The impact of race/ethnicity on the clinical outcomes of people with type 2 diabetes admitted to hospital with COVID-19: an observational multi-national analysis

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Abstract

Aims: To describe the relationship between race/ethnicity and adverse outcomes related to coronavirus disease 2019 (COVID-19) in adults with T2DM admitted to hospital in the UK, France and USA.

Methods: Study data from the UK ABCD nationwide COVID-19 audit, the French CORONADO nationwide initiative and the USA AMERICADO multi-centre study were analysed to assess the association between race/ethnicity and severe COVID-19. Severe COVID-19 was defined as death in hospital and/or admission to the intensive care unit (ICU). Logistic regression models were used to generate age-adjusted odds ratios.

Results: Data from 3,471 patients in the ABCD audit, from 2,451 CORONADO patients and from 9,321 AMERICADO patients admitted with COVID-19 and T2DM were analysed. Race/ethnicity data were available for 3,410 (98%), 2,173 (89%) and 8,893 (95%) patients, respectively. In the UK ABCD audit cohort, Asian and Black race/ethnicity were associated with an increased risk of death/ICU admission compared to White when adjusted for age and sex (OR 2.14; 1.38-3.29 and OR 2.09; 1.17-3.74, respectively). When adjusted for additional confounders the association was stronger (Asian OR 2.88; 1.72-4.82 and Black OR 2.20; 1.12-4.30). In the CORONADO cohort Middle Eastern/North African race/ethnicity was protective against death/ICU admission (OR 0.57; 0.36-0.91).

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There was no association between ethnicity and death alone in the AMERICADO dataset.

Conclusion: **In those with T2DM admitted to hospital with COVID-19, a non-White race/ethnicity was associated with higher risk of death/ICU admission in the UK ABCD data but not in French CORONADO or USA AMERICADO datasets. Further research is required to improve our understanding of the observed discrepancies in outcomes.**

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Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that may cause coronavirus disease 2019 (COVID-19) has claimed almost 7 million lives globally.[1] There have been a number of publications on the epidemiology of COVID-19, including risk factors and clinical presentation. These studies have consistently shown that a number of chronic conditions, including diabetes, cardiovascular disease, chronic kidney disease (CKD) and respiratory diseases, are key risk factors for severe COVID-19 including intensive care unit (ICU) admission and death.[2] In addition, very early in the pandemic, data from the United Kingdom (UK) and United States (US) reported a disproportionate COVID-19 impact in ethnic/racial populations, including hospitalisation and mortality.[3,4] These disparities also included historically minoritised ethnic/racial populations with chronic diseases including diabetes.

The reasons for the higher incidence and severity of COVID-19-related outcomes in ethnic/racial groups are not yet fully understood but may include differences in co-morbid conditions (e.g. diabetes), socioeconomic disparities and differences in exposure to risk such as living in multigenerational or overcrowded housing and essential worker roles.[5] The first reports of these disparities were from the UK in South Asian and Black populations;[5] subsequently, reports emerged from the US of a disproportionate impact of COVID-19 in Black and Hispanic populations.[6] A number of studies have been published during the pandemic on the impact of COVID-19 in ethnic minority populations. These include a systematic review of 50 studies covering 18,728,893 people. It reported increased risk of COVID-19 infection for individuals of Black (RR 2.02; 1.67-2.44) and Asian (RR 1.50; 1.24–1.83) race/ethnicity compared to White individuals, with Asians being at a higher risk of intensive care unit admission (RR 1.97; 1.34–2.89) and death (RR 1.22; 0.99–1.50), compared to White individuals.[7]

Despite this and other publications, our knowledge about the impact of COVID-19 in ethnic minority populations with diabetes is limited. Uncertainties arise from differences in definitions, small study sizes, use of retrospective databases and limited populations (mainly from the US and UK). The largest study used a national population database in England and included 264,390 people with type 1 diabetes (T1DM) and 2,874,720 people with type 2 diabetes (T2DM).[8] In people with T1DM, South Asian (HR 1.57; 1.16-2.12), Black (HR 1.77; 1.25-2.49), Mixed (HR 1.77; 1.25-2.49) and Other ethnic groups (HR 1.89; 1.03-2.37) had significantly higher mortality risk from COVID-19 compared to White populations.[8] For people with T2DM, the risk of in-hospital mortality was greater for Asian (HR 1.08, 95% CI 1.01-1.15), Black (HR 1.63; 1.51-1.77) and Mixed ethnic groups (HR 1.30; 1.10-1.55).[8] However, a multi-centre study of 4,413 COVID-19 patients with T2DM reported no significant association between race/ethnicity and mortality.[9]

In view of these inconsistent findings, we sought to determine whether race/ethnicity influences the risk of COVID-19 related death and/or ICU admission across three countries (UK, France, USA).

Research design and methods

ABCD COVID-19 audit

The methodology for the Association of British Clinical Diabetologists (ABCD) national diabetes and COVID-19 audit has been described in detail.[10] Contributors were asked to collate data from patient records and to transfer the data in anonymized form to the NIHR Health Informatics Collaborative Coordinating Centre within the Oxford University Hospitals NHS Foundation Trust (OUH). Data collection included admissions between March and October 2020. Data were transferred securely using the National Health Service (NHS) network. The UK audit was registered with the OUH and a Data Protection Impact Assessment was carried out and reviewed by the OUH Caldicott Guardian and the Public Benefit and Privacy Panel in Scotland (reference 2021-0111). The NHS supports audit with clear guidance for the contributing centres on the use of routine clinical practice data submitted in anonymized form via the secure NHS network. As the audit was retrospective, and comprised routinely collected healthcare data only, there was no requirement for approval by a research ethics committee.

CORONADO study

The aim of the CORONADO study was to describe the phenotypic characteristics and prognosis of people with diabetes admitted with COVID-19. The initiative has been described previously.[11,12] CORONADO is a retrospective study of people with diabetes who were admitted with COVID-19 to one of 68 French hospitals between March 10th and April 10th, 2020. The study was sponsored by Nantes University Hospital and designed in accordance with the Declaration of Helsinki. It obtained all required regulatory approvals.

AMERICADO study

The AMERICADO (American Corona Analysis/Diabetes Outcomes) study participants were previously reported.[9] This study included people with T2DM and COVID-19 in 13 out of 27 Northwell Health System hospitals in the New York area. Inclusion dates ranged from January 1st to May 31st, 2020.

Study outcomes

For all participants (ABCD COVID-19 Audit, CORONADO and AMERICADO) the follow-up period ended at the point of death in hospital or discharge from hospital within 28 days of admission. The primary outcome was death or admission to the intensive care unit (ICU) for the ABCD COVID-19 audit and the CORONADO study and death alone for the AMERICADO study.

Definition of race/ethnicity

In the ABCD UK COVID-19 audit, race/ethnicity was categorised as White European, Asian, Black/Afro-Caribbean or Other, extracted from hospital records. In the CORONADO study race/ethnicity categories were Europid, Asian, Middle East and North Africa (MENA) or Afro-Caribbean according to the team involved in the patient's care or extracted from medical files, and if missing extracted from the patient's general practitioner. In the AMERICADO study categories were White, Asian, Black or Other, extracted from the electronic medical records. For consistency and due to small numbers, American Indian, Alaska Native, Native Hawaiian and Other Pacific Islander were grouped in the Other category. It should be noted that in the US race is categorized as White, Black or African American, American Indian or Alaska Native, Asian, and Native Hawaiian or Other Pacific Islander, while ethnicity is Hispanic/Latino and Non-Hispanic/Latino. For the purposes of this paper, US-based race categories will be referred to as race/ethnicity for consistency across countries.

Statistical analysis

Baseline clinical characteristics are reported as frequency and percentages for categorical variables, and as mean and standard deviation for continuous variables. Patient characteristics were compared using traditional statistical tests (ANOVA, Kruskal-Wallis test or c^2 test). Univariate logistic regression was used to assess the association between race/ethnicity and death/ICU. Odds ratio (OR) and 95% confidence intervals (95% CI) were calculated for each study population. The multivariate model was then adjusted for age, sex, admission glucose, creatinine, pre-COVID-19 characteristics and co-morbidities. Statistical analyses were performed with SAS version 9.4 (SAS Institute, Cary, NC), R statistical software version 4.1.0 in the US, version 4.0.3 in France and 3.6.3 version 3.3 in UK, GraphPad Prism software version 8.0 (La Jolla, CA) and RevMan software (Version 5.4. The Cochrane Collaboration). P values < 0.05 were considered statistically significant.

Results

Study population

Ethnicity, age and sex data were available for 3,410 of the 3,741 people in the ABCD COVID-19 audit, for 2,173 of 2,514 people in CORONADO and 8,993 of 9,321 people in the AMERICADO study. Of those with complete data, the proportions of people of White, Asian and Black race/ethnicity, respectively, were 79%, 12% and 6% in the ABCD COVID-19 audit population; 57%, 3% and 17% in the CORONADO study population; and 38%, 12% and 23% in the AMERICADO population. MENA ethnicity accounted for 22% of the CORONADO population and Other for 27% of the AMERICADO population.

Demographic and clinical characteristics

Forty five UK NHS centres submitted data to the ABCD COVID-19 diabetes national audit for 3,741 inpatients with T2DM who were hospitalised between March and October 2020. Of these 920 had a complete dataset, including the primary outcome (discharged or died or admitted to ICU). In France 68 centres submitted data for 2,173 inpatients, of whom 611 had full data; and in the USA 13 centres submitted data for 9,321 inpatients, of whom 5,246 had a full data set.

Table 1 summarises the clinical characteristics of the study population with a full data set, according to country. There was a slightly higher proportion of men in the data from all three countries. The UK ABCD cohort were slightly older (mean[SD] age 73(13) years vs 70(12) years in CORONADO and 67(14) years in AMERICADO). Mean(SD) BMI was 29(7) kg/m² in UK ABCD, 30(6) in CORONADO and 30(12) in AMERICADO. The mean(SD) latest available HbA_{1c} was 7.9 (4.1)%, 63(21) mmol/mol in the UK ABCD; 8.1 (4.0)%, 65(20) in CORONADO; and 8.0 (4.0)%, 64(20) in AMERICADO. The prevalence of microvascular complications (any reported diabetic nephropathy, foot ulcer, retinopathy, peripheral neuropathy) was highest in UK ABCD (51%), then CORONADO (43%), with a lower proportion in AMERICADO (21%). Macrovascular disease (any reported peripheral vascular disease, ischaemic heart disease, cerebrovascular disease) was reported among 54% of patients in UK ABCD, 38% in CORONADO and 37% in AMERICADO. The most common glucose-lowering treatment was metformin (50% in UK ABCD cohort, 62% in CORONADO), followed by insulin (37% in UK ABCD, 45% in CORONADO). Treatment data were not available for the AMERICADO cohort. Those from a White/Europid background were older (70-75 years vs 62-69 years) while those from a Black/Afro-Caribbean background were more likely to present with diabetic ketoacidosis (4-17% vs 2-3%). Appendix 1 (found online at www.bjd-abcd.com) summaries the clinical characteristics, stratified by country and data completeness.

Table 2 presents the age-adjusted odds ratio and 95% confidence intervals for death and/or ICU admission for different clinical variables. No variable was consistently associated with the outcome of death/ICU admission across all three countries. In the AMERICADO dataset, male sex, DKA on admission, admission plasma glucose level, smoking, HbA_{1c} above 75mmol/mol, micro- and macrovascular disease, dementia and COPD were associated with death/ICU. In the UK ABCD audit data Asian and Black race/ethnicity, COPD and malignant neoplasm were associated with death/ICU. The CORONADO data showed a positive association with death/ICU admission for male sex, admission plasma glucose level and hypertension.

Table 3 presents the multivariable models which describe the association between race/ethnicity and death/ICU for each country. In the UK ABCD audit cohort, Non-White race/ethnicity was associated with an increased risk of death/ICU compared to White (OR 1.89; 1.35-2.65) when adjusted for age and sex. When adjusted for additional confounders, including admission plasma glucose, creatinine, pre-COVID characteristics, co-morbidities and treatments, the association persisted and became stronger (OR 2.22; 1.49-3.30). More specifically, Asian and Black race/ethnicity were associated with an increased risk of death/admission to ICU compared to White race/ethnicity when adjusted for age and sex (OR 2.14; 1.38-3.29 and OR 2.09; 1.17-3.74, respectively). When adjusted for additional confounders including admission plasma glucose, creatinine, pre-COVID characteristics, co-morbidities and treatments, the associa-

Table 1 Clinical characteristics of the T2DM population with complete data by ethnic group.

	AMERICADO				ABCD				CORONADO			
	White (N=1999)	Asian (N=605)	Black (N=1215)	Other (N=1427)	White (N=719)	SA (N=109)	Black (N=54)	Other (N=38)	Afro-Caribbean (N=105)	MENA (N=136)	Asian (N=21)	Europid (N=349)
Sex M/total (%)	1244 (62%)	380 (63%)	611 (50%)	851 (59%)	464 (64%)	73 (67%)	39 (72%)	20 (53%)	70 (67%)	88 (65%)	11 (52%)	207 (59%)
Age years (SD)	69.9 (13)	65 (13)	65 (14)	64 (14)	75 (12)	64 (15)	69 (16)	68 (15)	62(10)	68(12)	67(17)	73(12)
Admission features												
DKA on admission	66 (3%)	7 (1.2%)	49 (4%)	49 (4%)	15 (2%)	3 (3%)	9 (17%)	1 (3%)	11 (11%)	6 (4%)	0 (0%)	9 (3%)
Admission glucose (mmol/l) (SD)	11.0 (6.3)	11.2 (5.3)	13.1 (9.3)	11.7 (6.4)	10.4 (5.9)	11.1 (6.0)	15.8 (11.7)	11.7 (5.4)	11.6 (6.6)	10.6 (5.1)	12.0 (8.6)	10.1 (5.0)
Creatinine (µmol/l)	142 (125)	133 (151)	199 (235)	147 (205)	120 (62)	111 (64)	129 (70)	113 (67)	144 (126)	141 (161)	128 (144)	122 (123)
Pre-COVID characteristics												
Smoker	511 (25.5%)	33 (6%)	170 (14%)	142 (10%)	59 (8%)	6 (6%)	4 (7%)	6 (16%)	4 (4%)	10 (7%)	0 (0%)	19 (5%)
BMI (kg/m^2)	31.1 (9.1)	28.0 (10.7)	31.3 (10.0)	30.1 (14.8)	29.7 (7.5)	28.5 (6.7)	29.3 (7.1)	28.7 (5.8)	28 (4.6)	29.3 (5.5)	26.2 (5.2)	30.2 (5.7)
HbA_{1c} (%)	7.6 (6.4, 8.5)	8.0 (6.8,8.7)	8.4 (6.7,9.7)	8.3 (6.7, 9.3)	7.8 (4.1)	8.0 (4.2)	8.8 (5.0)	7.6 (4.0)	8.7 (4.6)	8.1 (3.9)	8.4 (4.3)	7.8 (3.7)
HbA_{1c} (mmol/mol)	60 (46, 69)	64 (51, 72)	68 (50, 83)	67 (50, 78)	62 (21)	64 (22)	73 (31)	60 (20)	72 (27)	65 (19)	68 (24)	62 (17)
Microvascular disease*	492 (25%)	87 (5%)	302 (25%)	238 (8%)	373 (52%)	49 (45%)	32 (59%)	19 (50%)	37 (35%)	59 (43%)	8 (38%)	158 (45%)
Macrovascular disease**	890 (44.5%)	212 (35%)	420 (35%)	421 (30%)	404 (56%)	42 (39%)	27 (50%)	19 (50%)	22 (21%)	50 (37%)	10 (48%)	152 (44%)
Comorbidities												
Hypertension	1647 (83%)	514 (85%)	1071 (88%)	1124 (79%)	472 (66%)	82 (75%)	40 (74%)	26 (68%)	83 (79%)	106 (78%)	15 (71%)	295 (85%)
Dementia	205 (10%)	31 (5%)	88 (7%)	78 (6%)	111 (15%)	7 (6%)	5 (9%)	10 (26%)	0 (0%)	1 (1%)	2 (10%)	1 (0%)
Asthma	198 (10%)	70 (12%)	147 (12%)	153 (11%)	80 (11%)	26 (24%)	7 (13%)	3 (8%)	3 (3%)	4 (3%)	0 (0%)	11 (3%)
COPD	300 (15%)	31 (5%)	114 (9%)	96 (6.8%)	153 (21%)	6 (6%)	5 (9%)	5 (13%)	3 (3%)	20 (15%)	3 (14%)	40 (12%)
Malignant neoplasm	297 (15%)	46 (8%)	113 (9%)	101 (7%)	134 (19%)	10 (9%)	8 (15%)	3 (8%)	7 (7%)	13 (10%)	0 (0%)	39 (11%)
Outcomes												
Death	409 (21%)	112 (19%)	233 (19%)	244 (17%)	294 (42%)	49 (46%)	25 (46%)	11 (31%)	8 (8%)	21 (15%)	4 (19%)	62 (18%)
Death/ICU	N/A	N/A	N/A	N/A	323 (45%)	62 (57%)	32 (59%)	17 (45%)	43 (41%)	40 (29%)	8 (38%)	132 (38%)

*Microvascular disease includes diabetic nephropathy, foot ulcer, retinopathy and peripheral neuropathy. **Macrovascular disease includes peripheral vascular disease, ischaemic heart disease and cerebrovascular disease.

tion persisted and became stronger (Asian OR 2.88; 1.72-4.82 and Black OR 2.20; 1.12-4.30). In contrast, in the CORONADO cohort a MENA race/ethnicity was protective against the risk of death/ICU admission compared to Europid race/ethnicity when adjusted for age and sex (OR 0.64; 0.41-0.99) and other confounders (OR 0.57; 0.36-0.91). There was no statistically significant association between race/ethnicity and death in the AMERICADO dataset (Non-white vs White OR 0.95; 0.82-1.09; Asian vs White OR 1.04; 0.82-1.33; Black vs White OR 1.14; 0.94-1.37).

Discussion

This analysis provides insight into the relationship between race/ethnicity and COVID-19 outcomes in a large cohort of people with T2DM across three different countries. In the UK population, the odds ratio for death/ICU admission for people of non-White race/ethnicity was approximately double that of people of White ethnicity after adjustment for confounders. This contrasts with data from CORONADO and AMERICADO in which this relationship was not observed. Those of a MENA background in the CORONADO study had a lower risk of death/ICU compared to those of an Europid, Asian and Afro-Caribbean background.

There are many reasons why a relationship between race/ethnicity and adverse outcomes from COVID-19 might be different between populations. The data presented are from a subset of those admitted to hospital with T2DM and COVID-19, and these patients may not have been representative of the national populations. For instance, the proportion of people with complete data was lower for the subset of patients of minority ethnic background than for the entire dataset in the UK ABCD cohort. Furthermore, those with complete data had a significantly greater likelihood of death and/or ICU admission than the whole cohort; the opposite was true for the CORONADO and AMERICADO datasets. However, the UK ABCD audit data are consistent with the National Diabetes Audit data from England and Wales which, from just under 3 million people hospitalised with T2DM, identified an increased risk of mortality in those from Asian, Black or Mixed ethnic groups.[8] This fits with the national picture across the whole UK population regardless of diabetes status. Analyses of data from 17 million adults in England demonstrated higher ICU admission and mortality risk in those of a South Asian, Black and Mixed ethnic group compared to people of White race/ethnicity.[13] The disparity in health outcomes between ethnicity groups in the UK is a source of national concern and efforts to understand it are underway. A report by Public Health England identified that COVID-19 mortality risk for those of Bangladeshi ethnicity was twice that of people with White

Table 2 Age-adjusted odds ratios with 95% confidence intervals of death and/or ICU admission for different clinical variables after adjustment in sub-set with complete data.

	AMERICADO		ABCD		CORONADO	
Clinical features	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Men vs women	1.65 (1.43, 1.92)	**<.001**	1.24 (0.94-1.62)	0.13	1.50 (1.06-2.13)	**0.021**
Race/ethnicity (vs White)	Asian 1.04 (0.82, 1.31)	0.85	Asian 2.14 (1.39-3.30)	**<0.001**	Asian 0.96 (0.38-2.39)	0.925
	Black 1.06 (0.88, 1.28)	0.53	Black 2.12 (1.19-3.78)	**0.01**	Afro-Caribbean 1.03 (0.64-1.65)	0.918
	Other 0.98 (0.81, 1.17)	0.80	Other 1.16 (0.60-2.27)	0.66	MENA 0.65 (0.42-1.01)	0.053
Admission features						
DKA on admission vs not	1.89 (1.30, 2.74)	**<0.001**	1.35 (0.63-2.89)	0.45	1.72 (0.78-3.80)	0.177
Admission blood glucose (mmol/L)	1.43 (1.23, 1.65)	**<0.001**	1.16 (0.89-1.51)	0.27	1.71 (1.22-2.39)	**0.002**
Above vs equal or below the median (>= 8.9)	>=1.21 (ref)	**<0.001**	74-107 (ref)		74-107 1 (ref)	
Creatinine (μmol/L)	2.52 (2.04, 3.10)		Creatinine <74 0.79 (0.54-1.16)	0.23	<74 0.92 (0.59-1.42)	0.697
			Creatinine >107 1.64 (1.20-2.24)	**0.002**	<107 1.75 (1.16-2.62)	**0.007**
Pre-COVID characteristics						
Smoker	1.21 (1.01, 1.45)	**0.04**	1.20 (0.75-1.93)	0.45	1.14 (0.55-2.34)	0.725
BMI (kg/m^2)	1.00 (0.99. 1.01)	0.88	0.99 (0.97-1.01)	0.06	1.01 (0.98-1.04)	0.501
HbA_{1c} (>=9%, 75mmol/mol)	1.24 (1.05, 1.46)	**0.01**	0.99 (0.99-1.00)	0.11	1.00 (0.99-1.00)	0.355
Microvascular disease*	1.25 (1.06, 1.47)	**0.01**	1.09 (0.84-1.42)	0.51	1.14 (0.80-1.63)	0.478
Macrovascular disease**	1.19 [1.03, 1.37)	**0.02**	1.12 (0.85-1.46)	0.43	1.05 (0.74-1.49)	0.799
Co-morbidities						
Hypertension	1.08 (0.88, 1.33)	0.47	0.95 (0.72-1.26)	0.72	1.74 (1.10-2.75)	0.019
Dementia	0.64 (0.49, 0.84)	**0.001**	0.72 (0.49-1.06)	0.10	1.98 (0.27-14.3)	0.500
Asthma	0.86 (0.68, 1.10)	0.23	1.03 (0.70-1.53)	0.87	0.86 (0.32-2.32)	0.760
COPD	1.29 (1.05, 1.60)	**0.02**	1.80 (1.27-2.54)	**0.001**	1.19 (0.70-2.02)	0.517
Malignant neoplasm	0.82 (0.65, 1.03)	0.08	1.49 (1.05-2.12)	**0.03**	0.71 (0.39-1.30)	0.268

*Microvascular disease includes diabetic nephropathy, foot ulcer, retinopathy and peripheral neuropathy. Macrovascular disease includes peripheral vascular disease, ischaemic heart disease and cerebrovascular disease.

Table 3 Odds ratios from multivariable models describing association between race/ethnicity and death/ICU with complete data

	Adjustments					
Race/ethnicity	Age and sex	Age, sex, admission glucose	Age, sex, admission glucose and creatinine	Age, sex, admission glucose and creatinine, pre-COVID characteristics	Age, sex, admission glucose and creatinine, pre-COVID characteristics, comorbidities	Age, sex, admission glucose and creatinine, pre-COVID characteristics, comorbidities, treatments
AMERICADO						
Non-white vs white	0.95 (0.82, 1.09)	0.97 (0.83, 1.12)	1.01 (0.87, 1.17)	0.99 (0.85, 1.15)	0.99 (0.85, 1.16)	N/A
Asian vs white	1.04 (0.82, 1.33)	1.05 (0.83, 1.33)	1.03 (0.81, 1.32)	1.10 (0.86, 1.42)	1.11 (0.86, 1.43)	N/A
Black vs white	1.14 (0.94, 1.37)	1.07 (0.88, 1.29)	0.99 (0.81, 1.20)	1.03 (0.84, 1.25)	1.03 (0.84, 1.26)	N/A
Other vs white	1.01 (0.84, 1.21)	0.99 (0.83, 1.19)	0.97 (0.81, 1.17)	1.02 (0.85, 1.24)	1.01 (0.84, 1.23)	N/A
ABCD						
Non-white vs white	**1.89 (1.35-2.65)**	**1.88 (1.34-2.63)**	**1.83 (1.28-2.62)**	**1.85 (1.29-2.67)**	**2.14 (1.46-3.12)**	**2.22 (1.49-3.30)**
Asian vs white	**2.14 (1.38-3.29)**	**2.14 (1.39-3.30)**	**2.13 (1.35-3.37)**	**2.17 (1.36-3.47)**	**2.55 (1.57-4.14)**	**2.88 (1.72-4.82)**
Black vs white	**2.09 (1.17-3.74)**	**2.05 (1.14-3.68)**	**1.93 (1.02-3.65)**	**2.03 (1.06-3.86)**	**2.16 (1.13-4.14)**	**2.20 (1.12-4.30)**
Other vs white	1.19 (0.61-2.33)	1.18 (0.60-2.32)	1.14 (0.56-2.33)	1.10 (0.53-2.25)	1.35 (0.65-2.81)	1.23 (0.58-2.60)
CORONADO						
Non-EU vs EU	0.79 (0.55-1.12)	0.76 (0.53-1.08)	0.69 (0.47-0.99)	0.70 (0.48-1.03)	0.69 (0.47-1.02)	0.70 (0.47-1.03)
Afro-Caribbean vs EU	1.00 (0.62-1.62)	0.99 (0.61-1.60)	0.86 (0.52-1.41)	0.91 (0.54-1.54)	0.91 (0.53-1.54)	0.90 (0.53-1.54)
MENA vs EU	**0.64 (0.41-0.99)**	**0.60 (0.38-0.94)**	**0.56 (0.35-0.87)**	**0.57 (0.36-0.90)**	**0.56 (0.36-0.90)**	**0.57 (0.36-0.91)**
Asian vs EU	0.99 (0.40-2.48)	0.95 (0.38-2.40)	0.91 (0.36-2.31)	1.02 (0.39-2.65)	0.92 (0.35-2.47)	0.92 (0.34-2.49)

*Microvascular disease includes diabetic nephropathy, foot ulcer, retinopathy and peripheral neuropathy. Macrovascular disease includes peripheral vascular disease, ischaemic heart disease and cerebrovascular disease.

race/ethnicity and that people of Chinese, Indian, Pakistani, Other Asian, Black Caribbean and Other Black ethnicity also had higher (10–50%) risk of death compared to White British, even after adjustment for age, sex, income, education, housing and an area-based measure of socio-economic deprivation.[14]

In the UK ABCD COVID-19 dataset, those of non-White race/ethnicity formed only 21% of the study population; this was lower than in the CORONADO and AMERICADO datasets, where Asian, Black and Other ethnicities represented 43% and 62% of inpatients, respectively. These data suggest that the

marked disparity in outcomes may be specific to the UK. However, a recent systematic review and meta-analysis of 58 studies spanning seven countries with data from almost 10 million individuals identified a similar disparity in Brazil. While the risk of being diagnosed with SARS-CoV-2 infection was higher in most ethnic minority groups, once hospitalised no clear inequalities existed in COVID-19 outcomes except for a higher risk of death in ethnic minorities in Brazil.[15]

Many factors might contribute to disparity in outcomes in relation to race/ethnicity. We adjusted our analysis for admission characteristics (DKA on admission, admission blood glucose, creatinine), pre-COVID characteristics (smoking status, BMI, HbA_{1c}) and co-morbidities (hypertension, dementia, asthma, COPD and malignant neoplasm); but insufficient data were available to permit adjustment for socioeconomic status and deprivation, which are established risk factors for poor outcomes in relation to both COVID-19 and the complications of diabetes.[16] Associations between race/ethnicity and deprivation may differ between countries, which might explain why MENA background was protective in the CORONADO cohort. A further key consideration is risk of exposure to SARS-CoV-2, which may vary between ethnicity groups because of differences in frequency of multigenerational housing and public-facing occupations.

Access to healthcare is another important consideration. The UK NHS provides free, tax-funded healthcare at the point of need but access to free healthcare may be limited by health and social inequalities between ethnicity groups. Data from other UK datasets have highlighted similar disparities to those observed in the current study. Access to healthcare is an area of concern for those from minority backgrounds. For example, women of Black and Asian ethnicities are, respectively, four times and twice as likely to die in the UK during pregnancy or childbirth compared to women of White ethnicity. [17] This raises concern, particularly given the contrast in the current study between outcomes in the UK and those in France and the USA, that structural issues may be to blame. Such structural issues may include differences before and during the pandemic in access to and availability of primary and specialist care support, the quality of care available and/or willingness or ability to access these services.

Other factors may also be relevant, however. In particular, the lack of association between race/ethnicity and mortality in the AMERICADO dataset may reflect inclusion of a more selected population with medical insurance. Furthermore, some of the hospitals in the Northwell Health system are poorly served by public transport, limiting access by those from more deprived backgrounds. Interestingly, the findings from the AMERICADO dataset contrast with early findings from the general population in the USA which reported a higher risk of death for those of Black or Hispanic background compared to white race/ethnicity.[18] Subsequent analyses from Louisiana and Georgia in the USA did not identify race as an independent predictor of mortality.[19,20] Limitations in reporting and completeness of data may explain differences in findings.[16] A review of published data from the USA and UK suggests that those from ethnic minority groups (with and without diabetes) are disproportionately affected by COVID-19 both in terms of admission to ICU and mortality.[7]

Further potential sources of variation in outcome include lack of homogeneity of social status which, for any given ethnic group, may differ within and between countries, and not necessarily in relation to minority population status, while cultural, behavioural, social and religious practices differ widely. The categorisation of race/ethnicity is not standardised across countries, which is a significant limitation of international comparisons such as our study.[21]

The strengths of this study include the large multi-national cohort of people with T2DM and the level of detail about characteristics and co-morbidities, including data on macro- and microvascular complications. The data were adjusted for confounders; the insights gained were lacking in previously published datasets. Key limitations to acknowledge are the observational nature of the multi-national data which were collected retrospectively and the lack of standardisation in coding for race/ethnicity globally. Due to the real-world nature of this study, there are missing data (Appendix 1 online at www.bjdabcd.com). Furthermore, our study lacks a comparator arm, either those with T2DM who were admitted to hospital without COVID-19 or those with T2DM who were not admitted. Variability in the reporting of and categorisation of race/ethnicity is a universal limiting factor in the study of race/ethnicity with clinical outcomes.[16] Furthermore, ICU admission as an outcome and diabetes treatment data were not available for the AMERICADO cohort limiting comparison to the UK ABCD audit and CORONADO cohorts. Lastly, centres in France reported death within 28 days as an outcome, whereas in the UK and USA death during the admission was reported. However, this is unlikely to confound results substantially given that almost all deaths occur within the first 28 days.

Key messages

- There are limited data exploring the relationship between adverse outcomes related to COVID-19 and race/ethnicity in people with diabetes.
- In this study, observational data from the UK, France and the USA were utilised to explore the relationship between race/ethnicity and the risk of death/ICU admission in those with T2DM admitted to hospital with COVID-19. A non-White race/ethnicity was associated with higher risk of death/ICU admission in the UK ABCD data but not in French CORONADO or USA AMERICADO datasets.
- Further research is required to improve our understanding of the relationship between race/ethnicity and adverse outcomes from COVID-19 in people with diabetes.

Conclusion

In conclusion, we report unique multinational data on outcomes of adults with T2DM admitted to hospitals with COVID-19 in the UK ABCD audit and the CORONADO and AMERICADO study datasets. In this study population, non-White race/ethnicity was associated with the primary outcome of death and/or ICU admission in the UK ABCD audit population but not in the French CORONADO or US AMERICADO populations.

Novelty statement

What is already known?

- People living with diabetes who contract COVID-19 infection have a heightened risk of adverse outcomes
- Our understanding of the impact of COVID-19 in people with diabetes from minority ethnic backgrounds is limited

What this study has found

- People with type 2 diabetes (T2DM) from a non-White race/ethnicity who were admitted to hospital with COVID-19 in the UK experienced an increased risk of intensive care admission and/or death compared to those of a White background
- This relationship did not exist in those with T2DM who were admitted to hospital with COVID-19 in the USA or French cohorts

What are the implications of the study?

- These data highlight the disparities in outcomes in people with T2DM admitted to hospital with COVID-19 in the UK. Efforts are required to understand and address the social and systemic factors contributing to this disparity

Conflict of interest No potential conflicts of interest relevant to this article were reported.

BC reports grants and personal fees from Amgen, personal fees from AstraZeneca, personal fees from Akcea, personal fees from Genfit, personal fees from Gilead, personal fees from Eli Lilly, personal fees from Novo Nordisk, personal fees from Merck (MSD), grants and personal fees from Sanofi, grants and personal fees from Regeneron.

PD reports personal fees from Novo Nordisk, Sanofi, Eli Lilly, MSD, Novartis, Abbott, AstraZeneca, Boehringer Ingelheim, Mundipharma.

JFG reports personal fees and non-financial support from Eli Lilly, Novo Nordisk, and AstraZeneca, Personal fees from Bristol-Myers Squibb, Gilead and Bayer, all disclosures above unrelated to this presentation.

PG reports personal fees from Abbott, personal fees from Amgen, personal fees from AstraZeneca, personal fees from Boehringer Ingelheim, personal fees from Eli Lilly, personal fees from MSD, personal fees from Mundipharma, grants and personal fees from Novo Nordisk, personal fees from Sanofi, personal fees from Servier.

SaH reports personal fees and non-financial support from AstraZeneca, grants and personal fees from Bayer, personal fees from Boehringer Ingelheim, grants from Dinno Santé, personal fees from Eli Lilly, non-financial support from LVL, personal fees and non-financial support from MSD, personal fees from Novartis, grants from Pierre Fabre Santé, personal fees and non-financial support from Sanofi, personal fees and non-financial support from Servier, personal fees from Valbiotis.

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RRo reports grants, personal fees and non-financial support from Sanofi, grants, personal fees and non-financial support from Novo Nordisk, personal fees and non-financial support from Eli Lilly, personal fees from Mundipharma, personal fees from Janssen, personal fees from Servier, grants and personal fees from AstraZeneca, personal fees from MSD, personal fees from Medtronic, personal fees from Abbott, grants from Diabnext, personal fees from Applied Therapeutics.

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SHW attends meetings of the Scottish Study Group of Diabetes in the Young that receives support from Novo Nordisk.

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All other authors declare no competing interests.

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Author contributions RRe, EGW, SHW, SoH, BCTF, REJR, PN, YR and KK designed the ABCD COVID-19 national Audit study. KAV conducted data management and governance and YR conducted the statistical analysis for the ABCD study.

AKM, MSW, XZ and RP designed the AMERICADO study. Y.L. compiled the data and MSW conducted the statistical analysis.

MW, PG, SaH and BC designed the CORONADO study. PG, LK, RR, J-FG, P-JS, SaH, and BC participated in patient recruitment. MW conducted the statistical analysis for the CORONADO study and for joint analysis.

EGW, KK and SW drafted the first version of the manuscript. All authors approved the final manuscript. EGW, KK, SW, SH, MW, BC, AM and MSW are the guarantors of this work.

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Appendix 1. Clinical characteristics of the study populations by source and presence/absence of complete data

	AMERICADO			ABCD			CORONADO		
	Complete data (N=5246)	**Incomplete data(N=4075)**	**p**	**Complete data (N=920)**	**Incomplete data (N=2492)**	**p**	**Complete data (N=611)**	**Incomplete data(N=1562)**	**p**
Sex M/total (%)	3086/5246 (58.8%)	2211/4075 (54%)	**<0.001**	596/920 (65%)	1701/2820(60%)	0.11	376/611 (61.5%)	1019/1562 (65.2%)	0.111
Mean Age years (SD)	66.7(13.6)	69.0 (14.5)		73(13)	72(14)	0.13	70 (12)	71 (13)	0.061
Ethnicity	Asian 605/5246(11%) Black 1215/5246 (23%) Other 1427/5246 (27%) White 1999/5246 (38%)	Asian 432/4075 (12%) Black 814/4075 (22%) Other 849/4075 (22%) White 1652/4075 (44%)	**<0.001** **<0.001** **<0.001** **<0.001**	White 719/920 (79%) Asian 109/920 (12%) Black 54/920 (6%) Other 38/920 (3%)	White 1413/2492(57%) Asian 411/2492(16%) Black 182/2492(7%) Other 486/2492(20%)	**<0.01** **<0.01** **<0.01** **<0.01**	Afro-Caribbean 105/611 (17%) MENA 136/611 (22%) Asian 21/611 (3%) Europid 349/611 (57%)	Afro-Caribbean 252/1562 (16.1%) MENA 330/1562 (21.1%) Asian 62/1562 (4%) Europid 918/1562 (58.8%)	0.785
Admission features									
DKA on admission	161/5246 (3%)	96/4075 (2%)	**<0.001**	28 (3%)	92/2277(4%)	0.32	26/611 (4%)	70/1392 (5%)	0.497
Admission blood glucose (mmol/l)	11.7 (7.10)	10.8 (7.3)	**<0.001**	10.9 (6.5)	11.3(7.1)	0.08	10.5(5.5)	11.3(6.6)	**0.010**
Creatinine(µmol/l)	156 (183)	173 (194)	**<0.001**	119(63)	119(67)	0.42	130 (133)	120 (97)	0.097
Pre-COVID characteristics									
Smoker	856/5246 (16.3%)	878/4075 (22%)	**<0.001**	75/920 (8%)	69/903(8%)	0.82	33/611 (5%)	55/1193 (4.6%)	0.489
BMI (kg/m^2)	30.5 (11.3)	29.6 (8.1)	**<0.001**	29.5 (7.3)	29.2(7.0)	0.42	29.5(5.5)	29.4(6.1)	0.653
HbA1c(mmol/mol)	64 (20)	65 (20)	**<0.001**	63 (22)	56(27)	**<0.01**	65 (20)	66.3(21.7)	0.117
Microvascular disease*	1119/5246 (21%)	1070/4075 (26%)	**<0.001**	473/920 (51%)	812/1975(41%)	**<0.01**	262/611 (43%)	415/915 (45.4%)	0.344
Comorbidities									
Macrovascular disease**	1943/5246 (37%)	1819/4075 (45%)	**<0.001**	492/920 (54%)	966/2326(41.5%)	**<0.01**	234/611 (38%)	571/1431 (39.9%)	0.52
Hypertension	4358/5246 (83%)	3544/4075 (87%)	**<0.001**	620/920 (67%)	1890/2585(73.1%)	0.11	499/611 (82%)	1222/1542 (79.2%)	0.211
Dementia	402/5246 (8%)	552/4075(14%)	**<0.001**	133/920 (14%)	356/2150(16.6%)	0.29	4/611 (1%)	5/1562 (0.3%)	0.279
Asthma	568/5246 (11%)	457/4075 (11%)	**<0.001**	116/920 (13%)	321/2197(14.6%)	0.24	18/611 (3%)	54/1562 (3.5%)	0.596
COPD	541/5246 (10%)	592/4075 (15%)	**<0.001**	166/920 (18%)	302/2052(14.7%)	**<0.01**	66/611 (11%)	130/1511 (8.6%)	0.116
Malignant neoplasm	557/5246 (10%)	536/4075 (13%)	**<0.001**	155/920 (17%)	363/2292(15.8%)	**0.04**	59/611 (10%)	141/1517 (9.3%)	0.806
Outcomes									
Death	998/5246 (19%)	909/4075 (22%)	**<0.001**	379/920 (42%)	887/2511(35.3%)	**0.02**	95/611 (16%)	356/1558 (22.8%)	**<0.001**
Death/ICU	N/A	N/A	N/A	434/920 (47%)	1055/2665(39.6%)	**0.01**	223/611 (37%)	687/1560 (44.0%)	**0.001**

Appendix 2. CORONADO Collaborators list

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