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The percentage of children who developed type 1 diabetes after rotavirus vaccination—Reply

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We thank Dr. Rogers for her interest in our article¹. The question of whether rotavirus vaccination may affect the risk of type 1 diabetes (T1D) is certainly one that is worthwhile to investigate using a variety of epidemiologic methods. Although information from cohort studies can be analyzed in several different ways, we feel that MarketScan[®] data, which we used in our analysis, is best analyzed with person-time as the denominator¹, as was done by Dr. Rogers and colleagues in their study on this topic². While the timing of viral challenge with wild-type rotavirus may be unknown in our study population, the timing of vaccination is well documented due to the use of insurance claims data and the inclusion criterion of continuous enrollment since birth. In contrast, once a child is lost to follow-up, the timing and occurrence of T1D is unknown. Furthermore, loss to follow-up (caused by change in insurance status) may be different in children who are completely unvaccinated as compared to children who receive routine vaccinations—one reason for which we subset our main analysis population to those children who had received at least one dose of diphtheria-tetanus-pertussis (DTaP) vaccine by one year of age. Lastly, T1D risk in children is not static, and tends to increase with age^{3,4}.

To further examine the associations between rotavirus vaccination and T1D in our dataset, we performed 3 additional subset analyses. In the first analysis, we used extended Cox regression with age in weeks as the timescale and controlled for year of birth, as previously¹, but censored all participants at 5 years of age, since recent analysis has suggested a possible secular decrease in T1D incidence in children <5³. We again found null results: the adjusted hazard ratio (aHR) was 0.98 (95% Confidence interval [CI]: 0.76 – 1.26) for full-series rotavirus vaccination, and 0.84 (95% CI: 0.60 – 1.16) for partial-series rotavirus vaccination. In a second analysis, we subset the analysis population to include only children with continuous enrollment to at least age 5 years who had received at least one dose of DTaP vaccine and no T1D diagnosis at the age of 1 year. This resulted in a total of 284,181 children, of whom 187,791 (66%) were fully vaccinated against rotavirus, 42,385 (15%) were partially vaccinated against rotavirus, and 54,005 (19%) were unvaccinated against rotavirus. Between the ages of 1 and 5 years, there were 117 (0.062%) T1D diagnoses observed in the fully vaccinated group, 34 (0.080%) in the partially vaccinated group, and 41

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(0.076%) in the unvaccinated group; the Chi Squared p value was 0.31 for this unadjusted analysis. Extended Cox regression among this group of children followed for at least 5 years found a non-significant aHR of 1.36 (95% CI: 0.89 – 2.07) for the effect of full rotavirus vaccination on the risk of developing T1D between 5 and 12 years of age.

These additional analyses support our original conclusion that there is no evidence of an association between rotavirus vaccination and the risk of T1D in our study cohort.

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