Spatial analysis of Pertussis Outbreaks and Herd Immunity

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Abstract

Over the last 10-15 years, pertussis outbreaks have been on the rise in the United States after fifty years of low infection rates. Although long-lasting effects of the disease are rare in adolescents and adults, potentially fatal outcomes can result in infants or immune depressed individuals. With pertussis being highly transmissible ($R_{0,}$ of 12-17), herd immunity, or the protection of the vulnerable population, requires 92%-95% immunization of the surrounding community. When below this threshold, there is a greater risk of endemic disease transmission. In this study, spatial analysis was used to examine pertussis incidence amongst the general population and immunization percentages of kindergarteners in the United States of America. First pertussis cases were analyzed at a national level. Secondly, the geographic and temporal variance of pertussis incidence over the past six years was examined for California to assess the correlation between pertussis incidence, vaccination rates and different socioeconomic and demographic factors. Results indicate that pertussis incidence is on the rise in the USA (% over 20 years). High clusters of pertussis were found in northern states and low clusters in the Southeastern states. Although California was found to have the highest total number of reported cases since 1993 when compared with the rest of the states based on per 100,000 population, it ranked 30th (mean=3.8 (SE=0.91)). During the past 6 years, California has had two outbreaks 2010 (N=9,159 cases) and 2014 (N= 11,203 cases) with rates as high as 24.5 and 29.3, respectively. Correlations between PBE's and Vaccination Rates were moderate (r=-0.67). The findings from this study can be used to enhance prevention campaigns by targeting specific school districts and zip codes within counties containing high pertussis rates.

Introduction

One of the greatest accomplishment in recent history has been the development of vaccines. Diseases such as smallpox and polio have been eliminated from many countries or eradicated from the world (College of Physicians of Philadelphia, 2014). Pertussis, commonly known as whooping cough, is another disease which could potentially be eliminated through vaccination. While the number of reported cases in the United States has fallen dramatically from the peak of 265,269 in 1934, to a low of 1,010 in 1976, it is beginning to rebound with 48,277 cases in 2012 (CDC, 2014). Even though this disease has been observed to have cyclical peaks occurring every two to five years, this rise is a disturbing trend that should not be taken lightly (Cherry, 2010). Similar bimodal distribution patterns have been seen with diseases such as smallpox in the 19th century. The incidence of smallpox fell between 1802 and 1840 from the widely accepted belief that vaccination was an effective tool at preventing disease. Through the 1850s however, advocates of nonstandard medical theories challenged vaccine usage. As vaccination decreased, smallpox made a major comeback in the 1870s (Omer *et al.*, 2009). A recent trend among some parents to delay or fore-go vaccination due to personal beliefs, apathy about vaccinations in general (Lundquist 2010), the replacement of the DTwP (Diptheria and tetanus toxoids and whole-cell pertussis) vaccine with the DTaP (Diptheria, Tetanus, and acelluar pertussis) for the completed childhood vaccination series (DeBolt, 2012), and the waning effectiveness of the vaccine itself (CDC 2012) have been identified as possible candidates for pertussis resurgence and mirrors the challenges seen with smallpox one and a half centuries ago. Although not as life threatening as smallpox, many adults and adolescents which contract pertussis will have relatively mild symptoms ranging from a sustained cough with possible fever, vomiting, sweating, and syncope which can even be misdiagnosed as bronchitis or asthma (CDC, 2000). Newborns and infants, however; who have no immunity to the disease and must rely on the immunity of the surrounding population for protection can suffer much greater impacts from infection with roughly half of cases leading to hospitalization and rarely, even death (CDC, 2013) (Auger, Patrick, Davis, 2013). Therefore, significant efforts need to be undertaken to minimize the spread of vaccine-preventable diseases.

Herd immunity and vaccination (R_0)

An important factor to consider with any disease is the transmission rate from a single case to a susceptible population, also known as the R_0. The R_0 is also used to assess the severity of an outbreak as well as the strength of the medical and/or behavioral interventions necessary for control (Breban, Vardavas, Blower, 2007) (see Table 1 for different diseases). Rates less than one indicate that the disease will die off on its own, but numbers greater than one indicate that an outbreak will generate an epidemic. Diseases such as polio and smallpox, which have been eradicated from the United States, each had an R_0 of 5-7 (CDC Smallpox Course), meaning that one case would lead to 5-7 secondary cases of the disease assuming the surrounding population was uninfected and had no immunity (Fraser *et al.*, 2009; Table 1). With a disease such as pertussis having an R_0 ranging between 12 and 17, it is considered highly transmissible between humans (Heininger, 2012) and very difficult to control in a vulnerable population. In order to prevent an epidemic outbreak of disease, the percentage of the vaccinated population needs to be above $1 – 1/ R_0$ (Gay, 2004), or between 92-94% (Table 1).

Disease	**Transmission**	**R_0**	**Herd immunity threshold**
Mumps	Airborne droplet	4–7	75–86%
Polio	Fecal-oral route	5–7	80–86%
Rubella	Airborne droplet	5–7	83–85%
Smallpox	Social contact	6–7	83–85%
Diphtheria	Saliva	6–7	85%
Measles	Airborne	12–18	83–94%
Pertussis	**Airborne droplet**	**12–17**	**92–94%**

Table 1: Transmission method, herd Immunity thresholds for vaccine preventable diseases (CDC Smallpox Course)

For those who cannot be immunized such as infants and individuals with depressed immune systems, it is especially vital that the surrounding community maintain this collective immunity level (Winter *et al.*, 2012). This theory is known as community or herd immunity, where individuals that cannot be vaccinated themselves are protected from a disease through the immunity of the surrounding populace (Vaccines Today, 2013).

When herd immunity begins to wane, outbreaks in disease become increasingly likely. When portions of the population begin to receive vaccination from a disease however, those that cannot or are not receiving vaccination also become protected. One study in 2000 showed that once American children started receiving the pneumococcal conjugate vaccine, the disease incidence rate amongst the 50 and older population (a demographic not receiving vaccination) fell by 55% (Lexau, 2005)). This example relates to Figure 1C where the older demographic was receiving protection from child vaccination. In a similar effort designed to protect vulnerable newborns and infants from diseases such as pertussis, the Centers for Disease Control and Prevention (CDC) recommended a "cocooning strategy" in 2006. This effort involved immunizing expectant mothers and close relatives of the child to limit disease exposure (Halperin, 2012). This was largely unsuccessful however, since even one missed friend or relative can lead to failure and potential infection. Furthermore, a recent study found that a leading cause of pertussis transmission to infants is through older siblings (de Greeff, 2010), highlighting the need to encourage vaccination rates, especially amongst school children, and the importance of immunizing family members coming into direct contact with vulnerable infants.

Vaccination rates

Within the United States, parents can forgo vaccinations for their children based on religious, philosophical or medical reasons depending upon the state laws in which they reside. As of 2013, all states allow medical exemptions, forty eight allow religious exemptions, and nineteen allow philosophical exemptions: Washington, California, Idaho, Utah, Arizona, Colorado, New Mexico, Texas, Oklahoma, North Dakota, Minnesota, Wisconsin, Arkansas, Louisiana, Michigan, Ohio, Pennsylvania, Vermont, and Maine (CDC, 2015). Due to an increase in vaccination refusals in the United States, within the last decade there has been a rise in vaccine-preventable disease outbreaks (e.g. measles in California during 2010 (Sugerman *et al.*, 2010); pertussis (California, 2010 (Halperin, 2012), Washington state, 2012 (DeBolt *et al*, 2012). With other diseases such as measles, vaccination exemptions due to personal beliefs were seen in 68% of measles cases in the United States from 2004-2008 (Parker-Fibelkorn, 2010). With a disease such as pertussis, exemptions or delays to vaccination can be very damaging due to the high R_0 and waning immunization of populations due to missed booster shots (Reinberg, 2013). Although a drop in vaccination rates may play an important role in the widespread outbreaks of pertussis and other diseases (e.g. measles), understanding where incidence are on the rise and how these correlate with vaccination coverage is important for reducing future outbreaks as well as guiding future strategies.

Geographic Information Systems (GIS) has been used extensively for analyzing the spatial distribution of disease (e.g. pertussis (Chen, Waters & Green, 2002), measles (Metcalf *et al.*, 2010) and examples therein (Cromley & McLafferty, 2012); their relationship between different causal factors (e.g. high median income (Sugerman *et al.*, 2010), percent unemployed or percent of children attending day care (Wilking *et al.*, 2012)) and health outcomes (e.g. low immunization rates leading to higher disease percentages (Chen, Waters & Green, 2002). By combining multiple types of data, GIS can be used to identify locational or demographic trends and target outreach and disease prevention tactics.

Thus, the key objectives of this study were to:

(1) Examine pertussis cases in the USA over the past 22 years (1993 – 2014) and how these relate to exemptions and vaccination rates.
(2) Examine spatial and temporal cases of pertussis in (California (highest number of cases over the past 22 years)) during the most recent six years (2009-2014)
(3) Assess correlation between pertussis outbreaks/vaccination rates with socioeconomic and demographic compositions.

METHODS

Pertussis is a highly contagious disease (R_0 = 12-17, herd immunity required > 92%, Table 1), requiring five doses between 2 months and 4-6 years of age as well as booster shots at least every 10 years beginning at 11-12 years of age (CDC, 2014, Figure S4). In this study we examined the prevalence of pertussis incident rates and personal belief exemption rates at state and county levels to identify "disease hotspots."

Data: A variety of data was used in this study and is summarized in Table 2. Details of the data and how they were used are described in more detail within the relevant analysis sections.

State	Years	Scale	Data	Source
USA	1993-2013	State	1. Total Number of cases within each state for a given year	CDC http://www.cdc.gov/pertussis/surv-reporting.html#surv
	1993-2013	State	1. Population estimates within each state for a given year	US Census http://www.census.gov/popest/data/historical/2010s/vintage_2013/index.html
	2012-13	State	1. Kindergarten Personal Belief Exemption Rates 2012-13 school year	http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6230a3.htm
California	2009-14	County	1. Number of pertussis cases/year 2. Pertussis incident rates per 100,000 population	The California Department of Health http://www.cdph.ca.gov/programs/immunize/Pages /PertussisSummaryReports.aspx
	2014	County	1. Population estimates effective January 1, 2014	Demographic Research Unit, California Dept. of Finance http://www.dof.ca.gov/research/demographic/reports/estimates/e-1/view.php
	2014-15	School Districts	1. Elementary School Districts 2. Unified School Districts	https://www.census.gov/cgi-bin/geo/shapefiles2014/main
	2014	Zip Code	1. Zip Code Tabulation Areas	https://www.census.gov/cgi-bin/geo/shapefiles2014/main
	2000-01 – 2013-14	School district,	1. Total number of kindergarteners vaccinated	http://www.cdph.ca.gov/programs/immunize/pages/immuniza

		city, county	2. Number of kindergarteners with permanent exemption from one or more vaccinations	tionlevels.aspx
	2014-15	Individual Schools	1. Total number of kindergarteners at each school with 10+ enrolled 2. Personal Belief Exemption for Kindergarteners at school with 10+ enrolled	https://www.cdph.ca.gov/programs/immunize/Pages/ImmunizationLevels.aspx geocoded to lat/long by LA Times: http://spreadsheets.latimes.com/immunization-levels-california/
	2010, 2013	Socioeconomic and demographic data	Average Household Size, Average Family Size % Vacant Homes % Husband/Wife Families % Husband/Wife Families with Children % Husband/Wife Families with Children < 6 years old % Husband/Wife Families with no Children % Households with 3+ generations % Households with < 3 generations % Hispanic/Latino % Mexican % White % Black % Asian % Population < 5 years old % Population 5-9 years old % Population 10-14 years old % Houses for Rent % Houses for Recreational or Seasonal Purposes % Population with only High School Diploma % Population with only Associate's Degree % Population with only Bachelor's Degree % Population with only Master's Degree % Population with Doctorate Degree % Population with at least	2010 Census Data (http://factfinder.census.gov/faces/nav/jsf/pages/download_center.xhtml) 2013 American Community Survey 5-Year Average.

			an Associate's Degree % Population with at least a Bachelor's Degree % Population with at least a Master's Degree % Population with a Professional Degree % Unemployment Median Household Income % Population with Health Insurance	

Table 2: Data sources used in this study as compiled from the listed sources.

Analysis

Analysis were conducted at several spatial scales throughout the USA. First a comprehensive analysis was performed at the national level to investigate pertussis incidence throughout the USA. Next we selected the state with the highest number of reported cases, California and conducted a more detailed analysis to understand spatial and temporal patterns that are occurring.

National-Level: At the national level pertussis cases were obtained from the CDC (Table 2) analyzed between 1993 and 2014 by state (including the District of Columbia). The total number of cases recorded for each year for each State were totaled from 1993 to 2014 by state to identify the state with the highest number of cases reported. To account for variation in population the total number of pertussis cases was divided by the estimated total population for that state and an incidence rate per 100,000 of the population was calculated and used for the analysis (Table 2). Population data and estimates for each year was obtained from the US Census Bureau Population Statistics. All data were projected to NAD 83 Contiguous USA Albers using the Project tool in ESRI ArcGIS 10.2.

Although, 22 years were examined, only the most recent years (2009-2014) were analyzed spatially for trends. For this analysis, the average pertussis incident rates per 100,000 for 2009-2014 were calculated by totaling the incidence rates for years 2009-2014 by state and dividing by the total number of years, in this case six.

Patterns of pertussis incidence per 100,000 population were examined using the Global Moran's I and Anselin Local Moran's I (LISA) methods. The Moran's I Spatial Autocorrelation tool was run on each year 1993 through 2014 on the pertussis cases per 100,000 population in that state. For the Global Moran's I, an inverse distance was used to ensure that neighboring polygons had larger influences compared to those farther away based on a straight line distance. Included with the Global Moran's *I*, a z-score and p-value were calculated, where a z-score indicates the number of standard deviations above or below the mean value, and whether or not the null hypothesis can be rejected. In the case of this study, a mean value of 0 is used as the null hypothesis since the anticipated outcome would be equal distribution of disease with no spatial clustering. The p-value indicates the probability that the observed spatial pattern was the result of random chance. The Moran's *I* values range from -1 (strong negative spatial autocorrelation) to +1 (strong positive autocorrelation) with values close to 0 indicating no spatial autocorrelation. Values with a Moran's *I* score above 0.3 or below -0.3 are a good indicator of relatively strong autocorrelation. While the Global Moran's *I* is a good indicator of spatial autocorrelation for an entire dataset it does not identify regions where autocorrelation is strongest or weakest. Instead the LISA, which compares values for each area against one another rather than the average of their neighbors, was used to identify localized clusters and outliers.

Analysis of pertussis incidence and vaccination exemption rates was examined for the year with the highest incidence of pertussis cases, 2012 (N=48,277). Both the pertussis cases per 100,000 population and the 2012-13 school year estimated vaccine exemption rates among kindergarteners were gathered. In order to compare the states using equal reporting metrics, the total number of reported pertussis cases within a state were divided by the estimated population of that state by the US Census Bureau for that year and multiplied by 100,000. To determine the correlation between pertussis cases and kindergarten vaccination exemptions, a correlation coefficient was calculated in Microsoft Excel for each State.

Analysis of Pertussis in California: For California, pertussis incidence was examined at various scales due to the availability of the data. Each of the analysis are described next.

County-Level: For the state of California, pertussis cases were examined between 2009 and 2014 at the county level (Table 1). Pertussis case data was not publicly available at higher levels of geographic detail. Case rates were standardized to 2010 Census data by the California Department of Finance to enable cross comparisons between years. All data were projected to NAD 83 California Teale Albers Feet. PBE rates of kindergarteners from the 2000-01 to the 2014-15 school years was also obtained from the California Department of Health in order to compare with case rates.

Similar to the national level, a Moran's Index was calculated for the years 2009 through 2014 at the county level based on the pertussis case rates per 100,000 population. This tool created a z-score and p-value to help determine if clustering had occurred through random chance. For the years in which clustering occurred, LISA was used to determine the location of high and low clusters as well as outliers. Correlations between pertussis case rate and PBE rates for kindergarteners were examined using the correlation coefficient function in Microsoft Excel and spatially by creating map overlays.

Elementary school analysis:

Elementary School Immunization and PBE's: The location of each elementary school was made available through the addition of latitude and longitude values to California Department of Public Health data (http://www.cdph.ca.gov/programs/immunize/pages/immunizationlevels.aspx) for the number of student enrollments, the name of the school district, school type (e.g. public or private), the number and rate of personal belief exemptions rates, and MMR immunization rate for the 2014 school year (Smith, 2014). A total of 7,804 schools were listed. Schools with less than 10 students and certain private schools were not included since they did not report as part of a school district. Schools with no latitude or longitude coordinates were also excluded. Thus a total of 7,033 schools were used in this study representing 532,037 students. MMR immunization rates were used to represent pertussis vaccination rates as these were the values included in the geocoded data table.

Areas of low and high PBE's were highlighted by kriging the PBE's and 2014 school year vaccination rates recorded at each school. An Empirical Bayesian kriging method was used to account for low sampling values and create a continuous surface.

Elementary School District-Level: Elementary school district boundaries were obtained from US Census Bureau for 2014 and available in two datasets, the Elementary School Districts (only contains elementary schools) and Unified School Districts (contains elementary, middle, and high schools) (Table 2). These were combined into a single dataset to create a comprehensive dataset containing all school districts in California (N=842). Using the tables made available by the L.A. Times, total student enrollment and PBE numbers were calculated for school district by summarizing the student enrollment and PBEs at each school within each district. PBE rates were calculated by dividing the number of PBE by the total student population, which provided an overall averaged rate across the school district. A total of 696 school districts were matched and used for the district level analysis. Of the 842 school districts, 18 were excluded since they did not contain any student enrollments.

Using the school-district aggregated PBEs and MMR vaccination rate, a scatter plot was created to assess the relationship between the two variables. In lieu of pertussis cases, PBE's were used to assess pertussis incidence since positive correlations have been observed between exemption rates and disease incidence (Sugarman, 2010). Similar to the national level the Global Moran's I was used to assess if clustering of PBE's occurred in California at the school district level using the rates for 2014. These were also used to identify localized clustering using the LISA analysis. To assess areas of influence and how these related to county-level pertussis rates, High-High PBE Clusters obtained from the LISA analysis were overlaid with county-level pertussis case rates.

Zip Code-Level: Lastly, to better understand factors that might be contributing to disease outbreaks in California several socio-economic factors were analyzed. These included median income, ethnic composition, unemployment, household size, marital status, seasonal housing, education levels (see list in Table 2); factors that were found to be significant in outbreaks of measles in San Diego, CA (Sugarman, 2010) and rotavirus in Berlin, German (Wilking, 2012).

The 2014 California zip code boundaries were obtained from the US Census Bureau (Table 2). Socio-economic and demographic factors listed in Table 2 were obtained for the 2010 US Census and 2013 American Community Survey (ACS) 5-year average variables and examined at the zip code level (N=1,812). Elementary school data was spatially joined to each zip code. Once joined the total number of students, mean PBE rates and vaccination rates were calculated for each zip code with a school. Zip codes without a school were excluded from the analysis (N= 471). A total of 1,341 zip codes were analyzed.

The PBE rates were then compared with each Census or ACS factor and linear correlation coefficients, or Pearson correlations, calculated using the correlation function in Microsoft Excel. Correlation values are measures from -1 (strong negative) to +1 (strong positive) with values near 0 indicating no correlation. Values from 0.20 to 0.29 have weak relationships, 0.30 to 0.39 have moderate relationships, 0.40 to 0.69 strong relationships, and above 0.70 there exist very strong relationships. Given the large sample size of zip codes, correlations were determined to be significant if above or below an absolute value of 0.0703 (Social Science Statistics, 2015). In addition, clustering of zip-code level 2014-15 PBE rates for kindergarteners were assessed using the Moran's I and LISA methods, as described in previous sections.

Results

National Level Analysis: During the past 22 years, a total of 341,255 cases have been reported in the USA with the number of cases increasing since 2003 and peaking in 2012 (Figure 1A). Clustering of pertussis cases was found to occur during 15 of the 22 years (Table 3). Although, California reported the highest total number of pertussis cases in the United States, (N=36,252, Figure 1B), the highest mean rate per 100,000 population occurred in Vermont (22.2, SE=4.78), Wisconsin (17.3, SE=6.66) and Minnesota (15.1, SE=3.35) (Figure 1B, 1C).

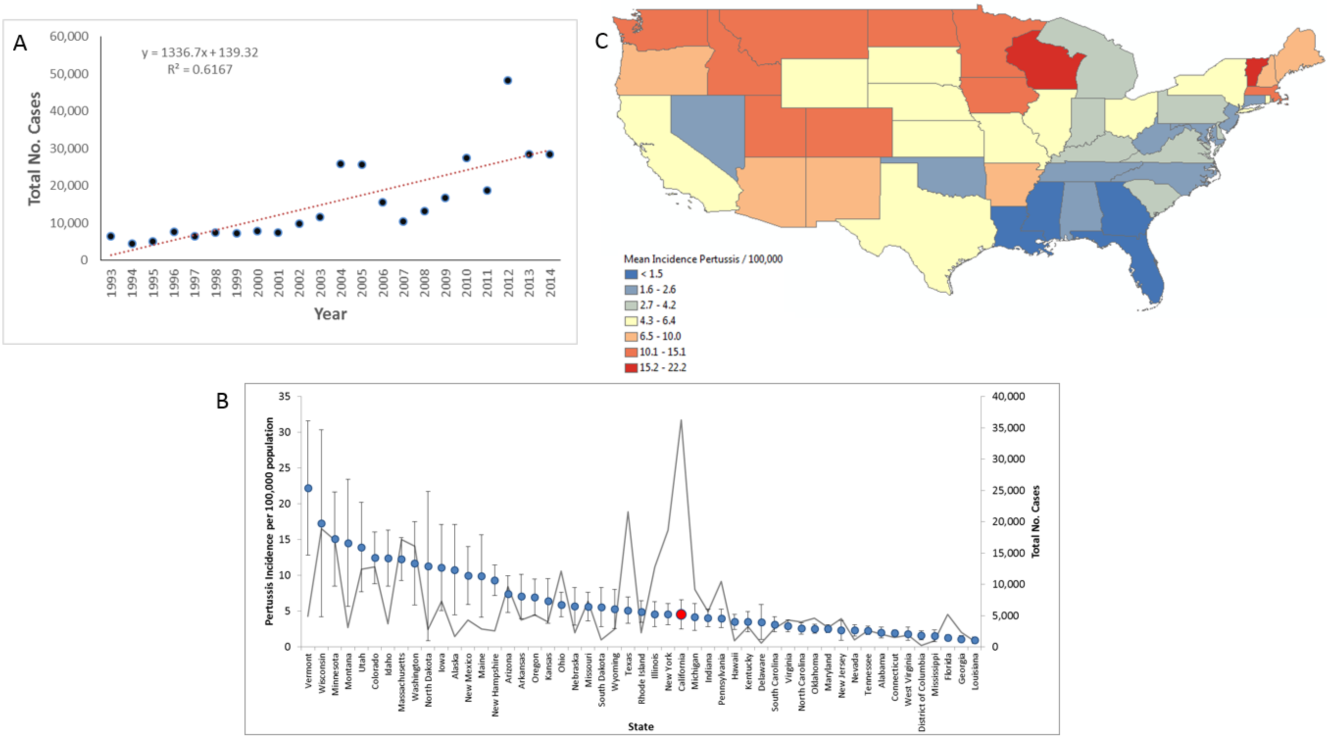

Figure 1: (A) Total number of pertussis cases reported yearly; **(B)** Mean incidence of pertussis cases per 100,000 population (+/- Standard error) (blue dots) and the total number of cases reported (grey line) by State; and **(C)** mean incidence of pertussis cases per 100,000 population mapped by State between 1993 and2014.

Year	Moran's Index	Z-score	P-value	Clustered
1993	0.13	4.25	0.00	Yes
1994	0.02	1.05	0.23	No
1995	0.10	3.13	0.00	Yes
1996	0.01	1.02	0.31	No
1997	0.03	1.34	0.18	No
1998	0.09	2.98	0.00	Yes
1999	0.13	3.85	0.00	Yes
2000	0.10	3.93	0.00	Yes
2001	-0.02	0.13	0.90	No
2002	0.03	1.38	0.17	No
2003	0.07	2.34	0.02	Yes
2004	0.03	1.54	0.12	No
2005	0.16	4.80	0.00	Yes
2006	0.15	4.54	0.00	Yes
2007	0.07	2.51	0.01	Yes
2008	0.04	1.83	0.07	No
2009	0.09	2.94	0.00	Yes
2010	0.15	4.41	0.00	Yes

2011	0.11	3.40	0.00	Yes
2012	0.06	2.08	0.04	Yes
2013	0.10	3.27	0.00	Yes
2014	0.08	2.53	0.01	Yes

Table 3: Moran's I results, Z-Score, P-Value, and whether there is clustering at a $p<0.05$ confidence for pertussis incident rates per 100,000 population by year measured at the state level for the United States.

Nineteen states allow non-medical, or personal belief exemptions (PBE) for school children (Table 4, Appendix Table 1). During the past 6 years the highest incidence of pertussis cases occurred in Montana and Wisconsin (Figure 2). Of these PBE's rates in Montana ($mean_{2009-2014}$=3.3) and Wisconsin ($mean_{2009-2014}$=2.7) were low.

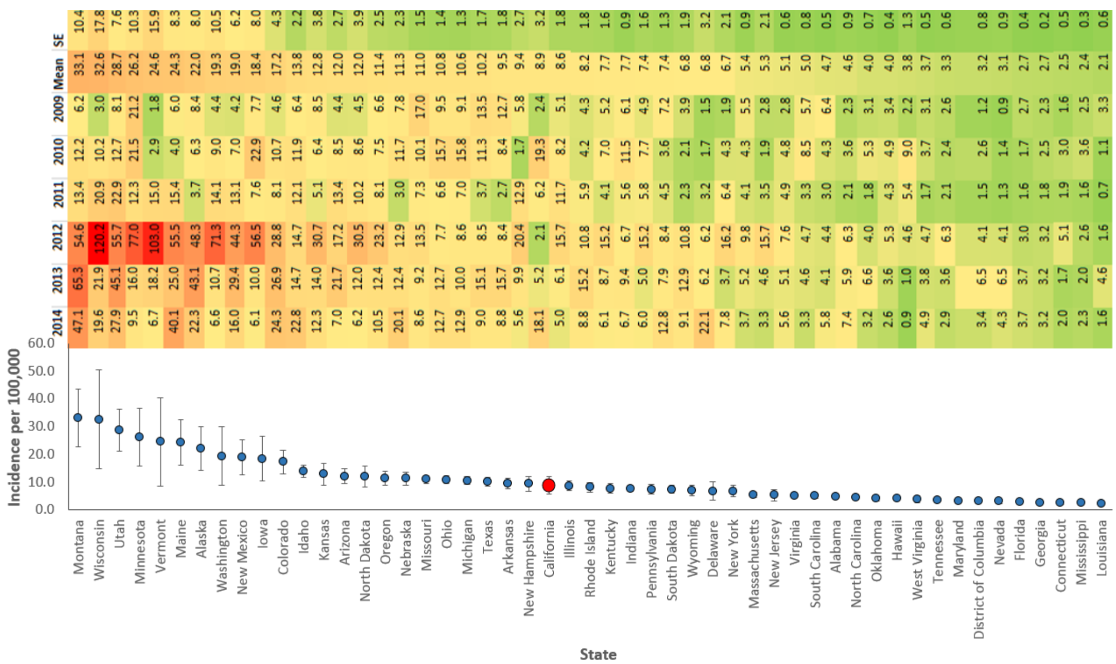

Figure 2: Pertussis Incidence per 100,000 population between 2009 and 2014.

During the past 6 years, pertussis was highest in the States of Montana, Wisconsin and Utah with rates in excess of 30 (Figure 2). Clustering of pertussis cases were found (Table 3) and are clearly shown for each year (Figure 3). Clusters varied by year but typically showed a trend towards high-high clusters in the upper Midwest or Mountain West portion of the country, with consistently low-low clusters in the Southeastern States of the USA.

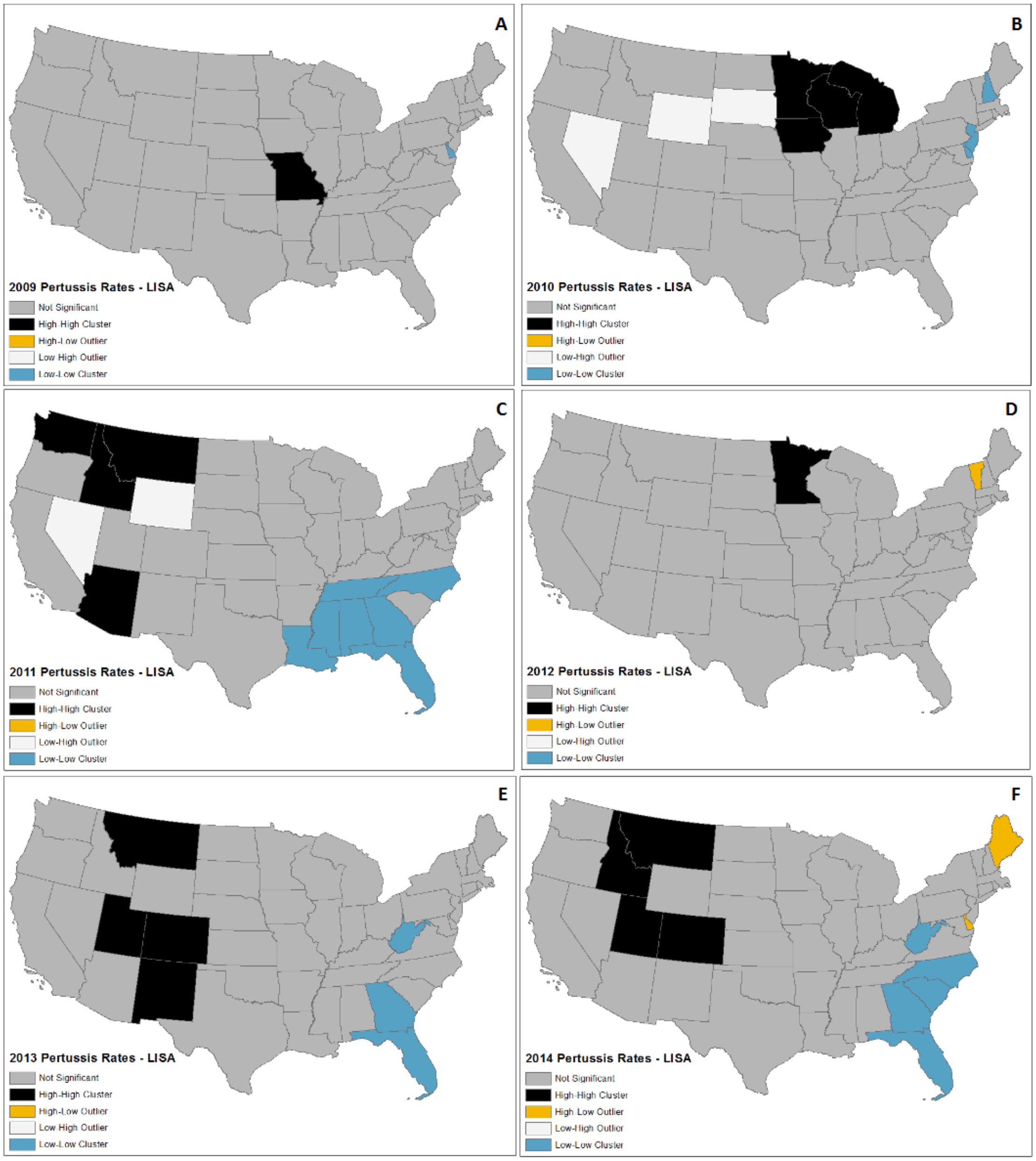

Figure 3: LISA cluster analysis of the lower 48 states by year with **(A)** 2009, **(B)** 2010, **(C)** 2011, **(D)** 2012, **(E)** 2013, **(F)** 2014.

When a single year was analyzed, 2012, the Southeast appeared to have low pertussis rates while parts of the upper Midwest, Mountain West and Northeast appeared to have higher rates with no strong correlation between cases and PBE's and the number of pertussis cases per 100,000 population were found (Figure 4A, B).

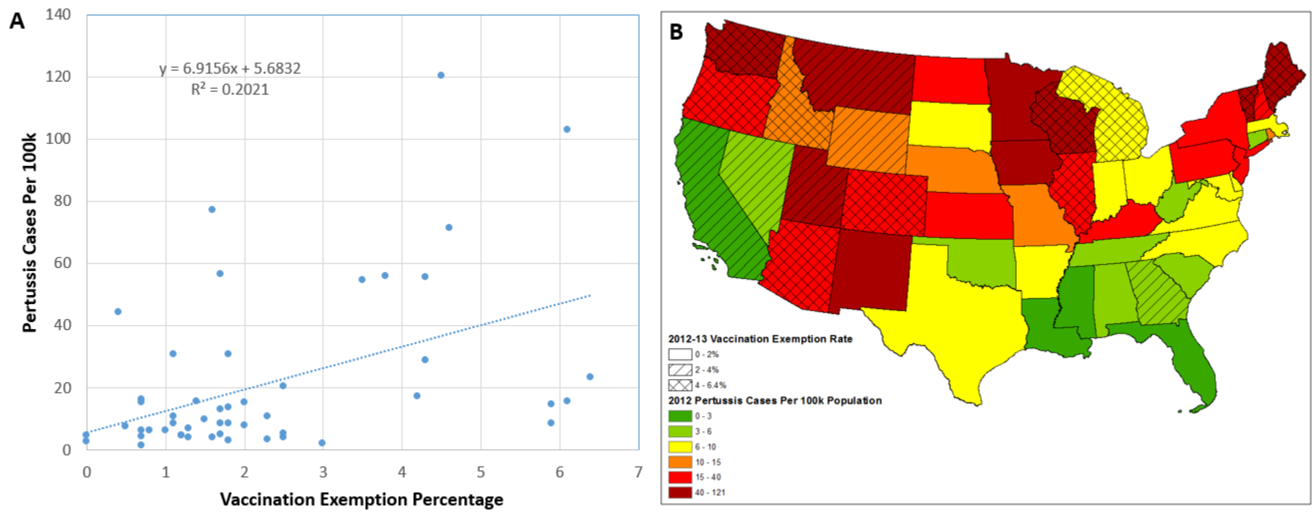

Figure 4: (A) Vaccination exemption rates and pertussis cases per 100,000 population during 2012; and **(B)** vaccination exemption rates for kindergarteners during the 2012-13 school year overlayed with pertussis incidence rates per 100,000 population during the 2012 in the USA.

Analysis of Pertussis in California: Between 2009 and 2014, California experienced two outbreak years during 2010 (N=9,159 cases) and 2014 (N= 11,203 cases) with rates as high as 24.5 and 29.3 respectively per 100,000 population (Table 4). Clustering of cases were identified (Table 4) with weak correlations between PBE's and the number of pertussis cases. The distribution of pertussis can be seen in Figure 5 with particular spikes occurring in Humboldt, Marin, and Sonoma Counties (Figure 6) where exemption rates were in excess of 5%.

Year	Total Cases	Cases Per 100k Population	Moran's Index	Z-score	P-value	Clustered	Correlation Coefficient
2009*	530	1.35	-0.040641	-0.475658	0.634318	No	0.41
2010	9,159	24.50	0.116902	2.333948	0.019598	Yes	0.18
2011	3,016	8.00	-0.053223	-0.607139	0.543759	No	0.01
2012	1,023	2.70	-0.001746	0.630526	0.528350	No	-0.02
2013	2,537	6.60	0.026131	0.851378	0.394560	No	0.36
2014	11,203	29.30	0.148877	2.931486	0.003373	Yes	0.13

Table 4: Total number of pertussis cases reported; incidence rates per 100,000 population; Moran's Index (Z-score, P-value, clustering ($p<0.05$)); and correlation coefficient (pertussis rates and PBE's by County) in California from 2009-2014. Cases per 100,000 population were standardized to the 2010 census. *Cases in 2009 were only reported January 1 – September 7.

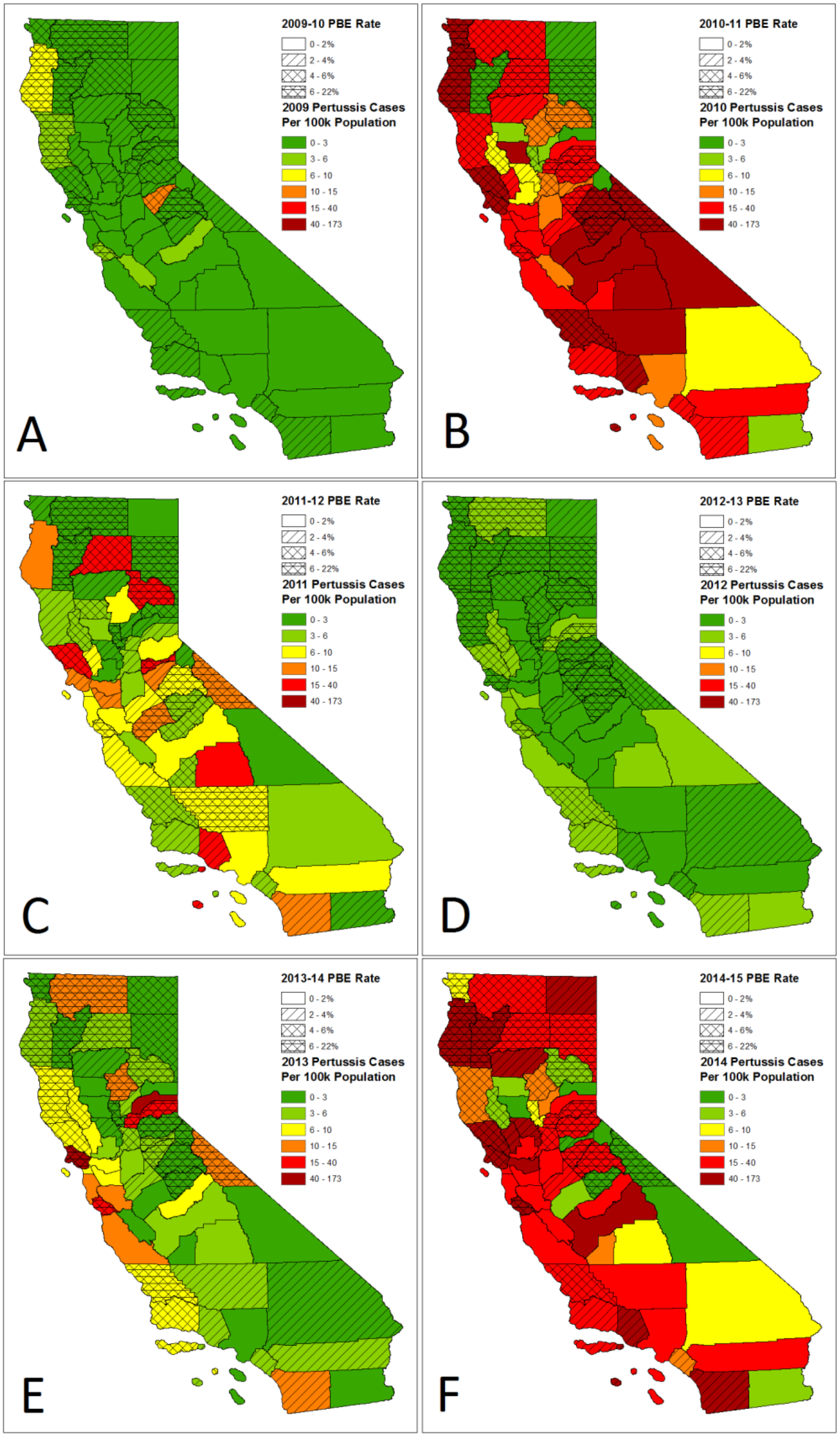

Figure 5: Pertussis cases by county in California overlaid with kindergarten PBE's for the associated school years **(A)** 2009-10, **(B)** 2010-11, **(C)** 2011-12, **(D)** 2012-13, **(E)** 2013-14, **(F)** 2014-15.

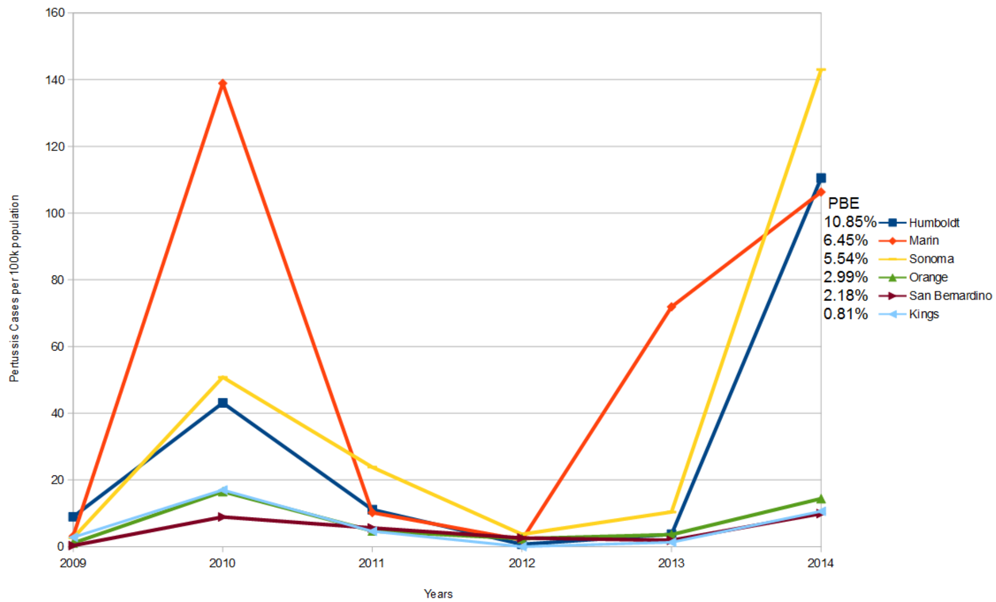

Figure 6: A chart of pertussis rates per 100,000 population in California's Humboldt, Marin, Sonoma, Orange, San Bernardino, and Kings Counties from 2009-2014 with PBE rates from 2014-15.

During the outbreak years, no correlation was found between PBE's and pertussis rates (Figure 7A,B). Clusters were identified in counties in central California during 2010 and along the coastal areas north of San Francisco extending into wine country of Napa and Sonoma Counties during 2014 (Figure 7C,D).

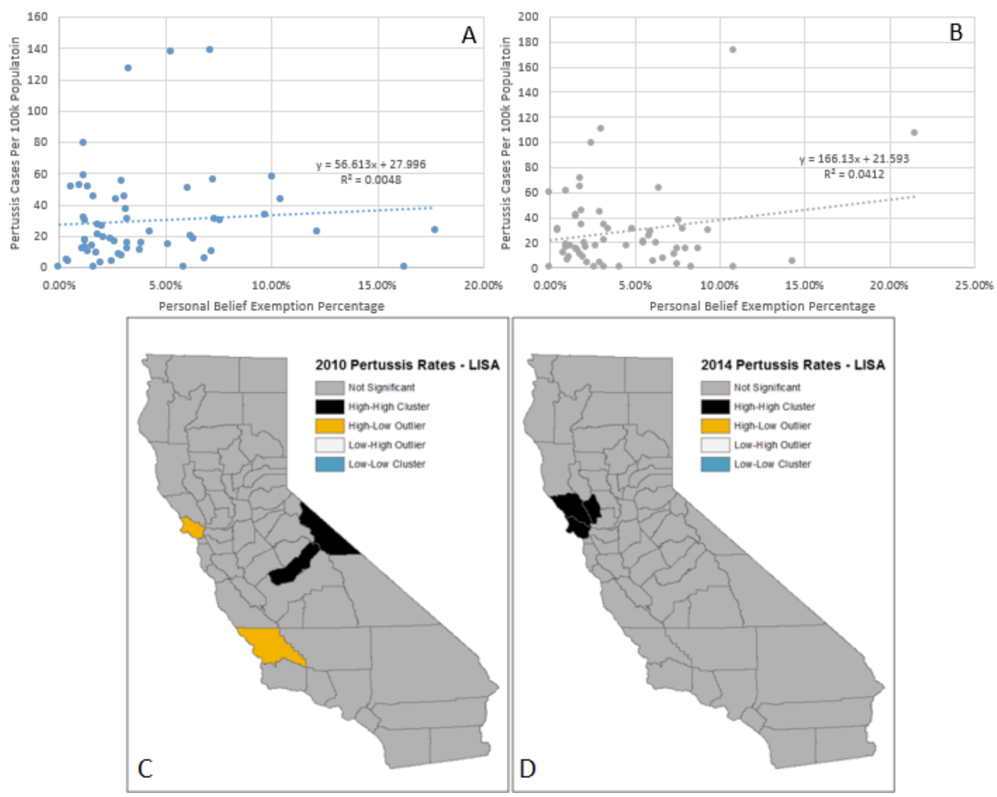

Figure 7: Scatter Plot of **(A)** 2010 and **(B)** 2014 personal belief exemptions for kindergarteners on the X-axis and pertussis cases per 100,000 population on the Y-axis for each county within California; and LISA cluster analysis of pertussis rates in California during **(C)** 2010 and **(D)** 2014 by County.

Elementary Schools

Empirical Bayesian kriged surfaces of schools created seamless overviews of vaccination rates and PBE rates for 2014 that enabled greater geographic detail than data reported at the county level (Figure 8). Thus highlighting areas where vaccination rates were low and below herd immunity thresholds (e.g. rates < 92% (Table 1)) (Figure 8A) as well as areas where PBE's were high (Figure 8B). During the 2014 school year, a strong inverse relationship was observed between vaccination rates and PBEs (Correlation = -6.91) (Figure 9).

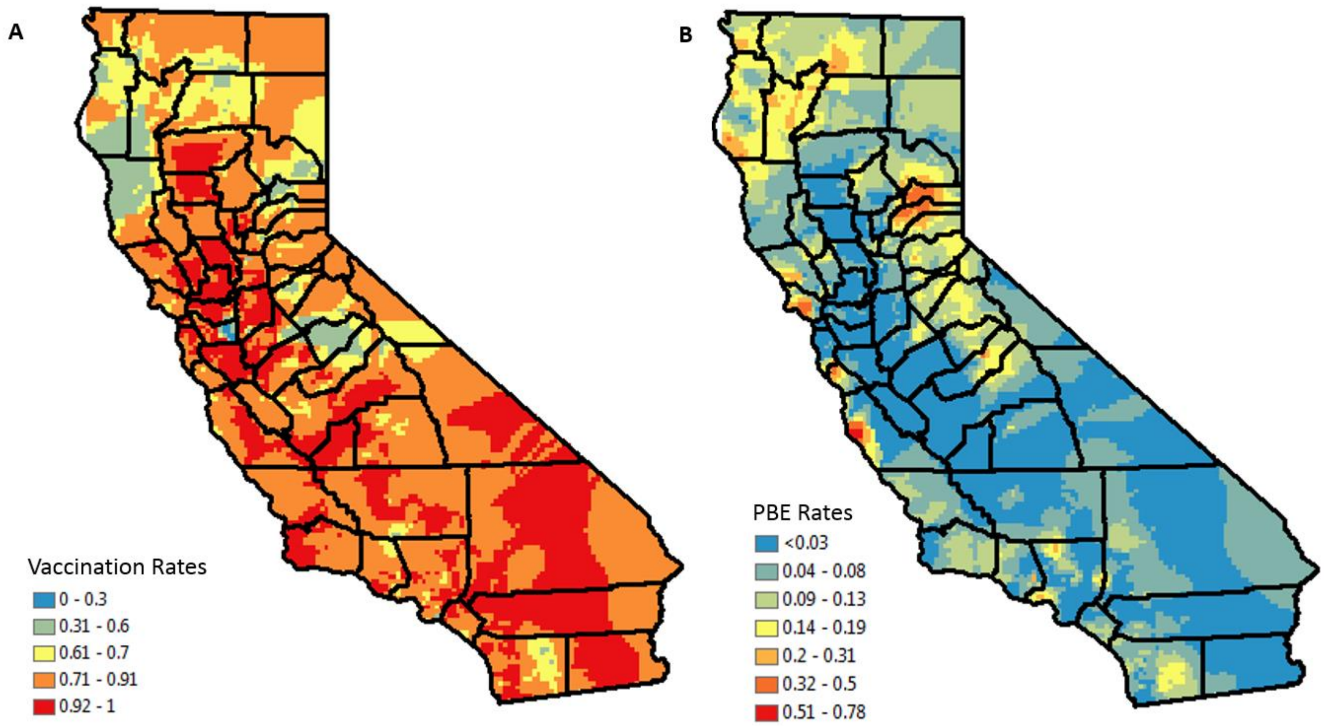

Figure 8: Vaccination Rates **(A)** and PBE Rates **(B)** for the 2014 School Year in California.

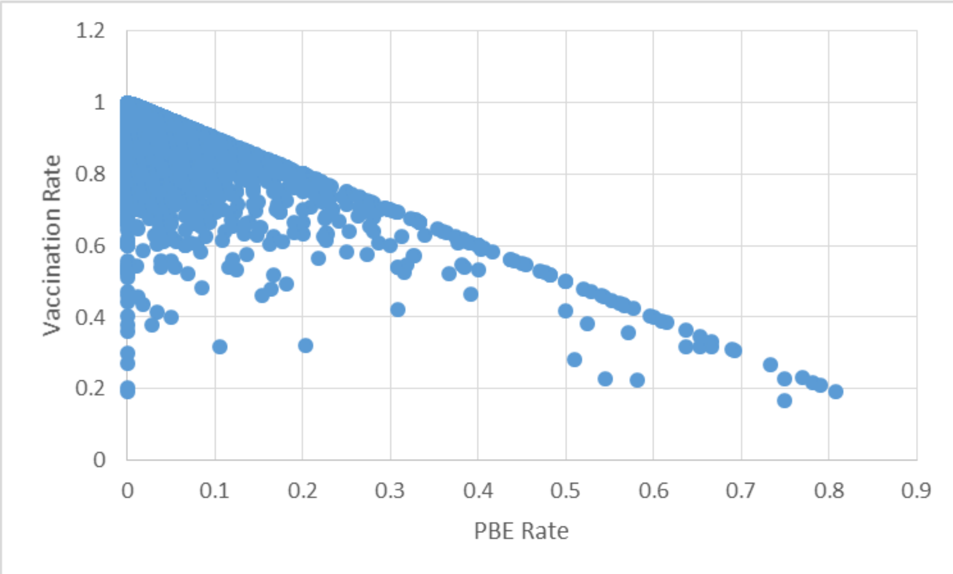

Figure 9: Vaccination Rate and PBE Rate by School (N=5645)

When PBE High-High clusters were compared to pertussis rates during 2014, the majority of these occurred in counties with rates in excess of 15 (Figure 10). The High-High school district PBE clusters fell within 14 out of 58 California counties containing 62.64 cases per 100,000 population. Only 5 of the 12 counties with pertussis rates greater than 40 contained school district containing High-High PBE clusters.

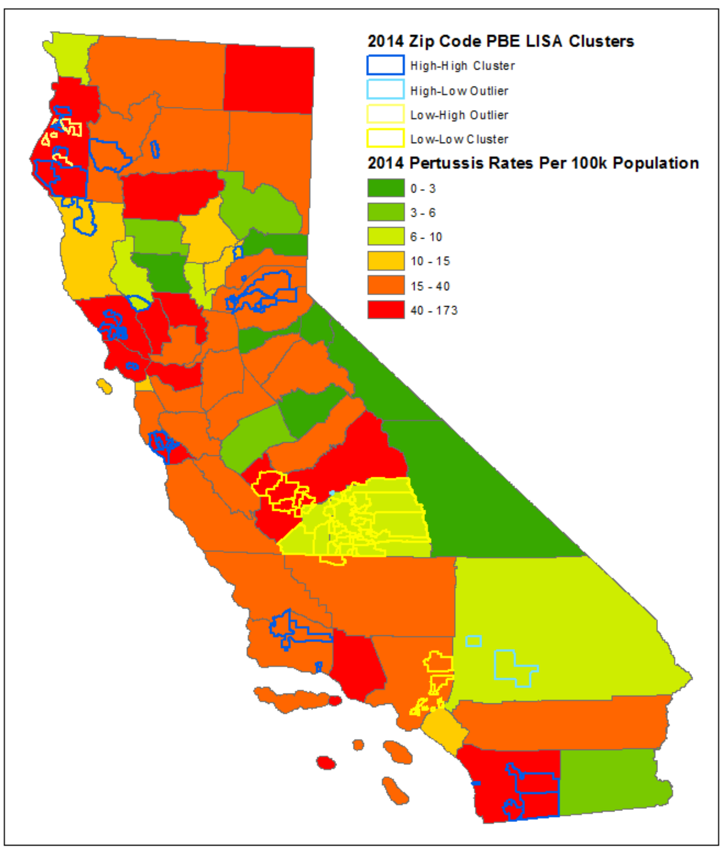

Figure 10: Pertussis cases by California counties overlaid with LISA Clustering results at the Elementary and School District for PBE rates in 2014.

Zip Codes

A weak correlation was found for PBE rates in schools (Moran's I= 0.145; p-score=, z-score=16.5) at the school district level and even weaker at the zip code level (Moran's I= 0.075; p-score=, z-score=21.25) (Figure 11). Of the 94 High-High PBE clusters observed at the zip code level, these intersected all three of the High-High County Pertussis rate clusters and 23 of the 38 (61%) High-High School District PBE clusters (Figure 11). Of the 143 Low-Low PBE clusters observed at the zip code level, there were no Low-Low County Pertussis Rate clusters, but they intersected 57 of the 82 (70%) Low-Low School District PBE clusters (Figure 11).

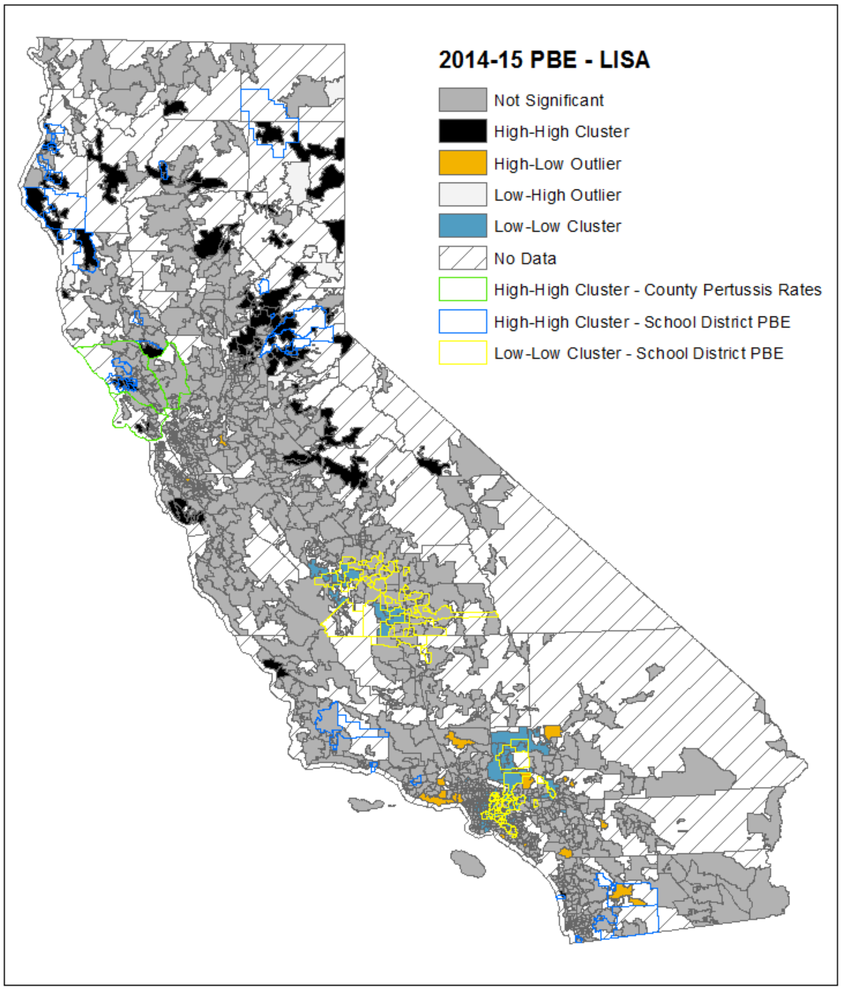

Figure 11: Clusters of PBE rates for 2014-2015 at the different geographies.

Socio-economic factors associated with PBE's: All factors were observed to be significant (p<0.01) (Table 4) when correlated with PBE's, but none of these showed a very strong correlation (value > 0.70). Factors with a strong correlation (values between 0.40 and 0.69) included: average family size (-), and the percentage of housing with seasonal/recreational purposes (+). Factors with a moderate correlation (values betweem 0.30 and 0.39) included: the average household size, percentage of households with 3+ generations, Hispanic/Latino's, Mexican's, children under 5 years of age (-); and vacant housing, husband/wife families with no children, and households with less than 3 generations (+). Weak correlations (values between 0.20 and 0.29) included: husband/wife families with children, population from 5 to 9 years old, population from 10 to 14 years old, and houses for rent (-); and husband/wife families, white's, at least an Associate's degree (+).

Factors	PBE Correlation Coefficient
Average Household Size	-0.3553
Average Family Size	-0.6717
Percentage of Vacant Houses	0.3125
Percentage of Husband/Wife Families	0.2099
Percent of Husband/Wife Families with Children	-0.2909
Percent of Husband/Wife Families with Children under 6 years old	-0.0934
Percent of Husband/Wife Families with no Children	0.3860
Percentage of Households with 3 or more generations	-0.3766
Percentage of Households with less than 3 generations	0.3766
Percentage of Hispanic or Latino population	-0.3559
Percentage of Mexican population	-0.3338
Percentage of White population	0.2089
Percentage of Black population	-0.1029
Percentage of Asian population	-0.1569
Percentage of the population under 5 years old	-0.3282
Percentage of the population from 5 and 9 years old	-0.2889
Percentage of the population from 10 and 14 years old	-0.2663
Percentage of houses for rent	-0.2809
Percentage of houses used for recreational/seasonal purposes	0.4196
Percentage of the population with highest education as a high school diploma	-0.1126
Percentage of the population with highest education as an Associate's degree	0.1715
Percentage of the population with highest education as an Bachelor's degree	0.1779
Percentage of the population with highest education as an Master's degree	0.1651
Percentage of the population with highest education as an Doctorate degree	0.1239
Percentage of the population at least an Associate's Degree or above	0.2025
Percentage of the population at least a Bachelor's Degree or above	0.1796
Percentage of the population at least a Master's Degree or above	0.1609
Percentage of the population with a Professional Degree	0.1513
Unemployment Rate	-0.1662
Median Household Income	0.0776
Percentage of the Population with Health Insurance	0.1636

Table 4: Socioeconomic and demographic factors from 2010 US Census Bureau and 2013 5-year American Community Survey with the Pearson correlation coefficient calculated based on the zip code level.

Discussion

Over the past two decades there has been a steady rise in vaccine preventable diseases such as pertussis, as examined in this study. In particular, during the past 6 years, some clustering of pertussis incidence were found at the state level that shifted from year-to-year. Low incidence rates clustered in the Southeast and high incidence rates were found to cluster in the mid to north western states, in particular Montana which was identified to be highly clustered during 3 of the 6 years (Figure 12).

Observing a clustered pattern for pertussis disease rates at the national level is increasing as overall disease rates increase; with clustering observed six times out of twelve from 1993 to 2004, but nine times out of ten from 2005 to 2014 as noted in Table 3.

The upper mid-west and Rocky Mountain portions of the continental United States appear to have high-high clusters, while southeastern states tend to have low-low clusters (Figure 12) from 2009-14. Demographic analysis at the state level would likely provide insufficient results for any conclusions to be drawn to relate any factors to this occurrence, but targeted studies could be performed in those state such as Montana, Idaho, Utah, Colorado, and Minnesota to observe clustering at finer geographies and comparison with community compositions.

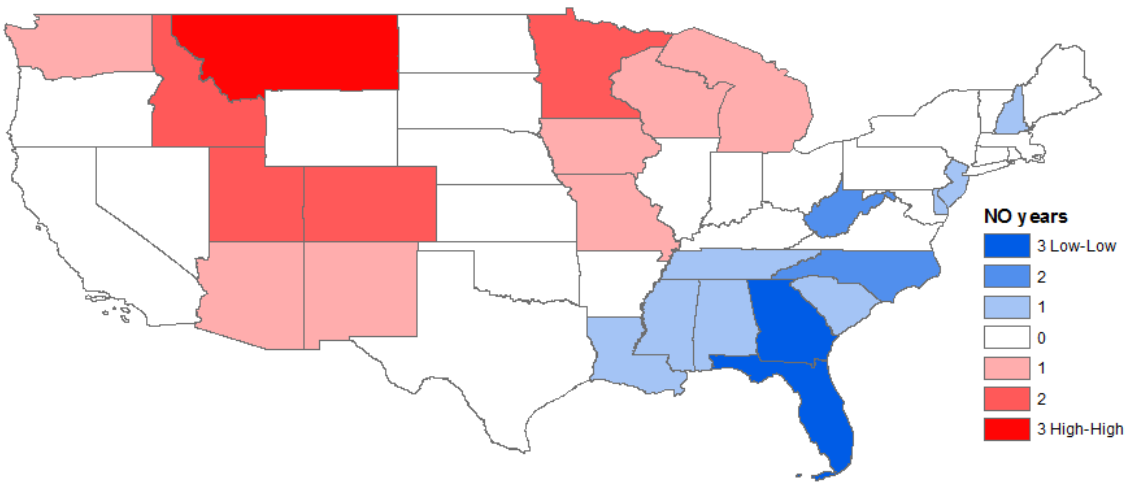

Figure 12: A map of the continental United States with the number of year a state was observed to have a high-high and low-low clusters of pertussis case rate.

Pertusssis clusters in California counties were only observed in epidemic outbreak years with little to no correlation found between PBE and disease rates during non-outbreak years. The location of these clusters also varied between outbreak years (Figure 7). Some overlapping, but many different clustering patterns were also found when PBE's were examined at the school district and zip code level. Pertussis rates were highest during epidemic years in counties with higher PBEs. For example, during 2014nearly three times the disease rate was observed in counties which contained High-High school district PBE clusters compared to those that did not. By examining the rates and PBE's at different geographies, different clustering patterns became apparent, highlighting key areas that may be contributing to the current disease outbreak. By analyzing the relationships between socio-economic and demographic factors at the zip code level, we can begin to draw conclusions about the composition of communities at high-risk of disease outbreaks and increased transmission.

Californian infants were the most impacted from pertussis (Winter, 2014) and are unable to receive full vaccination, therefore it is vital that caregivers and family members become vaccinated to protect these children. This includes keeping up-to-date with booster shots since vaccine effectiveness wanes over time (CDC, 2015) as reflected in the caseloads seen in this age range compared to younger and older children (Figure 13). Pertussis is deadly, and with case rates soaring to levels not seen in generations, the public should be reminded (especially those in areas with high clusters of cases and PBE rates) that during a time period before a pertussis vaccine existed (1940 to 1948), pertussis caused the deaths of more babies under 1 year of age in the United States than measles, meningitis, scarlet fever, diphtheria, and poliomyelitis combined. (Espinoza, 2014). Therefore understanding a relationship between PBEs and pertussis cases and identifying the make-up of high PBE communities is important for vaccination campaigns and disease prevention tactics. Further work will need to be done to completely address this relationship.

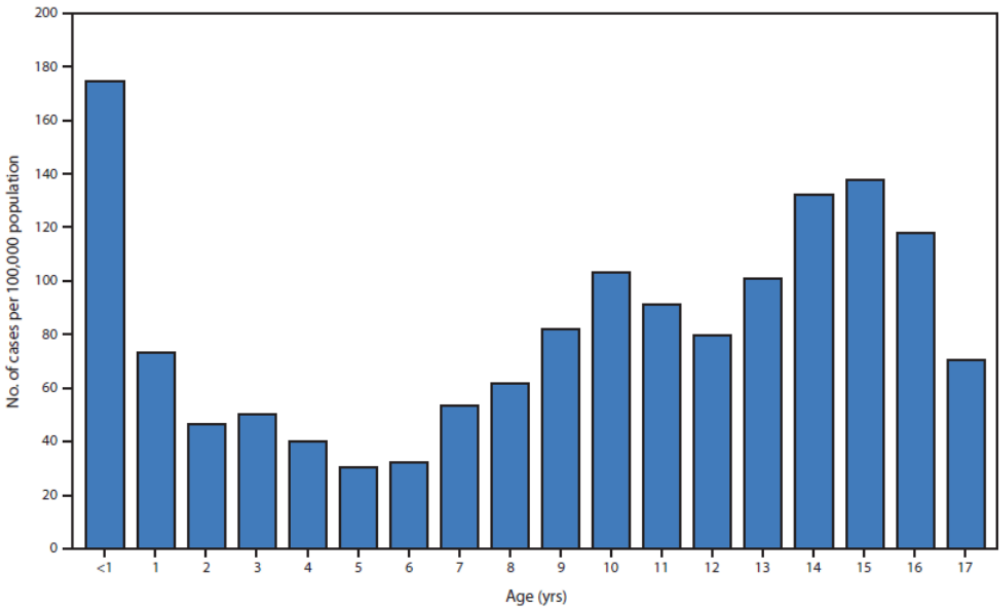

Figure 13: Pertussis cases per 100,000 population by age range as reported to the California Department of Public Health as of November 26, 2014 (Winter *et al*, 2014).

Similar studies have been performed to analyze disease in terms of under-vaccinated populations. One study published in the journal Pediatrics analyzed a 2008 outbreak of measles in San Diego amongst pockets of under-vaccinated school children (Sugarman, 2010). The disease outbreak subsided after 11 cases due to community vaccination rates above 90% and public awareness campaigns, but the end results could have been far different with higher levels of vaccination exemptions. Similar to this study, it was observed that higher PBE rates were strongly related to lower vaccination rates. The families that chose exemptions were also nearly all white, college educated, and had higher than average salaries. Although relatively weak correlations were found in this study, increased PBE's were also seen to be related to whiter communities with education levels at or above an Associate's degree, but the correlation to median income was too small to be considered relevant. Conversely, these communities would have lower than average family sizes, fewer husband/wife families with children, less households with 3+ generations, and lower proportions of Hispanic/Latinos.

With the strongest factors of average family size being negatively correlated and percentage of houses used for recreational/seasonal purposes being positively correlated with PBE, we can begin to create community trends for PBEs. These trends can be extended to other parts of the country which may not contain the same quality of data and could be used to anticipate similar PBEs and disease case rates. A tool could be built to weigh each factor by its correlation which would allow us to better model the expected PBEs in other communities. This knowledge will allow health professionals to anticipate vaccine demand, medical personnel requirements, and potential opposition to any vaccine drives or health campaigns.

Limitations:
Scale: The key limitation of this study was obtaining data at an appropriate geographic scale. Due to the restrictions and confidentiality of health records pertussis case information was not publicly available for geographies finer than the county level. Thus incidence rates were obtained at the state and county level through the CDC and California Department of Health. The data scale hinders auto-correlation and clustering analysis and may prevent the identification of high, low, or outlier communities due to their aggregation with more normalized neighbors. Similarly, the lack of pertussis case information at the zip code, school district, or ideally the census tract level lessens the validity of socio-economic results that can be compared to pertussis case rates or personal belief exemptions due to the aggregation of populations at larger geographies, a direct result of the Modifiable Areal Unit Problem.

Modifiable Areal Unit Problem: The Modifiable Areal Unit Problem (MAUP) is a phenomena that can cause an observer to draw different conclusions based on varying geographic aggregation scales and boundaries. This has the strong ability to impact results when analyzing data collected and combined at various scales of geographic detail. Since each pertussis case relates back to an individual, the aggregation of results into census tracts, zip codes, counties, or states can inadvertently allow the reviewer to draw different conclusions based on the data aggregation method.

Reporting: The pertussis data were available at the county and state level and thus representative of the entire population at those levels.

1. Comparisons were made between PBE rates and pertussis cases, but the PBE rates were obtained only for kindergarteners at schools with 10 or more students enrolled. Thus, small and private schools were omitted due to lack of reporting requirements and their lack of affiliation with a school district.
2. Aggregation of schools to the zip code level likely caused some students to be counted in a county where they do not reside due to the lack of individual school zoning across the state. This left some zip codes as reporting no students and their neighboring zip code which contained the school as reporting all students.

However, regardless of the limitations of this study, by mapping and applying various spatial analysis methods, it was possible to identify areas within California where vaccination rates were below those required for herd immunity against pertussis which is highly transmittable (e.g. Figure 8A (areas < 0.92)). By mapping the overlap of county rates with High-High PBE clusters at different geographies (e.g. school district boundaries, zip code boundaries) it then becomes possible to identify key communicates to target. For example, in some communities throughout the state, like those in Sonoma County, which experienced the highest pertussis case rate in 2014 at 142.18 cases per 100,000 population, the areas west of Santa Rosa, CA showed High-High clusters at all three geographies for pertussis cases and PBE. The results of this study can be used to identify very high-risk communities such as these across the state in order to target vaccination campaigns.

Future work should include spatial and temporal analysis of incidence and a breakdown by age to better understand the timing of pertussis cases both at different times of the year as well as how these relate spatially. Analysis comparing case rates and PBE at different latitudes or climates may also shed light onto disease transmission, the cyclical nature of the disease and whether epidemic frequency is related to either, or other as yet unobserved characteristics.

Pertussis is a preventable disease that can be vaccinated. With the recent outbreaks of measles at Disneyland and increasing news coverage on vaccine-preventable disease outbreaks, legislation is beginning to work its way through the systems of government to curtail personal belief vaccination exemptions. As of June 30, 2015, voters in California and Vermont have voted to repeal personal belief exemptions for school children, but campaigns can be pushed in the remaining PBE states to further similar legislation (NCSL, 2015). This requirement should increase the overall vaccination coverage rate, strengthen herd immunity, and make it less likely for vaccine-preventable disease outbreaks to occur. Thus, understanding spatial patterns of disease incidents, vaccination percentages, personal belief exemptions, and various socio-economic and demographic factors can help target likely areas to experience future outbreaks as well as educational campaigns or legislation to protect vulnerable populations. To help in targeting of these vaccinations, analyses as illustrated here will help identify key zipcode’s and school areas.

References

Atwell, J., Van Otterloo, J., Zipprich, J., Winter, K., Harriman, K., Salmon, N., Neal, H., Omer, S. (2013). *Nonmedical Vaccine Exemptions and Pertussis in California, 2010.* Pediatrics, 132(4):624-630.

Auger, K., Patrick, S., Davis, M. (2013). *Infant Hospitalization for Pertussis Before and After Tdap Recommendations for Adolescents.* Pediatrics, 132(5):e1149-e1155.

Breban, R., Vardavas, R., Blower S. (2007). *Theory versus Data: How to Calculate R0?.* PLoS ONE. 2(3): e282.

Centers for Disease Control and Prevention. (2000). *Guidelines for the control of pertussis outbreaks*. Retrieved March 28, 2014, from http://www.cdc.gov/pertussis/outbreaks/guide/

Centers for Disease Control and Prevention. (2003). Course: "Smallpox: Disease, Prevention, and Intervention". Retrieved April 5, 2014, from http://www.bt.cdc.gov/agent/smallpox/training/overview/pdf/eradicationhistory.pdf (herd immunity picture as well)

Centers for Disease Control and Prevention. (2012). *Pertussis Epidemic – Washington, 2012,* Morbidity and Mortality Weekly Report, 61(28): 517-522.

Centers for Disease Control and Prevention. (2013). *Signs & Symptoms*. Retrieved March 26, 2014, from http://www.cdc.gov/pertussis/about/signs-symptoms.html

Centers for Disease Control and Prevention. (2014). *Pertussis Cases by Year (1922-2013)*. Retrieved March 28, 2014, from http://www.cdc.gov/pertussis/surv-reporting/cases-by-year.html

Centers for Disease Control and Prevention. (2015). *School Vaccination Requirements, Exemptions and Web links.* Retrieved August 8, 2014, from http://www2a.cdc.gov/nip/schoolsurv/schlmmRqmtReport.asp

Chen, Y., Waters, E., Green, J., (2002). *Geospatial analysis of childhood pertussis in Victoria, 1993-1997.* Australian and New Zealand Journal of Public Health, 26(5):456-461.

Cherry, J. D. M.D. (2010). *The present and future control of pertussis.* Clinical Infection Diseases, 51 (6): 663-7.

The College of Physicians of Philadelphia. (2014). *Disease Eradication.* Retrieved March 29, 2014, from http://www.historyofvaccines.org/content/articles/disease-eradication

Cromley, E., McLafferty, S. (2012). GIS and Public Health, Second Edition.

DeBolt, C., Tasslinmi, A, Bardi J., Leader, B. Hiatt, B. Quin X., Patel M., Martin S., Tondella M., Cassiday P., Faulkner A., Messonnier N., Clark T., Meyer S. (2012). *Pertussis Epidemic – Washington 2012,* Morbidity and Mortality Weekly Report. 61(28):517-522.

de Greeff, S., Mooi, F., Westerhof, A., Verbakel, J., Peeters, M., Huevelman, C., Notermans, D., Elvers, L., Schellekens, J., de Melker, H. (2010) *Pertussis Disease Burden in the Household: How to Protect Young Infants*. Clinical Infectious Diseases, 50(10):1339-1345.

Dittman, S., Wharton, M., Vitek, C., Ciotti, M., Galazka, A., Guichard, S., Hardy, I., Kartoglu, U., Koyama, S., Kreysler, J., Martin, B., Mercer, D., Rønne, T., Roure, C., Steinglass, R., Strebel, P., Sutter, R., Trostle, M. (2000). *Successful control of epidemic diphtheria in the states of the Former Union of Soviet Socialist Republics: lessons learned.* Journal of Infectious Disease. 181(Suppl 1):S10-22.

Fraser, C., Donnelly, C., Cauchernez, S., Hanage, W., Ven Kerkhove, M., Hollingsworth, T., Griffin, J., Baggaley, R., Jenkins, H., Lyons, E., Jombart, T., Hinsley, W., Grassly, N., Balloux, F., Ghani, A., Ferguson, N., Rambaut, A., Pybus, O., Lopez-Gatell, H., Alpuche-Aranda, C., Chapela, I., Zavala, E., Guevara, D., Checchi, F., Garcia, E., Hugonnet, S., Roth, C. (2009). *"Pandemic Potential of a Strain of Influenza A (H1N1): Early Findings"*. Science. 324(5924):1557-1561.

Gay, N (2004). *The Theory of Measles Elimination: Implications for the Design of Elimination Strategies.* Journal of Infectious Diseases, 189(Suppl 1): S27-35.

Halperin, S. A M.D. (2012). Infectious Disease News. *Myriad Causes contributed to California*

Pertussis Outbreak. Retrieved March 15, 2014, from http://www.healio.com/pediatrics/news/print/infectious-diseases-in-children/%7B13404fa4-f570-4d7f-9e99-9fa5d1f5e7eb%7D/myriad-causes-contributed-to-california-pertussis-outbreak

Heininger, U. M.D. (2012). *What the Pediatric Infection Disease Specialist Should Know.* The Pediatric Infectious Disease Journal. 31(1):1-2.

Heymann, D., Aylward R. (2006). *Mass vaccination: when and why.* Current Topics in Microbiology and Immunology. 304:1-16.

Lesau, C., Lynfield, R., Danila, R., Pilishvili, T., Facklam, R., Farley, M., Harrison, L., Schaffner, W., Reingold, A., Bennett, N., Hadler, J., Cieslak, P., Whitney, C. (2005). *Changing ;Epidemiology of Invasive Pneumococcal Disease Among Older Adults in the Era of Pediatric Pneumococcal Conjuage Vaccine*. The Journal of the American Medical Association. 294(16)2043:2051.

Lundquist, L. (2010). Whooping cough risingin vaccine-averse idaho. *McClatchy - Tribune Business News*. Retrieved from http://search.proquest.com/docview/731783684?accountid=13158

Metcalf, C., Bjornstad, O., Ferrari, M., Klepac, P., Bharti, N., Lopen-Gatell, H., Grenfell, G. (2010). *The epidemiology of rubella in Mexico: seasonality, stochasticity and regional variation.* Epidemiology & Infection, 2011(139):1029-1038.

Omer, S., Salmon, D., Orenstein, W., deHart, P., Halsey, N. (2009). *Vaccine Refusal, Mandatory Immunizations, and the Risks of Vaccine-Preventable Diseases*. The New England Journal of Medicine. 360:1981-8.

Parker Fiebelkorn, A., Redd, S., Gallagher, K., Rota, P., Rota, J., Bellini, W., Seward, J. (2010). *Measles in the United States during the Postelimination Era.* Journal of Infectious Disease, 202(10):1520-1528.

Reinberg, S. (2013). *Whooping Cough Risk Higher Among Kids Who Miss Vaccinations: Study.* U.S. News & World Report. Retrieved on May 11, 2014 from http://health.usnews.com/health-news/news/articles/2013/09/09/whooping-cough-risk-higher-among-kids-who-miss-vaccinations-study

Sugerman, D., Barskey, A., Delea, M., Ortega-Sanchez, I., Bi, D., Ralston, K., Rota, P., Waters-Montijo, K., LeBaron, C. (2010). *Measles Outbreak in a Highly Vaccinated Population, San Diego, 2008: Role of the Intentionally Undervaccinated.* Pediatrics. 125(4):747-755.

Vaccines Today (2013). *What is herd immunity?* Retrieved March 28, 2014, from *http://www.vaccinestoday.eu/vaccines/what-is-herd-immunity/*

Weil, A., Chowdhury, F., Khan, A., Leung, D., Uddin, T., Begum, Y., Saha, N., Charles, R., Lorocque, R., Harris, J., Ryan, E., Qadri, F., Calerwood, S. (2012). *Frequency of reexposure to Vibrio cholerae 01 evaluated by subsequent vibriocidal titer rise after an episode of severe cholera in a highly endemic area in Bangladesh.* American Journal of Tropical Medicine and Hygiene. 87(5):921-6.

Wilking, H., Höhle, M., Velasco, E., Suckau, M., Eckmanns, T. (2012). *Ecological analysis of social risk factors for Rotavirus infections in Berlin, Germany, 2007-2009.* International Journal of Health Geographics, 11(37):1-12.

Winter, K., Harriman, K., Zipprich, J., Schechter, R., Talarico, J., Watt, J., Chavez, G. (2012). *California Pertussis Epidemic, 2010.* Journal of Pediatrics, 61(6):1091-1096.

Winter, K., Glaser, C., Watt, J., Harriman, K. (2014). *Pertussis Epidemic – California 2014.* Morbidity and Mortality Weekly Report (MMWR), 63(48):1129-2231.

Wiysonge, C., Nomo, E., Mawo, J., Ofal, J., Mimbouga, J., Ticha, J., Ndumbe, P. (2008). *Yellow fever control in Cameroon: where are we now and where are we going?* BMC Medicine. 6:3

Appendix

Table A1: Pertussis Cases per 100,000 population by year and the average for each state between 2009 and 2014 and whether or not Personal Belief Exemptions are allowed

State	2009	2010	2011	2012	2013	2014	2009-14 Average	PBE
Montana	6.20	12.21	13.43	54.62	65.30	46.70	33.08	N
Wisconsin	3.00	10.25	20.88	120.15	21.90	19.56	32.62	Y
Utah	8.08	12.68	22.92	55.72	45.10	27.52	28.67	Y
Minnesota	21.23	21.47	12.31	77.00	16.00	9.44	26.24	Y
Vermont	1.76	2.88	15.00	103.03	18.20	6.70	24.60	Y
Maine	6.02	3.99	15.43	55.45	25.00	40.00	24.31	Y
Alaska	8.44	6.30	3.73	48.26	43.10	22.26	22.02	N
Washington	4.36	9.00	14.10	71.28	10.70	6.56	19.33	Y
New Mexico	4.17	6.97	13.13	44.31	29.40	15.97	18.99	Y
Iowa	7.75	22.85	7.57	56.47	10.00	6.08	18.45	N
Colorado	4.65	10.70	8.13	28.80	26.90	23.90	17.18	Y
Idaho	6.37	11.90	12.12	14.73	14.70	22.52	13.72	Y
North Dakota	4.51	8.60	10.22	30.59	12.00	14.47	13.40	Y
Kansas	8.47	6.37	5.05	30.74	14.00	12.29	12.82	N
Arizona	4.37	8.52	13.41	17.24	21.70	6.89	12.02	Y
Oregon	6.62	7.45	8.12	23.23	12.40	10.40	11.37	N
Nebraska	7.78	11.70	3.04	12.93	12.40	19.98	11.31	N
Missouri	17.03	10.07	7.29	13.53	9.30	8.59	10.97	N
Ohio	9.51	15.66	6.65	7.74	12.70	12.64	10.81	Y
Michigan	9.09	15.83	7.00	8.55	10.00	12.84	10.55	Y
Texas	13.54	11.28	3.75	8.51	15.10	8.81	10.16	Y
Arkansas	12.74	8.38	2.72	8.41	15.80	8.73	9.46	Y
New Hampshire	5.77	1.75	12.90	20.37	9.90	5.95	9.44	N
California	2.35	19.27	6.15	2.09	5.30	17.91	8.85	Y
Illinois	5.06	8.23	11.73	15.74	6.10	4.97	8.64	N
Rhode Island	4.27	4.18	5.90	10.76	15.20	8.81	8.19	N
Kentucky	5.24	6.97	4.10	15.20	8.70	6.07	7.71	N
Indiana	6.07	11.51	5.63	6.75	9.40	6.64	7.67	N
Pennsylvania	4.86	7.70	5.82	15.24	5.00	6.04	7.44	Y
South Dakota	7.19	3.55	4.49	8.40	7.90	12.66	7.37	N
Wyoming	3.93	2.13	2.29	10.76	12.90	9.07	6.85	N
Delaware	1.46	1.67	3.19	6.22	6.20	21.91	6.77	N
New York	1.88	4.29	6.41	16.20	6.40	4.41	6.60	N
Massachusetts	5.49	4.33	4.10	9.75	5.20	3.66	5.42	N
New Jersey	2.79	1.92	3.53	15.74	4.60	3.27	5.31	N
Virginia	2.80	4.78	4.92	7.64	5.10	5.57	5.14	N
South Carolina	5.71	8.46	3.34	4.74	4.60	3.25	5.02	N
Alabama	6.41	4.31	2.98	4.40	4.10	5.75	4.66	N
Oklahoma	3.15	5.27	1.80	4.04	6.60	3.15	4.00	Y
Hawaii	3.42	4.91	4.28	5.24	3.60	2.54	4.00	N
West Virginia	2.16	8.95	5.45	4.58	1.00	0.86	3.83	N
Tennessee	3.12	3.67	1.72	4.72	3.80	4.89	3.65	N
North Carolina	2.33	3.59	2.05	6.28	5.90	0.45	3.43	N
Maryland	2.58	2.40	2.11	6.27	3.60	2.89	3.31	N
District of Columbia	1.18	2.64	1.45	4.11	6.50	3.34	3.21	N
Nevada	0.89	1.41	1.25	4.06	6.50	4.19	3.05	N

Florida	2.66	1.74	1.64	2.98	3.70	3.62	2.72	N
Georgia	2.32	2.54	1.82	3.21	3.20	3.18	2.71	N
Connecticut	1.57	2.99	1.90	5.07	1.70	2.00	2.54	N
Mississippi	2.53	3.57	1.65	2.58	2.00	2.30	2.44	N
Louisiana	3.32	1.10	0.68	1.56	4.60	1.57	2.14	Y

County	PBE 2009	PBE 2010	PBE 2011	PBE 2012	PBE 2013	PBE 2014	Pertussis Cases per 100k 2009	Pertussis Cases per 100k 2010	Pertussis Cases per 100k 2011	Pertussis Cases per 100k 2012	Pertussis Cases per 100k 2013	Pertussis Cases per 100k 2014
ALAMEDA	1.36%	1.24%	2.67%	1.65%	1.78%	1.54%	1.05	30.2	14.6	4.4	8.6	25.1
ALPINE	0.00%	0.00%	4.29%	10.53%	8.33%	0.00%	0	0.0	0.0	0.0	0.0	0.0
AMADOR	2.98%	3.86%	7.22%	7.72%	9.46%	2.61%	2.51	10.6	29.5	2.7	5.5	2.8
BUTTE	4.25%	5.15%	1.84%	5.75%	6.99%	5.96%	0.88	14.5	7.3	1.4	14.9	14.9
CALAVERAS	6.09%	6.20%	3.22%	10.64%	10.84%	8.33%	14.83	19.8	11.1	0.0	4.4	37.3
COLUSA	0.54%	1.35%	1.25%	0.74%	0.47%	0.50%	0	51.2	4.7	0.0	0.0	0.0
CONTRA COSTA	1.96%	2.13%	1.76%	2.19%	2.32%	1.90%	1.31	19.5	10.7	2.2	6.4	44.1
DEL NORTE	5.75%	7.30%	3.15%	10.96%	8.13%	7.55%	0	56.1	0.0	0.0	0.0	7.2
EL DORADO	5.84%	7.64%	1.26%	8.19%	9.16%	7.61%	1.07	29.8	6.1	1.6	2.2	19.6
FRESNO	0.98%	1.20%	1.13%	1.52%	1.62%	1.03%	2.07	59.0	6.2	1.7	4.6	40.9
GLENN	1.47%	0.42%	5.29%	1.50%	1.01%	0.96%	0	3.6	3.5	0.0	0.0	3.5
HUMBOLDT	10.25%	10.47%	2.06%	11.46%	11.87%	10.85%	8.95	43.1	11.1	0.7	3.7	110.5
IMPERIAL	0.30%	0.41%	3.21%	0.22%	0.64%	0.45%	0	5.1	1.7	4.5	1.7	5.6
INYO	1.34%	2.73%	1.83%	1.42%	1.03%	2.06%	0	43.2	0.0	5.3	0.0	0.0
KERN	1.50%	1.63%	9.76%	1.75%	2.69%	1.77%	0.12	44.7	5.8	0.2	3.6	18.8
KINGS	1.44%	1.26%	6.38%	0.76%	0.87%	0.81%	2.8	17.0	4.6	0.0	1.3	10.6
LAKE	3.68%	2.95%	5.88%	5.76%	4.88%	4.85%	0	7.7	4.7	3.1	4.7	4.7
LASSEN	3.05%	1.95%	12.18%	7.30%	5.56%	7.82%	0	2.8	0.0	0.0	0.0	15.3
LOS ANGELES	1.42%	1.58%	1.38%	1.88%	2.22%	1.62%	0.91	14.1	6.6	2.2	3.6	21.2
MADERA	1.06%	1.17%	6.07%	2.30%	2.17%	2.00%	3.16	79.3	5.3	0.0	6.5	30.7
MARIN	7.13%	7.15%	3.26%	7.83%	7.57%	6.45%	3.16	138.9	10.2	2.0	71.9	106.3
MARIPOSA	4.00%	2.98%	6.88%	11.68%	13.11%	14.29%	0	55.0	5.6	1.0	0.0	0.0
MENDOCINO	7.11%	7.35%	3.92%	8.71%	9.33%	6.30%	4.33	30.7	3.4	0.0	6.8	11.3
MERCED	0.57%	0.56%	16.30%	0.94%	1.07%	0.98%	1.87	51.2	10.4	0.0	0.4	3.4
MODOC	3.68%	1.65%	0.97%	3.48%	5.71%	2.70%	0	0.0	0.0	0.0	0.0	64.7
MONO	2.65%	3.31%	10.07%	4.76%	8.11%	10.81%	0	126.4	14.0	146.1	14.1	0.0
MONTEREY	1.40%	1.16%	3.08%	1.50%	1.66%	1.60%	0.23	31.7	9.0	4.0	11.5	30.4
NAPA	1.94%	2.41%	2.87%	3.86%	0.04%	3.18%	5.68	18.3	8.0	4.3	9.3	98.5
NEVADA	18.92%	17.72%	2.51%	22.44%	21.26%	21.55%	0	23.3	2.0	5.1	71.5	16.3
ORANGE	2.75%	2.67%	2.67%	3.03%	3.65%	2.99%	1.07	16.5	4.7	2.4	3.6	14.4
PLACER	5.00%	4.29%	4.29%	8.14%	7.68%	8.00%	2.05	22.8	5.3	3.1	23.6	33.4
PLUMAS	15.43%	7.22%	7.22%	9.31%	10.19%	6.71%	0	10.0	20.1	0.0	5.2	5.2
RIVERSIDE	1.53%	1.84%	1.84%	2.32%	2.88%	2.48%	1.56	21.3	7.5	2.0	3.5	20.7
SACRAMENTO	2.57%	3.22%	3.22%	4.32%	5.39%	4.54%	1.18	12.3	4.8	2.4	4.8	30.9
SAN BENITO	1.06%	1.25%	1.25%	0.77%	0.87%	1.23%	3.2	12.7	5.4	1.8	1.7	19.2
SAN BERNARDINO	1.19%	1.76%	1.76%	2.54%	2.86%	2.18%	0.33	8.9	5.6	2.6	1.9	9.9
SAN DIEGO	2.64%	3.15%	3.15%	3.88%	4.49%	3.46%	2.59	36.7	12.7	5.1	12.8	63.4
SAN FRANCISCO	1.60%	1.26%	1.26%	1.38%	1.64%	1.80%	2.58	17.5	8.6	3.6	7.1	15.4
SAN JOAQUIN	0.97%	1.13%	1.13%	1.01%	0.02%	1.13%	0.69	12.2	3.9	2.1	3.7	30.5
SAN LUIS OBISPO	3.92%	5.29%	5.29%	5.68%	8.26%	5.53%	0	137.5	5.6	5.2	6.3	16.6
SAN MATEO	1.85%	2.06%	2.06%	2.10%	2.26%	1.85%	1.36	26.5	8.0	3.1	14.0	17.4
SANTA BARBARA	3.01%	3.21%	3.21%	4.27%	4.72%	2.94%	4.88	15.6	4.2	2.6	6.5	27.8
SANTA CLARA	1.49%	1.83%	1.83%	1.69%	1.72%	1.57%	0.6	28.8	9.7	2.5	13.7	29.0
SANTA CRUZ	6.50%	9.76%	9.76%	9.61%	9.54%	9.35%	10.12	33.1	8.3	4.8	19.9	60.8
SHASTA	6.18%	6.38%	6.38%	8.33%	8.56%	7.53%	0	18.0	15.2	1.1	3.9	18.5
SIERRA	3.45%	5.88%	5.88%	0.00%	0.00%	0.00%	0	0.0	0.0	0.0	0.0	0.0
SISKIYOU	13.59%	12.18%	12.18%	12.16%	15.22%	6.08%	2.13	22.3	0.0	4.4	11.1	15.5
SOLANO	0.82%	1.38%	1.38%	1.55%	1.55%	1.80%	0.46	9.7	2.9	2.4	3.5	34.0
SONOMA	5.30%	6.07%	6.07%	6.33%	6.04%	5.54%	2.65	50.8	23.8	3.7	10.4	143.0
STANISLAUS	2.02%	3.26%	3.26%	4.06%	4.08%	3.25%	2.18	30.9	8.3	2.1	3.0	17.4
SUTTER	1.92%	6.88%	6.88%	8.55%	7.30%	5.83%	2.51	5.3	1.1	0.0	2.1	8.3
TEHAMA	3.27%	3.92%	3.92%	4.93%	4.24%	4.15%	1.55	15.8	1.6	0.0	0.0	59.9
TRINITY	7.61%	16.30%	16.30%	15.93%	18.80%	8.77%	0	0.0	0.0	0.0	0.0	44.6
TULARE	1.07%	0.97%	0.97%	1.26%	1.55%	0.96%	1.75	51.9	17.2	6.0	5.5	8.1
TUOLUMNE	13.06%	10.07%	10.07%	12.27%	15.41%	7.36%	0	258.0	7.3	1.8	3.7	29.5
VENTURA	2.21%	3.08%	3.08%	3.54%	3.46%	3.05%	0.35	5.1	19.6	1.8	4.3	41.5
YOLO	2.96%	2.87%	2.87%	3.63%	3.67%	3.23%	1.48	8.4	2.5	2.9	1.9	71.3
YUBA	0.84%	2.51%	2.51%	2.65%	2.56%	2.22%	1.27	4.1	0.0	1.4	5.5	13.7

Table 6: PBE and Pertussis Case Rates per 100,000 population by California county from 2009-2014. 2009 data only reflects cases reported from January 1 – September 7 of that year.