



The Correlation of Nonmedical Vaccine Exemptions and Clusters of Pertussis Cases in the United States, 2012

Citation

Aloe, Carlin F. 2016. The Correlation of Nonmedical Vaccine Exemptions and Clusters of Pertussis Cases in the United States, 2012. Master's thesis, Harvard Extension School.

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The Correlation of Nonmedical Vaccine Exemptions and
Clusters of Pertussis Cases in the United States, 2012

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A Thesis in the Field of Biology
for the Degree of Master of Liberal Arts in Extension Studies

Harvard University

May 2016

Abstract

The aim of this investigation was to determine if there was a correlation between nonmedical vaccine exemptions and clusters of pertussis cases in the United States during 2012. It was hypothesized that counties that have high rates of nonmedical vaccine exemptions will also have high rates of reported pertussis cases. Kindergarten immunization data as well as pertussis cases at the county level were examined. This study used incidence rates, linear regression models, and a statistical analysis program called SaTScan version 9.4 to determine if there was a correlation between geographical clusters of nonmedical vaccine exemptions and geographic clusters of pertussis cases in the United States during 2012. The results of the investigation indicated that there is a moderate correlation between nonmedical vaccine exemptions and pertussis cases at the county level. It was concluded that geographic clusters of nonmedical vaccine exemptions do pose a risk to the surrounding communities. The results suggest that states should actively monitor trends in nonmedical vaccine exemptions at the county level to better understand the impact of nonmedical vaccine exemptions on public health. In addition, states should reconsider allowing nonmedical vaccine exemptions because of the potential impact that these exemptions have on public health.

Acknowledgments

Many thanks to Dr. Barry Bloom, Dr. Martin Kulldorff, Dr. James Morris, and Harvard University's Center for Geographic Analysis for their kindness, support, and invaluable assistance with this thesis.

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Chapter I

Introduction

Vaccines are one of the greatest achievements in medicine and public health. Studies have indicated that vaccine programs in the United States have significantly decreased the number of cases of vaccine preventable diseases over the past century (Wang, et al., 2014; Panhius, et al., 2013; Roush & Murphy, 2007; Armstrong, et al., 1999; CDC, 1999). The Centers for Disease Control and Prevention (CDC) has estimated that childhood vaccines will prevent 322 million illnesses, 21 million hospitalizations, and 732,000 deaths among children born in the United States in the last twenty years (CDC, 2014). One of the reasons why the United States has had such success with a reduction in vaccine preventable diseases is because of the school immunization requirements (Wang, et. al., 2014; Omer, et al., 2006).

However, over the past decade the CDC has reported that there has been a rise in the number of cases of certain vaccine preventable diseases (CDC, n.d. a). Pertussis also known as whooping cough is one of the vaccine preventable diseases that has been on the rise in the United States (CDC, n.d. a). In 2012 there were 48,277 cases of pertussis reported in the United States (CDC, n.d. b). This is the highest number of cases of pertussis reported in the U.S. since 1955 (CDC, n.d. a). According to the Centers for Disease Control and Prevention the number of pertussis cases in the U.S. has been gradually increasing since the early 1980s (CDC, n.d. a). Yet, if one looks closely at the data of reported pertussis cases in the U.S., one can see that starting in the early 2000s the number of pertussis cases reported each year has increased significantly thus indicating

that something has changed with the effectiveness of the vaccination program in the United States since the early 2000s (CDC, n.d. a).

In 1905 the Supreme Court case *Jacobson vs. Massachusetts* ruled that a state is allowed to have vaccination requirements to protect public health (Mariner, et al. 2005). There are no federal laws regarding vaccination requirements and states have effectively enforced vaccination laws through school vaccine requirements (Orenstein & Hinman, 1999; Malone & Hinman, n.d.; CDC, n.d. c). Currently, all fifty states and the District of Columbia require vaccination upon school entry (Wang, et al., 2014; Blank, et al., 2013; Omer, et al., 2008; Orenstein & Hinman, 1999; Malone & Hinman, n.d.). Yet, the majority of states have amended the vaccination laws over the years and have allowed for vaccine exemptions. Currently, forty-seven of the fifty states offer religious and/or personal belief exemptions (also know as nonmedical vaccine exemptions) to the school vaccination requirements (California Legislative Information, 2015; Wang, et al., 2014; Blank, et al., 2013; Omer, et al., 2008; Orenstein & Hinman, 1999; Malone & Hinman, n.d.).

Nonmedical vaccine exemptions for school requirements have been on the rise in the U.S. (Wang, et al., 2014; Blank, et al., 2013; Omer, et al., 2009; Thompson, et al., 2007; Omer, et al., 2006). Studies have indicated that demographic variables such as income level and education attainment are associated with rates of vaccine coverage (Wang, et al., 2014; Atwell, et al., 2013; Omer, et al., 2009; Omer, et al., 2008). Specifically that white, college educated individuals with relatively high levels of income were more likely to obtain nonmedical vaccine exemptions for their children (Yang, et

al., 2016; Wang, et al., 2014; Atwell, et al., 2013; Birnbaum, et al., 2013; Richards, et al., 2013; Salmon, et al., 2005).

In addition, several studies have shown that where it is easier to obtain a nonmedical vaccine exemption in a state then that state will have higher rates of nonmedical vaccine exemptions (Blank, et al., 2013; Omer, et al., 2009; Thompson, et al., 2007; Omer, et al., 2006). Is it possible that nonmedical vaccine exemptions could be a cause of the 2012 pertussis outbreak in the United States?

There have been debates in the current literature about what has contributed to the recent pertussis outbreaks including the cyclical nature of the disease peaking every three to five years, the waning immunity due to the introduction of the acellular pertussis vaccine, the increased detection of cases, and/or the possibility of genetic changes in circulating strains of pertussis (Klein, et al., 2016; Atwell, et al., 2013; Shapiro, 2013; Cherry, 2012 a; Cherry, 2012 b; Klein, et al., 2012; Witt, et al., 2012; Misegades, et al., 2012; Mattoo & Cherry, 2005; CDC, n.d. d). Yet, there has been limited research on the impact that nonmedical vaccine exemptions from school immunization requirements have had on the recent increase of pertussis cases in the United States.

The aim of this investigation is to determine if there is a correlation between nonmedical vaccine exemptions and clusters of pertussis cases in the United States at the county level, using data from 2012. It is believed that counties in the U.S. that have high rates of nonmedical vaccine exemptions will also have high rates of reported pertussis cases. The hypothesis is based on the principle of herd/community immunity. When nonmedical vaccine exemption rates are high enough to compromise herd/community

immunity at the local level, the risk of a vaccine preventable disease outbreak increases (Lieu, et al., 2015; Glanz, et al., 2009; Omer, et al., 2008; Feikin, et al., 2000 a).

To determine if there is a correlation between rates of nonmedical vaccine exemptions and geographical clusters, I examined the incidence rate of pertussis in the forty-eight states that offer nonmedical vaccine exemptions vs. the incidence rate of pertussis in the two states (Mississippi and West Virginia) that did not offer nonmedical vaccine exemptions in 2012. Analysis and comparison of state pertussis datum will further help to better understand the relationship between nonmedical vaccine exemptions and outbreaks of pertussis.

I also completed a linear regression to compare the percentage of pertussis cases and percentage of nonmedical vaccine exemptions at the county and state levels in the five states (Arizona, New Jersey, Oregon, Utah, and Washington) that were studied in this investigation.

Lastly, I used SaTScan version 9.4, which is a free software program that analyzes spatial, temporal, and space-time scan statistics. SaTScan version 9.4 enabled me to analyze the relationship between nonmedical vaccine exemptions, cases of pertussis, and geography. I used SaTScan version 9.4 to conduct a spatial Poisson model and a Bernoulli space-time model to determine statistical significance of geographic clusters (SaTScan, 2015; Lieu, et al., 2015; Sherman, et al., 2014; Atwell, et al., 2013; Omer, et al., 2008). The end result of the analysis produced data tables of spatial clusters of nonmedical vaccine exemptions and spatial clusters of pertussis cases (Lieu, et al., 2015; Atwell, et al., 2013; Omer, et al., 2008).

The data from SaTScan version 9.4 were used to create maps and a linear regression model to better understand the relationship between geographic clusters of nonmedical vaccine exemptions and geographic clusters of pertussis cases. With the support from Harvard University's Center for Geographic Analysis, the data sets collected from SaTScan version 9.4 were used to create maps via a GIS software called ArcGIS. The maps created from the SaTScan data showed the overlap between geographic clusters of nonmedical vaccine exemptions and geographic clusters of pertussis cases.

The significance of this investigation is two fold. The first is if there is a correlation between nonmedical vaccine exemptions and pertussis cases then one could argue that in areas where there are high rates of nonmedical vaccine exemptions there could also be increased risk for cases of other vaccine preventable diseases. The second is the larger implication on public health in the U.S. and the impact that high rates of nonmedical vaccine exemptions have on the health of the country. If there is a correlation between high rates of nonmedical vaccine exemptions and increased rates of pertussis cases then both the State and Federal Governments would need to discuss policy regarding the school immunization programs and the efficacy of nonmedical vaccine exemptions.

Definition of Terms

“Acellular Pertussis Vaccine”: A type of pertussis vaccine that contains purified antigenic components of *Bordetella pertussis*. Meaning the vaccine contains certain components of *Bordetella pertussis* instead of the whole cell. The acellular pertussis vaccine was created to reduce adverse events from the original whole cell vaccine (CDC, 1997).

“Bernoulli space-time model”: A discrete probability distribution that expresses the probability of a given number of cases and controls in a fixed interval of time and/or space. This type of analysis is often used for data collected over a period of time (SaTScan, 2015).

“*Bordetella pertussis*”: A gram-negative bacteria that causes the illness pertussis also known as whooping cough (CDC, n.d. d).

“Community Pertussis Outbreak”: When the number of reported cases is higher than what is expected on the basis of previous reports during a non-epidemic period for a given population in a defined period of time.

“DTaP”: The vaccine that is given to children up to the age of seven years old to protect them against Diphtheria, Tetanus, and Pertussis. The “a” in DTaP stands for acellular.

“Efficacy”: The capacity for beneficial therapeutic effect of a given intervention. In medicine and public health if efficacy is established it means the intervention is likely to be as good as or better than other available interventions.

“Endemic”: An epidemiology term used to describe an infection that is common in a population.

“Encephalopathy”: A medical term used to describe a syndrome of altered brain function due to disease or injury.

“GIS (Geographic Information System)”: A system that is designed to analyze and present spatial and/or geographic data.

“Herd/Community Immunity”: Type of indirect protection from infectious disease within a community. It occurs when a large percentage of the population is immune to an infectious disease through vaccination or prior illness and makes it less likely that an infectious disease will spread from person to person. It is a type of immunity that protects individuals in a population that are unable to receive vaccines (infants, people who are allergic to vaccines, or people with chronic illnesses).

“Incidence Rate”: A measure of disease that indicates the number of new cases per population at risk in a given period of time. It allows one to determine a person’s probability of being diagnosed with a disease during a given period of time.

“Medical Vaccine Exemption”: An exemption law for the school immunization requirements. Individuals who have medical vaccine exemptions include those who have allergies to ingredients in vaccines or people who have a chronic illness and are unable to receive vaccines.

“Nonmedical Vaccine Exemption”: An exemption law for the school immunization requirements that is in place in forty-seven states (California Legislative Information, 2015; Wang, et al., 2014). The exemption law allows parents/guardians to opt out of vaccinating their children because of religious, philosophical, or personal beliefs.

“Polymerase Chain Reaction (PCR)”: A laboratory technique used to sequence DNA. In the case of *B. Pertussis* it is a technique used by healthcare providers to diagnosis pertussis. PCR can also be used by researchers to determine the genetic sequencing of different strains of pertussis.

“Pertussis”: Also known as whooping cough is a highly contagious respiratory illness caused by the bacterium *Bordetella pertussis*.

“School Immunization Requirements”: State laws that are in place to ensure that children who are enrolling into daycare and school have been vaccinated. The goal of these laws is to maintain high vaccination rates (CDC, n.d. c; Orenstein & Hinman, 1999).

“Spatial Scan Statistics”: Statistical method to relate the clustering of randomly positioned points. It is used to detect spatial or space-time clusters, to test whether a disease is randomly distributed over space, over time, or over space and time, and to evaluate the statistical significance of disease clusters (SaTScan, 2015).

“Spatial Poisson Model”: A discrete probability distribution that expresses the probability of a given number of events that occur in a fixed interval of time and/or space. This type of analysis is often used for data collected during a set point in time (SaTScan, 2015).

“Underimmunized”: A term used to describe children that do not receive the full number of recommended immunizations and thus are not fully vaccinated. This could be due to lack of access to healthcare, parental/guardian refusal of certain vaccines, and/or parental/guardian delaying vaccination.

“Vaccine Preventable Disease”: An infectious disease for which an effective preventive vaccine exists.

“Vaccine Selection Pressure”: Immunity from vaccination that reduces reproductive success of an infectious agent and causes the infectious agent to genetically evolve to have reproductive success.

“Virulent”: A term used in pathology to describe a pathogen’s ability to easily invade the tissue of the host and cause illness.

“Waning Immunity”: When vaccination for a disease does not provide protection against the disease for as long as expected.

Background of the Problem

Pertussis (also known as whooping cough) is an extremely contagious and endemic respiratory illness in the United States (CDC, n.d. d). Pertussis is caused by the bacterium called *Bordetella pertussis*. The bacterium is only found in humans and is spread from person to person primarily by the respiratory route (CDC, n.d. d). When an individual is infected with *Bordetella pertussis*, the bacteria attaches to the cilia (tiny hair like structures) in the upper airway (CDC, n.d. d). The bacterium releases toxins which damage the cilia as well as causes inflammation in the upper airway (CDC, n.d. d). Symptoms of pertussis include cold-like symptoms and severe coughing fits that can last between two to three weeks (CDC, n.d. d). In addition, pertussis can cause life-threatening complications in infants (less than one year old) and young children who are not fully vaccinated (CDC, n.d. d).

The clinical case definition of pertussis was updated in 2014 by the Centers for Disease Control and Prevention. “In the absence of a more likely diagnosis a cough illness lasting two weeks or more with one of the following symptoms: paroxysms of coughing (numerous rapid coughs at one time) or inspiratory “whoop” (noise a person

makes when breathing in after paroxysms of coughing) or posttussive vomiting (vomiting induced by paroxysm of coughing) or apnea (with or without cyanosis) for infants under the age of one year old” (CDC, n.d. d). According to the CDC, the best protection from pertussis is vaccination (CDC, n.d. d).

Pertussis Cases on the Rise

The number of reported cases of pertussis in the United States from 1922-2014 reflects an interesting history of public health and vaccination in the United States. As indicated in Figure 1, the number of reported cases of pertussis was in the hundreds of thousands prior to the availability of the pertussis vaccine in 1943 (Shapiro-Shapin, 2010; CDC, n.d. a). After the introduction of the vaccine, the annual reported cases of pertussis dropped dramatically indicating that the pertussis vaccine was an effective tool in preventing people becoming infected with *Bordetella pertussis* (Shapiro-Shapin, 2010; CDC, n.d. a).

Yet, according to the Centers for Disease Control and Prevention there has been a gradual rise in the number of pertussis cases reported in the United States since the 1980s (CDC, n.d. a). Even more significant is that since the early 2000s the number of cases reported each year has increased dramatically as seen in Figure 2. It is important to note that in 2012 there were 48,277 cases of pertussis reported in the United States (CDC, n.d. b). This is the highest number of cases of pertussis reported in the U.S. since 1955 (CDC, n.d. a). What could be causing the trend in the increase of reported cases of pertussis in the United States?

Figure 1: Reported Pertussis Cases in the United States from 1922-2014

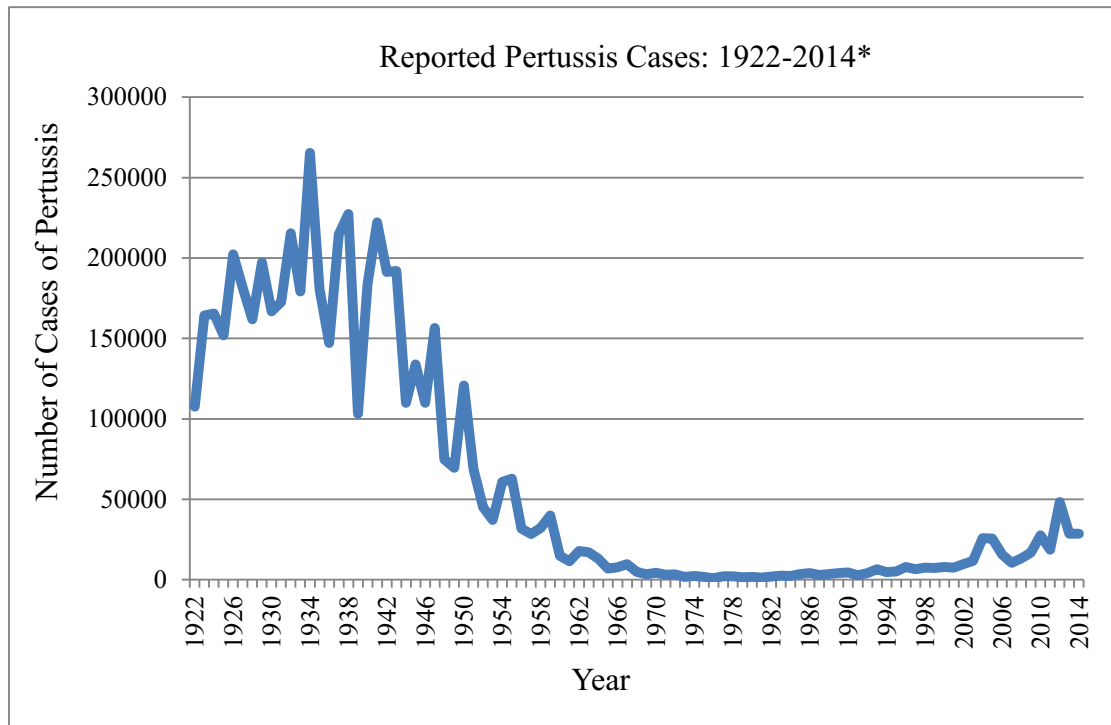
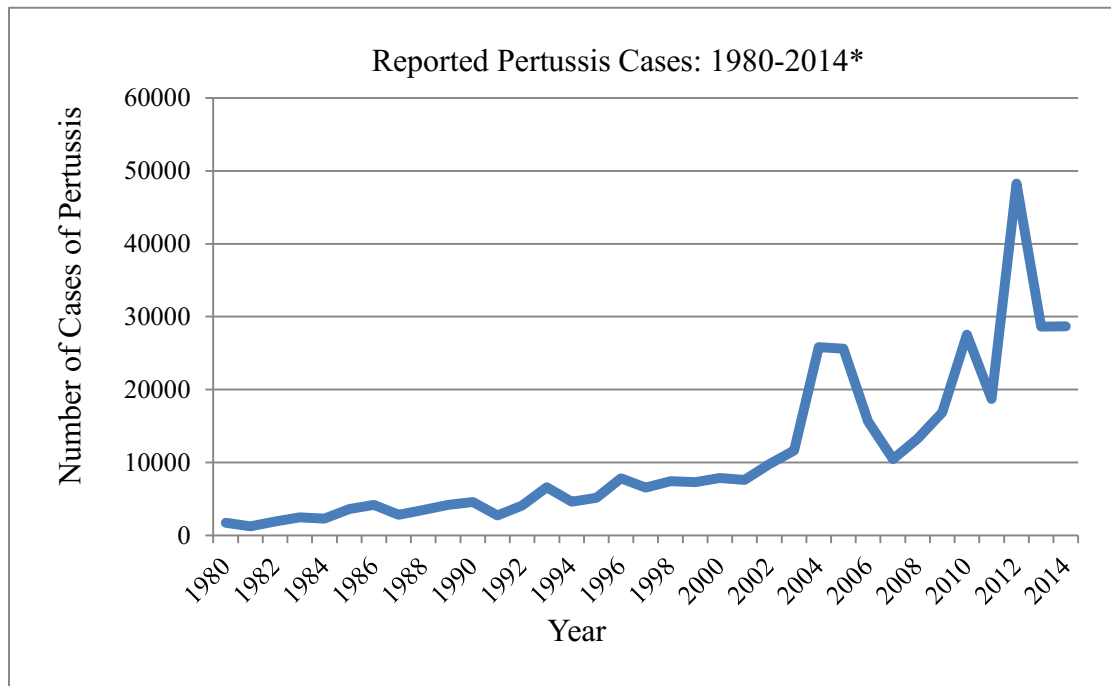


Figure 2: Reported Pertussis Cases in the United States from 1980-2014



* 2014 reported case numbers are provisional and are expected to increase as case counts are reconciled. Data source (CDC, n.d. a)

Acellular Pertussis Vaccine

The original pertussis vaccine was created as a killed whole cell vaccine meaning it contained inactive *Bordetella pertussis* (Shapiro-Shapin, 2010). Concerns about the safety of the whole cell vaccine were expressed because of the several adverse reactions that were reported after individuals received the vaccine (CDC, 1997 a). Some of the adverse reactions reported included redness, swelling and pain at the injection site as well as mild systemic events such as fever, drowsiness, and lack of appetite (CDC, 1997 a). Yet, it was the potential of the rare adverse event of acute encephalopathy that caused scientists, healthcare providers, and public health officials to be concerned about the safety of the whole cell pertussis vaccine. (CDC, 1997 a).

In the early 1990s the United States started to make the transition from using whole cell pertussis vaccine to DTaP (Klein, et al., 2016; Klein, et al., 2012). The DTaP vaccine is considered to be an acellular vaccine for pertussis because it contains defined protective antigens, including inactivated pertussis toxin, and one or more bacterial components such as proteins (CDC, 1997; Emsley, et al., 1996).

In 1992, the CDC recommended the current DTaP vaccination schedule which is a series of five doses of the DTaP vaccine at two months, four months, six months, between fifteen and eighteen months of age, and between four and six years old (Klein, et al., 2016; CDC, 1997 b). As the use of the DTaP vaccine became common practice in the late 1990s in the U.S. the number of reported cases of pertussis in the U.S. also increased as seen in Figure 2 (CDC, n.d. a). In addition, during the 1990s and early 2000s there was also an increase in reports of cases of pertussis in adolescents (Taroff, et al., 2013; Feikin, et al., 2000 b; Guris, et al., 1999). The increase in pertussis cases among

adolescents indicates that the DTaP vaccine only protects an individual four to six years after they complete the vaccination series and therefore could potentially indicate waning immunity (Klein, et al., 2016; Cherry, 2015; Taroff, et al., 2013; Cherry, 2012 b; Klein, et al., 2012; Skoff, et al., 2012).

Due to the increase in cases of pertussis in the U.S. in 2005 the CDC recommended that a child between the ages of eleven and twelve years old should receive a booster shot for the pertussis vaccine in the form of the Tdap (tetanus, diphtheria, and pertussis) vaccine (Acosta, et al., 2015; Taroff, et al., 2013; CDC, 2006; FDA, 2005). After the 2005 Tdap vaccination program began the number of pertussis cases being reported in adolescents reduced (Acosta, et al., 2015; Taroff, et al., 2013; Skoff, et al., 2012).

Since there was an overall increase in the number of reported cases of pertussis as well as an increase in the reported cases of pertussis in children between the ages of ten and eighteen years old, many experts have questioned the efficacy of the DTaP vaccine. Researchers have studied the trends in the correlation between the acellular vaccine and increased cases in pertussis (Taroff, et al., 2013; CDC, 2013; Shapiro, 2013; Cherry, 2012 b; Klein, et al., 2012; Skoff, et al., 2012; Witt, et al., 2012; Lugauer, et al., 2002; Olin, et al., 2003). Yet, according to the literature experts disagree if there is actually an association between the waning immunity of the DTaP vaccine and increased cases of pertussis. Therefore, it is inconclusive that the acellular pertussis vaccine is a cause of the increased cases of pertussis in the U.S.

Greater Awareness and Reporting of Pertussis

Advancements in medicine and public health have played a role in the increase in the number of pertussis cases being reported. In terms of medical advancements, healthcare providers have access to more sensitive diagnostic tools such as the routine use of polymerase chain reaction (PCRs) to help more accurately diagnosis a case of pertussis (CDC, n.d. h; Faulkner, et al., 2016; Cherry, 2015; Schmidt-Schlapfer, et al., 1997; Edelman, et al., 1996; Mead & Bollen, 1994). Since healthcare providers have access to PCRs and the use of single serum serologic testing there have been increased reports of pertussis (Faulkner, et al., 2016; Cherry, 2012 a; Schmidt-Schlapfer, et al., 1997; Edelman, et al., 1996).

In addition, during the 1980s and 1990s there was significant media attention about vaccine safety, the efficacy of whole cell vaccine vs. the DTaP vaccine, and there were hundreds of research articles published about pertussis and vaccines (Cherry, 2012 a). Due to the greater awareness of pertussis by healthcare providers, public health officials, and the public, the reporting of pertussis cases in the United State improved (Faulkner, et al., 2016; Cherry, 2012 a). That said, pertussis surveillance data are influenced by a number of factors such as provider awareness and diagnostic testing preferences which directly impacts case identification (Faulkner, et al., 2016).

Thus, it cannot be concluded that the recent trends of increased usage of PCR for pertussis diagnosis is the cause of increased reports of pertussis cases in the United States (Faulkner, et al., 2016). There are differences in the manner in which states investigate and diagnose a case of pertussis and the practices of how a state investigates and diagnosis a case of pertussis directly impacts the number of pertussis cases that are

reported (Faulkner, et al., 2016). Therefore, more sensitive diagnostic testing and greater awareness of pertussis cannot be the primary reason for the increased cases of pertussis in the United States.

Genetic Changes to Pertussis

Another theory about why there has been an increased rate of pertussis cases in the United States is regarding the genetic changes that have occurred in the bacterium *Bordetella pertussis*. Given the fact that *B. pertussis* has no nonhuman hosts or environmental niches, vaccine selected pressure is the most likely cause of the evolution of genetic changes in *B. pertussis* (Martin, et al., 2015; Lam, et al., 2014; Queenan, et al., 2013; Barkoff, et al., 2012; Hegerle, et al., 2012; Otsuka, et al., 2012). The genetic changes have altered the outer membrane proteins on the bacterium (Queenan, et al., 2013). Pertactin is an outer membrane protein of *Bordetella pertussis* and is a component of the acellular pertussis vaccine (Martin, et al., 2015; Queenan, et al., 2013; Barkoff, et al., 2012; CDC, 1997; Emsley, et al., 1996). This particular protein is a major virulence factor within *B. pertussis* because it promotes adhesion to epithelial cells in the trachea (Martin, et al., 2015; Emsley, et al., 1996).

It is believed that there is a strain of pertussis that is circulating that is pertactin-negative meaning that this particular strain of pertussis does not have the pertactin protein (Martin, et al., 2015; Queenan, et al., 2013; Barkoff, et al., 2012). The significance of the pertactin-negative strain of *B. pertussis* is three fold. Due to the genetic changes pertactin-negative strain of *B. pertussis* may be able to avoid vaccine-induced immunity,

the strain might be more virulent, and/or the strain might be more contagious (Martin, et al., 2015; Queenan, et al., 2013; Mooi, et al., 2014; Mooi, et al., 2009).

The *Bordetella pertussis* strain that lacks the pertactin protein has been identified in France, Japan, Finland and Australia (Lam, et al., 2014; Barkoff, et al., 2012; Hegerle, et al., 2012; Octavia, et al., 2012; Otsuka, et al., 2012). In 2011, the first identified cases of the pertactin-negative strain of pertussis was identified in the U.S. in the city of Philadelphia, PA (Queenan, et al., 2013).

Since the initial identification of pertactin-negative strain of *B. pertussis* in the United States there have been a handful of investigations to determine where in the country pertactin-negative strain of *B. pertussis* is circulating (Martin, et al., 2015; Bowden, et al. 2014; Pawloski, et al., 2014; Quinlan, et al., 2014; Schmidtke., et al, 2012). The pertactin-negative strain of *B. pertussis* was identified in several states and notably in the pertussis outbreak in California in 2010 as well as in the Washington state pertussis outbreak of 2012 (Martin, et al., 2015; Bowden, et al. 2014; Pawloski, et al., 2014; Quinlan, et al., 2014; Schmidtke., et al, 2012).

It is possible that the pertactin-negative strain of *Bordetella pertussis* might be causing increased cases of pertussis in the United States. Yet, the research on this particular topic has just started in the United States and in the other countries that have reported the presence of pertactin-negative strains of *B. pertussis*.

To date there has not been a large study conducted in the United States that has examined the clinical presentation, testing for various strains of *Bordetella pertussis*, and comparing the reported cases and strains of *Bordetella pertussis* to individual vaccination records (Martin, et al., 2015; Queenan, A., et al., 2013). In addition, the CDC has

reported very little information about pertactin-negative pertussis cases in the United States. The CDC has only published a website dedicated to explaining what the pertactin-negative strain of *B. pertussis* is and how the CDC is conducting research to determine if the pertactin-negative strain of *B. pertussis* relates to the increase in the number of cases of pertussis in the United States (CDC, n.d., g).

Due to the limited information that has been published about pertactin-negative pertussis in research and the limited information being provided by the CDC, one cannot conclude that the genetic changes to *Bordetella pertussis* is the main cause of the increased reports of pertussis cases in the United States.

Nonmedical Vaccine Exemptions

Currently, all fifty states and the District of Columbia require vaccination upon school entry though forty-seven of the fifty states offer either religious or personal belief exemptions to the school vaccination requirements (California Legislative Information, 2015; Wang, et al., 2014; Blank, et al., 2013; Omer, et al., 2008; Orenstein & Hinman, 1999; Malone & Hinman, n.d.). When one examines the vaccination rates in the United States from 2009-2012 the median vaccination rate coverage is impressive. According to the Centers for Disease Control and Prevention the median rate coverage in the U.S. of the DTaP vaccine for students that entered kindergarten between 2009-2012 was $\geq 90\%$ (CDC, 2011; CDC, 2012).

According to the CDC national and statewide rates of immunization are high (CDC, 2011; CDC, 2012). However, if one takes a closer look at the county level there is substantial local variation in vaccination rates throughout the U.S. (Lieu, et al., 2014;

Atwell, et al., 2013; Diekema, 2012; Duffy & Shea, 2012; Omer, et al., 2009; Omer, et al., 2008; Feikin, et al., 2000). In addition, recent studies have indicated that there is also an increase in the rate of parents who refuse to vaccinate their children and elect to use the nonmedical vaccine exemptions to avoid the school immunization requirements (Atwell & Salmon, 2014; Diekema, 2012; Omer, 2008; Wang, et al., 2014). Thus there are pockets of communities in the United States where the median vaccination rates are below >90%. For herd/community immunity to be effective for pertussis, 92-94% of the community needs to be vaccinated against pertussis (CDC, n.d. e).

Based on the studies that have been conducted about nonmedical vaccine exemptions and pertussis outbreaks in California and Michigan there is a potential correlation between nonmedical vaccine exemptions and outbreaks of pertussis (Atwell, et al., 2013; Duffy & Shea, 2012; Omer, et al., 2008). It is possible that high rates of nonmedical vaccine exemptions could be the cause of the increasing cases of pertussis in the United States.

Question and Hypothesis

The aim of this investigation is to determine if there is a correlation between nonmedical vaccine exemptions from school immunization requirements and clusters of pertussis cases in the United States during 2012. It is believed that counties in the U.S. that have high rates of nonmedical vaccine exemptions will also have high rates of reported pertussis cases. The hypothesis is based on the principle of herd/community immunity. When nonmedical vaccine exemptions rates are high enough to compromise herd/community immunity at the local level then the risk of vaccine preventable disease

outbreak increases (Lieu, et al., 2015; Glanz, et al., 2009; Omer, et al., 2008; Feikin, et al., 2000).

Implications of Research

The significance of this investigation is two fold. The first is if there is a correlation between nonmedical vaccine exemptions and pertussis cases then one could argue that in areas where there are high rates of nonmedical vaccine exemptions there could also be increased cases of other vaccine preventable diseases. The second is the larger implication on public health in the U.S. and the impact that high rates of nonmedical vaccine exemptions have on the health of the country. If there is a correlation between high rates of nonmedical vaccine exemptions and increased rates of pertussis cases then both the State and Federal Governments need to discuss policy regarding the school immunization programs and the efficacy of nonmedical vaccine exemptions.

Chapter II

Materials and Methods

This study evaluated several sets of data to determine if there was a correlation between nonmedical vaccine exemptions and pertussis cases. This included comparing the incidence rate of pertussis in the forty-eight states that offer nonmedical vaccine exemptions vs. the incidence rate of pertussis in the two states (Mississippi and West Virginia) that did not offer nonmedical vaccine exemptions in 2012. In addition, this study also used a linear regression analysis, SaTScan version 9.4, and ArcGIS to determine if there was a correlation between geographical clusters of nonmedical vaccine exemptions for students entering kindergarten during the 2011-2012/2012-2013 school years with geographic clusters of pertussis cases in 2012.

Incidence Rate

In 2012 forty-eight states allowed for nonmedical vaccine exemptions and two states (Mississippi and West Virginia) did not offer nonmedical vaccine exemptions. To compare the incidence rate of pertussis cases in states that offer nonmedical vaccine exemptions vs. the two states (Mississippi and West Virginia) that do not offer nonmedical vaccine exemptions, I used state data from 1997-2014 to calculate the incidence rate of pertussis in the forty-eight states that offer nonmedical vaccine exemptions and the two states (Mississippi and West Virginia) that do not offer nonmedical vaccine exemptions.

Data for Linear Regression & Geographic Cluster Analysis

The second set of data needed for the investigation included: nonmedical vaccination rates for students entering kindergarten during the 2011-2012 and the 2012-2013 academic years and the number of pertussis cases reported in children under the age of five years old at the county level from the nineteen states that had an incidence rate above 15.4 per 100,000 during the 2012 pertussis outbreak in the United States (CDC, n.d. b). The incidence rate above 15.4 per 100,000 was selected because the overall incidence of reported pertussis in the United States during the 2012 outbreak was 15.4 per 100,000 (CDC, n.d. b).

There were a total of nineteen states that had a pertussis incidence rate above 15.4 per 100,000 (Table 1). Kindergarten immunization data and cases of pertussis for children age five years and younger at the county level were collected from each state's Department of Public Health. Of the nineteen states that had an incidence rate above 15.4 per 100,000 during the 2012 pertussis outbreak in the United States only five states (Arizona, New Jersey, Oregon, Utah, and Washington) had the data for this investigation (CDC, n.d. b) (Table 1).

The state of Utah reported both the immunization data and pertussis cases at the health district level. In Utah a health district can be a single county such as the Davis county health district or a group of counties such as the Bear River health district which serves three counties. That said, the data from Utah's health districts were used because it provided information at the county level. In addition, it is important to note that Washington started to collect nonmedical vaccine exemption data during the 2012-2013 academic year.

Table 1: State Data Collection Information

State	Incidence rate (per 100,000) of pertussis in 2012) Data source: (CDC, n.d.b)	Did the state collected pertussis cases by county	School immunization data for students entering kindergarten 2011-2012 and 2012-2013 academic year by county
Alaska	48.3	Yes	Incomplete – <i>state does not collect school immunization data</i>
Arizona	17.2	Yes	Yes
Colorado	28.8	Yes	Incomplete - <i>state will begin to collect immunization data in 2016</i>
Illinois	15.7	Yes	Incomplete – <i>state had immunization data for entire school population not just kindergarten</i>
Iowa	56.5	Yes	Incomplete – <i>state does not collect school immunization data</i>
Kansas	30.7	Yes	Incomplete – <i>state has the kindergarten immunization data but did not collect nonmedical exemption rates at the county level</i>
Maine	55.5	Yes	Incomplete – <i>state did not begin to collect immunization data until the 2014-2015 school year</i>
Minnesota	77.0	Yes	Incomplete – <i>state does not collect school immunization data</i>
Montana	54.6	Yes	Incomplete – <i>state had immunization data for entire school population not just kindergarten</i>
New Hampshire	20.4	Yes	Incomplete – <i>state does not have immunization data at the county level</i>

Table 1: State Data Collection Information

State	Incidence rate (per 100,000) of pertussis in 2012) Data source: (CDC, n.d.b)	Did the state collected pertussis cases by county	School immunization data for students entering kindergarten 2011-2012 and 2012-2013 academic year by county
New Jersey	15.7	Yes	Yes
New Mexico	44.3	Yes	Incomplete - <i>state did not begin to collect immunization data until 2014</i>
New York* <i>*Does not include New York City</i>	24.2	Yes	Incomplete – <i>state did not provide kindergarten enrollment numbers. In addition, the immunization data for the 2012-2013 academic year is for the entire school populations</i>
North Dakota	30.6	Yes	Incomplete - <i>school's can elect to report data if they want therefore reporting each year is inconsistent</i>
Oregon	23.2	Yes	Yes
Utah	55.7	Yes	Yes
Vermont	103.0	Yes	Incomplete – <i>state had immunization data for entire school population not just kindergarten</i>
Washington	71.3	Yes	Yes – <i>however, the state only has nonmedical vaccine exemption data for the 2012-2013 school year</i>
Wisconsin	120.2	Yes	Incomplete- <i>state only had data on immunization rates for 24 month olds in the state and does not provide exemption data</i>

According to the Departments of Public Health from the five states analyzed in this investigation, the percent of nonmedical vaccine exemptions for students entering kindergarten during the 2011-2012 academic year was the following: Arizona at 3.4%, New Jersey at 1.1%, Oregon at 5.8%, and Utah at 3.5%. The percent of nonmedical vaccine exemptions for students entering kindergarten during the 2012-2013 academic year was the following: Arizona at 3.9%, New Jersey at 1.2%, Oregon at 6.4%, Utah at 3.8%, and Washington at 3.5%.

Arizona, Oregon, Utah, and Washington allow for religious and personal belief vaccine exemptions (Figures 9, 10, 11, and 13) (Arizona's Department of Health, n.d.; Oregon's Department of Health, n.d.; Utah Department of Health, n.d; Washington's Department of Health, n.d). Whereas, New Jersey only allows for religious vaccine exemptions (Figure 12) (New Jersey Department of Health and Senior Services, 2008).

Linear Regression Analysis

The nonmedical vaccination rates for students entering kindergarten during the 2011-2012 and the 2012-213 academic years and number of pertussis cases reported in children under the age of five years old at the county level and state level were used to create a linear regression in excel. The linear regression model helps to determine if there was a correlation between the percent of nonmedical vaccine exemptions and percent of pertussis cases.

Cluster Identification and Population Description

The nonmedical vaccination rates for students entering kindergarten during the 2011-2012 and the 2012-2013 academic years and number of pertussis cases reported in children under the age of five years old at the county level were also used to determine if there was a correlation between geographic clusters of pertussis cases and geographic clusters of nonmedical vaccine exemptions using SaTScan version 9.4.

To verify if there was a correlation between geographic clusters of pertussis cases and geographic clusters of nonmedical vaccine exemptions, I used Kulldorff's scan statistics through the free software program SaTScan version 9.4 (SaTScan, 2015; Lieu, et al., 2015; Atwell, et al., 2013; Omer, et al., 2008). This approach was useful in identifying localized, statistically significant geographic clusters of events (Lieu, et al., 2015; Atwell, et al., 2013; Omer, et al., 2008). I used the spatial Poisson model and the Bernoulli space-time model in SaTScan version 9.4 to determine if there was statistical significance in geographical clusters of nonmedical vaccine exemptions and geographical clusters of pertussis cases (SaTScan, 2015; Lieu, et al., 2015; Atwell, et al., 2013; Omer, et al., 2008).

The spatial Poisson model and the Bernoulli space-time model detected and evaluated geographic clusters. Since geographic clustering of nonmedical vaccine exemptions is a relatively long-term phenomenon a Bernoulli space-time model was selected to identify geographic clusters at the county level. The geographic clusters of pertussis cases on the other hand was considered to be a short-term phenomenon and the

spatial Poisson model was used to identify geographic clusters of pertussis at the county level.

Candidate spatial clusters of events and space-time clusters were identified -- in this case county location for exemption clusters and county location for pertussis clusters with a statistical significance level of $P < .05$. This was done by gradually scanning a circle variable size window across space noting the number of nonmedical vaccine exemptions as well as the number of cases of pertussis and calculated the likelihood for each (Lieu, et al., 2015; Omer, et al., 2008). The test statistic derived as a likelihood ratio (circle with the maximum likelihood was the most likely cluster meaning the cluster was least likely to be due to chance) and was calculated for each candidate cluster (Lieu, et al., 2015; Omer, et al., 2008). The end result of the analysis produced data tables of spatial clusters of nonmedical vaccine exemptions, data tables of spatial clusters of pertussis cases, geographical mapping of the data through Google maps, and data that can be used in GIS software (SaTScan, 2015; Lieu, et al., 2015; Atwell, et al., 2013; Omer, et al., 2008).

Studies have indicated that the demographic variables of income level and education attainment have been shown to be associated with rates of vaccine coverage (Yang, et al, 2016; Wang, et al., 2014; Atwell, et al., 2013; Omer, et al., 2009; Omer, et al., 2008). Research has shown that white, college educated individuals with relatively high levels of income were more likely to obtain nonmedical vaccine exemptions for their children potentially leading to clusters of communities that have high rates of children with nonmedical vaccine exemptions (Yang, et al, 2016; Wang, et al., 2014; Atwell, et al., 2013; Birnbaum, et al., 2013; Richards, et al., 2013; Salmon, et al., 2005).

In addition, studies have indicated that individuals whose income is below the poverty level tend to have higher rates of not being fully vaccinated potentially leading to clusters of communities where children are underimmunized (Lieu, et al., 2015; Wang, et al., 2014; Atwell, et al., 2013; Brinbaum, et al., 2013; Diekema, 2012). Since people with the same demographic variables tend to live in the same geographic area it was not necessary to consider these factors as covariates in this investigation.

The rationale to analyze data at the county level was two fold. First, most state's Departments of Public Health collect infectious disease and immunization data at the county level. Second, if one only examined data at the state level then there is the potential that pockets of localized clusters of pertussis cases and/or unimmunized individuals could not be seen due to the scale of state level analysis.

The rationale to adjust for age in the linear regression and SaTScan version 9.4 analysis was two-fold. The first is that children five years old and younger had the highest incidence rate of pertussis cases during 2012 (CDC, n.d. b). Since a large percentage of pertussis cases were diagnosed in children age five years and younger it is important to account for the this age group because pertussis is more likely to be diagnosed in a child under the age of five years.

The rationale to analyze vaccination rates for students entering kindergarten was because most state's Departments of Public Health collect immunization data from schools and report immunization data at various grades (kindergarten and 7th grade). The grade of kindergarten was selected for this study because when students begin their education in the United States they need to provide vaccination information to the school and most students begin their education in kindergarten.

Mapping of Geographic Clusters

SaTScan version 9.4 identified geographic clusters of nonmedical vaccine exemptions and geographic clusters of pertussis cases. This data were then used to create maps using the software ArcGIS to determine which geographic clusters overlap with one another. The visualization of the overlap of geographic clusters of nonmedical vaccine exemptions and the geographic clusters of pertussis cases on maps helps to determine if there was a correlation between nonmedical vaccine exemptions and pertussis cases in the geographic clusters identified by SaTScan version 9.4.

Linear Regression Analysis of Geographic Clusters

The data from SaTScan version 9.4 that identified geographic clusters of nonmedical vaccine exemptions and geographic clusters of pertussis cases that overlap with one another were used to create a linear regression in excel. The linear regression helps to determine if there was a correlation between nonmedical vaccine exemptions and pertussis cases in the geographic clusters identified by SaTScan version 9.4.

Analytical Tools

There were several reasons behind the rationale to use SaTScan version 9.4 for this investigation. This particular software performs statistical analysis, provides geographical mapping of the data through Google maps, and creates data that can be used in GIS software. SaTScan version 9.4 is a free software which analyzes spatial, temporal, and space-time data using spatial, temporal, or space-time statistics (SatScan, 2015).

SaTScan version 9.4 has been widely used in public health and other fields to identify

clusters of illness or other events across space and time (Lieu, et al., 2015; Sherman, et al., 2014; Atwell, et al., 2013; Omer, et al., 2008).

SaTScan version 9.4 was developed by Dr. Martin Kulldorff a professor and biostatistician in the Department of Population Medicine at Harvard Medical School. SaTScan version 9.4 was created when Dr. Kulldorff was working for the National Cancer Institute’s Division of Cancer Prevention (National Cancer Institute, n.d.). The goal of Dr. Kulldorff’s work was to create software that could identify geographic surveillance of disease, that could detect spatial or space-time disease clusters, and to determine if the disease clusters were statistically significant (National Cancer Institute, n.d.).

ArcGIS was the software used to create the maps from the data produced by SaTScan version 9.4. Harvard University’s Center for Geographic Analysis provided the support and access to ArcGIS to create the maps.

Table 2: Experimental Design Rationale

Logic	Experiment	Control & Why
1. To evaluate the incidence rate of pertussis and states that offer nonmedical vaccine exemptions vs. states that do not offer nonmedical vaccine exemptions.	Calculate and graph the incidence rate of pertussis cases in the states that offer nonmedical vaccine exemptions vs. states that do not offer nonmedical vaccine exemptions.	The dependent variable was the incidence rate of pertussis in Mississippi, West Virginia, and the forty-eight states that offer nonmedical vaccine exemptions and the independent variable was the calendar year.

Table 2: Experimental Design Rationale

Logic	Experiment	Control & Why
<p>2. To evaluate the relationship between nonmedical vaccine exemptions of students entering kindergarten during the 2011-2012 and 2012-2013 academic years and pertussis cases at the county and state levels in 2012.</p>	<p>A linear regression analysis created to compare the percent of nonmedical vaccine exemptions to percent of pertussis cases at the county and state levels in 2012.</p>	<p>The dependent variable was the percent of pertussis at the county level and the independent variable was the percent of nonmedical vaccine exemptions at the county level.</p>
<p>3. To determine if there were geographical clusters of nonmedical vaccine exemptions for students entering kindergarten during the 2011-2012 and 2012-2013 academic years.</p>	<p>A Bernoulli space-time model was run using the free computer software SaTScan version 9.4.</p>	<p>The dependent variable was the number of children who had nonmedical vaccine exemptions, the independent variable was the calendar year, and the offset variable was the number of children enrolling in kindergarten that year.</p>
<p>4. To determine if there were geographical clusters of pertussis cases during 2012.</p>	<p>A Poisson regression model was run using the free computer software SaTScan version 9.4.</p>	<p>The dependent variable was the number of pertussis cases, the independent variable was the calendar year, and the offset variable was the total population.</p>
<p>5. To evaluate the relationship the percent of nonmedical vaccine exemptions and annual number of pertussis cases per 100,000 people in the geographic clusters identified by SaTScan version 9.4.</p>	<p>A linear regression analysis created to compare the percent of nonmedical vaccine exemptions to the annual number of pertussis cases per 100,000 people in the geographic clusters identified by SaTScan version 9.4.</p>	<p>The dependent variable was the annual number of pertussis cases per 100,000 people in the geographic clusters identified by SaTScan version 9.4 and the independent variable was the percent of nonmedical vaccine exemptions in the geographic clusters identified by SaTScan version 9.4.</p>

Research Limitations

There were a handful of limitations of this investigation that were unavoidable. The first was accounting for immunization data from children in kindergarten who were homeschooled during the 2011-2012/2012-2013 academic years. States do not collect immunization data on children that are homeschooled. Therefore, this specific population in the local community was not accounted for within the research. That said, according to the United States Department of Education, in 2012 the reported number of children in the U.S. that were homeschooled for kindergarten was so small and that there were too few cases to report reliable estimates (U.S. Department of Education, 2015). Thus, not including this particular population should not lead to any bias in the data analysis because the population of home school kindergarteners is extremely small.

A second limitation of this investigation was that children who have medical exemptions from immunization laws were not included in the study. If one were to include medical exemptions in the data analysis there was a chance the medical exemptions could bias the data. Medical exemptions are not expected to be clustered and if this particular data were included the statistical analysis would be bias towards the null hypothesis because medical exemptions are located randomly.

A third limitation was that states do not have records of children that are underimmunized. When a child is underimmunized they are susceptible to becoming infected with vaccine preventable diseases. If a community has high rates of underimmunized children then there is the potential that the community will have higher rates of pertussis cases.

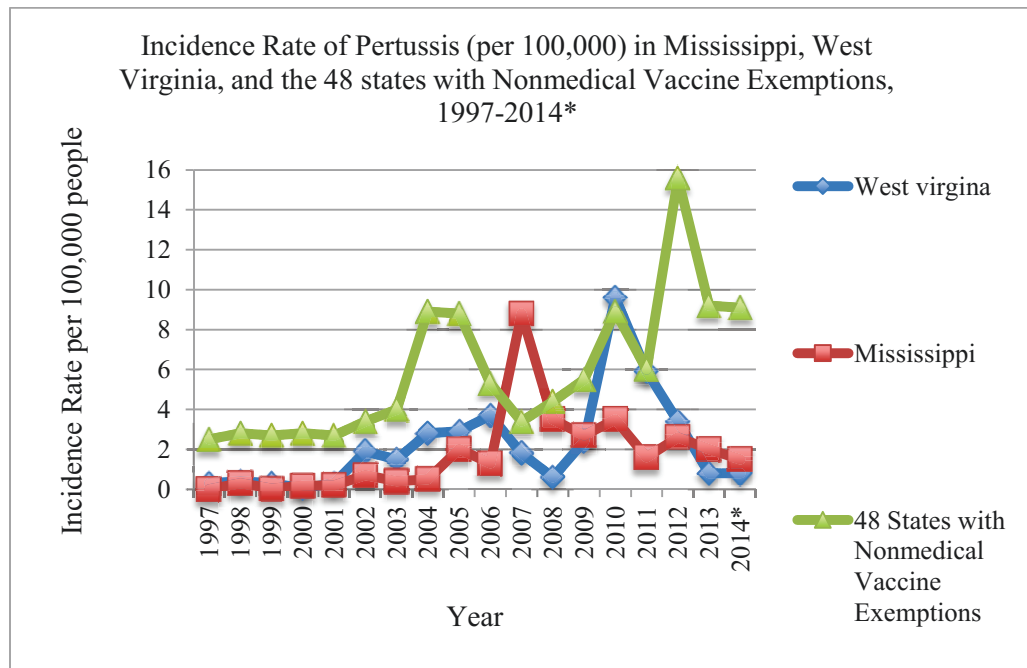
Chapter III

Results

Incidence Rate

The calculation of the incidence rate of pertussis cases used data from all fifty states in the United States. The data were used to calculate and graph the incidence rate of pertussis cases included the number of pertussis cases reported in each state from 1997-2014 and the total population in each state from 1997-2014 as reported by the U.S. Census Bureau (CDC, n.d. a; Mississippi State Department of Health, n.d.; West Virginia Department of Public Health, n.d.; U.S. Census Bureau, n.d.). The incidence rate was calculated using the equation: $(\text{total number of cases}/\text{total population}) \times 100,000$.

Figure 3: Incidence Rate of Pertussis (per 100,000) in Mississippi, West Virginia, and the 48 States with Nonmedical Vaccine Exemptions, 1997-2014



* 2014 reported case numbers are provisional and are expected to increase as case counts are reconciled. Data source: (CDC, n.d. a)

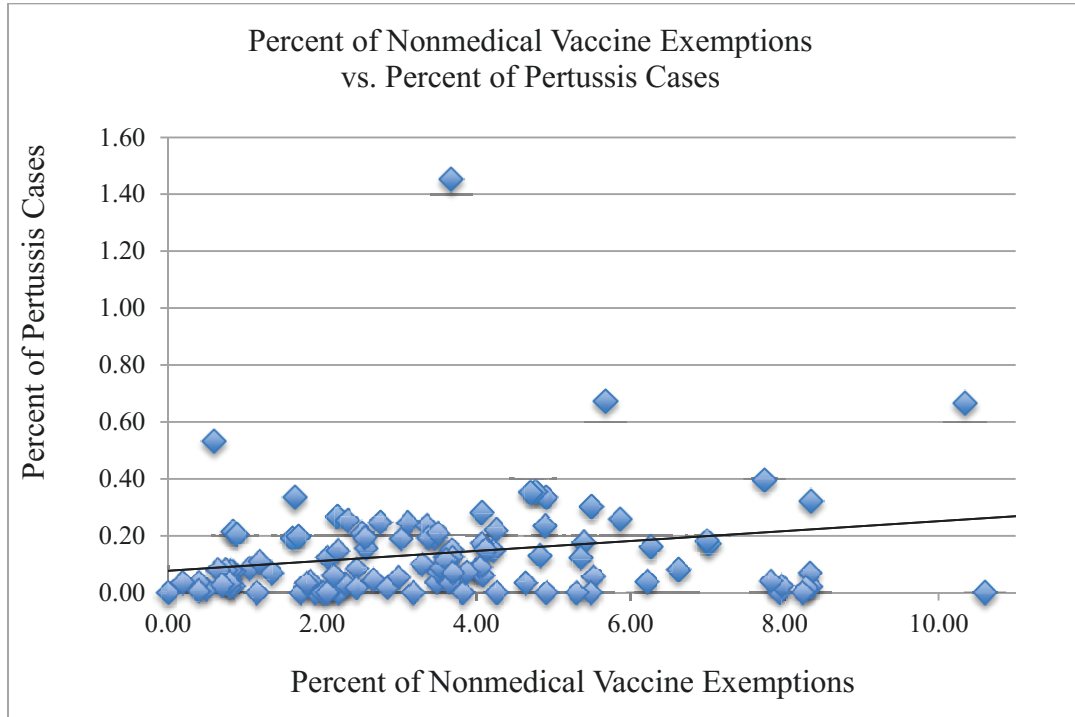
The incidence rate of pertussis cases per 100,000 people in states that offer nonmedical vaccine exemptions was greater than the states that do not offer nonmedical vaccine exemptions during the time period of 1997-2014. The only time that West Virginia had a higher incidence rate of pertussis cases between 1997-2014 was in the year 2010 (Figure 3). In addition, the only time that Mississippi had a higher incidence rate of pertussis cases between 1997-2014 was in the year 2007 (Figure 3).

Linear Regression Analysis

The data used for the linear regression at the county level were the percent of nonmedical vaccine exemptions of students entering kindergarten during the 2011-2012 and 2012-2013 academic years as well as percent of pertussis cases in children under the age of five years old 2012 at the county level in the states of Arizona, New Jersey, Utah, Oregon, and Washington.

The percent of nonmedical vaccine exemptions at the county level was calculated using the equation $(\text{total number of kindergarten students with nonmedical vaccine exemptions} / \text{total number of children enrolled in kindergarten}) \times 100$. The percent of pertussis cases was calculated using the equation $(\text{total number of pertussis cases in children under the age of five years old} / \text{population in the county under the age of five years old}) \times 100$. The percent of pertussis cases was adjusted for age because children under the age of five years old had the highest incidence rate of pertussis in 2012 (CDC, n.d. b).

Figure 4: Linear Regression Model for Percentage of Nonmedical Vaccine Exemptions vs. Percentage of Pertussis Cases at the County Level

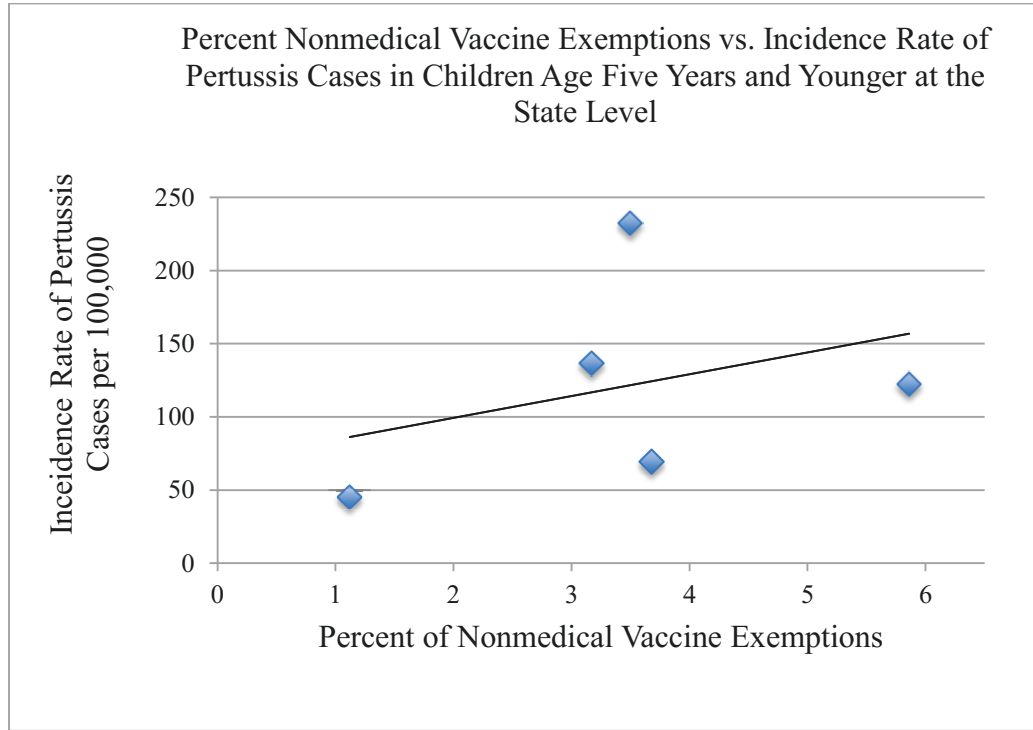


The data used for the linear regression at the state level was the percent of nonmedical vaccine exemptions of students entering kindergarten during the 2011-2012 and 2012-2013 academic years as well as the incidence rate of pertussis cases in children under the age of five years old 2012 at the state level in Arizona, New Jersey, Utah, Oregon, and Washington.

The percent of nonmedical vaccine exemptions at the state level was calculated using the equation $(\text{total number of kindergarten students with nonmedical vaccine exemptions} / \text{total number of children enrolled in kindergarten}) \times 100$. The incidence rate of pertussis cases was calculated using the equation $(\text{total number of pertussis cases in children under the age of five years old} / \text{population in the state under the age of five years old}) \times 100,000$. The incidence rate of pertussis cases was adjusted for age because

children under the age of five years old had the highest incidence rate of pertussis in 2012 (CDC, n.d. b).

Figure 5: Linear Regression Model for Percentage of Nonmedical Vaccine Exemptions vs. Incidence Rate of Pertussis Cases per 100,000 at the State Level



Based on the trend lines in Figure 4 and Figure 5, there is a weak correlation between the rates the pertussis cases and the rates of nonmedical vaccine exemptions. The data indicates that as the percent of nonmedical vaccine exemptions increases the percent of pertussis cases also increases.

Geographic Cluster Analysis

The data collected from Arizona, New Jersey, Oregon, Utah, and Washington were also entered into SaTScan version 9.4 to determine geographic clusters of nonmedical vaccine exemptions and geographic clusters of pertussis to complete the data analysis. SaTScan version 9.4 was programmed to perform cluster analysis with a cluster radius of 200km, a P-value of $<.05$, at both high rates and low rates of geographic clusters, and that there were no geographic overlaps with the identified clusters.

It is important to note that in the geographic cluster analysis some counties might be identified in both high and low rate clusters for nonmedical vaccine exemptions or in both the high and low rate clusters for pertussis cases. This occurred because a geographic location in the county was identified to be in the 200km radius for either a high or low rates cluster. This means that if a particular county is identified in both high and low rates geographic clusters that certain areas of the county have different vaccination rates or different rates of pertussis cases.

High Rates Analysis

The analysis of high rates of geographic clusters of nonmedical vaccine exemptions and high rates of geographic clusters of pertussis cases provides information about counties where there is a high number of reported pertussis cases and counties where the students enrolling in kindergarten have low vaccination rates.

Table 3: High Rates of Spatial Clusters of Nonmedical Vaccine Exemptions for the 2011-2012/2012-2103 Academic Years

Exemption Cluster	Cluster Centroid		Observed Exemptions	Expected Exemptions	Relative Risk	P value	Location (county & state)
	Latitude °N	Longitude °W					
1	43.92	122.89	4387	2293.28	2.17	<.0001	Lane, Linn, Marion, Polk, Coos, Deschutes, Yamhill, Jackson, Clackamas, Josephine, Benton, Tillamook, Multnomah, Douglas, Lincoln, and Washington, Oregon
2	33.34	112.49	5194	3710.15	1.54	<.0001	Maricopa, Pinal, and Yavapi, Arizona
3	43.06	118.98	816	295.89	2.83	<.0001	Harney and Malheur, Oregon
4	38.96	112.33	733	518.24	1.43	<.0001	Central Utah, Utah, Southwest, and Southeastern, Utah
5	47.35	123.18	2241	1883.45	1.21	<.0001	Mason, Kitsap, Thurston, King, Grays Harbor, Jefferson, Lewis, Pierce, Pacific, Island, Clallam, Wahkiakum, Snohomish, Clark, Cowlitz, San Juan, Skagit, Kittitas, and Whatcom, Washington Clatsop and Columbia, Oregon

Table 3: High Rates of Spatial Clusters of Nonmedical Vaccine Exemptions for the 2011-2012/2012-2103 Academic Years

Exemption Cluster	Cluster Centroid		Observed Exemptions	Expected Exemptions	Relative Risk	P value	Location (county & state)
	Latitude °N	Longitude °W					
6	48.53	117.27	309	185.87	1.67	<.0001	Pend Oreille, Stevens, Ferry, Spokane, Lincoln, Okanogan, and Whitman, Washington
7	40.87	110.96	379	305.28	1.25	.0061	Summit and Wasatch, Utah
8	35.39	110.32	290	227.07	1.28	.0087	Navajo, Apache, and Coconino, Arizona
9	40.96	112.09	338	274.07	1.24	.0263	Davis, Utah
10	40.56	74.91	104	85.27	1.22	.9913	Hunterdon, New Jersey
11	45.42	119.60	106	89.75	1.18	.9999	Morrow and Umatilla, Oregon

Table 4: High Rates of Spatial Clusters of Pertussis Cases, 2012

Exemption Cluster	Cluster Centroid Latitude °N Longitude °W		Observed Exemptions	Expected Exemptions	Relative Risk	P value	Location (county & state)
1	47.03	122.13	1045	539.85	2.79	<.0001	Pierce, Thurston, Lewis, King, Kitsap, Mason, Cowlitz, Clark, Kittitas, Snohomish, Yakima, Grays Harbor, Island, Pacific, Jefferson, Wahkiakum, Chelan Skagit, Klickitat, Clallam, Grant, San Juan, Douglas, Whatcom, Washington Columbia, Clatsop, Multnomah, Hood River, Washington, Oregon
2	46.90	117.52	139	73.91	1.94	<.0001	Whitman, Columbia, Adams, Spokane, Asotin, Lincoln, Walla Walla, Franklin, Stevens, and Benton, Washington
3	35.71	113.74	34	11.75	2.92	<.0001	Mohave, Arizona
4	40.66	111.92	297	229.35	1.92	.0014	Salt Lake Valley, Davis, Utah, and Weber-Morgan, Utah
5	43.06	118.98	8	2.97	2.70	.7976	Harney and Malheur, Oregon

Table 5: Percent Cases of Nonmedical Vaccine Exemptions in High Rate Geographic Clusters as Calculated by SaTScan version 9.4

Geographic Cluster Number	Percent of Nonmedical Vaccine Exemptions for the 2011-2012/2012-2013 Academic Year in Geographic Clusters with a P value <.05
SaTScan version 9.4 calculation for percent cases in the entire area	3.0
Cluster 1	5.7
Cluster 2	4.2
Cluster 3	8.2
Cluster 4	4.2
Cluster 5	3.6
Cluster 6	5.0
Cluster 7	3.7
Cluster 8	3.8

Table 6: Annual Number of Cases of Pertussis per 100,000 people in High Rates Geographic Clusters as Calculated by SaTScan version 9.4

Geographic Cluster Number	Annual Number of Cases of Pertussis per 100,000 people in Geographic Clusters with a P value <.05
SaTScan version 9.4 calculation for percent cases in the entire area	115.97
Cluster 1	224.0
Cluster 2	217.7
Cluster 3	334.8
Cluster 4	149.9

Table 7: Overlap of High Rates of Geographic Clusters of Nonmedical Vaccine Exemptions and High Rates of Geographic Clusters of Pertussis

Cluster	Percent of Nonmedical Vaccine Exemptions for the 2011-2012/2012-2013 Academic Year in Geographic Clusters with a P value <.05	Annual Number of Cases of Pertussis per 100,000 people in Geographic Clusters with a P value <.05
SaTScan version 9.4 calculation for the entire area	3.0	115.97
Eastern Washington State and Northern Oregon Cluster	3.6	224.0

Table 7: Overlap of High Rates of Geographic Clusters of Nonmedical Vaccine Exemptions and High Rates of Geographic Clusters of Pertussis

Cluster	Percent of Nonmedical Vaccine Exemptions for the 2011-2012/2012-2013 Academic Year in Geographic Clusters with a P value <.05	Annual Number of Cases of Pertussis per 100,000 people in Geographic Clusters with a P value <.05
Western Washington State Cluster	5.0	217.7
Utah Cluster	3.7	334.8

In the five states that were analyzed for high rates of geographic clusters of nonmedical vaccine exemptions and high rates of geographic clusters of pertussis cases, SaTScan version 9.4 identified seventy-two counties with a P-value of <.05, that were located in geographical clusters of nonmedical vaccine exemptions (Table 3 and Figure 7) and forty-five counties that geographical clusters of pertussis cases in 2012 (Table 4 and Figure 7). Of the forty-five counties that were identified to be a part of a geographic cluster of high rates of pertussis cases, twenty-six or fifty-eight percent of those counties were also associated with geographic clusters of high rates of nonmedical vaccine exemptions (Figure 7).

Low Rates Analysis

The analysis of low rates of geographic clusters of nonmedical vaccine exemptions and low rates of geographic clusters of pertussis cases provides information

about counties where there is a low number of reported pertussis cases and counties where the students enrolling in kindergarten have high vaccination rates.

Table 8: Low Rates of Spatial Clusters of Nonmedical Vaccine Exemptions for the 2011-2012/2012-2103 Academic Years

Exemption Cluster	Cluster Centroid		Observed Exemptions	Expected Exemptions	Relative Risk	P value	Location (county & state)
	Latitude °N	Longitude °W					
1	39.46	74.63	2588	6973.96	0.28	<.0001	Atlantic, Cumberland, Camden Burlington, Cape May, Ocean, Gloucester, Salem, Mercer, Monmouth, Middlesex, Union Somerset, Hunterdon, Passaic, Hudson, Essex, Morris, Warren, and Bergen, New Jersey
2	32.77	113.91	28	169.52	0.16	<.0001	Yuma, Arizona
3	46.45	120.73	24	120.52	0.20	<.0001	Yakima, Washington
4	31.52	110.84	613	868.70	0.70	<.0001	Santa Cruz, Cochise, and Pima, Arizona
5	47.73	119.69	25	58.21	0.43	<.0001	Douglas and Grant, Washington
6	46.98	118.56	19	47.75	0.40	.0004	Adams and Franklin, Washington
7	47.03	122.13	207	280.77	0.73	.0006	Pierce, Washington
8	41.75	111.81	644	766.00	0.84	.0007	Bear River and Weber-Morgan, Utah
9	35.38	109.49	26	47.90	0.54	.0810	Apache, Arizona

Table 8: Low Rates of Spatial Clusters of Nonmedical Vaccine Exemptions for the 2011-2012/2012-2103 Academic Years

Exemption Cluster	Cluster Centroid		Observed Exemptions	Expected Exemptions	Relative Risk	P value	Location (county & state)
	Latitude °N	Longitude °W					
10	40.66	111.92	414	482.16	0.86	.1678	Salt Lake Valley, Utah
11	47.14	123.82	29	45.00	0.64	.7286	Gray's Harbor, Mason, and Pacific, Washington
12	39.59	110.81	40	55.55	0.72	.9492	Southeastern, Utah
13	33.78	110.81	28	37.82	0.74	.9998	Gila, Arizona

Table 9: Low Rates of Spatial Clusters of Pertussis Cases, 2012

Exemption Cluster	Cluster Centroid		Observed Exemptions	Expected Exemptions	Relative Risk	P value	Location (county & state)
	Latitude °N	Longitude °W					
1	40.56	74.91	179	534.13	0.28	<.0001	Union, Essex , Mercer, Passaic, Burlington, Monmouth, Morris Middlesex, Somerset, Warren Hunterdon, Sussex, Hudson, Bergen, Gloucester, and Camden, New Jersey
2	33.34	112.49	249	451.79	0.49	<.0001	Maricopa, Yavapai, Yuma, Pinal, La Paz, Gila, and Pima, Arizona
3	43.28	123.15	53	107.15	0.48	<.0001	Douglas, Lane, Coos, Jackson, Josephine, Benton, Linn, Polk Lincoln, Deschutes, and Marion, Oregon
4	41.75	111.81	7	18.55	0.38	.2919	Bear River, Utah
5	40.46	113.12	1	6.31	0.16	.7191	Tooele, Utah
6	35.39	110.32	3	9.54	0.31	.8341	Navajo, Arizona
7	46.90	117.52	0	2.61	0.00	.9479	Whitman and Columbia, Washington
8	45.32	118.09	0	1.83	0.00	.9980	Union, Oregon

Table 9: Low Rates of Spatial Clusters of Pertussis Cases, 2012

Exemption Cluster	Cluster Centroid		Observed Exemptions	Expected Exemptions	Relative Risk	P value	Location (county & state)
	Latitude °N	Longitude °W					
9	46.92	122.83	11	18.21	0.60	.9995	Thurston, Washington
10	47.49	121.83	124	144.45	0.85	.9995	King, Washington
11	45.45	123.75	0	1.58	0.00	.9997	Tillamook, Oregon

Table 10: Percent Cases of Nonmedical Vaccine Exemptions in Low Rates of Geographic Clusters as Calculated by SaTScan version 9.4

Geographic Cluster Number	Percent of Nonmedical Vaccine Exemptions for the 2011-2012/2012-2013 Academic Year in Geographic Clusters with a P value <.05
SaTScan version 9.4 calculation for percent cases in the entire area	3.0
Cluster 1	1.1
Cluster 2	0.5
Cluster 3	0.6
Cluster 4	2.1
Cluster 5	1.3
Cluster 6	1.2
Cluster 7	2.2
Cluster 8	2.5
Cluster 9	1.6

Table 11: Annual Number of Cases of Pertussis per 100,000 people in Low Rates Geographic Clusters as Calculated by SaTScan version 9.4

Geographic Cluster Number	Annual Number of Cases of Pertussis per 100,000 people in Geographic Clusters with a P value <.05
SaTScan version 9.4 calculation for percent cases in the entire area	115.7
Cluster 1	38.8
Cluster 2	63.8
Cluster 3	57.2

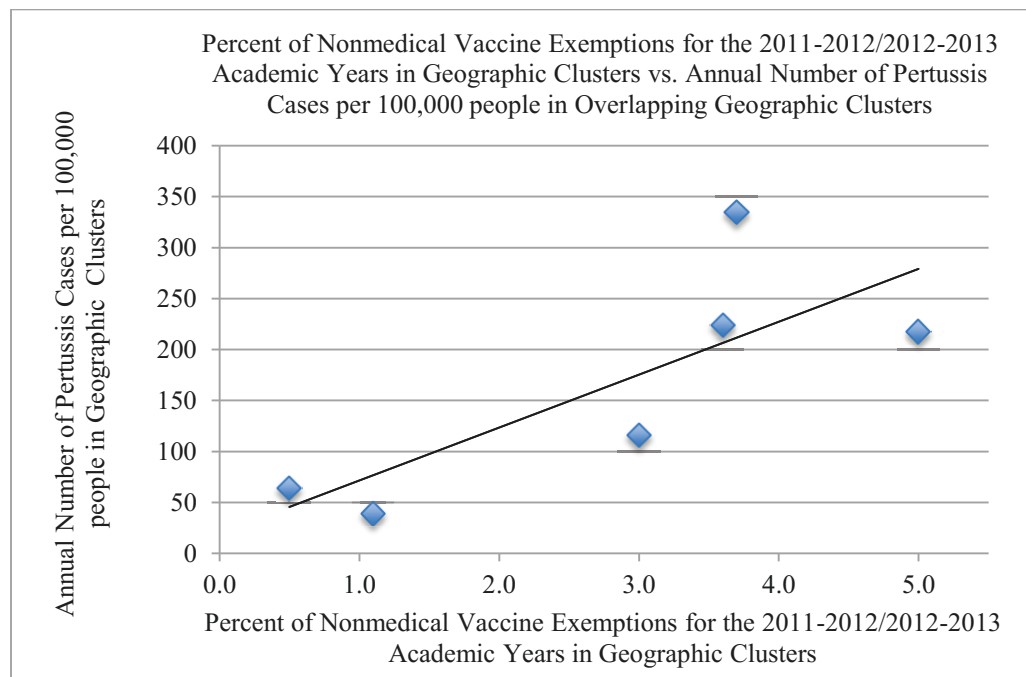
Table 12: Overlap of Low Rates of Geographic Clusters of Nonmedical Vaccine Exemptions and Low Rates of Geographic Clusters of Pertussis

Cluster	Percent of Nonmedical Vaccine Exemptions for the 2011-2012/2012-2013 Academic Year in Geographic Clusters with a P value <.05	Annual Number of Cases of Pertussis per 100,000 people in Geographic Clusters with a P value <.05
SaTScan version 9.4 calculation for the entire area	3.0	115.97
New Jersey	1.1	38.8
Arizona	0.5	63.8

In the five states that were analyzed for low rates of geographic clusters of nonmedical vaccine exemptions and low rates of pertussis cases, SaTScan version 9.4 identified thirty-six counties with a P-value of $<.05$ that were located in geographical clusters of nonmedical vaccine exemptions (Table 8 and Figure 8) and thirty-four counties that geographical clusters of pertussis cases in 2012 (Table 9 and Figure 8). Of the thirty-four counties that were identified to be a part of a geographic cluster of low rates of pertussis cases, fifteen or forty-four percent of those counties were also associated with geographic clusters of low rates of nonmedical vaccine exemptions (Figure 8).

Linear Regression of Geographic Clusters

Figure 6: Linear Regression Model of Percent of Nonmedical Vaccine Exemptions and Annual Number of Pertussis Cases per 100,000 people in Overlapping Geographic Clusters



Based on the trend line in Figure 6, there is a correlation between the percent of nonmedical vaccine exemptions in the geographic clusters and annual number of pertussis cases per 100,000 people in the geographic clusters that overlap with one another. The data indicate that as the percent of nonmedical vaccine exemptions increases the annual number of pertussis cases will also increase.

Chapter IV

Discussion

The results of the data indicated that in 2012 there was a correlation between counties with geographic clusters of nonmedical vaccine exemptions and counties that had geographic clusters of pertussis cases. In the high rates analysis which indicates counties that have a high number of reported pertussis cases, fifty-eight percent of those counties were also associated with geographic clusters of high rates of nonmedical vaccine exemptions (meaning students entering kindergarten have low vaccination levels). In the low rates analysis which indicates counties that have a low number of reported pertussis cases, forty-four percent of those counties were also associated with geographic clusters of low rates of nonmedical vaccine exemptions (meaning students entering kindergarten have high vaccination levels).

The data analysis indicates that there is a correlation between counties that have high rates of nonmedical vaccine exemptions there are high rates of pertussis cases. In addition, the analysis also indicates that in counties where there are low rates of nonmedical vaccine exemptions there are low rates of pertussis cases.

The trend lines in the three different linear regression models supports a correlation between nonmedical vaccine exemptions and pertussis cases. Specifically, when examining the percent of nonmedical vaccine exemptions vs. the percent of pertussis cases at both the county and state level the trend line indicates a weak correlation between the data. When using the data from the geographic clusters identified

by SaTScan version 9.4 to create a liner regression, the trend line indicates that there is a moderate correlation between an increase in nonmedical vaccine exemptions and an increase in pertussis cases at the county level.

The maps created from the data sets produced by the SaTScan version 9.4 analysis also reflect the correlation between nonmedical vaccine exemptions and pertussis cases. For example, in Washington, which had a large outbreak of pertussis, SaTScan version 9.4 identified thirty-four counties with high rates of geographic clusters of pertussis. Of those thirty-four counties with high rates of pertussis, twenty-three or sixty-seven percent of the counties also had high rates of nonmedical vaccine exemptions. In New Jersey the same correlation holds true with the low rates analysis, which indicated in counties where students enrolling in kindergarten had high vaccination rates then the county would have low rates of pertussis. SaTScan version 9.4 identified sixteen counties in New Jersey with low rates of geographic clusters of pertussis. Of those sixteen counties with low rates of pertussis, thirteen or eighty-one percent of the counties also had low rates of nonmedical vaccine exemptions.

Although correlation does not mean causation, the statistical analysis from this investigation has clearly proven that a relationship does exist between nonmedical vaccine exemptions and pertussis cases during the 2012 outbreak of pertussis in the United States.

The results of this investigation support the findings of prior research investigating the relationship between geographic clusters of nonmedical vaccine exemptions and geographic clusters of pertussis cases (Lieu, et al., 2015; Atwell, et al., 2014; Omer, et al., 2008). Two of the investigations took place in California and one of

the investigations took place in Michigan (Lieu, et al., 2015; Atwell, et al., 2014; Omer, et al., 2008). All three of the studies indicated that at the state level there are indeed geographic clusters of children that have nonmedical vaccine exemptions (Lieu, et al., 2015; Atwell, et al., 2014; Omer, et al., 2008). In addition, two of the studies also showed that at the state level there is a correlation between geographic clusters of nonmedical vaccine exemptions and geographic clusters of pertussis cases (Atwell, et al., 2014; Omer, et al., 2008).

Since prior research has solely focused on individual states this investigation offers additional information to help better understand the impact the nonmedical vaccine exemptions have on public health on a larger scale. This study provides both nonmedical vaccine exemption and pertussis data at the county level in multiple states during a single pertussis outbreak within the United States. In addition, since the current literature has only focused on California and Michigan this investigation provides data from additional states (Arizona, New Jersey, Oregon, Utah, and Washington) to help further support the findings that people who live in communities where there are high levels of nonmedical vaccine exemptions are at higher risk of becoming infected with vaccine preventable diseases (Lieu, et al., 2015; Atwell, et al., 2014; Omer, et al., 2008; Feikin, et al., 2000 b; Salomon, et al., 1999). Lastly, prior studies have only examined the relationship between high rates nonmedical vaccine exemptions and high rates of pertussis cases (Lieu, et al., 2015; Atwell, et al., 2014; Omer, et al., 2008). This study provides information about both high rates and low rates of geographic clusters of nonmedical vaccine exemptions and pertussis cases to better understand the relationship between nonmedical vaccine exemptions and pertussis cases.

This study demonstrated that there are pockets of high exemption rates within each of the five states analyzed despite the overall high levels of vaccination coverage in each state in 2012. The Centers for Disease Control and Prevention collects state-level vaccination rates for children between 19-35 months old via the National Immunization Survey (NIS) every year (CDC, n.d. f). These data enable the Centers for Disease Control and Prevention to better understand vaccination rates within every state in the United States. Yet, state level data can obscure nonmedical exemption rates that are at the county and individual community level.

It is important to recognize that there is not likely to be a single reason for the increase in the rates of pertussis cases in the United States and that there are a handful of factors that have contributed to the surge of pertussis cases. Studies have suggested that one factor that has led to the increase in pertussis cases is waning immunity from the DTaP vaccine (Klein, et al., 2016; Cherry, 2015; Taroff, et al., 2013; Cherry, 2012 b; Klein, et al., 2012; Skoff, et al., 2012). The resurgence of pertussis has been attributed to the switch from the whole cell pertussis vaccine to the acellular vaccine (DTaP) in 1992. However, the increase in reported cases of pertussis in the United States began in 1980 approximately 14 years before the use of the acellular vaccine was commonplace in the United States (CDC, n.d. a; Cherry, 2015). Therefore, one cannot solely blame the waning immunity from the acellular pertussis vaccine as the cause of the increases in cases of pertussis in the United States.

It is also important to take into account the new genetic strain of pertactin-negative pertussis that has been circulating in the United States (Martin, et al., 2015; Bowden, et al. 2014; Pawloski, et al., 2014; Quinlan, et al., 2014; Schmidtke., et al,

2012). Researchers do not know much about the virulence level of pertactin-negative pertussis, if this particular strain of pertussis is more contagious, and/or if the pertactin-negative strain is able to avoid vaccine induced immunity (Martin, et al., 2015; Queenan, et al., 2013; Mooi, et al., 2014; Mooi, et al., 2009). In the states that were part of this investigation it has been confirmed that the pertactin-negative strain of pertussis has been present in Arizona, Oregon, and Washington (Bowden, et al. 2014; Pawloski, et al., 2014). Yet, there has been no documentation of the pertactin-negative strain being present in Utah or New Jersey. Studies have also suggested that the pertactin-negative strain has been present in the United States for a number of years (Pawloski, et al., 2014; Schmidtke., et al, 2012). Yet, higher frequencies of the pertactin-negative strain were not reported until 2011 (Pawloski, et al., 2014; Schmidtke., et al, 2012). Again, the increase in reported cases of pertussis in the United State began in 1980 approximately 31 years before higher frequencies of pertactin-negative *B. pertussis* strains were reported (Figure 2) (CDC, n.d. a; Pawloski, et al., 2014; Schmidtke, et al, 2012). Therefore, one cannot conclude that genetic changes in the strains of pertussis circulating in the U.S. is the cause of increased cases of pertussis in the U.S.

Due to the greater awareness of pertussis by healthcare providers, public health officials, and the public the reporting of pertussis cases in the United States improved (Faulkner, et al., 2016; Cherry, 2012 a). In addition, advancements in medicine such as using PCR as a diagnostic tool for pertussis have contributed to more precise diagnosis of pertussis in the United States (Faulkner, et al., 2016; Cherry, 2012 a). That said, pertussis surveillance data is influenced by a number of factors such as provider awareness and diagnostic testing preferences which directly impacts case identification (Faulkner, et al.,

2016). Thus, it cannot be concluded that the recent trends of increased usage of PCR for pertussis diagnosis is the cause of increased reports of pertussis cases in the United States (Faulkner, et al., 2016). There are differences in the manner in which states investigate and diagnose a case of pertussis and the practices of how a state investigates and diagnosis a case of pertussis directly impacts the number of pertussis cases that are reported (Faulkner, et al., 2016). Therefore, ascertainment bias due to sensitive diagnostic testing and greater awareness of pertussis cannot be the primary reason for the increased cases of pertussis in the United States.

It is clear that the increase in the number of pertussis cases in the United States is complex due to the evolving strains of *B. pertussis*, a better understanding of the waning immunity associated with the DTaP vaccine, and the advancements in medicine and public awareness of pertussis. As stated earlier, correlation does not mean causation, yet, based on the data collected for this investigation it is difficult to deny that nonmedical vaccine exemptions have contributed to the increase cases of pertussis in the United States and that this impact should be further investigated.

Public Health Implications

There are several public health factors that need to be taken into consideration based on the results of this investigation. The first is the manner in which individual states collect immunization data. As indicated in Table 1, of the nineteen states that had a pertussis cases incidence rate above 15.4 per 100,000 people only five of the states had collected detailed information about the immunization status of school children in the state. For example - - the states of Alaska, Iowa, and Minnesota do not collect school

immunization data. It is evident that vaccines prevent the spread of infectious disease including pertussis (Wang, et al., 2014; Panhius, et al., 2013; Roush & Murphy, 2007; Armstrong, et al., 1999; CDC, 1999). Yet, if states do not collect immunization data then how can states truly understand outbreaks of vaccine preventable disease such as the outbreak of pertussis in 2012?

In addition, if a state does collected detailed immunization data then that information can be used to identify local clusters of vaccine exemptions and communities that have low vaccination rates. For herd/community immunity to be effective, 92-94% of the community needs to be vaccinated against pertussis (CDC, n.d. e). Information about local clusters of vaccine exemptions could allow public health officials to alert local healthcare providers about vaccination levels within a community as well as tailor public health campaigns at the community level. Identification of clusters of nonmedical vaccine exemptions within a state and establishing a correlation between clusters of exemptions and pertussis cases will influence public health interventions and will help to inform immunization policy.

The second public health factor that needs to be considered at the state level is the impact that nonmedical vaccine exemptions has on the incidence rate of vaccine preventable diseases in the state. Until 2016, there were only two states (Mississippi and West Virginia) that did not allow nonmedical vaccine exemptions. When comparing the incidence rate of pertussis cases in the states that do not have nonmedical vaccine exemptions vs. the states that offer nonmedical vaccine exemptions it is very clear that there is a greater incidence rate of pertussis in states that offer nonmedical vaccine exemptions (Figure 3).

Although not investigated in this study, it is likely that the rates for other vaccine preventable diseases such as measles or varicella (chicken pox) are also higher in the states that offer nonmedical vaccine exemptions. Again, the incidence rates of pertussis are higher in states that offer nonmedical vaccine exemptions because individuals who chose to have nonmedical vaccine exemptions are at higher risk for pertussis as well as infecting others in the community with pertussis (Lieu, et al., 2015; Atwell, et al., 2014; Omer, et al., 2008; Feikin, et al., 2000 b; Salomon, et al., 1999). Thus, states need to take these data into consideration when discussing vaccination laws and if nonmedical vaccine exemptions should be legal. Clearly, having nonmedical vaccine exemptions jeopardizes public health and causes greater risk for diseases and outbreaks within states.

On June 30, 2015, the state of California passed Senate Bill No. 227 which was a bill that ended nonmedical vaccine exemptions in California starting in 2016 (Figure 14) (California Legislative Information, 2015). Based on the law individuals cannot file for vaccine exemptions after December 31, 2015 and after July 1, 2016 any student that does not adhere to the school vaccination laws cannot enroll into school or advance past the seventh grade until the student has met the state vaccination laws (Figure 14) (California Legislative Information, 2015). The aim of Senate Bill No. 227 is to eliminate nonmedical vaccine exemptions and increase vaccination rates within the state of California to help reduce rates of vaccine preventable diseases in the state.

The state of California will provide an important case to study over the next few years to determine the impact that Senate Bill No. 227 has on public health and if there is a change in the incidence rates of vaccine preventable diseases in the state. Based on the results of this investigation and the handful of other studies conducted about the

correlation of nonmedical vaccine exemptions and outbreaks of pertussis it would not be surprising to see a decline in the incidence rate of pertussis and other vaccine preventable disease within the state of California (Lieu, et al., 2015; Atwell, et al., 2013; Omer, et al., 2008). Hopefully, other states will take notice of California's Senate Bill No. 227 as well as the vaccination laws in Mississippi and West Virginia because vaccines prevent the spread of disease and saves lives.

Conclusion

Geographic clusters of nonmedical vaccine exemptions at the county level pose a risk to the surrounding communities. States should actively monitor trends in nonmedical vaccine exemptions at the county level to better understand the impact of nonmedical vaccine exemptions on public health. In addition, states should reconsider allowing nonmedical vaccine exemptions because of the potential impact that these exemptions have on public health.

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Appendix

Figure 7: Map of the Overlap of High Rates of Spatial Clusters of Nonmedical Vaccine Exemption Clusters for the 2011-2012/2012-2013 Academic Year and High Rates of Spatial Clusters of Pertussis Cases in 2012

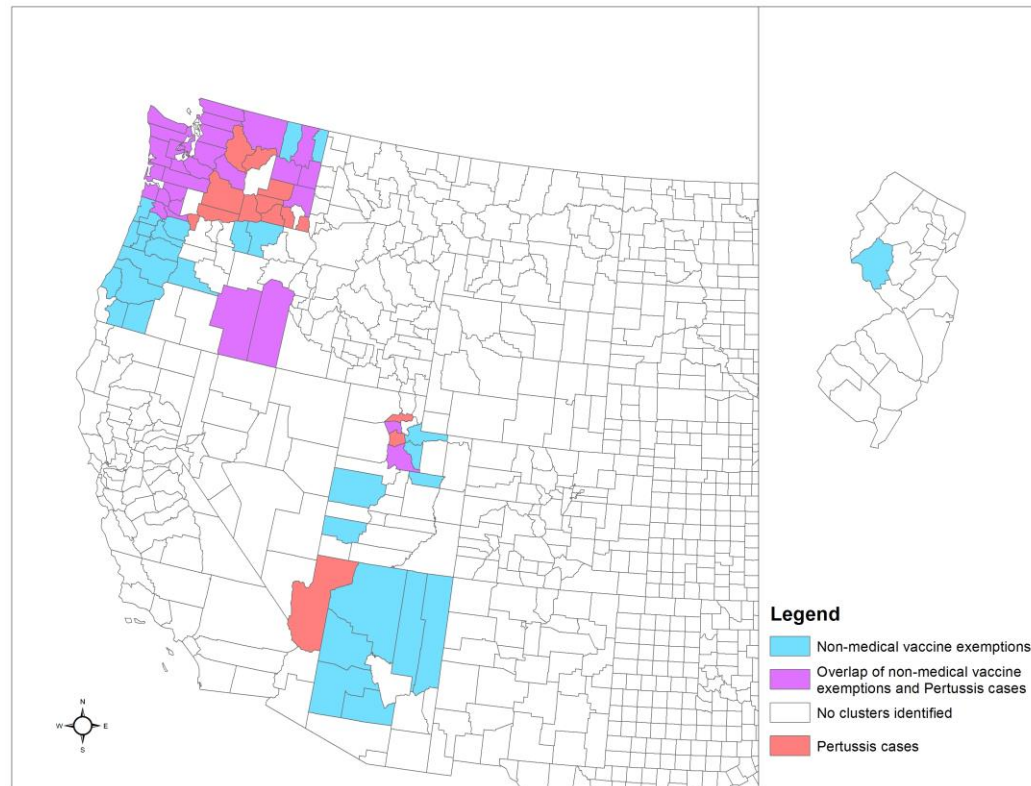


Figure 8: Map of the Overlap of Low Rates of Geographic Clusters of Nonmedical Vaccine Exemption Clusters for the 2011-2012/2012-2013 Academic Year and Low Rates of Geographic Clusters of Pertussis Cases in 2012

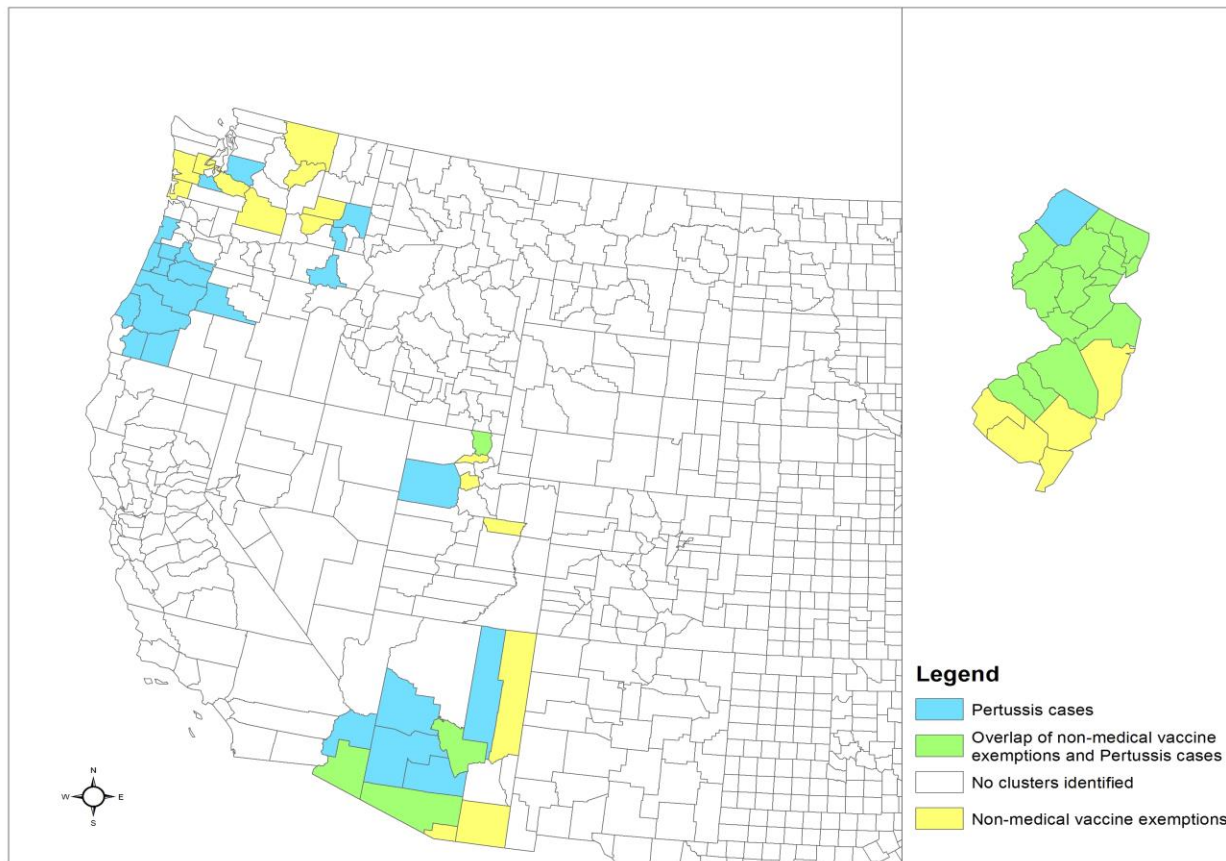


Figure 9: Arizona’s Department of Health Services Application Form for Nonmedical Vaccine Exemptions (Arizona’s Department of Health Services, n.d.)



Arizona Department of Health Services (ADHS) strongly supports immunization as one of the easiest and most effective tools in preventing diseases that can cause serious illness and even death. ADHS also respects the rights of parents to decide whether or not to vaccinate their child.

By state law, (A.R.S. §15-873) a child will not be allowed to attend school until either proof of immunization or a completed exemption form is submitted to the school. The information below is provided to ensure that parents are informed about the risks of not vaccinating.

Place an "X" in the box to the left of each disease listed to exempt your child from the vaccine. Initial and date the box on the right.

<input type="checkbox"/>	I have been informed that by not receiving this vaccine, my child is at increased risk of developing diphtheria if exposed to this disease. Serious symptoms and effects of this disease include: heart failure, paralysis (can't move parts of the body), breathing problems, coma, and death.	Date_____
<input type="checkbox"/>	I have been informed that by not receiving this vaccine, my child is at increased risk of developing tetanus if exposed to this disease. Serious symptoms and effects of this disease include: "locking" of the jaw, difficulty in swallowing and breathing, seizures (jerking and staring), painful tightening of muscles in the head and neck, and death.	Date_____
<input type="checkbox"/>	I have been informed that by not receiving this vaccine, my child is at increased risk of developing pertussis (whooping cough) if exposed to this disease. Serious symptoms and effects of this disease include: severe coughing fits that can cause vomiting and exhaustion, pneumonia, seizures (jerking and staring), brain damage, and death.	Date_____
<input type="checkbox"/>	I have been informed that by not receiving this vaccine, my child is at increased risk of developing polio if exposed to this disease. Serious symptoms and effects of this disease include: paralysis (can't move parts of the body), meningitis (infection of the brain and spinal cord covering), permanent disability, and death.	Date_____
<input type="checkbox"/>	I have been informed that by not receiving this vaccine, my child may be at increased risk of developing measles, mumps, and/or rubella if exposed to these diseases. Serious symptoms and effects of measles include: pneumonia, seizures (jerking and staring), brain damage, and death. Serious symptoms and effects of mumps include: meningitis (infection of the brain and spinal cord covering), painful swelling of the testicles or ovaries, sterility, deafness, and death. Serious symptoms and effects of rubella include: rash, arthritis, and muscle or joint pain. If a woman gets rubella while she is pregnant, she could have a miscarriage or her baby could be born with serious birth defects such as deafness, heart problems, and mental retardation.	Date_____
<input type="checkbox"/>	I have been informed that by not receiving this vaccine, my child may be at increased risk of developing hepatitis B if exposed to this disease. Serious symptoms and effects of this disease include: jaundice (yellow skin or eyes), life-long liver problems, such as scarring and liver cancer, and death.	Date_____
<input type="checkbox"/>	I have been informed that by not receiving this vaccine, my child may be at increased risk of developing varicella (chickenpox) if exposed to this disease. Serious symptoms and effects of this disease include: severe skin infections, pneumonia, brain damage, and death.	Date_____
<input type="checkbox"/>	I have been informed that by not receiving this vaccine, my child is at increased risk of developing meningococcal disease. Serious symptoms and effects of this disease include: neurological damage, sepsis, permanent scarring or loss of limbs and death.	Date_____
<p>Due to my personal beliefs, I request an exemption for my child from the required vaccine doses selected above. I am aware that if I change my mind in the future, I can rescind this exemption and obtain immunizations for my child. Initials_____</p> <ul style="list-style-type: none"> I am aware that additional information about vaccine preventable diseases, vaccines and reduced or no cost vaccination services is available from my local county health department and Arizona Department of Health Services (www.azdhs.gov/phs/immun/index.htm). I am aware that in the event the state or county health department declares an outbreak of a vaccine-preventable disease for which I cannot provide proof of immunity for my child, he or she may not be allowed to attend school for up to 3 weeks or until the risk period ends. <p>Child's Name _____ Date of Birth (month/day/year)_____</p> <p>Parent/Guardian Signature _____ Date (month/day/year)_____</p>		

Figure 9: Arizona’s Department of Health Services Application Form for Nonmedical Vaccine Exemptions (Arizona’s Department of Health Services, n.d.)



Arizona law requires that childcare facilities and preschools use this official ADHS form, signed and completed by the child’s parent/guardian, to document a religious beliefs exemption to immunization.

Arizona Department of Health Services (ADHS) strongly supports immunization as one of the easiest and most effective tools in preventing diseases that can cause serious illness and even death. ADHS also respects the rights of parents who are raising their child in a religion whose teachings are in opposition to immunization to make the decision not to vaccinate their child.

Place an “X” in the box to the left of each disease listed to exempt your child from the vaccine. Initial and date the box on the right.

<input type="checkbox"/>	Diphtheria (DTaP, DT, Tdap, Td): I have been informed that by not receiving this vaccine, my child may be at increased risk of developing diphtheria if exposed to this disease. Serious symptoms and effects of this disease include: heart failure, paralysis (can't move parts of the body), breathing problems, coma, and death.	Initials_____
<input type="checkbox"/>	Tetanus (DTaP, DT, Tdap, Td): I have been informed that by not receiving this vaccine, my child may be at increased risk of developing tetanus if exposed to this disease. Serious symptoms and effects of this disease include: "locking" of the jaw, difficulty in swallowing and breathing, seizures (jerking and staring), painful tightening of muscles in the head and neck, and death.	Initials_____
<input type="checkbox"/>	Pertussis (Whooping Cough) (DTaP, Tdap): I have been informed that by not receiving this vaccine, my child may be at increased risk of developing pertussis (whooping cough) if exposed to this disease. Serious symptoms and effects of this disease include: severe coughing fits that can cause vomiting and exhaustion, pneumonia, seizures (jerking and staring), brain damage, and death.	Initials_____
<input type="checkbox"/>	Polio: I have been informed that by not receiving this vaccine, my child may be at increased risk of developing polio if exposed to this disease. Serious symptoms and effects of this disease include: paralysis (can't move parts of the body), meningitis (infection of the brain and spinal cord covering), permanent disability, and death.	Initials_____
<input type="checkbox"/>	Measles, Mumps, Rubella (MMR): I have been informed that by not receiving this vaccine, my child may be at increased risk of developing measles, mumps, and/or rubella if exposed to these diseases. Serious symptoms and effects of measles include: pneumonia, seizures (jerking and staring), brain damage, and death. Serious symptoms and effects of mumps include: meningitis (infection of the brain and spinal cord covering), painful swelling of the testicles or ovaries, sterility, deafness, and death. Serious symptoms and effects of rubella include: rash, arthritis, and muscle or joint pain. If a woman gets rubella while she is pregnant, she could have a miscarriage or her baby could be born with serious birth defects such as deafness, heart problems, and mental retardation.	Initials_____
<input type="checkbox"/>	Haemophilus Influenza type b (Hib): I have been informed that by not receiving this vaccine, my child may be at increased risk of developing Hib if exposed to this disease. Serious symptoms and effects of this disease include: meningitis (infection of the brain and spinal cord covering), pneumonia, severe swelling in the throat that makes it hard to breathe, infections of the blood, joints, bones, and covering of the heart, and death.	Initials_____
<input type="checkbox"/>	Hepatitis B: I have been informed that by not receiving this vaccine, my child may be at increased risk of developing hepatitis B if exposed to this disease. Serious symptoms and effects of this disease include: jaundice (yellow skin or eyes), life-long liver problems, such as scarring and liver cancer, and death.	Initials_____
<input type="checkbox"/>	Hepatitis A: I have been informed that by not receiving this vaccine, my child may be at increased risk of developing hepatitis A if exposed to this disease. Serious symptoms and effects of this disease include: jaundice (yellow skin or eyes), "flu-like" illness, hospitalization, and death.	Initials_____
<input type="checkbox"/>	Varicella (Chickenpox): I have been informed that by not receiving this vaccine, my child may be at increased risk of developing varicella (chickenpox) if exposed to this disease. Serious symptoms and effects of this disease include: severe skin infections, pneumonia, brain damage, and death.	Initials_____
<p>Due to my religious beliefs, I request an exemption for my child from the required vaccine doses selected above. I am aware that if I change my mind in the future, I can rescind this exemption and obtain immunizations for my child. Initials_____</p> <ul style="list-style-type: none"> I am aware that additional information about vaccine preventable diseases, vaccines and reduced or no cost vaccination services is available from my local county health department and Arizona Department of Health Services (www.azdhs.gov/phs/immun/index.htm). I am aware that in the event the state or county health department declares an outbreak of a vaccine-preventable disease for which I cannot provide proof of immunity for my child, he or she may not be allowed to attend childcare for up to 3 weeks or until the risk period ends. <p>Child's Name _____ Date of Birth (month/day/year) _____</p> <p>Parent/Guardian Signature _____ Date (month/day/year) _____</p>		

Figure 10: Oregon's Department of Public Health Application Form for Nonmedical Vaccine Exemptions (Oregon's Department of Public Health, n.d.)



**Oregon Certificate of Immunization Status
Oregon Health Authority, Immunization Program**

Oregon law requires proof of immunization be provided or an exemption be signed prior to a child's attendance at school, preschool, child care or home day care. This information is being collected on behalf of the Oregon Health Authority, Immunization Program and may be released to the Authority or the local public health department by the school or children's facility upon request of the Authority. Please list immunizations in the order they were received.

<i>Child's Last Name Apellido</i>	<i>First Primer Nombre</i>	<i>Middle Initial Segundo Nombre</i>	<i>Birthdate Fecha de Nacimiento</i>	Complete for all	
<i>Mailing Address Dirección</i>	<i>City Ciudad</i>	<i>State Estado</i>	<i>Zip Code Codigo Postal</i>		Up-to- date
<i>Parents' or Guardians' Names Nombre de los padres o guardian</i>		<i>Home Telephone Number Número de Teléfono</i>			Medical
Non medical					

Vaccines	Dose 1	Dose 2	Dose 3	Dose 4	Dose 5
Diphtheria/Tetanus/Pertussis (DTaP, Tdap, Td)	(mm/dd/yy)	(mm/dd/yy)	(mm/dd/yy)	(mm/dd/yy)	(mm/dd/yy)
Booster Dose Tdap					
Polio (IPV or OPV)					
Varicella (Chickenpox) [VZV or VAR] <input type="checkbox"/> Check here if child has had chickenpox disease _____ (mm/dd/yy)					
Measles/Mumps/Rubella (MMR) <i>or</i> Measles vaccine only Mumps vaccine only Rubella vaccine only					
Hepatitis B (Hep B)					
Hepatitis A (Hep A)					
Haemophilus Influenzae Type B (Hib) (Only children less than 5 years)					

I certify that the above information is an accurate record of this child's immunization history.

Signature* _____ Date _____

Update Signature _____ Date _____

Update Signature _____ Date _____


Update Signature _____ Date _____

For school/facility use only
School/facility Name
Student ID Number
Grade

*Parent, guardian, student at least 15 years of age, medical provider or county health department staff person may sign to verify vaccinations received.

Continued On Reverse Side

Figure 10: Oregon's Department of Public Health application form for nonmedical vaccine exemptions (Oregon's Department of Public Health, n.d.).



Oregon Certificate of Immunization Status, Page 2
Oregon Health Authority, Immunization Program

Child's Last Name
Apellido

First
Primer Nombre

Middle Initial
Segundo Nombre

Birthdate
Fecha de Nacimiento

Recommended Vaccines	Recommended Vaccines	Dose 1	Dose 2	Dose 3	Dose 4	Dose 5
	Pneumococcal (PCV) (Only in children less than 5 years)					
Meningococcal (MCV4, MPSV4)						
Human Papilloma Virus (HPV) (9 years or older)						
Influenza (Flu)						
Other Vaccine Please specify:						
Other Vaccine Please specify:						

For medical exemptions:
Please submit a letter signed by a licensed physician stating:

- Child's name
- Birth date
- Medical condition that contraindicates vaccine
- List of vaccines contraindicated
- Approximate time until condition resolves, if applicable
- Physician's signature and date
- Physician's contact information, including phone number

For Immunity Documentation (history of disease or positive titer): **Please submit a letter signed by a licensed physician stating:**

- Child's name and birth date
- Diagnosis or lab report
- Physician's signature and date

Nonmedical Exemption:
 I have received information regarding the benefits and risks of immunizations. I understand that my child may be excluded from school or child care attendance if there is a case of disease that could be prevented by vaccine. I have attached the required document from (check one):

A health care practitioner
 The vaccine educational module approved by the Oregon Health Authority

I understand that I may decline one or more vaccinations for my child and request that my child be exempted from the following required immunizations (check all that apply):

<input type="checkbox"/> Diphtheria/ Tetanus/Pertussis	<input type="checkbox"/> Hepatitis B
<input type="checkbox"/> Polio	<input type="checkbox"/> Hepatitis A
<input type="checkbox"/> Varicella	<input type="checkbox"/> Hib
<input type="checkbox"/> Measles/Mumps/Rubella	

Signature of Parent or Guardian _____ Date _____

Optional:
 ORS 433.267 states that this document may include the reason for declining the immunization. Immunization is being declined because of:

Religious belief Philosophical belief Other

I certify that the above information is an accurate record of this child's immunization history and exemption status.

Signature _____ Date _____

Update Signature _____ Date _____

Update Signature _____ Date _____

Update Signature _____ Date _____

53-05A (01/2014)

Figure 11: Image of Utah’s Department of Health Website about the Application Form for Nonmedical Vaccine Exemptions. (Utah Department of Health, n.d)

UTAH DEPARTMENT OF HEALTH

Home | Health Services | A-Z List | FAQ | Data | About Us

Home > Information For The Public > Immunization Recommendations > Exemptions

Utah Department of Health
IMMUNIZATION PROGRAM
 Immunize for healthy lives

INFORMATION for THE PUBLIC →

INFORMATION for HEALTH CARE PROVIDERS →

SCHOOL & EARLY CHILDHOOD PROGRAM REQUIREMENTS →

» About Us
 » Contact Us

→ Home

→ Immunization Services

→ Vaccines for Children Program

→ Statistics

→ Immunization Reporting

→ Order Educational Materials

→ Travel Vaccines

→ Medical Assistant Training

HIGHLIGHTS

Immunization Exemptions

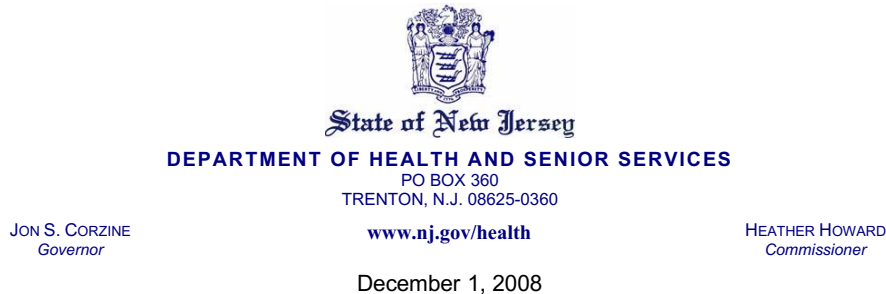
CLAIMING AN EXEMPTION
 A parent may claim an exemption to immunization for medical, religious, or personal reasons, as allowed by Section 53A-11-302 of the Utah Statutory Code. Each exemption claimed must be accompanied by the appropriate Utah Department of Health Exemption Form.

MEDICAL EXEMPTION
 If a parent/guardian claims a medical exemption for a student, a Medical Exemption Form must be completed and signed by the student’s licensed physician (Utah Statutory Code - Section 53A-11-302). [The Medical Exemption Form may be obtained from the student’s physician.](#) The appropriate copy must be filed with the school or early childhood program.

RELIGIOUS EXEMPTION
 If a parent/guardian claims a religious exemption for a student, a Religious Exemption Form must be completed and signed by the parent/guardian. [The Religious Exemption Form may be obtained from a local health department.](#) A local health department representative must witness and sign the Religious Exemption Form. The appropriate copy must be filed with the school or early childhood program.

PERSONAL EXEMPTION
 If a parent/guardian claims a personal exemption for a student, a Personal Exemption Form must be completed and signed by the parent/guardian. [The Personal Exemption Form may be obtained from a local health department.](#) A local health department representative must witness and sign the Personal Exemption Form. The appropriate copy must be filed with the school or early childhood program.

Figure 12: Information about How to Apply for Nonmedical Vaccine Exemptions in New Jersey (New Jersey's Department of Health and Senior Services, 2008).



N.J.A.C. 8:57-4.3 and 4.4 Immunization of Pupils in Schools rule,
Religious and Medical Exemption

The New Jersey Department of Health and Senior Services (NJDHSS) has received numerous inquiries regarding enforcement of N.J.A.C. 8:57 – 4, Immunization of Pupils in School. The issue of exemptions to mandatory immunizations has been reviewed by the NJDHSS Office of Legal and Regulatory Affairs and the New Jersey Office of the Attorney General. Below is a summary of the advice received from legal council regarding exemptions to immunization(s).

- Religious Exemptions:
N.J.S.A. 26:1A – 9.1 provides an exemption for pupils from mandatory immunization “if the parent or guardian of the pupil objects thereto in a written statement signed by the parent or guardian upon the grounds that the proposed immunization interferes with the free exercise of the pupil’s religious rights.” All schools, child care centers, and local health officers may be advised that the religious exemption extends to private, parochial, and public institutions. When a parent or guardian submits their written religious exemption to immunization, which contains some religious reference, those persons charged with implementing administrative rules at N.J.A.C. 8:57 – 4.4, should not question whether the parent’s professed religious statement or stated belief is reasonable, acceptable, sincere and bona fide. In practice, if the written statement contains the word “religion” or “religious” or some reference thereto, then the statement should be accepted and the religious exemption of mandatory immunization(s) granted. The language requiring how the administration of immunizing agents conflicts with the student’s religious beliefs does not mandate specificity as to membership in a recognized church or religious denomination. NJDHSS will seek to amend the rules at N.J.A.C. 8:57 – 4.4 through the Administrative Rules process to be consistent with N.J.S.A. 26:1A – 9.1.
- Medical Exemptions:
N.J.A.C. 8:57 – 4.3 allows for exemptions to immunizations which are medically contraindicated. A written statement shall be submitted to the school, preschool, or child care center from a physician licensed to practice medicine or osteopathy or an advanced practice nurse (certified registered nurse practitioner or clinical nurse specialist) indicating that an immunization is medically contraindicated for a specific period of time, and the reason(s) for the medical contraindication, based upon valid medical reasons as enumerated by the Advisory Committee on


Figure 12: Information about How to Apply for Nonmedical Vaccine Exemptions in New Jersey (New Jersey's Department of Health and Senior Services, 2008).

Immunization Practices (ACIP) or the American Academy of Pediatrics (AAP) guidelines.

Objections to vaccination based on grounds which are not medical or religious in nature and which are of a philosophical, moral, secular, or more general nature continue to be unacceptable.

NJDHSS hopes that the information provided will enable schools, child care facilities, and local health departments to process requests for exemptions in a more uniform and expeditious manner. NJDHSS remains committed to ensuring that our children and communities are protected against vaccine-preventable diseases. The dramatic decrease in the morbidity and mortality of vaccine-preventable diseases is attributed, in large part, to enforcement of school immunization requirements. The Department remains grateful for all the work expended locally to implement and enforce these important health regulations within the proscribed authority.

Figure 13: Washington State’s Department of Health Application Form for Nonmedical Vaccine Exemptions (Washington’s Department of Public Health, n.d.).



Washington State Department of Health
DOH 348-104 Jun 2013

Certificate of Exemption

SIDE A:
For Religious, Personal, Philosophical, and Medical Exemptions¹

PART 1: PARENT OR GUARDIAN INSTRUCTIONS

In order for this form to be valid for religious, personal, philosophical, or medical reasons, please:

Step 1: Fill in your child’s information in Boxes 1-4
Step 2: Read the Parent/Guardian Declaration
Step 3: Provide your initials where indicated
Step 4: Print your name, sign, and date in Boxes 5-6
Step 5: Have a provider complete Part 2 of this form

1. Child’s Last Name

2. Child’s First Name and Middle Initial

3. Birthdate (mm/dd/yyyy)

4. Gender
 Male
 Female

I am the parent or legal guardian of the above named child. One or more required vaccines are in conflict with my personal, philosophical, or religious beliefs.

Parent/Guardian Declaration

I understand that:

- My child may not be allowed to attend school or child care during an outbreak of the disease that my child has not been fully vaccinated against. _____ (initial)
- Exempting my child from any or all required vaccine(s) may result in serious illness, disability, or death to my child or others. I understand the risks and possible outcomes of my decision to exempt my child. _____ (initial)
- The information provided on this form is complete and correct. _____ (initial)

5. Print Parent/Guardian Name

6. Parent/Guardian Signature and Date

PART 2: HEALTHCARE PROVIDER INSTRUCTIONS

In order for this form to be valid, please:

Step 1: Mark which disease(s) and what type of exemption is requested. If medical write a **T** for Temporary or **P** for Permanent.
Step 2: Discuss the benefits and risks of immunizations with the parent or guardian
Step 3: Read the Provider Declaration
Step 4: Print your name, credentials, sign, and date in Boxes 7-8

Vaccine	Personal/Philosophical	Religious	Medical (T/P)*	Exemption Code for Reporting Purposes
Diphtheria				
Hepatitis B				
Hib				
Measles				
Mumps				
Pertussis				
Pneumococcal				
Polio				
Rubella				
Tetanus				
Varicella				
All				

Provider Declaration

I declare that:

- I have discussed the benefits and risks of immunizations with the parent/legal guardian as a condition for exempting their child.
- I am a qualified MD, ND, DO, ARNP or PA licensed under Title 18 RCW.
- The information provided on this form is complete and correct.

7. Print Provider Name and Credential (see 48.35.040 RCW)

8. Provider Signature and Date

¹RCW 28A.210.090-093 "Before or on the first day of every child's attendance at any public and private school or licensed child care center in Washington State, the parent or guardian must present proof of either (1) full immunization, (2) the initiation of and compliance with a schedule of immunization, as required by rules of the State Board of Health, or (3) a certificate of exemption signed by a parent or guardian and if either A) signed by a licensed healthcare provider or B) demonstrates membership in a church or religious body that precludes healthcare practitioners from providing medical treatment to children."

FOR OFFICE USE ONLY CHILD'S LAST NAME

FIRST NAME

M.I.

Figure 14: The Introduction to California’s Senate Bill No. 227 (California Legislative Information, 2015).

Senate Bill No. 277

CHAPTER 35

An act to amend Sections 120325, 120335, 120370, and 120375 of, to add Section 120338 to, and to repeal Section 120365 of, the Health and Safety Code, relating to public health.

[Approved by Governor June 30, 2015. Filed with
Secretary of State June 30, 2015.]

LEGISLATIVE COUNSEL’S DIGEST

SB 277, Pan. Public health: vaccinations.

Existing law prohibits the governing authority of a school or other institution from unconditionally admitting any person as a pupil of any public or private elementary or secondary school, child care center, day nursery, nursery school, family day care home, or development center, unless prior to his or her admission to that institution he or she has been fully immunized against various diseases, including measles, mumps, and pertussis, subject to any specific age criteria. Existing law authorizes an exemption from those provisions for medical reasons or because of personal beliefs, if specified forms are submitted to the governing authority. Existing law requires the governing authority of a school or other institution to require documentary proof of each entrant’s immunization status. Existing law authorizes the governing authority of a school or other institution to temporarily exclude a child from the school or institution if the authority has good cause to believe that the child has been exposed to one of those diseases, as specified.

This bill would eliminate the exemption from existing specified immunization requirements based upon personal beliefs, but would allow exemption from future immunization requirements deemed appropriate by the State Department of Public Health for either medical reasons or personal beliefs. The bill would exempt pupils in a home-based private school and students enrolled in an independent study program and who do not receive classroom-based instruction, pursuant to specified law from the prohibition described above. The bill would allow pupils who, prior to January 1, 2016, have a letter or affidavit on file at a private or public elementary or secondary school, child day care center, day nursery, nursery school, family day care home, or development center stating beliefs opposed to immunization, to be enrolled in any private or public elementary or secondary school, child day care center, day nursery, nursery school, family day care home, or development center within the state until the pupil enrolls in the next grade span, as defined. Except as under the circumstances described above, on and after July 1, 2016, the bill would prohibit a governing authority from unconditionally admitting to any of those institutions for the first time or

Figure 14: The Introduction to California's Senate Bill No. 227 (California Legislative Information, 2015).

admitting or advancing any pupil to the 7th grade level, unless the pupil has been immunized as required by the bill. The bill would specify that its provisions do not prohibit a pupil who qualifies for an individualized education program, pursuant to specified laws, from accessing any special education and related services required by his or her individualized education program. The bill would narrow the authorization for temporary exclusion from a school or other institution to make it applicable only to a child who has been exposed to a specified disease and whose documentary proof of immunization status does not show proof of immunization against one of the diseases described above. The bill would make conforming changes to related provisions.