COVID-19 Severity Is Tripled in the Diabetes Community: A Prospective Analysis of the Pandemic's Impact in Type 1 and Type 2 Diabetes

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OBJECTIVE

To quantify and contextualize the risk for coronavirus disease 2019 (COVID-19)–related hospitalization and illness severity in type 1 diabetes.

RESEARCH DESIGN AND METHODS

We conducted a prospective cohort study to identify case subjects with COVID-19 across a regional health care network of 137 service locations. Using an electronic health record query, chart review, and patient contact, we identified clinical factors influencing illness severity.

RESULTS

We identified COVID-19 in 6,138, 40, and 273 patients without diabetes and with type 1 and type 2 diabetes, respectively. Compared with not having diabetes, people with type 1 diabetes had adjusted odds ratios of 3.90 (95% CI 1.75–8.69) for hospitalization and 3.35 (95% CI 1.53–7.33) for greater illness severity, which was similar to risk in type 2 diabetes. Among patients with type 1 diabetes, glycosylated hemoglobin (HbA_{1c}), hypertension, race, recent diabetic ketoacidosis, health insurance status, and less diabetes technology use were significantly associated with illness severity.

CONCLUSIONS

Diabetes status, both type 1 and type 2, independently increases the adverse impacts of COVID-19. Potentially modifiable factors (e.g., HbA_{1c}) had significant but modest impact compared with comparatively static factors (e.g., race and insurance) in type 1 diabetes, indicating an urgent and continued need to mitigate severe acute respiratory syndrome coronavirus 2 infection risk in this community.

The medical community currently lacks sufficient data to adequately mitigate the impact of the novel coronavirus disease 2019 (COVID-19) in the type 1 diabetes community. At present, our knowledge is largely extrapolated from recent retrospective analyses of hospitalized patients (1–5), which have strongly suggested "diabetes" increases risk for COVID-19 morbidity and mortality. These studies did not, however, distinguish between type 1 diabetes and type 2 diabetes—two pathophysiologically distinct conditions. Although reports of COVID-19 in type 1 diabetes are emerging, the scope of these investigations to date has been limited by including only hospitalized

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patients (6,7), patients referred to a registry (8), or an analysis of mortality as the sole outcome without directly verifying patient-specific factors (9,10). Thus, there remains a need to ascertain a wider range of clinical outcomes across a broader spectrum of patients with type 1 diabetes infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Although clinical outcome data for the SARS-CoV-2 virus in type 1 diabetes are lacking, some evidence suggests people with type 1 diabetes are prone to worse outcomes when infected with other respiratory viruses (11). Both type 1 diabetes–related factors, such as dysglycemia, type 1 diabetes duration, BMI, and vascular disease, and demographic factors, such as age, race/ethnicity, and social determinants of health, may modify these risks.

To address these critical gaps in our knowledge, we aimed to answer two questions. First, among patients with COVID-19, to what extent does a diagnosis of type 1 diabetes increase risk for hospitalization, greater severity of illness, and death compared with patients without diabetes or those with type 2 diabetes? Second, which covariates increase risk for a more severe outcome among people with type 1 diabetes? To answer these questions, we conducted a prospective cohort study to identify case subjects with COVID-19 using the electronic health record (EHR), categorizing each patient by diabetes category: no diabetes, type 1 diabetes, or type 2 diabetes.

RESEARCH DESIGN AND METHODS

Data Collection

We retrieved data by querying the Epic Clarity data warehouse at Vanderbilt University Medical Center (VUMC). This data warehouse encompasses the entire EHR at VUMC, a network of 137 primary care, urgent care, and hospital facilities that manages >2 million ambulatory and inpatient visits annually. During the prospective study period between 17 March and 7 August 2020, VUMC tested all patients admitted to the hospital for any reason and all patients prior to any surgical procedure. Additionally, tests were conducted on patients presenting to VUMC primary care, after-hours, urgent care, and minor medical clinics. Using our EHR query, we identified all individuals with a positive COVID-19 test at VUMC, as determined by a positive Centers for Disease Control and Prevention SARS-CoV-2 Real-Time PCR diagnostic panel, with probes and primers provided by Integrated DNA Technologies (Coralville, IA). We then categorized these case subjects by diabetes category, as shown in the flowchart in Supplementary Fig. 1, according to problem list diagnoses. If a patient's problem list included both type 1 diabetes and type 2 diabetes, the primary investigator (J.M.G.) adjudicated which diagnosis was more likely. Type 1 diabetes was assigned if the patient had a history of having autoantibodies associated with type 1 diabetes or required multiple daily injections. Type 2 diabetes was assigned if the patient required multiple oral antihyperglycemic medications. We retrieved prespecified clinical outcomes related to COVID-19 and covariates thought to potentially affect illness severity (listed in Supplementary Tables 1–3), as documented in the EHR. Beginning with the first case subject with COVID-19 in March 2020, we prospectively repeated the query every 2 weeks to identify case subjects, outcomes, and covariates. We also accessed publicly available data sets from the Tennessee Department of Health to determine the number of positive and total COVID-19 tests that were conducted in the local community around VUMC (i.e., Davidson County and its six surrounding counties, accessed on https://www.tn.gov/content/tn/health/cedep/ncov/data.html).

To further characterize factors that modulate risk for COVID-19 severity, we conducted a detailed chart review on all case subjects in patients with type 1 diabetes and attempted to contact them by telephone. After obtaining written, informed consent via electronic document, patients completed a survey over the phone, including questions about their medical history and social determinants of health (as listed in Supplementary Tables 1–3).

The research team managed study data using secure Research Electronic Data Capture (REDCap) electronic data tools (12). The Institutional Review Board of Vanderbilt University approved the study protocol.

Calculations and Data Analysis

To quantify the magnitude of COVID-19 severity, we defined an ordinal outcome variable for illness severity with six mutually exclusive levels that had to occur within 14 days of a positive PCR test for SARS-CoV-2:

- No hospitalization
- Hospitalization for any reason without any respiratory support
- Hospitalization for any reason with lower acuity respiratory support (e.g., oxygen by nasal canula, nonrebreather mask, or continuous or bilevel positive airway pressure)
- Intensive care unit (ICU) admission for any reason
- Endotracheal intubation and mechanical ventilation for any reason
- Death for any reason

Hospitalization was analyzed as a binary outcome using logistic regression. Disease severity was analyzed using the proportional odds ordinal logistic regression model. In all models, we included diabetes status and adjusted for a set of prespecified covariates that could potentially confound the association between diabetes status and illness severity. These covariates included age, sex, BMI, diabetes category, smoking history, race, and a history of hypertension. Results are presented as odds ratios (ORs) with corresponding 95% CIs. For all analyses, multiple imputation (10 imputed data sets) for missing covariates was performed using the "aregImpute" function available in the rms package for R version 3.6.3 (13).

After detailed chart review and patient surveys, we further analyzed the risk factors listed in Supplementary Table 3 for worsening illness severity among the patients with type 1 diabetes. To quantify the effect size of each independent variable on the ordinal variable for illness severity, we determined the unadjusted OR for worse illness severity for each independent variable using univariate ordinal regression.

RESULTS

Demographic and Clinical Characteristics of Patients With COVID-19 Identified by EHR Query

During the prospective study period between 17 March and 7 August 2020, VUMC obtained 83,437 SARS-CoV-2 PCR results for 69,701 unique individuals at VUMC, 6,451 of whom tested positive for COVID-19 (7.7% positive). By comparison, 45,456 of 372,779 SARS-CoV-2 PCR tests (12.2%) were positive in Davidson County, TN, and its six surrounding counties over the same interval. Of the COVID-19–positive individuals at VUMC, 6,138 had no diabetes, 40 had type 1 diabetes,

and 273 had type 2 diabetes. Table 1 summarizes demographic and clinical characteristics of these patients. The median age and BMI of patients with type 1 diabetes were similar to the group without diabetes, while patients with type 2 diabetes were two decades older and had a BMI ~20% higher than the other two groups. Pediatric patients (i.e., aged <18 years) comprised 9.4%, 20.0%, and 0% of the groups with no diabetes, type 1 diabetes, and type 2 diabetes, respectively. The type 1 diabetes cohort had a higher percentage for White race and a lower percentage for Hispanic ethnicity. The percentage of individuals taking medications to treat hypertension or who had a diagnosis of hypertension or asthma was lowest for those without diabetes, intermediate for those with type 1 diabetes, and highest for those with type 2 diabetes.

Unadjusted Outcome Data for Patients With COVID-19 Identified by EHR Query

Supplementary Table 1 summarizes unadjusted COVID-19 hospitalization rates and illness severity for patients categorized by diabetes status. Whereas hospitalization was three times more likely to occur in patients with type 1 diabetes than patients without diabetes (22.5% vs. 7.1%; $P < 0.001$), hospitalization in the group with type 2 diabetes occurred two times more often than in the group with type 1 diabetes (44.3% vs. 22.5%; $P = 0.009$), which was two decades younger. No deaths occurred in the group with type 1 diabetes, but deaths occurred in 0.5% of patients without diabetes ($P = 0.67$ vs. type 1 diabetes) and 4.8% of patients with type 2 diabetes ($P = 0.368$ vs. type 1 diabetes and $P < 0.001$ vs. no diabetes). Unadjusted for other covariates, illness severity for patients with type 1 diabetes was worse than those without diabetes ($P < 0.001$), but less severe than those with type 2 diabetes ($P < 0.001$).

Adjusted Outcome Data for Patients With COVID-19 Identified by EHR Query

Because of key differences in baseline risk factors between the groups (e.g., older age in the group with type 2 diabetes), we used multivariable regression to adjust for age, race, sex, hypertension, smoking, and BMI. Figure 1 summarizes adjusted ORs for hospitalization rates and illness severity. After statistical adjustment, groups with both type 1 and type 2 diabetes had similarly increased odds of hospitalization and worsening illness severity relative to individuals without diabetes (Fig. 1*A* and *C*). In type 1 diabetes, the adjusted ORs were 3.90 (95% CI 1.75–8.69) for hospitalization and 3.35 (95% CI 1.53–7.33) for worsening illness severity. For type 2 diabetes, the adjusted ORs were 3.36 (95% CI 2.49–4.55) for hospitalization, 3.42 (95% CI 2.55–4.58) for worsening illness severity, and 3.21 (95% CI 1.54–6.70) for death. Across all ages, patients with type 1 diabetes had a higher probability of hospitalization than patients without diabetes (Fig. 1*B*). Next to age, the presence of diabetes was the most important factor in the multivariable ordinal regression model for illness severity (Fig. 1*D*).

Clinical Factors Associated With Worse COVID-19 Outcomes in Type 1 Diabetes

Because an EHR query is limited in its ability to capture some risk factors for a

Table 1—Baseline characteristics of patients with COVID-19 grouped by diabetes status (no diabetes, type 1 diabetes mellitus [T1DM], and type 2 diabetes mellitus [T2DM])

Baseline characteristic	No diabetes (n = 6,138)	T1DM (n = 40)	T2DM (n = 273)	Percent missing
Age, years (interquartile range, total range)	33 (23–48, <1 day–97 years)	37 (21–51, 4–80)	58 (49–97, 22–91)	0
Male sex, % (n)	46.8 (2,871)	42.5 (17)	56.0 (153)	0
BMI, kg/m^2	26.6 (22.8–31.5)	25.0 (21.5–28.6)	32.6 (28.1–37.6)	28
Weight, kg	77.1 (62.9–93.0)	74.0 (62.5–81.7)	97.1 (81.7–114.8)	23
Most recent HbA_{1c} within past year, %	5.3 (5.1–5.6)	8.0 (7.1–9.1)	7.5 (6.5–8.8)	89*
Most recent HbA_{1c} within past year, mmol/mol	34 (32–38)	64 (54–76)	58 (48–73)	89*
Diagnosis of hypertension, % (n)	9 (568)	33 (13)	71 (194)	0
Diagnosis of asthma, % (n)	6 (345)	5 (2)	10 (28)	0
Smoking status, % (n)				
Never smoker	81 (3,590)	82 (31)	67 (171)	
Former smoker	10 (430)	18 (7)	23 (59)	27
Some days smoker	0 (0)	0 (0)	0 (0)	
Every day smoker	10 (424)	0 (0)	11 (27)	
Taking ACE-I, % (n)	3 (207)	32 (13)	28 (75)	0
Taking ARB, % (n)	4 (212)	12 (5)	22 (59)	0
Taking any antihypertensive medication other than ACE-I or ARB, % (n)	9 (542)	18 (7)	50 (135)	0
Race, % (n)				
White	67 (3,106)	79 (30)	53 (141)	
Black	15 (676)	18 (7)	34 (91)	
Asian	3 (117)	0 (0)	3 (8)	24
American Indian/Alaska Native	0 (13)	0 (0)	1 (2)	
Unknown	15 (684)	3 (1)	8 (22)	
Native Hawaiian/Pacific Islander	0 (6)	0 (0)	0 (1)	
Hispanic ethnicity, % (n)	10 (559)	3 (1)	11 (29)	12

Continuous variables are summarized as medians (interquartile range). Categorical and ordinal variables are expressed as percentages (counts). ACE-I, ACE inhibitor; ARB, angiotensin receptor blocker. *HbA_{1c} was missing for 92% of patients without diabetes, 17% of patients with T1DM, and 39% of patients with T2DM.

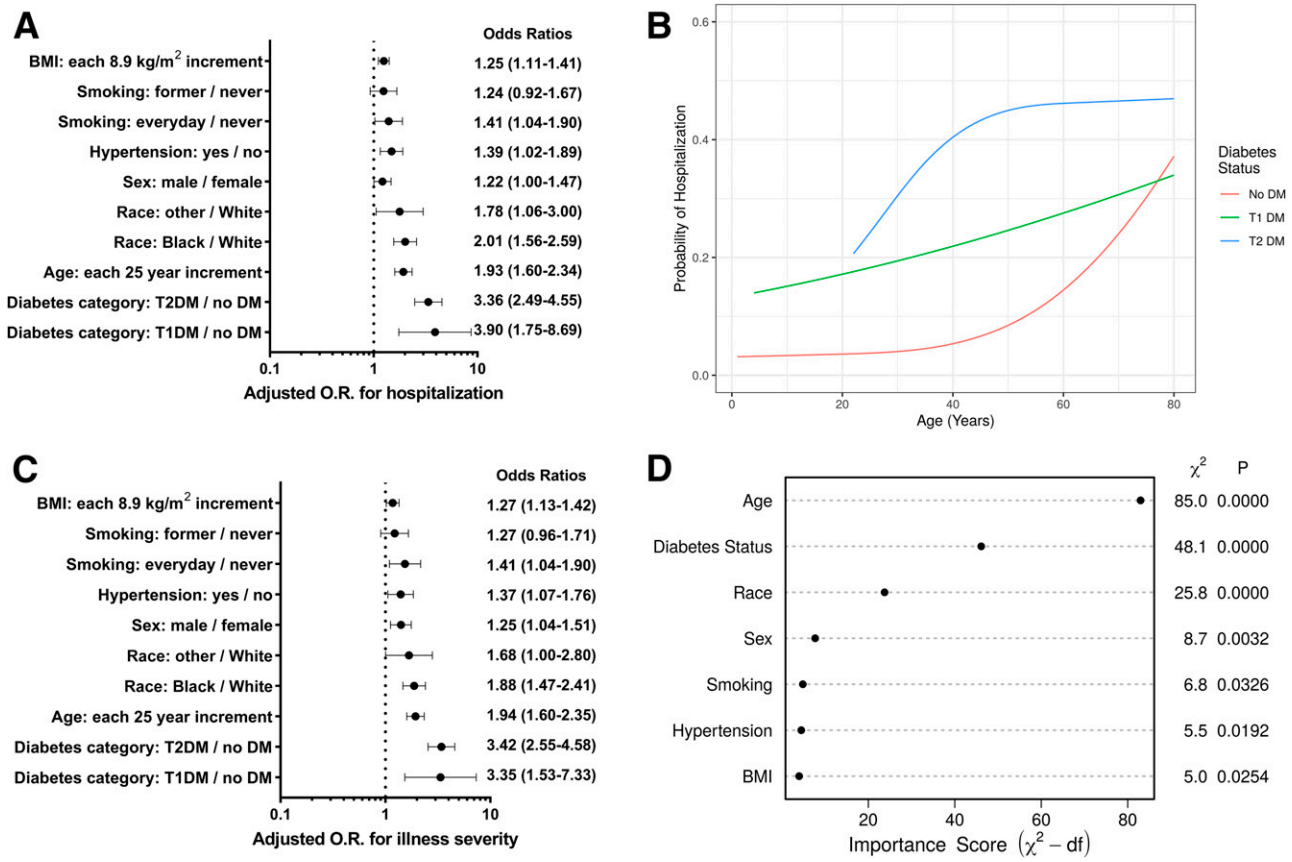

Figure 1—*A*: OR plot displaying adjusted ORs and 95% CIs for independent variables associated with hospitalization with COVID-19 within 14 days of a positive test. *B*: Probability of COVID-19–positive hospitalization by age, categorized by diabetes type, adjusted to a BMI of 26 kg/m^2. *C*: OR plot displaying adjusted ORs and 95% CIs for independent variables associated with worsening illness severity with COVID-19 within 14 days of a positive test. *D*: ANOVA plot depicting the importance of clinical factors in the multivariable ordinal regression model for illness severity. DM, diabetes mellitus; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

worse outcome in type 1 diabetes, we conducted a detailed chart review on 37 out of 40 patients with type 1 diabetes infected with SARS-CoV-2. Fifteen of these patients consented to participate in a telephone survey to further characterize clinical factors that might worsen sequelae from COVID-19. Of the 37 chart-reviewed case subjects, 76% required no hospitalization, 14% were hospitalized without need for respiratory support or ICU admission, 3% were hospitalized and required low-acuity respiratory support, 5% required ICU admission, and 3% required endotracheal intubation and mechanical ventilation. No deaths occurred within 14 days of positive SARS-CoV-2 testing. None of the patients were diagnosed with myocarditis, acute cardiac injury, or arrythmia. Only one patient was hospitalized with diabetic ketoacidosis (DKA) within 14 days of positive SARS-CoV-2 testing.

Table 2 lists summary statistics and ORs for the association of clinical factors with COVID-19 illness severity in type 1 diabetes. Clinical factors significantly associated with greater COVID-19 illness severity ($P < 0.05$) included having a previous diagnosis of hypertension, higher glycosylated hemoglobin (HbA_{1c}), taking any antihypertensive medication other than an ACE inhibitor or angiotensin receptor blocker, having at least one DKA admission in the past year, and not using a continuous glucose monitor (CGM). There was insufficient evidence to determine whether patients with a past medical history of microvascular disease tended to have worsening illness severity.

Of the 11 patients previously diagnosed with hypertension, 55% were hospitalized. By comparison, only 12% of the 25 patients not diagnosed with hypertension were hospitalized. The unadjusted OR for greater illness severity was 7.06 in the hypertensive patients versus patients without hypertension ($P = 0.020$).

Social determinants of health were also significantly related to severity outcome. Eleven percent of patients who identified race as White were hospitalized, and the unadjusted OR for greater illness severity was 0.091 for White race versus not White race ($P = 0.007$). Seventy-one percent of patients who identified as Black or African American were hospitalized, and the unadjusted OR for worse illness severity was 10.4 for Black race versus not Black race ($P = 0.009$). While 8% of patients with private insurance were hospitalized, 60% of patients with public insurance only were hospitalized and 67% of patients with no insurance were hospitalized. The unadjusted OR for increased illness severity was 30.7 for public or no insurance versus private insurance ($P = 0.001$). Although the survey included questions about income category and highest level of education, we found patients who were hospitalized were less likely to take phone calls or report this information.

Similarly, patients using higher levels of technology to manage their diabetes were less likely to have worse outcomes.

Table 2—Clinical characteristics, unadjusted ORs for more severe illness, and *P* values for key variables correlating with COVID-19 severity among 37 patients with type 1 diabetes mellitus (T1DM) whose charts were reviewed

Variable	Value	Percent missing	OR	*P* value
Age, years	32 (21–48)	0	1.23*	0.317
Male sex, % (*n*)	40.5 (15)	0	1.04	0.754
BMI, kg/m^2	24.8 (21.5–28.6)	3	0.133	0.465
Weight, kg	73.9 (62.5–80.2)	0	1.06†	0.574
Most recent HbA_{1c} within past year, %	8.0 (7.1–9.5)	14	1.52	0.045
Most recent HbA_{1c} within past year, mmol/mol	64 (54–80)	14	—	0.045
T1DM duration, years	18 (9–29)	11	0.98	0.631
Number of DKA admissions within past year, % (*n*)				
Zero	91 (29)			
One	3 (1)	14	18.26‡	0.21
Two	3 (1)			
Three	3 (1)			
Primary glucose monitoring device, % (*n*)				
Blood glucose meter	41 (15)	0	8.70	0.016
Continuous glucose meter	58 (22)			
Primary insulin delivery method, % (*n*)				
≥3 injections daily	53 (18)	8	7.07	0.085
Insulin pump	47 (16)			
Has seen an endocrinologist within the past year, % (*n*)	94 (30)	14	0.10	0.101
Any nephropathy, % (*n*)	17 (6)	5	5.21	0.071
Any retinopathy, % (*n*)	11 (4)	5	6.49	0.070
Any neuropathy, % (*n*)	11 (4)	3	6.07	0.080
Smoking status, % (*n*)				
Never smoker	80 (30)			
Former smoker	20 (6)	3	4.45	0.104
Some days smoker	0 (0)			
Every day smoker	0 (0)			
Had flu immunization in past year, % (*n*)	74 (23)	16	0.35	0.349
Taking ACE-I, % (*n*)	32 (12)	0	2.16	0.321
Taking ARB, % (*n*)	11 (4)	0	3.04	0.288
Taking any antihypertensive medication other than ACE-I or ARB, % (*n*)	14 (5)	0	14.60	0.007
Diagnosis of hypertension, % (*n*)	31 (11)	3	7.06	0.020
Previous diagnosis of asthma, % (*n*)	6 (2)	6	2.34	0.561
Race % (*n*)				
White	78 (28)			
Black	19 (7)			
Asian	0 (0)	3	10.94§	0.007
American Indian/Alaska Native	0 (0)			
Unknown	3 (1)			
Native Hawaiian/Pacific Islander	0 (0)			
Health insurance type, % (*n*)				
No insurance	16 (16)			
Public insurance only	14 (5)	0	30.72‖	0.001
Private insurance only	68 (25)			
Both private and public insurance	3 (1)			

Percent missing indicates that chart review could determine the variable of interest and values are reported for nonmissing data only. Continuous variables are summarized as medians (interquartile range). Categorical and ordinal variables are expressed as percentages (counts). ACE-I, ACE inhibitor; ARB, angiotensin receptor blocker. *OR is for each 10-year increase in age. †OR is for each 10-kg increase in weight. ‡OR is for any DKA admissions in the past year vs. none. §OR is for non-White race vs. White race. ‖OR is for public or no insurance vs. private insurance.

Whereas only 9% of patients using a CGM as the primary means of glucose monitoring were hospitalized, 47% of patients using a blood glucose monitor as the primary means of glucose monitoring were hospitalized. The unadjusted OR for worse illness severity was 8.70 for a blood glucose monitor versus CGM ($P = 0.016$). While only 6% of patients using an insulin pump were hospitalized, 33% of patients using multiple daily injections were hospitalized. The unadjusted OR for greater illness severity was 7.07 for multiple daily injections versus insulin pump use ($P = 0.085$).

CONCLUSIONS

Two principal themes emerge from these data regarding the severity of COVID-19 in type 1 diabetes. First, after adjustment for age, race, and other risk factors, the odds of a COVID-19–related hospitalization and greater illness severity for patients

with type 1 diabetes are three- to fourfold higher than patients without diabetes. This increased risk is approximately the same for patients with type 2 diabetes (Fig. 1*A* and *C*). Second, COVID-19 outcome severity in type 1 diabetes is associated with glycemic, vascular, and socioeconomic risk factors.

Before adjustment for baseline characteristics that differed between groups, patients with type 1 diabetes appeared to have a risk for hospitalization and greater illness severity that was intermediate between the group with no diabetes and the group with type 2 diabetes. Importantly, however, once our analysis adjusted the odds of hospitalization and greater illness severity for other known COVID-19 risk factors, especially age, both groups with diabetes had similar odds of worsening morbidity compared with the group without diabetes. The three- to fourfold adjusted OR for hospitalization and greater illness severity seen in this investigation is comparable to the adjusted OR for mortality recently reported by the National Health Service (NHS) in England. In this large population study, the adjusted ORs for in-hospital death with COVID-19 was 3.5 for people with type 1 diabetes and 2.0 for people with type 2 diabetes (both relative to people without diabetes) (9).

Whereas our data agree with an increasing body of evidence suggesting hospitalization rates are low in individuals without diabetes and rise considerably after 40 years of age (14), our analysis additionally suggests the probability of hospitalization is substantially higher for patients with type 1 diabetes than patients without diabetes until nearly the eighth decade of age (Fig. 1*B*). Although the NHS investigators reported low absolute risk for mortality for patients with type 1 diabetes $<$40 years of age, when we examine the more common outcome of hospitalization, we find the probability ranges between $\sim$15% and $\sim$22% for patients $<$40 years of age, after adjustment for BMI. This probability is considerably greater than the $\sim$5% risk seen over that age range in individuals without diabetes. Thus, the increased risk for COVID-19–related hospitalization remains markedly higher for people with type 1 diabetes until the seventh decade of life.

An EHR query is limited in its ability to accurately capture many risk factors for COVID-19 morbidity, particularly among people with type 1 diabetes. For this reason, our detailed chart review of 37 out of the 40 COVID-19–positive patients with type 1 diabetes enhanced our ability to analyze associations between potential clinical covariates and outcome severity. Our analysis suggests chronic hyperglycemia and vascular disease, social determinants of health, and decreased use of diabetes technology correlate significantly with outcome severity; these factors represent common characteristics between type 1 and type 2 diabetes and suggest that addressing modifiable factors will reduce risk in all patients with diabetes. These relationships are not surprising given the linkage between these risk factors and worse illness with COVID-19 reported in previous studies that did not focus on type 1 diabetes. For example, the heightened risk of poor outcomes for patients with type 1 diabetes with hypertension reported in this study is consistent with findings from previous meta-analyses of the broader Chinese population (15,16). Whereas previous reports have indicated proportionally higher rates of hospitalizations from COVID-19 among Black patients and those with public insurance (17), this study is the first to show a similar finding in the population with type 1 diabetes. Although our investigation identified an inverse correlation between diabetes technology use and illness severity, we found that patients with worse illness severity answered questions about socioeconomic status at a lower rate. Thus, our analysis cannot exclude the possibility that greater amounts of diabetes technology use are a surrogate for higher socioeconomic status. Somewhat surprisingly, we did not observe a significant correlation between type 1 diabetes duration and COVID-19 severity. Moreover, we did not find statistically significant associations between the illness severity and age and sex within the type 1 diabetes cohort. We suspect these relationships would have been stronger had the sample size been larger, since these correlations were robust in the larger EHR cohort.

Interestingly, only 1 out of 40 patients with type 1 diabetes diagnosed with COVID-19 was also hospitalized for DKA. This finding contrasts with a preliminary report from the T1D Exchange Collaboration, which found 46% of 33 COVID-19–positive patients had DKA (8). One possible reason for this significant discrepancy is that clinicians and patients were more likely to refer more severe case subjects to the T1D Exchange multicenter registry. Similarly, physicians participating in the registry may have been unaware of less severe case subjects in the community. This tendency for referral bias may have been particularly true during the early weeks of the unfolding pandemic when the preliminary report was published.

Strengths of our study include the ability of the EHR query to broadly and prospectively identify case subjects with COVID-19 across our entire EHR in an unbiased fashion. Further, testing at Vanderbilt captures a wide cross-section of illness severity. In contrast with two recent studies characterizing clinical characteristics of patients with type 1 diabetes hospitalized with COVID-19 (6,7), our analysis included not only every hospitalized patient, but also numerous patients in outpatient primary care, minor medical, and urgent care clinics (i.e., many patients with milder symptoms). Additionally, our hospital tests all patients immediately prior to an elective surgical procedure (i.e., many entirely asymptomatic patients). Because this approach does not rely on clinics to report case subjects with COVID-19 in type 1 diabetes, it is less prone to referral bias than other current approaches (8). Furthermore, our approach determined the presence of COVID-19 in a straightforward, standardized fashion across the EHR: to have COVID-19 for our study, the patient simply had to have a positive SARS-CoV-2 PCR test. In addition, our phone survey allowed us to collect more detailed information about social determinants of health. Thus, our approach complements that of our colleagues who are also working to characterize COVID-19 in type 1 diabetes.

Three significant limitations of this study warrant consideration. First, data were accrued from a single academic health system largely serving urban and suburban populations. Although the VUMC system includes many outpatient testing locations throughout the local community (e.g., primary care, minor medical, and urgent care clinics), we were unable to access detailed information about case subjects with COVID-19 identified outside the VUMC system. Second, although all hospitalized and presurgical patients at VUMC received COVID-19 testing during the prospective study period, our study cannot exclude the possibility that clinicians in the outpatient setting were more likely to

test patients with diabetes than without diabetes because of the perception that patients with diabetes were at greater risk. Third, although we extensively characterized risk factors and outcomes for patients with COVID-19 in this study, the sample size remains relatively small compared with whole-population studies. This smaller sample size prevented us from conducting some multivariate regression analyses within the group with type 1 diabetes and from better characterizing COVID-19 outcomes in Hispanic patients with type 1 diabetes. Additionally, more rare outcomes, such as death, are difficult to adequately characterize. This is likely the reason for the striking difference seen in the death rate in our study (0 out of 40 COVID-19–positive patients with type 1 diabetes) and that of the whole-population study done by NHS England (9,10), which focused on mortality as the outcome of interest. Because the present investigation involved a comparatively smaller sample size, it can neither support nor refute the NHS study's finding of high mortality in COVID-19–positive patients with type 1 diabetes. Instead, our analysis complements the NHS study by showing the adjusted odds of hospitalization and the severity of illness with COVID-19 are three- to fourfold higher in type 1 diabetes versus a comparable population of individuals who do not have diabetes.

Our data have important implications for the community with diabetes as colder temperatures emerge in the Northern hemisphere. As social activities move inside, humidity decreases, and the will to maintain social distancing practices wanes, experts have expressed considerable concern that SARS-CoV-2 transmission will increase sizably (18). Our investigation suggests that as COVID-19 hospitalizations rise, patients with both type 1 and 2 diabetes will comprise a disproportionally higher number of those admissions and, once hospitalized, demonstrate a greater degree of illness severity. Thus, unless the community with type 1 diabetes reamplifies its efforts to mitigate the spread of SARS-CoV-2 in the coming months, physicians should anticipate an imminent escalation in the number of these patients with severe illness, including both adults and children. In light of these data, we call on our colleagues to emphasize the importance of social distancing measures and hand hygiene, with particular emphasis on patients with diabetes, including those in the most vulnerable communities whom our study affirms will face the most severe impact.

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