Complex Science Society

A Guide to the Vaccination Debate

Contributors:
Students:
Annie Collier ’16
Robert Hammond ’16
Spencer Kennedy ’16
Takumi Matsuzawa ’16
Dylan Polcyn ’16
Muyang Sun ’16
Morgan Walker ’15

Project Manager:
Mojtaba Akhavantafti ’15

Faculty:
Dr. Tom Askew, Department of Physics
Dr. Eric Barth, Department of Mathematics
Dr. Mark Beougher, Department of Political Science
Dr. Max Cherem, Department of Philosophy
Dr. Péter Érdi, Department of Physics
Dr. Jennifer Furchak, Department of Chemistry
Dr. Laura Furge, Department of Chemistry
Dr. Gary Gregg, Department of Psychology
Dr. Ahmed Hussen, Department of Economics
Dr. Maksim Kokushkin, Department of Sociology
Dr. Christopher Latiolais, Department of Philosophy
Dr. Eric Nordmoe, Department of Mathematics
Dr. Thomas Smith, Department of Chemistry
Dr. Charles Stull, Department of Economics
Dr. Jan Tobochnik, Department of Physics
Dr. Amanda Wollenberg, Department of Biology

Fall 2014
Thanks to:
Michael McDonald- Provost
J. Ward and Mary Greiner- Grant Funding
Karla Aguilar- Program Coordinator of Arcus Center for Social Justice Leadership
Alison Geist- Director of the Center for Civic Engagement
Dr. Mark Largent- Associate Professor at Michigan State University
Dr. Douglas Homnick- Medical Director of
the Kalamazoo County Health and Community Services
Penny Born- Supervisor of the Immunization Area and Communicable Disease
Roxanne Ellis- Immunization Coordinator for Kalamazoo County
Dawn Smith- Immunization Coordinator for Kalamazoo County
Grace Kelley ’13- Former Student Researcher
Philip Mulder ’15- Former Student Researcher
Tyler Nichols ’15- Former Student Researcher
Introduction

Maintaining high vaccination rates in order to lower the risk of vaccine-preventable diseases is a constant struggle for public health officials in communities across America. This has been the case for officials since the inception of the smallpox vaccine in the 19th century (History of Anti-Vaccination Movements 2014), but the manner in which it is achieved has changed drastically over the years. In particular, the vaccine debate between patients, parents, and healthcare providers across the nation has developed over the past decade to create distinct and recognizable groups on both sides of the controversy. There are three distinct groups noticeable in parents today, all with varying degrees of opposition to vaccines:

“Individuals who have no specific objections to vaccines but are concerned because of the emotional, fervent rhetoric that they have encountered in the media and elsewhere, individuals concerned about specific vaccines or the recommended vaccination schedule who prefer a modified approach to vaccination, individuals with objections to all vaccines without exception, including those with religious or “philosophical” reasons for this position.” (Schwartz 2011)

The first group is the largest, including nearly 40% of parents in America; they are often referred to as “vaccine-anxious parents” (Largent 2012). These individuals play an important role in public health, because how they are treated by the many healthcare providers that come into contact with their child or themselves will determine whether they will or will not follow the recommended vaccination schedule. Whoever administers a vaccine to a patient is effectively its representative.

Just as there are multiple ways in which parents respond to vaccination, there are also multiple ways in which healthcare providers respond to those refusing vaccination. In this situation, health care providers have two principal alternatives: “either to document refusal and continue the doctor-patient relationship or to discharge the patient and direct them to seek care elsewhere” (Schwartz 2011). Doctors may refuse to see a patient refusing vaccination for a variety of reasons, but upon doing so they eliminate any opportunity to educate them further on the benefits of vaccination for themselves, their child, and their community.

In the United States, individuals and parents may be able to exempt themselves or their children from state required immunizations in three different forms. Depending on what their state laws permit and how they are interpreted, the forms are medical exemptions (50 states), religious exemptions (48 states), and philosophical, or personal belief (PBE), exemptions. (20 states) (“Vaccination Exemptions” 2014). Vaccination rates remain high in the U.S. Even after a decade of continual attention on the alleged risks of vaccines, Americans still overwhelmingly believe in the importance of vaccines (Schwartz 2011). The unique challenge that exemptions, especially PBEs, create for public health officials is the tendency of those who get them to cluster in one area (Omer 2006). Even if the vaccination rate in a state is high, a community with a large amount
of exemptions could compromise the herd immunity, putting many at risk (Omer 2008).

Though vaccines over the years have been proven to be an excellent form of preventative health care, the anxiety of those seeking exemptions is real and stems from a variety of sources, both credible and illegitimate. Healthcare providers must take the time to understand these individuals in order to quell the growing risk that PBEs pose to herd immunity in communities across America. This begs the question: what is the best way to approach individuals seeking exemptions and ensure that the community is protected from vaccine-preventable diseases? It is important to understand the roles of both healthcare providers and individuals seeking exemptions when addressing the debate. It is the purpose of public health officials to educate and protect their communities from communicable diseases. In order to do this they must first understand that it is the patient or guardian who decides whether or not to get vaccinated. This is a right that all Americans have, and by respecting this, healthcare providers will hopefully have some common ground between themselves and those who are anxious towards vaccines. It is also important to understand the overwhelming scientific evidence that shows vaccines as extremely effective and efficient with risks that are relatively minor and rare. No vaccine is 100% effective, but they have stopped the ravage of many diseases on our society and allowed us to progress to where we are today. Anti-vaccinators and vaccine anxious parents only want what is best for their children, as do physicians and all other healthcare providers.

Ultimately, the decision to vaccinate is up to the patient or guardian, and officials must take a very careful approach to educate the different groups of parents mentioned above rather than alienate them further. Creating a space in which proper education is provided in a friendly environment should be the goal of any healthcare provider facing a patient considering not vaccinating. Anyone that is opposed to vaccines should fully understand the risks they are taking for their child and community. The goal of this paper is to illustrate the importance of vaccines as an excellent preventative healthcare measure, explore how communities can design ways to work with those who are vaccine-hesitant, and bridge the perspectives of patients, parents, and healthcare providers to foresee a viable future for vaccines in public health.
Efficacy of Vaccine

Functions of the Human Immune System

The advancement of technology gave society the means to combat infectious agents that have long caused death, disability, and disease. Today, we have many treatments to fight against a particular disease such as antibiotics and surgeries, but no medical treatment in America has caused more uproar than vaccines. Why is this the case in a society that has seen so much progress in technology and science? Much research has been done on the immune system of the human body, infectious diseases, and vaccines. All of this research in conjunction demonstrates that vaccines are generally safe. Despite the statistically proven safety of vaccines, parents in America still have various anxieties about the safety of vaccines for their children.

Vaccines were developed even with limited knowledge of how the mammalian immune system functioned. The general requirement for a live vaccine was that the product was safe and effective at protecting the vaccinated if they were exposed to the disease sometime in the future. The mammalian immune system consists of two subsystems that are known as the innate immune system and the adaptive immune system. The innate immune system consists of specialized cells that include macrophages, neutrophils, natural killer cells (NKs), and dendritic cells (DCs), alongside various other products such as the cytokines; $\alpha$, $\beta$, and $\gamma$-interferons (IFNs), and proteins of the complement cascade (Plotkin & Orenstein, 1999). Parts of the innate system can be rapidly activated, which is necessary as the adaptive system can take several days to be activated. Furthermore, both systems are closely related. For example, the $\gamma$-interferon (an important activator of macrophages) (Schroder, Hertzog, Ravasi, & Hume, 2004) is produced by effector T cells of the adaptive system and natural killer cells of the innate system. On the other hand, the adaptive immune system developed later in evolution and has great specificity and memory. Both of these properties are a feature of a white blood cell type called the lymphocyte and are the features that the practice of vaccination depends on (Plotkin & Orenstein, 1999).

There are two separate responses within the adaptive immune system: the humoral response and the cell-mediated response. The humoral response consists of B cells that interact with the epitopes of antigens that enter the body. This interaction is the first step in a process that leads to the activation and differentiation of the cell that leads to an antibody-producing plasma cell and a memory B cell (Plotkin & Orenstein, 1999). Antibodies are secreted from the plasma cell and act independently of the cell, where they can neutralize antigens or tag them for degradation. The cell-mediated immune response is somewhat of a misnomer, as many processes in this response are instead mediated by a type of cytokine called an interleukin (IL), a type of protein that is involved in cellular signalling. B cells have receptors that respond to cytokines, but T cells are major producers and also have receptors for cytokines. T cells have three different types of receptors that allow their function: the specific T cell receptor
(TCR) which recognizes antigens presented by the antigen-presenting cell (APC), a receptor specific to the co-stimulator molecule expressed by the APC, and receptors recognizing different cytokines (Plotkin & Orenstein, 1999). The two main types of T cells express either CD4 or CD8 differentiation antigens and act as accessory molecules to the TCR. One role of CD4+ T cells is to help activate B cells, thus they are called T helper cells. There are two main types of T helper cells, namely Th1 and Th2 cells. These two helper cells are different because of the types of cytokines they secrete and their functions. Th2 cells help activate B cells and their subsequent differentiation into antibody-producing plasma cells. Meanwhile, Th1 cells help manage the delayed-type hypersensitivity immune response, exhibit antimicrobial functions against viruses, and give support to cytotoxic T lymphocytes (CTLs) and macrophages. On the other hand, CD8+ T cells have the capability to target and lyse infected cells, thus they are called cytotoxic T lymphocytes (Plotkin & Orenstein, 1999).

With the capability to prevent, reduce, control, and clear antigens, the immune system needs a way to distinguish between antigens that are foreign and antigens that are a part of the body. If the immune system attacks parts of the self, allergies and autoimmune disorders result. APCs recognize foreign antigens, which they endocytose for processing, and then display on their surface to activate other cells. Certain types of APCs include B cells and dendritic cells (Plotkin & Orenstein, 1999). B cells recognize a foreign antigen by the B cell receptor or a membrane-bound antibody, which allows them to engulf it, digest it, then display it to a Th2 cell. Furthermore, dendritic cells (DCs) constantly sample their surroundings for pathogens, and are highly capable of endocytosing antigens. The DC digests the antigen and then presents it to an immature T cell to activate it (Plotkin & Orenstein, 1999).

How Vaccines Work

All the information described above gives the basis for an immune response in the body. The same immune response is induced by a vaccine, but the response is not as involved as it is for a wild pathogen. Adjuvants are a component of a vaccine that help boost the functions of the immune system. Adjuvants work in many different ways such as: moving antigens towards the lymph nodes to allow T and B cells to have greater activity, providing protection to antigens, which allows the immune system response to be prolonged and thus allowing it to boost immune memory in the meantime, and adjuvants can induce the release of inflammatory cytokines to attract more T and B cells at the site of infection and also increase the frequency of transcription to create a net increase in the amount of immune cells (Plotkin, Orenstein, & Offit 2008). When a vaccine is injected into the body, the pathogen-associated patterns contained in the antigens attract DCs, monocytes, and neutrophils. If the antigens/adjuvants create enough danger signals, then monocytes and DCs are activated. This creates an inflammatory environment and causes the cells to change their surface receptors, allowing responses by other cells. The activated DCs next migrate towards lymph nodes, where
the activation of T and B cells occurs (Plotkin, Orenstein, & Offit 2008).

The activation of T and B cells by protein antigens in a T-dependent response results in the induction of an efficient B cell differentiation pathway through structures known as germinal centers (GCs). It is here where activated B cells can proliferate and differentiate into plasma cells or memory B cells. Inactivated B cells that are generated in the bone marrow circulate until they encounter an antigen to which they can bind. This antigen binding activates the B cell and drives the upregulation of CCR7, a chemokine receptor that causes the antigen-specific B cell to migrate towards the outer T cell zone of secondary lymphoid tissues (Plotkin, Orenstein, & Offit 2008). It is here where the antigen-specific B cells are exposed to recently activated DCs and T cells that contain upregulated surface molecules which provide B cell differentiation signals, driving the B cells into plasma cells that secrete low affinity antibodies. This is called the extrafollicular reaction. This reaction is rapid, and doesn’t last very long since the cells usually die from apoptosis in a few days, thus the extrafollicular reaction plays a minor role in vaccine efficacy (Plotkin, Orenstein, & Offit 2008).

Furthermore, antigen-specific B cells that obtain sufficient help from antigen-specific T cells instead proliferate in germinal centers. The induction of GCs occurs by the upregulation of CXCR5, a type of chemokine receptor, in antigen-specific B cells which then migrate towards follicular dendritic cells (FDCs). These FDCs play a major role in B cell responses by attracting antigen-specific B and T cells and capture antigens for long periods of time. B cells that are attracted by FDCs become the creators of GCs in which the antigen-specific B cells receive additional activation and survival signals from FDCs and follicular T cells. This allows the B cells to undergo massive clonal proliferation allowing them to differentiate into many plasma cells that then secrete large amounts of antigen-specific antibodies (Plotkin, Orenstein, & Offit 2008). The GC reaction results in a maturation of B cell affinity and results from a hypermutation process within the immunoglobulin genes. The development of the GC reaction requires a couple of weeks, such that the hypermutated antibodies specific to protein vaccine antigens first appear within the blood about 10-14 days after antigen exposure. It is the magnitude of the GC responses that controls the intensity of B cell differentiation into plasma cells, and thus the peak of vaccine antibodies to be reached about 4-6 weeks after immunization (Plotkin, Orenstein, & Offit 2008).

With the effects of primary immunization, it is a hallmark of the adaptive immune to be able to provide lifelong immunity against the same infection. When B cells differentiate during the primary T-dependent response, memory B cells are generated. These cells do not produce antibodies or in other words, they do not provide protection unless there is re-exposure to the same antigen (Plotkin, Orenstein, & Offit 2008). Upon re-exposure, the memory B cells differentiate into higher affinity, antibody producing plasma cells in a very rapid process. The memory B cells that are produced then migrate towards the extrafollicular areas of the spleen and nodes. The antigen-specific memory cells are more numerous and better fit than inactivated B cells by producing larger amounts of antibodies (Plotkin, Orenstein, & Offit 2008).

There are several requirements for successful vaccination and these are described
as:

1. The activation of APCs, involving the processing of antigens by the lysosomal or cytoplasmic pathways, the expression of co-stimulatory factors and chemokine receptors at the cell surface, and the secretion of certain cytokines.

2. The activation, replication and differentiation of T and B lymphocytes leading to the generation of large pools of memory cells of both types (Plotkin & Orenstein, 1999).

3. The incorporation of sufficient B cell epitopes to generate strong neutralizing antibody responses, and of T-cell determinants that bind with high affinity to at least the major regional HLA haplotypes so that the complex is recognized by the T-cell receptor.

4. The long-term persistence of conformationally intact antigen, preferably as aggregates complexed with antibody and held at the surface of FDCs in lymphoid tissues. This allows the continuing production of cells that secrete antibody of increasingly higher affinity, and of memory B cells (Plotkin & Orenstein, 1999).

Addressing Parents’ Concerns

As described in Mark Largent’s book, parents have various concerns about the effects of vaccines on their children. These concerns may be warranted, but most of them are misunderstandings about how vaccines and the immune system function. These concerns include, but are not limited to:

- We give too many vaccines too close together, overwhelming a child’s immune system
- Children’s immune systems are not capable of handling vaccines
- Not enough research has been done on the long-term effects of vaccines

Parents care deeply for their children and naturally worry about their child’s health and safety, but these worries about vaccines give way to misunderstandings of an infant’s immune system (Largent, 2012).

Neonates develop the ability to respond to antigens before they are born. They develop B and T cells by 14 weeks of gestation, which even express a large number of antigen-specific receptors. Despite this ability, when neonates are in utero they aren’t normally exposed to foreign antigens, thus many of their immune cells are inactive by the time they are born (Offit, et al., 2002). Furthermore, neonates are completely capable of generating humoral and cell-mediated responses to foreign antigens at birth.
Active immunity includes the full range of cell responses including: the B cell response, cytotoxic T cell responses, Th1 cells in the cell-mediated response, and Th2 cells that assist the B cell response. This early development of the immune system by a newborn is necessary to meet the environmental challenges that are faced at birth, thus it shouldn’t be surprising that a newborn has an almost fully developed immune system. The main deficiency that faces an infant immune system is the B-cell response to T-independent antigens such as polysaccharides that coat the surface of bacteria in Haemophilus influenzae type B and Streptococcus pneumoniae, for example. To overcome this limitation in the Hib and S pneumoniae vaccines, the polysaccharides are linked to proteins (such as diphtheria toxoid or tetanus toxoid) in order to activate the Th cells. By converting from a T-independent response to a T-dependent response, an infant’s B cells are capable of responding to conjugate vaccines and thus provide better protection than a natural immune response (Offit, et al., 2002). Some infants may be immunocompromised and if they receive live viral vaccines, they may develop infections with the attenuated antigens. However, children in the United States no longer receive a live viral vaccine until 12-15 months of age. Most children with severe T cell deficiencies will usually be diagnosed by 6 to 8 months of age (Offit, et al., 2002). Moreover, some parents believe that children with a mild illness are in a sense, immunocompromised, and if these children are vaccinated during this time then their immune systems won’t respond to the vaccine and may develop adverse reactions. They also believe that a child’s immune system shouldn’t be burdened with more infections. However, vaccine antibody responses and rates of adverse reactions due to vaccines in children with mild illness are comparable to those of healthy children. On the other hand, it is generally recommended for severe infections that a child is delayed in receiving a vaccines in order to prevent superimposing a reaction to a vaccine on top of a preexisting condition (Offit, et al., 2002).

Research done on the diversity of antigen receptors has shown that the immune system has the ability to respond to extremely large numbers of foreign antigens. Data shows that the theoretical capacity would allow for 10^9 to 10^11 different antibody specificities. Another way to show that a child’s immune system can diversely respond is by estimating the number of vaccines a child can respond to as described by Cohn and Langman (1990);

“If we assume that 1) approximately 10 ng/mL of antibody is likely to be an effective concentration of antibody per epitope (an immunologically distinct region of a protein or polysaccharide), 2) generation of 10 ng/mL requires approximately 103 B-cells per mL, 3) a single B-cell clone takes about 1 week to reach the 103 progeny B-cells required to secrete 10 ng/mL of antibody (therefore, vaccine-epitope-specific immune responses found about 1 week after immunization can be generated initially from a single B-cell clone per mL), 4) each vaccine contains approximately 100 antigens and 10 epitopes per antigen (i.e., 103 epitopes), and 5) approximately 107 B cells are present per mL of circulating blood, then each infant would have the theoretical capacity to respond to about 10 000 vaccines at any one time (obtained by dividing 107 B cells per mL by 103 epitopes per vaccine).”
Even so, most vaccines contain much less than 100 antigens and thus this is a very conservative estimate (Offit, et al., 2002).

Due to the more or less passive nature of vaccines, it is very difficult to determine the long term effects that vaccines pose. As such there hasn’t been much research done on the long term effects of vaccines due to this challenge and more research on the subject is always welcomed. Furthermore, the information that has been described is an introduction into the functions of the human immune system and its subsystems. Immunology is a very broad topic and contains a lot of detailed information, but the necessities to understanding vaccines and how they prevent disease are available. Concepts of immunology shouldn’t be overshadowed by the misunderstanding of parents, especially when the public health system is at risk.

Do Vaccines Work?

As new vaccines are introduced, it is necessary but difficult to determine whether the candidate vaccine prevent the diseases that it is designed to prevent. Some of those who refuse to get vaccines argue that vaccines are intended to act as placebo agents. In fact, a vaccine comes to market after it has been tested for safety and efficacy. The test begins with scientific modelling, followed by a series of animal and target population tests. (Largent, 2012).

A Mathematical Estimate

Vaccine Effectiveness (VE) is normally the measure used to examine the extent to which a vaccine is effective. Besides the efficacy of a vaccine, vaccination coverage, contact patterns, diagnostic performance and other factors that govern the transmission dynamics of infectious diseases also play roles in vaccine effectiveness (Omori, Cowling, and Nishiura, & 2012). Vaccine efficacy is often confused with vaccine effectiveness. Efficacy refers to whether the intervention can be successful when it is properly implemented under controlled conditions, whereas effectiveness refers to whether the intervention typically is successful in actual clinical practice (Marlowe, 2014).

Mathematical deduction of vaccine efficacy is nearly 100 years old. Vaccine efficacy is generally expressed as the following two formulas:

\[
Efficacy = \frac{ARU - ARV}{ARU} \times 100 \quad (1)
\]

\[
Efficacy = (1 - RR) \times 100 \quad (2)
\]

These two formulas would give the same outcome, yet they represent two different ways we understand vaccine efficacy. Eq.(1) stands for a proportionate reduction in disease attack rate (AR) between the unvaccinated (ARU) and vaccinated (ARV) study cohorts.
Eq. (2), however, shows that vaccine efficacy is calculated from the relative risk (RR) of disease among the vaccinated group (Weinberg and Szilagyi, 2010).

Vaccine efficacy measures how much antibody a vaccine could produce; vaccine effectiveness (VE), on the other hand, measures how the vaccine prevents diseases in real world. There are several studies designed to measure VE: 1) retrospective case control analysis-in which the rates of vaccination among a set of infected cases and appropriate controls are compared; 2) “indirect cohort” or “quasi-cohort” study, in which different responses in the same vaccinated population are used to examine vaccine effectiveness; 3) “case-coverage” or “case-cohort” method, in which vaccination rates among cases are compared with those in a similar cohort (which may include individuals who develop cases) over a defined period of time; 4) ecologic or observational in nature, examining changes in disease burden over time (e.g. before and after introduction of routine vaccination) (Weinberg and Szilagyi, 2010).

Health organizations and research groups commonly present vaccine effectiveness (VE) as a single point estimate: for example, 75%. This point estimate represents the reduction in risk provided by the vaccine. In addition to VE, a confidence interval (CI) is provided to give context for understanding the precision or exactness of a VE point estimate. Rather than relying on a single statistic as an estimate of VE, the CI gives a range of plausible values for VE. Thus, the wider the confidence interval, the less exact the point value estimate of vaccine effectiveness becomes.

Table 1: Vaccines and their efficacy

<table>
<thead>
<tr>
<th>Name of Vaccine</th>
<th>VE</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMR during 1999-2004</td>
<td>90%</td>
<td>88.8%-91.1%</td>
</tr>
<tr>
<td>“2009 H1N1” virus</td>
<td>62%</td>
<td>53%-69%</td>
</tr>
<tr>
<td>Seasonal Flu for 2013-14</td>
<td>61%</td>
<td>52%-68%</td>
</tr>
<tr>
<td>DTap (after second dose) in Germany during 1997-2000</td>
<td>91.8%</td>
<td>84.7%-95.7%</td>
</tr>
<tr>
<td>DTap (estimate after 4 dose) in Germany</td>
<td>98.6%</td>
<td>-</td>
</tr>
<tr>
<td>Polio (3+ doses) in Gambia in 1992</td>
<td>72%</td>
<td>57%-82%</td>
</tr>
</tbody>
</table>

VE and CI respectively stand for vaccination effectiveness and confidence interval.

Usually, there are many different outcomes for vaccine effectiveness studies. Results of studies may vary based on study design, population, and time and places in which the vaccine was studied. These differences can make it difficult to compare one study.’

---

1A data set was retrieved from http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6007a1.htm.
3A data set was retrieved from the following link. http://cid.oxfordjournals.org/content/35/2/162.long#cited-by.
4A data set was retrieved from the following link. http://www.who.int/immunization/polio_grad_opv_effectiveness.pdf
To address the efficacy of vaccine, a vaccine trial would be launched before the vaccine is licensed. A vaccine trial usually involves two groups from the target population and each individual may be randomly assigned to receive either a candidate vaccine or a control treatment. Researchers collect data on antibody production and health outcomes. Collected data would be processed through statistical software and final analysis would be shown within statistical discipline. A two-sided test is performed to see whether the observed differences in the results between the vaccine and placebo group could reach statistical significance level (usually, p-value=0.05). If the value is less than 0.05, the vaccine is effective. If the candidate vaccine is determined as non-effective, the researchers would figure out what makes the vaccine unable to work. At the same time, adverse effects of the vaccine will be considered whether to license it.

The outcomes in three groups is shown in the table below.

Table 2: Results of efficacy trials of RV144 in Thailand (Gilbert, Berger, Stablein, Becker, Essex, Hammer, Kim, DeGruttola, 2010)

<table>
<thead>
<tr>
<th>Efficacy trial</th>
<th>HIV risk group</th>
<th>Population</th>
<th>Nv(nv)</th>
<th>Np(np)</th>
<th>Estimated VE, %</th>
<th>95% CI</th>
<th>2-Sided P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV144</td>
<td>General population</td>
<td>ITT</td>
<td>8202(56)</td>
<td>8200(76)</td>
<td>26</td>
<td>-4 to 48</td>
<td>.08</td>
</tr>
<tr>
<td>Thailand</td>
<td>Mostly at risk</td>
<td>MITT</td>
<td>8197(51)</td>
<td>8198(74)</td>
<td>26</td>
<td>1 to 51</td>
<td>.04</td>
</tr>
<tr>
<td>Thailand</td>
<td>Heterosexual risk</td>
<td>PP</td>
<td>6176(36)</td>
<td>6336(50)</td>
<td>26</td>
<td>-13 to 52</td>
<td>.16</td>
</tr>
</tbody>
</table>

In statistical significance testing, the p-value is the probability of obtaining a test statistic result at least as extreme as the one that was actually observed, assuming that the null hypothesis is true. In this context of RV144, the null hypothesis is that there is no statistically significant difference in the infection rates between vaccine and placebo groups. In the MITT group, p-value is equal to 0.04, lower than statistical significance level (p-value=0.05), so it does reject null hypothesis. That means there was a statistically significant lower rate of infection in the vaccine group compared to the placebo group in MITT population. However, by the other two methods of analysis, there was no statistical significance in infection rates between the vaccine and placebo groups, with p=0.08 for the ITT population and p=0.16 for the PP population. That means there is no significant lower rate of infection in ITT and PP vaccine population vaccine. Though VE of the candidate HIV vaccine does not meet the requirements of vaccine license, its modest VE makes the vaccine be safe, well tolerated, and suitable for large-scale further research.

Each vaccine would undergo VE model estimate and statistical analysis before licensed. Just like famous “Thai Trial”, the candidate vaccine must pass a rigorous round of testing. Not all candidate vaccines are able to pass. Without a high estimate...
VE in computing model, there is not real clinic trial; If the VE in clinical trial does not reach the requirement of license, the tested candidate vaccine would not be put in use. So, there is great confidence in trusting licensed vaccines.

**Statistical Results**

Do vaccines work? Yes, the licensed vaccines do work. Vaccination is one of the greatest achievements in modern medicine and protect thousands of people from transmissive disease around the world.

National Network for Immunization Information website collected data as following:

1. Before 1985, Haemophilus Influenzae type b (Hib) caused serious infections in 20,000 children each year, including meningitis (12,000 cases) and pneumonia (7,500 cases). In 2002, there were 34 cases of Hib disease.

2. In the 1964-1965 epidemic, there were 12.5 million cases of rubella (German measles). Of the 20,000 infants born with congenital rubella syndrome, 11,600 were deaf, 3,580 were blind, and 1,800 were mentally retarded as a result of the infection. There were 9 cases of rubella in 2004 and only four cases of congenital rubella between 2001 and 2004.

3. Before 1963, more than 3 million cases of measles and 500 deaths from measles were reported each year. More than 90% of children had measles by age 15. In 2002, there were 44 cases of measles.

4. In 1952, polio paralyzed more than 21,000 people. In 2002, there were no cases of polio in the United States.

5. In the early 1940s, there was an average of 175,000 cases of pertussis (whooping cough) per year, resulting in the deaths of 8,000 children annually. In 2002, 9,771 cases were reported.

6. In the 1920s, there were 100,000 to 200,000 cases of diphtheria each year and 13,000 people died from the disease. In 2002, there was only one case of diphtheria in the United States.

With introduction of vaccines, many of diseases have been potentially eliminated. However, it does not mean we do not need vaccines any more. Without vaccines, there is the possibility for the diseases we are now protected from to return. At the same time, licensed vaccines have high effectiveness after being modeled and test, but they are not completely effective for 100 percent people.
Are the Benefits Worth It?

Even if vaccines work and do prevent disease, the next question to ask is whether or not these benefits are worth the costs. The way economists handle this type of question is to do cost-benefit analyses and find the benefit-to-cost ratio (BCR). Any BCR above 1 means that the benefits exceed the cost and that it is a worthwhile program.

Doing a cost-benefit analysis on vaccines is extremely difficult because coming up with all of the possible benefits and costs, let alone measuring them, can be difficult, but Fangjun Zhou has done an evaluation of the vaccination program twice, once in 2001 and once again in 2009. In these papers he included the cost of the vaccine, administrative cost, vaccine-associated adverse events, costs associated with travel, and work time lost due to getting the vaccination. Even with all of these costs in 2001 he found direct and societal BCR’s of 5.3 and 16.5 respectively and that in the worst possible scenario the BCR’s were 1.8 and 6.5 (Zhou 2005). In 2009 when redoing his analysis for the new schedule he found direct and societal BCR’s of 3.0 and 10.1 and that in the worst possible scenario that Zhou could find these values were 1.2 and 5.1 (Zhou 2014). Even in the worst possible scenario vaccinations are a program we should invest in, and in the best possible scenario it is one of the best public health investments ever implemented.

Similar analyses by other researchers have shown comparable results, although they typically have looked at specific vaccines rather than being completely comprehensive like these two papers. A cost-benefit analysis of the 2-dose MMR vaccine lead by Alan Hinman found direct and societal BCR’s of 14.2 and 26.0 (Hinman 2004). A 1997 analysis by Donatus Ekwueme of the DTaP and DTwP vaccines found a societal BCR of 27.0 (Ekwueme 2000). Another analysis done by Zhou, that looked specifically at the 2-dose varicella program, found a societal BCR of 2.73 (Zhou 2008).

In Zhou’s paper he also noted that “the BCR of 10.1 is substantially lower than the 16.5 noted in 2001” (Zhou 2014). The decrease is largely due to the introduction of three new vaccines added since 2001: PCV7, Hepatitis A, and Rotavirus. Specifically the HepA and Rota vaccines have BCR’s less than 1, “but they are still cost-effective from the societal perspective” (Zhou 2014). If one only looks at the personal benefit of getting the vaccine it is an inefficient purchase because the probability of contracting these diseases is so low and the even if a child has the disease its symptoms are typically easily treatable and not very life-threatening. However, once other benefits are factored in, such as the savings to the public health sector that the affected family will not feel and the overall number of cases of the disease that are prevented simply because the child never gets them, it is in the best interest of everyone in the U.S. if each person were to get the vaccine.

After examining the literature on the subject, it seems clear that vaccines are a cost-effective tool in public health. In general, both from a direct and societal perspective the benefits of vaccines far exceed the costs, and in no cases do the societal costs exceed the societal benefits. Even under the worst possible scenario, that Zhou could find, the vaccination schedule was a cost-effective tool.

One of the major benefits of vaccines we have learned about since their introduction
is that of “herd immunity”. Herd immunity is the idea that once vaccination rates reach a certain, high level the community will be so well-defended against the disease that even those who did not vaccinate will still be protected. The question is how high do rates have to be in order to reach herd immunity? We believe that the best way to answer that question is through the mathematical modeling of diseases.

How Mathematical Model Can Support Experiential Policy-Making on Vaccination

Mathematical modeling is typically the only way to examine the possible impact of a disease. It can answer the following questions: What fraction of a population must be vaccinated to prevent epidemics from happening? What kind of control measures are most efficient? Despite the benefits of models, applying the models to actual policy-making processes needs special care because simple models cannot capture the complexity of epidemics dynamics. Several important aspects of epidemics, such as the response of a population to certain events, are difficult to quantify.

There are two kinds of models in mathematical epidemiology; there are deterministic models and stochastic models. All mathematical models require assumptions to build upon. Deterministic models translate these into differential equations, which decide the dynamics. Only parameters are adjusted so that the equations follow the actual epidemic behavior (Towers 2013). The second is called stochastic models, which recognize random nature of transmission events using simulations. Both kinds are built upon the simplification of the complexity of epidemics. Researchers consider transmission path, age/social structure, network structure, and patch structure to make the assumptions. All models have advantages and disadvantages. It is also very important to apply an appropriate model for a certain type of disease. While the SIR model is appropriate for infectious diseases that confer lifelong immunity, such as measles or pertussis, the SIS model is predominantly used for sexually transmitted diseases (STDs) such as chlamydia or gonorrhea, where repeat infections are common (Keeling & Eames 2005).

The SIR model is a very fundamental deterministic model, and can be applied for most vaccine-preventable diseases such as measles, pertussis, mumps, and rubella. Basically, it categorizes people in a community into three groups: susceptible, infected, and removed/recovered. In the simplest SIR model, only susceptibles can get infected. At a fixed rate, infected people get removed/recovered, gaining lifelong immunity. To see the significance of vaccines, let’s think about a community where everybody is not vaccinated. A disease would spread to everybody after its outbreak. Probably, you would also expect that speed of the propagation of a disease to be very fast at first, but decrease as the number of recovered people increases. The SIR model predicts exponential growth. This situation can be mostly used at the initial stage of epidemics. For instance, the number of infected people of a new influenza (H1N1) in Mexico has a good fit to an exponential curve right after the outbreak (Boëlle, Bernillon, & Desenclos 2009).
Any models define a quantity called a basic reproduction number, $R_0$, which is an average number of secondary individuals infected by one primary case. If there is no change in the total population, everybody gets infected eventually if $R_0$ is greater than 1.

Let’s allow birth and death in the population while we keep the population constant. There is a supply of susceptible people, and people in any phase may die. If an infected person averagely infects more than one susceptible person, a disease spreads in a community. If not, a disease eventually gets eradicated. Hence, $R_0$ represents the strength of transmission. It is an independent quantity for each disease within a short timescale. It is useful to define such a quantity so that we can understand in what condition epidemics occur; if $R_0 > 1$, it will be epidemic. If $R_0 = 1$, it will be endemic. If $R_0 < 1$, a disease will be eradicated eventually. The basic reproduction number depends on organism characteristics such as infectivity and duration of infectiousness, and population characteristics such as mixing patterns, demographics and population density. Hence, the basic reproduction number of the same infection but in different areas may differ.

Vaccination lowers $R_0$. The concept of vaccination is lowering the susceptible population so that an infection has less chance to propagate. This means a lower $R_0$. The SIR model shows how vaccination lowers $R_0$ to effective reproduction number $R_{eff}$ by the following equation.

$$R_{eff} = (1 - v)R_0$$

(3)

$v$ represents the ratio of vaccinated people out of the total population. For example, if everybody in a community is vaccinated, $R_{eff}$ becomes zero, meaning that a disease does not spread. To eradicate a disease, we must lower $R_{eff}$ to less than 1 by increasing a vaccination rate. As long as $R_{eff}$ is less than 1, a disease gets eliminated eventually. Hence, the vaccination coverage must exceed the critical threshold $H$. The critical thresholds for major diseases are shown on Table 3.

$$H = 1 - \frac{1}{R_0}$$

(4)

According to Healthy People 2020 objectives about immunization and infectious diseases, which aims to “achieve and maintain effective vaccination coverage levels for universally recommended vaccines among young children”, the target vaccination coverages for DTaP, MMR, polio, hepatitis B, and varicella vaccine are all 95%. Measles and pertussis need especially extra care because the average age of infection for these diseases is 4-5, so the target vaccination coverage must be achieved before children attend kindergarten. Actually, high vaccination coverage for infections among young children can be quantitatively explained by the SIR model. We assume following conditions. 1) Everybody dies at age, $L$. 2) There is the same number of people at every age. 3) Children who are younger than the average age of infection, $A$, are susceptible, while
Table 3: Basic reproduction number $R_0$ and critical vaccination coverage $H$ for major infections

<table>
<thead>
<tr>
<th>Infection</th>
<th>Serial interval(range)</th>
<th>$R_0$</th>
<th>$H$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>2 - 30 days</td>
<td>6-7</td>
<td>83-86</td>
</tr>
<tr>
<td>Malaria</td>
<td>≥20 days</td>
<td>5-100</td>
<td>80-100</td>
</tr>
<tr>
<td>Measles</td>
<td>7-16 days</td>
<td>12-18</td>
<td>92-94</td>
</tr>
<tr>
<td>Mumps</td>
<td>8-32 days</td>
<td>4-7</td>
<td>75-86</td>
</tr>
<tr>
<td>Pertussis</td>
<td>5-35 days</td>
<td>12-17</td>
<td>92-94</td>
</tr>
<tr>
<td>Polio</td>
<td>2-45 days</td>
<td>5-7</td>
<td>80-86</td>
</tr>
<tr>
<td>Rubella</td>
<td>7-28 days</td>
<td>6-7</td>
<td>83-86</td>
</tr>
<tr>
<td>Smallpox</td>
<td>9-45 days</td>
<td>5-7</td>
<td>80-86</td>
</tr>
</tbody>
</table>

others are immunized. Then, the basic reproduction number can be rewritten as $R_0 = \frac{L}{A}$. This is a very optical assumption, but it is valid as long as $L$ is sufficiently greater than $A$. After all, the basic reproduction number becomes greater as there are more susceptible people. It makes sense why infections such as measles and pertussis have a higher basic reproduction number, because their average age of infection is very young.

Table 4: Target vaccination coverage in the U.S. for DTaP, MMR, Polio, Hepatitis B, and Varicella vaccine (Healthy People 2020)

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Target dose in kindergarten</th>
<th>Target vaccination rate in kindergarten</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTaP vaccine</td>
<td>4</td>
<td>95%</td>
</tr>
<tr>
<td>MMR vaccine</td>
<td>2</td>
<td>95%</td>
</tr>
<tr>
<td>Polio vaccine</td>
<td>3</td>
<td>95%</td>
</tr>
<tr>
<td>Hepatitis B vaccine</td>
<td>3</td>
<td>95%</td>
</tr>
<tr>
<td>Varicella vaccine</td>
<td>3</td>
<td>95%</td>
</tr>
</tbody>
</table>

How do we know these values of critical vaccination coverage are valid? In Finland, there were about 15,000 cases of measles a year before 1975. The vaccination coverage was lower than 70% then. By 1986, measles incidence had declined by 93% compared to 1982, although vaccine coverage had reached only 80.9%. In 1990, the vaccination coverage for MMR finally reached 96% for children. Since 1996, there has been no domestic transmission of measles in Finland. In 1997, Finland also became the first country documented to be free of mumps of rubella thanks to the high coverage of MMR vaccine. In the recent outbreak of pertussis in California, a state report showed that “vaccine coverage for pertussis among Bay Area kindergartners was generally high,

---

5If $L$ is not sufficiently larger than $A$, $R_0$ is equal to $1 + \frac{L}{A}$. 
Table 5: Average age of infection for several infections

<table>
<thead>
<tr>
<th>Infection / Infection agent</th>
<th>Average age of infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>4-5</td>
</tr>
<tr>
<td>Pertussis</td>
<td>4-5</td>
</tr>
<tr>
<td>Mumps</td>
<td>6-7</td>
</tr>
<tr>
<td>Rubella</td>
<td>9-10</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>11-14</td>
</tr>
<tr>
<td>Polio virus</td>
<td>12-15</td>
</tr>
</tbody>
</table>

except for Marin County, where just 86 percent of kids received their recommended shots” (Gross 2013). This makes sense because the coverage had not been above the critical vaccination coverage of 92-94%. The critical vaccination coverage is an optimistic estimate because it is based upon simplified assumptions. The SIR model assumes the following conditions. 1)Everybody has the same probability of interacting with others. 2)The population does not change over the duration of epidemics. 3)People get life-long immunity once recovered from a disease. Hence, the results may not be 100% accurate. The expected critical vaccination coverages are reasonably close to experiential values. It is suggested to keep an eye on the results of mathematical epidemiology in addition to the current experiential approach because mathematical models suggest us better strategies of vaccination. The vaccination rate in a community should always exceed the critical value. In particular, infections which harm young children must achieve very high vaccination rates to prevent epidemics. Hence, vaccination for diseases such as measles and pertussis should be prioritized over others. It is very important to make an effort to increase the vaccination rates even after achieving the critical values shown above because vaccines are not 100% effective. For example, a single dose of MMR vaccine is 95% effective according to the Center for Disease Control and Prevention (CDC). Referring to the results of mathematical modeling is important to support the current experiential approach on vaccination.

---

6Please check our website, http://complex-science-society.tumblr.com, to see mathematical proofs with more detail.

7Effort by the Public Health Office in Finland deserves credit for its effective campaigns. You can find the details on the following link.


8If we considered the effectiveness of vaccines is not 100%, we can rewrite the effective reproduction number as (1-ev)R0 where e is the effectiveness of vaccines. For multiple doses of vaccines, it is written a little differently. You can follow how to compute the susceptibility of a community on our website.
Undervaccination in Children

How Children Become Un- or Under-Vaccinated

To make the best use of mathematical modeling in real world settings, public health officials need to understand how people interact with the vaccination process, as well as how children come to be un- or under-vaccinated. Many people attribute unvaccinated children exclusively to the “anti-vaccination movement” and PBE’s (Blume 2006). Actually, the reasons why parents choose to seek PBE’s for their children are poorly understood, and PBE’s are not the only reason that children go unvaccinated. In reality, about 40% of American parents have delayed or refused a recommended or mandated vaccine, in addition to the less than 1% of parents who reject vaccines wholesale (Largent 2012; Committee on the Assessment of Health Outcomes Related to Recommended Childhood Immunization Schedule 2013). That 40% possess views on vaccines ranging from suspicion of the lobbying process through which vaccines become mandated to concern over the number of vaccines that children receive in their first 3 years of life (Largent 2012; Omer, Salmon, Orenstein, deHart, & Halsey 2009). The ways in which healthcare professionals communicate with such parents needs to be dynamic and compassionate in order to address parents’ true concerns.

Since the late 90’s, these anxieties have been expressed in fights over mercury in vaccine preservatives and MMR’s link to autism. Public health authorities have continuously responded to these claims by pointing to studies disproving the link to autism or proving the safety of the specific type of mercury in vaccines, without making any genuine gain in assuaging parents’ fears. Not only do people tend to believe personal stories over studies and statistics (Small, Loewenstein, & Slovic 2005), but autism and mercury are not actually the root of parents’ fears regarding vaccines. Nyhan, Reifler, Richey, & Freed (2014) gave parents one of four interventions to determine the effectiveness of messages designed to increase vaccination rates. One of the strategies included explaining the lack of evidence that MMR causes autism. After hearing the information, the parents who heard this intervention were less likely to believe that vaccines caused autism, but they were also less willing to get their child vaccinated. This supports the assertion that parents’ real concern lies not with concerns over mercury and autism, but with the vaccination process itself.

Parents are most often concerned about the immunization schedule and the side effects that sometimes result from vaccinations. Frequently, parents fear that the amount of vaccinations given together in one visit will overwhelm or weaken their child’s immune system (Largent 2012; Offit, Quarles, Gerber, Hackett, Marcuse, Kollman, Gellin, & Landry 2002). Parents of unvaccinated or under-vaccinated children are more likely than parents of up-to-date children to think that children these days receive too many vaccinations (Omer, Salmon, Orenstein, deHart, & Halsey 2009). Children can get as many as 8 vaccinations in one visit in accordance with the recommended vaccination schedule (“2014 recommended immunizations” 2014). The number of vaccinations
compounds if children have missed doctor’s visits or are ill at the time of the visit, as well as if an adopted child is missing vaccinations and needs be caught up (Largent 2012). Though children’s immune systems face thousands of challenges every day, and the entire list of recommended vaccinations represents only 150 such challenges (“Too Many Vaccines” 2012), watching a child be held down while doctors jab multiple needles into them leaves a powerful impression on parents’ minds. If a child exhibits side effects such as irritability or a fever, parents’ negative impressions of vaccination grows. Side effects are particularly worrying to parents (Omer, Salmon, Orenstein, deHart, & Halsey 2009), for while they are usually minor and rather rare, no parent wants their child to be one of the 3.52 children per 10,000 children to have a febrile seizure from the MMRV vaccine (MacDonald, Dover, Simmonds, & Svenson 2014). Additionally, some parents would rather have their child suffer from catching the disease than fall ill from an action in which they participated, namely vaccination (Downs, de Bruin, & Fischhoff 2008; Largent 2012). The vaccine schedule and the rare but possible side effects of vaccines are not the only concerns of vaccine-anxious parents, but they are two of the most widespread culprits in undermining parents’ trust in vaccination.

These concerns are linked to alternative medicine, which has become more and more mainstream within the past few decades. Alternative medicine, in this case, means those forms of treatment, such as faith healing, which are not accepted by traditional medical communities. Regarding vaccine-preventable diseases, alternative medicine tends to promote more “natural” methods of prevention, such as special diets meant to boost the immune system (Parker 2011). The concept of “natural immunity” also tends to be lauded by those connected to alternative medicine communities. Natural immunity is the concept that the antibodies obtained as a result from fighting off the disease are superior to the antibodies produced as the result of manufactured vaccines. A large portion of chiropractors have unfavorable views toward vaccination, and so chiropractics are one of the main places to which parents turn when they are alienated by the traditional medical community (Largent 2012).

Yet others object to the mandatory nature of vaccines, rather than their safety. They see the mandated schedule as the government diminishing their choices, and therefore their rights. While the Supreme Court has recognized the authority of the states to require citizens to be vaccinated since 1905, the court and the United States in general have since become more oriented towards individuals’ rights than ever before. This emphasis on individual rights and choices has turned getting vaccinated into a political decision for some parents.

Because of the wide range of concerns about vaccines, each parent must be met at his or her own level of understanding and belief in order for healthcare professionals to truly address his or her concerns and help the parent make the best decision for the child. Healthcare providers are the most frequently used source of information about vaccination (Omer, Salmon, Orenstein, deHart, & Halsey 2009; Largent 2012) and so are the key to connecting with parents. Parents want healthcare providers to provide information on their specific concerns, so there is no one speech that will quell all parents’ fears (Omer, Salmon, Orenstein, deHart, & Halsey 2009). Parents with
anxieties about vaccines can easily become parents seeking exemptions if they encounter authoritarian healthcare workers. Contentious relationships with healthcare providers may push anxious individuals towards other, more alternative forms of healthcare, which tend to confirm their fears about vaccination instead of assuaging them.

Maintaining respectful, working relationships between healthcare providers and vaccine-anxious parents is crucial to keeping the community safe from vaccine-preventable diseases. Recently some healthcare providers have refused to treat unvaccinated children to protect their more vulnerable patients from vaccine-preventable diseases (Parker 2011). Transmission of diseases in sites of healthcare is not an idle threat. From January 1 to April 25 of 2008, there were five measles outbreaks in the U.S. 44 of the 64 total measles cases had a known transmission site, and 18 of those 44 cases were transmitted in a healthcare facility. Furthermore, 13 of the 64 cases were in children who were too young to be vaccinated (Omer, Salmon, Orenstein, deHart, & Halsey 2009). Despite the risk to other vulnerable patients, the best way to limit the spread of vaccine-preventable disease is to continue to treat those who choose to remain unvaccinated. Unlike practitioners of alternative medicine, traditional healthcare providers like pediatricians and family practice doctors are trained to diagnose and treat diseases such as the measles. Early recognition and reporting of a vaccine-preventable disease is crucial to containing the spread of a disease. These factors also likely contributed to the high percentage of measles cases that were known to be transmitted in a healthcare facility in 2008. Seeing unvaccinated children only at the beginning or the end of the day may be one way to mitigate the risk to vulnerable patients while continuing to treat unvaccinated children (personal communication with Dr. Douglas Homnick July 22, 2014). Upholding relationships between vaccine-anxious parents and traditional healthcare providers is essential for protecting the health of both individual children and the community.

It would be incorrect, however, to say that parents seek exemptions for their children purely as a result of doctor recommendation or deliberation on the merits of vaccines. While parent beliefs certainly play a part in how children come to be exempted from vaccines, a number of factors can lead a parent to seek an exemption for their child. 9 Vaccination is not just the result of an individual choice, but a process consisting of a number of interconnected structures, including but not limited to education, healthcare, the economy, the legal system, and local norms.

Sometimes individual or collective circumstances can lead to parents seek exemptions for their children. In states with “easy” PBE laws, getting an exemption is actually less of a hassle than bringing children up to date on immunizations. In those states, exemptions are sometimes used as a way to keep children in school while waiting for a doctor’s appointment. Other parents use exemptions to put their children on alternative vaccine schedules, wherein the child eventually receives all recommended shots, just not on the recommended schedule (Largent 2012). Additionally, not all children with

9Proof of immunization is required only for schools or daycares, so when we speak of exemptions, we are speaking of school-age children or younger. Thus, we refer mainly to the concerns of parents instead of the concerns of the patients or students themselves.
exemptions are exempt from all vaccines. Those with medical exemptions may be able to handle some immunizations but not others, and those with philosophical exemptions may have parents who object to only one or two vaccines. For example, a child with an immune deficiency may not be able to handle live-virus vaccines, but he or she may be able to have vaccines made with the dead virus. Such children would be susceptible to some diseases but protected from others (personal communication with Dr. Douglas Homnick July 22, 2014). Getting an exemption for a child is not always the result of clear choice against vaccines.

In many cases, the barriers to vaccination are just as if not more potent than the attitude of healthcare providers in affecting how a child comes to be vaccinated or unvaccinated. Each community presents its own barriers to vaccination. In addition to differences in the level of difficulty required to obtain an exemption, location-specific barriers can include historical circumstances and local norms. Haitian immigrant communities, for example, tend to be suspicious of the HPV vaccination because of the stigma that might result from getting the vaccination. Such immigrants fear that getting the HPV vaccine marks Haitians as likely carriers of sexually transmitted infections, much as Haitians had been stigmatized as carriers of HIV (Stephens & Thomas 2013). Those who have ties to or practice alternative medicine may likewise cluster in communities. Omer, Enger, Moulton, Halsey, Stokley, & Salmon (2008) found significant clusters of PBE’s in Michigan, suggesting that either parents influence each other’s vaccination choices and/or like-minded parents tend to live in the same area. Either way, the clustering of parents that has serious doubts or objections to vaccination can make not vaccinating children seem like the norm instead of the exception, thus providing peer pressure to not vaccinate.

Recognizing and mitigating barriers to vaccination is important, as a large amount of children remain under-vaccinated. Though the highest exemption rate for any state is 6.4% (“Vaccination coverage” 2013), nationally, only about 71.9% of children age 19-35 months are fully up to date on the 4:3:1:3:3:1 vaccination series (“Estimated vaccination coverage” 2012). This means that nearly a quarter or more of 19-35 month old children in the U.S. are under-vaccinated without an exemption. Some of the gap between the vaccination rate and the exemption rate can be accounted for by the age range on which the National Immunization Survey collects immunization information. Most children do not go to kindergarten until age 5 or 6, so if a child does not attend daycare or preschool, he or she would not need to show proof of immunization or obtain an exemption until a couple years after the 35 month marker. Additionally, the parents of homeschooled children do not need to present proof of immunization even once their children reach school age, so they would not need to obtain exemptions for un- or under-vaccinated children. School procedure can also confuse exemption rates, as some schools permit children to have PBE’s even when the state does not authorize them. In Massachusetts and Missouri, where PBE’s are not legally authorized, 18.1% and 17.0% of schools respectively allow children to have philosophical exemptions (Salmon, Omer, Moulton, Stokley, deHart, Lett, Norman, Teret, & Halsey 2005). All of these explanations account for some of the under-vaccinated or unvaccinated children without
documented exemptions, but not all.

It is likely that a child’s individual circumstances have some bearing on his or her ability to be fully immunized, contributing to the gap between vaccination rates and exemption rates. Factors associated with under-vaccination include having a mother who is black; has less than a high school education; is single, has multiple children; and has an income that is less than 50% of the federal poverty level (Luman, McCauley, Shefer, & Chu 2003). Under-vaccinated children are also more likely than either fully vaccinated or completely unvaccinated children to be younger; be foreign-born; live in a central city; live in a household that has moved across state lines; have a low socioeconomic status (as measured by per capita income); and have had less than continuous healthcare coverage within last 12 months (Smith, Chu, & Barker 2004; Williams, Milton, Farrell, & Graham 1995; Allred, Wooten, & Kong 2007). Unvaccinated children, on the other hand, are more likely than under-vaccinated children to be male, white, in households with a higher income, have college-educated mothers, and live with four or more children. These characteristics suggest that factors related to socio-demographic characteristics and the healthcare system play a significant role in preventing under-vaccinated children from staying up-to-date with the recommended immunization schedule, while unvaccinated children are likely part of families that have deliberately chosen to remain unvaccinated (Omer, Salmon, Orenstein, deHart, & Halsey 2009). Though children who are unvaccinated without an exemption cannot attend public school, children who are under-vaccinated can attend public school if the child has had at least one dose of each mandated vaccine and intends to receive the rest of the required doses at a later date. Under-vaccinated children may also be slipping through cracks in the school system due to clerical or other human error. The mechanisms through which the gap between vaccination rates and exemption rates occurs are not well understood, but finding ways to decrease the discrepancy is crucial to reaching and maintaining herd immunity.

More research within a community is needed to determine the vaccination barriers specific to that location, but several barriers are consistent across the board regardless of location. Cost is one of the biggest barriers to immunization. While recommended vaccinations themselves must be covered by all insurance plans under the Affordable Care Act without charging a deductible, copayment, or coinsurance, healthcare providers can charge an administrative fee that differs by state (“The Affordable Care Act and immunization” 2012; “Vaccines For Children Program” 2013). These fees, when added to the cost of transportation to the doctor’s office and possibly time off work, can quickly become insurmountable for poorer families. The Affordable Care Act, however, simply sets minimum standards for health insurance; the mandated vaccination coverage does not apply to those who have neither private nor public insurance. There are also some health insurance plans that were grandfathered in under the Affordable Care Act, for whom the vaccination coverage would not apply (Konrad 2011). The Vaccines For Children Program (VFC) covers this gap, providing free vaccines to children who are uninsured, underinsured, American Indian or Alaska Native, or who are eligible for Medicaid. While the administrative fee can still be applied, the vaccine must still be
provided if the family cannot afford the fee ("Vaccines For Children Program" 2013; “Free preventive care” n.d.). Lower out-of-pocket cost has been correlated with higher vaccination rates (Molinari, Kolasa, Messonnier, & Schieber 2007), so encouraging participation of eligible families in programs like VFC can reduce the cost barrier for a number of families.

Time is another significant barrier to immunization, as those who are under-vaccinated are more likely to be in a single-parent household. It takes numerous doctor visits to complete the recommended immunization schedule, and scheduling appointments around work and childcare is difficult. However, even a small reduction in these barriers or minor changes in doctor or clinic practices can be extremely beneficial. In a study of African American preschoolers, 26.2% of students were under-vaccinated. 72.6% of those who were under-vaccinated needed only one additional visit to be completely up-to-date with their immunizations, and 78.3% of those who needed only one additional visit had already had enough doctor visits to have completed their recommended immunizations (Daniels, Jiles, Klevins, & Herrara 2001). If children are receiving care from multiple sources instead of one main source, healthcare providers may not consistently check the vaccination status of children. Having all healthcare providers check a child’s immunization status at every visit may be enough to increase immunization rates by as much as 15.0% among African American preschoolers. However, those children who have had almost enough visits to be fully vaccinated may have been sick and unable to receive any immunizations during one of their visits, meaning that ensuring regular checks of vaccination status is not enough; the removal of time and cost barriers is crucial to helping children stay up-to-date. Workplaces can help in this respect by providing more full time equivalent (FTE) weeks of pay for maternity leave. Dabu, Raub, and Heymann (2012) found in their global study of vaccination rates that an additional 10% in FTE weeks produced a 15% increase in DTaP vaccination rates. Changes in practice in healthcare providers and in workplaces can work together to increase vaccination rates in communities.

Reminders and participation in Women, Infants, and Children (WIC) can also help increase vaccination rates by making parents aware of their child’s vaccination status. Parents often simply forget about vaccinations, especially considering the sheer amount of vaccinations that children are recommended to have. Reminder texts, emails, or calls can help parents remember to schedule visits to get their child vaccinated (Butler 2013). Participation in WIC can also help parents get their child vaccinated by making parents aware of the vaccination status of their child. WIC is a federally funded program that gives supplemental food, health referrals, and nutrition education to women who qualify. Screening immunization records of children under the age of two has been a routine part of WIC certification visits since 2000, and those who participate in WIC have been shown to have higher vaccination rates than those who are eligible but do not participate ("Women, Infants, and Children" 2013; Lumen, McCauley, Shefer, & Chu 2003). Efforts that make parents aware of their child’s vaccination status can help increase vaccination rates.

Children come to be un- or under-vaccinated through a variety of processes,
some of which include more intentionality on the part of parents than others. Those parents who seek out exemptions are more likely to be intentionally keeping their child unvaccinated than the parents of children who are under-vaccinated but are not exempt. The reasons behind such intentional lack of immunization include worry over the safety of the number of vaccines given to children, concern about the usually minor and rare side effects, objection to the mandatory nature of vaccines, and distrust of the lobbying process through which vaccines get placed on states’ mandatory vaccine lists. The wide variation in such concerns demands that healthcare providers address each parent’s concern on an individual basis, which will keep parents connected to traditional medicinal communities that can best identify and treat vaccine-preventable disease. For those who are not intentionally unvaccinated, barriers such as the cost (both direct and indirect) of getting a child vaccinated and the time and number of visits required to complete the recommended vaccination schedule prevent many children from becoming vaccinated. Strategies that reduce these and other, more community specific barriers are crucial to maintaining high immunization rates and protecting communities from vaccine-preventable diseases. In fact, the prevalence of these factors and how much they prevent children from getting vaccinating calls into question the direct relationship between exemptions and vaccination rates.

**How do Exemption and Vaccination Rates Interact?**

The CDC publishes all of the NIS results for vaccination in children 18-35 months old by state on their website. This includes data on both specific vaccines and certain vaccine series. The 4:3:1 series, 4:3:1:3 series, 4:3:1:3:3 series, and 4:3:1:3:3:1 series. In order those numbers represent 4 doses of Diphtheria, Tetanus, and acellular Pertussis, 3 doses of Polio, 1 dose of Measles, Mumps, Rubella, 3 doses of Haemophilus Influenzae type B, 3 doses of Hepatitis B, and 1 dose of Varicella. We were primarily interested in these series data because in most states these were the vaccines required to attend school. Students in most states not having the complete 4:3:1:3:3:1 series should, theoretically, have to get an exemption. The data is available from 1995-2012. Armed with this data we can begin to look empirically at some interesting questions about the interaction between exemptions and vaccination rates.

**Do Exemptions Decrease Vaccination Rates?**

At first glance this question seems like it has a very obvious answer, a child getting an exemption is a child not getting fully vaccinated, but after some empirical analysis it might not be so simple. First, I ran a simple linear regression between states’ vaccination rates for all of these series and their exemption rates. There was no correlation in any of them, and even if the R-squared values were not near zero, a 1% increase in exemption rates caused only a 0.5% decrease in 4:3:1:3:3:1 series vaccination rates. How is this possible? The nationwide coverage rate for only the 4:3:1 series
(keep in mind that this does not include all of the vaccinations that would require an exemption to attend school) is 80.5+/-1.4%, and the highest exemption rate in any state is 6.4% in Oregon ("National Immunization Survey" 2013; "Vaccination Coverage" 2013). 49% of toddlers born from 2004 to 2008 were not fully up to date by their second birthday, but only 2% had outright refused vaccinations. These kids were missing shots for other reasons, such as parents’ work schedules, transportation problems, and insurance hiccups (Butler 2013). This is possible because at two years old most kids had not faced the situations that would typically force them to vaccinate, schools and daycares, and as a result they have no incentive to. Later these children avoid both getting vaccinated and getting exemptions through homeschooling, loopholes in school vaccination laws, and other unknown ways. These children, and the fact that they represent a much larger proportion of the population than the children getting exemptions, could be the reason that exemptions do not directly decrease vaccination rates.

Does the Difficulty of an Exemption Decrease Vaccination Rates?

In 2006 Saad Omer, an associate professor at the Rollins School of Public Health at Emory University, published a paper about exemptions(Omer 2006). One part of the paper classified states based on the difficulty of getting an exemption. He used 4 factors (whether it was a form vs a letter from a parent, whether the parent obtained the form from the school or the public health department, whether or not the form needed to be notarized, and if a letter from the parent was required) to label each state with non-medical exemptions as either 1, 2, or 3 (1 being the most difficult to get an exemption and 3 being the easiest). Omer showed, and we confirmed through a similar analysis, that there was a statistically significant difference in exemption rates between the three categories. However, when looking at 2006 vaccination rates, there is no statistically significant difference between the vaccination rates of states with easy, medium, or hard exemption laws. It appears that the ease of getting an exemption affects the exemption rates but not the vaccination rates.
This does not prove there is no relationship between the difficulty of getting an exemption and vaccination rates, rather it casts the assumption that there is one into doubt. Ideally we could track the changes in vaccination rates for states that switched categories before and after they made the switch. Unfortunately, Omer classified states only once, and to do so he had access to specifics about state laws that we are unable to obtain. For now we will take the difference found in states’ exemption rates to back up Omer’s findings and to show that easier exemptions do lead to more exemptions. The lack of difference for vaccination rates means we have to consider an interesting possibility. Vaccination rates might be unaffected by the ease of getting an exemption.

**Do Personal Belief Exemptions Affect Vaccination Rates?**

The majority of exemptions are personal belief exemptions. 18 states offered personal belief exemptions as of 2012, 19 if you count Missouri but that only applies for preschool(States 2012). In every series there was a statistically significant difference in both vaccination rates and exemption rates between states with personal belief exemptions and states without. Interestingly, the rise in exemptions does not account for all of the decrease in vaccination rates in those states.

This can be explained in two ways. One, the people who are getting exemptions are being trendsetters and affecting the people who are simply slipping through the cracks. Two, there is something systematically different about the states with personal belief exemptions, such as states more likely to allow personal belief exemptions are states that are ahead of the trend of falling vaccination rates, which could even imply that personal belief exemptions actually have little to no impact on vaccination rates. To test this we need to see what happens when states change their laws.

Using the difference in the lists of states with PBE’s in 2012 and the list that Saad Omer used for his paper, we know that since 2004, Texas, Arkansas, and Arizona added PBE’s and New Mexico and Oregon took theirs away. If we compare these states’ vaccination rates from 2004 with theirs now, we can get a clearer picture of
what impact personal belief exemptions have on vaccination rates. States that didn’t change their laws experienced a significant average drop in vaccination rates across the board. How did the states that added personal belief exemptions fair? On average for the 4:3:1 and 4:3:1:3 series they were exactly the same. For the longer series, their losses were slightly above average, but not significantly so. The lack of significance is partially because there are only three states that added this law, so we’re dealing with a very small sample size, and partially because the difference was small. States that removed personal belief exemption laws saw lower losses than average for some series and higher for others, but there was no significance again (even a smaller sample size this time). When comparing the difference between states that added personal belief exemptions to states that took theirs away there was still no statistical significance. Still this could just be a case of having too small of sample sizes. These results do not back up causation with respect to PBE’s, in fact they provide evidence against it, but hopefully with more data we could get a more definitive answer.

All of the questions we have asked so far can be summed up into one: do exemptions decrease vaccination rates? It appears to be a no. Only PBE’s had any evidence supporting them, but even then we were unable to show any causation. The difficulty of obtaining exemptions and the rate of exemptions most likely do not affect vaccination rates, even though difficulty does affect exemption rates. But why are we concerned about vaccination rates? We are trying to prevent disease. This leads us to, perhaps, a more appropriate question.

Figure 2: Vaccination Series vs. Drop in Vaccination Rates 2004-2012 Separated by PBE Law Changes
Do Exemptions Cause an Increased Rate of Disease?

Interestingly, while we were unable to find anyone who had looked at the relationship between exemptions and vaccination rates, we were able to find several times when somebody had looked at the interactions between exemption rates and rates of diseases. In the previously mentioned paper on exemptions, Saad Omer also showed that states with less difficult exemptions and states with higher exemption rates had more outbreaks of pertussis (Omer 2006). But if the exemption rates are not correlated with vaccination rates and the difficulty of exemption does not affect vaccination rates, how do they directly affect rates of pertussis? People with nonmedical exemptions tend to “cluster” together. In states that offer these forms of exemptions, there are identifiable clusters of people who have gotten them. 39 such clusters were found in a California study, and these clusters “were 2.5 times as likely to be in a pertussis cluster” (Atwell 2013). In Michigan, 23 exemptions clusters were found. These also had a statistically significant overlap with pertussis outbreaks in Michigan (Omer 2008). In Colorado, a 1% increase in exemption rates in a county increased the rate of measles by 1.6 times and of pertussis by 1.9 times (Feiken 200). While these studies only looked at pertussis or measles, it is reasonable to assume that these results can be expanded to other highly contagious, vaccine-preventable diseases.

The critical value for vaccination coverage to prevent measles is 92-94%, very close to our actual national coverage rate with the MMR vaccine. The problem is that this target vaccination rate only works if it is evenly distributed for every population level: national, state, even county. Even though exemption rates do not affect vaccination rates on the state level, those with exemptions cluster, creating counties with very high exemption rates, some being as high as 26% in Washington (Omer 2009) and are well below the critical value, putting them at a high risk of these diseases.

What Can Reduce Exemptions?

One of the most profound findings in Omer’s paper about exemption difficulty was that simple requirements that make it more difficult to get an exemption can decrease the rates of exemptions and, as a result, diseases in a state. Omer found that the difference in exemption rates between states in the easy and medium categories was much greater than the difference between states in the medium and hard categories (Omer 2006). Even though it was not statistically significant, we found that the highest vaccination rates were actually found in states with medium difficulty. Simply adding the requirement of getting the form notarized or a parent sending in a signed letter stating the reason for the exemption could prevent a lot of disease. In our view, these simple added requirements making it slightly more difficult to get an exemption are the best policies to focus on moving forward.
Conclusion

Role of the Public Health Office

All across the country, local and state public health officials take on the challenge of ensuring that vaccination rates remain high in their communities in order to prevent the spread of communicable diseases. The threat of disease changes from year to year, with PBEs being a primary influence on how quickly diseases like measles and pertussis spread. The state of Michigan is one of twenty states that offer a personal belief exemption and in most counties the process to waive vaccinations is easier to fulfill than to take your child through the recommended vaccine schedule. Saad Omer’s study in 2006 analyzes the exemption laws of forty-seven states, eventually classifying them as either “easy, medium, or hard” to receive an exemption. Michigan is classified as an “easy” state to receive an exemption because in most cases a parent needs only to obtain a state-created exemption form from their school office, choose which vaccines they would like to waive, sign it, and turn it back in. Since there are so many natural barriers to getting vaccinations; such as, scheduling conflicts, transportation, accessibility, etc., it was not uncommon for parents to simply sign a waiver form rather than going through the hassle of getting their child the necessary shots to enter school. However, some counties within Michigan have taken it upon themselves to make the exemption process more educational without the use of formal laws.

In 2010, Michigan experienced one of the largest outbreaks of whooping cough (pertussis) in years with a total of over 1500 cases reported (Whooping Cough in Michigan). The Kalamazoo Public Health Department in Kalamazoo County handled the outbreak in their county. After the outbreak had subsided the health department received criticism from community members who thought more should have been done by the health department to prevent the epidemic. In truth, the burden of the outbreak was shared; not enough people were getting vaccinated and there was not enough education on vaccines readily available for those seeking exemptions. Therefore, the county decided to make policy changes to how PBEs are handled in Kalamazoo County.

First, the Kalamazoo County Public Health Department collaborated with Kalamazoo Public Schools and all private schools within the county to take the exemption forms out of the schools, instead locating them at the public health office. All schools, both religious and not, have been extremely cooperative with this measure as it is not in any way a formal law, but rather a new policy implemented by the officials.

The second change made by the department was the implementation of an educational course before parents receive a waiver. No parent has to go through the course if they don’t want to, as it is their right by law to get a waiver and leave. Many, though, stay and leave with an entirely different view on vaccination and public health. The reason being is that when a parent arrives specially trained nurses hear their concerns and let them know that they understand the place they are coming from. They follow by showing scientific articles showing the effectiveness and safety of vaccines,
explanations of herd immunity and its importance to the community, what these vaccine preventable diseases look like in children, and the long term ailments from these diseases when contracted at a young age. After the course if a parent would still like a waiver, there is little or no argument. These nurses respect that it is the decision for the parent to make and understand that a balance between public health and civil liberties must be maintained. Before they leave they make sure to teach them one last thing, which is how to recognize the symptoms of common childhood communicable diseases like measles and mumps. It is often that parents who choose to exempt their children from vaccines will also choose to take their child to an alternative health care provider. This individual may be proficient within their field, but they are not specialized in recognizing communicable diseases in children like pediatricians; therefore, if a parent chooses to exempt their child from vaccines they should have the knowledge and understanding to know what these diseases are. In response to parents seeking waivers, some community’s pediatricians have decided as a group to not see unvaccinated children. Kalamazoo County is one such community. These pediatricians, like many others across the nation, made this choice because of the risk that unvaccinated children can be to other patients. Some people argue that if a pediatrician simply splits their schedule between unvaccinated and vaccinated children, they will be able to provide care for all. Pediatricians recognize the unfortunate truth, though, which is that they are running a business and parents want to bring their children between four and six in the afternoon when they get off of work. Accommodating this minority group of parents could pose a financial threat for many pediatricians, a risk many will not take. From a public health perspective, pediatricians choosing not to see unvaccinated children is a huge issue. These doctors are a public health official’s lifeline to a community to be kept up to date on what the presence of certain diseases look like in their community. The varying reasons why a pediatrician choose to not see unvaccinated children can be justified in their own way, but at the end of the day those children continue to live in your community without monitoring or available education on the health and safety of their child. The decision is challenging, but perhaps sacrifice might need to be made by doctors to make up for a lack of it among parents who choose to not vaccinate their children.

The overall movement for public health offices across Michigan is to change policies so that the exemption process is one of education rather than a passive system that reinforces uninformed decision making. It’s a logical and relatively easy set up, a challenge that is manageable and necessary for public health officials to overcome. How healthcare officials handle these sorts of situations will determine vaccination rates in the upcoming years, a responsibility that physicians should not take lightly and a situation that all parents should be aware of (personal communication with Dr. Douglas Homnick, Penny Born, Roxanne Ellis, and Dawn Smith July 22, 2014).
What States Can Do

So far our recommendations have been oriented to the county level, largely because they can institute changes almost immediately, but, as we have mentioned above, this is not where the authority lies in terms of mandating vaccination. If we want to make lasting changes, we need to work at the state level, where a new law or new interpretation of current laws can permanently change the vaccination landscape. There are two sets of policies that we believe can be incredibly helpful to a state; one is designed to decrease exemption rates and the other to increase vaccination rates.

Decreasing Exemption Rates Through the State

Increased rates of exemptions within a state are strongly associated with increased outbreaks of disease. Clustered exemptions are often the center of such outbreaks. Furthermore, increased difficulty of getting an exemption is associated with lower exemption rates. Our recommendation to states is to make exemptions harder to obtain. Part of this can be accomplished simply by making sure that schools are following existing laws in states without PBE’s. Though the Salmon et al (2005) study included only Massachusetts and Missouri, it is likely that schools in other states without PBE’s are also accepting non-authorized exemptions. Regarding creating new legislation in states with PBE’s, emulating the states that Omer (2006) classified as “hard” to get an exemption in is a good place to start. Mandating that the form be obtained in the public health department rather than the schools, requiring that the form be notarized to be accepted and requiring a signed letter from the parent stating the reason for the exemption together would move a state into the “hard” category. Moving the exemption forms into the public health office is particularly important, as the knowledge, attitudes, and beliefs of school personnel and school procedures have been shown to influence exemption rates in individual schools (Salmon et al 2005; Salmon, Moulton, Lawrence, Omer, Chace, Klassen, Talebian, & Halsey 2004). Taking exemption forms out of schools would eliminate both of these influences and encourage lower exemption rates. By making the exemption process more inconvenient the large portion of parents seeking exemptions who are simply anxious are deterred from going through the process. How a public health office handles people seeking exemptions can impact exemption rates. We recommend similar policies to what the Kalamazoo County Public Health Department instituted, with an available informational session on vaccines and how to identify early symptoms, care for a sick child, and prevent the disease from spreading before giving an exemption form. Lastly, while the Michigan attorney general’s opinion that it is up to the counties to decide which exemption forms to accept could and should inspire counties to create their own form, it is just one person’s interpretation of the law. We recommend adding a section onto the law that clearly gives power to the counties to create their own exemption form and to choose which forms they will not accept.
We recognize that the political realities of states vary and that in most states a law including everything we highlighted above would be extremely controversial and difficult to pass. We hope that legislators will be able to choose which of these recommendations are right for their state. Even adding just one of our recommendations could be extremely helpful and reduce the incidence and spread of vaccine preventable diseases.

Increasing Vaccination Rates

There is no correlation between the difficulty of getting an exemption and the vaccination rate of a state, therefore none of our recommendations above will actually increase vaccination rates on a state level. Vaccination rates are falling across the country. From 2004-2012, 4:3:1:3:3:1 series vaccination rates fell by an average of nearly 2.5%. In Michigan, they fell by 7% and in some states they fell by over 10%. Even if states followed every one of our recommendations above and greatly reduced the number of exemptions, without taking steps to reverse the trend of falling vaccination rates, we will never achieve the critical values needed to completely eradicate these diseases. This is why we also need to institute some policies to increase the vaccination rates.

The issues that lead to low vaccination rates, rather than high exemption rates, are much more difficult to address. They include ways that children slip through the cracks of the healthcare and school systems, often due to sociodemographic factors. The cost and time requirements of the recommended vaccination schedule are significant barriers to poorer families and single-parent households. Less systematic factors, like moving across state lines, forgetting to schedule visits, or a child being sick at the time of a well-child visit also contribute to unintentionally under-vaccinated children. Many of these barriers can be lessened through changes on the local level. County health offices can work with local practices to make sure that all healthcare providers are checking every child’s vaccination status at every doctor visit and providing reminder texts, calls, or emails to parents. Practices and clinics can also make vaccination more convenient by offering extra hours for and setting up vaccination clinics through schools and other easily accessible places. These practices, however, command healthcare providers’ resources.

State governments can facilitate these changes on the local level by providing infrastructure support. For example, many states have vaccination databases which can be accessed by any healthcare provider at any time. Keeping up these databases, continuing to make them easier to use, and encouraging practices to use them will make checking the vaccination status of children at every visit faster and easier. States can also increase awareness of and participation in the WIC and VFC programs, which can reduce the cost of vaccination and make parents aware of which vaccines their children are missing. Furthermore, additional funding from state or federal sources to help cover administrative costs can offset the costs involved in making getting vaccinated
more convenient. Rein, Honeycutt, Rojas-Smith, & Hersey (2006) found a 1.6% increase in vaccination coverage of 19-35 month olds for every additional $10 per person provided through the CDC’s Section 317 Immunization Grants Program, which provides operational funding for vaccination (as opposed to funding for the purchase of vaccines). Support for vaccination infrastructure and operations from state and federal governments can complement local efforts to reduce barriers to vaccination to increase vaccination rates.

**Final Remarks**

In the realm of public health, nothing is simple. It is a place where multiple disciplines collide in an attempt to show their truths. We have shown the efficacy of vaccines, provided insight into current feelings on vaccines in America, and discussed steps and solutions that could help protect your community or state. In the end the parent decides because it is a civil liberty that protects American citizens from governmental mistakes. Accepting this reality allows Dr.’s and public health officials to understand the individual seeking an exemption as well as implement one last suggested solution: earn the trust of your patients.
References


[51] 著者名、本のタイトル（出版社）


