

# **HHS Public Access**

Author manuscript *Vaccine*. Author manuscript; available in PMC 2016 November 17.

Published in final edited form as:

Vaccine. 2015 November 17; 33(46): 6250-6256. doi:10.1016/j.vaccine.2015.09.075.

# MMR vaccination status of children exempted from school-entry immunization mandates

Alison M. Buttenheim<sup>a</sup>, Karthik Sethuraman<sup>b</sup>, Saad B. Omer<sup>c</sup>, Alexandra L. Hanlon<sup>a</sup>, Michael Z. Levy<sup>b</sup>, and Daniel Salmon<sup>d</sup>

Alison M. Buttenheim: abutt@nursing.upenn.edu; Karthik Sethuraman: k.seth1993@gmail.com; Saad B. Omer: somer@emory.edu; Alexandra L. Hanlon: alhanlon@nursing.upenn.edu; Michael Z. Levy: mzlevy@mail.med.upenn.edu; Daniel Salmon: dsalmon@jhsph.edu

<sup>a</sup>Department of Family and Community Health, School of Nursing, University of Pennsylvania. 235L Fagin Hall, 418 Curie Boulevard, Philadelphia, PA 19104 USA

<sup>b</sup>Department of Biostatistics and Epidemiology, Perelman School of Medicine, University of Pennsylvania. 714 Blockley Hall 423 Guardian Drive Philadelphia, PA 19104-6021 USA

<sup>c</sup>Global Health and Epidemiology, Rollins School of Public Health, Emory University. Claudia N Rollins Bldg 7017. 1518 Clifton Rd, Atlanta, GA 30322 USA

<sup>d</sup>International Health, Bloomberg School of Public Health, Johns Hopkins University. 615 N. Wolfe Street Room W5035 Baltimore, Maryland 21205 USA

# Abstract

**BACKGROUND**—Child immunizations are one of the most successful public health interventions of the past century. Still, parental vaccine hesitancy is widespread and increasing. One manifestation of this are rising rates of nonmedical or "personal beliefs" exemptions (PBEs) from school-entry immunization mandates. Exemptions have been shown to be associated with increased risk of disease outbreak, but the strength of this association depends critically on the true vaccination status of exempted children, which has not been assessed.

**OBJECTIVE**—To estimate the true measles-mumps-rubella (MMR) vaccination status of children with PBEs.

**METHODS**—We use administrative data collected by the California Department of Public Health in 2009 and imputation to estimate the MMR vaccination status of children with PBEs under varying scenarios.

**RESULTS**—Results from 2009 surveillance data indicate MMR1/MMR2 coverage of 18–47% among children with PBEs at typical schools and 11–34% among children with PBEs at schools with high PBE rates. Imputation scenarios point to much higher coverage (64–92% for MMR1 and

Correspondence to: Alison M. Buttenheim, abutt@nursing.upenn.edu. CONFLICT OF INTEREST: None.

**Publisher's Disclaimer:** This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

25–58% for MMR2 at typical schools; 49–90% for MMR1 and 16–63% for MMR2 at high PBE schools) but still below levels needed to maintain herd immunity against measles.

**CONCLUSIONS**—These coverage estimates suggest that prior analyses of the relative risk of measles associated with vaccine refusal underestimate that risk by an order of magnitude of 2–10 times.

#### Keywords

Immunization; Imputation; Measles; Measles Mumps Rubella Vaccine; Primary Schools; Vaccination

### INTRODUCTION<sup>1</sup>

Following more than a decade of low measles incidence in the United States, reported cases increased from 37 in 2004 to 668 in 2014 [1, 2]. The "Disneyland" outbreak in late 2014 spread from southern California to 7 states and 2 countries [3]; by April 2015, 169 cases from 5 outbreaks had been recorded [4]. These recent outbreaks suggest that herd immunity against measles is compromised in the United States.

Assessing herd immunity and outbreak risk requires accurate immunization surveillance data. The prevalence of nonmedical exemptions (NMEs) from state-mandated immunizations is commonly used as a measure of modifiable gaps in immunization coverage for school-aged children. News coverage of the Disneyland outbreak used NME rates to report "vaccine coverage" or "undervaccination" [5–12]. Published studies investigating parental vaccine refusal and its relationship to outbreak risk use exemptions as a primary outcome measure [13, 14] or as a proxy for vaccination rates [15–21].

While higher exemption rates have been shown to be associated with disease outbreak [15, 16, 22–25], the strength of this association theoretically depends on the true vaccination status of exempted children. Prior studies correlating exemption prevalence or clustering with outbreaks assume that exempted children are unvaccinated. If these children are in reality partially or fully vaccinated, then the relative risk associated with vaccine refusal is *underestimated* due to overestimation of the denominator for incidence estimates among unvaccinated children [24, 25]. At the same time, school-level practices for recording student immunization histories or encouraging parents to claim an exemption when medical records cannot be located may *overstate* the relative risk associated with NMEs, as exempted children in both scenarios may have received more vaccine doses than school immunization records show. NME rates can therefore misestimate outbreak risk in both directions.

Only 2 prior studies have attempted to assess the vaccination status of exempted children. The first, based on parental report, found that among exempted children in 4 states, 22% were fully vaccinated, 7% had medical contraindication, 17% had received no vaccines, and

<sup>&</sup>lt;sup>1</sup>Abbreviations: MMR Measles, mumps, rubella; CDPH California Department of Public Health; CSIR California School Immunization Record; KRS Kindergarten Retrospective Survey; NME Non-medical exemption; PBE Personal beliefs exemption; CDC Centers for Disease Control and Prevention; OOB Out-of-bag.

Vaccine. Author manuscript; available in PMC 2016 November 17.

53% were partially vaccinated [26]. The second, based on data from the Arkansas Department of Health on exemption request types, found that 71% of exemption requests were for all vaccines, 9% were for 2+ vaccines, and 20% were for a single vaccine [27]. Neither of these studies, however, reviewed children's medical records to confirm vaccination status.

The purpose of this study therefore is to provide estimates of the true vaccination status of children with NMEs. We focus specifically on measles vaccination in California for 3 reasons: the recent widespread measles outbreaks in California and elsewhere [3, 4]; the high herd immunity threshold of measles (up to 88–95% of the population needs to receive 2 doses of the Measles-Mumps-Rubella (MMR) vaccine to maintain herd immunity [28, 29]); and the controversy surrounding the purported link between the MMR vaccine and autism, which has remained a persistent driver of parental vaccine refusal [30]. Using data routinely collected by the California Department of Public Health (CDPH), we use imputation methods to estimate the MMR coverage status of California kindergarteners with NMEs. We hypothesize that the majority of children with exemptions are at least partially vaccinated with MMR. We further hypothesize that exempted children at schools with higher exemption rates have received fewer doses of MMR than exempted children at schools with average exemption rates; this hypothesis is motivated by the assumption that schools with higher exemption rates reflect a parent population that has stronger anti-vaccine convictions and does not vaccinate, while schools with lower exemption rates reflect a parent population that may at least partially or fully vaccinate their children but exempt due to convenience.

# MATERIALS AND METHODS

#### Data and measures

To enroll a child in kindergarten, parents in California must provide evidence of immunization, file a medical exemption (requiring health care provider documentation) or file a non-medical exemption (called a "personal beliefs exemption" or PBE in California) [31, 32]. Prior to 2014, a PBE was obtained by signing an affidavit on the California School Immunization Record (CSIR). During kindergarten registration, school staff (usually a registrar, health clerk, or nurse) transfer immunization histories from medical records provided by parents to the CSIR.

We use data from the Kindergarten Retrospective Survey (KRS) and the Selective Review (SR), conducted by the California Department of Public Health (CDPH) Immunization Branch to monitor immunization and exemption tracking. The KRS provides estimates of kindergarten immunization coverage from a stratified random sample of 2–3% of the more than 8,000 schools in the state with kindergartens. Local health departments visit schools in person and record data from the CSIR of every sixth student, including dates of receipt for each required vaccine dose and limited demographic data. Given rising rates of PBEs in California, the CDPH added two additional student samples to the 2009 KRS (KRS09): (1) All kindergarteners with PBEs from the stratified random sample of 256 schools; and (2) all children with PBEs from the 50 schools with the highest number of kindergarten PBEs in the state. The SR, conducted on the same sample of schools as the KRS, validates school-level reporting of immunization coverage and assesses school policies and procedures for

tracking exemptions over the course of the school year and in the case of an infectious disease outbreak (see Table 1 for SR questions on school immunization tracking policies and procedures). This study was approved by the Institutional Review Board of the University of Pennsylvania.

#### Analytic approach

To estimate MMR coverage, we use immunization dates recorded on the CSIR by school staff and collected in the KRS. As noted above, these data are obtained directly from the student's medical records provided by the parents, and are not obtained from the California state immunization registry. Many exempted kindergarteners in the KRS dataset have no dates recorded for some or all state-mandated vaccine doses; in fact, the modal number of reported vaccine doses among exempt kindergarteners is 0, in contrast to up-to-date kindergarteners who have 18–19 doses reported. A missing date on the CSIR may indicate that the child has truly not received that vaccine dose, or that the child has received the dose but the date of immunization was not recorded on the CSIR. This could occur primarily for 2 reasons: (1) the parent did not provide any vaccine records to the school when seeking an exemption (although provision of existing vaccine records is required under California's exemption law); or (2) the vaccine records provided by the parent were incomplete for some immunizations. Coverage estimates based on the KRS09 are therefore likely an unrealistic *lower* bound of MMR coverage among exempted students.

To address this high degree of missingness, we employ a stratified multiple imputation scheme. We divide exempted kindergarteners into 2 groups: those with 1 or more vaccine doses noted in the CSIR ("partial"), and those with no vaccine doses recorded on the CSIR ("blank"). We begin the imputation process with the partial stratum by creating an indicator variable for the status of each MMR dose where 1 = vaccination date recorded on the CSIR, otherwise missing. To successfully impute, we convert missing MMR status indicators to 0 (where 0 = no vaccine dose received) for some children using the following algorithm:

- 1. If the CSIR indicated that a California Immunization Record (CIR), a California state immunization form (IZ), or a CDPH immunization form was presented, we assume that a blank MMR date indicates that the child did not receive the vaccine.
- 2. If the exempted kindergartener received any other vaccine dose at 12–17 months old (for MMR1) or at 45–65 months old (for MMR2), we assume the child is unvaccinated for MMR. For example, if a child's status for MMR1 is unrecorded and the child received another vaccine dose at 12 months old, we convert the blank MMR1 status indicator to 0 (no vaccine dose received). This assumption is informed by the CDC/ACIP recommended immunization schedule, which includes a first dose of MMR at 12–15 months and a second dose at 4–6 years [33], as well as other doses at the same ages.
- **3.** Because all kindergarteners observed in the dataset only have MMR2 immunization conditional on MMR1 immunization, we further assume that a kindergartener unvaccinated for MMR1 is unvaccinated for MMR2.

Having converted some MMR1 and MMR2 status indicators to 0 (unvaccinated), we then perform a multiple imputation over all children with partial records using missForest, a nonparametric imputation scheme that predicts missing values by training a random forest on the observed values in the dataset [34, 35]. missForest is a good alternative to other parametric imputation schemes (such as MICE) as it does not require any assumptions about the distribution of variables; and is appropriate for high-dimensional data with mixed (continuous and categorical) data [34, 35]. The imputation algorithm includes additional child-level factors including the status of other vaccine doses, race/ethnicity, and type of immunization record provided to complete the CSIR; and school-level factors including number of PBEs, number of missing vaccination doses among exempted children, school immunization and surveillance policies, and proportion of students eligible for free or reduced-price lunch as a proxy for school-level socioeconomic status (see Table 1 for the complete list of factors). The imputation procedure predicts MMR1 and MMR2 vaccination status for each child with a partial record; reports "out of bag" (OOB) error, the probability that the random forest model misclassified a child; corrects for imputation error through a permutation approach; and accounts for binomial variability by resampling the observed and imputed values [35]. We repeat the imputation process and non-parametrically sample a large number of imputation sets to create robust 95% confidence intervals.

To address the remaining exempt kindergarteners with no recorded vaccine doses, we construct 3 scenarios in which we assume that these kindergarteners' MMR1 and MMR2 status is the same as 1) the *least-vaccinated* partially-recorded exempt kindergartener; 2) the mode of the partially-recorded exempt kindergarteners; or 3) the most-vaccinated partiallyrecorded kindergartener at that child's school. If an exempt kindergartener with unrecorded MMR1 and MMR2 doses does not attend school with a partially-recorded exempt kindergartener, we take the kindergartener to be unvaccinated in the first scenario and vaccinated in the second and third scenarios. The first and third scenarios provide upper and lower bounds respectively on the coverage of unrecorded kindergarteners and the second scenario provides a reasonable median estimate. To obtain an estimate of MMR1 and MMR2 coverage across all exempted individuals, we combine the results of the imputation with the results of the scenario analyses above and report it with accompanying 95% confidence intervals and by subsample. For policy relevance, we also calculate school-level MMR coverage rates for 3 groups of children: those with 0, 1 and 2 doses of MMR vaccine. All statistical analyses were conducted in R version 3.02 (The R Foundation for Statistical Computing).

# RESULTS

The KRS09 stratified random sample included 2,659 students from the every-sixth-student sample (including 15 kindergarteners with PBEs) plus an additional 247 kindergarteners with PBEs from 103 schools in the sample with at least 1 PBE. The KRS09 high-PBE sample included 1,107 kindergarteners with PBEs from 50 schools (Table 2). Some key differences emerge across the 2 subsamples: The average school-level PBE rate for exempted children in the random sample of schools is 10%; in the high-PBE schools, it is 49%. In other words, the average exempted kindergartener in California who attended a high-PBE school in 2008–09 was in a kindergarten cohort in which half the students had an

exemption from school-mandated vaccines; the comparable exempted child at a typical school in California was in a school environment where only 1 in 10 kindergarteners was exempted. For both subsamples, around half of exempted students reported no vaccine doses on the CSIR. Twice as many exempted children from randomly-selected schools produced California Immunization Records at the time of kindergarten enrollment compared to exempted children from high-PBE schools (31% vs. 16%). Reported dose-specific coverage of mandated vaccines ranged from a low of 1% for Varicella 2 to a high of 54% for DTaP2. MMR1 and MMR2 coverage rates for exempted children were 47% and 18% in the random sample and 34% and 11% respectively in the high-PBE sample.

MMR1 and MMR2 coverage rates estimated from the imputation scenarios are shown in Table 3. As hypothesized, MMR coverage rates for exempted students vary by school subsample. Imputed MMR1 coverage in the random sample ranges from 64% (minimum scenario) to 92% (maximum scenario); the comparable range in the high-PBE sample is 48–90%. For MMR2, coverage is much lower: only 25–58% of exempted children in the random sample and 16–63% of students at high-PBE schools are estimated to have received MMR2. Across both vaccine doses and samples, the minimum and maximum imputation scenarios increase coverage estimates by about 10 and 50 percentage points, respectively, compared to the KRS. In the bottom panel of Table 3, MMR1 and MMR2 coverage rates for all children in the random sample are near 100% in all imputation scenarios, just slightly higher than that observed in the KRS. MMR1 coverage rates are only below 95% in the high-PBE schools in the minimum coverage scenario; however, MMR2 coverage rates for all students at high-PBE schools range from 75–89%, only reaching herd immunity threshold in the maximum coverage imputation scenario.

School-level MMR2 coverage rates are presented in Figure 1, stratified by school type, number of MMR doses the child received, and scenario. Each bar represents a different risk pool for measles infection, with those who have received 0 doses most susceptible, and those who have received 2 doses least susceptible. The 88–95% herd immunity threshold is shown for comparison. Kindergarteners in the random sample who are reported in the KRS as receiving 0 MMR doses attend schools where on average 89% of the kindergarten cohort has received MMR2. The minimum and maximum imputation scenarios report 88% and 91% MMR2 coverage respectively. Kindergarteners with 1 or 2 doses of MMR2 experience kindergarten MMR2 coverages rates of 93–99%, within the herd immunity threshold. At the high-PBE schools, the picture is much riskier. For children with no doses of MMR, school-level MMR coverage rates observed in the KRS are as low as 53%; imputation scenarios increase this to only 55–82%, well below the herd immunity threshold. For children with 1 dose of MMR, MMR2 coverage is slightly higher, and for those with 2 doses, coverage is around 80–90%, but still below the herd immunity threshold.

#### DISCUSSION

In this analysis we used surveillance data from the California Department of Public Health to report the MMR vaccination status of kindergarteners with personal beliefs exemptions (PBEs) from school-entry vaccine mandates. Due to substantial proportions of missing data on vaccination status, we imputed vaccination status under varying scenarios. While MMR1

and MMR2 coverage rates for exempted children were very low in the surveillance data, credible imputation scenarios suggest that coverage is in reality 10–50 percentage points higher. However, even with substantially higher coverage, MMR2 coverage for exempted children remains below herd immunity thresholds, and overall kindergarten cohort coverage is also low at schools with high exemption rates, and for children with no MMR doses. These results highlight that many students and schools are vulnerable to a measles outbreak were the virus to be introduced. Another important finding is the substantial variation in coverage and risk between schools with typical vs. high PBE rates; these stark differences emphasize the strong clustering of exempted and undervaccinated students at the school and community level [13–15, 17].

The recent history of measles outbreaks in California and elsewhere across the US [3, 4, 36–41] indicates that herd immunity against the disease is compromised. Given measles epidemiology, MMR coverage of schoolchildren is a key driver of outbreak risk. In the wake of recent outbreaks, school exemption rates have been used as the best proxy for vaccine coverage; however, missing data makes this at best a noisy proxy. The imputation methods used here can help to construct more realistic estimates of coverage and outbreak risk, and to identify epidemiologic "hot spots."

Our results offer both good and bad news: while our imputation results suggest that MMR1 and MMR2 coverage rates for exempted children are likely higher than those observed in surveillance data, they also highlight the fact that measles outbreaks can still take hold and spread in communities where vaccine coverage is actually higher than reported in surveillance data. Prior studies have found a 22–35 times increased risk of measles associated with vaccine refusal [24, 25]; these analyses assumed that exempted children were unvaccinated. Using our low estimate that 50% of exempted children in typical schools have received at least 1 MMR dose, the denominators in those original relative risk analyses are too large by a factor of 2 (assuming that half of the exempted children are actually vaccinated and should therefore not be in the denominator); the revised relative risks are therefore 44–70 times higher. Our high estimate of 90% coverage with imputation suggests that the denominators are too large by a factor of 10 (assuming 90% of the exempted children should be removed from the denominator of the risk calculation); the relative risk associated with vaccine refusal in this scenario is therefore 220–350 times higher.

The gap between reported coverage and our imputation scenarios also suggests that immunization recording and tracking procedures at schools could be improved. In its reporting of kindergarten vaccination coverage, the CDC acknowledges not being able to distinguish exempted children from up-to-date children, and recommends more routinized and standardized collection of these data [42–45]. The exemption law in effect in California at the time of data collection (2009) did require parents to provide immunization records even when requesting an exemption; however, compliance with this requirement is clearly spotty. California's new PBE law, which went into effect in January 2014, reinforces this requirement with new regulations and forms that should improve reporting [46]. For example, parents must indicate the specific vaccine(s) for which they are requesting an exemption. The new law also requires a health care provider signature on the exemption application, which should reduce exemptions that parents obtain out of "convenience" vs.

"conviction" (as was the case in Washington State following a similar regulatory change); however, the smaller number of children who do obtain exemptions going forward may be on average less vaccinated than exempted children in prior years [13]. Furthermore, the epidemiology of exemptions is likely to change when California implements a recently-passed law eliminating personal beliefs exemptions entirely [47].

It is important to note some limitations to our imputation methods. Results are sensitive to the assumptions driving the imputation algorithm. For example, we assumed that missing vaccination dates for any student presenting an immunization record at the time of kindergarten registration could be interpreted as the child not having received that vaccine. A second set of assumptions concerns documented receipt of other vaccines at the time when MMR1 or MMR2 was due. However, we have placed realistic bounds on our analyses with minimum and maximum coverage scenarios based on the vaccination histories of other exempted children at the same school; given the social patterning of vaccine behavior, we are confident that this is a reasonable assumption. Our coverage estimates have very wide ranges and should be interpreted with caution. Coverage estimates are particularly unstable in schools with lower enrollments where the addition or subtraction of one exempt or vaccinated student can change coverage estimates dramatically. Finally, with the unique sampling scheme of the KRS09, we were not able to combine the random and the high-PBE samples of schools in one set of estimates; future iterations of the KRS will permit this, and will elucidate any implications of new state exemption legislation for patterns of vaccine coverage.

#### Conclusion

Estimates of the true vaccination status of children with nonmedical exemptions are critical for surveillance and outbreak risk analysis. Our imputation scenarios suggest that MMR1 and MMR2 coverage among exempted kindergarteners in California is 10–50% higher than reported in surveillance data, but remains below herd immunity thresholds, particularly in schools with high exemption rates. At the same time, recent measles outbreaks in California have been able to spread despite these higher coverage rates. Going forward, surveillance and targeting efforts that account for high rates of missingness in routinely-collected data are needed, particularly as new exemption legislation rolls out in California and elsewhere.

### Acknowledgments

This research was supported by the Eunice Kennedy Shriver National Institute for Child Health and Human Development (5R03HD080732), which had no role in the design, execution, or submission of this study. The authors thank Teresa Lee and Steve Nickell from the California Department of Public Health Immunization Branch for access to these data, and Eileen Wang for manuscript assistance.

### References

- 1. Centers for Disease Control and Prevention. Measles--United States, 2004. MMWR Morb Mortal Wkly Rep. 2005; 54:1229–31. [PubMed: 16340938]
- 2. Centers for Disease Control and Prevention. Measles Cases and Outbreaks. 2015.
- Zipprich J, Winter K, Hacker J, Xia D, Watt J, Harriman K. Measles outbreak—California, December 2014–February 2015. MMWR Morb Mortal Wkly Rep. 2015; 64:153–4. [PubMed: 25695321]

- Clemmons NS, Gastanaduy PA, Fiebelkorn AP, Redd SB, Wallace GS. Measles—United States, January 4–April 2, 2015. MMWR Morb Mortal Wkly Rep. 2015; 64:373–6. [PubMed: 25879894]
- 5. Xia, RX.; Lin, R-G., II; Poindexter, S. Los Angeles Times. 2015. Many California child-care centers have low measles vaccination rates. Local ed
- 6. Szabo, L. USA Today. 2015. Measles outbreak raises question of vaccine exemptions.
- 7. Nagourney, A.; Goodnough, A. The New York Times. 2015. Measles Cases Linked to Disneyland Rise, and Debate Over Vaccinations Intensifies.
- Ingraham, C. California's epidemic of vaccine denial, mapped. Wonkblog: The Washington Post; 2015.
- 9. Esquivel, P.; Poindexter, S. Los Angeles Times. 2015. Plunge in kindergartners' vaccination rate worries health officials. Local ed
- 10. Levs, J. CNN. 2015. The unvaccinated, by the numbers.
- 11. Reuters, Thompson. Measles outbreak: Measles cases in the US are on the rise. 2015.
- 12. Hensley, S.; Rizzo, M.; Hurt, A. NPR News. 2015. Rise in measles cases marks a 'wake-up call' for U.S.
- Jones M, Buttenheim A. Potential effects of California's new vaccine exemption law on the prevalence and clustering of exemptions. Am J Public Health. 2014; 104:e3–e6. [PubMed: 25033149]
- Buttenheim A, Jones M, Baras Y. Exposure of California kindergartners to students with personal belief exemptions from mandated school entry vaccinations. Am J Public Health. 2012; 102:e59– e67. [PubMed: 22698009]
- Omer SB, Enger KS, Moulton LH, Halsey NA, Stokley S, Salmon DA. Geographic clustering of nonmedical exemptions to school immunization requirements and associations with geographic clustering of pertussis. Am J Epidemiol. 2008; 168:1389–96. [PubMed: 18922998]
- Atwell JE, Van Otterloo J, Zipprich J, Winter K, Harriman K, Salmon DA, et al. Nonmedical vaccine exemptions and pertussis in California, 2010. Pediatrics. 2013; 132:624–30. [PubMed: 24082000]
- Ernst K, Jacobs ET. Implications of philosophical and personal belief exemptions on re-emergence of vaccine-preventable disease: The role of spatial clustering in under-vaccination. Hum vaccin immu. 2012; 8:838–41.
- Omer SB, Salmon DA, Orenstein WA, deHart MP, Halsey N. Vaccine refusal, mandatory immunization, and the risks of vaccine-preventable diseases. N Engl J Med. 2009; 360:1981–8. [PubMed: 19420367]
- Salmon DA, Sotir MJ, Pan WK, Berg JL, Omer SB, Stokley S, et al. Parental vaccine refusal in Wisconsin: A case-control study. WMJ. 2009; 108:17–23. [PubMed: 19326630]
- Omer SB, Pan WK, Halsey NA, Stokley S, Moulton LH, Navar AM, et al. Nonmedical exemptions to school immunization requirements: Secular trends and association of state policies with pertussis incidence. JAMA. 2006; 296:1757–63. [PubMed: 17032989]
- Sugerman DE, Barskey AE, Delea MG, Ortega-Sanchez IR, Bi D, Ralston KJ, et al. Measles outbreak in a highly vaccinated population, San Diego, 2008: Role of the intentionally undervaccinated. Pediatrics. 2010; 125:747–55. [PubMed: 20308208]
- Imdad A, Tserenpuntsag B, Halsey NA, Easton DE, Shaw J. Religious exemptions for immunization and risk of pertussis in New York state, 2000–2011. Pediatrics. 2013; 132:37–43. [PubMed: 23733795]
- Centers for Disease Control and Prevention. Brief report: Imported measles case associated with nonmedical vaccine exemption --- Iowa, March 2004. MMWR Morb Mortal Wkly Rep. 2004; 53:244–6.
- Salmon DA, Haber M, Gangarosa EJ, Phillips L, Smith NJ, Chen RT. Health consequences of religious and philosophical exemptions from immunization laws: Individual and societal risk of measles. JAMA. 1999; 282:47–53. [PubMed: 10404911]
- Feikin DR, Lezotte DC, Hamman RF, Salmon DA, Chen RT, Hoffman RE. Individual and community risks of measles and pertussis associated with personal exemptions to immunization. JAMA. 2000; 284:3145–50. [PubMed: 11135778]

- Salmon DA, Moulton LH, Omer SB, DeHart MP, Stokley S, Halsey NA. Factors associated with refusal of childhood vaccines among parents of school-aged children: A case-control study. Arch Pediatr Adolesc Med. 2005; 159:470–6. [PubMed: 15867122]
- Safi H, Wheeler JG, Reeve GR, Ochoa E, Romero JR, Hopkins R, et al. Vaccine policy and Arkansas childhood immunization exemptions: A multi-year review. Am J Prev Med. 2012; 42:602–5. [PubMed: 22608376]
- 28. Centers for Disease Control and Prevention. History and epidemiology of global smallpox eradication. Atlanta, GA: US Dept of Health and Human Services, Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases (NCIRD);
- 29. Hutchins SS, Bellini WJ, Coronado V, Jiles R, Wooten K, Deladisma A. Population immunity to measles in the United States, 1999. J Infect Dis. 2004; 189:S91–7. [PubMed: 15106096]
- 30. Nyhan B, Reifler J, Richey S, Freed GL. Effective messages in vaccine promotion: a randomized trial. Pediatrics. 2014; 133:e835–e42. [PubMed: 24590751]
- 31. California Department of Health Services. California Immunization Handbook: School and Child Care Immunization Requirements for Schools and Child Care Programs. 7. Richmond, CA: Center for Infectious Diseases, Division of Communicable Disease Control, Immunization Branch; 2003.
- 32. California Department of Public Health. California School Immunization Law. Richmond, CA: Center for Infectious Diseases, Division of Communicable Disease Control, Immunization Branch;
- McLean HQ, Fiebelkorn AP, Temte JL, Wallace GS. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: Summary recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2013; 62:1–34. [PubMed: 23760231]
- 34. Breiman L. Random forests. Machine learning. 2001; 45:5-32.
- 35. Stekhoven DJ, Bühlmann P. MissForest—non-parametric missing value imputation for mixed-type data. Bioinformatics. 2012; 28:112–8. [PubMed: 22039212]
- 36. Centers for Disease Control and Prevention. Measles United States, January 1–August 24, 2013. MMWR Morb Mortal Wkly Rep. 2013; 62:741–3. [PubMed: 24025755]
- Hill M, Risk I, Burnett C, Garcia W, Carter A, Guerra L, et al. Two measles outbreaks after importation-Utah, March–June 2011. MMWR Morb Mortal Wkly Rep. 2013; 62:222–5. [PubMed: 23535688]
- Lynfield R. Notes from the field: Measles outbreak --- Hennepin County, Minnesota, February– March 2011. MMWR Morb Mortal Wkly Rep. 2011; 60:421. [PubMed: 21471950]
- Collier M. Notes from the field: Measles outbreak --- Indiana, June–July 2011. MMWR Morb Mortal Wkly Rep. 2011; 60:1169. [PubMed: 21881549]
- Redd S, Kutty P, Parker A, LeBaron C, Barskey A, Seward J, et al. Measles--United States, January 1–April 25, 2008. MMWR Morb Mortal Wkly Rep. 2008; 57:494–98. [PubMed: 18463608]
- Grigg M, Brzezny A, Dawson J, Rietberg K, DeBolt C, Linchangco P, et al. Update: Measles— United States, January–July 2008. MMWR Morb Mortal Wkly Rep. 2008; 57:893–6. [PubMed: 18716580]
- Seither R, Masalovich S, Knighton CL, Mellerson J, Singleton JA, Greby SM. Vaccination coverage among children in Kindergarten—United States, 2013–14 school year. MMWR Morb Mortal Wkly Rep. 2014; 63:913–20. [PubMed: 25321068]
- Centers for Disease Control and Prevention. Vaccination coverage among children in Kindergarten — United States, 2011–12 school year. MMWR Morb Mortal Wkly Rep. 2012; 61:647–52. [PubMed: 22914226]
- Centers for Disease Control and Prevention. Vaccination coverage among children in Kindergarten — United States, 2012–13 school year. MMWR Morb Mortal Wkly Rep. 2013; 62:607–12. [PubMed: 23903595]
- Stokley S, Stanwyck C, Avey B, Greby S. Vaccination coverage among children in Kindergarten —United States, 2009–10 school year. MMWR Morb Mortal Wkly Rep. 2011; 60:700–4. [PubMed: 21637184]
- 46. State of California Health and Human Services Agency. California Department of Public Health. Personal Beliefs Exemption to Required Immunizations. 2013.
- 47. Public health: vaccinations. Education Code, Health and Safety Code. 2015–2016



#### Figure 1.

Average school-level MMR2 coverage rate experienced by kindergarteners with 0, 1, or 2 doses of measles-containing vaccine, and by school type (random or high-PBE sample). Coverage estimates are provided from observed data in the KRS, and from minimum and maximum coverage imputation scenarios. Imputations are conducted with the missForest procedure. 95% confidence intervals are shown for each estimate. The herd immunity threshold of 88–95% is shown in the horizontal gray bar. MMR2 second dose of measles, mumps, rubella vaccine; KRS 2009 California Department of Public Health Kindergarten Retrospective Survey; Min Imputation and risk estimate under the minimum scenario where exempted children are as vaccinated as the least vaccinated kindergartener at their school; Max Imputation and risk estimate under the maximum scenario where exempted children are as the most vaccinated kindergartener at their school.

Factor	Type	Level	Notes
Other (non-MMR) vaccine status	Categorical	Child	Number of doses of other vaccines missing (polio, varicella, DTaP, HepB, HiB)
Race/ethnicity	Categorical	Child	White non-Hispanic, Hispanic, black, other
Place of Birth	Categorical	Child	Same country, within state, other state, Mexico, other country, unknown, or not stated
Type of Immunization Record	Categorical	Child	CA immunization record, other immunization record, other state school record, other medical record, CHDP Form PM171, other, unknown, or not stated
Varicella History	Categorical	Child	Reported history of varicella
School sample	Categorical	School	Random, High-PBE
School type	Categorical	School	Public, private
Charter	Categorical	School	Yes, no
Latitude, Longitude	Continuous	School	Zip code-based latitude and longitude of school
Number of kindergarteners by type	Continuous	School	Number of kindergartners up-to-date, PBE, conditional acceptance, medical exemption
Number of kindergarteners requiring specific vaccines	Continuous	School	Number of kindergartners missing vaccine doses for (polio, DTaP, MMR, HepB, and Varicella).
Percent of students receiving free or reduced lunch	Continuous	School	Free and reduced lunch prevalence as reported by CDE for public and charter schools in 2007
Who completes CSIR at school?	Categorical	School	School, school asks parent, not using CSIR, other
Who verifies and copies CSIR at school?	Categorical	School	Secretary, school nurse, volunteer, health clerk, other
What happens to an entrant requiring a vaccination?	Categorical	School	Refuse entry, allow entry, offer parent PBE, both allow entry and offer PBE, other
Who follows up on missing vaccinations?	Categorical	School	Secretary, school nurse, volunteer, health clerk, no follow up, other
If parent signs PBE, what is recorded on CSIR?	Categorical	School	No required vaccinations, all required vaccinations, some but not all, other
Computerized records used?	Categorical	School	Yes, no
Are parents given PBE as temporary option?	Categorical	School	Yes, no, other

Vaccine. Author manuscript; available in PMC 2016 November 17.

California Department of Education database. CSIR California School Immunization Record; CDE California Department of Education; DTaP Diphtheria, tetanus, pertussis; Hib Hemophilus influenza B;

MMR Measles, mumps, rubella; PBE personal beliefs exemption; CSIR California School Immunization Record; CHDP: Child Health and Disability Prevention program (State of California Health and Human Services Agency).

Author Manuscript

Author Manuscript

Author Manuscript

# Table 1

#### Table 2

Selected Characteristics of Samples of Kindergarteners With Personal Beliefs Exemptions, California Department of Public Health Kindergarten Retrospective Survey and Selective Review, 2009 (N=1,368)

	Random sample of schools	High-PBE schools
Variable	Mean (SD) or proportion	Mean (SD) or proportion
School-level variables		
K enrollment	77.9 (42.5)	70.9 (34.8)
PBE rate	0.10	0.49
School offers PBE*	0.14	0.75
School type		
Public school	0.82	0.29
Public charter school	0.03	0.48
Private school	0.14	0.23
Child-level variables		
Number of vaccine doses reported	5.5 (5.6)	5.1 (6.4)
No vaccine doses recorded	0.44	0.53
Source of vaccine records:		
Not stated	0.52	0.71
California Immunization Record	0.31	0.16
Other records	0.17	0.13
Mandated dose recorded on CSIR:		
DTaP 1	0.54	0.45
DTaP 2	0.51	0.42
DTaP 3	0.36	0.39
DTaP 4	0.41	0.33
DTaP 5	0.15	0.13
Hepatitis B 1	0.03	0.33
Hepatitis B 2	0.03	0.29
Hepatitis B 3	0.03	0.26
Hib 1	0.48	0.30
Hib 2	0.42	0.27
Hib 3	0.38	0.24
Hib 4	0.36	0.11
MMR 1	0.47	0.34
MMR 2	0.18	0.11
Polio 1	0.52	0.39
Polio 2	0.50	0.37
Polio 3	0.45	0.32
Polio 4	0.19	0.14
Polio 5	0.01	0.01
Varicella 1	0.03	0.26
Varicella 2	0.01	0.04

	Random sample of schools	High-PBE schools
Variable	Mean (SD) or proportion	Mean (SD) or proportion
Ν	262	1106

DTaP Diphtheria, tetanus, pertussis; Hib Hemophilus influenza B; MMR Measles, mumps, rubella. PBE personal beliefs exemption; CSIR California School Immunization Record.

Author Manuscript

# Table 3

Proportion Covered by MMR1 and MMR2 Vaccine Doses Under Different Imputation Scenarios and by School Type, Kindergarteners With Personal Beliefs Exemptions, California Department of Public Health Kindergarten Retrospective Survey and Selective Review, 2009.

	MMR1 Coverage [9:	5% CI]	MMR2 Coverage [95	% CI]
	Random sample	High-PBE schools	Random sample	High-PBE schools
All exempted kindergarteners at s	sampled schools (N=1,3	(62)		
As reported in KRS09	0.473 [0.413-0.534]	0.339 [0.311–0.367]	0.184 [0.138–0.232]	0.107 [0.089–0.125]
Imputation <sup><math>d</math></sup> + Minimum Coverage	0.643 [0.599–0.683]	0.485 [0.463–0.507]	0.251 [0.202–0.306]	0.160 [0.141 - 0.180]
Imputation + Median Coverage	0.909 $[0.870-0.942]$	$0.860 \ [0.841 - 0.880]$	0.490 [0.439–0.546]	0.217 [0.194–0.241]
Imputation + Maximum Coverage	0.921 [0.885 - 0.950]	$0.900 \ [0.884 - 0.916]$	0.581 [0.527–0.637]	$0.629 \ [0.606-0.651]$
All kindergarteners at sampled sc	hools (N=11,210)			
As reported in KRS09	0.990 [0.990-0.991]	0.799 [0.786–0.812]	0.985 [0.984 - 0.985]	0.729 [0.714–0.743]
Imputation + Minimum Coverage	0.994 [0.986 - 0.990]	0.843 [0.836 - 0.849]	0.985 [0.983–0.987]	0.745 [0.740-0.751]
Imputation + Median Coverage	0.998 [0.997–0.999]	0.957 [0.951–0.962]	0.990 [0.989–0.991]	0.762 [0.755–0.770]
Imputation + Maximum Coverage	0.998[0.997-0.999]	0.969 [0.964 - 0.974]	0.992 [0.991 - 0.993]	0.888 [0.881 - 0.894]

<sup>d</sup>Imputations were conducted with the missForest procedure under scenarios of minimum coverage, median coverage, and maximum coverage where exempted children are as vaccinated for MMR1 and

MMR2 as the least, average, and most vaccinated child at their school respectively.