Trends and Characteristics of Unvaccinated Children in the United States: The National Immunization Survey, 2002−2010

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INTRODUCTION

The United States has seen a resurgence of infectious diseases once nearly eradicated with the development of immunizations. Pockets of vaccine-preventable disease have been reported by the Centers for Disease Control and Prevention (CDC) with hundreds, sometimes thousands, of cases being contracted in localized outbreaks across the country.[1-5] Although these diseases can result from a variety of factors, many recent outbreaks have occurred among “clusters" of children either too young to be vaccinated or left unvaccinated by parents concerned about vaccine safety.[6-11] Not only are unvaccinated children many times more likely to contract measles and pertussis than fully-vaccinated children,[12-14] but these diseases are more likely to be transmitted in communities with lower herd immunity (where immunization rates fall below disease-specific thresholds of elimination).[15-20] To develop health policies and immunization programs that reduce the risk of infectious disease by minimizing childhood vaccine refusal, we need to understand the current trends and characteristics of unvaccinated children across the US.

Despite the evidence linking unvaccinated children with outbreaks of infectious disease, only one study to date has assessed the number and profile of unvaccinated children in this country.[11] Looking at National Immunization Survey (NIS) data from 1995−2001, Smith, Chu and Barker (2004) found that unvaccinated children were "distinctly different” from under-vaccinated children and significantly more likely to have high socioeconomic status (SES) parents. Given the importance of vaccine refusal as a factor in disease outbreaks,[21] the ongoing controversy

surrounding vaccine safety,[22-23] and the availability of more recent NIS data, the current study updates our understanding of the trends and characteristics of unvaccinated children in the United States.

This paper asks three questions. First, did the proportion of unvaccinated children change significantly between 2002 and 2010? Second, were children with certain characteristics more (or less) likely to be unvaccinated during these nine years? And third, did the odds of being unvaccinated increase (or decrease) for children with certain characteristics over the period?

METHODS

To monitor progress in reaching goals set forth in the Childhood Immunization Initiative, the NIS has collected cross-sectional vaccine data on US children between the ages of 19−35 months each year since 1995.[24-25] NIS data are collected in two phases: (1) a Random Digit Dialing (RDD) telephone survey of parents is used to obtain a child's vaccine history, as well as demographic, socioeconomic and geographic characteristics of the child, mother and household; then, given parental consent to contact the child's vaccine provider(s) by mail, (2) the Provider Record Check (PRC) Study collects a vaccination history from the child's medical records.[26-34] Each year, approximately 30,000 households (about 85% of contacted households with age-eligible children) complete an RDD household survey, of which about 70% (20,000 households) also have adequate PRC provider data. Together, RDD and PRC data are available from the CDC in annual Public-Use Data Files.[35-43]

Unfortunately, the NIS has changed over time how it defines unvaccinated children.[44] Prior to 2002, children with no PRC data were coded as missing on all their vaccination measures. However, since some of these children were in fact unvaccinated (and so had no immunization

data for their providers to report), the number of unvaccinated children went under-reported. Starting in 2002, children have been coded as unvaccinated if either their RDD data indicated they had not received any vaccines (so provider data were appropriately missing) or their PRC data showed they were in fact unvaccinated. Because pre- and post-2002 vaccine status data are inconsistently coded, this study analyzes unvaccinated children only since 2002.

From 2002 to 2010, the NIS has collected RDD and PRC data on over 173,000 US children (un-weighted sample size). Applying sampling (probability) weights provided by the NIS, these data constitute a nationally representative annual population of about six million children (weighted count), with data pooled across nine years representing more than 54 million children.

Dependent Variable

Six vaccines make up the standard 4:3:1:3:3:1 immunization series recommended by the US Advisory Committee on Immunization Practices (ACIP) for children between birth and 18 months of age, 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 1 specifies the recommended timing (by child age) for administration of each dose in the 4:3:1:3:3:1 vaccine series (so called for the number of doses for each vaccine, yielding a total of 15 doses).[45-46]

[Table 1 about here]

The dependent variable for this analysis is "vaccine status," a dichotomous measure that identifies children as either: completely "unvaccinated" (vaccine status = "1" = child received none (0) of the recommended vaccine doses in the 4:3:1:3:3:1 series); or "not unvaccinated" (vaccine status = "0" = child received some (1 to 14) or all (15) of the recommended doses)

including both under- and fully-vaccinated children.

This paper focuses on completely unvaccinated children because they have been a key factor in recent outbreaks of infectious disease across the US. As Smith, Chu and Barker stated, unvaccinated children are "at increased risk of acquiring and transmitting vaccine-preventable disease" and parents of unvaccinated children are "much more concerned about vaccine safety" than parents of vaccinated children.[11] While getting some (but not all) vaccine doses may be a function of various factors beyond a parent's control (including lack of health insurance or inaccessibility of health services), forgoing all immunizations requires a conscious choice on the part of a parent. This study aims to inform outreach efforts by updating our understanding of which children are most at risk of being completely unvaccinated.

Independent Variables

This study considers the year of NIS interview (2002 through 2010) and eleven categorical measures of child, mother and household characteristics: 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 of residence[†], and state philosophical exemption status (a binary measure of residence in a state that did or did not allow philosophical exemptions from vaccination).[47] Each measure was used to create a series of dummy variables that was then included in the analysis with a specified reference category ("ref" in Table 3).

There are several potential limitations of the NIS public use data files downloaded for this

[†] Census regions include the following states, as defined by the U.S. Department of Commerce: Northeast = CT, MA, ME, NH, NJ, NY, PA, RI & VT; Midwest = IA, IL, IN, KS, MI, MN, MO, ND, NE, OH, SD & WI; South = AL, AR, DC, DE, FL, GA, KY, LA, MD, MS, NC, OK, SC, TN, TX, VA & WV; and West = AK, AZ, CA, CO, HI, ID, MT, NM, NV, OR, UT, WA & WY.

study. First, limited detail was available for some child, mother and household characteristics: most measures were coded as categorical variables (even child's and mother's age); and household annual income was top-coded at "above $50,000." Second, some NIS coding became even more collapsed over time (for example, mother's marital status combined "never" and "previously" married into one category in 2009), further limiting the interpretation of these measures. Finally, some state laws regulating philosophical exemptions from vaccination have changed over time. However, since only a few states changed their policies during the period of analysis, philosophical exemption status was coded for all years based on whether or not the child lived in one of 17 states that allowed philosophical exemptions in 2005-2006.[‡]

Models

This paper runs three sets of analyses. First, a trend analysis was conducted using two-tailed *t*-tests to determine if the proportions of unvaccinated children changed significantly between 2002 and each subsequent year through 2010. Given the large NIS sample size with a relatively small number of unvaccinated children, un-weighted standard deviations around weighted means (proportions unvaccinated) were used to calculate un-weighted 95% confidence intervals (CIs) so as not to overstate the significance of the association over time (which likely would have occurred if weighted standard deviations had been applied instead).

Binomial logistic regression models of vaccine status (1=unvaccinated, 0=not unvaccinated) on time (NIS interview year) confirmed this trend analysis by estimating a child's unadjusted odds of being unvaccinated across the period. In three separate regressions, time was coded in

[‡] In 2005-2006, the 17 states that allowed philosophical exemptions from vaccination were: AR, CA, CO, ID, LA, ME, MI, MN, NM, ND, OH, OK, TX, UT, VT, WA and WI.

three different ways: discrete years (2002 through 2010); a binary measure with only two years of data (2002 and 2010); and, a binary measure of time split between earlier (2002−06) and later (2007−10) periods, coinciding with lower and higher rates of unvaccinated children in the trend analysis. While all three regressions found significantly more unvaccinated children over time, subsequent models were run with time split between the earlier and later periods both to utilize all years of available NIS data and perhaps to help explain the observed jump in proportions of unvaccinated children between 2006 and 2007.

Second, a main effects regression model (Model 1) of vaccine status on year of interview (0=2002−06, 1=2007−10) *plus* all eleven child, mother and household measures estimated the adjusted odds of being unvaccinated for different groups of children. Wald chi-square tests were evaluated both to determine if year was still significant after controlling for these main effects (indicating change in vaccine status over time was significant beyond changing US population characteristics) and to estimate the odds of being unvaccinated across the nine-year period for children with various characteristics. When interpreting this model, the odds ratio (OR) for a main effect measure reflects the ratio of the odds of being unvaccinated for a child with a specific characteristic to the odds of being unvaccinated for a child with the reference level characteristic for that measure (whose odds of being unvaccinated, by definition, equals 1.0).

Third, six interaction terms (created by crossing NIS year with each of the six main effect measures significantly associated with vaccine status) were sequentially added to Model 1. Again using Wald statistics, two significant interaction terms were identified (indicating two measures were associated with a change over time in a child's odds of being unvaccinated). An interaction model (Model 2) was created (by adding these two interaction terms to Model 1) to

see if the odds of being unvaccinated changed significantly between the earlier and later periods for certain children. When interpreting this final model, the odds ratio for an interaction term is the *change* over time (between the earlier and later periods) in the ratio of the odds of being unvaccinated for a child with a specific characteristic relative to the odds of being unvaccinated for a child with the reference level characteristic.

Stata software was used to run all statistical tests throughout this analysis.[48]

RESULTS

Trend Analysis

The proportion and number of unvaccinated children in the US increased between 2002 and 2010, representing both a statistically and practically significant rise in children who received none of the 15 recommended doses of the 4:3:1:3:3:1 vaccine series.

[Table 2 and Figure 1 about here]

The proportion of unvaccinated children rose significantly over the period, from about one-quarter of one percent in 2002 (0.27%) to over half of one percent in 2004 (0.56%), over three-quarters of one percent in 2007 (0.80%), and remaining high through 2010 (0.81%). While these proportions are very small, they represent a substantive change in the risk of disease over time: the number of unvaccinated children in the US doubled between 2002 and 2004 (from below 16,000 to over 32,000 children), increased by nearly 20,000 children in 2007 alone, and tripled by 2010 (to over 50,000 children nationally).

Three simple regressions confirmed that a child's unadjusted odds of being unvaccinated increased significantly across the period of analysis, regardless of how time was coded. On average, a child's odds of being unvaccinated increased 12% annually over the nine years

(OR=1.12, 95%CI=1.08−1.16), a child was three times more likely to be unvaccinated in 2010 than in 2002 (OR=3.00, 95%CI=2.00−4.48), and a child's odds of being unvaccinated increased by 77% (OR=1.77, 95%CI=1.47−2.13) between the earlier and later periods of analysis (2002−06 and 2007−10).

Multivariate Analyses

Even after controlling for child, mother and household characteristics, Model 1 (the main effects model) showed a child's adjusted odds of being unvaccinated still increased 75% between the earlier and later periods (OR=1.75), so this trend was not simply due to changes in the US population composition. Wald chi-square tests showed six main effect measures were significantly associated with a child's odds of being unvaccinated: Child's Race/Ethnicity (Wald=48.82, p=0.0000); Child's Firstborn Status (Wald=4.18, p=0.0410); Mother's Education (Wald=19.60, p=0.0002); Household's Number of Children (Wald=89.63, p=0.0000); Household's Census Region (Wald=19.02, p=0.0003); and Household's State Philosophical Exemption Status (Wald=4.39, p=0.0362).

[Table 3 about here]

White non-Hispanic children were two to three times more likely to be unvaccinated than either Blacks (1.0/0.54=1.85) or Hispanics (1.0/0.34=2.94). Firstborn children were 35% more likely to be unvaccinated than younger siblings. Mothers who graduated from college were 35% more likely to have an unvaccinated child than mothers with only some college (1.0/0.74=1.35), but mothers who had dropped out of high school were 61% more likely to have an unvaccinated child than college graduates. Children living in the largest households (with four or more children) were five times more likely to be unvaccinated than only children, but even children in

two- or three-child households were twice as likely as only children to be unvaccinated. Children living in the West (and, to a lesser extent, in the Midwest) were more likely to be unvaccinated than children living in the South (1.0/0.59=1.69) or Northeast (1.0/0.57=1.75), and children living in states that allowed philosophical exemptions were 24% more likely to be unvaccinated.

Finally, looking at measures associated with vaccine status over time, the odds of being unvaccinated changed significantly between the earlier and later periods for children identified by either race/ethnicity (Wald=10.49, p=0.0148) and their household's number of children (Wald=12.56, p=0.0019). Including these two interaction terms in Model 2 (the interaction model) showed children of other or multiple race/ethnicities were only one third as likely to be unvaccinated in the later period (relative to White non-Hispanics) as they had been in the earlier period (OR=0.35) while children in two- or three-child households were twice as likely to be unvaccinated in the later period (relative to only children) as they had been earlier (OR=2.04).

DISCUSSION

This study finds three times more unvaccinated children in the United States in 2010 than there had been just nine years earlier. And while the proportion of unvaccinated children approaches one percent of all children across the total US, this national average understates the higher prevalence of vaccine refusal in communities with clusters of unvaccinated children.[49]

Consistent with Smith et al. (2004), this analysis found White non-Hispanic children are still more likely than some others to be unvaccinated, as are children living in the largest households, in Western states, and in states where philosophical exemptions from vaccination are allowed. However, in contrast to Smith et al., the range of child, mother, and household characteristics associated with vaccine refusal have become more heterogeneous over time.

Some demographic characteristics now have a weaker association with vaccine refusal than in the past. Whereas Smith et al. found boys were more likely than girls to be unvaccinated, this analysis shows child gender is no longer significantly associated with vaccine status. Also, older mothers (over age 30) now are no more likely than mothers in their twenties to refuse vaccines, and currently married mothers are no more likely than never/previously married mothers to have unvaccinated children. Although household size is still strongly associated with vaccine status, children in two- and three-child households are increasingly likely to be unvaccinated.

Likewise, vaccine refusal now appears to be less a function of socioeconomic status than it once was. Previously, maternal education was strongly associated with vaccine refusal, but now mothers without a high school diploma are even more likely than college graduates to have unvaccinated children. Also, unvaccinated children are no longer found primarily in the highest income households (perhaps a function of income data being top-coded at $50,000), but now are equally likely to live in households with more moderate (or even below poverty) incomes.

These findings may serve to inform programs and policies that aim to improve vaccine coverage in the US. While this paper does not attempt to evaluate current immunization efforts, understanding key characteristics associated with vaccine refusal may aid in developing programs that educate parents about the importance and safety of childhood vaccines. For example, beyond efforts aimed at school-based populations (who often share similar socioeconomic and demographic characteristics), perhaps a regional approach could reach a more diverse group of parents. Conversely, outreach campaigns (via the internet, radio, or television) tailored towards younger, unmarried or divorced mothers, or lower SES parents might reach a broader audience with information to counter media sources that discourage vaccination.

Also, state and local health and education systems, alongside federal agencies and the CDC, could coordinate to address individual vaccine concerns while providing parents with a greater appreciation of the community benefits gained by increased immunization compliance.

CONCLUSION

The United States has recently seen a sharp rise in both the proportion and number of unvaccinated children, experienced numerous outbreaks of vaccine-preventable disease, and engaged in a heated debate about vaccine safety. While the overall prevalence of vaccine refusal has grown, children with increasingly diverse demographic and socioeconomic characteristics are being left unvaccinated. Efforts aimed at reducing the incidence of infectious disease need to take these findings into account when developing programs and policies that attempt to reach clusters of unvaccinated children around the country.

Future research could investigate single vaccines or diseases (MMR, measles, pertussis) and conduct small area analyses to improve our understanding of trends in local communities. Also, updated information from the CDC on parental knowledge and attitudes about immunizations could shed light on the diffusion of beliefs about childhood disease and the risk assessment parents go through in deciding whether or not to vaccinate their child. Parents' social networks, traditional news sources, and internet media all have increased the public's awareness of vaccine refusal as an alternative, albeit a controversial one. Having a better understanding of these influences, and the current factors associated with vaccine refusal, will enable program and policy makers to develop interventions that reach a more heterogeneous population of parents, address their concerns about vaccine safety, lower the prevalence of unvaccinated children, and hopefully, reduce the incidence of vaccine-preventable disease.

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TABLES & FIGURES

TABLE 1: Recommended Immunization Schedule, with Type of Vaccine and Number of Doses in the 4:3:1:3:3:1 Vaccine Series, by Age of Child at Vaccination.

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		

Ref: CDC, Recommended Immunization Schedules for Persons Aged 0 Through 18 Years – United States, 2010. *MMWR Morb Mortal Wkly Rep*. 2010;58(51&52):1−4.

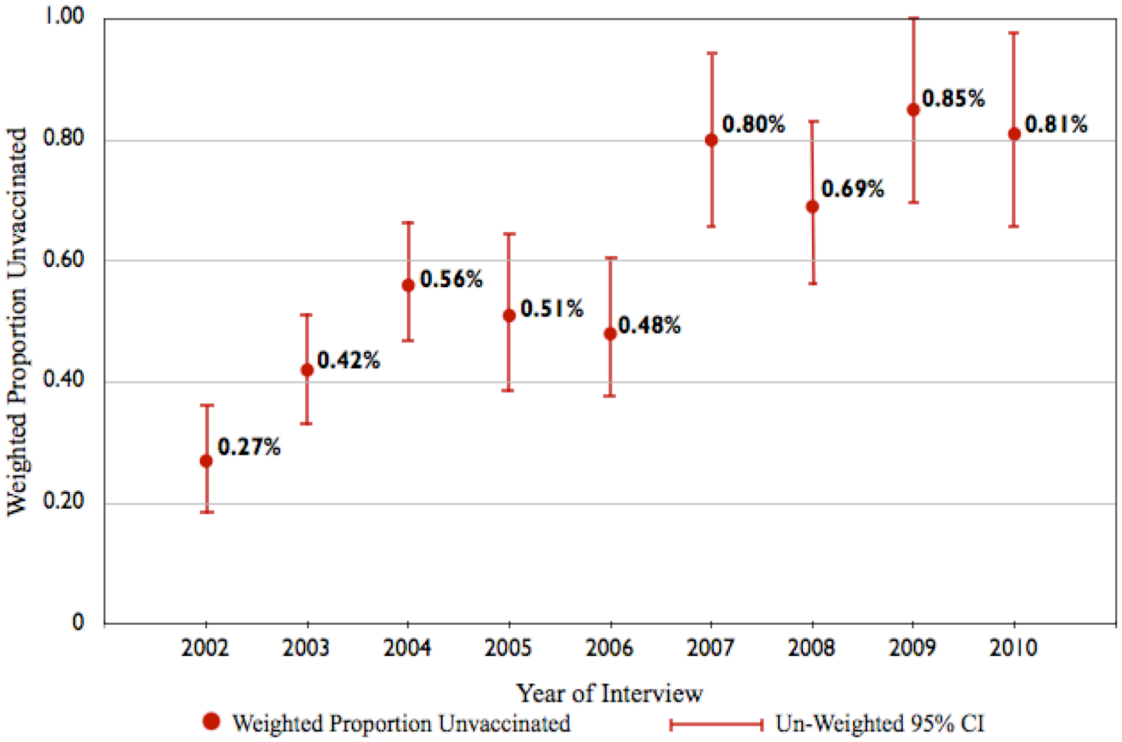
TABLE 2: NIS Sample Size and US Count of Children Aged 19−35 Months; Number and Proportion [with 95% CI] of Unvaccinated Children; and P-values from T-test Comparison of Proportions Unvaccinated in 2002 and 2003−2010.

Year	NIS Sample Size[a]	US Count[b]	Number of Unvaccinated Children[c]	Proportion of Unvaccinated Children[d]	95% CI[e]	P-value[f]
2002	21,410	5,845,539	15,958	0.27%	0.18-0.36%	-
2003	21,310	5,899,319	24,533	0.42%	0.32-0.51%	0.0327
2004	21,998	5,874,424	32,780	0.56%	0.46-0.66%	0.0000
2005	17,563	5,935,947	30,041	0.51%	0.38-0.64%	0.0038
2006	21,044	6,010,243	28,964	0.48%	0.37-0.60%	0.0049
2007	17,017	6,025,082	48,052	0.80%	0.65-0.94%	0.0000
2008	18,430	6,168,021	42,774	0.69%	0.56-0.83%	0.0000
2009	17,313	6,297,794	53,525	0.85%	0.69-1.01%	0.0000
2010	17,004	6,159,994	50,119	0.81%	0.65-0.98%	0.0000

Ref: CDC (2003−2011), 2002−2010 National Immunization Survey.

[a] *Total un-weighted number of children in NIS sample with "adequate provider data."*
[b] *Weighted number of children age 19−35 months in the US that NIS data represent.*
[c] *Weighted number of children in the US who are unvaccinated.*
[d] *Weighted proportion of children in the US who are unvaccinated.*
[e] *Un-Weighted 95% CI for proportion of children in the US who are unvaccinated.*
[f] *Significance of change in proportion of unvaccinated children each year since 2002.*

FIGURE 1: Weighted Proportion of Unvaccinated Children, by Year of Interview, with Un-Weighted 95% Confidence Intervals.



Ref: CDC (2003-2011), 2002-2010 National Immunization Survey.

TABLE 3: Binomial Logistic Regression Models of Vaccine Status on Year, Characteristics and Interaction Terms: Odds Ratios [and 95% CIs], N=160,576.

	Model 1	Model 2
Year of NIS Interview (ref: 2002−06)	1.75 [1.44-2.14]	1.26 [0.83-1.92]
Child Characteristics		
Race/Ethnicity (ref: White, Non-Hispanic)		
Hispanic	0.34 [0.24-0.49]	0.33 [0.20-0.53]
Black, Non-Hispanic	0.54 [0.37-0.79]	0.63 [0.37-1.05]
Other or Multiple Race/Ethnicity	0.44 [0.30-0.63]	0.75 [0.45-1.24]
Gender (ref: Male)		
Female	1.02 [0.83-1.25]	1.02 [0.83-1.25]
Child's Age (ref: 30−35 Months)		
19−23 Months	1.12 [0.88-1.42]	1.12 [0.88-1.42]
24−29 Months	0.96 [0.74-1.24]	0.96 [0.74-1.24]
First Born (ref: No)		
Yes	1.35 [1.01-1.79]	1.31 [0.99-1.75]
Mother Characteristics		
Education Level (ref: GE 16 years)		
LT 12 Years	1.61 [1.01-2.57]	1.62 [1.01-2.58]
12 Years	1.00 [0.73-1.37]	1.00 [0.73-1.37]
13−15 Years	0.74 [0.57-0.96]	0.74 [0.57-0.96]
Mother's Age (ref: 30 years or older)		
Under 20 Years	0.79 [0.37-1.70]	0.78 [0.37-1.67]
20−29 Years	1.20 [0.92-1.56]	1.20 [0.92-1.56]
Marital Status (ref: Never/Previously Married)		
Currently Married	1.17 [0.87-1.59]	1.17 [0.87-1.59]
Household Characteristics		
Income & Poverty Status (ref: Income <= Poverty)		
Income > Poverty but <= $50K	1.16 [0.84-1.59]	1.16 [0.85-1.59]
Income > $50K	0.95 [0.64-1.41]	0.95 [0.64-1.41]
Number of Children in HH (ref: One Child in HH)		
Two-Three Children in HH	2.06 [1.52-2.79]	1.36 [0.91-2.01]
Four or More Children in HH	5.25 [3.67-7.52]	5.06 [3.18-8.03]
Census Region (ref: West)		
Northeast	0.57 [0.41-0.79]	0.57 [0.41-0.79]
Midwest	0.75 [0.58-0.97]	0.75 [0.58-0.97]
South	0.59 [0.45-0.77]	0.59 [0.45-0.77]
Philosophical Exemption (ref: No)		
Yes	1.24 [1.01-1.51]	1.24 [1.01-1.51]
Interaction Terms		
Year*Child's Race/Ethnicity (ref: White, Non-Hispanic)		
Year * Hispanic	-	1.04 [0.53-2.02]
Year * Black, Non-Hispanic	-	0.78 [0.38-1.61]
Year * Other & Multiple R/E	-	0.35 [0.18-0.68]
Year*Number of Children in HH (ref: One Child)		
Year * Two-Three Children	-	2.04 [1.25-3.33]
Year * Four or More Children	-	1.08 [0.63-1.85]

Ref: CDC (2003−2011), 2002−2010 National Immunization Survey.