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The Dual Burden of Type 1 Diabetes and COVID-19

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In the year following identification of the first case of COVID-19 in the United States on January 21, 2020, the nation's death toll from the virus passed 400,000, a number on par with American fatalities in World War II (405,399) (1). From as early as February 2020, data from China indicated that the COVID-19 case fatality rate was three times higher in patients with diabetes than in patients without diabetes (2). As the pandemic spread beyond China, mounting evidence showed that, although individuals with diabetes were no more prone to SARS-CoV-2 infection than the overall population, they comprised a disproportionately higher percentage of severe COVID-19 cases (3). These early analyses largely did not distinguish between types of diabetes. Yet, because of its higher worldwide prevalence, these data likely largely reflected the experience of patients with type 2 diabetes (T2DM). This early lack of data specifically on patients with type 1 diabetes may have influenced the Center for Disease Control's (CDC) current guidance, which states adult patients with T2DM "are at increased risk" of severe illness from COVID-19, while those with T1DM "might be at an increased risk" for severe illness(4)., How should physicians extrapolate what we know about SARS COV-2 and type 2 diabetes to patients with type 1 diabetes (T1DM)?.

Fortunately, by the second half of 2020 data emerged quantifying COVID-19-related morbidity and mortality in patients with T1DM (5–8). Compellingly, these analyses showed patients with T1DM experienced markedly higher adjusted odds of hospitalization (6), severity of illness (6, 8), and mortality (5, 8) compared with patients who did not have T1DM (Table). In conflict with present CDC guidance, these data further demonstrate that, when compared to individuals without diabetes, people with T1DM have similar to slightly higher adjusted risk for adverse COVID-19 outcomes compared to people with T2DM. Notably, we have found that patients with COVID-19 and well-controlled T1DM have threefold higher unadjusted odds for hospitalization compared with COVID-19 patients who do not have diabetes. This evidence indicates that COVID-19 presents an elevated threat to those living with T1DM.

In addition to quantifying the excess risk for poor COVID-19 outcomes in T1DM, recent studies shed light on patient subgroups that are particularly vulnerable. For example, a

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CONFLICTS OF INTEREST:

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population-wide analysis of 264,390 patients with T1DM found that the adjusted hazard ratio for COVID-19 related death for Black versus White patients was 1.77 (95% CI 1.25–2.49) (7). When patients in the most deprived quintile of the deprivation index were compared against the least deprived quintile, the adjusted hazard ratio for mortality was 1.93 (95% CI 1.36–2.72). By comparison, when the investigators analyzed the association of mortality and glycemic control, the only statistically significant association was among patients with the HbA1c > 10.0% compared to those with HgBA1c 6.5%–7% (adjusted hazard ratio 2.23 (95% CI 1.50–3.30)). Collectively, available evidence suggests that even patients with well-controlled T1DM are at increased risk of poor outcomes from COVID-19 compared to individuals without diabetes.

In December 2020, Pfizer-BioNTech(9) and Moderna(10) reported safety and efficacy data from placebo-controlled randomized clinical trials of their COVID-19 vaccines to the Food and Drug Administration. The effectiveness of the vaccines in preventing confirmed COVID-19 were 95.0% (95% CI 90.3–97.6%) and 94.5% (95% CI 86.5–97.8%), respectively. Moreover, severe COVID-19 occurred only once among vaccinated participants. Importantly, efficacy findings were consistent across nearly every subgroup analyzed, including racial and ethnic minorities, participants older than age 65, and participants with a high-risk condition. People with diabetes comprised 8.4% and 9.4% of each trial's participants (although neither report identified types of diabetes) and derived 94.7% (95% CI 66.8–99.9%) and 100% efficacy from each vaccine. Thus, the vaccines were not only profoundly protective against COVID-19, but they were equally effective in preventing the virus in participants with and without diabetes.

In 1848 Horace Mann, the first great American advocate for public education, famously wrote, “Education then, beyond all other devices of human origin, is a great equalizer of the conditions of men — the balance wheel of the social machinery.” At this critical moment in our history, we believe a new great equalizer has come to the fore: the COVID-19 vaccine. The existing evidence clearly shows the vaccine presents a golden opportunity to rectify health inequities experienced by people with T1DM. While these individuals have a markedly higher risk for severe COVID-19—and higher still for those who are also socially disadvantaged—we now possess an effective tool to mitigate this risk. Presently, individual states are on the threshold of vaccinating persons with high-risk medical conditions and many do not include T1DM in this category. This shortcoming needs prompt remediation to prevent further excessive morbidity and mortality in the T1DM population.

By prioritizing patients with T1DM, states will maximize the vaccine's benefit by decreasing the excess individual burden of severe illness and reducing hospitalizations that strain healthcare systems. Further, this prioritization will mitigate health inequities that are demonstrably present among disadvantaged subgroups of patients with T1DM. In light of these considerations, we urge the ACIP to identify the more than 1.6 million Americans who live with T1DM as individuals at increased risk for poor COVID-19 outcomes.

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TABLE:

Adjusted odds ratios for adverse COVID-19 outcomes in patients with type 1 and type 2 diabetes.

Outcome	Population Analyzed	Number of patients analyzed (No Diabetes vs T1DM vs. T2DM)	Adjusted O.R. T1DM vs. No Diabetes	Adjusted O.R. T2DM vs. No Diabetes
Mortality [*] (5)	England, March 1-May 11, 2020	58,244,220 vs. 263,830 vs. 2,864,670	3.51 (3.16–3.90)	2.03 (1.97–2.09)
Mortality or ICU admission [†] (8)	Scotland, March 1-July 31, 2020	5,143,951 vs. 34,383 vs. 275,960	2.40 (1.82–3.16)	1.37 (1.28–1.47)
Hospitalization [‡]	Vanderbilt Health System, March 17-December 24, 2020	19,422 vs. 136 vs. 1,100	4.60 (3.04–6.98)	3.42 (2.94–3.99)
1st HbA1c quartile		19,422 vs. 26	2.96 (1.11–7.86)	
2nd HbA1c quartile		19,422 vs. 26	2.96 (1.11–7.86)	
3rd HbA1c quartile		19,422 vs. 24	5.12 (2.12–12.35)	
4th HbA1c quartile		19,422 vs. 25	9.76 (4.42–21.54)	

^{*} Adjusted for age, sex, deprivation index, ethnicity, and geographical region.

[†] Adjusted for age and sex.

[‡] Adjusted for age, race, sex, hypertension, smoking, and BMI.