# THE FIRST ORAL ROTAVIRUS VACCINE 1998-1999: ESTIMATES OF UPTAKE FROM THE NATIONAL IMMUNIZATION SURVEY

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**ABSTRACT**

***Objective***. On August 31, 1998, the rhesus-human reassortant rotavirus vaccine (RRV-TV) was licensed for use in the U.S. During the next nine months, 15 cases of intussusception were reported among infants who received the vaccine. Case-control and cohort studies showed a significantly increased risk of developing intussusception within one week of receiving the vaccine; subsequent ecologic studies did not. In this paper, we use data on RRV-TV vaccination rates from the National Immunization Survey (NIS) to estimate state and national RRV-TV uptake rates and factors associated with receiving RRV-TV. These estimates are a key component in evaluating published ecologic studies designed to investigate the relationship between receipt of the vaccine and intussusception.

***Methods***. We analyzed NIS data for children aged 19-35 months who were eligible to receive RRV-TV between September 1998 and July 1999. We estimated vaccine coverage and the number of doses administered by State, NIS sampling quarter, and birth cohort, and analyzed demographic and socioeconomic variables to evaluate their relationship with receiving RRV-TV.

***Results.*** We estimate that approximately 1 million doses of RRV-TV were administered to 504,585 (±61,854) children, 13.4% (±1.6%) of eligible children. The estimated number of doses administered and the vaccination coverage rate varied greatly from state to state. Children living in households with higher socioeconomic conditions were more likely to receive the vaccine.

***Conclusion***. Ecologic studies had a limited ability to detect a significant increase in the population incidence rate of intussusception that could be attributed to RRV-TV because populations in these studies consisted primarily of children who did not receive the vaccine. The example from RRV-TV demonstrates some of the challenges of assessing

the magnitude of the association between a vaccine and an uncommon or rare adverse event.

***Abbreviations:*** ACIP, Advisory Committee on Immunization Practices; CDC, Centers for Disease Control and Prevention; CI, confidence interval; NIS, National Immunization Survey; OR, odds ratio; RRV-TV, RotaShield®; VAERS, Vaccine Adverse Event Reporting System.

## BACKGROUND

Rotavirus is the most common cause of severe diarrhea among infants worldwide.[1] In the United States, approximately 2.7 million children < 5 years of age are infected with rotavirus diarrhea each year, resulting in 500,000 physician visits and 50,000 hospitalizations at an estimated $274 million in medical care and more than $1 billion in societal costs.[2,3] In developing countries, an estimated 800,000 deaths per year are caused by rotavirus.[4,5]

An oral, live, tetravalent, rhesus-human reassortant rotavirus vaccine, RotaShield® (RRV-TV), was developed and found to be effective in clinical trials among children in North America, South America, and Europe.[6] On the basis of these studies, RRV-TV was licensed on August 31, 1998 for use among infants in the United States.[7]

In the prelicensure studies of candidate live attenuated rhesus-human reassortant rotavirus vaccines administered orally, intussusception occurred in five of 10,054 vaccine recipients and in one of 4,633 controls.[8] While these data suggested a possible relationship between vaccination with the candidate vaccines and intussusception, the difference between these estimated rates was not statistically significant. As a precaution, intussusception was listed in the vaccine package insert as a possible adverse reaction, and the Advisory Committee on Immunization Practices (ACIP) recommended post-licensure surveillance for intussusception.[9]

Within nine months of licensure of RRV-TV, 15 cases of intussusception among recipients of RRV-TV were reported to the Vaccine Adverse Event Reporting System (VAERS).[10] Based on these data and data from the manufacturer's prelicensure studies, the Centers for Disease Control and Prevention (CDC) recommended on July 16, 1999 that health-care providers and parents postpone administration of RRV-TV while further investigation was undertaken.[11] Subsequently, the manufacturer ceased distribution of the vaccine.

In response to these reports, CDC conducted case-control[12] and cohort studies[13] that demonstrated that the risk of intussusception was increased significantly following administration of the first dose of RRV-TV, by approximately one case in 10,000 vaccinees. On October 1999, the ACIP withdrew its recommendation for the administration of RRV-TV in the U.S.[14,15]

Two ecologic studies, conducted by Simonsen et al.[16] and Chang et al.[17] questioned whether RRV-TV was, in fact, associated with increased risk of intussusception. Estimates of vaccine coverage are a key component in ecologic analyses to detect a significant increase in the population incidence rates of intussusception over the rate of intussusception in the absence of RRV-TV. The assumption is that the increase could be attributed to RRV-TV. The conclusions of the two studies depended on state-level estimates of the number and percentage of children receiving RRV-TV. To estimate these statistics, both studies used preliminary marketing and distribution data from the manufacturer. Since doses distributed to a state may be redistributed to other states or

stored for future administration, coverage estimates derived from these data may be inaccurate.

We analyzed data from the 1999-2001 National Immunization Survey (NIS), a large probability sample survey conducted by the CDC, to accurately estimate the number of doses of RRV-TV administered, the percentage of children receiving one or more doses, and the socioeconomic and demographic factors associated with receipt of the vaccine. We used these surveillance statistics to examine the ability of the ecological analyses to detect an increased risk of intussusception following vaccination with RRV-TV, if such an increased risk existed.

## METHODS

### RRV-TV Surveillance: The National Immunization Survey

The NIS is conducted in 78 Immunization Action Plan (IAP) areas, consisting of the 50 states, the District of Columbia, and 27 other large urban areas. During each quarter of the calendar year, the NIS obtained an independent sample of telephone numbers to identify households that had children 19-35 months of age in each IAP area. At the completion of the telephone interview of households with age-eligible children, consent was requested to contact the children's vaccination providers to obtain their vaccination histories. Data obtained from the vaccination providers were used to determine whether the sampled children were up-to-date with respect to recommended vaccines. Estimates of vaccination coverage rates were obtained from each quarterly survey and provided a

measure of the extent to which children were adequately vaccinated with respect to recommended vaccines. Descriptions of the NIS sampling design, survey weights, and statistical methods for estimating vaccination coverage rates are given by Smith et al.[18,19]

**Determination of Birth Cohorts Eligible for the RRV-TV Vaccine**

RRV-TV was licensed on August 31, 1998 and became available at different times in different geographic areas in the U.S. For each IAP, we assumed that vaccine became available in the month of the earliest dose reported by providers of children sampled by the NIS. RRV-TV administration effectively ceased in each IAP by July 16, 1999, when the CDC recommended that health-care providers and parents discontinue its use. Children who received the vaccine as recommended (no first dose after 6 months of age and no dose before 6 weeks of age) when it was available were born no earlier than 7 months before the month in which it was available in each area and no later than May 31, 1999 in all areas.

**Statistical Analysis of RRV-TV Uptake Rates**

NIS vaccination coverage rates were estimated for each quarter the survey was conducted and information was collected on children's RRV-TV vaccination histories. To accommodate the complex sampling design and sample survey weights of the NIS, we used SUDAAN Version 7.5[20] for all statistical analyses of RRV-TV uptake rates and all related RRV-TV surveillance statistics. We used bivariate logistic regression to estimate odds ratios to evaluate the association between the receipt of one or more doses of RRV-TV and children's demographic and socioeconomic characteristics.

## RESULTS

### Quarterly NIS Estimates of RRV-TV Uptake

Over the seven NIS quarterly surveys conducted between the third quarter of 1999 and the first quarter of 2001, 14,889 children were sampled by the NIS who were age-eligible to receive RRV-TV during the time it was recommended. The estimated number of doses administered when the vaccine was available was reported in the third quarter survey of 1999 to be less than 1,000 doses and increased to 1,037,000 doses reported in the first quarter survey of 2001 (Table 1). Because Quarter 1, 2001 NIS data include all birth cohorts eligible to receive RRV-TV, data from this quarter estimate the total number of RRV-TV doses administered in the U.S. The estimated RRV-TV coverage rate increased from 2.3% (±2.5%) in the fourth quarter survey of 1999 to 12.2% (±1.4%) in the first quarter survey of 2001. The estimated RRV-TV coverage rate peaked at 13.4% (±1.6%) in the fourth quarter survey of 2000. The decrease in estimated coverage from 13.4% in the fourth quarter survey of 2000 to the 12.2% in first quarter survey of 2001 was not statistically significant. This apparent decline was attributable to the cohort born during the second quarter of 1999 that was eligible to receive RRV-TV for only 2½ months before vaccine usage was suspended.

Using data from the NIS, we determined that doses had been received by sampled children in 77 of the 78 IAPs by July 16, 1999 (Figure 1). No providers reported administering RRV-TV to children sampled by the NIS in New Mexico. By the end of October 1998, doses were reported by the providers of sampled children in 34 IAPs

(44%) and by the end of December 1998, doses were reported by the providers of sampled children in 65 IAPs (84%). In the seven NIS quarterly surveys included in the analysis, 1,562 children sampled by the NIS were reported by vaccination providers as having been administered RRV-TV. Of these, 43 (2.8%) received doses after July 16, 1999 when CDC recommended that administration of the vaccine be suspended.

**National and State Estimates of RRV-TV Uptake**

Data from the NIS survey conducted in the first quarter of 2001 included the most recent available information about RRV-TV vaccination histories for birth cohorts that could have been administered the vaccine. Table 2 gives the quarterly estimates of the number of doses administered and the percent of children receiving one or more doses of RRV-TV by State using NIS data reported in this quarter. Among the 5.5 million children between the ages of 19 and 35 months and were eligible to be sampled by the NIS in this quarter, approximately 4.4 million children were eligible to have received RRV-TV according to ACIP recommendations during the time when it was available. Estimates of the number of doses administered and the RRV-TV coverage varied widely from state to state: the estimated number of doses administered ranged from less than 1,000 (NH, NM, ND, OR, SD, VT, WA, WY) to 105,000 (NY); and the estimated coverage rate ranged from less than 1% (NM, OR, SD, WA) to 29.4% (NE). Overall, 504,585 (±61,854) children received one or more doses of RRV-TV.

**RRV-TV Coverage by Birth Cohort**

Table 3 shows RRV-TV quarterly coverage estimates by birth cohort as the cohorts progressed over time. Children belonging to older birth cohorts were less likely to have received the vaccine. The oldest birth cohort eligible to receive RRV-TV was born in the second quarter of 1998. The estimated uptake in this birth cohort increased from 0% in the third NIS sampling quarter of 1999 to 2.6% in the first NIS sampling quarter of 2001. More recent birth cohorts had higher coverage rates, achieving a maximum of 22.8% for the cohort born in the first quarter of 1999 and sampled in the fourth quarter of 2000.

**Factors Associated with the Receipt of RRV-TV**

Table 4 shows the estimated percent of children receiving one or more doses of RRV-TV for 15 variables collected in the NIS. Also, this table shows the estimated odds ratios for the association between the receipt of one or more doses of RRV-TV and the children's demographic and socioeconomic characteristics and their vaccination providers' characteristics. Children who received one or more doses of RRV-TV were more likely to be white; to have received vaccinations from providers in a private practice setting; to be in a household that reported an annual income exceeding $75,000; and to have a mother who was at least 30 years old, who was married and attended college. Children who received one or more doses of RRV-TV were less likely to have participated in the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) and their vaccination providers were less likely to have participated in the Vaccines for Children (VFC) program.

## DISCUSSION

Data from the NIS provide the first estimates of RRV-TV uptake in the U.S. using standard sampling techniques.[21] NIS interviews conducted from 1999 to 2001 provide data on all cohorts that could have received the vaccine according to ACIP recommendations during the period that the vaccine was available. These data suggest that approximately one million doses of RRV-TV were administered to 504,585 (±61,854) children living in the United States. Approximately 13.4% of all children who were eligible to receive RRV-TV were administered one or more doses of the vaccine. In general, the likelihood of receiving RRV-TV was significantly greater among children living in households with higher socioeconomic status.

By using the same data collection methodology and survey instruments in all areas, the NIS produces vaccination coverage levels that are comparable among areas and over time. Considerable resources are applied to eliminating the effects of data collection and field operations that could bias results. The NIS is designed to produce annual estimates of vaccination coverage levels within each of 78 areas with a coefficient of variation of no more than 5%. Previous studies[22] have shown that vaccination coverage estimates obtained from the National Health Interview Survey[23] are very similar to those obtained from the NIS, and provide a validation of the methods and results in this paper.

RRV-TV vaccination coverage estimates obtained from the NIS are useful for evaluating the conclusions of research designed to investigate the relationship between receipt of the vaccine and intussusception. For example, Simonsen et al.,[16] investigated the risk of intussusception attributable to vaccination with RRV-TV using an ecologic study design. In this study, hospital discharge reports of children 6 weeks to 7 months old with any mention of intussusception were extracted from electronic databases of 10 states. The authors estimated the attributable risk by dividing the number of excess cases of intussusception during the period of vaccination by the estimated number of vaccinated children based on doses of vaccine distributed. Chang et al.[17] used essentially the same method in their ecologic analyses of data from New York State. Unlike the case case-control study[12] and cohort study[13] that estimated the attributable risk of RRV-TV to intussusception to be approximately one case among 10,000 vaccinees, the ecologic studies did not detect an attributable risk of this magnitude.

To examine the discrepant findings of the ecologic studies versus the case-control and cohort studies, we used the RRV-TV vaccination coverage rates estimated from NIS data to examine the ability of the ecological analyses to detect an increased risk of intussusception, if such an increased risk existed. Using NIS data we estimated that the RRV-TV coverage rate was 12.2% (±1.4%) in the 10 states of Simonsen's ecological study and 17.7% (±7.8%) in New York State. Assuming these levels of vaccine coverage and a background intussusception rate of 34.40 cases per 100,000 derived from data reported by Simonsen et al., the chance of detecting an attributable risk of approximately one case of intussusception among 10,000 vaccinees was no more than 22% for

Simonsen's ecologic study and no more than 16% for Chang's ecologic study. Given the NIS national estimate of 13.4% coverage (± 1.6%), if Simonsen's ecological study were expanded to include all 50 states and the District of Columbia, the chance of detecting an attributable risk of approximately one case among 10,000 vaccinees would be no more than 46%. Even given the highest estimate of attributable risk of one case among 5000 vaccinees[12], the chance of detecting an increased risk attributable to RRV-TV was < 40% in Simonsen et al's 10 state analysis, was approximately 80% if the Simonsen et al. analysis were extended to all 50 states and the District of Columbia, and was only 25% in Chang et al. ecological study. The power of the ecologic studies to detect substantial levels of the attributable risk was low because few infants were vaccinated with RRV-TV in the study populations. As a result, although the risk of intussusception may have been substantial among children receiving RRV-TV, the risk to the entire population of predominantly unvaccinated children was quite small because relatively few children were administered the vaccine. Ecologic studies may not provide reliable evaluations of the association between vaccination with RRV-TV and intussusception.

Both ecologic studies used manufacturer distribution data as the basis for estimating RRV-TV coverage in the states investigated in their evaluations. These estimates were substantially higher than those obtained by the NIS. Reasons for this difference may include doses that were never used rather than being administered, doses that were wasted or returned, and some doses that were distributed to one state and administered to children living in another state.

Development of rotavirus vaccines is desirable because safe and effective vaccines could save as many as 800,000 lives each year. Accurate estimates of the magnitude of the association between RRV-TV and intussusception are useful for designing vaccine trials with a new generation of rotavirus vaccines, and will affect national policy for use of these vaccines

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**APPENDIX**

The baseline risk of intussusception in the absence of RRV-TV was derived from the data published in Table 1 of the paper by Simonsen et al.[16] In estimating this risk, we used data pertaining to children 45-210 days old because the first dose of RRV-TV was recommended no sooner than 45 days (~6 weeks) of age and no later than after 210 days (~6 months) of age. This table also indicates that 125 children in this age group had intussusception in the 9 month period before RRV-TV was available, beginning October 1, 1998 and ending June 20, 1999. The estimated annualized number of intussusceptions is n=166.7=125/0.75, since the 9 month period represents 3/4 of a year. Also, this table shows 1,076,715 children belonged to the 12 month 1998 birth cohort. Assuming the children are born uniformly across the year, the annualized number 167 "represents" intussusception cases from approximately (210-45)/365=0.45 of the entire 1998 birth

cohort, i.e., .45 x 1,076,715 = 484,521.75 children. Using these statistics, the estimated background rate of intussusception in the absence of RRV-TV is 167/484,521.75 = 34.40 per 100,000. Assuming the estimate of Murphy et al.[12] and Kramartz et al.[13] of one case in 10,000 as the increased risk of intussusception attributable to RRV-TV, the risk of intussusception among children receiving RRV-TV that is attributable to both the background rate and the rate attributable to RRV-TV is (34.40 + (10,000 * 0.0001 ) ) / 10,000= 44.4 per 10,000. Using the estimated national RRV-TV coverage rate of 13.4% reported in Table 1 of our paper, the population risk of intussusception assuming an attributable risk of 1 in 10,000 is 10.000 x [(1-0.134) x 0.00340 + 0.134 x 0.000444] = 35.74 per 10,000. If the Simonsen's ecologic study had been expanded to the *entire* U.S. annual birth cohort of 4.5 million children, the statistical power of Simonsen's methods would have 45.7% to detect a difference between the population risk of intussusception and the baseline risk of intussusception, using a one-sided statistical test designed to have no more than a 5% chance of erroneously concluding that differences existed if they actually did not exist. The mathematical formulae for these power calculations are described[24,25] and available in the binomial.sample.size() function of S-Plus.[26] A similar approach was used to estimate the statistical power of Simonsen's 10-state ecologic study, and Chen's ecologic study of New York State.

**Table 1: Quarterly Estimates of RRV-TV Uptake. National Immunization Survey: April 1, 1999 – March 31, 2001.**

| NIS Quarterly Survey Quarter/Year | Sample Size[a] | Population Size[b] | Estimated Number of Eligible Children[c] | Estimated Numbers in Thousands of Doses Administered Number (95% CI[d]) | Estimated Coverage One or More RRV-TV Doses % (95% CI) |
|---|---|---|---|---|---|
| Q3/1999 | 12 | 5,493,972 | 8,708 | <1 (±<1 ) | <1 (±<1 ) |
| Q4/1999 | 287 | 5,412,542 | 253,552 | 13 (±15 ) | 2.3 (±2.5 ) |
| Q1/2000 | 1084 | 5,813,749 | 1,013,896 | 96 (±43 ) | 3.9 (±1.6 ) |
| Q2/2000 | 2085 | 5717,,510 | 2,207,071 | 452 (±105) | 8.0 (±1.8 ) |
| Q3/2000 | 3132 | 5,813,855 | 3,103,959 | 746 (±124) | 10.3 (±1.6 ) |
| Q4/2000 | 3761 | 5,372,071 | 3,753,774 | 979 (±125) | 13.4 (±1.6 ) |
| Q1/2001 | 4528 | 5,509,950 | 4,413,058 | 1,037 (±132) | 12.2 (±1.4 ) |

[a] The NIS quarterly sample size is the unweighted number of children 19-35 months of age at the time of the NIS interview who were determined from date of birth to have been eligible to have received RRV-TV according to ACIP recommendations during the period when RRV-TV was administered.
[b] The NIS quarterly estimate of the number of children in the U.S. 19-35 months of age.
[c] The NIS quarterly estimate of the number of children in the U.S. who were eligible to have received RRV-TV according to ACIP recommendations during the period when RRV-TV was administered.
[d] 95% Confidence interval.

**Table 2: RRV-TV Uptake of Children 19-35 Months of Age: National and State Estimates. NIS, 1st Quarter of 2001.**

| | Sample Size | Population Size | Estimated Number of Eligible Children | Estimated Numbers in Thousands of Doses Administered Number (95% CI) | Estimated Coverage One or More RRV-TV Doses % (95% CI) |
|---|---|---|---|---|---|
| U.S. Total | 4528 | 5509950 | 4,413,058 | 1,037 (±132) | 12.2 (±1.4 ) |
| Alabama | 126 | 83373 | 70,578 | 35 (±15 ) | 25.3 (±9.8 ) |
| Alaska | 57 | 13576 | 10,105 | 2 (±2 ) | 10.6 (±8.5 ) |
| Arizona | 92 | 114318 | 74,508 | 3 (±4 ) | 1.5 (±2.1 ) |
| Arkansas | 75 | 49563 | 38,291 | 4 (±4 ) | 4.9 (±4.8 ) |
| California | 255 | 779001 | 640,609 | 103 (±58 ) | 8.1 (±4.4 ) |
| Colorado | 69 | 88145 | 68,391 | 19 (±13 ) | 11.1 (±7.7 ) |
| Connecticut | 57 | 50173 | 40,584 | 9 (±7 ) | 12.9 (±8.6 ) |
| Delaware | 52 | 13001 | 10627 | 3 (±2 ) | 17.0 (±11.2) |
| Dist. of Columbia | 62 | 11930 | 9,341 | 1 (±1 ) | 8.4 (±6.8 ) |
| Florida | 147 | 293893 | 203,006 | 35 (±35 ) | 7.8 (±6.5 ) |
| Georgia | 119 | 161283 | 128,219 | 11 (±9 ) | 4.1 (±3.3 ) |
| Hawaii | 42 | 20728 | 17,057 | 1 (±1 ) | 5.9 (±8.0 ) |
| Idaho | 68 | 32266 | 26,605 | 8 (±6 ) | 13.0 (±8.1 ) |
| Illinois | 144 | 236265 | 203,433 | 48 (±26 ) | 11.9 (±5.8 ) |
| Indiana | 120 | 118991 | 101813 | 34 (±21 ) | 16.5 (±9.5 ) |
| Iowa | 53 | 49443 | 40,909 | 9 (±7 ) | 14.5 (±9.3 ) |
| Kansas | 52 | 48501 | 39,531 | 9 (±8 ) | 12.3 (±9.3 ) |
| Kentucky | 64 | 68392 | 58,789 | 9 (±7 ) | 7.9 (±6.0 ) |
| Louisiana | 115 | 94581 | 79,996 | 28 (±17 ) | 14.4 (±7.9 ) |
| Maine | 64 | 23656 | 17,575 | 2 (±2 ) | 9.5 (±7.1 ) |
| Maryland | 133 | 125536 | 102,899 | 32 (±15 ) | 18.6 (±8.6 ) |
| Massachusetts | 101 | 112434 | 90,459 | 19 (±13 ) | 13.4 (±7.8 ) |
| Michigan | 99 | 176285 | 122,227 | 40 (±26 ) | 19.9 (±11.2) |
| Minnesota | 68 | 97015 | 87,489 | 24 (±14 ) | 18.4 (±9.5 ) |
| Mississippi | 58 | 53137 | 45,917 | 3 (±4 ) | 4.5 (±4.5 ) |
| Missouri | 56 | 104761 | 87,855 | 42 (±23 ) | 23.5 (±11.8) |
| Montana | 65 | 14466 | 13,157 | 4 (±2 ) | 17.4 (±9.3 ) |
| Nebraska | 63 | 32328 | 27,933 | 18 (±8 ) | 29.4 (±11.8) |
| Nevada | 62 | 45839 | 36,368 | 3 (±3 ) | 4.3 (±4.9 ) |
| New Hampshire | 50 | 17122 | 11,563 | <1 (±<1 ) | 1.8 (±3.6 ) |
| New Jersey | 125 | 212528 | 181,835 | 44 (±31 ) | 15.0 (±9.2 ) |
| New Mexico[a] | 0 | 39369 | 0 | 0 (±0 ) | 0 (±0 ) |
| New York | 124 | 340288 | 282,489 | 105 (±51 ) | 17.7 (±7.8 ) |
| North Carolina | 55 | 136342 | 119,447 | 31 (±19 ) | 14.1 (±8.8 ) |
| North Dakota | 42 | 9005 | 5,090 | <1 (±<1 ) | 6.2 (±8.3 ) |
| Ohio | 186 | 219246 | 178,473 | 56 (±35 ) | 12.1 (±6.8 ) |
| Oklahoma | 69 | 74037 | 61,938 | 7 (±7 ) | 6.2 (±5.7 ) |

| | | | | | |
|---|---|---|---|---|---|
| Oregon | 40 | 60717 | 32,625 | <1 (±<1 ) | <1 (±<1 ) |
| Pennsylvania | 114 | 190092 | 155,825 | 61 (±32 ) | 20.5 (±9.5 ) |
| Rhode Island | 60 | 18269 | 13,195 | 2 (±2 ) | 9.5 (±8.1 ) |
| South Carolina | 62 | 82440 | 63,366 | 22 (±13 ) | 17.7 (±9.7 ) |
| South Dakota | 49 | 13011 | 9,913 | <1 (±<1 ) | <1 (±<1 ) |
| Tennessee | 178 | 97438 | 80,645 | 12 (±7 ) | 9.4 (±5.2 ) |
| Texas | 347 | 444785 | 384,542 | 53 (±34 ) | 7.6 (±4.3 ) |
| Utah | 46 | 58574 | 34,484 | 7 (±6 ) | 11.7 (±9.2 ) |
| Vermont | 56 | 11242 | 7,510 | <1 (±1 ) | 2.8 (±3.8 ) |
| Virginia | 54 | 137297 | 121,171 | 48 (±31 ) | 19.3 (±11.5) |
| Washington | 97 | 108845 | 67,179 | <1 (±1 ) | 0.6 (±1.2 ) |
| West Virginia | 52 | 27626 | 23,806 | 8 (±7 ) | 17.5 (±11.3) |
| Wisconsin | 126 | 91437 | 77,407 | 25 (±12 ) | 17.2 (±7.8 ) |
| Wyoming | 58 | 7357 | 6,281 | <1 (±1 ) | 2.2 (±4.2 ) |

[a] No children sampled in New Mexico received RRV-TV.

## Table 3: RRV-TV Coverage by Birth Cohort

| Birth Cohort (Quarter / Year) | Quarterly Survey (Quarter / Year) | Sample Size | Estimated Coverage 1+ RRV-TV Doses % (95% CI) |
|---|---|---|---|
| Q2 / 1998 | | | |
| | Q3 / 1999 | 4 | 0.0 (±0.0 ) |
| | Q4 / 1999 | 228 | 2.7 (±3.1 ) |
| | Q1 / 2000 | 729 | 2.7 (±1.5 ) |
| | Q2 / 2000 | 769 | 2.9 (±2.1 ) |
| | Q3 / 2000 | 774 | 3.8 (±1.7 ) |
| | Q4 / 2000 | 706 | 3.8 (±2.2 ) |
| | Q1 / 2001 | 804 | 2.6 (±1.2 ) |
| Q3 / 1998 | | | |
| | Q4 / 1999 | 1 | 0.0 (±0.0 ) |
| | Q1 / 2000 | 292 | 7.3 (±4.4 ) |
| | Q2 / 2000 | 973 | 10.1 (±3.0 ) |
| | Q3 / 2000 | 1081 | 7.6 (±2.4 ) |
| | Q4 / 2000 | 986 | 7.2 (±2.1 ) |
| | Q1 / 2001 | 972 | 8.2 (±2.5 ) |
| Q4 / 1998 | | | |
| | Q2 / 2000 | 310 | 14.6 (±5.7 ) |
| | Q3 / 2000 | 991 | 16.6 (±3.5 ) |
| | Q4 / 2000 | 982 | 17.6 (±3.6 ) |
| | Q1 / 2001 | 1018 | 17.4 (±3.5 ) |
| Q1 / 1999 | | | |
| | Q3 / 2000 | 231 | 19.8 (±7.3 ) |
| | Q4 / 2000 | 882 | 22.9 (±4.0 ) |
| | Q1 / 2001 | 1023 | 19.2 (±3.7 ) |
| Q2 / 1999 | | | |
| | Q4 / 2000 | 166 | 19.8 (±9.2 ) |
| | Q1 / 2001 | 665 | 13.7 (±3.9 ) |

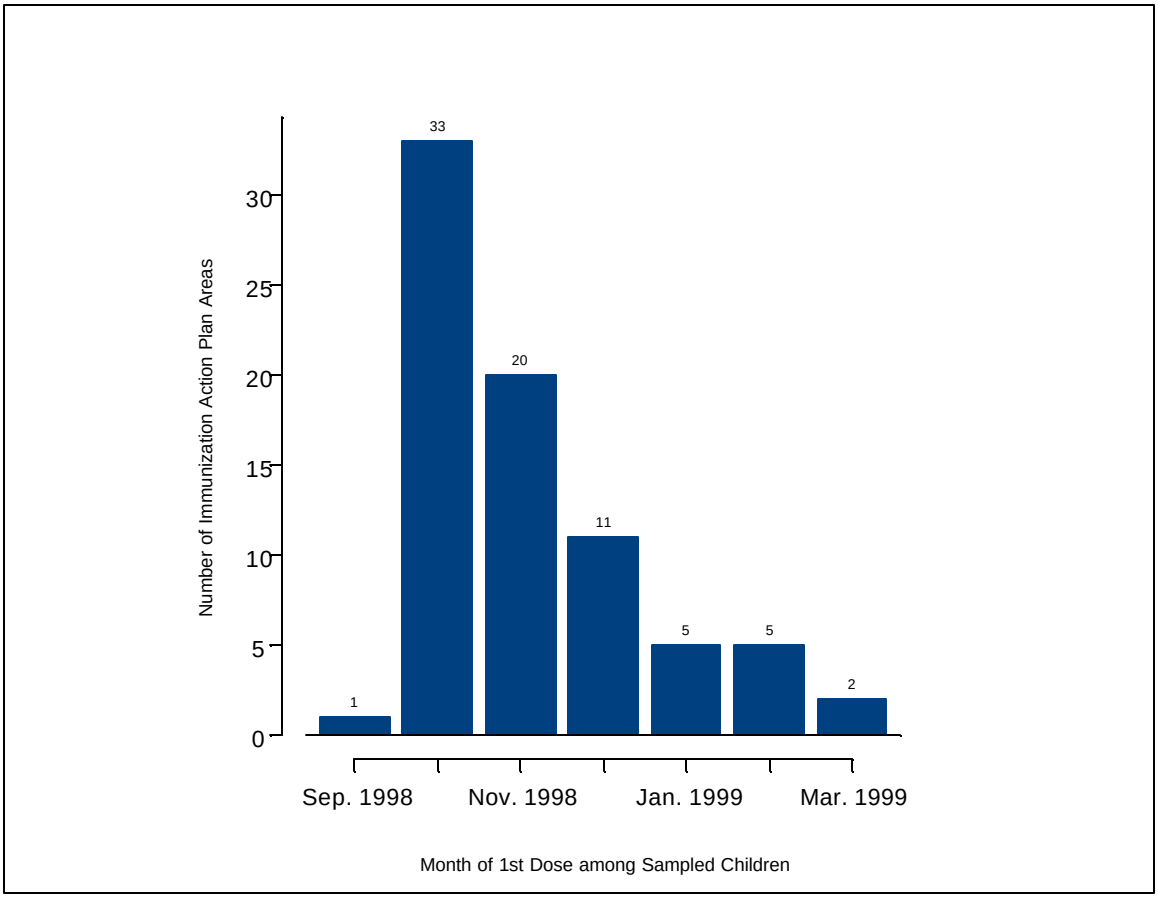
Table 4: Analysis of Factors Associated with Receiving One Or More Doses of RRV-TV.

| Variable | Sample Size | Percent Received One or More RRV-TV Doses % (95% CI) | OR[a] | 95% CI for the OR |
|---|---|---|---|---|
| **Age of child (months)** | | | | |
| 19 - 24 | 1517 | 17.0 (±2.9 ) | 4.5 | [3.0, 6.8] |
| 25 - 29 | 1610 | 14.7 (±2.5 ) | 3.7 | [2.4, 5.5] |
| 30 - 35† | 1401 | 4.8 (±1.6 ) | 1.0 | [1.0, 1.0] |
| **Number of children ≤ 18 years of age in the household** | | | | |
| 1 child† | 1257 | 14.0 (±2.9 ) | 1.0 | [1.0, 1.0] |
| 2-3 children | 2739 | 12.4 (±1.8 ) | 0.9 | [0.6, 1.2] |
| 4+ children | 532 | 7.6 (±3.0 ) | 0.5 | [0.3, 0.8] |
| **Number of vaccination providers** | | | | |
| 1 provider† | 3120 | 13.3 (±1.8 ) | 1.0 | [1.0, 1.0] |
| 2 providers | 1153 | 11.1 (±2.6 ) | 0.8 | [0.6, 1.2] |
| 3+ providers | 255 | 3.6 (±2.2 ) | 0.2 | [0.1, 0.5] |
| **Educational Status of the mother** | | | | |
| <12 years | 609 | 5.2 (±2.5 ) | 0.3 | [0.2, 0.5] |
| 12 years | 1383 | 10.0 (±2.4 ) | 0.5 | [0.4, 0.7] |
| >12, non-college graduatet | 805 | 11.9 (±3.1 ) | 0.6 | [0.4, 0.8] |
| College graduate† | 1731 | 18.5 (±2.8 ) | 1.0 | [1.0, 1.0] |
| **Poverty status** | | | | |
| Annual household income ≥ $75K† | 806 | 18.5 (±3.8 ) | 1.0 | [1.0, 1.0] |
| Above Poverty, household income <$75K | 2415 | 13.0 (±1.9 ) | 0.6 | [0.5, 0.9] |
| Below poverty | 835 | 5.8 (±2.4 ) | 0.3 | [0.2, 0.5] |
| Unknown | 472 | 10.7 (±4.4 ) | 0.6 | [0.3, 1.0] |
| **Age of mother** | | | | |
| ≤ 19 | 162 | 7.3 (±5.5 ) | 0.5 | [0.2, 1.1] |
| 20 - 29 | 1967 | 9.0 (±2.0 ) | 0.6 | [0.4, 0.8] |
| 30+† | 2399 | 15.1 (±2.0 ) | 1.0 | [1.0, 1.0] |
| **Marital status of mother** | | | | |
| Widowed/divorced/separated | 363 | 9.6 (±4.3 ) | 0.7 | [0.4, 1.2] |
| Never married | 866 | 8.3 (±2.9 ) | 0.6 | [0.4, 0.9] |
| Married† | 3297 | 13.5 (±1.7 ) | 1.0 | [1.0, 1.0] |
| **Moved to a Different State Since Birth** | | | | |
| Yes† | 403 | 9.0 (±5.1 ) | 1.0 | [1.0, 1.0] |
| No | 4125 | 12.5 (±1.5 ) | 1.4 | [0.7, 2.8] |
| **MSA[b]** | | | | |
| MSA, central city† | 2036 | 11.9 (±2.4 ) | 1.0 | [1.0, 1.0] |
| MSA, non-Central City | 1557 | 13.5 (±2.1 ) | 1.1 | [0.8, 1.5] |
| Non MSA | 935 | 9.4 (±2.9 ) | 0.6 | [0.4, 1.0] |
| **Facility type** | | | | |
| All public/non-hospital | 663 | 3.0 (±2.0 ) | 0.2 | [0.1, 0.3] |

| | | | | |
|---|---|---|---|---|
| All hospital | 342 | 8.6 (±5.3 ) | 0.4 | [0.2, 0.9] |
| All private/non-hospital | 2457 | 15.9 (±2.1 ) | 1.0 | [1.0, 1.0] |
| All military/other | 72 | 0.6 (±1.2 ) | 0.0 | [0.0, 0.2] |
| Mixed | 332 | 7.2 (±3.5 ) | 0.4 | [0.2, 0.7] |
| Type of provider unknown | 662 | 11.6 (±3.4 ) | 0.7 | [0.5, 1.0] |
| **Race/ethnicity of child** | | | | |
| Hispanic | 851 | 7.1 (±2.6 ) | 0.5 | [0.3, 0.8] |
| White, non Hispanic† | 2726 | 15.7 (±2.0 ) | 1.0 | [1.0, 1.0] |
| Black, non Hispanic | 716 | 6.0 (±2.5 ) | 0.3 | [0.2, 0.5] |
| America Indian, non-Hispanic | 58 | 5.3 (±6.5 ) | 0.3 | [0.1, 1.1] |
| Asian, non Hispanic | 176 | 15.1 (±7.9 ) | 1.1 | [0.5, 2.1] |
| **Dose card** | | | | |
| Dose card† | 2456 | 12.6 (±2.0 ) | 1.0 | [1.0, 1.0] |
| Non dose card | 2072 | 11.8 (±2.0 ) | 0.8 | [0.6, 1.1] |
| **Gender** | | | | |
| Male† | 2325 | 11.2 (±1.8 ) | 1.0 | [1.0, 1.0] |
| Female | 2203 | 13.3 (±2.1 ) | 1.2 | [0.9, 1.6] |
| **VFC[c] participation** | | | | |
| All providers | 3296 | 11.2 (±1.6 ) | 0.7 | [0.5, 1.0] |
| Some but not all providers† | 769 | 15.8 (±3.8 ) | 1.0 | [1.0, 1.0] |
| **Ever on WIC[d]** | | | | |
| Received WIC† | 2247 | 7.0 (±1.6 ) | 1.0 | [1.0, 1.0] |
| Never received WIC | 2240 | 17.6 (±2.3 ) | 2.7 | [2.0, 3.6] |

[a] Odds ratio adjusted for difference in coverage rates between states.
† Reference cell.
[b] Metropolitan statistical area.
[c] The Vaccine for Children, or VFC, program buys vaccines for children in certain groups who can't afford to buy vaccines.
[d] The Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) is a federal grant program administered by the Food and Nutrition Service of the U.S. Department of Agriculture.

Figure 1: Distribution of Month of Earliest 1st RRV-TV Dose among sampled children in each Immunization Action Plan Area.



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