK.

HPV infection does not only manifest in cervical cancer and it can have deleterious effects for men as well as women. Overall, the burden of HPV-associated invasive cancers in cancer registries data from 1998 to 2003 demonstrated approximately 15,000 cancers in females each year and 7,000 in men. A particularly concerning statistic was that the rate of anal cancer seemed to be increasing, at a rate of about 2.7% per year from 1992 to 2004. While overall incidence of anal cancer is higher in women (around 1.5 per 100,000) compared to men (1 per 100,000), data indicated that there was an increased risk of anal cancer in men who have sex with men (MSM, the term used in the ACIP proceedings).

Although anal cancer is a relatively rare disease in the overall population (about 2 in 100,000 people annually), among MSM, the rate of anal cancer is

280 Ibid., 133.
about 40 per 100,000. This rate is forty times greater in HIV-positive MSM, leading to about 80 cases per 100,000 cases annually. Anal cancer is caused by the same strains of HPV that cause cervical cancer, and therefore the Gardasil vaccine could provide prophylactic protection against anal cancer. Anal HPV is present in approximately 65% of HIV negative MSMs and 95% of HIV-positive MSMs. It can be spread through sexual skin-to-skin contact, and the use of condoms cannot completely eliminate the risk of contracting the infection.282

The FDA finally licensed the Gardasil vaccine for males in October 2009. At the October meeting, the ACIP made a permissive recommendation for the use of the vaccine in males. But still, the connection to anal cancer was not promoted in that recommendation. The vaccine was initially indicated for protection against genital warts, with no mention of the other potential downstream effects of HPV infection.283 A central factor that was emphasized in the initial recommendation for males was the fact that vaccinating males would reduce the potential for transmission of HPV among the entire population. A 2009 study demonstrated that the addition of male vaccination between ages nine to twenty-six would dramatically decrease the incidence of genital warts, cervical cancer, and other cancer-related deaths.284

Estimates of the cost-effectiveness of male-vaccination varied greatly, and some models indicated that, perhaps, improving vaccination coverage of females would be the more cost-effective strategy for reducing the overall burden of HPV

in the population. However, by choosing to recommend the vaccine only to women when the vaccine was demonstrated to be safe and effective for men, the ACIP would be sending a message that it was not the responsibility of the male population to protect their current or future partners.

The conversation surrounding the risks associated with HPV and anal cancer did not really become critical to the ACIP’s process until October 2010, with Gardasil’s presentation on their male clinical trials. At this point, there was only a permissive recommendation for the HPV vaccine for males. The results from Merck’s clinical trials indicated high efficacy of Gardasil demonstrated against HPV 6, 11, 16 and 18-related HPV persistent infection and disease at multiple anogenital sites (cervical, vulvar, vaginal, anal and genital warts).

Again, there was the question of the best strategy for recommending the vaccine for men. The option of making a targeted recommendation for MSM was complicated because this would necessitate that physicians have a conversation about sexual orientation with preteens before their sexual debut. This would be challenging to implement, considering that about 50% of physicians do not even routinely discuss sexual orientation with any of their patients. However, it was obvious that refraining from implementing a male recommendation would be an unacceptable strategy because it would mean that one of the highest risk populations to HPV-related infection would remain unvaccinated (also a

286 Ibid., 123.
287 Ibid., 128.
population that would be less likely to feel the spillover effects of female vaccination even if rates of coverage in females were to improve).

Representatives from LGBTQ, HIV and AIDS advocacy groups lobbied aggressively to the ACIP for them to pass a universal recommendation for adolescent males. As stated in a letter sent by thirteen representatives from different advocacy groups, “a recommendation to routinely vaccinate only MSM would require self-reporting, a particularly sensitive issue among adolescent boys who may fear stigma from disclosing same-sex behavior and may result in missed opportunities to vaccinate those at increased risk of anal cancer... a vaccine exists that can decrease stigmatized and painful diseases from development in thousands of people.”

The WG ultimately decided it was not feasible to target young adolescent men based on their sexual orientation and instead a universal recommendation was made for all males aged eleven to twelve. Although this was made with the caveat that, for older males through age twenty-six that have disclosed their sexual orientation, "HPV vaccination could be recommended or a strong guidance provided." This risk-based approach was considered to be more feasible in adult men because of the increased likelihood that they may be open about or aware of their sexual orientation.

So why was cervical cancer the centerpiece of the original HPV campaign instead of the other HPV-related cancers? As I have demonstrated, the choice to frame the HPV vaccine as an anti-cervical cancer vaccine was driven by the

lucrative women's health movement. However, the complete answer to this question speaks directly to the stigmatization of certain health issues in society, and on an even bigger scale, the silencing of conversations about sex and sexual behavior in policy and health. Cervical cancer is an easy cancer to talk about in a policy capacity. The cervix is not a part of the body that has been sexualized. Although it is technically a female reproductive organ, this element of the anatomy is not been used to talk about sex or sexuality. The conversation about cervical cancer does not trigger images of female genitalia. The associations with the cervix are more comparable to those of the kidney or gallbladder than with the vagina. The same cannot be said of the anus.

This high-risk association between anal cancer and HPV was known from the outset of the ACIP’s deliberations. Data shown at the October 2005 Gardasil presentation specifically noted that in MSM, HPV was responsible for about 70% of anal cancers.²⁹⁰ But in spite of this knowledge, Merck had strategically chosen to market the vaccine as a defense against cervical cancer.

The reason that the ACIP did not recommend the HPV vaccine to MSM at that first meeting was the selective body of evidence provided by Merck’s clinical trials. The vaccine could not be recommended for gay men in those early meetings because there simply was not enough clinical data on the issue to defend a recommendation. Neither GSK nor Merck had conducted extensive clinical trials in males, nor had there been any studies done of the vaccine’s prophylactic efficacy against anal cancer. Without this evidence, the ACIP would

²⁹⁰ “Meeting of the Advisory Committee on Immunization Practices, October 29-30, 2005,”
not and could not make a recommendation for MSM without compromising the integrity of its recommendation process.

The brings us to an argument made by historian of science Robert Proctor, who has contended that any study of epistemology (examining the production of knowledge) should also contain a study of agnotology, “the study of what we don't know and why we don't come to know it.”^291 When it comes to the agnotology of the inclusion of anal cancer in clinical trials related to HPV, the lack of knowledge is the result of “the ideological lineages that have been forged in recent decades between a medically marginalized group [MSM], a socially invisible organ (the anus), and a socially stigmatized practice (anal sex).”^292 Anal cancer was estranged from the conversation because of the epistemic politics of the pharmaceutical industry.

The limitation of evidence-based recommendations is the reliance on the data that is available and the motives of those responsible for producing the data. The ACIP is responsible for evaluating this data and making the best recommendations based on the evidence available, but the committee’s role cannot extend further. The committee cannot be both a scientific body and still be able to pass judgment on the quality of evidence, as this would be a blatant conflict of interest. But this dichotomy means that the ACIP is constrained by the evidence produced by those conducting trials. This does not make the recommendation process biased, nor does it invalidate the quality of evidence.

^291 Wailoo et al., Three Shots at Prevention: The Hpv Vaccine and the Politics of Medicine's Simple Solutions, 63.
^292 Ibid.
guiding the recommendations, but it does demonstrate the influence of social factors on the committee’s recommendation process.

The HPV vaccine is exemplary of the way social and historical events have contextualized and shaped the ACIP’s recommendations. The legacy of the vaccine should be a greater understanding of how these events have impacted and shaped public health policy-making and a lesson going forward about how to effectively disseminate vaccine recommendations. The successes and failures of the HPV vaccine highlight the role of external considerations, politics, and social values in the transition from evidence into policy by public health experts at the ACIP.²⁹³

“What is essential in mass psychology is the art of persuasion. If you compare a speech of Hitler’s with a speech of (say) Edmund Burke, you will see what strides have been made in the art since the eighteenth century. What went wrong formerly was that people had read in books that man is a rational animal, and framed their argument on this hypothesis. We now know that limelight and a brass band do more to persuade than can be done by the most elegant of syllogisms.”

—Bertrand Russell, *The Impact of Science on Society* (1951)
Conclusion

In late March of 2016, the public was anxiously awaiting the announcement of that year’s lineup for The Tribeca Film Festival, one of the largest film festivals in the country. However, the announcement was met by general shock and outrage as the festival had included in its lineup an anti-vaccine documentary, *Vaxxed: From Coverup to Catastrophe*. This documentary was made by Andrew Wakefield, one of the most famous anti-vaxxers of all time. The backlash was immediate: members of the scientific, medical, and filmmaking community were outspoken in their disapproval of the decision to screen the documentary. Within days, the board of the committee pulled the documentary from the festival’s lineup.294

The director of the film, Andrew Wakefield, is notorious for the paper he co-authored in 1998, published in the *Lancet*, which suggested a causal association between the measles, mumps, rubella (MMR) vaccine and autism spectrum disorder. In spite of the small sample size of Wakefield’s study, and its poor design, the paper achieved wide publicity and raised alarm amongst many parents.295 The study prompted a series of epidemiological studies to measure whether there was any validity in Wakefield’s claims. These studies unanimously showed that these claims were completely unfounded, and the result of

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fraudulent, falsified data.296 The *Lancet*, as well as ten out of twelve of Wakefield’s co-authors, completely retracted the paper in February 2010. The co-authors admitted that the data used to back their allegations was insufficient and was in no way indicative of a causal link between autism and the vaccine.297 Also, it was revealed that Wakefield had failed to disclose the fact that when he published the paper he was being funded by lawyers who were in the midst of anti-vaccination lawsuits; a clear conflict of interest.298 Wakefield has since had his medical license revoked and he is likely to go down “as one of the most serious frauds in medical history.”299

In spite of the complete retraction of the study, and the high volume of epidemiological studies refuting the allegation, the study has still had an immense impact on public perception of the MMR vaccine. The study was the origin of many parent's decisions to abstain from getting their children vaccinated out of fear of the risk of autism. This led to a dramatic reduction in immunization coverage of the MMR vaccine throughout the United Kingdom, Ireland, and the United States (to name a few). This led to measles outbreaks in all three countries.300 In 2012 in the UK, there were nearly 2,000 cases of

296 Ibid.
297 Ibid., 96.
299 Rao and Andrade, "The Mmr Vaccine and Autism: Sensation, Refutation, Retraction, and Fraud."
measles, an unprecedented number given the high efficacy of the vaccine.\textsuperscript{301} Clearly, the evidence presented by scientists that disproved Wakefield’s conclusion was not enough to entirely alleviate the fears of parents that the vaccine could cause autism.

A climactic turn of events took place in 2015 after a large measles outbreak that started at Disneyland in California. In response to the outbreak, Governor Jerry Brown signed in a new bill which eliminated the option for philosophical or religious exemptions from school vaccine mandates in California.\textsuperscript{302} This bill suggested an increased public understanding of the benefits of the MMR vaccine, and a universal rejection of the claim that the vaccine causes autism. But one year later we can see that this rhetoric is far from obsolete. The addition of \textit{Vaxxed} to the Tribeca Film Festival, one of the most well renowned film festivals in the US, demonstrates that in spite of all the evidence against Wakefield, and the outbreaks in CA, some people still believe in his claims.

\textit{Screening Vaxxed} at a venue as prestigious as the Tribeca Film Festival, gives legitimacy to Wakefield’s claim. Wakefield’s past disgraces, the refutation of his claims, even his financial stake in the issue, were not mentioned on the Tribeca Film Festival’s website or anywhere in the announcement about the lineup. Robert De Niro, one of the founders of the festival, defended his choice to include the film, “[My wife] and I have a child with autism and we believe it is

\begin{footnotes}
\item[301] Nancy Shute, "Fifteen Years after a Vaccine Scare, a Measles Epidemic," http://www.npr.org/sections/health-shots/2013/05/21/185801259/fifteen-years-after-a-vaccine-scare-a-measles-epidemic.
\end{footnotes}
critical that all of the issues surrounding the causes of autism be openly discussed and examined... this is very personal to me and my family and I want there to be a discussion, which is why we will be screening *Vaxxed.* The underlying message of De Niro’s statement and the Film Festival’s decision to include the documentary is that equal weight should be given to ‘all sides’ of the vaccine argument. This is nice in theory, but it ignores that reality not all arguments are built on the same quality of evidence.

At the core of this message is a prevalent modern ideology that rejects the possibility that there is an objective stance in the production of knowledge, that objectivity and scientific knowledge are, “merely a matter of elite consensus.” At the core is a deep suspicion of the sciences. This ideology is perpetuated throughout many institutionalized systems in the 21st century, in media, television, and even academia. This ideology questions the legitimacy of traditional ‘experts’ in the scientific community, and may actually prioritize personal accounts and parent testimonials over scientific data.

There is an inevitable disconnect between the ACIP’s strict adherence to evidence-based decisions and the widespread skepticism of the scientific method and expert evidence. As this ideology continues to dominate many of the leading sources of information (internet, media, academia), it is challenging for the ACIP to successfully gain the public trust using an appeal to scientific evidence.

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Parents are told that it is their responsibility as caretakers to become well educated in issues related to their children’s health, to become ‘informed consumers.’ Consumers strive to be empowered and knowledgeable, to use the tools at their disposal to make their own choices about their health. Informed consumers have autonomy over their own body and health. Unfortunately this is easily muddled by the conflicting and unreliable collection of information available.

The Internet and media are overrun with anti-vaccine information: personal horror stories, videos propagating the dangers of vaccines, and unbacked medical advice. There is no distinction between the information that comes from a single person and the entire scientific community. The Internet “flattens” these sources, presenting each with equal legitimacy. The Internet, social media, online communities etc. have become tools for promoting individual experiences as undeniable facts. In these outlets it is challenging to recognize the bias that shapes each source of information. Information from all sides will be given an equal opportunity to shape the consumer- anyone from the radical anti-vaxxer, the conspiracy theorist, and the moderate critic. Celebrities, such as De Niro, have coopted high profile spaces to share anti-vaccine information and give these claims legitimacy and influence that they would not otherwise have. Informed consumers must navigate this overwhelming amount

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of information and make decisions about what data they consider to be trustworthy based on their own judgments.

In conclusion, let’s come full circle and return to our home metaphor: We can all consider ourselves potential homebuyers. If we are committed to living in the best and strongest home possible then it is our responsibility to do our own research based off the best available evidence.

So too, with our evaluation of the recommendations produced by the ACIP: We should not just listen to the terrifying claims we read on the internet, or the advice of celebrities, or even blindly accept the advice given to us by medical professionals or the appeal to ‘consensus.’ We should be actively engaging with the evidence to make our own judgments about the safety and efficacy of vaccines and the integrity of vaccine recommendations.

I hope that this examination of the ACIP will leave us all with a new way of thinking about evidence: how it is produced and why it is produced. At the same time, I hope it will help us understand that not all evidence is created equal. While the ACIP may never be completely flawless, it has created a system for transparently evaluating quality of evidence, in order to produce the strongest recommendations possible, given the available evidence.
Appendix 1. ACIP Recommended schedule for children through age 18 as of January 1, 2016

Source: http://www.cdc.gov/vaccines/schedules/index.htm
Appendix 2. ACIP Recommended Adult Immunization Schedule as of January 1, 2016

Recommended Adult Immunization Schedule—United States - 2016

Note: These recommendations must be read with the footnotes that follow containing number of doses, intervals between doses, and other important information.

### Figure 1. Recommended immunization schedule for adults aged 19 years or older, by vaccine and age group

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>Ages (years)</th>
<th>ACIP®/OPV#</th>
<th>19-29</th>
<th>30-49</th>
<th>50-69</th>
<th>≥ 70</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>1 dose annually</td>
<td>1 dose annually</td>
<td>1 dose annually</td>
<td>1 dose annually</td>
<td>1 dose annually</td>
<td>1 dose annually</td>
</tr>
<tr>
<td>Tetanus, diphtheria, pertussis (Tdap)</td>
<td>Td booster annually</td>
<td>Td booster annually</td>
<td>Td booster annually</td>
<td>Td booster annually</td>
<td>Td booster annually</td>
<td>Td booster annually</td>
</tr>
<tr>
<td>Pneumococcal 13-valent conjugate (PCV13)</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
</tr>
<tr>
<td>Pneumococcal 23-valent polysaccharide (PPV23)</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>2 doses</td>
<td>2 doses</td>
<td>2 doses</td>
<td>2 doses</td>
<td>2 doses</td>
<td>2 doses</td>
</tr>
<tr>
<td>Meningococcal C vaccine or conjugate (MenC)</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
</tr>
<tr>
<td>Meningococcal A (MenA)</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
</tr>
<tr>
<td>Meningococcal W (MenW)</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
</tr>
<tr>
<td>Anthrax vaccine type B (ANB)</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
</tr>
</tbody>
</table>

Report all adverse events to the Vaccine Adverse Event Reporting System (VAERS). Reporting forms and instructions on filing a VAERS report are available at www.vaers.hhs.gov or by telephone, 800-822-7967.

Information on how to file a Vaccine Injury Compensation Program claim is available at www.hrsa.gov/vaccinecompensation or by telephone, 800-338-2382 (in a claim for vaccine injury). Contact the U.S. Court of Federal Claims, 717 Madison Place, N.W., Washington, DC 20001; telephone, 202-502-4498.

Additional information about the vaccines in this schedule, sources of available data, and comments about the recommended adult dose are available at www.cdc.gov/vaccines or from the CDC/HHS, National Center for Immunization and Respiratory Diseases (NCIRD), 1600 Clifton Rd., Atlanta, GA 30333, or by phone, 800-232-4636, in Eastern Time, Monday–Friday, excluding holidays.

Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

The recommendations in this schedule were approved by the Centers for Disease Control and Prevention’s (CDC) Advisory Committee on Immunization Practices (ACIP), the American Academy of Family Physicians (AAFP), the American College of Physicians (ACP), the American College of Obstetrics and Gynecologists (ACOG), and the American College of Nurse-Midwives (ACNM).

### Figure 2. Vaccines that might be indicated for adults aged 19 years or older based on medical and other indications

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>Indications</th>
<th>Doses</th>
<th>Administration</th>
<th>Interval</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>1 dose annually</td>
<td>1 dose annually</td>
<td>1 dose annually</td>
<td>1 dose annually</td>
<td>1 dose annually</td>
</tr>
<tr>
<td>Tetanus, diphtheria, pertussis (Tdap)</td>
<td>Td booster annually</td>
<td>Td booster annually</td>
<td>Td booster annually</td>
<td>Td booster annually</td>
<td>Td booster annually</td>
</tr>
<tr>
<td>Pneumococcal 13-valent conjugate (PCV13)</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
</tr>
<tr>
<td>Pneumococcal 23-valent polysaccharide (PPV23)</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>2 doses</td>
<td>2 doses</td>
<td>2 doses</td>
<td>2 doses</td>
<td>2 doses</td>
</tr>
<tr>
<td>Meningococcal C vaccine or conjugate (MenC)</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
</tr>
<tr>
<td>Meningococcal A (MenA)</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
</tr>
<tr>
<td>Meningococcal W (MenW)</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
</tr>
<tr>
<td>Anthrax vaccine type B (ANB)</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
</tr>
</tbody>
</table>

Source: http://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html
### Appendix 3. Liaison and Ex. Officio Representatives as of June 30, 2016

| Liaison representatives | American Academy of Family Physicians (AAFP), American Academy of Pediatrics (AAP), American Academy of Physician Assistants (AAPA), American College Health Association (ACHA), American College of Nurse Midwives (ACNM), American College of Obstetricians and Gynecologists (ACOG), American College of Physicians (ACP), American Geriatrics Society (AGS), America’s Health Insurance Plans (AHIP), American Medical Association (AMA), American Nurses Association (ANA), American Osteopathic Association (AOA), American Pharmacists Association (APhA), Association of Immunization Managers (AIM), Association for Prevention Teaching and Research (APTR), Association of State and Territorial Health Officials (ASTHO), Biotechnology Industry Organization (BIO), Council of State and Territorial Epidemiologists (CSTE), Canadian National Advisory Committee on Immunization (NACI), Department of Health, United Kingdom, Infectious Diseases Society of America (IDSA), National Association of County and City Health Officials (NACCHO), National Association of Pediatric Nurse Practitioners (NAPNAP), National Foundation for Infectious Diseases (NFID), National Immunization Council and Child Health Program, Mexico, National Medical Association (NMA), National Vaccine Advisory Committee (NVAC), Pediatric Infectious Diseases Society (PIDS), Pharmaceutical Research and Manufacturers of America (PhRMA), Society for Adolescent Health and Medicine (SAHM), Society for Healthcare Epidemiology of America (SHEA) |
| Ex officio representatives as of June 30, 2016 | Centers for Medicare and Medicaid Services (CMS), Department of Defense (DoD), Department of Veterans Affairs (DVA), Food and Drug Administration (FDA), Health Resources and Services Administration (HRSA), Indian Health Service (IHS), National Vaccine Program Office (NVPO), National Institutes of Health (NIH) |

Source: [http://www.cdc.gov/vaccines/acip/committee/members.html](http://www.cdc.gov/vaccines/acip/committee/members.html)
Appendix 4. MMR Requirements for Childcare 2007-2008

<table>
<thead>
<tr>
<th>State or Territory</th>
<th>Dosage Requirements and Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alabama</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Alaska</td>
<td>1 dose (on or after age 1 year)</td>
</tr>
<tr>
<td>American Samoa</td>
<td>1 dose (at age 15 months)</td>
</tr>
<tr>
<td>Arizona</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Arkansas</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>California</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Colorado</td>
<td>1 dose (by age 15 months)</td>
</tr>
<tr>
<td>Connecticut</td>
<td>1 dose (after age 1 year) or proof of immunity</td>
</tr>
<tr>
<td>Delaware</td>
<td>1 dose (measles after age 15 months; mumps and rubella after age 12 months)</td>
</tr>
<tr>
<td>District of Columbia</td>
<td>1 dose (after age 1 year); 2 doses (at age 4 years)</td>
</tr>
<tr>
<td>Federated States/Micronesia</td>
<td>Did not report requirements</td>
</tr>
<tr>
<td>Florida</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Georgia</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Guam</td>
<td>2 doses (age appropriate; after age 1 year; dose 2 between ages 4-6 years)</td>
</tr>
<tr>
<td>Hawaii</td>
<td>1 dose (at or after age 1 year)</td>
</tr>
<tr>
<td>Idaho</td>
<td>2 doses (age appropriate; after age 1 year; dose 2 between ages 4-6 years)</td>
</tr>
<tr>
<td>Illinois</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Indiana</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Iowa</td>
<td>1 dose (after age 1 year): measles and rubella; mumps not required</td>
</tr>
<tr>
<td>Kansas</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Kentucky</td>
<td>1 dose (after age 16 months)</td>
</tr>
<tr>
<td>Louisiana</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Maine</td>
<td>Required (age appropriate)</td>
</tr>
<tr>
<td>Marshall Islands</td>
<td>Did not report requirements</td>
</tr>
<tr>
<td>Maryland</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Michigan</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Minnesota</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Mississippi</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Missouri</td>
<td>1 dose (following ACIP recommendations)</td>
</tr>
<tr>
<td>Montana</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>N. Mariana Islands</td>
<td>2 doses</td>
</tr>
<tr>
<td>Nebraska</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Nevada</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>New Hampshire</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>New Jersey</td>
<td>1 dose (at age 16-19 months)</td>
</tr>
<tr>
<td>New Mexico</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>New York</td>
<td>1 dose (at age 1 year or earlier than 4 days before age 1 year); or proof of immunity must provider diag or pus sore test</td>
</tr>
<tr>
<td>North Carolina</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>North Dakota</td>
<td>Required (age appropriate)</td>
</tr>
<tr>
<td>Ohio</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Oklahoma</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Oregon</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Palau</td>
<td>Did not report requirements</td>
</tr>
<tr>
<td>Pennsylvania</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Puerto Rico</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Rhode Island</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>South Carolina</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>South Dakota</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Tennessee</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Texas</td>
<td>1 dose (age appropriate on or after age 1 year)</td>
</tr>
<tr>
<td>Utah</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Vermont</td>
<td>Required (age appropriate)</td>
</tr>
<tr>
<td>Virgin Islands</td>
<td>Required (age appropriate following ACIP recommendations)</td>
</tr>
<tr>
<td>Virginia</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Washington</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>West Virginia</td>
<td>1 dose (on or after age 1 year); measles and rubella; mumps not required</td>
</tr>
<tr>
<td>Wisconsin</td>
<td>1 dose (after age 1 year)</td>
</tr>
<tr>
<td>Wyoming</td>
<td>1 dose (after age 1 year)</td>
</tr>
</tbody>
</table>

Appendix 5. Effect of Pneumococcal (PCV) Vaccine on Costs of Childhood Vaccines

![Graph showing the effect of pneumococcal vaccine on costs of childhood vaccines]

Note: DTP = diphtheria and tetanus toxoids and acellular pertussis vaccine; DTPP = diphtheria and tetanus toxoids and whole-cell pertussis vaccine; HBV = hepatitis B vaccine; Hib = Haemophilus influenzae type b vaccine; IPV = inactivated poliovirus vaccine; MMR = measles-mumps-rubella vaccine; Var = varicella vaccine. Each bar represents attributable change in cost for the vaccines indicated. Bars of different shades distinguish costs for different vaccines in years in which more than 1 change in recommendations occurred. New combination vaccines are indicated with "/" in the vaccine name. All costs are in 2001 US dollars.

FIGURE 2—Changes in cumulative costs per child of vaccine series attributable to changes in recommendations.


![Graph showing cumulative cost of recommended vaccine series per child at public-sector prices, 1975-2001.](image)

Note. Vaccine series considered for children through age 6 years. All costs are in 2001 US dollars.

**FIGURE 1—Cumulative cost of recommended vaccine series per child at public-sector prices, 1975-2001.**

<table>
<thead>
<tr>
<th>Source of Funding</th>
<th>Private/Manufacturer Assistance Programs</th>
<th>Eligibility</th>
<th>VFC</th>
<th>Public/State</th>
<th>Medicare Part B</th>
<th>Manufacturer Assistance Programs</th>
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Appendix 8. Select images from Merck’s ‘One Less Campaign’
https://www.youtube.com/watch?v=hJ8x3KR75fA
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