RESPONSE TO COMMENT ON GREGORY ET AL.

COVID-19 Severity Is Tripled in the Diabetes Community: A Prospective Analysis of the Pandemic's Impact in Type 1 and Type 2 Diabetes. Diabetes Care 2021;44:526–532

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We thank Maahs et al. for their insightful comments (1) regarding our prospective cohort study quantifying the impact of coronavirus disease 2019 (COVID-19) in patients with diabetes (2). We are pleased to learn no death or mechanical ventilation related to COVID-19 in pediatrics has been reported to the T1D Exchange registry to date. Death and mechanical ventilation are fortunately rare events in all of pediatrics, however. For this reason, comparing the odds of hospitalization or a greater severity of illness against a matched control group may better quantify excess COVID-19 risk in pediatric diabetes and guide policy.

Our initial report analyzed COVID-19 cases identified through 7 August 2020. Since then, our patient accrual has grown from 6,138 to 21,929 with no diabetes, 40 to 160 with type 1 diabetes, and 273 to 1,316 with type 2 diabetes. The number of COVID-19 cases in pediatric patients (i.e., aged ≥12 months and <18 years) with type 1 diabetes has increased from 8 to 22. Of these, 12 were not hospitalized and 10 were hospitalized without mechanical ventilation or death. By comparison, of 2,405 pediatric COVID-19 patients without diabetes, 2,311 were not hospitalized, 86 were hospitalized without mechanical ventilation, 5 required mechanical ventilation, and 3 died (94 hospitalizations). These data yield an unadjusted odds ratio of 20.49 (95% CI 8.63–48.62) for hospitalization and 19.39 (95% CI 8.47–44.42) for severity. Notably, the number of pediatric hospitalizations associated with both COVID-19 and diabetic ketoacidosis (DKA) increased since August 2020. Of the 10 hospitalizations in pediatric patients with type 1 diabetes, 9 were associated with DKA. With the available data, we cannot determine whether COVID-19 directly caused DKA leading to hospitalization or whether COVID-19 coincidentally occurred in children presenting in DKA. However, given the substantial threats of both COVID-19 and DKA, the capacity of viral infection to drive DKA—especially among the most vulnerable—and the potential interaction of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and islet function (3), we remain concerned about the virus's impact in pediatric type 1 diabetes. In addition, as cases rise, the increased odds for hospitalization and severe outcomes in the smaller pediatric data set mirrors the larger adult data set, and our data suggest that there is no discrete cutoff in type 1 diabetes at which younger age mitigates increased COVID-19 risk.

Our community will soon need to pragmatically address questions from patients, families, and policy makers with the best available evidence. A more highly transmissible variant of SARS-CoV-2, B.1.1.7, has potential to increase the U.S. pandemic trajectory in the coming months (4). Concurrently, Pfizer's COVID-19 vaccine is approved down to age 16 years, and an adolescent phase 2/3 trial of Moderna's vaccine is ongoing. Whether SARS-CoV-2 is causally or incidentally associated with pediatric DKA admissions, a safe, efficacious vaccine targeted to patients with type 1 diabetes should reduce COVID-19 hospitalizations and may protect against as-yet unknown sequelae in this population. For this reason, while we eagerly await additional high-quality data to further our understanding of COVID-19 in pediatric diabetes, we encourage recommended viral mitigation measures including prioritized vaccination for those with type 1 diabetes in approved age-groups.

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