RESEARCH LETTER

Gastroenteritis Hospitalizations in Older Children and Adults in the United States Before and After Implementation of Infant Rotavirus Vaccination

Implementation of infant rotavirus vaccination in 2006 has substantially reduced the burden of severe gastroenteritis among US children younger than 5 years. The role of rotavirus in adult gastroenteritis has been less well appreciated. Recent studies report rotavirus detection rates of 18% in emergency departments\(^1\) and 5% from February through May in hospitalized patients,\(^2\) and estimates of 81 000 emergency department visits\(^3\) and 18 000 hospitalizations\(^4\) in the United States annually. Whether indirect protection (due to reduced transmission of rotavirus) extends to adults remains unclear. Previous studies suggesting such indirect protection were limited to 1 postintroduction season\(^5\) or 1 hospital setting,\(^6\) so prudent interpretation was warranted. We assessed patterns of gastroenteritis hospitalizations among children aged 5 years or older and among adults before and after implementation of infant rotavirus immunization.

**Methods** Rotavirus-coded and cause-unspecified gastroenteritis discharges from January 2000 through December 2010 were retrieved from a nationally representative database of hospital inpatient stays, the Nationwide Inpatient Sample, as previously described.\(^5\) Cause-unspecified discharges were examined because testing for rotavirus is infrequently performed in adults. We fitted time series regression models assuming a Poisson distribution of 2 separate outcomes: monthly counts of rotavirus-coded or cause-unspecified discharges. We estimated annual and monthly incidence rate ratios (RR) of the postvaccine years (2008, 2009, and 2010) separately and combined vs the prevaccine years (2000-2006), controlling for month, secular trends, and population size; 2007 was a transition year with limited coverage and was excluded. Separate models were fit for each of the 6 age groups. The study was exempt from institutional review board approval because deidentified aggregated data were used. Significance was assessed as a 2-sided \(P\) value of .05 using Stata version 12.0 (StataCorp).

**Results** Compared with prevaccine years, during 2008-2010, statistically significant reductions were observed in rotavirus-coded gastroenteritis hospitalizations among children aged 4 years or younger (Table). In older children and adults, no significant changes were observed.


<table>
<thead>
<tr>
<th>Age Group, y</th>
<th>2000-2006</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2008-2010</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unweighted Annual Mean*</td>
<td>Unweighted No.*</td>
<td>Weighted RR (95% CI)*</td>
<td>Unweighted No.*</td>
<td>Weighted RR (95% CI)*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotavirus-coded gastroenteritis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-4</td>
<td>6651</td>
<td>2058</td>
<td>0.22 (0.14-0.33)</td>
<td>2562</td>
<td>0.29 (0.19-0.42)</td>
</tr>
<tr>
<td>5-14</td>
<td>372</td>
<td>155</td>
<td>0.29 (0.18-0.45)</td>
<td>227</td>
<td>0.43 (0.29-0.65)</td>
</tr>
<tr>
<td>15-24</td>
<td>26</td>
<td>14</td>
<td>0.35 (0.14-0.85)</td>
<td>25</td>
<td>0.73 (0.34-1.60)</td>
</tr>
<tr>
<td>25-44</td>
<td>24</td>
<td>22</td>
<td>0.68 (0.39-1.30)</td>
<td>17</td>
<td>0.57 (0.27-1.20)</td>
</tr>
<tr>
<td>45-64</td>
<td>35</td>
<td>35</td>
<td>0.77 (0.45-1.30)</td>
<td>56</td>
<td>1.24 (0.72-2.10)</td>
</tr>
<tr>
<td>≥65</td>
<td>54</td>
<td>78</td>
<td>0.79 (0.51-1.20)</td>
<td>114</td>
<td>1.08 (0.68-1.70)</td>
</tr>
<tr>
<td>Cause-unspecified gastroenteritis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-4</td>
<td>16 176</td>
<td>10 499</td>
<td>0.61 (0.52-0.71)</td>
<td>9578</td>
<td>0.61 (0.52-0.71)</td>
</tr>
<tr>
<td>5-14</td>
<td>5106</td>
<td>3707</td>
<td>0.71 (0.65-0.77)</td>
<td>3667</td>
<td>0.75 (0.68-0.82)</td>
</tr>
<tr>
<td>15-24</td>
<td>4158</td>
<td>4472</td>
<td>0.82 (0.86-0.98)</td>
<td>4120</td>
<td>0.87 (0.81-0.94)</td>
</tr>
<tr>
<td>25-44</td>
<td>13 451</td>
<td>14 449</td>
<td>0.97 (0.92-1.01)</td>
<td>13 363</td>
<td>0.92 (0.88-0.97)</td>
</tr>
<tr>
<td>45-64</td>
<td>16 461</td>
<td>21 320</td>
<td>1.01 (0.97-1.10)</td>
<td>20 422</td>
<td>0.98 (0.93-1.03)</td>
</tr>
<tr>
<td>≥65</td>
<td>24 134</td>
<td>30 116</td>
<td>1.02 (0.96-1.10)</td>
<td>28 387</td>
<td>0.97 (0.90-1.04)</td>
</tr>
</tbody>
</table>

Abbreviation: RR, rate ratio.

* Because the Nationwide Inpatient Sample is a sample probability approximating 20% of US community hospitals, the number of states, hospitals, and discharges included in the Nationwide Inpatient Sample increases every year; thus, unweighted numbers may not reflect actual reductions in discharges.

\(^{\dagger}\) All models controlling for secular and seasonal variation and accounting for population size.

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coded discharges by age group as follows: 0-4 years (RR, 0.20 [95% CI, 0.14-0.28]; \(P<.001\)), 5-14 years (RR, 0.30 [95% CI, 0.21-0.44]; \(P<.001\)), and 15-24 years (RR, 0.47 [95% CI, 0.24-0.94]; \(P = .03\)). Similarly, significant reductions were observed in cause-unspecified discharges by age group as follows: 0-4 years (RR, 0.58; 95% CI, 0.50-0.66), 5-14 years (RR, 0.70; 95% CI, 0.65-0.76), 15-24 years (RR, 0.89; 95% CI, 0.84-0.95), and 25-44 years (RR, 0.94; 95% CI, 0.90-0.98) (\(P<.001\) for all; Table). Compared with prevaccine years, significant reductions in rotavirus-coded discharges occurred up to age 25 years in 2008, age 15 years in 2009, and across all age groups in 2010, with similar patterns for cause-unspecified discharges. Cause-unspecified reductions across all age groups and postvaccine years were focused in the late winter and early spring (Figure); in 2010, significant reductions were observed in March or April for all age groups.

Discussion | The pattern of observed reductions in gastroenteritis discharges among unvaccinated older children and adults is consistent with indirect protection resulting from infant rotavirus vaccination. First, reductions occurred primarily in March and April, the peak months of rotavirus hospitalization prevaccine. Second, reductions mirrored the biennial epidemiology of childhood rotavirus during postvaccine years (ie, a large reduction in 2008, followed by a relatively smaller reduction in 2009, and the most pronounced reduction in 2010). Third, reductions persisted for 3 contiguous years and thus were unlikely due to year-to-year secular variations. In addition, reductions coincided with increasing vaccine coverage; significant reductions were observed across all ages in 2010, which is when the greatest decline in rotavirus hospitalizations among vaccine-eligible young children occurred.

Study limitations include the ecological design, lack of specificity of cause-unspecified discharges, and unknown specificity and infrequent use of rotavirus codes among adults. However, these limitations would only result in a bias if coding practices changed over time; broadly consistent results based on cause-unspecified and rotavirus-coded discharges suggest otherwise.

Based on the observed reductions, annual reductions in gastroenteritis discharges after introduction of rotavirus vaccine in the United States, particularly in the 5- to 44-year age group, are likely. These results point to the primacy of chil-
Children in the transmission of rotavirus and illustrate how indirect benefits may amplify the effect of the US rotavirus vaccination program.

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Acquisition of data: Curns, Parashar, Lopman.
Analysis and interpretation of data: Gastañaduy, Curns, Parashar, Lopman.
Drafting of the manuscript: Gastañaduy, Parashar.
Critical revision of the manuscript for important intellectual content: Curns, Parashar, Lopman.
Statistical analysis: Gastañaduy, Curns, Lopman.
Administrative, technical, or material support: Gastañaduy, Curns, Parashar.
Study supervision: Parashar, Lopman.

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


COMMENT & RESPONSE

Vitamin D Supplementation During First 12 Months of Life
To the Editors The study by Ms Gallo and colleagues1 investigated the effect of vitamin D supplementation at different doses during the first 12 months of life. The major confounder with respect to vitamin D levels is endogenous synthesis from UV radiation, which at recommended exposure levels should equate to 1000 IU/d of vitamin D. The authors corrected for the effects of sun exposure using the results of the study by Barger-Lux et al.2 However, in that study the sample population was healthy men who had just completed a summer season of extended outdoor activity working in landscaping, construction work, and farming (as well as other outdoor jobs). This index has not been validated and the questionnaire has not been used for an infant population.

The mean sun index (hours of sun exposure per week × percentage of body surface area) for the adult cohort was only 11.5 (interquartile range, 6.7-18.1),2 whereas the sun index in the infants aged 9 months was 71 (interquartile range, 42-101).1 It is peculiar that a 9-month infant would have an almost 7-fold higher sun index than an adult. This discrepancy and lack of validation requires explanation because sun exposure is likely to significantly confound the results and complicate interpretation of this study.

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In Reply Drs Sofiyan and Nanan highlight an important issue within the vitamin D research field. The estimation of sunlight exposure is often imprecise due to recall bias and is particularly challenging among children with sporadic patterns of exposure. We chose to estimate UV exposure using the sun index. Although more objective measures of UV exposure are available, such as dosimeters, they do not incorporate capacity for cutaneous vitamin D synthesis on the basis of body surface area (BSA) exposed.

The sun index measure is based on detailed sun exposure questions including season, time of day, duration, travel, and BSA exposed to direct sunlight, including clothing worn. The calculation of the sun index used in our study was the product of hours per week of sun exposure and percentage of BSA exposed (× 100 as a whole number), which was adapted from child burn charts described by the World Health Organization.1 In adults, BSA is calculated slightly differently2 due to differences in the ratio of head and neck to limbs.

Although calculations such as the sun index are frequently used in research studies, there is no standard,3,4 and none have been validated to quantify sun exposure in infants. Hence the discrepancy between our mean sun index values of infants at 9 months (71 [interquartile range, 42-101]; calculated as hours/week × percentage × 100 of BSA) vs those described by Barger-Lux et al1 (11.5 [interquartile range, 6.7-18.1]; calculated as hours/week × fraction of BSA) was due to differences in the units of BSA exposed (percentage of BSA as a whole number vs a fraction of BSA). Although BSA has been