Increased Diversity Among Un-Vaccinated Children in the United States:

An Analysis of the National Immunization Survey (NIS), 2002-2007

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ABSTRACT

This analysis uses data from the National Immunization Survey (NIS), a nationally-representative annual sample of approximately 20,000 children in the United States, to show significantly increased rates of un-vaccinated children between 2002 and 2007, from 0.27% to 0.80%, tripling the number of un-vaccinated children from 16,000 to 48,000 within five years. This trend supports epidemiological evidence that suggests recent outbreaks of vaccine-preventable diseases have occurred because of higher rates of un-vaccinated children in some segments of the population. However, this analysis also concludes that, while certain child, mother and household characteristics continue to be significantly associated with vaccine status, children with economically, culturally, and geographically diverse characteristics are now more likely to be un-vaccinated than previous research has shown. This finding suggests that new interventions may be needed to reduce the risk of future disease outbreaks among an increasingly diverse population of children.

[144 words]

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BACKGROUND

Recently, the United States has seen a resurgence of childhood illnesses once nearly eradicated with the development of immunizations. Pockets of vaccine-preventable disease, including measles, mumps, meningitis (Hib) and whooping cough (pertussis), have been reported by the Centers for Disease Control and Prevention (CDC) with hundreds, sometimes thousands, of cases being contracted in localized outbreaks reminiscent of the more widespread epidemics a century ago. In the first seven months of 2008, measles cases in the U.S. more than doubled (to 131) from an annual average of 63 between 2000 and 2007 (CDC, 2008a), and in the first 19 weeks of 2011, already 118 measles cases have been reported, more than any year since 1996 (CDC 2011a). The U.S. saw over 6,500 cases of mumps in 2006, the largest outbreak of the disease since 1987 (Dayan et al. 2008), and in 2008, Minnesota reported five cases of Hib (and one death) among children under age 5 years, the highest number of cases in the state since the Hib vaccine became available in 1992 (CDC 2009a). Additionally, 27,550 cases of pertussis were reported in the U.S. in 2010, including 9,143 cases in California alone, the highest number of cases in that state since 1947 (CDC 2011b).

Although disease outbreaks generally result from a combination of factors creating an opportunity for infection – vaccine failure (incomplete vaccine effectiveness), immunodeficiency (a body's inability to fight infectious disease), and exposure among the elderly who were born before vaccines were developed (Schaffzin et al. 2007; Tugwell et al. 2004; CDC 1999; CDC

2009b) – epidemiological evidence concludes another important factor is at play: several outbreaks have occurred in communities with large numbers of un-vaccinated children. In a March 2011 outbreak of measles in Minnesota, 11 of 13 cases were either too young to be vaccinated or had not been vaccinated because of parental concern about the MMR vaccine (CDC 2011c). Likewise, there was a 2005 measles outbreak in Indiana where all but two of the 34 cases were un-vaccinated, many of them children whose parents had refused to have them vaccinated (Parker et al. 2006). Similarly, three of the five reported cases in the 2008 Minnesota Hib outbreak were among children who had not been vaccinated because of parent "deferral or refusal" (CDC 2009a: 58). Overall, the CDC has determined that as many as 91% of the measles cases across the U.S. between January and July 2008 were among people un-vaccinated against the disease, and future outbreaks of measles will most likely occur in populations with "sizable clusters" of un-vaccinated persons (CDC 2008a).

Un-vaccinated children put at risk both the children who fail to receive vaccines and the community at large. First, un-vaccinated children are much more likely to contract vaccine-preventable diseases than children who receive immunizations on schedule. For example, un-vaccinated children have 6-23 times the risk of contracting pertussis, and 22-60 times the risk of contracting measles, compared to vaccinated children (Feikin et al. 2000; Meissner, Strebel and Orenstein 2004; Salmon et al. 1999). Additionally, the resistance to infection within a community is higher when a large enough proportion of the population is immune to disease (Haber et al. 2007). This so-called "herd immunity" protects a group of people from illness (even people not immune to the disease) via "random mixing," the even distribution of disease susceptibility across a population (Gordis 2009:24-25). When enough people are vaccinated, the likelihood of either contracting or transmitting disease is lower: a person's risk of exposure is reduced because fewer other people are sick, and fewer people become ill because one's own susceptibility to disease is lower (Lewit and Mullahy 1994).

However, because un-vaccinated children are themselves at greater risk of illness, they in turn can transmit disease to others in the community who might not otherwise become ill. Outbreaks can occur in communities where vaccine coverage falls below a disease-specific "threshold of elimination," the proportion beyond which the transmission of disease may no longer be prevented (Hyde et al. 2006:S146). In these communities, "susceptibility clustering" lowers herd immunity and increases the probability that un-vaccinated children will encounter people transmitting disease, both becoming ill themselves and transmitting disease to others (Salathé and Bonhoeffer 2008:1508).

In some communities where more parents have obtained "philosophical exemptions" from vaccination (freedom from school immunization requirements based on personal beliefs, as distinguished from medical reasons or religious convictions), immunization rates have fallen below the levels needed to prevent disease (Omer et al. 2006). In particular, disease outbreaks have occurred among children whose parents refused to have them vaccinated, either because of concerns about the safety of childhood vaccines (Parker et al. 2006:447) or because the perceived risk associated with vaccines is high while the probability of contracting a vaccine-preventable disease is relatively low (Steinhauer 2008). Parents of un-vaccinated children are more likely than others to express concerns about vaccine safety, often citing either the debated link between the measles-mumps-rubella (MMR) vaccine and autism (Wakefield et al. 1998), voicing doubts about combination vaccines, or fearing their child's immune system may be weakened by the vaccines themselves (Kutty 2009).

Unfortunately, despite evidence linking clusters of un-vaccinated children with recent outbreaks of disease, most research on childhood immunization focuses on children who are either fully-vaccinated (who have received all six vaccines in the recommended 4:3:1:3:3:1 series) or partly-vaccinated (who have received some, but not all, of the recommended series), rather than looking at children who are completely un-vaccinated (who have received none of the recommended vaccines). In particular, few studies have been conducted to determine whether the proportion of completely un-vaccinated children in the U.S. has increased in recent years, and little is known about the characteristics of children who remain completely un-vaccinated.

To my knowledge, only one study (Smith, Chu and Barker 2004) has specifically analyzed the trends and characteristics of un-vaccinated children. Using NIS data from 1995-2001 to look at un-vaccinated children in the U.S. between the ages of 19-35 months (the age by which children should been completed the recommended 4:3:1:3:3:1 vaccine series), Smith et al. (2004) estimated that the number of un-vaccinated children in the U.S. increased (from less than 15,000 to about 17,000) between 1995 and 2001. They also concluded that the characteristics of un-vaccinated children were “distinctly different” from partly-vaccinated children (Smith et al. 2004:192). Whereas partly-vaccinated children were more often Black, living with a younger, un-married mother who had not graduated from college, in a household near the poverty level, completely un-vaccinated children were more likely to be White, have an older mother who was married with a college degree, and live in a household with annual income exceeding $75,000. Parents of un-vaccinated children also were more likely to express concern about vaccine safety. Finally, un-vaccinated children “clustered geographically" (Smith et al. 2004:187), living in states that allowed philosophical exemptions from immunization, thus increasing the risk of transmitting disease to both other un-vaccinated children and to partly-vaccinated children before they were old enough to receive all their recommended vaccine doses.

RESEARCH QUESTIONS

Given the dearth of research examining trends and characteristics of un-vaccinated children in the U.S., the importance of un-vaccinated children as a factor in disease outbreaks, and the recent media focus on vaccine safety concerns (Steinhauer 2008; Wallace 2009) which may have increased even further the number of un-vaccinated children in some communities, this paper attempts to answer three questions. First, did the rate of un-vaccinated children change significantly between 2002 and 2007? Second, were children with certain characteristics more likely than others to remain un-vaccinated during this period? And third, did the risk of being un-vaccinated change (increase or decrease) significantly among children with some characteristics more than others across these six years?

The first question will help us understand how large a concern the presence of un-vaccinated children has become across the United States, while the second and third questions serve to inform policies aimed at educating particular groups of parents about the importance and safety of vaccines in hopes of reducing the risk of future disease outbreaks.

DATA AND METHODS

The National Immunization Survey (NIS) has collected vaccine data on children between the ages of 19-35 months in the United States each year since 1995 in order to monitor progress towards reaching national childhood immunization goals set forth in the Childhood Immunization Initiative (U.S. Department of Health and Human Services (DHHS) 1993).

NIS Sample

The NIS uses two phases of data collection to obtain vaccination information: (1) a Random Digit Dialing (RDD) telephone survey of parents to obtain a child's vaccine history as well as demographic, socioeconomic and geographic characteristics of the child, mother and household; then, given informed consent from a parent to contact the child's vaccine provider(s) by mail, the NIS also collects data with (2) the Provider Record Check (PRC) Study, a provider-reported history of vaccination from the child's medical records (U.S. DHHS 2003-2008: *2002-2007 DUG*; Smith et al. 2001). Each year, about 70% of children with a completed RDD household survey also have adequate PRC provider data. Together, RDD and PRC data are available through the CDC website in the form of annual Public-Use Data Files (U.S. DHHS 2003-2008: *2002-2007 NIS*).

Unfortunately, the NIS changed how un-vaccinated children were coded beginning in 2002. Prior to 2002, NIS defined children with no provider (PRC) data as though their vaccine status was missing; however, because vaccine data for these children were not missing at random (rather, they often had no vaccine data to report because they were un-vaccinated), the numbers of un-vaccinated children in the NIS were under-reported. Starting in 2002, children were coded as un-vaccinated if either the child had no provider data (because a parent reported they had not been vaccinated) or all providers reported that the child received no vaccines (Smith et al. 2005: 18-19). Since not all children with missing provider data prior to 2002 were un-vaccinated (indeed, some were simply missing vaccine data), pre- and post-2002 vaccine status data are inconsistent and cannot be reconciled. Therefore, because this study focuses on the small number of un-vaccinated children in the NIS (as few as 98 in 2002), this analysis will focus exclusively on data since 2002.

With annual samples of about 20,000 children, the NIS collected data on over 120,000 children (un-weighted sample size) in the U.S. between 2002 and 2007 (Table 1). Using sampling (probability) weights provided by the NIS, these data constitute a nationally representative sample each year of almost six million children (weighted count) ages 19-35 months. Across the six years, the pooled data represent more than 35 million U.S. children between one and a half years and three years of age.

[Table 1 about here]

Dependent Variable

For this period of analysis, six vaccines made up the 4:3:1:3:3:1 series of immunizations recommended by the U.S. Advisory Committee on Immunization Practices (ACIP) for children in the United States between birth and 18 months of age (CDC 2006a), including: Diphtheria-Tetanus-acellular Pertussis (DTaP); Inactivated Poliomyelitis "Polio" Virus (IPV); Measles-Mumps-Rubella (MMR); *Haemophilus influenzae* Type b (Hib); Hepatitis B (HepB); and Varicella "chicken pox" (VRC). Table 2 specifies the recommended number of doses for each vaccine in the 4:3:1:3:3:1 series (so called for the number of doses of each vaccine) and the recommended timing for the administration of these doses by the age of the child.

[Table 2 about here]

The dependent variable for this analysis, vaccine status, is a dichotomous measure that identifies children as being either 1 = completely "un-vaccinated" or 0 = "not un-vaccinated" (including either partly- or fully-vaccinated) based on an assessment of RDD and PRC data.

Between 2002 and 2007, the NIS defined as completely “un-vaccinated” (vaccine status = 1) those children who received none of the six recommended vaccines in the 4:3:1:3:3:1 series. For these children, either: (1) RDD household data indicated they had not received any vaccine doses (so PRC data were missing); or (2) PRC provider data indicated they had received no vaccines.

Alternatively, children were defined as “not un-vaccinated” (vaccine status = 0) if their PRC provider data indicated they were partly- or fully-vaccinated. These children had received either some (1 to 14) or all (15) of the recommended doses of the six vaccines in the 4:3:1:3:3:1 series (where 4+3+1+3+3+1 = 15 doses).

Independent Variables

This study uses as independent variables eleven pre-defined categorical measures of child, mother and household characteristics available in the NIS: child's race/ethnicity, gender, age, and first-born status; mother's level of education, age, and marital status; and household's income & poverty status, number of children, census region, and philosophical exemption status. Each measure was included in this analysis as a series of dummy variables with a reference category ("ref") identified for each measure. The analysis also included NIS year of interview (from 2002 through 2007) with 2002 as the reference category.

For comparison purposes, most of the independent measures included in Smith et al. (2004) were included in this study. However, one difference between these two studies is the lack of public access to data identifying households with annual incomes over $75,000. While these income data were available to Smith et al. (presumably because of their affiliation with the CDC), public-use data downloaded for this analysis only identified households with annual incomes above $50,000. Unfortunately, given Smith et al.'s finding that un-vaccinated children tended to live in households with the highest levels of annual income (above $75,000), this difference may be important when comparing the results of these two studies.

Methods

To answer my first research question, I conducted a trend analysis to determine whether the rates of un-vaccinated children changed significantly between 2002 and 2007. To measure the statistical significance of this change, I ran two-tailed t-tests that compared the vaccine status of children in 2002 to each subsequent year. So as not to overstate the significance of this association (that might have occurred if I used weighted standard deviations with a weighted mean in this large sample of children), I used instead un-weighted standard deviations around weighted means to calculate these t-test statistics.

Second, to assess whether children with certain characteristics were more or less likely to be un-vaccinated in any given year, I conducted a bivariate analysis using Pearson chi-square to determine the unadjusted associations between vaccine status and child, mother and household characteristics in each year (and in a pooled sample of children across all six years).

Third, to determine whether vaccine status changed among certain groups of children between 2002 and 2007 (whether children with certain characteristics became more or less likely to be un-vaccinated over time), I conducted a multivariate analysis using a series of binomial logistic regression models. The three main effects models (Models 1-3) determined which characteristics were associated with vaccine status across the six years (first adjusting for Year of NIS data, next adding all child, mother, and household characteristics, and then just including those characteristics significantly associated with vaccine status). The two interaction models

(Models 4-5) then assessed whether the odds of being un-vaccinated changed for some children more than others between 2002 and 2007. Models 4(a-f) sequentially added to Model 3 six interaction terms (Year by each significant main effect), and Model 5 includes all significant main and interaction effects to determine whether children with certain characteristics were more or less likely to be un-vaccinated in 2007 than children with that characteristic had been in 2002.

I used Stata software to run all the statistical tests throughout this analysis (StataCorp 2008).

RESULTS

Trend Analysis

This analysis confirms the expected increase in the number and proportion of un-vaccinated children in the United States between 2002 and 2007. This increase represents both a statistically and practically significant rise in un-vaccinated children across the period (with especially large increases between 2002 and 2004, and between 2002 and 2007). Results are presented both in tabular form (in Table 3) and visually (in Figure 1).

[Table 3 and Figure 1 about here]

Across the period, there was a statistically significant rise in the proportion of un-vaccinated children (who received none of the 15 recommended doses of the 4:3:1:3:3:1 series), with the largest differences being found between the proportions of un-vaccinated children in 2002 compared to 2004, and the proportions in 2002 compared to 2007. The rate of un-vaccinated children rose from 0.27% (about one-quarter of one percent) in 2002, to 0.56% (over half of one percent) in 2004, and to more than 0.80% (over three-quarters of one percent) in 2007.

While these proportions are very small, they represent a significant practical change in disease risk over time. While Smith et al. (2004) found approximately 17,000 un-vaccinated children in the U.S. each year between 1995 and 2001, the number of un-vaccinated children doubled in the U.S. (from below 16,000 to over 32,000 children) between 2002 and 2004, and tripled between 2002 and 2007 (to over 48,000 un-vaccinated children in just five years).

Bivariate Analysis

This analysis describes the unadjusted association between vaccine status and child, mother and household characteristics by assessing whether the crude odds of being un-vaccinated are higher among children with some characteristics than others.

Table 4 shows the weighted percent of un-vaccinated children by category for every independent variable in each year separately between 2002 and 2007 (and in pooled data, for all six years combined). The p-value for a Pearson chi-square statistic reflects the variation in proportions of un-vaccinated children across categories of each measure, and is significant if the proportions of un-vaccinated children are sufficiently different across the categories in that year.

[Table 4 about here]

Looking at child characteristics, race/ethnicity was significantly associated with vaccine status: for all six years combined, 0.64% of White non-Hispanic children were un-vaccinated compared to only 0.35% to 0.40% of Hispanics, Black non-Hispanics, and children of other & multiple races/ethnicities. Across the six year period (from 2002 to 2007), the proportion of White non-Hispanics who were un-vaccinated became significantly higher than the proportions among children of the other race/ethnicity categories. Also, for the whole period, children were significantly more likely to be un-vaccinated if they were not the first-born child in their family: 0.57% of lower birth order siblings were un-vaccinated compared with only 0.42% of older siblings, possibly reflecting the recently increased rates of un-vaccinated children overall.

Mother's marital status also was significantly associated with vaccine status: children whose mothers were widowed, divorced, separated or deceased (0.79%) were more likely to be un-vaccinated than children whose mothers were currently married (0.52%) or never married (0.36%). Surprisingly, given the results from Smith et al. (2004), vaccine status did not vary significantly by mother's level of education.

Among household characteristics, vaccine status was significantly associated with several factors: number of children in the household, census region, and philosophical exemption. Using pooled data for all six years, children were more likely to be un-vaccinated if they lived in a household with four or more children (1.11%), lived in the western United States (0.68%), or lived in a state that allowed parents to obtain a philosophical exemption from immunization (0.60%). In contrast to the earlier work by Smith et al. (2004), but similar to the results above for mother's education level, this bivariate analysis found no significant difference in vaccine status among children by household income & poverty status.

Multivariate Analysis

Model Building

This analysis used binomial logistic regression (three main effect and two interaction models) to estimate the adjusted association between vaccine status and child, mother and household characteristics, and to determine if children with a certain characteristic were more or less likely to be un-vaccinated in 2007 than children with the same characteristic had been in 2002.

In Model 1, I simply regressed vaccine status on Year of NIS Interview (0 = 2002, 1 = 2007). Mirroring the trend analysis described above, the odds of being un-vaccinated increased dramatically for children in the United States across the six years: on average, a child was nearly three times more likely to be un-vaccinated in 2007 than in 2002 (OR=2.937, p=0.000).

In Model 2, I controlled for Year of NIS Interview (Year) as well as the complete set of independent variables by adding dummy variables for each child, mother and household characteristic (with a reference category identified for each measure). Children were still significantly (over three times) more likely to be un-vaccinated in 2007 than children had been in 2002, and looking at Wald chi-square statistics for each set of dummy variables, six measures were at least marginally associated with a child's odds of being un-vaccinated:

- *Child's Race/Ethnicity:* Wald chi2 (df=3) = 25.67, p = 0.0000;
- *Child's Gender:* Wald chi2 (df=1) = 2.91, p = 0.0880;
- *Child's Age:* Wald chi2 (df=2) = 6.07, p = 0.0482;
- *Mother's Marital Status:* Wald chi2 (df=2) = 10.75, p = 0.0046;
- *Household's Income & Poverty Status:* Wald chi2 (df=2) = 15.37, p = 0.0005; and
- *Number of Children in the Household:* Wald chi2 (df=2) = 9.73, p = 0.0077.

In Model 3, I ran a revised binomial logistic regression model that included Year and only these six significant main effect characteristics. Then, using this subset of characteristics, I created six interaction terms by crossing Year with each significant main effect measure, and added these interaction terms sequentially to Model 3 to create six separate interaction models, Models 4(a-f). Again using Wald tests, I determined just two of these interaction terms were significant, indicating that the odds of being un-vaccinated changed significantly between 2002 and 2007 for children across only these two sets of characteristics:

- *Year*Child's Race/Ethnicity:* Wald chi2 (df=3) = 8.91, p=0.0306; and
- *Year*Number of Children in the Household:* Wald chi2 (df=2) = 7.71, p=0.0212.

Finally, I included just these two significant interaction terms (along with Year and the six significant main effect measures) in the final binomial logistic regression model, Model 5, to estimate the adjusted associations between vaccine status and these characteristics.

[Table 5 about here]

Interpretation

An odds ratio for a main effect measure reflects the ratio of the odds of being un-vaccinated for a child with a particular characteristic to the odds of being un-vaccinated for a child with the reference level characteristic for that measure (whose odds of being un-vaccinated, by definition, equaled 1.0) for all six years combined (from 2002 to 2007). An odds ratio for an interaction term is the *change* between 2002 and 2007 in the ratio of the odds of being un-vaccinated for a child with that characteristic relative to the odds of being un-vaccinated for a child with the reference level characteristic for that measure.

First, looking at the main effects estimates in Model 5, certain children did have significantly higher adjusted odds of being un-vaccinated: vaccine status varied significantly by child's race/ethnicity, mother's marital status, and household's income & poverty status.

White non-Hispanic children were almost ten times more likely to be un-vaccinated than Hispanic children across the whole period from 2002 to 2007 (OR=1.000/0.102=9.8, p=0.000); Black children also were much more likely to be un-vaccinated than Hispanic children between

2002 and 2007 (OR=0.860/0.102=8.4). Additionally, boys were somewhat more likely to be un-vaccinated than girls, but this difference was only marginally significant.

Children of currently married mothers were almost three times as likely to be un-vaccinated as children whose mothers had never been married (OR=1.000/0.358=2.8, p=0.001). However, children with previously married mothers had even higher odds of being un-vaccinated than children whose mothers were currently married, so they also were significantly more likely to be un-vaccinated than children whose mother had never been married (OR=1.210/0.358=3.4).

Finally, children who lived in households with incomes below poverty were four times more likely to be un-vaccinated than children in households with incomes above $50,000 per year (OR=1.000/0.248=4.0, p=0.000). This result contrasts with Smith et al. (2004) who found the highest rates of un-vaccinated children in households with annual incomes above $75,000 (although this finding may simply be a result of the limited income data available for public analysis, as mentioned in the section on Independent Variables, above).

Next, looking at interaction terms in Model 5, the relative odds of being un-vaccinated changed significantly across the period for two groups of children, as indicated by estimates for the measures Year*Child's Race/Ethnicity and Year*Number of Children in Household.

Between 2002 and 2007, the odds of being un-vaccinated decreased significantly among Black non-Hispanic children (relative to White non-Hispanics). The ratio of the odds that a Black child was un-vaccinated in 2007 (relative to a White child) was only one third as great as a Black child’s relative odds of being un-vaccinated in 2002 (OR=0.281/0.860=0.327, p=0.044).

[Figure 2 about here]

Also across the period, the odds of being un-vaccinated changed significantly among children living in households with two-three children (relative to children living in one child households). The odds that children with one or two siblings were un-vaccinated in 2007 (relative to only children) were almost four times greater than their relative odds in 2002 (OR=3.208/0.844=3.800, p=0.008). In addition, the relative odds of being un-vaccinated nearly doubled between 2002 and 2007 among children living in households with four or more children. Although this change was not statistically significant, it may reflect a practical significance with respect to the overall number of un-vaccinated children across the country and the potential focus of efforts to decrease the number of un-vaccinated children in some populations.

[Figure 3 about here]

DISCUSSION

The trend analysis conducted here finds a small but growing proportion of children in the United States remain un-vaccinated. Given previous studies showing that un-vaccinated children tend to live in clusters, that un-vaccinated children are at greater risk of contracting infectious diseases, and that disease outbreaks more often occur within clusters of un-vaccinated children, this trend appears to support the CDC's prediction that outbreaks of vaccine-preventable disease are likely to continue.

Regression models in this analysis indicate that, consistent with Smith et al. (2004), certain characteristics are associated with a child's odds of being un-vaccinated. Child's race/ethnicity, mother's marital status, and household's number of children are all significantly associated with vaccine status: White non-Hispanics, children with married mothers, and children living in households with four or more children are still more likely to be un-vaccinated than Hispanics, children with never married mothers, and only children.

However, in contrast to Smith et al. (2004), this analysis finds other characteristics are not significantly associated with vaccine status. Among child characteristics, Hispanic children are significantly less likely to be un-vaccinated than either Whites or Blacks (while Smith et al. (2004) found only Whites were more likely to be un-vaccinated). Also, gender is only marginally associated with vaccine status: boys are only slightly more likely to be un-vaccinated than girls.

Among mother's characteristics, level of education does not significantly predict vaccine status: mothers with a college degree are no more likely to have un-vaccinated children than mothers who have not finished high school. Also, previously married mothers are at least as likely to have un-vaccinated children as currently married mothers, and while Smith et al. (2004) found mothers over age 30 were more likely to have un-vaccinated children, this analysis finds mother's age does not significantly predict vaccine status.

Finally, among household characteristics, while a household's number of children is significantly associated with vaccine status, households with two-three children (in addition to households with four or more children) are now also more likely to have un-vaccinated children relative to households with an only child. Also, while Smith et al. (2004) found un-vaccinated children were significantly more likely to live in western states, this analysis showed census region is now not a significant determinant of vaccine status. Likewise, un-vaccinated children are not any more likely to live in states that allow philosophical exemption from immunization. Finally, household income is not significantly associated with vaccine status: households with incomes below poverty are at least as likely to have un-vaccinated children as households with annual incomes above $50,000.

CONCLUSION

While a change in the NIS coding of un-vaccinated children precludes my combining the 1995-2001 data used by Smith et al. (2004) with the 2002-2007 data used in this analysis, several characteristics that were previously associated with vaccine status no longer appear to predict a child's odds of being un-vaccinated. Both comparing the results of this analysis with Smith et al. (2004) and assessing the change in characteristics that predict vaccine status across the six years between 2002 and 2007, the factors associated with a child's odds of remaining un-vaccinated have become more economically, culturally and geographically diffused over time.

Higher socioeconomic status no longer appears to be significantly associated with a child's vaccine status. While Smith et al. found un-vaccinated children were more likely to live in households with the highest annual incomes, this study found children living in households with incomes below poverty had even higher odds of being un-vaccinated than children in moderate and high income households. Also, while Smith et al. found college educated mothers were more likely to have un-vaccinated children than mothers with lower levels of education, this analysis indicates mother’s education is no longer a significant determinant of vaccine status.

Culturally, un-vaccinated children now may be found in more varied living arrangements. While Smith et al. concluded that children who lived with currently married mothers were more likely to be un-vaccinated, this study found children are equally likely to be un-vaccinated if their mother is either currently or previously married (rather than never married). Also, while children living in the largest households (with four or more children) are still more likely to be un-vaccinated than only children, households with 2-3 children became significantly more likely to include un-vaccinated children in 2007 than they had been just six years earlier.

Finally, un-vaccinated children seem to have become more widely distributed geographically across the United States. Although Smith et al. found children living in western states were more likely to be un-vaccinated than children living in other areas of the country, census region no longer significantly predicts vaccine status. Likewise, this analysis found that un-vaccinated children are no longer more likely to live in states that allow philosophical exemptions than in states that do not.

Taken together, these findings suggest a recent shift has taken place across the United States in the characteristics associated with un-vaccinated children. Regardless of whether we consider a child's gender or socio-economic status (as measured by mother's level of education or household income), mother's marital status or age, the presence of siblings in one's household, or one's state of residence across the country, the combination of factors that predict a child's vaccine status has become increasingly heterogeneous.

Perhaps this shift has occurred in conjunction with the recently debated link between the MMR vaccine and autism, or as a result of the increased media attention given to vaccine safety concerns in general. No matter the reason, the rising numbers and increased diversity of un-vaccinated children found here represent a heightened risk of vaccine-preventable disease across the country. Given the importance of un-vaccinated children as a factor in recent disease outbreaks in the United States, this understanding of the changing rates and characteristics associated with vaccine status among children is essential in developing policies and interventions to prevent future outbreaks of disease.

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TABLES

Table 1.
Un-Weighted Sample Size, Weighted Count and Percent of Total Pooled, by Year, NIS Each Year and Combined, 2002 through 2007.

	Un-Weighted		Weighted	
Year	**Sample Size[a]**	**Percent of Total Pooled**	**Count[b]**	**Percent of Total Pooled**
2002	21,410	17.79%	5,845,539.05	16.42%
2003	21,310	17.71%	5,899,319.14	16.58%
2004	21,998	18.28%	5,874,423.78	16.51%
2005	17,563	14.59%	5,935,946.53	16.68%
2006	21,044	17.49%	6,010,242.66	16.89%
2007	17,017	14.14%	6,025,081.72	16.93%
Total Pooled	120,342	100.00%	35,590,552.89	100.00%

[a]*Un-Weighted Sample Size = total number of children in NIS with "adequate provider data."*
[b]*Weighted Count = estimated number of children the NIS data represent (based on un-weighted sample size and yearly provider weights).*

Table 2:
Type of Vaccine, Number of Doses in the 4:3:1:3:3:1 Vaccine Series, and Recommended Immunization Schedule, by Age of Child at Vaccination.[a]

Type of Vaccine	Number of Doses	Age of Child							
		At Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months
DTaP	4			DTaP	DTaP	DTaP		DTaP	
Polio	3			IPV	IPV	IPV			
MMR	1						MMR		
Hib	3			Hib	Hib		Hib		
HepB	3	HepB	HepB			HepB			
VRC	1						VRC		

[a] *Centers for Disease Control and Prevention, 2006b:Q2*

Table 3:
T-test Comparison of Weighted Number and Proportion of Un-Vaccinated Children in 2002 and 2003-07 (NIS 2002-2007).

Year	Weighted Count	Weighted Mean	Un-Weighted Standard Deviation	Un-Weighted 95% Confidence Interval	2-tailed T-test	p-value	Signif-icance
2002	15,958	0.0027	0.0675	0.0018 - 0.0036	-	-	
2003	24,533	0.0042	0.0707	0.0032 - 0.0051	-2.1363	0.0327	*
2004	32,780	0.0056	0.0775	0.0046 - 0.0066	-4.0884	0.0000	***
2005	30,041	0.0051	0.0873	0.0038 - 0.0064	-2.8975	0.0038	**
2006	28,964	0.0048	0.0844	0.0037 - 0.0060	-2.8137	0.0049	**
2007	48,052	0.0080	0.0977	0.0065 - 0.0094	-5.9632	0.0000	***

*Significant Change in Weighted Mean between Years: + $p<0.1$, * $p<0.05$, ** $p < 0.01$, *** $p<0.001$.*

Table 4:
Weighted Percent of Un-Vaccinated Children by Independent Measures and Significantly Different Percents, Each Year and Pooled 2002-2007.

Child Characteristics	2002	2003	2004	2005	2006	2007	Pooled
Race/Ethnicity				*		***	***
White, non-Hispanic (ref)	0.35	0.50	0.54	0.72	0.55	1.16	0.64
Hispanic	0.12	0.19	0.53	0.30	0.46	0.47	0.35
Black, non-Hispanic	0.30	0.58	0.48	0.15	0.42	0.36	0.38
Other & Multiple Race/Ethnicity	0.21	0.36	0.87	0.41	0.25	0.32	0.40
Gender						+	
Male (ref)	0.30	0.45	0.49	0.58	0.52	0.97	0.56
Female	0.24	0.38	0.63	0.42	0.44	0.61	0.46
Child's Age	+						
19-23 months	0.42	0.59	0.52	0.38	0.56	0.91	0.57
24-29 months	0.20	0.33	0.63	0.60	0.50	0.61	0.48
30-35 months (ref)	0.22	0.36	0.51	0.52	0.39	0.88	0.48
First Born					**		*
No (ref)	0.32	0.48	0.58	0.57	0.64	0.87	0.57
Yes	0.20	0.31	0.52	0.43	0.30	0.72	0.42
Mother Characteristics							
Education Level					**		
LT 12 years	0.25	0.44	0.75	0.40	0.95	0.95	0.64
12 years	0.25	0.48	0.52	0.57	0.24	0.98	0.50
13-15 years	0.27	0.40	0.43	0.26	0.47	0.62	0.42
GE 16 years (ref)	0.31	0.33	0.55	0.58	0.46	0.62	0.48
Mother's Age			+		+		
Under 20 years	0.04	0.09	0.02	0.08	1.43	0.44	0.36
20-29 years	0.29	0.39	0.68	0.57	0.55	0.81	0.54
30 years or older (ref)	0.27	0.46	0.48	0.48	0.38	0.80	0.48
Marital Status						+	*
Currently married (ref)	0.29	0.38	0.50	0.60	0.49	0.85	0.52
Widow/div/sep/deceased	0.38	0.79	0.91	0.43	0.62	1.63	0.79
Never married	0.19	0.38	0.59	0.23	0.40	0.36	0.36
Household Characteristics							
Income & Poverty Status	+					*	
Income below poverty (ref)	0.17	0.33	0.67	0.35	0.37	1.12	0.52
Income above poverty, <= $50k	0.39	0.53	0.48	0.48	0.56	0.96	0.55
Income > $50k	0.21	0.43	0.55	0.56	0.45	0.49	0.45
Number of Children in HH	*	***	***	***	**	**	***
One child (ref)	0.23	0.22	0.40	0.41	0.22	0.33	0.30
Two-Three children	0.23	0.36	0.35	0.37	0.46	0.90	0.45
Four or more children	0.57	1.02	1.74	1.22	0.98	1.10	1.11
Census Region				+	***		**
Northeast	0.37	0.30	0.32	0.56	0.15	0.54	0.38
Midwest	0.27	0.49	0.53	0.79	0.34	0.75	0.53
South	0.19	0.37	0.53	0.31	0.44	0.79	0.44
West (ref)	0.32	0.50	0.78	0.52	0.89	1.02	0.68
Philosophical Exemption			*		*		**
No (ref)	0.27	0.37	0.41	0.47	0.37	0.71	0.43
Yes	0.28	0.48	0.75	0.55	0.63	0.91	0.60

*Significant Difference in Percent Un-Vaccinated: + p<0.1, * p<0.05, ** p < 0.01, *** p<0.001.*

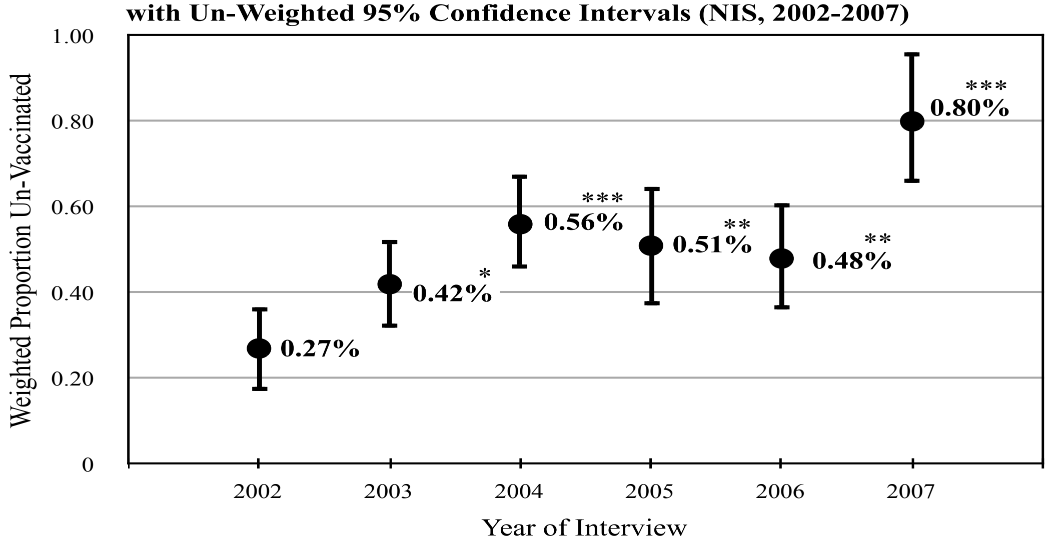
Table 5:
Binomial Logistic Regression Models of Vaccine Status on Year of NIS Interview, Child, Mother, and Household Characteristics, and Interaction Terms: Odds Ratios (and Standard Errors) for NIS Data in 2002 and 2007.

	Model 2	Model 3	Model 5
Year of NIS Interview	3.147 (0.659)***	3.214 (0.647)***	1.315 (0.570)
Child Characteristics			
Race/Ethnicity (ref=White, non-Hispanic)			
Hispanic	0.184 (0.070)***	0.238 (0.085) ***	0.102 (0.055)***
Black, non-Hispanic	0.449 (0.156)*	0.413 (0.129) **	0.860 (0.349)
Other & Multiple Races/Ethnicities	0.309 (0.098)***	0.367 (0.109) **	0.600 (0.317)
Gender (ref=Male)			
Female	0.690 (0.150)+	0.688 (0.148)+	0.687 (0.148)+
Child's Age (ref=30-35 months)			
19-23 months	1.282 (0.340)	1.270 (0.341)	1.275 (0.343)
24-29 months	0.715 (0.183)	0.719 (0.187)	0.716 (0.187)
First Born (ref=No)			
Yes	1.292 (0.373)	-	-
Mother Characteristics			
Education Level (ref=GE 16 years)			
LT 12 years	1.081 (0.539)	-	-
12 years	0.992 (0.351)	-	-
13-15 years	0.718 (0.207)	-	-
Mother's Age (ref=30 years or older)			
Under 20 years	0.668 (0.493)	-	-
20-29 years	0.865 (0.256)	-	-
Marital Status (ref=Currently married)			
Widow/div/sep/deceased	1.275 (0.579)	1.237 (0.586)	1.210 (0.575)
Never married	0.381 (0.119)**	0.365 (0.110) **	0.358 (0.108)**
Household Characteristics			
Income & Poverty Status (ref=Income < poverty)			
Income above poverty, <= $50k	0.688 (0.228)	0.665 (0.186)	0.655 (0.183)
Income > $50k	0.247 (0.102)***	0.254 (0.075) ***	0.248 (0.074)***
Number of Children in HH (ref=One child in HH)			
Two-Three children in HH	2.462 (0.745)**	2.086 (0.534) **	0.844 (0.315)
Four or more children in HH	3.094 (1.266)**	2.571 (0.770) **	1.747 (0.761)
Census Region (ref=West)			
Northeast	0.475 (0.178)*	-	-
Midwest	0.553 (0.162)*	-	-
South	0.645 (0.181)	-	-
Philosophical Exemption (ref=No)			
Yes	1.217 (0.283)	-	-
Interaction Terms			
Year*Child's Race/Ethnicity (ref=White, non-H)			
Year * Hispanic	-	-	2.573 (1.660)
Year * Black, non-Hispanic	-	-	0.327 (0.182)*
Year * Other & Multiple Races/Ethnicities	-	-	0.495 (0.309)
Year*Number of Children in HH (ref=One Child)			
Year * Two-Three Children	-	-	3.800 (1.913)**
Year * Four or more Children	-	-	1.914 (1.121)

*Significant Difference in Percent Un-Vaccinated: + p<0.1, * p<0.05, ** p < 0.01, *** p<0.001.*

FIGURES

Figure 1:
Weighted Proportion of Un-Vaccinated Children with Un-Weighted 95% Confidence Intervals (NIS, 2002-2007)



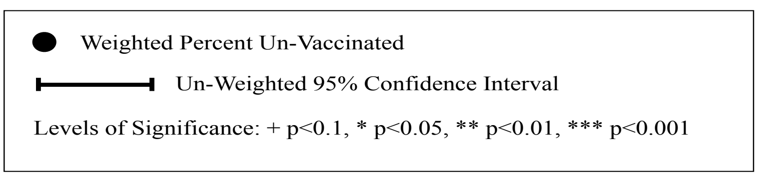
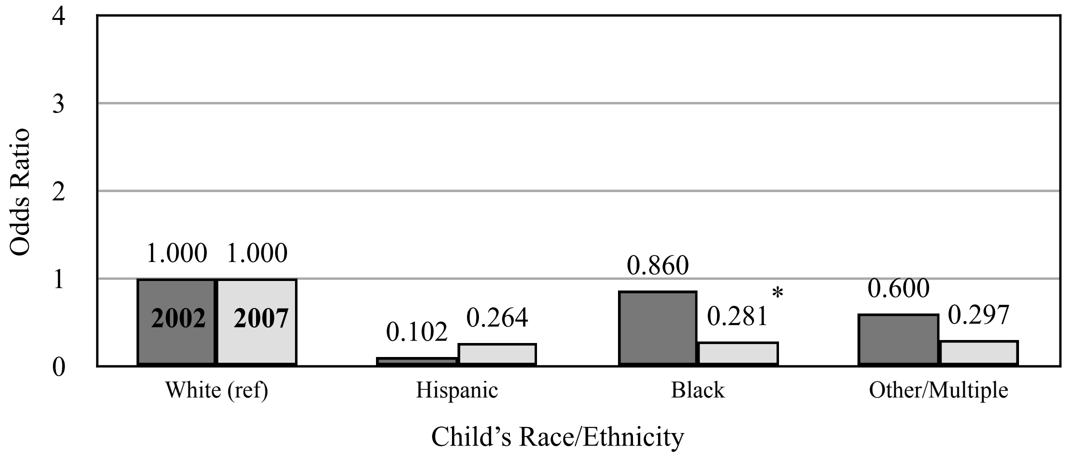
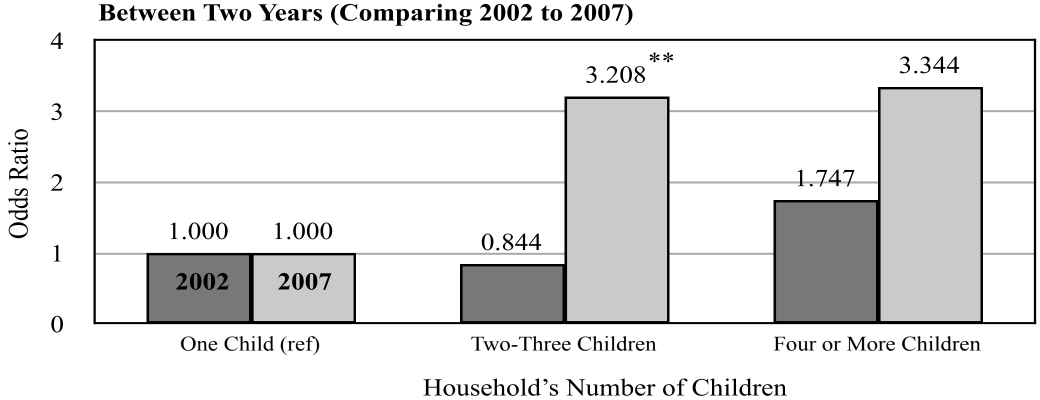


Figure 2.
2002 and 2007 Odds Ratio of Vaccine Status, by Child's Race/Ethnicity:
Change in Odds of Being Un-Vaccinated Relative to White non-Hispanic Children, Between Two Years (Comparing 2002 to 2007)



Levels of Significance: + p<0.1, * p<0.05, ** p<0.01, *** p<0.001

Figure 3.
2002 and 2007 Odds Ratio of Vaccine Status, by Household's Number of Children: Change in Odds of Being Un-Vaccinated Relative to One Child Households, Between Two Years (Comparing 2002 to 2007)



Levels of Significance: + $p<0.1$, * $p<0.05$, ** $p<0.01$, *** $p<0.001$