












ORIGINAL RESEARCH

Association Between Hypertension and Diabetes Control and COVID-19 Severity: National Patient-Centered Clinical Research Network, United States, March 2020 to February 2022

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BACKGROUND: Hypertension and diabetes are associated with increased COVID-19 severity. The association between level of control of these conditions and COVID-19 severity is less well understood.

METHODS AND RESULTS: This retrospective cohort study identified adults with COVID-19, March 2020 to February 2022, in 43 US health systems in the National Patient-Centered Clinical Research Network. Hypertension control was categorized as blood pressure (BP) <130/80, 130 to 139/80 to 89, 140 to 159/90 to 99, or ≥160/100 mmHg, and diabetes control as glycated hemoglobin <7%, 7% to <9%, ≥9%. Adjusted, pooled logistic regression assessed associations between hypertension and diabetes control and severe COVID-19 outcomes. Among 1 494 837 adults with COVID-19, 43% had hypertension and 12% had diabetes. Among patients with hypertension, the highest baseline BP was associated with greater odds of hospitalization (adjusted odds ratio [aOR], 1.30 [95% CI, 1.23–1.37] for BP ≥160/100 versus BP <130/80), critical care (aOR, 1.30 [95% CI, 1.21–1.40]), and mechanical ventilation (aOR, 1.32 [95% CI, 1.17–1.50]) but not mortality (aOR, 1.08 [95% CI, 0.98–1.12]). Among patients with diabetes, the highest glycated hemoglobin was associated with greater odds of hospitalization (aOR, 1.61 [95% CI, 1.47–1.76] for glycated hemoglobin ≥9% versus <7%), critical care (aOR, 1.42 [95% CI, 1.31–1.54]), mechanical ventilation (aOR, 1.12 [95% CI, 1.02–1.23]), and mortality (aOR, 1.18 [95% CI, 1.09–1.27]). Black and Hispanic adults were more likely than White adults to experience severe COVID-19 outcomes, independent of comorbidity score and control of hypertension or diabetes.

CONCLUSIONS: Among 1.5 million patients with COVID-19, higher BP and glycated hemoglobin were associated with more severe COVID-19 outcomes. Findings suggest that adults with poorest control of hypertension or diabetes might benefit from efforts to prevent and initiate early treatment of COVID-19.

Key Words: blood pressure ■ COVID-19 ■ diabetes ■ glycated hemoglobin ■ hypertension

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CLINICAL PERSPECTIVE

What Is New?

- In this study of 1.5 million patients with COVID-19 in the United States, higher blood pressure and glycated hemoglobin were associated with worse COVID-19 outcomes.
- This was the largest study of its kind, and unlike prior work, assessed hypertension and diabetes control based on assessments before SARS-CoV-2 infection, rather than measurements taken during acute COVID-19 illness.

What Are the Clinical Implications?

- These findings highlight the importance of ongoing chronic disease management during a pandemic, including through out-of-office services, such as telehealth, and strategies such as disease self-management education and support.
- In addition, clinicians can encourage adults with poorly controlled hypertension or diabetes to adhere to COVID-19 vaccination recommendations and encourage these patients to seek early treatment for COVID-19 to prevent progression to severe disease.

Nonstandard Abbreviations and Acronyms

PCORnet National Patient-Centered Clinical Research Network

Poorly managed hypertension and diabetes are known risk factors for a range of adverse health events, including cardiovascular morbidity and mortality.¹ Although these conditions can be managed through medical treatment and lifestyle modifications, such as dietary change and physical activity, control of these conditions is often suboptimal.¹ In recent national estimates, approximately one-quarter (24.3%) of US adults with hypertension had blood pressure (BP) levels that met recommended treatment targets for control (defined as BP <130/80 mmHg).² Among adults with diabetes, approximately two-thirds (66.8%) met the standard glycated hemoglobin (HbA1c) target of <7%.³ The COVID-19 pandemic adversely affected chronic disease management through disruptions to health care access and daily life, leading to reduced ability for adults to obtain preventive health care or engage in behaviors known to promote control of hypertension and diabetes.^{1,4,5}

Hypertension and diabetes are 2 of the most common comorbidities among adults hospitalized with

COVID-19⁶ and have been associated with severe disease outcomes and mortality.⁷⁻⁹ Poor BP or glycemic control might also be associated with worse COVID-19 outcomes, but research gaps persist regarding any independent associations between severe COVID-19 outcomes and standard measures of chronic disease control such as BP and HbA1c.¹⁰⁻¹² A prior study described greater prevalence of severe COVID-19 outcomes across higher strata of BP and HbA1c; however, these results did not account for differences in demographic and clinical characteristics across patient populations by BP or HbA1c level.¹³ In this study, we build on these previous descriptive analyses by assessing the independent association between hypertension control and diabetes control and severe COVID-19 outcomes among a large multisite US cohort of adults with COVID-19 from March 2020 to February 2022. We hypothesized that patients with hypertension who had the highest preinfection BP levels and patients with diabetes who had the highest preinfection HbA1c levels would have greater odds of severe COVID-19 outcomes relative to those with the lowest respective levels, after adjusting for demographic and clinical characteristics. These results can be used to guide clinical and public health practice by identifying populations who might be most at risk for poor COVID-19 outcomes and who might benefit most from enhanced chronic disease management, COVID-19 prevention strategies, and early treatment with medications known to reduce progression to severe COVID-19.¹⁴

METHODS

Participants and Procedures

This cross-sectional study aggregated ambulatory, emergency department, and inpatient electronic health record data in 43 sites (each representing ≥1 health systems) participating in PCORnet, the National Patient-Centered Clinical Research Network.^{15,16} All adults aged ≥20 years with COVID-19 identified by positive SARS-CoV-2 polymerase chain reaction (98%) or antigen (3%) lab test in an ambulatory, emergency department, or inpatient care setting during March 1, 2020, to February 28, 2022 were included (N=1 494 837). (Some patients tested positive by both polymerase chain reaction and antigen tests.) If a patient had multiple positive tests for COVID-19, we used the first positive record as the COVID-19 index date. Patient diagnoses and characteristics were identified by querying procedure codes (ie, Current Procedure Terminology; Healthcare Common Procedure Coding Systems, 9th and 10th Revisions), diagnostic codes (ie, *International Classification of Diseases, 10th Revision, Clinical Modification* [ICD-10-CM]), laboratory codes (ie, Logical Observation Identifiers Names and Codes),

or prescribing codes (ie, National Drug Code, RxNorm concept unique identifiers). This activity was deemed not to be research as defined in 45 CFR 46.102(l); informed consent and institutional review board review were not required. The data for this study were shared using existing data use agreements between sites involved. PCORnet has a standardized process called the Front Door to query and request data across participating systems. Requests can be made here: <https://pcornet.org/front-door/>.

Measures

Hypertension Control

Using a 3-year lookback period before the COVID-19 index date, we defined patients as having hypertension based on (1) prescription for an outpatient antihypertensive medication (not including centrally acting agents, loop diuretics, or beta blockers, as these are commonly used for other conditions); (2) outpatient centrally acting agents, loop diuretics, or beta blockers and either an *ICD-10-CM* diagnostic code for hypertension (I10–I16) or outpatient BP $\geq 130/80$ mmHg; (3) 2 outpatient BP readings $\geq 130/80$ on separate days; or (4) 2 *ICD-10-CM* codes for hypertension on separate days in any care setting. We identified hypertension control status by the outpatient BP measurement most recently available before the COVID-19-positive lab test, with values identified in the 18-month to 2-week period before the positive COVID-19 lab test. Excluding the 2-week period before infection avoided use of values during the acute illness, and including measures up to 18 months before accounted for the possibility that patients might have gone long periods without a measured BP, especially during the COVID-19 pandemic. Patients without a BP value during this period were not classified into hypertension control categories. Hypertension control was categorized into 4 strata (BP $< 130/80$, $130\text{--}139/80\text{--}89$, $140\text{--}159/90\text{--}99$, or $\geq 160/100$ mmHg; these cutpoints were selected a priori), using the higher systolic or diastolic value if a patient's values fell into multiple levels.

Diabetes Control

Using a 3-year-lookback period, we defined patients as having type 1 or type 2 diabetes based on (1) having ≥ 1 prescriptions for an outpatient diabetes medication, (2) HbA1c $\geq 6.5\%$, (3) 1 *ICD-10-CM* code for diabetes (E10–E11) plus metformin, or (4) 2 *ICD-10-CM* codes for diabetes in any care setting. Using an 18-month lookback period, we categorized diabetes control into 3 strata (HbA1c $< 7\%$, $7\%\text{--}< 9\%$, $\geq 9\%$; these cutpoints were selected a priori) using the most recently measured HbA1c before the index COVID-19 date. Adults

without an HbA1c measurement during this period were not categorized into diabetes control categories.

Severe Disease Outcomes

Hospitalization (defined as receiving ≥ 1 diagnosis for any reason in an inpatient setting), receipt of critical care (defined by procedure codes), and receipt of mechanical ventilation (defined by procedure and diagnostic codes) were assessed from 1 day before through 16 days after the COVID-19 index date, accounting for delayed worsening of COVID-19 illness that can extend into the second week of illness. We also captured deaths from any cause that occurred ≤ 60 days from the COVID-19 index date.

Demographic and Clinical Characteristics

Demographic variables included age in years, sex (male, female), race (White, Black, Asian, other [including American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, Multiple Race, other]), and Hispanic ethnicity (yes, no). Patients were classified as having obesity according to their body mass index (≥ 30 kg/m² versus < 30 kg/m²) and by smoking status by the most recent value recorded in the electronic health record (current, former, never, unknown). History of 32 comorbidities within a 3-year lookback period was assessed individually (see [Table 1](#); comorbidities with prevalence $\geq 5\%$) and collectively using the Combined Comorbidity Index score.¹⁷ COVID-19 treatment variables included use of dexamethasone, monoclonal antibodies, or remdesivir within 14 days before or after the COVID-19 index date. COVID-19 index dates were also classified according to date ranges corresponding to pandemic phase (March 1, 2020–April 30, 2020 early pandemic, May 1, 2020–February 28, 2021 summer and winter waves, March 1, 2021–June 30, 2021 rising vaccination rates, July 1, 2021–December 19, 2021 Delta variant predominance, and December 20, 2021–February 28, 2022 Omicron variant predominance).¹⁸

Statistical Analysis

Each PCORnet site ran a statistical program that conducted descriptive and multivariable analyses using patient-level data that remained behind each health system's firewall. They returned aggregate results to the study data coordinating center. For multivariable models, pooled logistic regression models generated the parameter estimates, SEs, covariance matrices, convergence status, and number of observations. If models did not converge at sites, typically because of limited sample size, results were discarded; this was especially true for children's hospitals that had few patients in the data with the conditions of interest

Table 1. Demographic and Clinical Characteristics of Patients With COVID-19, Overall and by COVID-19 Outcomes, PCORnet, March 2020 to February 2022

Characteristic	All COVID-19		Hospitalization	Critical care	Mechanical ventilation	60-day mortality*
Number of unique patients	1 494 837	100%	188 188 (12.6%)	43 357 (2.9%)	22 346 (1.5%)	31 094 (2.1%)
Age group						
20–39y	607 239	41%	18%	12%	10%	3%
40–54y	388 201	26%	19%	19%	19%	10%
55–64y	230 500	15%	20%	22%	24%	17%
65–74y	153 868	10%	20%	24%	27%	26%
75–84y	81 232	5%	15%	16%	16%	26%
85+ y	33 797	2%	8%	7%	5%	19%
Sex†						
Female	835 254	56%	50%	42%	39%	42%
Male	659 026	44%	50%	58%	61%	58%
Hispanic ethnicity†						
Yes	249 445	17%	19%	16%	20%	16%
No	1 106 884	74%	76%	79%	73%	77%
Race†						
Asian	42 665	3%	3%	3%	3%	3%
Black	245 015	16%	23%	23%	23%	21%
White	942 985	63%	53%	57%	51%	56%
Pandemic phase						
March 1, 2020–April 30, 2020	59 836	4%	11%	12%	20%	19%
May 1, 2020–February 28, 2021	660 518	44%	41%	40%	39%	39%
March 1, 2021–Jun 30, 2021	89 500	6%	10%	9%	8%	7%
July 1, 2021–December 19, 2021	270 093	18%	20%	23%	21%	20%
December 20, 2021–February 28, 2022	414 890	28%	18%	17%	12%	15%
Hypertension						
No hypertension	857 014	57%	40%	35%	42%	32%
All hypertension‡	637 823	43%	61%	65%	58%	69%
Diabetes						
No diabetes	1 311 676	88%	69%	58%	57%	59%
All diabetes‡	183 161	12%	32%	41%	43%	42%
Other comorbidities§						
Combined Comorbidity Index score (mean)	1 494 837	1.1	3.4	4.7	4.8	5.2
Chronic pulmonary disorders	197 721	13%	25%	29%	28%	29%
Mental health disorders	187 948	13%	20%	21%	19%	20%
Anemia	141 639	9%	26%	33%	35%	34%
Arrhythmia	136 473	9%	29%	43%	45%	47%
Asthma	119 764	8%	12%	11%	11%	9%
Severe obesity (BMI ≥40 kg/m ²)	117 400	8%	16%	20%	21%	15%
Coronary artery disease	100 203	7%	22%	28%	26%	33%
Chronic kidney disease	91 538	6%	23%	29%	29%	35%
Cancer	69 582	5%	11%	12%	10%	17%
Congestive heart failure	73 737	5%	19%	27%	27%	31%
Pregnancy	70 442	5%	6%	1%	1%	0%

(Continued)

Table 1. Continued

Characteristic	All COVID-19	Hospitalization	Critical care	Mechanical ventilation	60-day mortality*
Smoking status					
Current smoker	72 359	5%	5%	5%	3%
Former smoker	146 896	10%	13%	16%	16%
Never smoker	506 885	34%	24%	29%	21%
Unknown or missing	768 697	51%	58%	51%	60%
COVID-19 treatments					
Dexamethasone	107 777	7%	40%	54%	52%
Monoclonal antibodies	34 682	2%	2%	2%	1%
Remdesivir	66 210	4%	29%	39%	38%
BMI					
<30 kg/m ²	426 797	29%	37%	41%	34%
≥30 kg/m ²	363 352	24%	34%	39%	38%
BMI missing [†]	704 688	47%	28%	20%	28%

*60-day mortality refers to in-hospital mortality.

[†]Missing and "Other" not shown.

[‡]All hypertension and diabetes included patients who did not have a documented blood pressure measurement or glycated hemoglobin, respectively, within 18 months before COVID-19, so control status could not be categorized.

[§]Comorbidities with prevalence ≥5% are displayed; other comorbidities with prevalence <5% included rheumatoid arthritis, systemic lupus erythematosus, seizures or epilepsy, alcohol use disorder, chronic obstructive pulmonary disease, cirrhosis, dementia, Down syndrome, end-stage renal disease, HIV, hemiplegia, inflammatory bowel disorder, multiple sclerosis, peripheral vascular disorders, Parkinson disease, pulmonary circulation disorders, chronic pulmonary disorders, sickle cell disease, or weight loss.

^{||}BMI was missing if patients did not have a recorded height and weight within 18 months of the index positive test.

BMI indicates body mass index; and PCORnet, National Patient-Centered Clinical Research Network.

(diabetes or hypertension) or with severe COVID-19 outcomes. For example, the highest number of sites that had convergence was 38 for hypertension models and 32 for diabetes models that were unadjusted with hospitalization as the outcome; for fully adjusted models with mechanical ventilation as the outcome, convergence was achieved only for 23 sites for hypertension and 21 sites for diabetes models. Results from sites that did converge were combined using meta-analytic techniques, with the random-effects model based on the DerSimonian and Laird method generating pooled estimates.¹⁹ Each COVID-19 outcome was tested in a separate model. Models generated crude (OR) and adjusted (aOR) odds ratios and 95% CIs using a type 1 error rate of 5% to determine statistical significance. Adjusted models included the following covariates: age in years, age squared, sex, race, ethnicity, obesity, Combined Comorbidity Index score, smoking status, receipt of dexamethasone, receipt of remdesivir, receipt of monoclonal antibodies, and pandemic phase.

RESULTS

Among 1 494 837 adults with COVID-19, 56% were female, and the median age was 46.7 years (SD=17.5; Table 1). The largest race groups were White (63%) and Black (16%); 17% were of Hispanic ethnicity (Table 1). Overall, 637 823 (43%) patients with COVID-19 had hypertension (among whom, n=518 293 had data

available to allow classification into hypertension control categories; Table 2), and 183 161 (12%) had diabetes (among whom, n=123 557 had data available to allow classification into diabetes control categories; Table 3).

Among all patients with COVID-19, 13% required hospitalization, 3% required critical care, 2% were mechanically ventilated, and 2% died within 60 days of the COVID-19 index date (Table 1). The most frequent COVID-19 treatment was dexamethasone (7%), followed by remdesivir (4%) and monoclonal antibodies (2%). Older age, male sex, Black race, COVID-19 illness early in the pandemic, and a greater number of comorbidities before COVID-19 illness were disproportionately represented among those with severe COVID-19 outcomes (hospitalization, critical care, mechanical ventilation, or 60-day mortality, Table 1).

Hypertension and Severe COVID-19 Outcomes

Among patients with COVID-19, severe COVID-19 outcomes were twice as frequent among those with hypertension compared with those without hypertension: 18% versus 9% for hospitalization, 4% versus 2% for critical care, 2% versus 1% for mechanical ventilation, and 3% versus 1% for 60-day mortality (Table 2). Of 518 293 (81%) patients whose hypertension control could be classified, 35% had BP <130/80, 37% had BP 130 to 139/80 to 89, 22% had BP 140 to 159/90 to 99, and 7% had BP ≥160/100. The

Table 2. Demographic and Clinical Characteristics of Patients With COVID-19, by Hypertension and Control Status, PCORnet, March 2020 to February 2022

	Hypertension		Blood pressure control category			
	No	Yes*	<130/80	130–139/80–89	140–159/90–99	≥160/100
Number	857 034	638 128	180 021	192 728	111 519	34 025
Mean age, y	41.1	54.1	52.8	51.1	55.6	58.5
Sex						
Female	55%	57%	64%	58%	53%	53%
Male	45%	43%	36%	42%	47%	47%
Hispanic ethnicity†						
Yes	19%	13%	13%	13%	12%	12%
No	67%	83%	85%	85%	85%	86%
Race‡						
Asian	3%	2%	2%	2%	2%	2%
Black	15%	19%	16%	17%	20%	26%
White	59%	68%	72%	71%	69%	62%
Combined Comorbidity Index score (mean)	0.4	2.0	2.4	1.6	2.0	2.5
Body mass index (mean)‡	24.9	28.0	27.0	28.6	29.0	27.5
COVID-19 outcomes						
Hospitalization	9%	18%	15%	11%	16%	22%
Critical care	2%	4%	4%	3%	4%	6%
Mechanical ventilation	1%	2%	2%	1%	2%	3%
60-d mortality‡	1%	3%	3%	2%	3%	4%

PCORnet indicates National Patient-Centered Clinical Research Network.

*Includes 119835 who met criteria for hypertension but could not be classified by control status (ie, did not have blood pressure measurement within 18 months before COVID-19). Blood pressure control categories shown in mmHg.

†Missing and “Other” not shown.

‡60-day mortality refers to in-hospital mortality.

frequency of hospitalization, critical care, mechanical ventilation, and 60-day mortality were lowest among patients with BP 130 to 139/80 to 89 (11% hospitalized, 3% critical care, 1% mechanically ventilated, 2% 60-day mortality), higher among those with BP 140 to 159/90 to 99 (16% hospitalized, 4% critical care, 2% mechanically ventilated, 3% 60-day mortality) and highest among patients with BP ≥160/100 (22% hospitalized, 6% critical care, 3% mechanically ventilated, 4% 60-day mortality). Those with the lowest BP (<130/80) were older, had higher Combined Comorbidity Index scores, and had slightly worse COVID-19 outcomes than those with BP 130 to 139/80 to 89.

In unadjusted analyses among patients with hypertension, the poorest BP control level was significantly associated with greater odds of hospitalization (OR, 1.48 [95% CI, 1.41–1.55] for BP ≥160/100 versus BP <130/80), critical care (OR:1.59 [95% CI, 1.48–1.71]), mechanical ventilation (OR, 1.63 [95% CI, 1.45–1.84]), and 60-day mortality (OR, 1.34 [95% CI, 1.22–1.47]) (Table S1). In adjusted analyses, associations remained statistically significant for BP ≥160/100 versus BP <130/80 for hospitalization (aOR, 1.30 [95% CI, 1.23–1.37]), critical care (aOR, 1.30 [95%

CI, 1.21–1.40]), and mechanical ventilation (aOR, 1.32 [95% CI, 1.17–1.50]), but not 60-day mortality (aOR, 1.08 [95% CI, 0.98–1.12]) (Figure 1 and Table S2). There was a less pronounced but statistically significant association for BP 140 to 159/90 to 99 versus BP <130/80 for hospitalization (aOR, 1.05 [95% CI, 1.00–1.09]), critical care (aOR, 1.13 [95% CI, 1.10–1.20]), and mechanical ventilation (aOR, 1.17 [95% CI, 1.06–1.29]). Among patients with hypertension, Black and Hispanic adults were more likely to be hospitalized, receive mechanical ventilation, or receive critical care, compared with White adults (Table S2). Other characteristics independently associated with more severe COVID-19 outcomes included higher comorbidity score, male sex, and COVID-19 illness during the earliest phase of the pandemic.

Diabetes and Severe COVID-19 Outcomes

Among patients with COVID-19, the frequency of severe COVID-19 outcomes was 3 to 7 times higher for those with diabetes than those without: 32% versus 10% for hospitalization, 10% versus 2% for critical care,

Table 3. Demographic and Clinical Characteristics of Patients With COVID-19, by Diabetes and Control Status, PCORnet, March 2020 to February 2022

	Diabetes		HbA1c control category		
	No	Yes*	<7%	7%–<9%	≥9%
Number	1 311 896	183 266	57 892	41 457	24 208
Mean age, y	44.9	59.5	60.4	61.5	55.0
Sex					
Female	56%	52%	54%	50%	49%
Male	43%	48%	46%	50%	51%
Hispanic ethnicity†					
Yes	16%	18%	15%	18%	26%
No	73%	78%	82%	79%	71%
Race‡					
Asian	3%	3%	3%	3%	2%
Black	15%	24%	24%	21%	29%
White	64%	58%	60%	61%	49%
Combined Comorbidity Index score (mean)	0.7	3.4	3.9	3.5	3.3
Body mass index (mean)‡	25.8	30.4	30.6	30.5	31.5
COVID-19 outcomes					
Hospitalization	10%	32%	28%	30%	37%
Critical care	2%	10%	9%	9%	11%
Mechanical ventilation	1%	5%	4%	5%	6%
60-d mortality‡	1%	7%	6%	7%	6%

PCORnet indicates National Patient-Centered Clinical Research Network.

*Includes 59 709 who met criteria for diabetes but could not be classified by control status (ie, did not have glycated hemoglobin measurement within 18 months before COVID-19).

†Missing and “Other” not shown.

‡60-day mortality refers to in-hospital mortality.

5% versus 1% for mechanical ventilation, and 7% versus 1% for 60-day mortality (Table 3). Among 123 557 (67%) adults with diabetes whose control status could be classified, 47% had HbA1c <7%, 34% had HbA1c 7% to <9%, and 20% had HbA1c ≥9%. The frequency of hospitalization, critical care, and mechanical ventilation was lowest among patients with HbA1c <7% (28% hospitalized, 9% critical care, 4% mechanically ventilated) and highest among patients with HbA1c ≥9% (37% hospitalized, 11% critical care, 6% mechanically ventilated). In-hospital 60-day mortality was similar among patients regardless of HbA1c level.

Among patients with diabetes, there was a graded association between higher HbA1c and more severe COVID-19 outcomes. In unadjusted analyses, higher HbA1c was significantly associated with greater odds of hospitalization (OR, 1.52 [95% CI, 1.40–1.64] for HbA1c ≥9% versus HbA1c <7%; OR, 1.10 [95% CI, 1.04–1.17] for HbA1c 7% to <9% versus <7%), critical care (OR, 1.51 [95% CI, 1.38–1.65] for HbA1c ≥9% versus HbA1c <7%, OR, 1.10 [95% CI, 1.02–1.19] for HbA1c 7%–<9% versus <7%), and mechanical ventilation (OR, 1.35 [95% CI, 1.22–1.48] HbA1c ≥9% versus HbA1c <7%; OR, 1.12 [95% CI, 1.01–1.23] for HbA1c 7% to <9% versus <7%) (Table S1). After adjustment, associations were

statistically significant for hospitalization (aOR, 1.61 [95% CI, 1.47–1.76] for HbA1c ≥9% versus HbA1c <7%; OR, 1.10 [95% CI, 1.05–1.16] for HbA1c 7% to <9% versus <7%), critical care (aOR, 1.42 [95% CI, 1.31–1.54] for HbA1c ≥9% versus HbA1c <7%; OR, 1.08 [95% CI, 1.00–1.16] for HbA1c 7% to <9% versus <7%), mechanical ventilation (aOR, 1.12 [95% CI, 1.02–1.23] for HbA1c ≥9% versus HbA1c <7%; not significant for HbA1c 7% to <9% versus <7%), and 60-day mortality (aOR, 1.18 [95% CI, 1.09–1.27] for HbA1c ≥9% versus HbA1c <7%; OR, 1.07 [95% CI, 1.01–1.15] for HbA1c 7% to <9% versus <7%) (Figure 2 and Table S3). Among adults with diabetes, Black adults were more likely to be hospitalized than White adults, and Hispanic adults were more likely to be hospitalized, receive critical care, and receive mechanical ventilation than White adults (Table S3). Higher comorbidity score, male sex, and COVID-19 illness during the earliest phase of the pandemic were also associated with more severe COVID-19 outcomes.

DISCUSSION

In a large-scale, multisite study of nearly 1.5 million US adults, we observed that poor control of hypertension

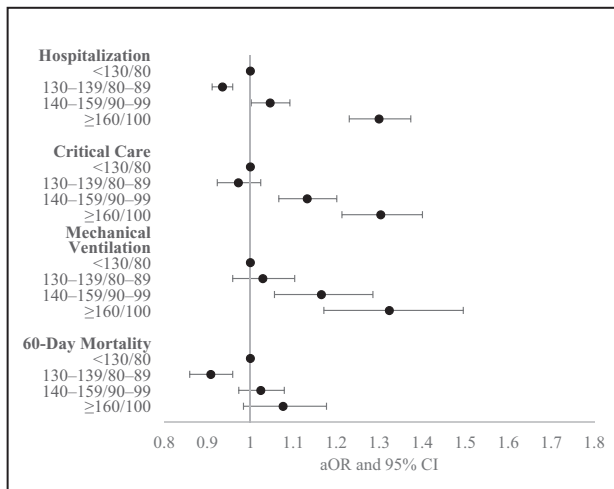


Figure 1. Adjusted odds ratios for COVID-19 outcomes by hypertension control status, PCORnet, March 2020 to February 2022.

This figure shows adjusted odds ratios for inpatient hospitalization, critical care use, mechanical ventilation, and 60-day in-hospital mortality by strata of blood pressure control, with blood pressure <130/80 mmHg as the referent category. Models controlled for age in years, age squared, sex, race, ethnicity, obesity, Combined Comorbidity Index score, smoking status, COVID-19 treatments (receipt of dexamethasone, receipt of remdesivir, receipt of monoclonal antibodies), and pandemic phase. This analysis was limited to patients with hypertension whose blood pressure control status could be categorized ($n=518293$ overall; model sample sizes varied depending on participating PCORnet sites). The number of sites that had model convergence was 32, 24, 23, and 29 for each of the outcomes, respectively. aOR indicates adjusted odds ratio; PCORnet, National Patient-Centered Clinical Research Network.

and diabetes was associated with greater odds of severe COVID-19 outcomes. In adjusted models of adults with hypertension, those with least controlled BP levels had approximately 30% greater odds of hospitalization, 30% greater odds of critical care, and 32% greater odds of mechanical ventilation compared with those with the most controlled BP level. Among adults with diabetes, those with the least controlled HbA1c level had approximately 61% greater odds of hospitalization, 42% greater odds of critical care, 12% greater odds of mechanical ventilation, and 18% greater odds of 60-day mortality compared with those with the most controlled HbA1c level. Overall, findings from this study address a research gap regarding the independent associations of BP and HbA1c control with COVID-19 severity, identifying those with least control as subpopulations at greatest risk for severe COVID-19 outcomes. Strengths of our study include the large population size across a broad geographic area, study period encompassing multiple pandemic phases, ability to assess BP and HbA1c before SARS-CoV-2 infection rather than upon hospital admission, and adjustment for differences in demographic and clinical characteristics

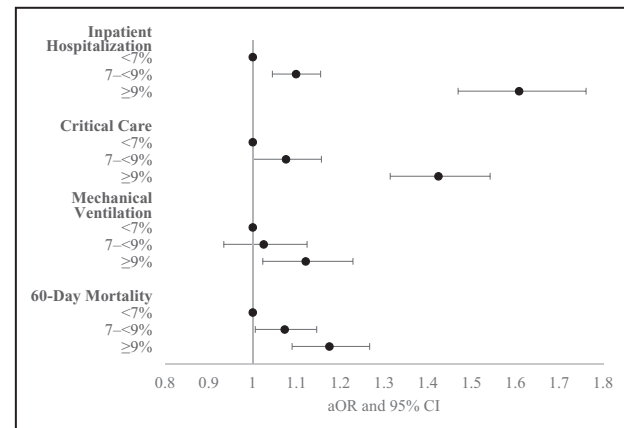


Figure 2. Adjusted odds ratios for COVID-19 outcomes by diabetes control status, PCORnet, March 2020 to February 2022.

This figure shows adjusted odds ratios for inpatient hospitalization, mechanical ventilation, critical care use, and 60-day in-hospital mortality by strata of HbA1c control, with HbA1c <7% as the referent category. Models controlled for age in years, age squared, sex, race, ethnicity, obesity, Combined Comorbidity Index score, smoking status, COVID-19 treatments (receipt of dexamethasone, receipt of remdesivir, receipt of monoclonal antibodies), and pandemic phase. This analysis was limited to patients with diabetes whose HbA1c control status could be categorized ($n=123557$ overall; model sample sizes varied depending on participating PCORnet sites). The number of sites that had model convergence was 29, 22, 21, and 26 for each of the outcomes, respectively. aOR indicates adjusted odds ratio; HbA1c, glycated hemoglobin; PCORnet, the National Patient-Centered Clinical Research Network.

among adults across BP and HbA1c control levels during a large proportion of the pandemic.

An important contribution of this study is that it clarifies the independent association between hypertension and severe COVID-19 outcomes, which some studies have suggested might be driven by age or other comorbidities.^{20,21} These results add to an emerging body of research that has presented conflicting findings. One study of 12548 patients with hypertension and COVID-19 in the Kaiser Permanente system in Southern California found that uncontrolled BP (>130/80) was not associated with hospitalization or mortality.²² Our study included a much larger population and more refined strata of baseline BP and observed stronger associations between hypertension control and hospitalization, mechanical ventilation, and critical care in the highest stratum (BP ≥160/100). Our findings were consistent with 2 studies from Wuhan, China. One of these assessed 803 hospitalized patients with hypertension and COVID-19 and found that higher systolic and diastolic BP were associated with adverse outcomes including intensive care unit admission and mortality.²³ The other, which consisted of 2864 hospitalized patients, also found that worse BP control was associated with worse COVID-19 outcomes.²⁴ An

important difference between our study and these 2 was our use of baseline, pre-COVID-19 measures of BP instead of in-hospital BP assessment, during which SARS-CoV-2 infection itself and the hospital environment might have influenced BP levels.²⁵

One proposed mechanism by which hypertension could exacerbate COVID-19 risk is through elevated immunological activity and inflammation.²⁶ The relationship between uncontrolled hypertension and severe COVID-19 outcomes is especially concerning given the high prevalence of uncontrolled hypertension in the United States² and increases in mean systolic and diastolic BP during the COVID-19 pandemic.²⁷ Such population-level increases in BP might be related to increased alcohol consumption and stress or decreased physical activity and access to medical care.^{4,27,28} To improve hypertension management, some clinical practices have made concerted efforts to increase use of telehealth services and support for self-measured BP monitoring.^{29,30}

Counterintuitively, severe COVID-19 outcomes were less frequent among adults with hypertension who had BP 130 to 139/80 to 89 compared with the lowest BP level of <130/80. Prior research has shown that adults with hypertension and lower BP tend to be older, with more comorbidities, and with a longer history of hypertension.^{31,32} Adults with hypertension in our study with BP <130/80 were older than those with BP 130 to 139/80 to 89; however, worse COVID-19 outcomes among those with BP <130/80 persisted in adjusted regression models that controlled for age and comorbidity score. Such findings suggest the possibility of residual confounding by factors we could not capture or a potential association between low BP or hypotension (which would have been grouped with BP <130/80) and frailty as well as severe COVID-19 outcomes.^{33–35}

Severe COVID-19 outcomes were 3 to 7 times higher for those with diabetes compared with those without, and adjusted models demonstrated a stepped association between higher HbA1c levels and more severe COVID-19 outcomes. Our findings are consistent with prior studies that have found associations of higher HbA1c with COVID-19 severity and mortality.^{11,12,36} As with hypertension, proposed mechanisms of increased risk of severe COVID-19 from diabetes include chronic inflammation and dysregulated immune function.¹² Also potentially related to inflammation or autoimmunity, emerging evidence suggests that COVID-19 might increase diabetes incidence and hyperglycemia, indicating a bidirectional relationship.^{37,38} Potentially exacerbating risk, HbA1c levels might have increased during the pandemic for some patients^{5,39} due to less screening and monitoring and to behavior changes related to the pandemic.⁴⁰ Among young and middle-aged adults with diabetes, a majority reported delaying medical care due to COVID-19 concerns (63%–87%),

and many reported difficulty accessing medications (26%–44%).⁴¹ Technologies such as telehealth and home monitoring of blood glucose might help support diabetes management, especially in the context of health care disruption due to the pandemic.³⁹

In addition to hypertension and diabetes, other factors observed to be independently associated with more severe COVID-19 outcomes were consistent with prior studies. Higher Combined Comorbidity Index scores, indicating more comorbidities, were associated with greater odds of severe COVID-19 outcomes. In prior studies, multiple comorbidities have been associated with COVID-19 risk, including obesity, chronic liver disease, chronic kidney disease, chronic neurologic disease, chronic pulmonary disease, diabetes, and heart disease.^{42,43} We also observed greater odds of severe COVID-19 outcomes among male adults⁴² and adults whose COVID-19 index event was in the earliest phase of the pandemic (March 1 through April 30, 2020), as other research has shown.⁴⁴ Black adults and Hispanic adults were more likely to experience severe COVID-19 outcomes, which is consistent with prior studies demonstrating disparities in COVID-19 risk.^{42,45,46} These effects were independent of comorbidity score and control of hypertension or diabetes. It should be noted that race is not a biological construct, and observed disparities could be driven by differences in social determinants of health,¹ health care access, other societal and health system inequities, or residual confounding by other underlying health conditions.^{45–47} At a population level, potential effects of poor hypertension and diabetes control on COVID-19 outcomes could disproportionately affect Black and Hispanic adults, given longstanding disparities in chronic disease management¹ and potential exacerbation of these disparities during the pandemic due to factors such as reduced access to telehealth, internet access, and other technological supports for chronic disease management.⁴⁸

This study had several limitations. First, patients in this study might not be generalizable to the US population; most of the institutions included were tertiary care academic medical centers in urban settings. In addition, many patients with COVID-19 were not captured in our data set, particularly those who tested in community settings, tested using at-home kits, or did not test at all. This likely biases our study toward inclusion of patients at higher risk for more severe COVID-19, which does not affect internal validity but might limit generalizability. However, if patients at higher risk for more severe COVID-19 were also more likely to have poorly controlled hypertension or diabetes, then collider bias could have influenced our findings. Second, some patients' hypertension or diabetes control status could not be classified because they did not have a BP or HbA1c within 18 months before the COVID-19 index date. Missing

data could bias results if there was differential missingness by BP and HbA1c level. Third, patient hypertension or diabetes control status could have been misclassified if BP or HbA1c measures changed from between the date of assessment and the COVID-19 index date or if the patient experienced transient high BP levels in health care settings (ie, the “white coat hypertension” phenomenon). Fourth, we cannot causally attribute the patient’s hospitalization, critical care, mechanical ventilation, or death to their laboratory-confirmed SARS-CoV-2 infection; it is possible that some patients were hospitalized, treated, or died for reasons independent of their SARS-CoV-2 infection. Fifth, not all sites were included in final models; if a model did not converge for a particular DataMart (typically because of small sample sizes or small number of events among patients at those sites, especially at children’s hospitals that had few patients aged 20 years and older), those data were discarded rather than pooled. Sixth, we did not distinguish between type 1 and type 2 diabetes, which might have differential relationships with COVID-19 outcomes and warrant further study. Finally, residual confounding might have occurred due to factors such as body mass index (which was missing in nearly half of patients, although we included both obesity status and an indicator for missing body mass index in our models) or unmeasured factors. We were unable to adjust for COVID-19 vaccination status due to poor capture of COVID-19 vaccination status in electronic health records for vaccinations that were delivered outside of health systems. Future studies could confirm our findings in different electronic health record data systems and patient populations, could explore multivariable models comparing the nonhypertension (and nondiabetes) groups against various levels of chronic disease control, and could examine robustness of results across additional stratifications, such as by age, by pre- and postvaccination eras, by pre- and post-in-home-testing eras, and by additional categories of BP control (such as systolic BP 110–130).

CONCLUSIONS

In conclusion, this multisite study of nearly 1.5 million US adults demonstrated worse COVID-19 severity among patients with poorly controlled hypertension and diabetes. These results have important implications for clinical and public health practice, especially given existing disparities in chronic disease control and the role such disparities might play in exacerbating observed disparities in COVID-19 outcomes. Clinicians and public health professionals can encourage adults with poorly controlled hypertension or diabetes to adhere to COVID-19 vaccination recommendations and encourage these patients to seek early treatment for COVID-19 to prevent

progression to severe disease.^{14,49} Additionally, results underscore the importance of ongoing chronic disease management during a pandemic, including through out-of-office services, such as telehealth, and strategies such as disease self-management education and support, as well as self-measured BP monitoring and home blood glucose measurements with clinical support.^{30,50} Ongoing efforts to adapt care delivery to the changing needs of the population during the pandemic could potentially improve population health and COVID-19 outcomes or outcomes from other infectious diseases. Finally, improved capture of data related to COVID-19 care, particularly vaccination status, would help to mitigate the limitations cited as well as improve the reliability of research findings.

APPENDIX

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Supplemental Material

Tables S1–S3

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