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Assessment of Clustering of Kindergarteners Not-Up-To-Date on Vaccines After Elimination of Personal Belief Exemptions in California

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An abstract of

A thesis submitted to the Faculty of the

James T. Laney School of Graduate Studies of Emory University

in partial fulfillment of the requirements for the degree of

Master of Science

in Epidemiology

2018

Abstract

Assessment of Clustering of Kindergarteners Not-Up-To-Date on Vaccines After Elimination of Personal Belief Exemptions in California

By Sundia Cassandra Pingali

In 2015, California implemented the most stringent new vaccination policy passed in more than 30 years, known as California Senate Bill 277 (SB277). This new law eliminated the option of a personal belief exemption to the mandated immunization requirements for entry to private and public schools. Prior research on the impact of SB277 has focused on the overall rates of vaccine exemptions in the state with little focus on the potential changes in spatial heterogeneity of kindergarteners who are not-up-to-date on their vaccines. This is the first study to examine the impact of SB277 on the clustering of and exposure to kindergartners who are not-up-to-date on their vaccines. Using data from the California Department of Public Health from 2000 to 2017 we assessed the clustering and spatial heterogeneity of not-up-to-date kindergartners. We also calculated two state-level measures of likelihood of exposure to not-up-to-date kindergarteners among other kindergartners: the aggregation index and the interaction index. The interaction index measures the probability of contact between a kindergartener who is up-to-date and a kindergartner who is not-up-to-date on their vaccines within the state, while the aggregation index measures the probability of contact between two not-up-to-date kindergarteners. The interaction index peaked at 8.23 in 2013 and fell to 1.35 two years after SB277 was implemented. Similarly, the aggregation index peaked at 27.09 in 2014 and fell to 8.94 in 2017. Our spatial analyses also indicated a reduction in the spatial clustering of not-up-to-date kindergartners, and decreasing not-up-to-date rates for many areas of the state after SB277 was implemented. Our results indicate that SB277 has been successful in reducing the clustering and exposure to kindergartners who are not-up-to-date on their vaccines in California. Reducing the aggregation and clustering of kindergartners who are not up-to-date on their vaccines helps to minimize the likelihood of disease outbreaks due to low vaccination coverage. Other states considering similar legislation can use SB277 as an example of the positive public health impact pro-vaccine legislation can have.

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Introduction

Large scale immunization programs such as school mandated immunization requirements are one of the most effective public health tools of the last century.[1] In the United States, school immunization programs have been essential to maintaining high levels of immunization coverage and low rates of vaccine-preventable diseases.[2] In recent years an increasing number of parents have expressed concerns about the potential for adverse effects due to receipt of a childhood vaccination.[3] This trend of vaccine hesitancy, particularly among parents of school aged children, threatens the herd immunity established by decades of mandatory school immunization programs and increases the potential for disease outbreaks via low vaccine coverage.[4]

Many U.S. states have recently considered new legislation pertaining to the mandatory vaccination requirements to prevent potentially serious disease outbreaks due to low vaccine coverage. In the 2016 legislative period, twenty-two bills addressing the mandatory vaccine schedule for school aged children were introduced in twelve different states.[5] In 2015, in order to curb increasing vaccine refusal rates in the state, California implemented the most stringent new vaccination law enacted in over 30 years, known as California Senate Bill 277 (SB277).[6] California is known to have substantial within-state heterogeneity of immunization coverage, and prior studies have shown that parents who refused or delayed vaccines for their child cluster spatially within the state.[7–9] These clusters of children with no or few vaccines weaken the herd immunity protection of their communities, putting the population at higher risk for outbreaks of vaccine-preventable diseases. SB277 was implemented in hopes of substantially increasing vaccine uptake in the state. Beginning in January 2016, parents in California with school aged children would no longer have the option of obtaining a personal belief exemption to the vaccination requirements for entry to private and public schools in California.[6] This new

restriction included parents who objected to immunizations for religious reasons. The law allowed students with a previously approved personal belief exemption to remain enrolled in school until they entered the next grade span at the 7th grade level. Students entering private or public school for the first time or those advancing to the 7th grade level needed to be fully immunized or obtain a conditional or medical exemption.[6] The passage of SB277 in California provides a unique opportunity to evaluate the impact of eliminating nonmedical exemptions in a large heterogeneous state. Given California's size and diverse population, lessons learned from the implementation of SB277 may be relevant to other states considering similar legislation.

Prior research on the impact of SB277 has focused on the overall rates of vaccine exemptions in the state with little focus on the potential changes in spatial heterogeneity of kindergartners who are not-up-to-date on their vaccines. It is essential to evaluate the impact of SB277 on the patterns of spatial heterogeneity of not-up-to-date kindergarten clusters to fully understand the effects of this stringent new policy on the clustering and likelihood of exposure to kindergarteners who are not-up-to-date on their vaccines. Our objective was to identify any changes in the spatial heterogeneity of not-up-to-date kindergarteners and the exposure to kindergartners who were not-up-to-date on their vaccines in the two years since SB277 was implemented in California. To investigate this issue, we used annual kindergarten vaccine exemption data collected by the California Health Department from the 2000 to 2017 school years. We assessed clustering of schools with high rates of children who were not-up-to-date on their immunizations and the changes in the spatial heterogeneity of these clusters. We also calculated multiple measures of exposure to not-up-to-date kindergarteners to assess changes in the prevalence and aggregation of not-up-to-date kindergarteners within schools from 2000 to 2017. This is the first study in which the impact of SB277 on the spatial heterogeneity of not-up-

to-date kindergarteners has been evaluated, and lessons learned from this analysis will be pertinent to other states considering implementing similar legislation.

Methods

Data Sources

Kindergarten enrollment and vaccine exemption data were available from the California Department of Public Health (CDPH) for the 2000-2017 school years.[10] Each year, schools in California with kindergarten programs report enrollment levels and total number of vaccine exemptions in the school to CDPH. Currently, there are five mechanisms of school entry for kindergarteners who are not-up-to-date on one or more of the required immunizations as defined by CDPH. From 2000-2014, the three methods of entry were personal belief exemptions, permanent medical exemptions, and conditional entrance. Conditional entrants are children who have not received all required doses of the mandated immunizations or had a temporary medical exemption to one or more of the required doses. In recent years, two new categories have been added by CDPH: overdue and other. In 2015, the "overdue" category was created to identify children who were overdue for one or more required immunizations but did not have a personal belief exemption or permanent medical exemption, and were not a conditional entrance. In 2016, CDPH created the "other" category which we have termed "not-subject-to-immunization-requirements" in our analysis. These students are exempt from the immunization requirements because they attend home-based private schools or an independent study program without classroom-based instruction; such programs are exempt from SB277.[6] Kindergarteners with all required vaccinations at school entry are categorized as up-to-date.[11] The school entry mechanisms and the years they were in effect are summarized in Table 1.[12]

Our main outcome variable was a summary variable called "not-up-to-date vaccination rate". This variable represented the proportion of students in each school that were not-up-to-date on their vaccination requirements each year. This school-level variable was calculated as the sum of all kindergartners not-up-to-date under the various entry mechanisms, divided by the kindergarten enrollment in the school for the school year. The entry mechanisms included in the not-up-to-date calculations for each year are provided in Table 2.

We restricted our clustering analysis to the two school years before and after SB277 was implemented (2014-2016 vs. 2016-2018). We only had two years of data after the law was implemented so we chose to pool the two-year data in the pre-law and post-law periods to temporally stabilize the rates in the analysis. All other analyses used all the data available from the 2000-2017 school years. Institutional review board approval for this study was obtained through Emory University. All analyses were performed by using R v3.4.0., SaTScan v.9.4, and ArcGIS v10.6.[13–15]

Imputation Data

The CDPH made major changes to the publicly-available school-level vaccination data for the 2016 and 2017 school years. The first major change was that vaccination status data of all students in schools having fewer than 20 incoming kindergarteners was fully suppressed; previously, only data from schools with fewer than 10 students were suppressed [16]. The second major change was to left censor small counts in schools with 20 or more students. The censoring rules were designed to protect the vaccination status of individual students and, in cases where all students were fully up-to-date, to protect the vaccination status of each student. The censoring rules are implemented using a set of threshold percentages based on a school's total enrollment.

The specific threshold percentages for censoring small counts are ≤ 5% for schools with 20-49 students, ≤ 2% for schools with 50-99 students, and ≤ 1% for schools with 100 or more students. Using the threshold percentages and enrollment information, we calculated the potential actual values for schools having suppressed data: 20-39 students (0-1), 40-49 students (0-2), 50-199 students (0-1), 200-299 students (0-2), 300-399 students (0-3). For example, if a school with 35 students had a suppressed entry, the actual value of that suppressed entry could be 0 or 1 based on the censoring rules (but not 2 or more).

We used a multiple imputation approach to estimate the number of not-up-to-date students at each school with censored data. The imputation approach leverages the geographic location of the schools in the school-level data in combination with the county-level counts of not-up-to-date students and the statewide counts of not-up-to-date students attending public and private schools, which are provided in the CDPH yearly summary files [17]. The approach can be considered a constrained allocation approach in that it uses information from more course data (county- and state-level) to allocate missing counts to the schools with suppressed information. First, the count of not-up-to-date students censored in each county was identified by subtracting the county-level count of not-up-to-date students (in the summary file) from the sum of uncensored not-up-to-date students in the school-level data. Then, the number of censored not-up-to-date students in the county's public and private schools was estimated using the total students enrolled in that county's public and private schools and the ratio of not-up-to-date students in public and private schools at the state level. Next, the county-level censored not-up-to-date students were "allocated" back to the schools with censored values. The number of not-up-to-date students allocated to each censored school were based on a randomly generated not-up-to-date count created using a random draw from a Poisson distribution based on the overall

rate of suppressed not-up-to-date students within the county (conducted separately for public and private schools) and the enrollment of each school. In application, the approach iterated through each county separately, and for each county, iterated through the censored not-up-to-date students until all were allocated to the schools. The stochastic elements of this approach were introduced in the process of generating the not-up-to-date counts for each school and in choosing the order in which schools were allocated the not-up-to-date student(s) as the approach iterated through all schools in each county.

The imputation approach was implemented in a manner that the imputed not-up-to-date student counts were consistent with the censoring rules in the original data (i.e., the imputed value for the number of not-up-to-date students at a particular school could only be one of the potential censored values for that school based on its enrollment). Furthermore, the approach preserved the known information about the number of not-up-to-date students at the state- and county-level. First, the state-level number of not-up-to-date students was preserved in the imputed school-level data. Second, the state-level numbers of not-up-to-date students in public and private schools were both preserved in the imputed school-level data. Third, the number of not-up-to-date students in each county was preserved in the imputed school-level data. In total, 5,000 imputations were performed, of which 500 were used for analysis.

Interaction and Aggregation Indices

To measure the likelihood that a kindergartner would be exposed to other children who were not up to date with their vaccines at their school we used the interaction index and aggregation index. We implemented methods described by Buttenheim et al to calculate the interaction and aggregation indices at the state-level.[18] These indices were first used in the literature to estimate the exposure of racial minorities to a majority population in residential segregation studies, but

have been used previously to assess vaccine exemption contact in California.[19] The interaction index measures between-group contact and finds the probability that kindergarteners who were up-to-date on their vaccines would have contact with kindergarteners who were not up-to-date. The index is calculated as the proportion of not-up-to-date kindergarteners in each school weighted by the school's proportion of up-to-date kindergarteners, summed across all schools:

$$\text{Interaction Index} = \sum_{i=1}^{N} \left[\left(\frac{a_i}{A} \right) \left(\frac{x_i}{ki} \right) \right] * 100,$$

wherein a_i is the number of up-to-date kindergartners in school i, A is the total number of up-to-date kindergartners for all schools, x_i is the number of not-up-to-date kindergartners in school i, k_i is the total kindergarten enrollment in school i, and N is the number of schools in the state. A higher interaction index indicates that kindergartners who are up-to-date on their vaccines are more likely to encounter a kindergartener who is not up-to-date at their school. The interaction index has a maximum of the proportion of not-up-to-date kindergartners in the state. The interaction index can be thought of as a measure of disease risk for the kindergarteners who are up-to-date on their vaccines.

The aggregation index measures within-group contact and calculates the probability that a kindergartner who is not-up-to-date on their vaccines would have contact with another kindergartner who is also not-up-to-date. The index is calculated as the proportion of not-up-to-date kindergarteners in each school weighted by the school's proportion of not-up-to-date kindergartners, summed across all schools:

$$\text{Aggregation Index} = \sum_{i=1}^{N} \left[\left(\frac{x_i}{X} \right) \left(\frac{x_i}{ki} \right) \right] * 100,$$

where x_i is the number of not-up-to-date kindergartners in school i, X is the total number of not-up-to-date kindergartners for all schools, k_i is the total kindergarten enrollment in school i, and N is the number of schools in the state. A higher aggregation index indicates that kindergartners

who are not up-to-date on their vaccines are more likely to encounter another kindergartener who is not up-to-date at their school. The aggregation index runs near 0 asymptotically to 100. A higher aggregation index indicates that kindergartners who are not-up-to-date with their vaccines are more likely to attend school with other not-up-to-date kindergartners, and that there is a higher potential for a disease outbreak to occur due to the increased aggregation of susceptible kindergartners.[18]

Kriging

Using school data from 2000-2017, we used kriging tools in ArcMap v10.6 to create predicted not-up-to-date exemption rates for the whole state.[20] Schools in the 99th percentile for not-up-to-date vaccination rates were dropped before creating the predicted surface because kriging is known to be influenced by extreme values (Table 4).[21] We used ArcMap v10.6 to map the predicted not-up-to-date vaccination rates (predicted per 100) by year from 2000-2017.[14]

Clustering Analysis and Quantifying Change in Heterogeneity

The goal of the clustering analysis was to examine the number and location of high not-up-to-date rate clusters before and after the law was implemented. We also compared the odds of a school being located within a high rate not-up-to date cluster in the two years before SB277 was implemented compared to the two years after the law was in effect to assess potential change in spatial heterogeneity of clustering. We termed the two years before the law as “pre-law” and the two years after SB277 was termed “post-law”. We took the mean of not-up-to-date variable and kindergarten enrollment across the two years in the pre-law period and the post-law period, and excluded any schools which were not present for the entire pre-law period or post-law period

from the analysis. Of the 10,391 schools open in California from 2000 to 2017, we dropped 3,163 schools because they were not open in either the post-law period and/or the pre-law period.

Kulldorff's scan statistics were used to identify spatial clusters of high not-up-to-date rates from the two years before and the two years after SB277 was implemented. The within-school exemption rates are relatively stable from year to year (in absence of new vaccine legislation or interventions) meaning the clustering of vaccine exemptions is a long-term phenomenon at the school level.[22] Therefore, we chose a purely spatial Poisson model for identifying school-level not-up-to-date clusters. Using Kulldorff's scan statistics in the SaTScan v9.4 provided the number and location of the Poisson spatial clusters in the state.[15] SaTScan randomly generates data sets of not-up-to-date rates under a known null hypothesis and potential clusters are identified using a moving circular window that scans each census tract centroid.[15] A maximum likelihood ratio is calculated for each potential cluster, and the observed events are compared to the distribution of simulated events.[15] The simulated data sets follow a discrete Poisson distribution because our data includes counts of not-up-to-date kindergarteners in each school and uses the kindergartener enrollment as the population denominator. The upper limit of the cluster size was set to 50% of the kindergarten enrollment used in the analysis because this allowed for the largest applicable cluster size without preselection bias.[9]

The post-law period included imputation data so we ran the clustering analysis 500 times to account for the multiple realizations of the data using the imputations. Using the clustering data, we performed a chi-square analysis to assess the odds of being in a high not-up-to-date rate cluster in the two years before the law compared to the odds of being in a high not-up-to-date rate cluster in the two years after SB277 was implemented. The chi-square analysis was

performed on each of the 500 replicates from the cluster analysis, and the mean and median odds ratios were reported with error bounds based on the imputation data. The clusters in the pre-law and post-law periods were mapped using ArcMap v10.6.

Results

From 2000 to 2017 there were 10,391 schools open in California which reported kindergarten immunization data to CDPH. Around 500,000 kindergarteners are enrolled in about 6,000 public and private schools every year in California. Less than 10% of the schools which reported data to CDPH were private schools. Each year about 250 schools refused to report immunization data to CDPH and the majority were private schools. From 2000-2017, a higher proportion of kindergarteners in public schools were reported as up-to-date on their vaccines, compared to public schools.[11,23]

Interaction and Aggregation Indices

The interaction index climbed from a starting point of 6.62 in 2000 to a peak of 8.23 in 2013 (Figure 1). This means that the average up-to-date kindergartener in California in 2013 was enrolled in a school where the not-up-to-date vaccination rate was 8.23 per 100 kindergartners. The interaction index decreased from 5.96 in 2015 (year before SB277 was implemented) to 1.28 in 2016, and 1.35 in 2017. After SB277 was implemented an up-to-date kindergarten was much less likely to interact with kindergartners who were not-up-to-date with their vaccines in their school.

The aggregation index followed a similar pattern as the interaction index, with a starting point of 20.28 in 2000 to a peak of 27.09 in 2014. After SB277 was implemented the aggregation index fell to 7.57 in 2016 and 8.94 in 2017, implying that after the law was implemented not-up-

to-date kindergartners were much less likely to interact with other not-up-to-date kindergarteners (Figure 1).

Kriging

A steady yearly increase in the not-up-to-date vaccination rate is evident from 2000 to 2015 throughout most areas of California. Northern California had the highest levels of predicted not-up-to-date rates in every year with a predicted not-up-to-date rate of 10 not-up-to-date kindergarteners per 100 kindergartners. From 2007-2015 Southern California also had large pockets of high predicted not-up-to-date rates. After SB277 was implemented, most areas experienced a decrease in not-up-to-date rates with many areas in Southern California falling from a not-up-to-date rate of 10 per 100 to a rate of 2.51-5.00 per 100. Much of the state now has predicted not-up-to-date rates below 5 not-up-to-date kindergarteners per 100. Northern California still had the highest predicted not-up-to-date rate, and experienced little change after SB277 (Figure 2) was implemented.

Clustering Analysis and Quantifying Change in Heterogeneity

In the pre-law period (2014-2016), there were 143 clusters of high rate not-up-to-date clusters identified by SaTScan. The number of clusters dropped to 12 or fewer clusters in the post-law period in each of the 500 replicates. In the pre-law period the largest clusters were in Northern California with one extremely large cluster spanning the entire width of Northern California. There were many smaller clusters located throughout Central and Southern California. In the post-law period, all the clusters in Southern California and most of the clusters in Central California were eliminated. However, the large clusters in Northern California remained and only the largest cluster reduced slightly in size (Figure 3).

The mean of the 500 odds ratios calculated from the results of the 500 chi-square analyses was 7.37 and the median was 6.71, and 95% of the odds ratios fell between 1.90 and 15.54. Schools which were in a cluster before the law were 7 times more likely to be a cluster after the law than schools which were not in cluster before the law (Table 3).

Discussion

This study provides a unique understanding of the changes in clustering of kindergartners who are not-up-to-date on their vaccines in California after the elimination of personal belief exemptions. It also provides a look at the change in the likelihood of exposure to kindergartners who are not-up-to-date on their vaccines within schools. We found evidence of a decrease in not-up-to-date rates and the spatial clustering of high rate not-up-to-date clusters after SB277 was implemented. There were notable improvements in the not-up-to-date rates in the southern and central areas of the state. Moreover, we found that schools which were in a cluster before the law were 7 times more likely to be in a cluster after the law compared to schools which were not in a cluster before the law. Only 71 schools joined a high rate not-up-to-date cluster after SB277, while 2,104 schools were no longer located within a cluster. We also identified that there was a sharp decrease in the level of exposure among kindergarten students in California to other kindergarteners who were not-up-to-date on their vaccines as assessed by the interaction and aggregation indices. Our study indicates that SB277 has been very effective at reducing not just the number but also the clustering of not-up-to-date kindergartners in California in the two years since its implementation. Future studies could focus on exploring the characteristics of the persisting high not-up-to-date rate clusters identified in Northern California in the spatial analyses.

The study included a few limitations. First, our data was limited to schools with 10 or more students in the school. CDPH does not collect vaccination data from schools with less than 10 students because these schools are likely to be family home schools.[9] Schools with fewer than 10 students may have been more likely to have high not-up-to-date rates which may have caused the not-up-to-date rates to be underestimated particularly before SB277 was implemented. Additional analyses of immunization rates among children in small home schools in California should be explored. A second limitation is that the not-up-to-date variable does not capture the entire vaccination status of the kindergartener. For example, a child may have a conditional exemption because they have not fully completed a series of one vaccine, but they do have some of their vaccinations. We know that these students are lacking at least one immunization due to their conditional entrance, but we do not know how many immunizations they lack in total. This may have affected the disease risk if kindergartners who were not-up-to-date had the majority but not all vaccines making a disease outbreak less likely. Future analyses could explore the changes in vaccination coverage for different vaccines after SB277. A final limitation is that we only have two years of data in the post-law period for the analyses making it difficult to examine trends in the post-law period. However, all of our analyses indicated that SB277 has been very effective at reducing the number of not-up-to-date kindergartners in the state, and a previous analysis from Washington state showed that post-implementation trends quickly stabilized after the implementation of new vaccination legislation.[24]

Conclusion

This is the first study in which the spatial heterogeneity of not-up-to-date kindergarteners has been evaluated after the elimination of the personal belief exemption option to the school immunization requirements in California. More than ten other states have considered similar

legislation to restrict or eliminate access to personal belief exemptions in the 2016 legislative period alone.[5] Other states considering similar legislation in the future will be able to use analyses such as this to support the need and the effectiveness of eliminating personal belief exemptions. Our findings indicate that laws such as SB277 which eliminate personal belief exemptions to the mandated immunization schedule can substantially reduce the clustering and exposure to kindergartners who are not-up-to-date on their vaccines, which in turn could reduce the likelihood of disease outbreaks due to low vaccination coverage.

Acknowledgements

This research was supported by grant R01AI125405 from the National Institutes of Health (NIH). The funding source had no role in the design and conduct of the study; management, analysis, and interpretation of the data; or preparation of the final manuscript.

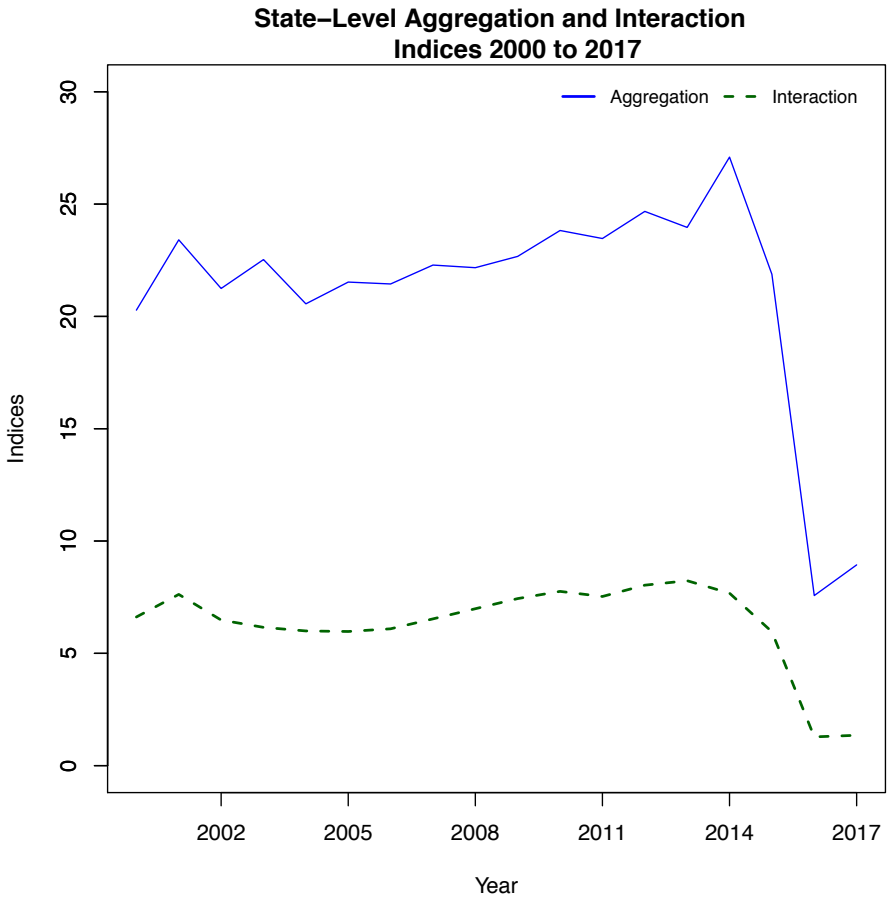

Figure 1. Aggregation Index (solid blue line) and Interaction Index (dashed green line) in California 2000-2017. The aggregation index runs from 0 to 100 and is the average not-up-to-date rate for up-to-date kindergarteners. The maximum value of the interaction index is the proportion of not-up-to-date kindergartners in the population and can be interpreted as the average not-up-to-date rate for not-up-to-date kindergartners.

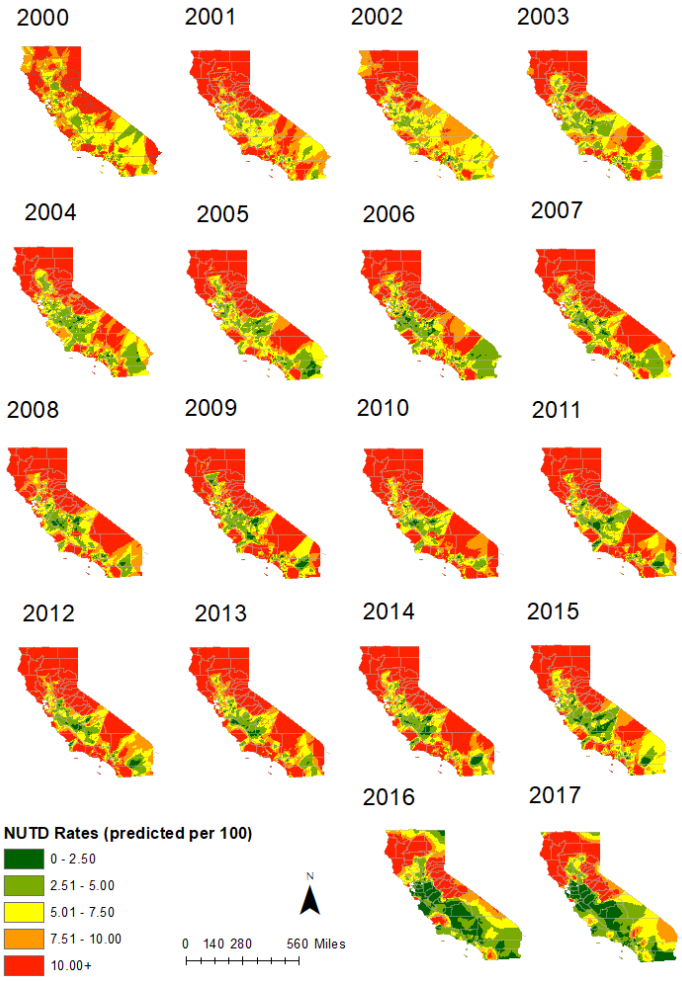

Figure 2. Predicted not-up-to-date (predicted per 100) rates in California 2000-2017.

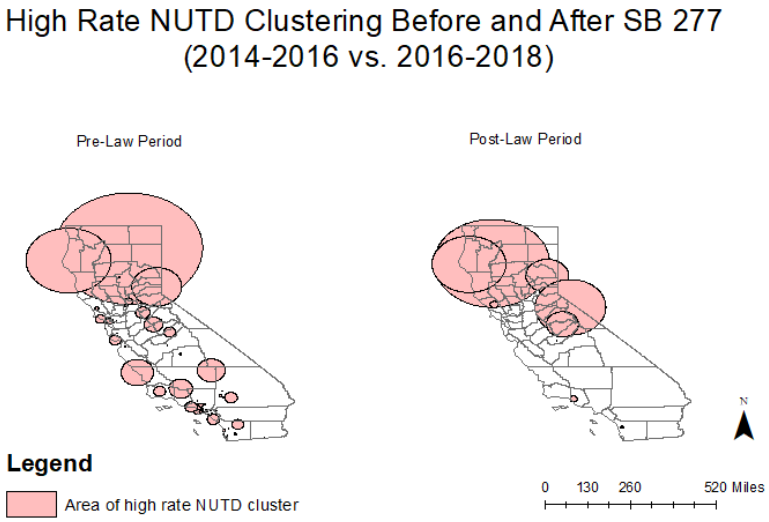

Figure 3. Clustering of high not-up-to-date rates in California pre-law (2014-2016) and post-law (2016-2018) periods.

Table 1. School entry mechanisms for kindergarteners not-up-to-date on one or more required vaccinations in California. Definition is a summary of the circumstances when the mechanism is used. Years available is when the particular requirements were in effect (beginning in 2000).

Mechanism Type	**Definition**	**Years Available**
Personal belief exemption	Nonmedical exemption based on parents' personal or religious beliefs	2000-2015
Medical exemption	Exemption due to a contraindication to vaccination	2000-2015
	Exemption due to a contraindication to vaccination with a doctor's signature	2016-current
Conditional entrance	a) Started but has not completed one or more series of required vaccinations or b) Temporary medical exemption	2000-current
Not Subject to Immunization Requirements	a) Attend home-based private schools or an independent study program without classroom-based instruction b) Cannot be denied access to special education services due to immunization status	2016-current
Overdue	Not-up-to-date on one or more series of required vaccines, but does not have a personal belief or medical exemption, is not exempt, or does not meet the requirements for conditional entrance	2015-current

Table 2. Exemption types included in the not-up-to-date variable by year.

School Year	**Exemption Types in the Not-Up-to-Date Variable**
2000-2015	Personal Belief Exemptions + Personal Medical Exemptions + Conditional Entrance
2015-2016	Personal Belief Exemptions + Personal Medical Exemptions + Conditional Entrance+ Overdue
2016-2017	Personal Belief Exemptions + Personal Medical Exemptions + Conditional Entrance+ Overdue + Not Subject to Immunization Requirements
2017-2018	Personal Belief Exemptions + Personal Medical Exemptions + Conditional Entrance+ Overdue + Not Subject to Immunization Requirements

Table 3. Table of school counts of cluster membership before and after the law. Table indicates the number of schools which were in a cluster of high not-up-to-date rates in the pre-law period and/or in the post-law period.

		In a cluster "pre-law"	
In a cluster "post-law"		Yes	No
	Yes	224	71
	No	2,104	4,829

Table 4. Count of schools in 99th percentile of not-up-to-date vaccination rate dropped in kriging analysis.

Year	Number of Schools Dropped
2000	73
2001	74
2002	74
2003	73
2004	74
2005	74
2006	73
2007	73
2008	72
2009	71
2010	71
2011	72
2012	72
2013	69
2014	71
2015	72
2016	47
2017	47

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