Effect of Rotavirus Vaccine on Reducing Acute Gastroenteritis in a Large Outpatient Pediatric Network

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Objectives: To measure the effect of rotavirus vaccine (RVV) on acute gastroenteritis (AGE) managed by primary care physicians in the first 2 rotavirus seasons following the introduction of RVV.

Design: Retrospective cohort study.


Participants: All children born from February 22, 2006 (date of RVV licensure), through February 29, 2008, and who received care at any network site.

Main Exposure: Receipt of RVV.

Outcome Measures: The primary outcomes were AGE-related office visits, telephone calls, and episodes (composite outcome consisting of all visits and calls within a 10-day period).

Results: Rates of AGE visits in the 2 rotavirus seasons following the introduction of RVV steadily decreased from 3.0 AGE visits per 100 total office visits in the 2005 season to 1.8 in the 2008 season. In 2007, vaccinations were administered to 9351 of 13 951 vaccine-eligible children (67.0%), and in 2008, they were administered to 9958 of 10 728 (92.8%). Among RVV-immunized children in 2007, AGE calls and episodes were significantly reduced with vaccine effectiveness of 53% and 46%, respectively. No significant difference was seen between RVV-immunized and RVV-nonimmunized children for any outcome in 2008.

Conclusions: Rotavirus vaccine was associated with a significant reduction in outpatient AGE calls and episodes among immunized children in our network in 2007. Despite a reduction in winter AGE rates in the network, no difference was detected between RVV-immunized and RVV-nonimmunized children for any outcome in 2008. Further study is needed to understand the lack of vaccine effect in 2008.

studies because not all children will require an outpatient office visit for an AGE episode. A large proportion of children will require only home care or a telephone call(s) to their primary care physician for AGE, making it difficult to gauge the full effect of RVV on less severe manifestations of AGE in young children. However, systematic capture of AGE-related telephone calls as well as AGE-related office visits will provide a more accurate assessment of the effect of RVV on the burden of AGE managed by primary care physicians. Using data from a large pediatric health care network, we measured the effect of RVV on the incidence of outpatient AGE outcomes, including office visits, telephone calls, and a composite variable, episodes, among children in the first 2 RV seasons following the introduction of RVV.

## METHODS

### STUDY DESIGN

We performed a retrospective cohort study to evaluate the effectiveness of RVV in preventing primary care AGE office visits, telephone calls, and episodes (all AGE-related visits and calls that occurred within 10 days of each other) during the first 2 full RV seasons after the introduction of RVV. The study was approved by The Children’s Hospital of Philadelphia (CHOP) Institutional Review Board.

### STUDY SETTING

The CHOP pediatric health care network includes 33 ambulatory pediatric practices (3 inner-city and 28 suburban). These ambulatory practices constitute the CHOP Pediatric Research Consortium (PeRC), a practice-based research network that has nearly 200,000 active patients, 60% of whom are younger than 5 years. Practices within PeRC use an electronic health record (EHR; EpicCare) and since December 2006 have shared a centralized after-hours nursing telephone call center. The triage nurses use the algorithm-driven Barton Schmitt outpatient telephone triage protocols, and contents of calls are recorded in a standardized and templated report that becomes part of the patient’s EHR.

The EHR used by PeRC was designed to facilitate research efforts in the ambulatory setting. The data procured have been validated in multiple studies. In particular, the immunization database within the EHR provides a comprehensive record of all vaccines received by a patient and is the sole immunization record used at all study practices. It has been used as the source of vaccine information in several studies and, in a study of vaccine registries in Philadelphia, was found to have the most complete information. Also, a recent infectious disease study in our network validated the use of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes from PeRC’s EHR. The ICD-9 codes agreed with the documentation in the clinician’s note with 95% sensitivity and specificity.

### STUDY POPULATIONS

The study population included any child born from February 22, 2006 (date of RVV licensure), through February 29, 2008, who had at least 1 office visit at a PeRC site before 2 months of age. To evaluate protection in the second season following immunization, children were divided into 2 cohorts: (1) the 2007 cohort included those children who were eligible for AGE outcomes in both the 2007 and the 2008 seasons, and (2) the 2008 cohort included children eligible for AGE outcomes in the 2008 season only (Figure 1). The cohorts were mutually exclusive. The 2007 season was from December 1, 2006, through May 31, 2007, and the 2008 season was from January 1, 2008, through June 30, 2008. Dates for AGE observations were selected to capture all seasonal RV activity on the basis of data from the CHOP Clinical Virology Laboratory. The AGE observation period began on the first day of the month with positive RV samples for 3 consecutive weeks and ended on the last day of the month in which there were 2 consecutive weeks without positive RV samples.

### EXPOSURES

The primary exposure of interest was receipt of RVV (RotaTeq [Merck], the only RVV available during the study period). Exposed children received 1, 2, or 3 doses of RVV. Unexposed children received 0 doses of RVV.

### OUTCOMES

The primary outcomes were AGE-related visits, calls, and episodes. Visits were defined as any office visits in the patient’s EHR with a primary diagnosis code for a diarrheal illness using the AGE ICD-9-CM codes (001-005, 006-007, 008-008.5, 008.6, 008.61, 008.8, 009-009.3, 558.9, 787-787.03, and 787.91). Calls were defined as all AGE-related after-hours telephone triage calls identified in the EHR by the use of standard protocols for vomiting, diarrhea, and dehydration. Because of inconsistencies in the way practice sites entered calls into the EHR during daytime office hours, we limited our data to calls made to the centralized triage center during night and weekend hours. Episodes were defined as all AGE-related visits and calls that occurred within 10 days of each other. The episode outcome was created to yield the best estimate of discrete diarrheal ill-

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Figure 1. Primary study design for cohort selection and outpatient acute gastroenteritis outcomes. Children were selected from the Pediatric Research Consortium, which is The Children’s Hospital of Philadelphia’s network of affiliated pediatric primary care practices. RVV indicates rotavirus vaccine.
nesses that each patient had during a season. This outcome accounts for variations in health care use and reduces the potential for bias if children had more than 1 visit and/or call for a single illness. Individual outcomes were not assessed until the child was at least 6 weeks of age (the earliest age at which RVV administration is recommended).

As a secondary outcome to contextualize our results, we determined the rates of AGE in the network during the period before and after the introduction of RVV (January 1, 2005, through December 31, 2008) by dividing the total number of monthly AGE visits (based on aforementioned ICD-9-CM codes) by the total number of monthly office visits for children 24 months or younger.

DATA COLLECTION

The EHR was retrospectively queried to identify all primary and secondary exposures and outcomes (number of RVV doses and number of AGE visits and calls) for children eligible for inclusion in the cohort. Data regarding demographic characteristics, other immunizations received, complex chronic conditions, number of sick and preventative care visits, and total numbers of calls were also abstracted.

STATISTICAL METHODS

We first characterized cohort subjects by all potential risk factors for AGE, including age (calculated as the age [in days] on the first day of their eligibility for an outcome in the first season in which they participated), demographic variables, and complex chronic conditions. Categorical variables, such as sex and race, were summarized by frequencies, whereas continuous variables, such as age, were summarized by mean (SD) or median (range). To compare demographic variables and characteristics of health care use between RVV-immunized and RVV-nonimmunized groups, χ² analysis was used for categorical variables and the t test or Wilcoxon rank sum test for continuous variables. Bivariable analysis was conducted using Poisson regression to determine the association between potential risk factors and each outcome.

For the multivariable analysis, Poisson regression was used to determine the association between exposure to RVV and the outcomes for each season. Receipt of RVV (exposure) was modeled as a binary variable, and each outcome was modeled as a count (total numbers of AGE visits, calls, and episodes per season). The total number of days the child was eligible for an outcome per season was calculated and included as the time variable in the regression. All variables with P < .20 on bivariable analysis were included in the multivariable model. Confounders and clinically relevant risk factors were also considered for inclusion in the multivariable model. Stratified analysis to assess effect modification was performed. Additional analyses were conducted to determine the association between receipt of RVV and VE after receipt of 1, 2, or 3 doses of vaccine and protection in the second season after vaccination.

Vaccine effectiveness in preventing AGE outcomes was calculated using a standard approach applied in other retrospective studies, with the formula VE = (1−incident rate ratio [IRR]) × 100, where the IRR is the adjusted ratio for each AGE outcome among vaccinated vs unvaccinated study subjects.

RESULTS

TRENDS IN NETWORK AGE RATES FOR CHILDREN 24 MONTHS OR YOUNGER

Monthly AGE office visit rates were calculated for all children 24 months or younger who were in the PeRC network to describe the context of our cohort findings. Before the introduction of RVV, the peak monthly AGE rate was 3.0 per 100 total office visits for 2005 and 2.7 for 2006 (Figure 2). For the 2007 and 2008 seasons, the peak monthly rates of AGE visits per 100 total visits were 2.4 and 1.8, respectively. The mean monthly winter AGE visit rate was significantly lower in 2007 and 2008 compared with those in 2005 and 2006 (P < .001). The mean summer baseline AGE rate (mean monthly rate of AGE visits for June through December 2005 through 2008) was 1.4 per 100 total visits.

CHARACTERISTICS OF STUDY POPULATION

The study population included a total of 24,679 children with a high rate of RVV vaccination; 78.2% of the cohort received at least 1 dose of RVV and 65.0% of the
The study population comprised 2 cohorts: 13,951 children in the 2007 cohort and an additional 10,728 children in the 2008 cohort. The rate of vaccination increased by nearly 50% between the 2007 and the 2008 cohorts. Among the 2007 cohort, 67.0% received at least 1 dose of RVV and 54.8% were fully vaccinated with RVV. For the 2008 cohort, 92.8% received at least 1 dose and 78.3% received 3 doses. The demographic characteristics of children in the cohorts were similar. In both cohorts, RVV-nonimmunized children were more likely to be black and to receive care at an urban pediatric practice than were children who had received 1 or more doses of RVV (Table 1).

Children not immunized with RVV had lower rates of health care use than their immunized peers; this disparity was more pronounced in the 2008 cohort compared with the 2007 cohort (Table 2).

**AGE OUTCOMES AMONG IMMUNIZED AND NONIMMUNIZED PATIENTS**

Unadjusted rates of AGE visits, calls, and episodes per 10,000 cohort days for RVV-immunized children remained constant across both cohorts for the 2007 and 2008 seasons (Figure 3). However, among RVV-nonimmunized children, rates for all outcomes dropped nearly 3-fold from 2007 to 2008. We calculated the IRR

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**Table 1. Demographic Characteristics of the Overall Cohort and the Individual 2007 and 2008 Cohorts**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall Cohort (N = 24,679)</th>
<th>2007 Cohort</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RVV-Immunized (n = 9351)</td>
<td>RVV-Nonimmunized (n = 4600)</td>
<td></td>
</tr>
<tr>
<td>Mean (SD) age, wk</td>
<td>15.9 (10.7)</td>
<td>10.2 (6.5)</td>
<td>26.4 (10.6)</td>
</tr>
<tr>
<td>Female sex</td>
<td>12,054 (48.8)</td>
<td>4561 (48.8)</td>
<td>2253 (49.0)</td>
</tr>
<tr>
<td>Race</td>
<td>2631 (28.1)</td>
<td>7179 (29.1)</td>
<td>1496 (32.5)</td>
</tr>
<tr>
<td>Black</td>
<td>4998 (53.5)</td>
<td>12,598 (51)</td>
<td>2315 (50.3)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1722 (18.4)</td>
<td>4802 (19.9)</td>
<td>789 (17.2)</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>286 (3.1)</td>
<td>713 (2.9)</td>
<td>136 (3.0)</td>
</tr>
<tr>
<td>Location</td>
<td>9085 (96.9)</td>
<td>23,966 (97.1)</td>
<td>4464 (97.0)</td>
</tr>
<tr>
<td>Urban</td>
<td>2031 (21.7)</td>
<td>5983 (24.2)</td>
<td>1247 (27.1)</td>
</tr>
<tr>
<td>Suburban</td>
<td>7320 (78.2)</td>
<td>18,696 (75.8)</td>
<td>3353 (72.8)</td>
</tr>
<tr>
<td>Median annual household income, $</td>
<td>50,943 (50.0)</td>
<td>52,377 (50.0)</td>
<td>49,649 (50.0)</td>
</tr>
<tr>
<td>Chronic condition</td>
<td>601 (6.4)</td>
<td>1588 (6.4)</td>
<td>338 (7.3)</td>
</tr>
<tr>
<td>Cardiac condition</td>
<td>144 (1.5)</td>
<td>383 (1.6)</td>
<td>90 (2.0)</td>
</tr>
<tr>
<td>GI condition</td>
<td>5 (0.1)</td>
<td>27 (0.1)</td>
<td>7 (0.2)</td>
</tr>
</tbody>
</table>

Abbreviations: GI, gastrointestinal; RVV, rotavirus vaccine.

**Table 2. Characteristics of Health Care Use for the Overall Cohort and the Individual 2007 and 2008 Cohorts**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall Cohort</th>
<th>2007 Cohort</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RVV-Immunized (n = 9351)</td>
<td>RVV-Nonimmunized (n = 4600)</td>
<td></td>
</tr>
<tr>
<td>Well-child visits up-to-date at 14 mo, No. (%) [SD]</td>
<td>15,185 (61.5)</td>
<td>6779 (72.5) [44.6]</td>
<td>2682 (58.3) [49.3]</td>
</tr>
<tr>
<td>Non-RV immunizations up-to-date at 7 mo, No. (%) [SD]</td>
<td>16,532 (67)</td>
<td>6957 (74.4) [43.6]</td>
<td>2719 (59.1) [49.2]</td>
</tr>
<tr>
<td>Sick-child visits, median (range)</td>
<td>6 (0-57)</td>
<td>8 (0-57)</td>
<td>7 (0-52)</td>
</tr>
<tr>
<td>Per patient</td>
<td>9.7 (0-90.4)</td>
<td>9.7 (0-70.81)</td>
<td>7.72 (0-53.62)</td>
</tr>
<tr>
<td>Per 1000 patient-days</td>
<td>2.5 (0-105)</td>
<td>2.77 (0-89.7)</td>
<td>1.97 (0-74.6)</td>
</tr>
<tr>
<td>After-hours calls per 1000 patient-days, median (range)</td>
<td>2.5 (0-94.96)</td>
<td>6 (0-39.09)</td>
<td>0 (0-46.82)</td>
</tr>
</tbody>
</table>

Abbreviations: RV, rotavirus; RVV, rotavirus vaccine.

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for each AGE outcome using Poisson regression. Adjusted models revealed that during the 2007 season, RVV-immunized children had significantly fewer AGE calls and episodes compared with RVV-nonimmunized children, with IRRs of 0.47 (95% CI, 0.33-0.65) and 0.54 (0.40-0.74), respectively. However, receipt of RVV was not associated with a significant reduction in either AGE calls or episodes for either cohort during the 2008 winter season (Table 3). Immunization with RVV was associated with a statistically nonsignificant reduction in AGE visits for the 2007 cohort in both seasons and for the 2008 cohort during the 2008 season (Table 3). The calculated VE was 53% for calls and 46% for episodes in the 2007 season.

AGE AND DOSE-STRATIFIED RESULTS

A stratified analysis was performed to determine the effectiveness of RVV among different age groups. On the basis of the distribution of age at study entry, the cohorts were divided into quartiles. On stratified analysis, there was no difference between the second and third quartiles; therefore, those age groups were combined, resulting in the 3 reported age groups: 6 weeks, 7 to 24 weeks, and 25 to 40 weeks. During the 2007 season, RVV was most effective in preventing AGE outcomes in the youngest age group (Figure 4A); this differential effect was seen for both cohorts in the 2008 season (Figure 4B and C) but was statistically nonsignificant. A subanalysis was performed for each age group to determine differences in protection from AGE on the basis of the number of RVV doses received. We found no significant difference in protection regardless of the number of doses of RVV received for AGE visits, calls, or episodes.

COMMENT

Although much attention has been focused on inpatient RV disease, this study instead examined AGE and its effect on disease managed by the primary care physician. In this cohort study within a large outpatient pediatric practice setting, receipt of RVV was not associated with a significant reduction in either AGE calls or episodes for either cohort during the 2008 winter season. Immunization with RVV was associated with a statistically nonsignificant reduction in AGE visits for the 2007 cohort in both seasons and for the 2008 cohort during the 2008 season. The calculated VE was 53% for calls and 46% for episodes in the 2007 season.

Figure 3. Median numbers of acute gastroenteritis (AGE) outcomes per 10,000 cohort days for the 2007 and 2008 cohorts. These numbers are adjusted for each child’s time in the cohort for each season. This graph demonstrates the decrease in numbers of AGE outcomes among rotavirus (RV) vaccine (RVV)–nonimmunized children from 2007 to 2008 and the lack of change in AGE outcomes between the 2 RV seasons among RVV-immunized children.

Table 3. IRRs and Calculated VE for AGE Outcomes for 2007 and 2008 Cohorts

<table>
<thead>
<tr>
<th>Variable</th>
<th>AGE Visits</th>
<th>AGE Calls</th>
<th>AGE Episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007 Cohort in 2007 season</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IRR (95% CI)</td>
<td>0.72 (0.42-1.21)</td>
<td>0.47 (0.33-0.65)</td>
<td>0.54 (0.40-0.74)</td>
</tr>
<tr>
<td>VE, %</td>
<td>28</td>
<td>53</td>
<td>46</td>
</tr>
<tr>
<td>2007 Cohort in 2008 season</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IRR (95% CI)</td>
<td>0.78 (0.54-1.13)</td>
<td>1.06 (0.77-1.46)</td>
<td>1.04 (0.79-1.38)</td>
</tr>
<tr>
<td>VE, %</td>
<td>22</td>
<td>-6</td>
<td>-4</td>
</tr>
<tr>
<td>2008 Cohort in 2008 season</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IRR (95% CI)</td>
<td>0.63 (0.29-1.37)</td>
<td>0.93 (0.49-1.76)</td>
<td>0.99 (0.55-1.77)</td>
</tr>
<tr>
<td>VE, %</td>
<td>37</td>
<td>7</td>
<td>1</td>
</tr>
</tbody>
</table>

Abbreviations: AGE, acute gastroenteritis; IRR, incidence rate ratio; VE, vaccine effectiveness.

aAll outcomes were adjusted for the following variables: age at the start of first season, race, practice location (urban vs suburban), presence of a chronic condition, well-child visits up-to-date at 14 months, non-rotavirus immunizations up-to-date at 7 months, total sick-child visits, and time in cohort. Because of the presence of effect modification, we included a term for interaction between rotavirus immunization and age.

bValues are statistically significant (P < .001).
practice–based research network, we found a significant reduction in AGE outcomes for RVV-immunized children. This study determined that children immunized with RVV had a reduced risk of AGE calls (VE of 53%) and episodes (VE of 46%) in 2007. We demonstrated a 3-fold reduction in rates of AGE visits, calls, and episodes among RVV-nonimmunized children in the cohort from the 2007 season to the 2008 season. Also, in our secondary analysis, we showed a significant reduction in winter AGE visit rates among children in our network in the 2 RV seasons following the introduction of RVV compared with the 2 RV seasons preceding RVV.

Our findings demonstrated a significant reduction in the IRR for AGE calls and episodes in 2007 for children immunized with 1 or more doses of RVV. By including calls and creating a composite episode variable, we demonstrated a more significant reduction in AGE-related outcomes among RVV-immunized children in the 2007 RV season than did Wang et al., with nearly half of AGE episodes reduced among RVV-immunized children in our network. Because RV has been estimated to cause more than 40% of outpatient AGE during the RV season, the AGE reductions found in our study correspond with expected reductions in RV-specific disease due to RVV. Although the IRR for visits alone did not reach the level of statistical significance, the trend we detected was similar to that reported by other investigators who demonstrated VE of 25% to 27%. The inability to achieve a statistically significant difference for the visit outcome is unclear but may be due to fewer numbers of visits than calls or fewer RVV-nonimmunized children in the 2008 cohort.

We found children’s age on entry into the 2007 season influenced the effectiveness of RVV. Stratified analysis demonstrated that RVV was most effective in preventing calls and episodes in the youngest age group. The reason for these results is unclear. We suspect that RVV is effective in preventing RV infection in children of all ages equally, but as children grow older, they are more likely to be exposed to non-RV AGE pathogens or their parents are less likely to call or to bring the children in for evaluation. Despite clear evidence in prelicensure studies for a dose-dependent response, we were unable to detect a difference based on number of doses in either cohort. This finding might be explained by a smaller sample size in each stratum that limited our ability to detect a statistically significant difference. Decreasing overall rates of disease may also have limited our ability to detect a difference on the basis of the number of doses received.

In 2008, essentially no vaccine effect was seen for AGE calls and episodes, despite a robust decrease in both of these outcomes among RVV-immunized patients in the 2007 season. These unexpected results contradicted our 2007 findings and the results from other studies. We suspect that indirect protection through herd immunity might have led to our inability to detect a difference between RVV-immunized and RVV-nonimmunized children in the 2008 season. High rates of vaccination in our cohort and the decrease in peak winter AGE rates in our network from the 2 RV seasons before the introduction of RVV to near-summer baseline levels by 2008 (after the introduction of RVV) support the possibility of indirect protection for RVV-nonimmunized children in the 2008 season. Other possible explanations for our inability to detect a difference between RVV-immunized and RVV-nonimmunized children in 2008 include limited RV disease activity, an increase in AGE caused by another pathogen, waning or short-lived immunity, or failure of the vaccine to protect against mild RV disease.

There were several limitations of this study. By using AGE as an outcome, we measured the AGE burden managed by primary care physicians, but we cannot truly assess the reduction in RV disease due to RVV. Testing for viral stool pathogens is uncommon in outpatient settings, so we could not capture RV-specific disease as a

retrospective outcome. To perform this study prospectively and to collect stool to test for RV during every AGE episode for more than 24,000 patients would have been costly and inefficient. Despite previous validation, the use of ICD-9-CM codes to identify AGE outcomes introduces the potential for error in both the physician diagnosis and the recorded codes. Also, we used retrospective data and captured only office visits and telephone calls within the PeRC network. If parents sought care for their children outside of the network, our data capture may be incomplete. Despite including 3 distinct factors in the models to account for variability in patterns of both well-child and sick-child primary care use, perhaps we did not adequately control for changes in health care use patterns in 2008 or other unmeasured factors, which could also explain the lack of a statistically significant difference between RVV-immunized and RVV-nonimmunized children in 2008.

In conclusion, our study demonstrates 46% VE against AGE episodes managed by primary care physicians in our cohort in the 2007 season. No difference was detected between RVV-immunized and RVV-nonimmunized children in 2008. Further studies are needed to determine whether the lack of VE seen in the 2008 season was the result of low RV disease activity, waning immunity, herd immunity, or other factors. Further study is also warranted to evaluate whether RVV is more effective in preventing disease among young infants compared with older infants and toddlers.

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Author Contributions: Dr Coffin received no commercial funding for this project, had full access to all the data in the study, and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Nolan, Fiks, Zaoutis, TenHave, and Coffin. Acquisition of data: Nolan, Prasad, Fiks, and Coffin. Analysis and interpretation of data: Nolan, Prasad, Fiks, Zaoutis, TenHave, and Coffin. Drafting of the manuscript: Nolan, Prasad, Fiks, and Coffin. Critical revision of the manuscript for important intellectual content: Nolan, Fiks, Zaoutis, TenHave, and Coffin. Statistical analysis: Nolan, Prasad, Fiks, TenHave, and Coffin. Obtained funding: Nolan. Administrative, technical, and material support: Nolan. Study supervision: Fiks, Zaoutis, and Coffin.

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Correction

Error in Calculation Reporting. In the article titled “Ex-
cess Body Mass Index–Years, a Measure of Degree and
Duration of Excess Weight, and Risk for Incident Dia-
betes” by Lee et al, published online on September 3, 2011,
and printed in the January 2012 issue of the Archives
(2012;166[1]:42-48), the reporting of the calculation for
excess body mass index (BMI)–years was erroneous. In
the “Main Exposure” subsection of the “Abstract” in print
on page 42, the first sentence should have read: “Excess
BMI-years, which were calculated by subtracting the ref-
erence BMI (25.0 for adults or 85th percentile for ado-
lescents) from the actual BMI for each study year and
cumulating excess BMI for the study duration.” In the
“Main Exposure” subsection of the “Methods” section
on page 43, left-hand column, lines 5 through 8 should
have read: “To calculate degree of excess BMI, we sub-
tracted the reference BMI (defined as BMI thresholds for
overweight of 25.0 for adults or 85th percentile [age- and
sex-adjusted] for adolescents) from the actual BMI.”