Protection Against Gastroenteritis in US Households With Children Who Received Rotavirus Vaccine

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We used Truven Health MarketScan claims database (2008–2011) to compare gastroenteritis rates during January–June among households whose child had received rotavirus vaccine with those whose child did not receive vaccine. Statistically significantly lower rates of hospitalization with a rotavirus gastroenteritis or unspecified-gastroenteritis discharge code occurred in vaccinated households among persons 20–29 years and females 20–29 years (2008/2009), and males 30–39 years (2009/2010). Lower emergency department gastroenteritis rates occurred in vaccinated households among females 20–29 years (2009/2010) and individuals 5–19 years (2010/2011). These data suggest rotavirus vaccination of infants provides indirect protection against moderate-to-severe rotavirus disease in young parents and older siblings.

Keywords. rotavirus vaccine; indirect protection; adults; household; rotavirus; diarrhea; gastroenteritis; immunization.

The introduction of rotavirus vaccine in the United States has resulted in a dramatic reduction in hospitalization and emergency department care for rotavirus disease among young children [1–3]. Indirect protection among unvaccinated, young children has been detected through active surveillance for rotavirus disease and by examining medical encounters in discharge databases, comparing post-introduction to the prevaccine period [1, 4, 5]. This indirect protection is believed related to overall reduction in rotavirus circulation in the community, with vaccination reducing the numbers of susceptible infants and young children who can transmit wild-type infection. The burden of rotavirus disease in older children and adults has been difficult to quantify because, in these age groups, rotavirus testing is uncommonly performed and the rotavirus-specific discharge code is infrequently applied. Hence, possible indirect protection to older individuals by the US infant vaccination program has further been assessed by comparing medical encounters for gastroenteritis with cause-unspecified (in addition to rotavirus-coded) during post and prevaccine periods and in calendar months when rotavirus circulates [6, 7]. Based on discharge data from community hospitals, hospitalization rates with cause-unspecified gastroenteritis were statistically significantly lower in persons aged 5–44 years (rate ratios 0.70 to 0.94, depending on age category) during the postintroduction period 2008 through 2010, compared to prevaccine baseline during 2000 through 2006 [7]. Rotavirus gastroenteritis can occur in family members of ill children [8–10]. We therefore sought to examine if there was indirect protection at the household level by comparing rates of medically attended gastroenteritis among individuals in households whose children had received rotavirus vaccine with those in households of children who did not receive rotavirus vaccine.

METHODS

The Truven Health MarketScan Commercial Claims and Encounters database containing data covering 2008 through 2011 was used. This MarketScan database contains detailed patient information linked with claims and encounter data from approximately 100 payers in the private health care sector.

To identify the household member population eligible for the analysis, we first identified 3 cohorts of children who were eligible to have received ≥1 dose of rotavirus vaccine (RV) and have a claim for that dose recorded in the database. Children eligible for vaccine-eligible cohort were those (1) born 1 April 2006 (rotavirus vaccine was recommended in the US in February 2006) through 31 July 2009; (2) born in a US state that did not have a universal RV program (ie, infants born in these states would not have a billing claim for RV: Alaska, Idaho, Maine, Massachusetts, New Hampshire, New Mexico, North Dakota, Oregon, Rhode Island, Vermont, Washington, Wisconsin, and Wyoming); (3) continuously enrolled in the insurance plan to at least age 5 months (to ensure that the first dose of RV would be captured in the database if it had been administered; national recommendation is that first dose be administered between ages 6 weeks and 14 weeks 6 days); and (4) had at least 1 "household" member (defined as having same family identification
number as the child) who was continuously enrolled in that insurance plan for the first 2 consecutive January–June (“rotavirus season”) periods after the child was eligible to have received the first dose of rotavirus vaccine. The first cohort were children born 1 April 2006 to 31 July 2007 and had household member(s) enrolled continuously during their follow-up of January–June of 2008 and 2009 (household group 1) (Supplementary Figure 1). The second cohort was born 1 August 2007 to 31 July 2008, with household members enrolled continuously during January–June 2009 and 2010 (household group 2). The third cohort was born 1 August 2008 to 31 July 2009, with household members enrolled continuously January–June 2010 and 2011 (household group 3). Based on dates of birth, the children in the latter 2 vaccine cohorts would have been aged 8–19 months, and 20–31 months, respectively, during the first and second March of the follow-up periods—March is typically the month of peak US rotavirus activity. Because the first cohort included an additional 4 months of birth eligibility, that cohort also includes children that would be 4 months older.

The households were designated “vaccinated” if the vaccine-eligible child had a ≥1 claim for RV (CPT code 90680 or 90681) and “unvaccinated” if there was no claim. Households were excluded if there was discordant RV status among multiple vaccine-eligible children within the same household.

Medical encounters for gastroenteritis among household members during the follow-up periods were identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes, and setting and date of service. An inpatient hospital admission was counted if a code for rotavirus (008.61) or diarrhea cause-unspecified (009.0 to 009.3, 558.9, 787.91, and 008.8) was listed in any of the 15 diagnosis categories from the dataset’s inpatient admission table. The inpatient analysis was also repeated using codes for all causes of gastroenteritis [1]. Emergency department and outpatient gastroenteritis encounters were counted if a code for gastroenteritis (any cause) was listed in 1 of 2 diagnosis fields; the specific rotavirus code is uncommonly used in these settings. Household members who presented to ≥1 setting for the same diarrheal event may be represented multiple times in the analysis.

The age group of a household member was categorized based on his/her age as of 1 January of his/her first follow-up period. The members were categorized into 7 age groups (0–4, 5–19, 20–29, 30–39, 40–49, 50–59, and ≥60 years), and by age with gender (20–29, 30–39 years) to better examine likely caregivers of young children. We did not analyze further household members aged 0–4 years (because this group contained fewer toddlers in each subsequent January–June follow-up period, as an increasing proportion of children in this age group had been eligible themselves for rotavirus vaccine) or ≥60 years (because of the small number).

Gastroenteritis encounters are presented per 10 000 persons during the 12-month total follow-up period. We calculated rate ratios (RRs) and 95% confidence intervals (CIs) based on a Poisson distribution and the natural log of the population, and P-values, by comparing rates among individuals in rotavirus-vaccinated households with those in unvaccinated households. P-values <.05 were considered statistically significant.

RESULTS

Approximately 90 000 households (200 000 individuals) contributed follow-up information for their respective household group. About 50% of the households were in southern United States (Table 1). The proportion of households that were considered rotavirus-vaccinated was lowest in group 1 (56%) and highest in group 3 (77%), as vaccine coverage among US infants increased over time (Table 1). Most (>65%) households had at least 3 individuals in the household in addition to the cohort child, about 65% of individuals were aged 20–49 years, and <1% were aged ≥50 years (Supplementary Table 1). The household size and age distribution of the household members included were similar across groups (Supplementary Table 1) and, within each group, among vaccinated and unvaccinated households (data not shown). Rates of gastroenteritis encounters among vaccinated and unvaccinated households were generally highest in group 1 and lowest in group 3.

Statistically significant lower gastroenteritis rates for those in vaccinated as compared with unvaccinated households occurred for hospital admissions with a rotavirus or unspeciﬁed-gastroenteritis code among group 1 adults aged 20–29 years (RR 0.59, 95% CI, .43–.82) and females aged 20–29 years (RR 0.57, 95% CI, .40–.82), and group 2 males aged 30–39 years (RR 0.68, 95% CI, .47–.99; Table 2). RR results were similar to results above when hospital admissions were examined using all codes for gastroenteritis (data not shown).

For gastroenteritis encounters in emergency departments, statistically significant lower rates for those in vaccinated as compared with unvaccinated households occurred among group 2 females aged 20–29 years (RR 0.84, 95% CI,. 71–.91) and group 3 individuals aged 5–19 years (RR 0.84, 95% CI, .71–1.00) (Table 2). Rates appeared lower among group 2 individuals aged 5–19 years, but the RR missed statistical significance.

For outpatient gastroenteritis encounters, rates were statistically significantly higher (by 5%–17%) among those in vaccinated as compared with unvaccinated households among 5–19 year olds in group 1 and among some adult age categories <50 years in each group, including among men (Table 2).

Overall, results were similar to those described above when households from the West were excluded (because of its difference in rotavirus seasons, with 2008 a higher and 2009 a lower season compared to other regions [1, 5]; data not shown) and when households from the South were examined separately using a restricted group 1 follow-up period (March–May 2008...
and January–May 2009, the specific periods of rotavirus circulation in the South [5, 11]; data not shown).

**DISCUSSION**

We found that privately insured adults aged 20–29 years (and men aged 30–39 years) had lower rates of hospital admission or emergency department encounters for gastroenteritis, if the child in the household had received RV. Emergency department rates were also lower among 5–19 year-olds in one group. These data suggest that, at least among privately insured individuals, directly protecting the child in the household with RV also protects against moderate-to-severe rotavirus disease in the child’s young parents and older siblings.

Indirect protection in the United States by RV has been examined in population- or hospital-level evaluations [6, 7, 12]. Lopman et al also found females (but not males) aged 15–24 years had lower rates of rotavirus-coded hospitalizations in 2008 compared to the prevaccine period 2000–2006 [7]. However, females did not have a lower annual rate for cause-unspecified gastroenteritis in 2008 compared to prevaccine. We extended these observations by examining data at the household level. Our finding of protection among younger women lends additional weight to the concept of household protection, because these may be the persons most frequently in direct contact with young children. It is possible that some protection is a result of exposure to vaccine-virus shed by infants.

It is not surprising that lower rates in vaccinated compared to unvaccinated households were not identified in each of the 3 follow-up groups, for at least 3 reasons. First, rates of gastroenteritis encounters among vaccinated and unvaccinated households were generally highest in group 1 and lowest in group 3, making any differences in rates harder to detect in the later groups. Second, we were interested in the impact over the first 2 follow-up seasons together for a more net effect of vaccination on household members. Although it is possible that results may have been different (ie, household protection more apparent) if examined for only the first follow-up season when the child is youngest and more likely to acquire and transmit rotavirus, the biennial pattern of rotavirus circulation observed after vaccine introduction makes single season assessment less meaningful. The third reason also relates to the biennial pattern. Although ages of the vaccine-eligible cohorts should be similar for each group, the first and second follow-up season for group 1 was a lower rotavirus season (2008) followed by a higher season (2009), whereas for group 2 the first season (2009) was high and the second (2010) was very low (Supplementary Figure 1). The order of the higher vs lower season affects the age each vaccine-eligible cohort would be during the period when at highest risk for acquiring and transmitting rotavirus, making it likely that findings would not be consistent for each group. Therefore, our analysis provides evidence that one component of the
## Table 2. Rate of Healthcare Encounters for Gastroenteritis During Follow-up Period per 10,000 Population, by Household Rotavirus Vaccination Status

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<tbody>
<tr>
<td>Total GE</td>
<td>Rate, vacc (+)</td>
<td>Rate, vacc (−)</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td>5–19</td>
<td>167 36 37 0.98 (73, 1.33) .92</td>
<td>142 31 38 0.80 (57, 1.13) .21</td>
<td>103 21 28 0.77 (50, 1.17) .22</td>
</tr>
<tr>
<td>20–29</td>
<td>148 27 46 0.59 (43, .82) .002</td>
<td>113 25 31 0.80 (54, 1.18) .26</td>
<td>94 21 18 1.19 (72, 1.97) .49</td>
</tr>
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<td>30–39</td>
<td>387 40 38 1.04 (85, 1.27) .70</td>
<td>311 31 38 0.83 (65, 1.06) .14</td>
<td>221 21 20 1.07 (78, 1.49) .67</td>
</tr>
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<td>40–49</td>
<td>110 62 66 0.95 (65, 1.37) .77</td>
<td>102 66 51 1.28 (81, 2.02) .29</td>
<td>54 28 32 0.89 (48, 1.63) .70</td>
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<td>50–59</td>
<td>13 65 119 0.54 (17, 1.73) .30</td>
<td>12 96 64 1.51 (39, 5.88) .56</td>
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<tr>
<td>20–29, female</td>
<td>121 34 60 0.57 (40, .82) .002</td>
<td>85 29 39 0.73 (47, 1.15) .17</td>
<td>74 26 20 1.30 (73, 2.32) .38</td>
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<tr>
<td>20–29, male</td>
<td>27 12 24 0.50 (23, 1.09) .08</td>
<td>28 20 16 1.05 (45, 2.41) .91</td>
<td>20 12 12 0.95 (34, 2.60) .91</td>
</tr>
<tr>
<td>30–39, female</td>
<td>250 47 51 0.92 (72, 1.18) .53</td>
<td>185 37 30 0.96 (69, 1.33) .79</td>
<td>121 22 21 1.05 (68, 1.62) .83</td>
</tr>
<tr>
<td>30–39, male</td>
<td>137 31 26 1.21 (86, 1.71) .27</td>
<td>126 25 36 0.68 (47, 0.99) .043</td>
<td>100 20 18 1.10 (68, 1.78) .71</td>
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<tr>
<td>5–19</td>
<td>968 211 209 1.01 (89, 1.15) .88</td>
<td>828 184 212 0.87 (75, 1.01) .061</td>
<td>664 140 167 0.84 (71, 1.00) .047</td>
</tr>
<tr>
<td>20–29</td>
<td>921 213 230 0.93 (81, 1.06) .25</td>
<td>952 217 247 0.88 (76, 1.01) .067</td>
<td>915 199 189 1.05 (90, 1.23) .51</td>
</tr>
<tr>
<td>30–39</td>
<td>2208 221 227 0.97 (89, 1.06) .52</td>
<td>1918 200 209 0.96 (86, 1.06) .40</td>
<td>1742 166 160 1.04 (92, 1.16) .54</td>
</tr>
<tr>
<td>40–49</td>
<td>440 275 237 1.16 (86, 1.40) .12</td>
<td>376 235 207 1.14 (90, 1.43) .28</td>
<td>272 145 149 0.97 (74, 1.28) .84</td>
</tr>
<tr>
<td>50–59</td>
<td>28 171 227 0.75 (36, 1.60) .46</td>
<td>26 187 190 0.98 (43, 2.27) .97</td>
<td>21 158 150 1.05 (38, 2.89) .92</td>
</tr>
<tr>
<td>20–29, female</td>
<td>692 247 273 0.91 (78, 1.05) .20</td>
<td>680 240 285 0.84 (71, 0.99) .038</td>
<td>644 221 204 1.08 (90, 1.30) .42</td>
</tr>
<tr>
<td>20–29, male</td>
<td>229 156 148 1.04 (80, 1.35) .77</td>
<td>272 176 188 0.94 (73, 1.23) .66</td>
<td>271 164 156 1.05 (97, 1.40) .72</td>
</tr>
<tr>
<td>30–39, female</td>
<td>1356 266 266 1.00 (90, 1.11) .98</td>
<td>1203 242 255 0.95 (83, 1.08) .42</td>
<td>1050 191 197 0.97 (84, 1.12) .67</td>
</tr>
<tr>
<td>30–39, male</td>
<td>852 176 181 0.97 (85, 1.11) .70</td>
<td>715 155 159 0.97 (82, 1.15) .76</td>
<td>692 139 124 1.12 (93, 1.34) .24</td>
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Abbreviations: CI, confidence interval; GE, gastroenteritis; RR, rate ratio; vacc (+), in household with child vaccinated against rotavirus; vacc (−), in household with child unvaccinated against rotavirus; y, years.

a Total gastroenteritis encounters among persons in the indicated care setting and age group.

b Rotavirus gastroenteritis code for unspecified gastroenteritis.

c Any gastroenteritis code.
overall indirect protection that has been observed occurs at the household level and the different findings across the follow-up groups is not unexpected.

Outpatient gastroenteritis encounters were modestly increased in some age categories in each group. One explanation could be that rotavirus illness occurred in some vaccinated households but was less severe because of lower overall shedding of wild-type rotavirus passed from a previously vaccinated infant (compared to an unvaccinated infant), so that care is more frequently received as an outpatient only and less frequently at a higher level. If this were true, the prevention of higher acuity care would nonetheless be highly beneficial. It is also possible that the proportion of analyzed gastroenteritis encounters during January–June that are truly due to rotavirus may be lower in outpatient encounters compared to those in the other settings, making our outpatient results for total gastroenteritis less informative overall. An evaluation using this same MarketScan database found that during July 2010–June 2011, rotavirus-vaccinated children had a similar rate of gastroenteritis outpatient encounters as unvaccinated children but a lower rate of gastroenteritis emergency department visits and hospitalizations [15].

Our findings suggest that the US infant vaccination program has provided additional, indirect protection against moderate-to-severe rotavirus gastroenteritis in some household members of vaccinated children.

Supplementary Data

Supplementary materials are available at The Journal of Infectious Diseases online (http://jid.oxfordjournals.org). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

Disclaimer. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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