ABSTRACT

A Spatiotemporal and Sociodemographic Analysis of Nonmedical Vaccine Exemptions for Texas Kindergarteners

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Across the United States, rates of nonmedical vaccine exemptions for schoolchildren have risen. Public health research has linked certain sociodemographic and school characteristics to higher nonmedical exemption rates. In Texas, analysis of change in nonmedical exemption rates and of associated risk factors has not been done at the school district level. This thesis analyzes data from the 2017 American Community Survey, the Texas Education Agency, and the Immunizations Epidemiology branch of the Texas Department of State Health Services to establish relationships between nonmedical exemption rates, sociodemographic characteristics, and school or school district characteristics. The data support our hypotheses: that nonmedical exemption rates in Texas are rising, and that they are positively associated with the proportion of non-Hispanic Caucasian students, median family income, educational attainment, rural schools, private schools, and charter schools. However, the exact details of the mechanisms influencing these trends and relationships have yet to be elucidated.

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A SPATIOTEMPORAL AND SOCIODEMOGRAPHIC ANALYSIS OF NONMEDICAL VACCINE EXEMPTIONS FOR TEXAS KINDERGARTENERS

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CHAPTER ONE

Introduction and Background Information on Vaccination and Immunization

The Advent of Vaccines to Modern Vaccines

Vaccines are one of medical science's greatest achievements. They have made a profound contribution to the substantial decrease in morbidity and mortality caused by infectious disease. Yet today, in times when deaths and life-changing disabilities from infectious disease are nowhere near as common as they once were, it can be easy to take vaccines- and their implications on individual and public health- for granted.

There once was a time when the life-saving vaccines as we know them today did not exist. In those days, our knowledge of immunity and of bacteria, viruses, and other infectious organisms was extremely limited. Many people suffered from infectious diseases that we rarely hear about and seldom (if ever) see today: diphtheria, measles, rubella, mumps, pertussis, tetanus, polio, and the devastating smallpox- now eradicated.

In fact, techniques harnessing the power of the immune system to recognize and destroy foreign substances- principles that vaccines even today rely upon- began with attempts to protect people against smallpox, the only human disease to have been permanently eliminated from the earth. In eastern and southern Asia, as well as parts of northern Africa, a practice known then as inoculation, or variolation, became common in the protection of individuals against smallpox. The exact process of variolation varied between practitioners in different regions of the world. During the 1500s, a form of variolation called insufflation became common in China and the Middle East. Insufflation was accomplished by grinding up dried scabs from patients who had survived a mild course of smallpox, combining them with various other substances, and blowing this concoction up a patient's nose (Boylston 2012). Around the same time, the Bengalese in modern day eastern India and Bangladesh practiced variolation when they dipped sharp needles into the pustules of those afflicted with smallpox, using those same needles to make tiny punctures in the upper arms of patients. All forms of variolation, though, involved gathering material from the pustules or scabs of previously infected individuals and introducing these materials to the immune systems of healthy individuals who had never suffered from the disease (Boylston 2012). It is remarkable that even then, before the discovery of inactivated and live attenuated vaccines, that people knew to use weakened forms of the pathogen to engender protection against the virulent form of the pathogen in those variolated. The demand for variolation was great: generations of variolators all from the same family closely guarded their trade secrets, passing them down only to younger members of the family who would take up the business (Boylston 2012). The method was imperfect. Deaths occurred from the application of improperly dried scabs or the scabs from individuals who suffered from a more severe form of infection (Lombard et al., 2007). Nevertheless, manuals describing the practice soon began to be spread, and the practice of variolation spread throughout the rest of Asia, Africa, and into Europe (Boylston 2012).

In 1749, the English scientist and physician Edward Jenner was born. Jenner, who would eventually create the first vaccine- against smallpox- was himself variolated against the disease in his teens. Later, he would observe that milkmaids, who were exposed to cowpox, were generally immune to the more dangerous smallpox. Jenner then conducted a series of experiments which involved scraping the hands or arms of subjects and then introducing material derived from cowpox blisters and pustules to the shallow wounds. The subjects would invariably fall ill with mild cases of cowpox. Jenner would then challenge the subjects with infectious smallpox material. In case after case, vaccinated individuals failed to develop smallpox. Vaccination, not to be confused with variolation (which is synonymous with inoculation in this context), ultimately proved to be a safer and more effective alternative to variolation in protecting individuals from smallpox. Variolation spread infectious material from smallpox victims, whereas vaccination spread infectious material from cowpox victims. Both techniques protected individuals from smallpox when successful, but variolation posed a greater danger than vaccination when unsuccessful. In 1798, Jenner published his findings for the scientific community to review (Lombard et al., 2007). The practice of variolation declined, and some countries even banned the practice outright.

The practice of using attenuated pathogens to vaccinate people against their more virulent forms was refined and developed by Louis Pasteur. In 1876, one of Pasteur's lab assistants cultured the bacteria *Pasteurella multocida,* which causes cholera in fowl, in a modified type of urine (Lombard et al., 2007). When the hen was vaccinated with these attenuated, or weakened cultures, it did not die. Subsequent immunologic challenges against the virulent form of the bacteria proved successful. The results of the experiment supported the idea that passaging a pathogen in a medium unlike the bodily fluids of the animal it naturally infects can attenuate the pathogen and produce material suitable for vaccination. Five years later, in 1881, Pasteur and his team had devised a similar method to attenuate anthrax. Sheep farmers in France watched in awe as Pasteur's heat-attenuated anthrax vaccine protected vaccinated sheep against challenges with *Bacillus anthracis,* while all unvaccinated sheep died. Pasteur then turned his attention to the rabies vaccine. In developing the rabies vaccine, Pasteur and his team developed a novel approach: rather than using sterile media or heat as an attenuating agent, the scientists decided to passage rabies virus through live dogs. The team dried the brains and spinal cords of rabbits who had died from the disease, and directly introduced this material to the brains of dogs (Lombard et al., 2007). This drying process was thought to have been enough to attenuate the virus, but it proved to be inconsistent and unpredictable. Individuals vaccinated with early forms of the rabies vaccine frequently developed serious side effects (Greenwood 2014). Nevertheless, this process was refined by later scientists- notably Albert Calmette and Camille Guerin, who in the 1910s passaged tuberculosis bacteria 230 times to produce a strain sufficiently attenuated for human vaccination, and Max Theiler and Hugh Smith, who in the 1930s passaged yellow fever virus in mouse and chicken embryonic tissue (Plotkin 2014).

In the 1950s, the incidence of polio in the United States had peaked. Polio, which is an infection that can cause permanent paralysis involving not only the skeletal muscles but also the respiratory system, started to come to American towns and cities in annual epidemics through the first half of the twentieth century. Fatality rates were quite high during the early years. In 1916, United States public health officials declared that polio had reached epidemic levels. That year, 27,000 cases of polio and 6,000 deaths were recorded in the United States- the most by far (Mehndiratta et al., 2014). The worst was yet to come, and the severity of polio epidemics in the United States was exacerbated by some specific factors. During the years in which polio reached epidemic proportions in the United States (1900-1955), the average age of people stricken with the disease increased (Nathanson & Kew, 2010). To make matters worse, the risk that a person infected with polio will die- the case-fatality rate- increases with increasing age: 19% of infants under three years of age infected with polio will develop paralysis involving the limbs and the respiratory system, while 55% of adults 25 and older will develop the same severity of symptoms (Nathanson & Kew, 2010). Fear of the ancient disease and calls for a vaccine grew quickly.

Jonas Salk's inactivated polio vaccine, introduced in 1955, and Albert Sabin's attenuated oral polio vaccine, introduced in 1961, drastically decreased the incidence of new polio cases in the United States. Both vaccines targeted all three strains, or serotypes, of the virus, including the most dangerous serotype- type 1- which caused 80% of paralytic cases of the disease. Within a year, the number of incident polio cases decreased to 5,600 from 58,000- a tenfold decrease. By the time Sabin's vaccine was finally ready, only 161 incident cases were recorded in the United States (Mehndiratta et al., 2014). Both Salk and Sabin were hailed as national heroes.

1973 was the first year in which no incident cases of polio appeared in the United States (Nathanson & Kew, 2010). Public health experts predicted that the rest of the world would eventually follow. Those predictions have turned out to be mostly true, as the prevalence of polio in the world has dropped 600-fold, from roughly 600,000 cases before the vaccine was introduced to fewer than 1000 cases by the turn of the millennium (Nathanson & Kew, 2010). The elimination of incident polio cases in the United States and its near elimination in the rest of the world represents one of vaccination's most notable and well-chronicled contributions to public health.

Because of vaccination, many of the diseases that plagued our families just one or two generations ago have dwindled into such obscurity that even physicians hardly ever encounter them. In many parts of the world, this is not (yet) the case. Because advances in transportation technology have made international travel easier and more accessible than ever before, there is still the risk that travelers from other countries or citizens returning from other countries will carry with them infectious diseases no longer endemic to the United States. In the case of the 2008 San Diego measles outbreak, which was the largest outbreak of the disease since 1991, a boy whose parents had intentionally refused to vaccinate against measles returned from Switzerland, and exposed 839 people to the disease, 48 of whom were too young to have been vaccinated against measles (Sugerman et al., 2010). Even in this highly vaccinated population, 11 people developed the disease, all of whom were unvaccinated children. Because of cases like this, the CDC still recommends immunization against diseases we rarely see. The CDC's schedule for immunization recommends that children and adolescents under the age of 18 be protected against 16 diseases: diphtheria, tetanus, and pertussis (through the DTaP and the Tdap vaccines); measles, mumps, and rubella (through the MMR vaccine); rotavirus, pneumococcal disease, varicella, influenza, polio, *Haemophilus influenzae* type B (HiB), human papillomavirus (HPV), meningococcal disease, and Hepatitis A and B (CDC).

Today, several organizations and programs promote vaccination to protect people in the United States from infectious disease. In 1964, the CDC created the Advisory Committee on Immunization Practices (ACIP) to promote the prevention of infectious diseases (Hotez 2018). ACIP is the organization tasked with creating recommended immunization schedules for all children, adolescents, and adults in the United States, and for developing protocols for the administration of such vaccines. Special care has been taken to eliminate any financial or other conflicts of interests. No ACIP committee member can work for a company that manufactures vaccines or have working relationships with employees of those companies. The fifteen members include experts in public health, vaccine research, vaccine safety, and those who have experience administering immunization programs at the local level (CDC). ACIP has a tremendous influence not only within the United States but also globally. Many countries use ACIP practices and guidelines as a part of their vaccination programs (Hotez 2018).

On a global level, the World Health Organization (WHO) coordinates most of the international effort to promote vaccination in countries where need remains high. In 1974, three years before smallpox was declared eliminated from the globe, the WHO set up the Expanded Program on Immunization (EPI). EPI took advantage of the global vaccine delivery infrastructure created in part by the effort to eradicate smallpox. The program delivered vaccines to children in remote and isolated areas. More recently, in 2000, the Global Alliance for Vaccines and Immunization (GAVI) was created to expand vaccination coverage to the 30 million children not fully immunized by the EPI program. This alliance has been very successful, reporting a 40% reduction in deaths from rotavirus and pneumococcal disease alone (Hotez 2018). It is even starting to help developing countries create their own vaccination infrastructures independent from GAVI. Humans have made huge strides in preventing infectious disease since inoculation was first used. Vaccines have made and continue to make an immense contribution to the decrease in illness and death due to such diseases.

How Vaccines Protect Individuals

It is an indisputable fact that vaccination saves lives. However, it was not until relatively recently that we have begun to grasp how immunization- the complex biochemical and immunologic changes in a vaccinated individual that protect it from infection- occurs.

On a basic level, vaccines take advantage of the immune system's ability to recognize self and distinguish it from non-self, which it does with great specificity (CDC). Furthermore, the immune system can mount an effective, strengthened response against antigens (portions of non-self organisms or substances) years or even decades after an initial exposure. Immunity against antigens can be measured by quantifying an organism's serum concentration of antibodies (proteins produced by plasma cells) against a specific antigen. There are two types of immunity: passive and active.

Passive immunity occurs when antibodies against an antigen are transferred between two different organisms. This transfer usually occurs between a mother and her infant when antibodies cross the placenta, giving the newborn temporary protection against particular diseases. Scientists have also developed transfusable blood products that contain high concentrations of a specific antibody. These blood products are often used post-exposure to grant their recipients a temporary boost against a particular antigen. In passive immunity, protection against an antigen is temporary because the organism's immune system plays no part in recognizing an antigen and developing an immune response against it.

Active immunity is a longer lasting form of immunity than passive immunity. Active immunity occurs when an organism's own immune system mounts a systemic response against an antigen. In the primary response, the activity of the immune system of low. Critically, the immune system creates memory cells that are specific to the antigen encountered in the primary response. These memory cells are what confer immunity to the antigen years after the primary response. In the secondary, or anamnestic response, the immune system mounts a much larger response against the antigen. Such a response is initiated by the surviving memory cells. There are two ways an organism can develop active immunity against an antigen. The organism can survive an infection by the antigen, or the organism can be vaccinated. Both modes of active immunity generate a long-lasting immune response, but vaccination stands out in that it is not associated with the infection's negative health effects (CDC).

There are different types of vaccines. Already briefly mentioned are the vaccines which use attenuated live pathogens and those which use inactivated killed pathogens or fragments of pathogens like protein subunits, polysaccharides, and polysaccharide-protein conjugates. When compared to inactivated vaccines dose-per-dose, attenuated vaccines induce a stronger and longer lasting immune response (and thus a more durable protective effect). This also means that it takes fewer doses of an attenuated vaccine than it does of an inactivated vaccine to achieve the same level of immunity. However, the live organisms which constitute attenuated vaccines may cause deleterious side-effects, especially in individuals with compromised immune systems. They can even mutate and revert to a more virulent state. In the case of the attenuated oral polio vaccine, this reversion has happened in exceedingly rare yet notable circumstances, and contributes (among other substantial factors) to some of the few vaccine-derived polio cases which now exist- in Syria, Nigeria, Pakistan, and especially Somalia (Greenwood 2014). And, while attenuated vaccines are, on average, less expensive to produce than their inactivated vaccine counterparts, they tend to be more sensitive to changes in temperature. This means that they are harder to produce and to transport, especially from their point of production in developed countries to the developing countries that need them most. Finally, attenuated vaccines induce both humoral (B-cell based) and cellular immunity (T-cell based), while inactivated vaccines only induce humoral immunity (CDC).

In the two centuries since Edward Jenner created his attenuated smallpox vaccine in 1796, the field of vaccinology has bloomed. The subsequent discoveries of inactivated vaccines, toxoid vaccines, recombinant protein vaccines, polysaccharide vaccines, conjugate vaccines, and subunit vaccines have protected humans against many serious diseases. There continue to be promising developments in vaccine technology, as researchers aim to use vaccines based on nanoparticles and nucleic acids to target an ever-broadening range of diseases (Plotkin 2014).

How Vaccines Protect Populations

Many billions of people have been vaccinated, and of those billions, a great many millions are saved from disfigurement and death. A 2019 estimate by the World Health Organization states that vaccination prevents 2-3 million deaths each year (WHO). However, there are people who- for medical reasons or not- remain unvaccinated. Does the vaccination of a population protect these unvaccinated individuals?

The answer is clear. When individuals susceptible to a disease are vaccinated against it, the incidence of the disease in that population drops: vaccines have direct benefits against disease in the vaccinated population. However, the incidence of disease in the susceptible unvaccinated population drops as well. This phenomenon, known as herd immunity, interferes with the ability of the infectious disease to transmit itself between susceptible individuals. Therefore, vaccinating even part of a population confers an indirect protection against the disease in the nonvaccinated individuals. The contribution of vaccines to the protection of a population thus relies on two factors: the direct benefit against disease in vaccinated individuals, and the indirect benefit (herd immunity) against disease in non-vaccinated individuals.

The success a vaccine has in indirectly protecting nonvaccinated individuals is related only to the success a vaccine has in preventing the transmission of the disease. For example, promising research has shown that a malaria vaccine which does not prevent sickness in the recipient, but rather prevents transmission from a sick human to a susceptible mosquito, can lower the incident rate of malaria in regions where it is endemic. (Zheng 2016)

The percentage of a population that needs to be immune to a disease for the disease to cease existing in the population- the herd immunity threshold- can be calculated with the equation

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

Where p_c represents the herd immunity threshold expressed as a proportion, and R_0 represents the basic reproduction number, the average number of new infections in a susceptible population caused by an infectious, diseased individual. When the basic reproduction number is high, the herd immunity threshold is higher. Measles, which has an estimated basic reproduction number of 15-18, thus has a herd immunity threshold of 93.3% to 94.4% (Fine et al., 2011).

It is important to consider that vaccines are not immunogenic in all their recipients, and that the degree of immunogenicity in recipients varies (Fine et al., 2011). Vaccination does not always lead to immunization. For example, only 95% of individuals who received the attenuated oral polio vaccine achieve immunity (Mehndiratta et al., 2014). As a result, there is an important distinction to be made between p_c, the herd immunity threshold, and v_c, the critical vaccination coverage threshold, that can be expressed by the following equation:

$$v_c = \frac{(1 - \frac{1}{R_0})}{E} = \frac{p_c}{E}$$

Where E represents the effectiveness of the vaccine at preventing transmission of the disease among the susceptible population. Some individuals, like those with severe immunodeficiency disorders, are not able to generate immune responses to vaccination. These individuals are still susceptible to the diseases vaccines prevent. Therefore, E is always less than 1. Because $E < 1$ for any given vaccine, then a greater proportion of the population than p_c, the herd immunity threshold, will need to be vaccinated for the incidence of the disease to decrease in the population.

It is also crucial to note that this model depends on the assumption that a population is homogenously distributed (Fine et al, 2011). We know from experience, however, that populations rarely distribute themselves evenly and interact randomly. Populations are heterogenous, and the patterns of interaction between individuals are hardly random. Groups coalesce within populations, and those groups which include highly interactive individuals are at greater risk for infectious disease than groups which feature individuals who interact with each other less frequently. Furthermore, there is a tendency for vulnerable individuals to concentrate themselves spatially and/or socially. Children, for example, are highly socially interactive and spend hours each school day in the same environments. Patients in hospitals, a population which tends to have a greater percentage of immunocompromised individuals than the general population, also congregate spatially. Communities which, for one reason or another, decline to vaccinate themselves and/or their children also tend to reside in the same locale. Because of this clustering, public health advocates have suggested selective vaccination as a viable practice to protect individuals or populations which are crucial in the transmission of the disease or particularly vulnerable to it (Fine et al., 2011).

In many ventures, there is difficulty in applying theory to practice. Public health and medical professionals increasingly face difficulties in gaining vaccine coverage equivalent to or greater than the critical vaccine coverage threshold in certain communities across the globe. Misinformation and mistrust of vaccines and the medical profession have made it more difficult to vaccinate populations and maintain herd immunity, which only exists when a sufficiently high proportion of the population is vaccinated and immunized. Individuals protected by herd immunity are still susceptible to disease and may become increasingly at risk for disease if the proportion of vaccinated and immunized individuals in the population drops over time (Fine et al., 2011). If a public health program aims to provide vaccination coverage equivalent to the critical vaccine coverage threshold, it will fall below that threshold, and there will be a risk for the incidence of the disease to increase. Thus, it should be a goal to obtain 100% vaccine coverage, fully knowing that while efforts to reach that goal will fall short, that they have a better chance of exceeding the critical vaccine coverage threshold.

The Beginnings of Doubt and Resistance

Doubt in vaccines is not a completely novel phenomenon. When Edward Jenner published his findings about the safety and efficacy of his smallpox vaccine, notable opponents of vaccination soon emerged. Chief among these opponents was the respected British scientist Alfred Russell Wallace, who published his observations in support of the theory of evolution by natural selection around the same time Charles Darwin did (Greenwood 2014). Even before Jenner created the first vaccine, the English Reverend Edmund Massey delivered a 1772 sermon in which he called the practice of inoculation a “diabolical operation” (Hussain et al., 2018). When England in the mid-1800s passed laws mandating the vaccination of children, parents formed the Anti Vaccination League (Hussain et al., 2018). To this day, doubt in vaccines continues to exist in nearly every part of the world.

Vaccine-hesitancy is not spread equally among vaccines. The MMR vaccine receives a large share of the opposition, while other vaccines like that against polio have not received nearly as much resistance. Resistance against a vaccine is influenced by the cost-benefit analysis performed by parents as they weigh the perceived benefits of the vaccine against its perceived risks (Hussain et al., 2018). Vaccination’s perceived benefits appear to be underestimated while its perceived risks appear to be overestimated.

In recent years, there has been a sharp increase in vaccine doubt. This modern rise in vaccine doubt can be traced to Andrew Wakefield, at the time a British physician, who in 1998 published a paper titled “Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children” in the *Lancet* (Wakefield et al., 1998). Wakefield and his colleagues studied the illnesses of 12 children who displayed gastrointestinal inflammation and developmental regression days to weeks after the administration of the MMR vaccine. Some of the immediate causes for concern included the uncontrolled nature of the experiment, the small n=12 sample size, and the strength of the conclusions drawn by Wakefield et al despite the lack of power (Rao & Andrade, 2011). Wakefield wrote that the groups of symptoms he and his colleagues observed reflected a “unique disease process” (Wakefield et al., 1998). The paper was ultimately retracted in 2010 (Hotez 2018). Among the *Lancet's* reasons to retract the paper included the findings of an extensive investigation, which included Wakefield's falsification of data, manipulation of results, and his dishonesty about the sampling technique (consecutive vs selective) he used to select patients (Rao & Andrade, 2011). The *British Medical Journal* published a series of articles which revealed financial conflicts of interest: Wakefield had received payments from lawyers involved in lawsuits against vaccine producers (Rao & Andrade, 2011). Consequently, Wakefield's license to practice medicine in the United Kingdom was revoked, and he has since relocated to Austin, Texas, where he continues to stand firm in his beliefs (Hotez 2018). This paper drew a huge share of the public attention and made many people incorrectly believe that the MMR vaccine caused autism. Consequently, MMR vaccination rates in the United Kingdom fell from over 90% in 1996 to 80% in 2003 (Hotez 2018). Measles, which was close to being declared officially eradicated from the United States by the end of the second millennium, has now made a comeback (Hotez 2018). People continue to believe, incorrectly, that the MMR vaccine causes autism despite the existence of methodologically sound, conflict-of-interest-free epidemiological studies conducted in Denmark, the United Kingdom, Canada, the United States, Japan, Australia, and more (Hotez 2018). The research provides solid evidence against the MMR-autism link.

Since the Wakefield paper, claims purporting to link vaccines to other detrimental health effects have been proposed. Some of the more recent views of those who are vaccine-resistant or vaccine-hesitant are that vaccines cause the very diseases they are meant to protect against. Others believe that trace amounts of formaldehyde left over from the inactivation process, as well as preservatives like thimerosal (ethyl mercury) and adjuvants (substances which boost the immune response to a vaccine) like aluminum, and squalene cause adverse side effects. There is no evidence to support these claims (Hotez 2018).

Some arguments against vaccination do not call into question the safety of vaccines' active or inactive ingredients. There are people who oppose vaccination on the grounds that any form of mandatory vaccination constitutes a broach of the right of individual freedom. Others cite religious beliefs to justify their opposition, though the relative effects of individual religious groups have yet to be extensively explored. Research conducted by Williams et al found that religious exemption rates in Vermont jumped from 0.5% to 3.7% after the state banned philosophical exemptions in 2016, suggesting that parents seeking exemptions used religious exemptions when philosophical exemptions became unavailable. Yet others appeal to the dichotomy between natural and unnatural substances, of which vaccines fall into the latter category.

The reasons people use to explain their doubt in vaccines seem to be as diverse as the illnesses vaccines are meant to prevent.

Celebrities and public figures who oppose vaccination have had a disproportionately negative impact on public perceptions of vaccines. The actor Jim Carrey, environmental activist Robert Francis Kennedy Jr, and actress Jenny McCarthy have all implicated vaccines as dangerous substances (Hussain et al., 2018). The news media continues to feed into the notion that there is a “controversy” over the safety of vaccines when, in fact, the vast majority of scientists and medical professionals agree that vaccines are safe and effective. These highly visible sources of misinformation have greatly contributed to the increase in nonmedical exemptions over the last two decades.

Because of the rising rates of nonmedical exemptions, some states have begun to draft or even pass legislation that would limit or even exclude nonmedical exemptions as valid reasons for a child’s non-vaccinated status. In 2015, the state of California passed Senate Bill 277, which eliminated personal belief exemptions. It was the first state in 30 years to have done so. California passed this law in response to a 2014 outbreak of measles at Disney, in a fifth of the 125 people who got sick had be hospitalized (Hotez 2018). Research by Paul Delamater and colleagues has shown that the year after the implementation of SB277 showed that in the first year after SB 277 had taken effect, the percentage of California kindergarteners who were not fully up to date on their vaccination requirements decreased. However, in the second year after SB 277 took effect, this percentage increased. The authors suggest that a “replacement mechanism” occurred during that second year: that parents who were unable to obtain personal belief exemptions for their children resorted to other mechanisms to bypass the law and enter schools (Delamater et al., 2019). Mohanty et al published research in 2018 which showed that the counties with the highest personal belief exemptions pre-SB 277 showed the largest increase in medical exemptions post-SB 277 (Mohanty et al., 2018). This lends credence to the observation that in post-SB 277 California, vaccine-hesitant parents who are no longer able to find personal belief exemptions for their children are finding sympathetic doctors who are willing to write medical exemptions. The authors of this study also interviewed California health officials, who were frustrated by the lack of clearance needed to establish a robust system reviewing such medical exemptions (Mohanty et al., 2018). In fact, one of the few regions in California which tried to keep official records of medical exemptions was sued (Mohanty et al., 2018).

In early 2019, local news organization Voice of San Diego published the results of a years-long investigation which revealed that one third of medical exemptions in San Diego since 2015 had come from a single doctor (Huntsberry 2019). This doctor had created a website which advertised “Evaluation for Medical Exemption to Vaccination” as a service their office provided. Soon after, on February 13, 2019, California Senate Bill 276 (SB276) was introduced to the California Legislature as a response to physicians like the aforementioned (California Legislative Information). If passed, SB 276 would restrict, but not eliminate, medical vaccine exemptions for California schoolchildren. Medical exemptions would have to be submitted into a state database. The California State Department of Public Health would be required to review the database and audit schools with an “overall immunization rate of less than 95%,” as well as physicians who submit more than 5 medical exemptions in a year. Importantly, SB 276 would require that all the information in the medical exemption forms be “true, accurate, and complete” under the "penalty of perjury" (California Legislative Information). Resistance to the bill has been extremely heated, and whether the bill will pass remains a question. The bill represents an important step in preserving public health: research has shown evidence of a positive association between the ease of obtaining vaccine exemptions to the incidence of the disease protected by the vaccine (Lo & Hotez, 2017).

Clusters of Nonmedical Vaccine Exemptions

Like-minded individuals tend to congregate together, and people who share opinions on vaccines are no exception to this general observation. Individuals who do not vaccinate themselves or their children, who tend to be in the minority, have a propensity to cluster together and form communities united by their stance on vaccines. Clustering may not necessarily be intentional. Parents who exempt their children for nonmedical reasons do not necessarily choose to deliberately move to places where other parents who favor nonmedical exemptions live. It could be the case that individuals with similar characteristics other than their stance on vaccines are guided by macro and micro-scale socioeconomic forces to live among one other. These primary characteristics such as such as income level, educational attainment, and racial/ethnic origin, that are the true drivers of clustering, might just be associated with their views on vaccines. This thesis aims to explore these associations as part of its research aims.

In this thesis, clustering is meant in the geographical or spatial sense of the word. However, in the age of instant communication, the tendency for like-minded individuals to congregate together need not be restricted by geographic boundaries or by distance. Social media platforms enable people who hold unfavorable views on vaccination to freely communicate with each other. Many of these platforms allow users to form private groups which vet prospective members before allowing them to join. This allows vaccine-hesitant individuals to hear and be swayed by the views of vaccine-resistant individuals. Individuals online tend to espouse bolder views in more dogmatic language than they would in person, and these online spaces become "echo chambers" that facilitate group polarization. Though researchers are coming up with new tools to quantify vaccine sentiment among the "general public" by trawling Twitter and other social media hotspots, this thesis does not seek to establish a relationship between online vaccine-sentiment clustering and the incidence of nonmedical vaccine exemptions (Blankenship et al., 2018).

Clustering is an important topic to discuss and account for in any research on vaccine exemptions involving spatial analysis. Overall vaccination coverage rates remain quite high in the United States despite the drop in recent years (Aloe et al., 2017). However, certain communities in the United States feature significantly high rates of nonmedical vaccine exemptions. These "hot spot" communities are at high risk for epidemic disease, since they have immunization rates well below the herd immunity threshold.

Some researchers have used geospatial software in conjunction with traditional social science statistical analysis techniques to identify hotspots of vaccine exemptions within the United States. Carlin Aloe led research in 2017 which linked spatial clusters of nonmedical exemptions and pertussis outbreaks in the United States (Aloe et al., 2017). Pertussis itself is a good candidate disease to study. Herd immunity requires that more than 90% of the susceptible population be immunized against pertussis, and thus the incidence of pertussis is more sensitive to drops in the immunization rate than for diseases with a lesser basic reproduction number. The researchers performed this level of analysis at the county level (Aloe et al., 2017). They identified 19 states in the union that in 2012, had an incidence rate of pertussis significantly higher than the national incidence rate. Unfortunately, only five states- Arizona, New Jersey, Oregon, Utah, and Washington state had county-level nonmedical exemption rate data and pertussis incidence rate data necessary for the research. Then, using the geographic statistical analysis software SaTScan, Aloe and colleagues used a spatial Bernoulli model to identify statistically significant clusters (counties) of nonmedical vaccine exemptions in those five states for children enrolled as kindergarteners for the 2011-2012 and 2012-2013 school years. The researchers then used a spatial Poisson model to identify statistically significant clusters of pertussis cases for children less than five years old and for children between 10 and 14 years old. New Jersey was the only state of the five the researchers analyzed that did not include a pertussis cluster or a nonmedical exemption cluster. Arizona, Oregon, Utah, and Washington all contained both pertussis clusters and nonmedical vaccine exemption clusters.

The proportion of kindergarteners with nonmedical exemptions in counties that were exemption clusters was 2.8 times higher than the comparable proportion in counties that were not exemption clusters (Aloe et al., 2017). Additionally, by superimposing the clusters of nonmedical exemptions upon the clusters of pertussis cases, the researchers were able to identify where pertussis clusters and nonmedical vaccine exemption clusters overlapped. In Washington, the researchers found 8 such clusters. In Oregon, researchers found 3 such clusters. In Utah, researchers found 2 such clusters. In the state of Arizona, Aloe et al found no pertussis clusters that were also nonmedical exemption clusters. This may be because Arizona only has 15 counties, compared to 36 in Oregon, 29 in Utah, and 39 in Washington (Aloe et al., 2017). A state with more counties allows for higher resolution analysis than states with fewer counties, since statistically significant clusters of nonmedical exemptions or pertussis cases found at the sub-county level will be less diluted by their non-statistically significant neighboring clusters. This makes it even more important that vaccine exemption data be collected and analyzed at the school, school district, or other sub-county level.

A separate study, conducted by Paul Delamater and colleagues in 2018, examined school level nonmedical exemptions for California kindergarteners and how the rates of these exemptions changed between the years 2000 and 2013 (Delamater et al., 2019).

Since at least 2000, the state of California has the enrollment numbers and the nonmedical exemption numbers for every school with more than 10 students (Delamater et al., 2016). The authors of this research were able to use ArcGIS v10.3.1 to geocode 8000-9000 such schools within the state of California between the years 2000 and 2013 to unique physical locations. With the statistical analysis software package R v3.2.4, these physical locations were then correlated to the block groups and census tracts, and school districts they were part of. The authors obtained a detailed picture of how the spatial distribution of nonmedical exemptions changed in California kindergarteners over time (Delamater et al., 2016).

Delamater and his colleagues found that nonmedical exemptions for California kindergarteners increased from 0.73% in 2000 to 3.09% in 2013 (Delamater et al., 2016). This finding is consistent with the general national trend. The researchers also found that vaccine cluster formation acts like a positive feedback process, with clusters of statistically significant high nonmedical exemptions accumulating these exemptions at a rate faster than areas not designated clusters. Furthermore, these “high NME use clusters” tend to expand in size over time, acting as what the authors call “seed locations” (Delamater et al., 2016). In 2000, 2.76% census tracts were identified as belong to such a cluster. In 2013, that number was 4.76% (Delamater et al., 2016). As expected, the proportion of clusters with no nonmedical exemptions decreased from 20.18% to 3.08% within that time period. Thus, the authors observed an expansion of nonmedical exemption use from areas of high use to areas of low use. The authors recommend focusing public health interventions that aim to decrease the rate of nonmedical exemptions use to not only the high-use clusters themselves, but also to the low-use clusters surrounding the high-use clusters, which are particularly susceptible to becoming high-use clusters themselves (Delamater et al., 2016). This approach is remarkably similar to the “ring vaccination” approach used by Donald Henderson and his international team as they eradicated smallpox from the earth (Hotez 2018).

Vaccine Exemptions and Factors Associated

In the United States, schoolchildren are required to have been vaccinated for certain diseases prior to entering school. However, parents of a school-age child may choose to exempt their child from vaccination. These exemptions fall into one of two categories: medical exemptions and nonmedical exemptions.

Parents may obtain a medical exemption for their child if their child has a condition which compromises his/her immune system, or if their child is taking medications that compromise their immune system. Parents may also obtain a medical exemption for their child if their child is known to have adversely suffered from vaccination or a known component of a vaccine.

Nonmedical exemptions fall into two categories: religious exemptions and philosophical or personal belief exemptions. The barriers parents must go through to obtain such exemptions for their children varies by state. In some states, all it takes for parents to obtain a nonmedical exemption is to have them fill out and sign a form. In other states, parents are required to discuss their beliefs about vaccination with a healthcare provider prior to obtaining a nonmedical exemption. As of 2019, five states- California, Maine, Mississippi, New York, and West Virginia- did not allow nonmedical exemptions for any vaccine (NCSL 2019).

Public health researchers have long attempted to link both personal factors and school-level factors to identify populations and communities most at risk from suffering low levels of vaccine coverage. A discussion of some of this research follows.

Personal Factors

Personal factors such as parental income level, parental education level, and race/ethnicity have been linked to increased nonmedical vaccine exemptions in children.

Ashley Gromis and Kayuet Liu conducted a spatial analysis of California which linked demographic factors to personal belief exemption clusters (2018). They found that while the spatial variance in demographic factors was not enough to explain the spatial variance in personal belief exemption rate, the demographic characteristic “proportion non-Hispanic white” had the strongest association with such high-use clusters (Gromis &

Liu, 2018). “Proportion non-Hispanic white” influenced personal belief exemption rate even more than the education levels of mothers, the next strongest factor. Analysis indicated that regions of Northern California, Central California, and major cities like San Francisco, Sacramento, San Diego, and Los Angeles contained disproportionately large amounts of high personal belief exemptions clusters.

Research conducted by McNutt and colleagues examined private kindergartens in California and focused on affluence as a predictor of vaccine hesitancy and refusal (2016). The research was conducted in 2015, one year before SB 277 came into force and eliminated personal belief exemptions. The results are in line with the rest of the literature. The percentage of California private kindergartens reporting more than 5% personal belief exemptions increased from 9% in the 2000-2001 school year to 31% in the 2014-2015 school year. However, most schools had fewer than 5% of their children covered by such exemptions (McNutt et al., 2016). Private kindergartens with tuitions greater than $10,000 were more than twice as likely to have personal belief exemption levels of more than 20% than private kindergartens with lower tuitions (McNutt et al., 2016). McNutt and colleagues cited possible explanatory factors underlying the association between affluence and vaccine hesitancy. They noted that people with greater socioeconomic status are more likely to behave in ways that beneficial to themselves but detrimental to the greater public, and that the “free rider” effect on the affluent on herd immunity is no exception (McNutt et al., 2016).

Canadian researchers Carpiano and Bettinger investigated the influence of demographic factors on personal belief exemption rates in British Columbian private and public kindergartens (2016). They found a negative association between the proportion of students speaking English at home (a rough estimate for the proportion of native-born children) with vaccine coverage levels. They also found the same negative association for students enrolled in English Language Learners programs (a rough estimate for the proportion of foreign-born children). Carpiano and Bettinger's data revealed a novel finding on the other end of the socioeconomic spectrum- that children of the highly affluent and children of the extremely poor were likely to not be complete in their vaccination schedules (2016). The authors remarked that the explanations for low vaccination coverage rates in these two distinct groups are fundamentally different. Highly affluent individuals tend to choose to refuse to vaccinate their children, while very poor individuals tend to not have the time or the transportation to access vaccination. These results may not be generalizable to populations within the United States. The demographic characteristics of the two countries differ, and there are programs within the United States such as the Vaccines for Children (VFC) program, which is an entitlement program designed to promote vaccine coverage among the most socioeconomically disadvantaged.

A study which examined personal belief exemptions in California kindergartens sought to identify spatial clusters of high personal belief exemptions, as many studies mentioned have done (Carrel & Bitterman, 2015). This study found that schools with higher percentages of non-Hispanic white students and low percentages of students on free and reduced lunch (FRL) were significantly associated with clusters containing high personal belief exemptions. Carrel and Bitterman also found that public charter schools had a higher proportion of non-Hispanic white students than public non-charter schools (2015). This study is consistent with the rest of the literature.

Yang et al conducted more research in California kindergarteners which provides evidence that non-Hispanic white population and high median household income are the strongest predictors of personal belief exemptions (2016). However, the research noted that educational attainment was not sufficiently significant to predict changes in personal belief exemptions.

In Arizona, Birnbaum and colleagues found that the trends observed in California applied to their state (2013). Arizona schools with a higher proportion of non-Hispanic white students and a low proportion of students receiving FRL lunches (a proxy of household income) were more likely than their counterparts to have high rates of personal belief exemptions (Birnbaum et al., 2013).

A separate study which used 2009 National Immunization Survey data to investigate household characteristics associated with vaccine hesitancy found that the following characteristics were more likely to be found in children with vaccine delays or exemptions: living in households earning more than four times the federal poverty level; having mothers who are married, over 30, English-speaking, college graduates, non-Hispanic white, and covered by private health insurance (Smith et al., 2011).

Finally, a 2014 systematic review of 42 published articles exploring nonmedical vaccine exemptions included 18 articles which explored sociodemographic predictors of high personal belief exemption status (Wang et al., 2014). This review summarized the findings from the literature: that the majority of research characterizes the population at greatest risk of high nonmedical exemptions as having a high median household income, as being non-Hispanic white race/ethnicity, and as having a college degree or higher level of educational attainment (Wang et al., 2014).

The research discussed does not attempt to explain why certain demographic factors are associated with nonmedical and personal belief exemptions. Some research, like the systematic review by Wang, elucidates such explanatory findings from qualitative studies. Parents, the studies say, who are skeptical of large institutions like the government, the pharmaceutical industry, and healthcare tend to have disproportionately negative views of the benefits vaccines provide. These parents also tend to underestimate the risk posed by vaccine-preventable disease, and this underestimation is likely due to the success of vaccines themselves (Wang et al., 2014).

A Methodological Problem in Linking Schools to Residences

Any research attempting to link school-level or district-level vaccination coverage levels to sociodemographic data gathered at the census-tract level will run into a problem. It is an assumption to infer that students who reside in one census tract necessarily attend the school(s) located within that census tract. Such students may commute outside of the census tracts containing the place of residence to attend schools in other census tracts. As a corollary, not all of the vaccination data associated with a school in a particular census tract is linked to the sociodemographic data associated with that census tract. The question then, is: how can researchers link vaccination coverage data at the school level to a census block (the highest level of Census data resolution) with multiple schools surrounding it (and perhaps one or more schools within it)? Delamater et al found an improved mathematical model- a “mobility-adjusted approach”- which factors in population mobility information to “estimate vaccination coverage at the community level” (2016). Such a model is limited, though, in its inability to fully account for factors such as the attractiveness of schools, the nonlinearity of distance between residence and school, and the use of "journey to work data as a proxy for parent/guardian mobility" (Delamater et al., 2016). The most accurate data to use in calculating a geographic region's vaccination coverage would be to link the addresses of households with schoolchildren to health information concerning the vaccination coverage of the schoolchildren. Such data is protected personal information and obtaining such data for all schoolchildren within a given state is infeasible. There remains room for further improvements in linking school-level vaccination coverage data with units of geography that government agencies use to collect demographic data.

California and Texas Vaccination Coverage Records

California is frequently chosen as a state to conduct high-resolution spatial and temporal analyses of vaccine coverage levels. One of the factors contributing to California's popularity among researchers is that it has documented the immunization records of all of its 8000-9000 schools with 10 or more students, including important data such as the number and percent of students fully up to date on recommended vaccines and the number and percent of students whose parents have filed a personal belief exemption on their behalf (Shots for School). California has records of this information for its kindergarteners since the 2000-2001 school year. For its students between the 7^{th} and 12^{th} grade, California has records of this information since the 2011-2012 school year (Shots for School). This abundance of data makes it possible for epidemiologists interested in the state to conduct detailed research going back nearly two decades.

Texas, on the other hand, has only kept records of school-level vaccination coverage levels for kindergarteners and 7th graders since the 2016-2017 school year (DSHS). It has kept conscientious exemption data by school district, charter school, and private school since the 2005-2006 school year (DSHS). This is 14 years-worth of data. Texas also keeps records of conscientious exemptions at the county level and has kept such records for 14 years. If one were to rely on the school-level vaccination coverage levels, one would only have three years of data- for the 2016-2017, 2017-2018, and 2018-2019 school years to work with. This amount of time is not suitable for analyses involving trends over time to be made at the school level. On the other hand, if one were to rely on the conscientious exemption data, one would have 14 years of data to conduct analyses, but the spatial resolution of results would be coarser.

School-Level Factors

While personal factors are important predictors of childhood nonmedical exemption status, certain characteristics of the schools children attend are also important in developing a clearer picture of the situation.

In the aforementioned 2008 San Diego measles outbreak, public health researchers noted that "substantial rates of intentional under vaccination occurred in public charter and private schools, as well as public schools in upper-socioeconomic areas" (Sugerman et al., 2010). The aforementioned study by Gromis and Liu found that in California, the nonmedical exemption rate was higher in charter schools than in private schools (2018). For example, in 2014, the rate of personal belief exemptions in California charter schools was 7.5%, while the comparable rate was 5.2% for private schools, and

2.1% in non-charter public schools (Gromis & Liu, 2018). According to that same research, even opening a charter school in the vicinity of public schools was found to stimulate personal belief exemptions in the neighboring public schools (Gromis & Liu, 2018).

Research mentioned earlier by McNutt focused in private kindergartens in California and examined the religious affiliation of the school as a factor associated with personal belief exemptions (2016). They found that private kindergartens that were secular or non-Catholic Christian were associated with personal belief exemption levels exceeding 20%, while Catholic, Jewish, and Islamic kindergartens had no such association (McNutt et al., 2016).

The study done by Carpiano and Bettinger on personal belief exemptions in British Columbian schools mostly corroborated data coming from the United States (2016). They found that private non-religious schools (Montessori and Waldorf-type schools in particular) were associated with a personal belief exemption rate far higher than their public counterparts.

The aforementioned research conducted by Carrel and Bitterman identified the proportion of private schools, public charter, and public non-charter schools in statistically identified hotspots of high personal belief exemptions (2015). Carrel and Bitterman found that private and public charter schools made up a higher-than-expected proportion of schools in high personal belief exemption clusters, while public non-charter schools were proportionally overrepresented in clusters of low personal belief exemptions. Among private schools, nonreligious schools were proportionally overrepresented in clusters of high personal belief exemptions, while religious schools were proportionally overrepresented in clusters of low personal belief exemptions. Suburban schools were more likely to be found in high exemption clusters than non-suburban schools (Carrel & Bitterman, 2015).

Birnbaum's investigation of sociodemographic predictors of high personal belief exemption rates in Arizona kindergartens found that kindergartens outside urban areas were more likely to have high rates of personal belief exemptions than their urban counterparts (Birnbaum et al., 2013). Furthermore, Birnbaum's research found that kindergarteners who attend charter schools in Arizona, which has the nation's highest concentration of charter schools, are 27 times more likely to be incomplete in their vaccination requirements than Arizona kindergarteners attending public non-charter schools.

One of the few studies to not have used geocoded data from state health departments is a research article published in 2005 by Salmon et al, who distributed surveys to a total of 1000 public and private elementary school officials. The researchers chose to send the surveys to officials in Colorado and Washington, two states that at the time allowed philosophical exemptions, and Missouri and Massachusetts, two states that do not allow philosophical exemptions (they only allow religious exemptions). Surprisingly, Salmon and his colleagues found that a fifth of the schools in Missouri and Massachusetts, the states which do not allow philosophical exemptions, went against state law by providing such exemptions. In accordance with the rest of published research, the study found that the proportion of exemptions in private schools was 8.2% compared to the significantly lower figure in public schools, which was 4.8% (Salmon et al., 2005).

An investigation of the San Diego measles outbreak published by Sugerman and colleagues in 2010 found the percentages of personal belief exemptions in the area's schools to be 1.8% among public schools, 11% among charter schools, and 5% among private schools. They also found 10 schools with a personal belief exemption rate of over 40%: 6 private schools, 2 public charter schools, and 2 public non-charter schools. These schools were located near each other: a megacluster of exemptions (Sugerman et al., 2010).

A separate study looking at California public schools and private schools came up with similar results. This research, published by Richards et al, established a novel finding: the rate at which personal belief exemptions increase in private schools is greater than that for public schools (2013). Richards also established that rural schools had 1.66 times the rate of personal belief exemptions compared to urban schools: for each 1000 person per square mile increase in population density, the rate of personal belief exemptions fell 3.3% (Richards et al., 2013).

The systematic review of 42 studies conducted by Wang et al found that schools with high rates of nonmedical exemptions tended to be found in rural, rather than urban areas, and that private schools had higher exemption rates than public schools (2014).

Hypotheses

This thesis hypothesizes that high rates of nonmedical vaccine exemptions in Texas kindergarteners are positively associated with non-Hispanic Caucasian race/ethnicity, high median family income level, and college-graduate-or-higher parental educational attainment levels. It is expected that the prevalence of nonmedical vaccine exemptions among private schools and public charter schools is higher than that among non-charter public schools, and that rural schools have higher nonmedical vaccine exemption rates than non-rural schools. Finally, it is also expected that the prevalence of nonmedical vaccine exemption rates for Texas kindergarteners has significantly increased since the data was first collected 14 years ago. This thesis attempts to answer questions involving the personal characteristics of those who cite nonmedical reasons in exempting their children from vaccination. This thesis also attempts to answer questions involving the characteristics of schools that contain a significant proportion of nonmedical exemptions. Finally, this thesis attempts to answer questions involving the change in nonmedical exemptions over time at the local level, and where clusters of high nonmedical exemptions exist.

CHAPTER TWO

Data and Methods

Data Sources

The data used to answer the research questions posted by this thesis can be grouped into three categories: nonmedical exemption data, geospatial data, and sociodemographic data. The data come from three major sources: the Texas Department of State Health Services' Immunization Unit, the Texas Education Agency's Public Open Data Site, and ProximityOne, a company that provides spatial and sociodemographic data to researchers and policymakers.

The pertinent data from the Texas Department of State Health Services' Immunization Unit include the outcome variable explored in this thesis: the rate and counts of kindergarten-level nonmedical (conscientious) vaccine exemptions by independent school district, public charter school, or private school. These data range from the 2005-2006 school year to the 2018-2019 school year.

The pertinent data from the Texas Education Agency's Public Open Data Site include shapefiles, which contain information about the boundaries of Texas school districts. The site also includes a "Snapshot" of ISD-level sociodemographic data ranging from the 1994-1995 school year to the 2017-2018 school year. Finally, the site includes data about ISD geographic classification (urban vs rural, city vs suburb vs town vs rural) ranging from the 2007-2008 school year to the 2017-2018 school year. Only the 2017-2018 school year "Snapshot" sociodemographic data and geographic classification data were used and linked with the nonmedical exemption data from the appropriate year.

The pertinent data from ProximityOne include US Census Bureau: American Community Survey five-year estimates from 2017. These extensive data can be grouped into four categories: general demographics, social characteristics, economic characteristics, and housing characteristics. From this source, data relevant to the scope of this thesis include the median family income and percent college graduates for each school district. Median income was chosen over mean income because the distribution of mean income in the United States is increasingly skewed towards higher incomes. As a result, mean income is significantly greater than median income and is not a good representation of the how much money most individuals make within any given geographic area. (US Census Bureau). Median family income was chosen over median household income because children are typically raised in families- two or more people related by birth, marriage, or adoption living in the same dwelling. Households, on the other hand, are comprised of one or more individuals living in a dwelling. This is a broader category and includes dwellings that are inhabited by one person (not an accurate representation of where school-age children live).

Data Analysis Methods

Facility boundaries were input into ArcMap 10.3.1. Data containing facility name, type, rural/urban classification, and nonmedical vaccine exemption rate were processed, cleaned, and linked with sociodemographic data like median family income, proportions of race/ethnicity, and percent college graduates. An Anselin Local Moran's I Spatial Autocorrelation analysis and a Getis-Ord Gi* Hot Spot analysis were performed in ArcMap 10.3.1. A linear regression was performed in to assess the overall trend in nonmedical vaccine exemption rates overall, and at the ISD, public charter school, and private school level. A t-test was performed to assess the difference in nonmedical vaccine exemption rates between rural and non-rural schools. Linear regressions were performed to evaluate the relationship between exemption rates and proportions of racial/ethnic makeup, median family income, and percent of individuals with a bachelor's degree or higher. An analysis of variance (ANOVA) with post-hoc Tukey HSD test was performed to determine differences between ISDs, public charter schools, and private schools. Data analysis was performed in RStudio using R x64 3.6.1.

Data Analysis Measures

Nonmedical Vaccine Exemptions

The state of Texas allows parents to pursue both medical and nonmedical vaccine exemptions for their school-age children, as is stated in the Texas Administrative Code §97.62. Nonmedical vaccine exemptions include both philosophical, or personal belief exemptions, and religious exemptions. This thesis explores trends in nonmedical vaccine exemptions. This thesis does not distinguish between subtypes of nonmedical vaccine exemptions- religious exemptions and philosophical exemptions.

Sociodemographic Indicators

"White": Data were collected from the Texas Education Agency's Public Open Data Site to determine the proportion of schoolchildren of Non-Hispanic White race within a school district's boundaries during the school year 2017-2018.

"Black": Data were collected from the Texas Education Agency's Public Open Data Site to determine the proportion of schoolchildren of Black or African American race within a school district's boundaries during the school year 2017-2018.

"Hispanic": Data were collected from the Texas Education Agency's Public Open Data Site to determine the proportion of schoolchildren of Hispanic ethnicity within a school district's boundaries during the school year 2017-2018.

"Asian": Data were collected from the Texas Education Agency's Public Open Data Site to determine the proportion of schoolchildren of Asian race within a school district's boundaries during the school year 2017-2018.

"Percent college graduates": Data were collected from US Census Bureau: American Community Survey five-year estimates released in 2017 to determine the proportion of individuals within a school district's boundaries who have obtained a bachelor's degree or higher.

"Median family income": Data were collected from US Census Bureau: American Community Survey five-year estimates released in 2017 to determine the median family income within a school district's boundaries.

School and School District Classification

"Independent school districts": Data was provided by the Texas Department of State Health Services' Immunization Unit. Public independent school districts are facilities with a "public" facility type and contain "ISD" or "CSD" or "CISD" within the facility name.

“Charter school”: Data were collected from the Texas Department of State Health Services’ Immunization Unit. Public charter schools are facilities with a “public” facility type and do not contain “ISD” or “CSD” or “CISD” within the facility name.

“Private school”: Data were collected from the Texas Department of State Health Services’ Immunization Unit. Private schools are facilities with a “private” facility type and do not contain “ISD” or “CSD” or “CISD” within the facility name.

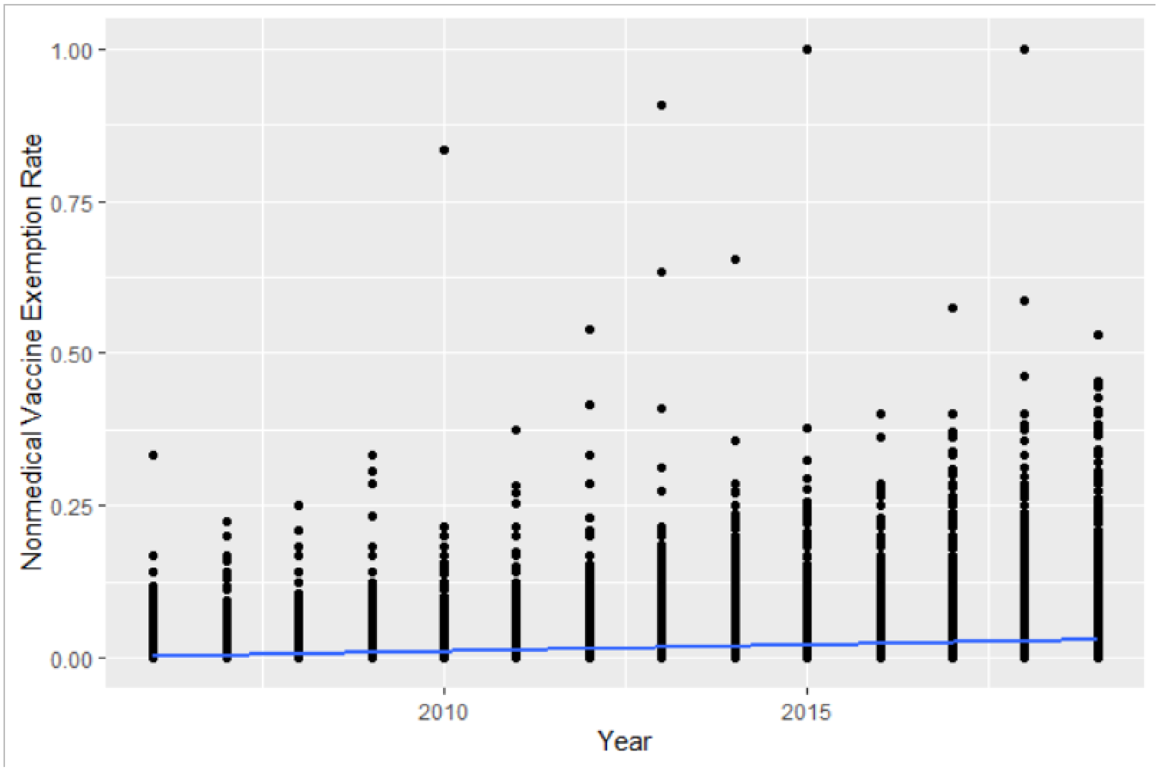
“Rural”: Data were collected from the Texas Education Agency’s Public Open Data Site. The Texas Education Agency classifies schools based on geographic type, and “rural” is one such classification.

“Non-rural”: Data were collected from the Texas Education Agency’s Public Open Data Site. The Texas Education Agency classifies schools based on geographic type: “major urban,” “major suburban,” “other central city,” “other central city suburban,” “independent town,” “non-metropolitan fast-growing,” and “non-metropolitan stable” were grouped together into the non-rural classification.

CHAPTER THREE

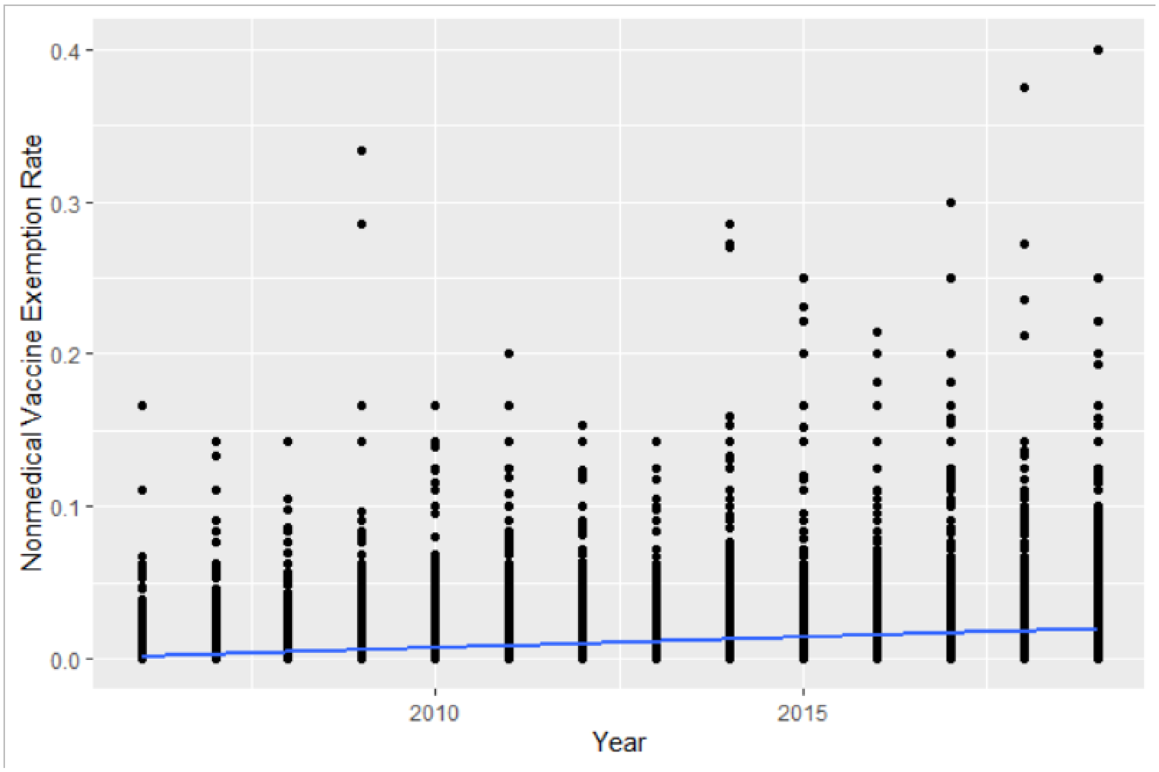
Results

Figure 1: Kindergarten Nonmedical Vaccine Exemption Rates, 2005-2006 to 2018-2019



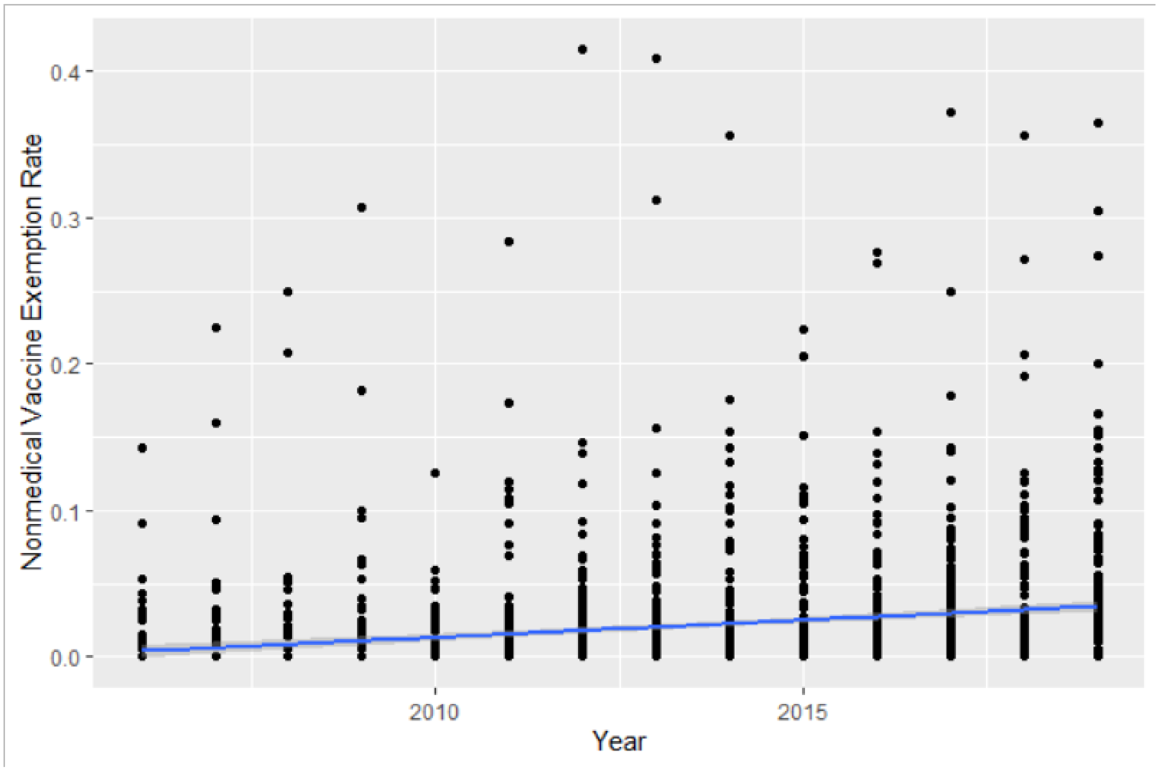
The coefficient for the predictor variable "Year" in this linear regression model was 2.109e-03, the standard error was 6.568e-05, the t value was 32.11, and $p<2e-16$. The coefficient is significantly greater than-zero at the $p<0.01$ threshold.

Figure 2: Kindergarten Nonmedical Vaccine Exemption Rates, 2005-2006 to 2018-2019, Independent School Districts



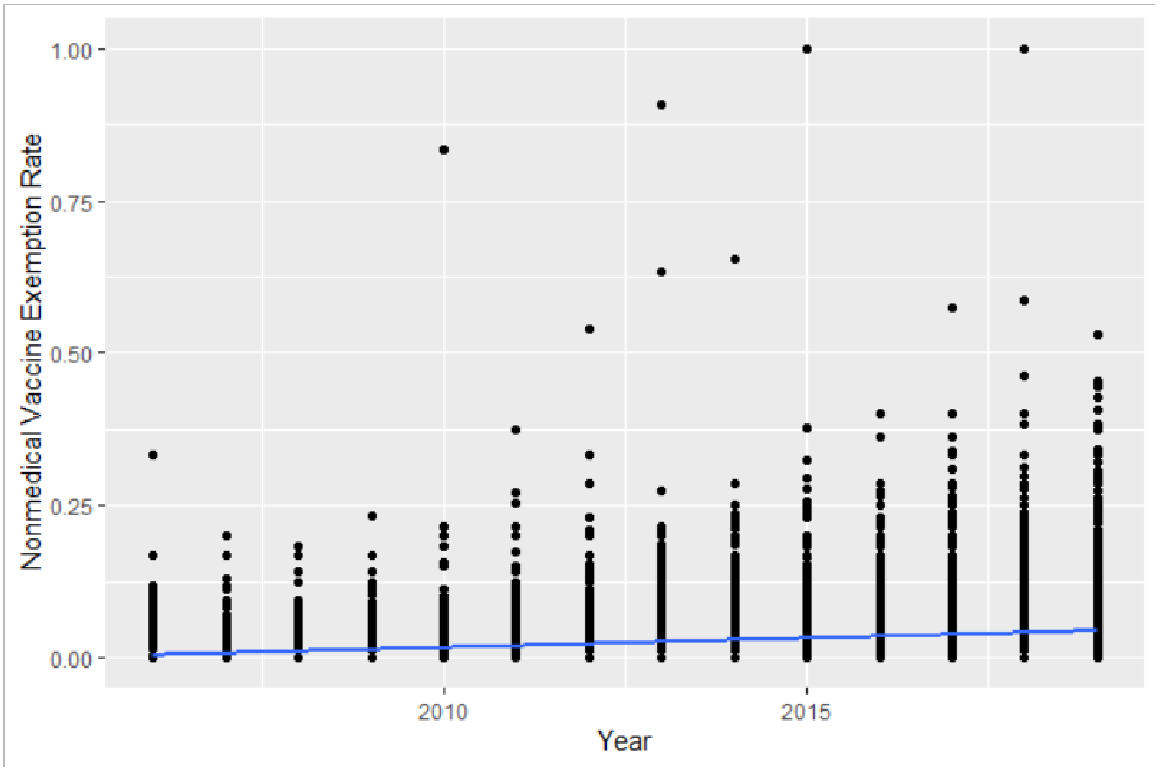
The coefficient for the predictor variable "Year" in this linear regression model was 1.401e-03, the standard error was 4.618e-05, the t value was 30.33, and p<2e-16. The coefficient is significantly greater than-zero at the p<0.01 threshold.

Figure 3: Kindergarten Nonmedical Vaccine Exemption Rates, 2005-2006 to 2018-2019, Charter Schools



The coefficient for the predictor variable "Year" in this linear regression model was 2.359e-03, the standard error was 2.731e-04, the t value was 8.640, and $p<2e-16$. The coefficient is significantly greater than-zero at the $p<0.01$ threshold.

Figure 4: Kindergarten Nonmedical Vaccine Exemption Rates, 2005-2006 to 2018-2019, Private Schools



The coefficient for the predictor variable "Year" in this linear regression model was 3.068e-03, the standard error was 1.719e-04, the t value was 17.84, and p<2e-16. The coefficient is significantly greater than-zero at the p<0.01 threshold.

Table 1: Counts and Percentages of Texas Kindergarteners with Nonmedical Vaccine Exemptions, 2005-2006 to 2018-2019

Year	# and % NME (Aggregated)	# and % NME (ISD)	# and % NME (Charter)	# and % NME (Private)
2005-2006	1073, 0.305%	959, 0.288%	26, 0.615%	88, 0.607%
2006-2007	1361, 0.381%	1206, 0.355%	36, 0.754%	119, 0.891%
2007-2008	1673, 0.480%	1512, 0.461%	39, 0.685%	112, 0.851%
2008-2009	1923, 0.573%	1720, 0.542%	46, 0.884%	157, 1.25%
2009-2010	2882, 0.769%	2665, 0.749%	61, 0.823%	156, 1.37%
2010-2011	3166, 0.820%	2811, 0.775%	114, 1.14%	241, 1.79%
2011-2012	3888, 1.00%	3448, 0.947%	168, 1.39%	272, 2.16%
2012-2013	4609, 1.15%	3988, 1.07%	231, 1.63%	390, 2.78%
2013-2014	5344, 1.35%	4664, 1.27%	286, 1.79%	394, 2.64%
2014-2015	5141, 1.29%	4383, 1.19%	296, 1.74%	462, 3.04%
2015-2016	5235, 1.34%	4401, 1.24%	352, 1.80%	482, 3.14%
2016-2017	5981, 1.55%	5034, 1.44%	432, 2.01%	515, 3.39%
2017-2018	6816, 1.80%	5708, 1.67%	560, 2.57%	548, 3.88%
2018-2019	8394, 2.17%	7042, 2.03%	678, 2.69%	674, 4.42%

Figure 5: Kindergarten Nonmedical Vaccine Exemption Rates, 2018-2019, ISD Students, Spatial Clustering

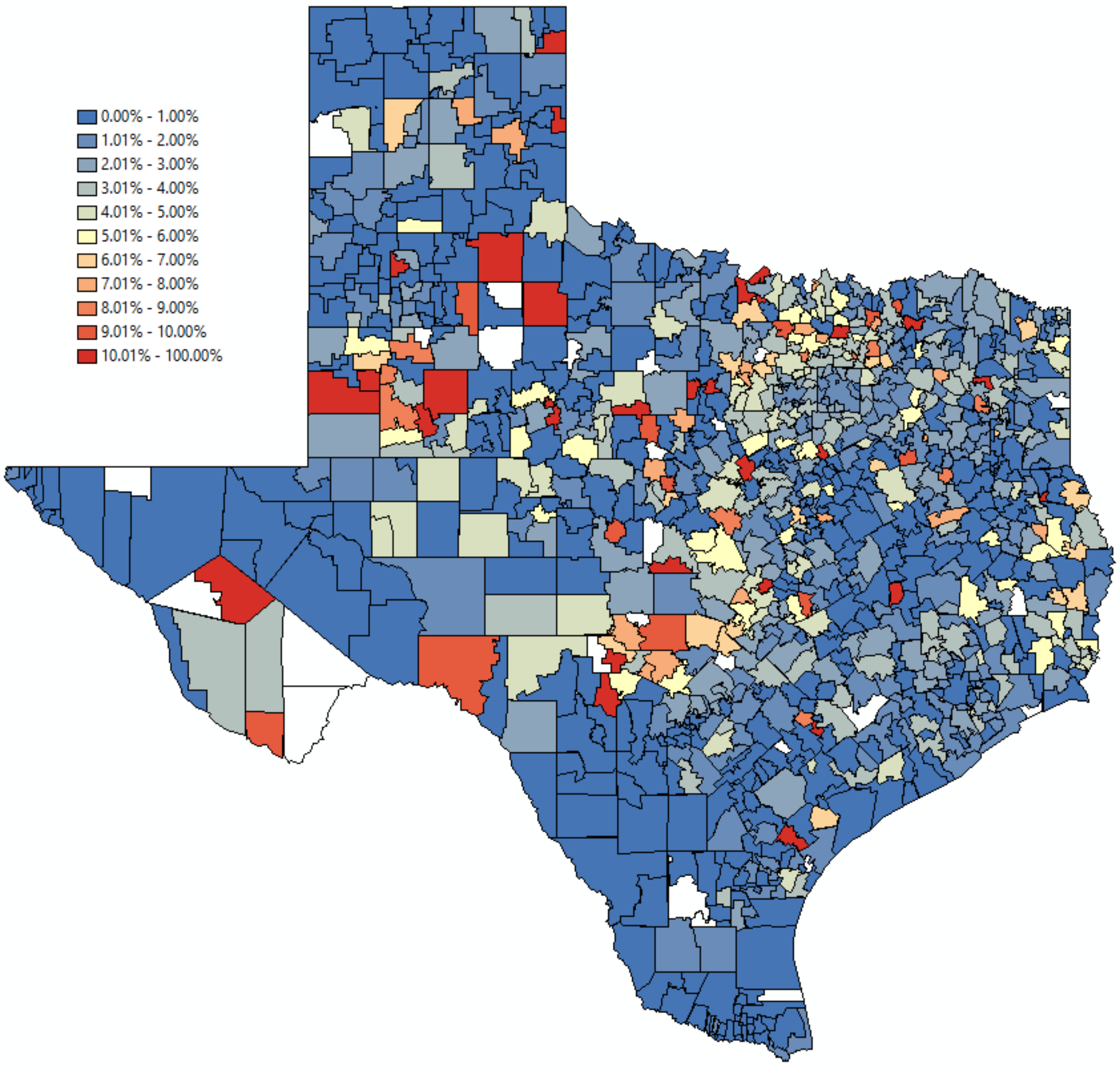
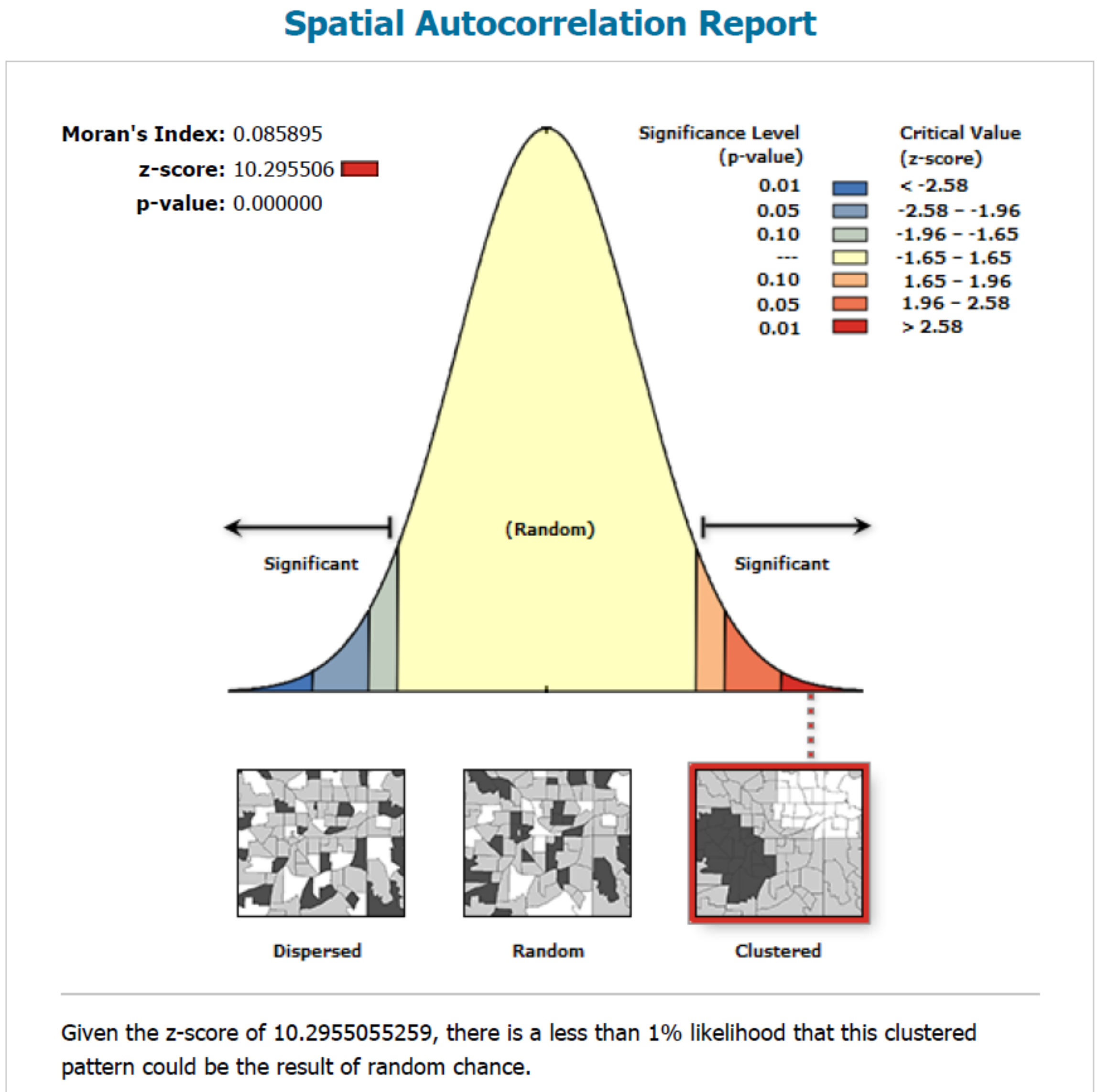
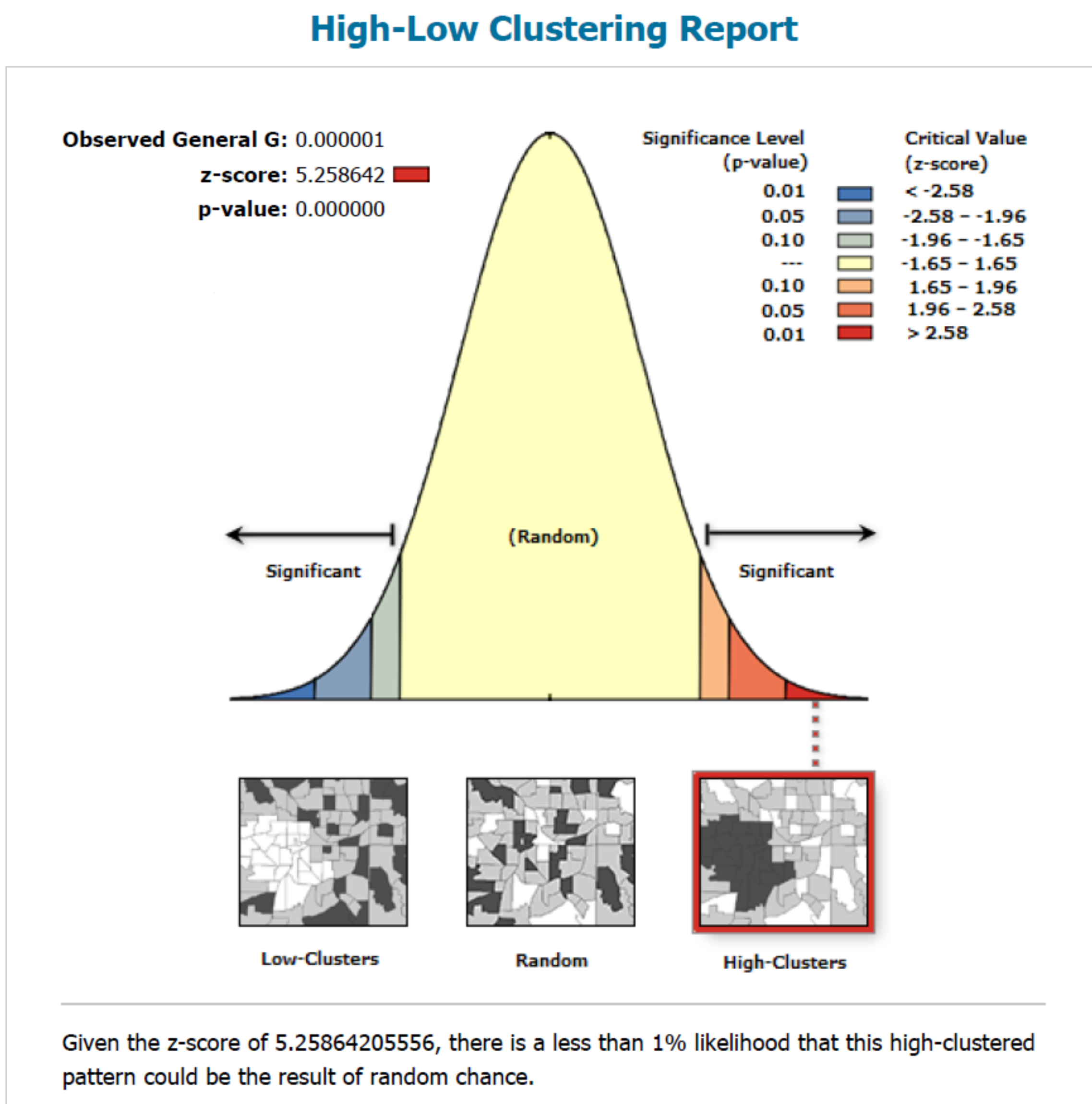


Figure 6: Kindergarten Nonmedical Vaccine Exemption Rates, 2018-2019, ISD Students, Anselin Local Moran's I Spatial Autocorrelation



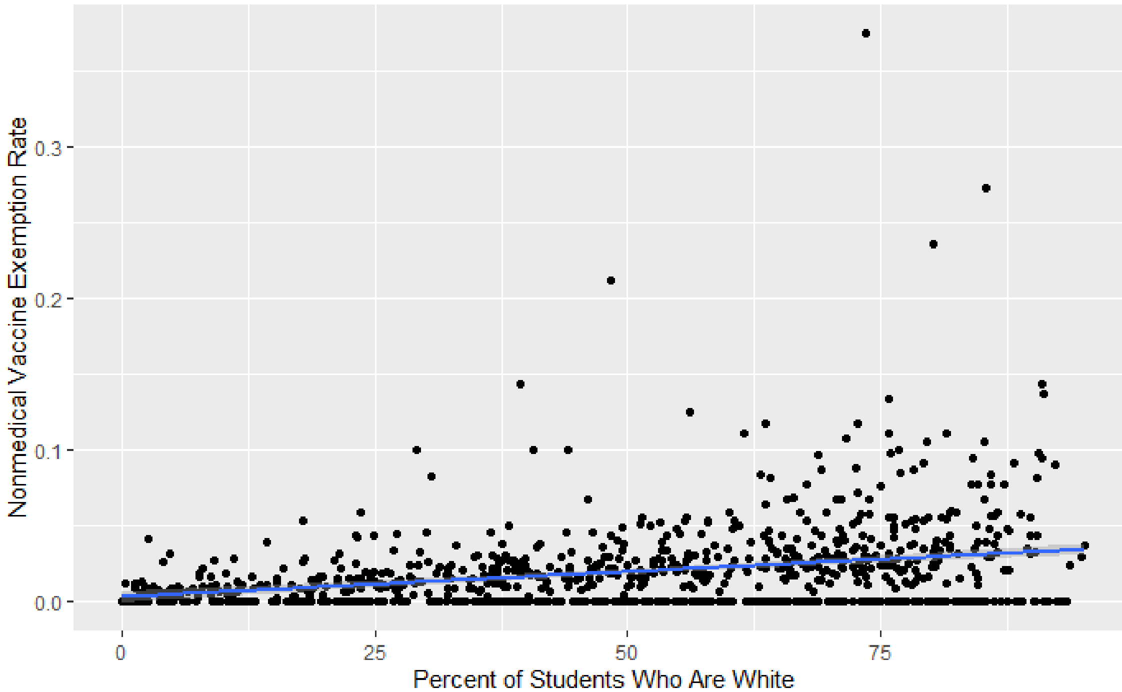
The Anselin Local Moran's I spatial autocorrelation analysis generated a Moran's Index of 0.0859 and a z-score of 10.296, corresponding to a p value of 0.00000. The p value is lower than the 0.01 threshold, which indicates that the clustered pattern was not the result of random chance.

Figure 7: Kindergarten Nonmedical Vaccine Exemption Rates, 2018-2019, ISD Students, Getis-Ord Gi* Hot Spot



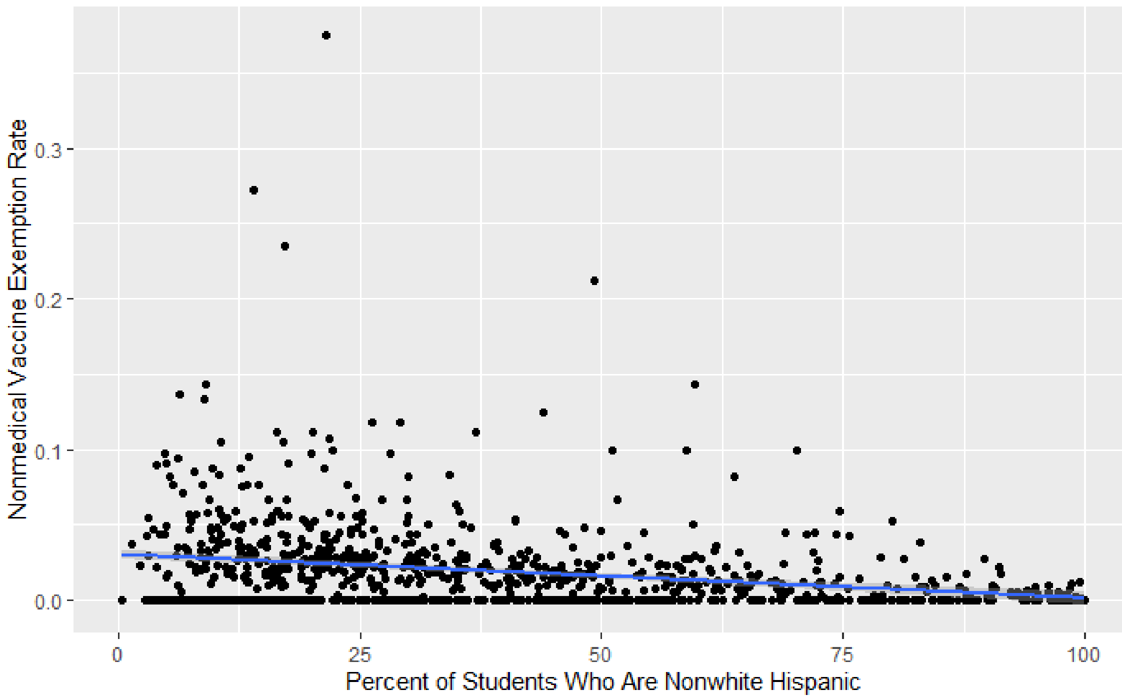
The Getis-Ord Gi* Hot Spot analysis generated a General G of 0.000001 and a z-score of 5.258, corresponding to a p value of 0.00000. The p value is lower than the 0.01 threshold, which indicates that the clusters of high nonmedical vaccine exemption rates were not due to random chance.

Figure 8: Kindergarten Nonmedical Vaccine Exemption Rates, 2017-2018, ISD Students, Percent White



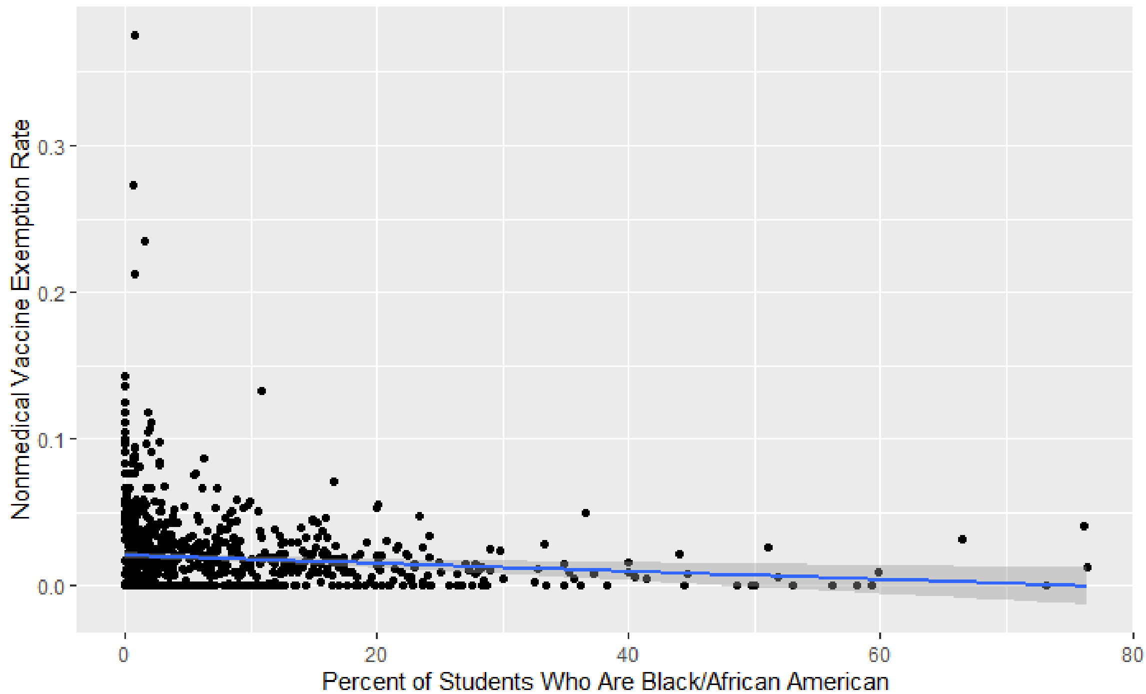
The coefficient for the predictor variable "Percent of Students Who Are White" in this linear regression model was 3.297e-04, the standard error was 3.404e-05, the t value was 9.685, and $p<2e-16$. The coefficient is significantly greater than-zero at the $p<0.01$ threshold.

Figure 9: Kindergarten Nonmedical Vaccine Exemption Rates, 2017-2018, ISD Students, Percent Nonwhite Hispanic



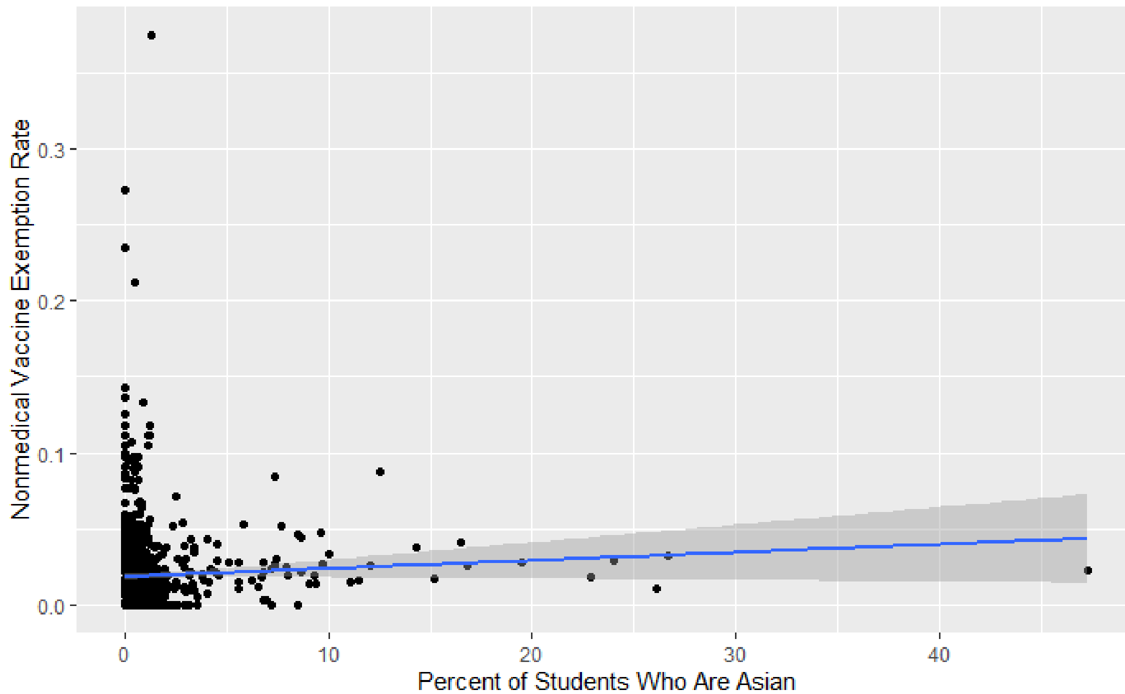
The coefficient for the predictor variable "Percent of Students Who Are Nonwhite Hispanic" in this linear regression model was -2.904e-04, the standard error was -3.387e-05, the t value was -8.574, and p<2e-16. The coefficient is significantly less than-zero at the p<0.01 threshold.

Figure 10: Kindergarten Nonmedical Vaccine Exemption Rates, 2017-2018, ISD Students, Percent Black/African American



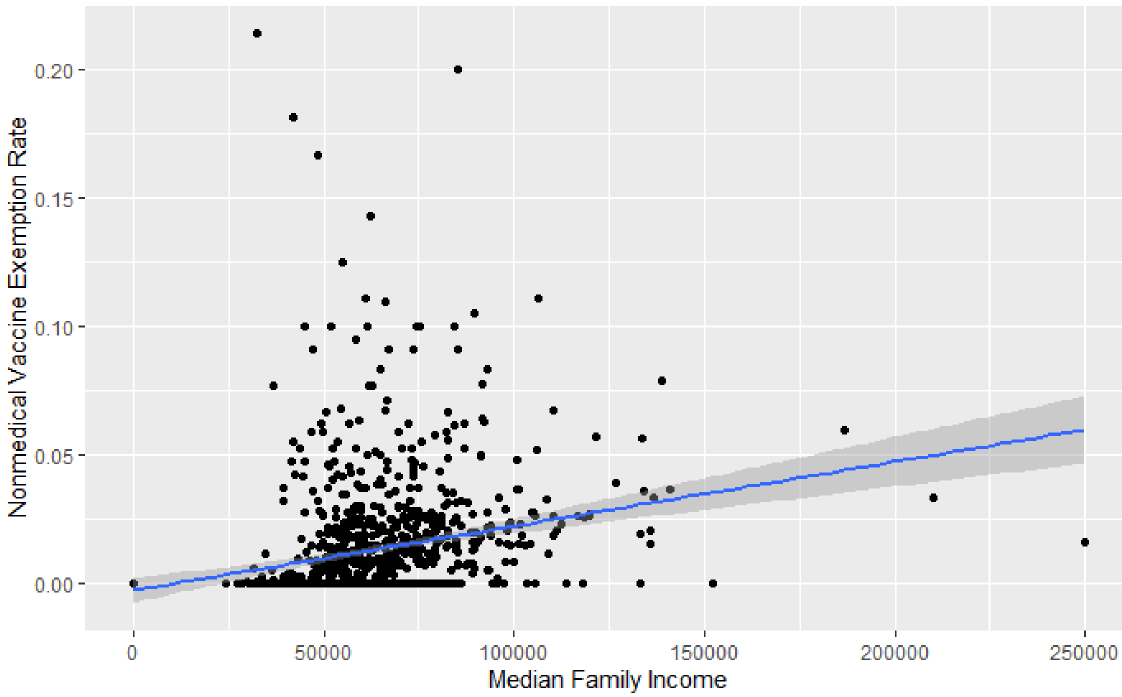
The coefficient for the predictor variable "Percent of Students Who Are Black/African American" in this linear regression model was -2.729e-04, the standard error was 9.032e-05, the t value was -3.021, and p<0.00259. The coefficient is significantly less than-zero at the p<0.01 threshold.

Figure 11: Kindergarten Nonmedical Vaccine Exemption Rates, 2017-2018, ISD Students, Percent Asian



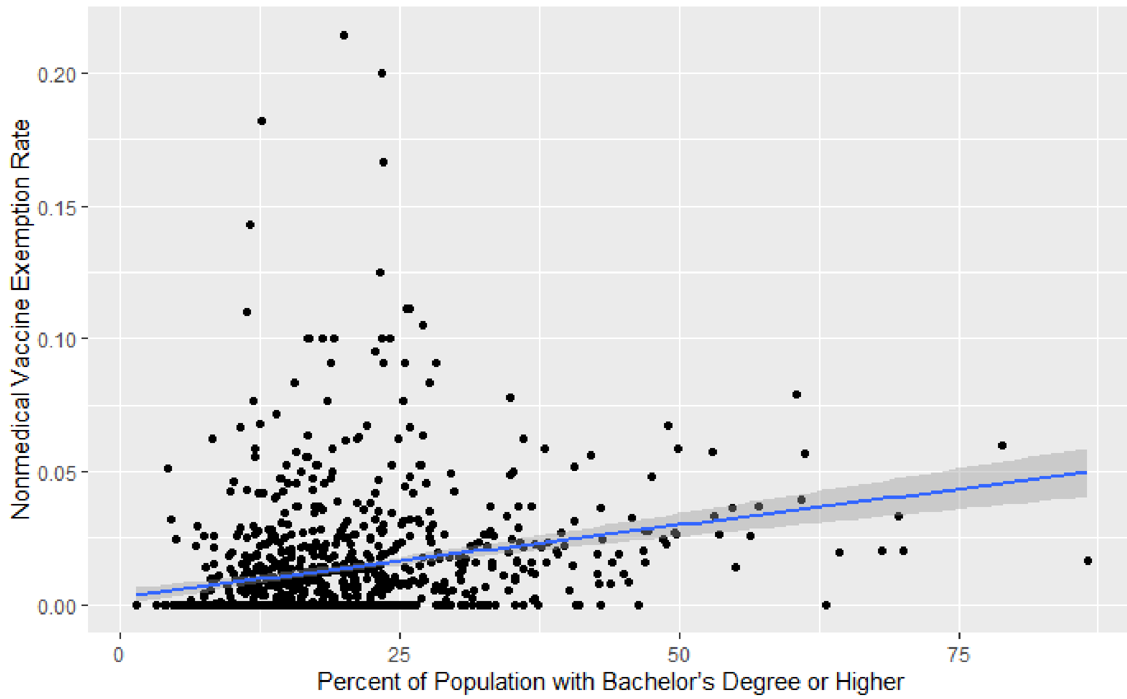
The coefficient for the predictor variable "Percent of Students Who Are Asian" in this linear regression model was 0.0005322, the standard error was 0.0003214, the t value was 1.656, and p<0.0981. The coefficient is not significantly greater than-zero at the p<0.01 threshold.

Figure 12: Kindergarten Nonmedical Vaccine Exemption Rates, 2015-2016, ISD Students, Median Family Income



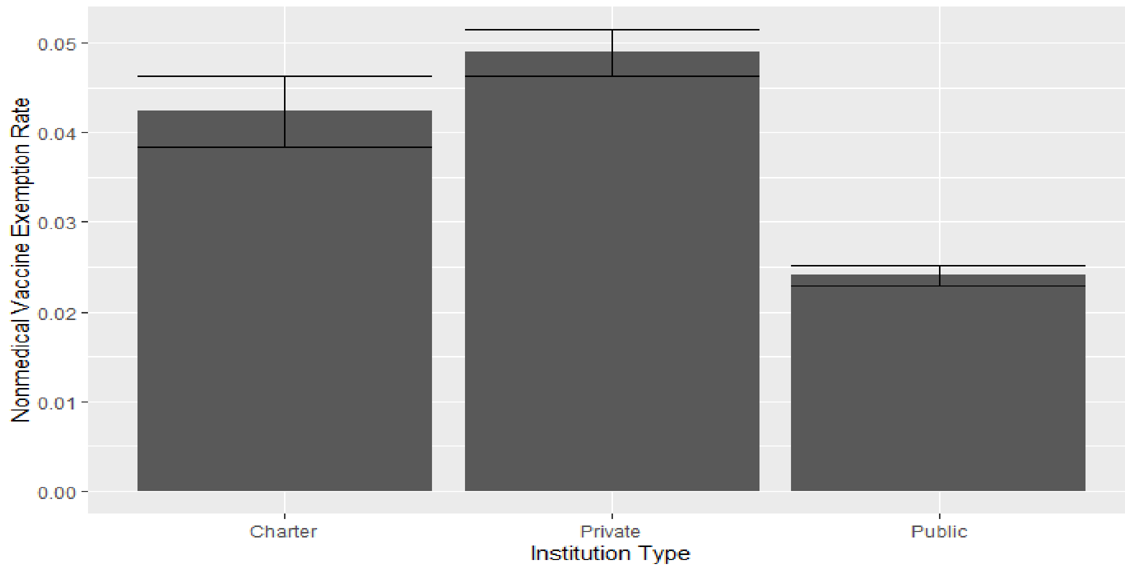
The coefficient for the predictor variable “Median Family Income” in this linear regression model was 2.506e-07, the standard error was 3.576e-08, the t value was 7.009, and p<4.43e-12. The coefficient is significantly greater than-zero at the p<0.01 threshold.

Figure 13: Kindergarten Nonmedical Vaccine Exemption Rates, 2015-2016, ISD Students, Percent of Population with Bachelor's Degree or Higher



The coefficient for the predictor variable "Percent of Population with Bachelor's Degree or Higher" in this linear regression model was 0.0005417, the standard error was 0.0000690, the t value was 7.850, and $p<1.07e-14$. The coefficient is significantly greater than-zero at the $p<0.01$ threshold.

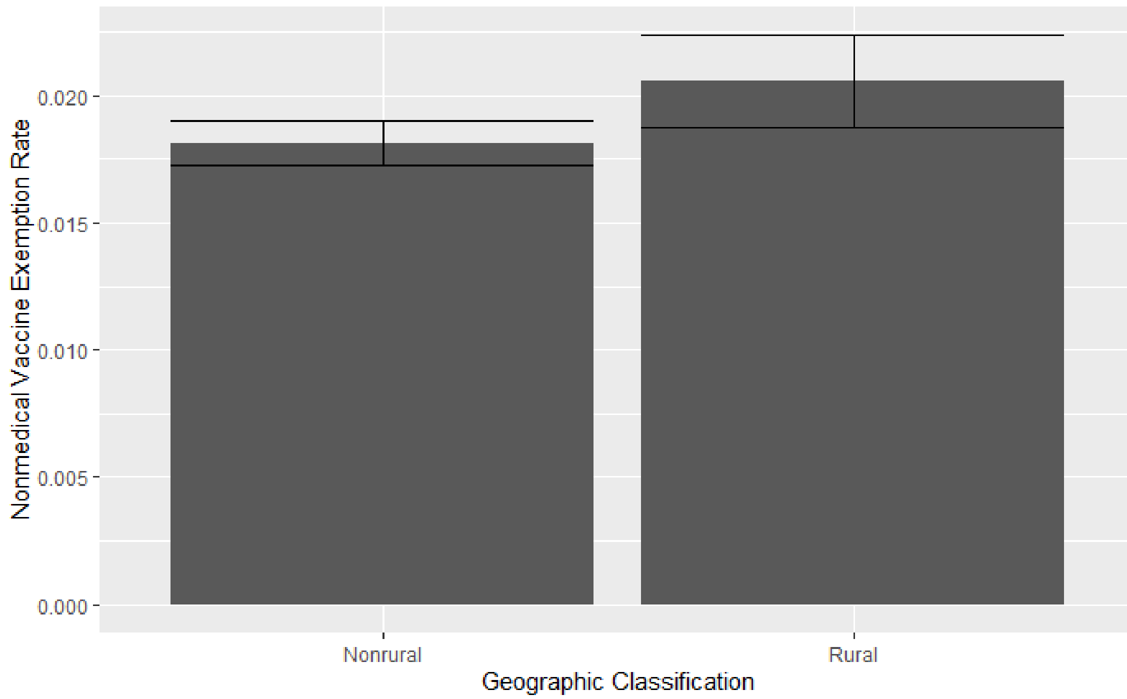
Figure 14: Kindergarten Nonmedical Vaccine Exemption Rates, 2018-2019, ISDs vs Charter Schools vs Private Schools



A one-way Analysis of Variance (ANOVA) produced an F statistic of 34.94 and a p value of 1.32e-15. This indicates that the difference in the mean nonmedical vaccine exemption rates between some of the groups is significant at the $p<0.01$ level.

A post-hoc Tukey HSD test was performed. The difference between private schools and charter schools was 0.00650, and the p value was 0.502. This indicates that there is no significant difference in the mean nonmedical vaccine exemption rates between private schools and charter schools. The difference between private schools and public ISDs was 0.0249, and the p value was 0.00. This indicates that private schools have a significantly higher mean nonmedical vaccine exemption rate than public ISDs. The difference between charter schools and public ISDs was 0.0184, and the p value was 0.00320. This indicates that charter schools have a significantly higher mean nonmedical vaccine exemption rate than public ISDs.

Figure 15: Kindergarten Nonmedical Vaccine Exemption Rates, 2017-2018, Rural vs Nonrural ISD



The two-sample t-test produced a t value of 1.165 and a p-value of 0.245. This indicates that the difference between the average nonmedical vaccine exemption rates of rural schools and nonrural schools, as classified by the Texas Education Agency, is not significant at the p<0.01 level.

CHAPTER FOUR

Discussion and Conclusion

Findings

This thesis hypothesized that rates of nonmedical vaccine exemptions for Texas kindergarteners have increased since data collection began for the 2005-2006 school year. This thesis also hypothesized that rates of nonmedical exemptions would be associated with non-Hispanic Caucasian race/ethnicity, high median family income, and high parental education level. Finally, this thesis hypothesized that rural schools would have higher nonmedical exemption rates than nonrural schools, and that private schools and charter schools would have higher nonmedical exemption rates than public ISDs.

This thesis found that among Texas kindergarteners, vaccination rates remain high overall: the proportion of Texas kindergarteners with a nonmedical exemption for any vaccine is 2.17%. It also found that the rate of nonmedical vaccine exemptions is increasing across all facility types. From the 2005-2006 school year to the 2018-2019 school year, nonmedical exemption rates rose from 0.305% to 2.17% overall; from 0.288% to 2.03% for public ISDs; from 0.615% to 2.69% for charter schools; from 0.607% to 4.42% for private schools. These findings complement the consensus of extant literature- that rates of nonmedical vaccine exemptions are increasing across the United States, and that the private schools and charter schools have higher rates than public non-charter schools. The patterns of spatial clustering in nonmedical vaccine exemptions were found to be greater than what could be attributed to random chance alone. Northeast

Texas, Central Texas, and some parts of East Texas are the most affected, while West Texas, South Texas, and the Texas Panhandle are the least affected.

While nonmedical vaccine exemption rates were negatively correlated with Hispanic and Black race/ethnicity, they were positively correlated with non-Hispanic Caucasian and Asian race/ethnicity, though the correlation with Asian race/ethnicity was not statistically significant.

Nonmedical exemption rates were positively associated with median family income and the proportion of the population with a bachelor's degree or higher. Rates in both private schools and charter schools were significantly higher than rates in public ISDs, but the data could not suggest that rates in private schools were higher than rates in charter schools.

Rural schools had higher rates of nonmedical exemptions than nonrural (suburban and urban) schools, but not at a level of statistical significance. How can we explain one aspect of the literature- that rural schools average higher nonmedical exemption rates than nonrural schools? Rural schools tend to be poorer than their nonrural counterparts. Based on the positive trend between median family income and nonmedical exemption rate, one should expect that poor rural schools have lower rates of nonmedical exemptions than their wealthier nonrural counterparts. This does not appear to be the case. However, there is a way to reconcile these conflicting observations. It may be the case that both trends are true for the nonmedical exemptions of Texas kindergarteners- that rural schools have higher rates than nonrural schools and that wealthier areas have higher rates than less wealthy areas. However, the relative effect sizes of rurality and wealth could very well differ. It is entirely possible that the increase in nonmedical exemption rates associated with a school district's rurality outweighs the decrease in nonmedical exemption rates associated with a rural school district's relative privation. This research does not address the relative effects of various school-level factors or personal factors on rates of nonmedical vaccine exemptions. Thus, it may be premature to address cases in which factors influencing nonmedical exemption rates seem to conflict each other. For example, schools and school districts with low proportions of non-Hispanic Caucasian individuals and relatively high median family incomes might be expected to have low nonmedical exemption rates associated with their racial/ethnic composition, but higher rates than expected due to their high incomes.

Limitations

Early on in this research, it was necessary to choose between analyzing exemptions for kindergarteners only and analyzing exemptions for all school students K-12. Obtaining data only from kindergarteners has the potential to make the counts of nonmedical exemptions from individual facilities too low to analyze statistically, since total kindergartener counts should be a mere fraction of total K-12 counts. The data itself supports this view, since it features many "0" and "0%" nonmedical exemption counts and rates. Furthermore, the low counts of the kindergartener-only data make them liable to sudden, random fluctuations in nonmedical exemption counts. In a kindergarten class of 20, a 10% change in nonmedical exemptions does not have the same significance as a 10% change in a kindergarten class of 200. Larger kindergarten classes protect against noise in the data. On the other hand, kindergartener-only data is the most accurate representation of how nonmedical vaccine exemptions (and vaccine sentiments) change from year to year, since it does not dilute data from incoming kindergarteners with data from twelve grades of students who have already obtained their exemptions. This is crucial to the temporal analysis this research performs and the understanding this research brings to quickly evolving public vaccine sentiment.

Even though participating in the DSHS's annual vaccine survey is required by law, there is no way to enforce this requirement. As a result, not all schools or school districts participate in the annual survey, and their data is left out. Private schools and public charter schools tend to participate at rates lower than public schools. With the resistance towards bills mandating individual school reporting (instead of ISD-level reporting), it is not implausible that the schools opting out of the survey have higher-than-average nonmedical exemption rates than the schools that respond. Public charter schools face an additional challenge. A significant proportion of charter schools are only partially represented in years between 2005-2006 and 2018-2019. This is because Texas closes charter schools that do not meet accreditation standards, and a significant number of charter schools only operate for a few years before they are closed by the state. As a result, those charter schools are only featured in the dataset for a fraction of the 14 school years for which data is available. This makes it difficult to analyze temporal trends in nonmedical vaccine exemption rates for charter schools, since the schools surveyed tend to differ year to year (more so than private schools or public ISDs).

The findings of this research are further limited by the relative underrepresentation of certain population groups in the statistical analysis. Non-Hispanic Caucasian students, which make up most Texas kindergarteners, are represented at every proportional level. There are kindergarten classes composed of nearly 100% non-

Hispanic Caucasian students, as there are classes composed of 75%, 50%, 25%, and nearly 0% non-Hispanic Caucasian kindergarteners. The same applies to Hispanic kindergarteners, who receive representation along the proportional spectrum. For Black/African American kindergarteners and especially for Asian American kindergarteners, this is not the case. These two racial/ethnic groups are not represented evenly along the proportional spectrum. There are only 12 kindergarten classes in which Black/African American students made up over 50% of the population. There are only 3 kindergarten classes in which Asian American students made up over 25% of the population. Similarly, the distribution of median family income and the percent of population with a bachelor's degree or higher are not evenly distributed along the continuum, with higher median family incomes and higher educational attainment levels vastly underrepresented. The statistical analyses conducted on these populations of students may not be robust enough to apply to populations of the same racial/ethnic origin in other states and may vary depending on the school year analyzed.

Another limitation of the scope of the conclusions drawn by this research arises from the discrepancy between the school/ISD-reported data on nonmedical vaccine exemptions and the DSHS's records of nonmedical exemption affidavits. In Texas, a nonmedical vaccine exemption affidavit lasts for two years before it must be renewed. Thus, parents wishing to exempt their child from vaccination for the duration of their K-12 school years must submit an affidavit before the child enters kindergarten, and renew before the second, fourth, sixth, eight, tenth, and twelfth grades. This creates seven classes of parents who have the opportunity to submit or renew their exemption. If parents who submit a nonmedical exemption affidavit always renew, and if each of the seven classes of parents had 8,394 exemptions (the 2018-2019 count of reported kindergarten exemptions) to renew, there would have been 7 * 8,394 = 58,758 exemption affidavits submitted that school year. Note that this figure is an overestimate, since kindergarten classes before 2018-2019 all had fewer than 8,394 exemptions. In 2018, Texas received 76,665 nonmedical exemption affidavits (DSHS). This leaves at least 17,907 affidavits unaccounted for- a significant proportion of the total. Some of the affidavits unaccounted for undoubtedly come from the schools that did not participate in the survey, and some come from institutions of higher education, pre-K facilities, and child-care facilities. Furthermore, it is important to note that the number of exemption affidavits received is not indicative of the total number of parents forgoing vaccination for their children. Homeschooled children do not have vaccination requirements and thus do not have to submit an exemption affidavit. This is an entire population of children that are unaccounted for- they are not even represented in the number of affidavits on file or the number of affidavits submitted per year. The number of Texas children who are homeschooled is significant: the Texas Home School Coalition estimates that around 350,000 children are taught at home (THSC). Texas does not track the vaccination status of homeschooled children, so the proportion of the estimated 350,000 homeschooled who are not vaccinated is unknown (Shaw et al., 2018).

There remain gaps in the literature that this research does not address. While this thesis establishes knowledge about geospatial trends in nonmedical exemption rates for public ISDs, analogous geospatial trends for private schools and charter schools do not exist. In the future, clusters of high nonmedical exemption rates for private schools and charter schools could be superimposed upon each other and upon the clusters for public schools. Relationships between the clustering patterns for public schools, private schools, and charter schools could be elucidated. Furthermore, the school-type compositions of clusters could be found.

Future Directions

This thesis only addresses kindergarten-level nonmedical exemption rates. Further research could address nonmedical exemption rates across K-12 grades. Analysis at this level would be less useful for establishing year-to-year trends in exemption rates and public vaccine sentiment, but more useful for understanding school communities holistically. The higher counts of nonmedical exemptions would also bring more meaning to changes in the exemption rate over time, differences in the exemption rate between populations, and ameliorate the effects of fluctuation.

Other gaps in the literature exist due to omissions in the data collected by the DSHS. Currently, the DSHS has no way to enforce the mandatory nonmedical exemption survey (Cheng & Byrne, 2019). For more detailed research to be done, some way to enforce the nonmedical exemption survey needs to be put in place so that schools- especially private and charter schools- submit their information.

In Texas, individual public schools are not required to report their vaccination data to the state, despite attempts by legislators to create such a requirement (Cheng & Byrne, 2019). Instead, public schools (and some charter schools) belonging to an ISD consolidate their data before reporting to the state. This prevents finer-grained analysis and identification of the individual schools most at risk from vaccine-preventable disease. It also prevents vaccine clusters from being compared to each other. This thesis only identifies clusters of high nonmedical exemption rates for public ISDs, which have clearly defined boundaries and draw their students from a defined area. Private schools, charter schools, and individual public schools, on the other hand, are represented by points. Clusters of points cannot be compared to clusters of areas. By codifying requirements for individual schools to report nonmedical exemption counts and rates to the state, Texas could prioritize resources to raising vaccination rates at the school level, rather than the district level.

It has been said that vaccines are a victim of their own success. In many parts of the world, they have made distant memories out of diseases which used to kill or permanently disfigure millions of people. Smallpox has been eradicated, polio is close to eradication, and many other infectious diseases are afflicting fewer people each year. Unfortunately, our inability to recall the devastating consequences of the diseases of the past jeopardizes our ability to protect ourselves against them in the future. Vaccine hesitancy and vaccine avoidance for conscientious reasons is on the rise in Texas, in the United States, and elsewhere in the world. Research like this can help us understand the characteristics of populations most at risk from vaccine-preventable diseases- populations in which herd community is compromised by low vaccination rates. By understanding these vulnerable populations, we can more effectively focus our efforts in protecting them and those around them from vaccine-preventable diseases.

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