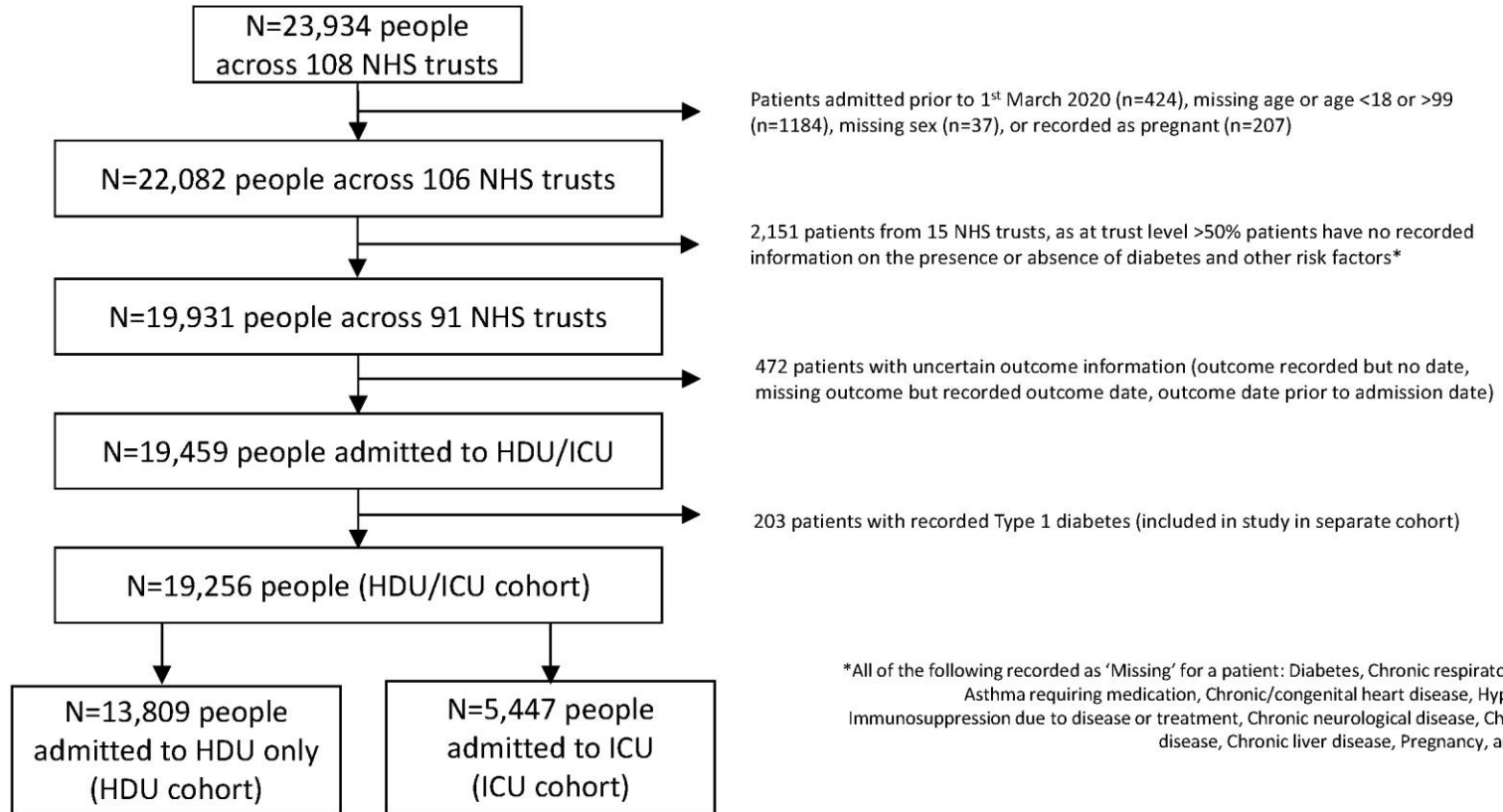**Supplementary Material for Diabetes and COVID-19 related mortality in the critical care setting: A national cohort study in England, March-July 2020**

Authors: John M. Dennis, Bilal A. Mateen, Raphael Sonabend, Nicholas J. Thomas, Kashyap A. Patel, Andrew T Hattersley, Spiros Denaxas, Andrew P. McGovern, Sebastian J. Vollmer

SFlowchart 1: Patient flow diagram

COVID-19 Hospitalisation in England Surveillance System (CHESS) daily reporting of persons requiring hospitalisation and HDU/ICU management (data download 27/07/2020)

N=23,934 people across 108 NHS trusts

Patients admitted prior to 1st March 2020 (n=424), missing age or age <18 or >99 (n=1184), missing sex (n=37), or recorded as pregnant (n=207)

N=22,082 people across 106 NHS trusts

2,151 patients from 15 NHS trusts, as at trust level >50% patients have no recorded information on the presence or absence of diabetes and other risk factors*

N=19,931 people across 91 NHS trusts

472 patients with uncertain outcome information (outcome recorded but no date, missing outcome but recorded outcome date, outcome date prior to admission date)

N=19,459 people admitted to HDU/ICU

203 patients with recorded Type 1 diabetes (included in study in separate cohort)
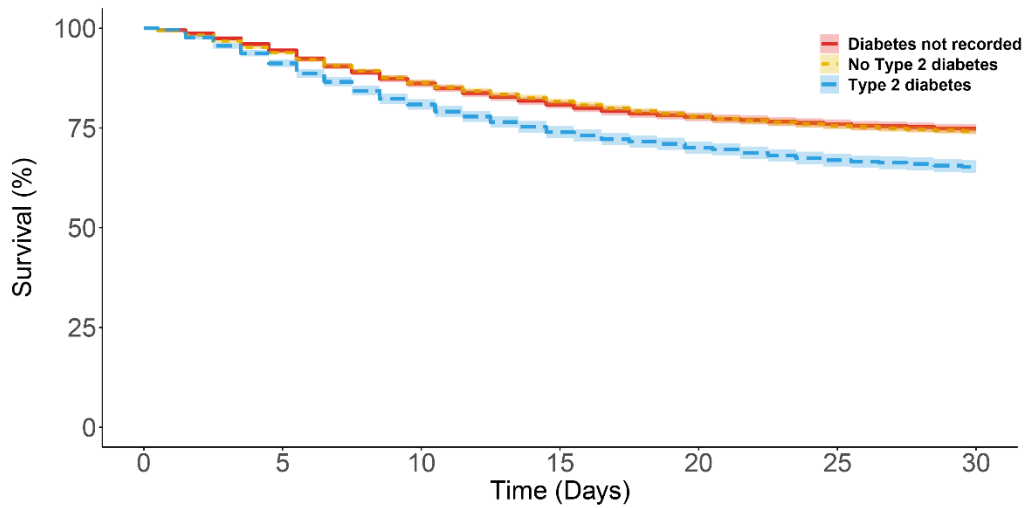
N=19,256 people (HDU/ICU cohort)

*All of the following recorded as 'Missing' for a patient: Diabetes, Chronic respiratory disease, Asthma requiring medication, Chronic/congenital heart disease, Hypertension, Immunosuppression due to disease or treatment, Chronic neurological disease, Chronic renal disease, Chronic liver disease, Pregnancy, and obesity.

N=13,809 people admitted to HDU only (HDU cohort)

N=5,447 people admitted to ICU (ICU cohort)

sTable 1: Recorded characteristics of study cohorts.

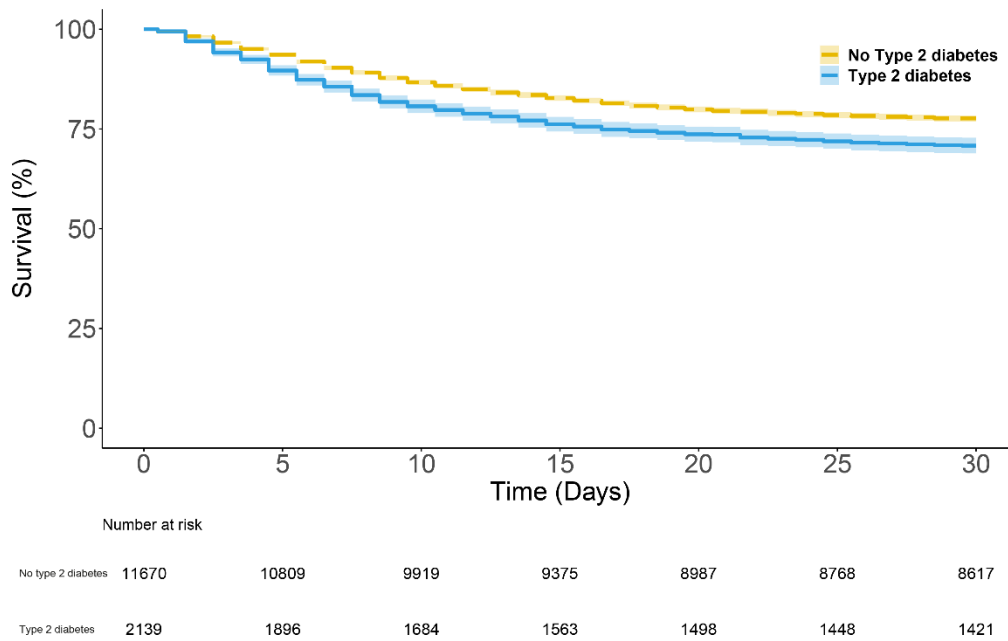|	HDU/ICU cohort (n=19,256)	HDU only cohort (n=13,809)	ICU cohort (n=5,447)
Age in years (Mean [SD])	67 (16.88)	70 (17.21)	58 (12.66)
Age Group			
18-24	172 (0.9)	134 (1.0)	38 (0.7)
25-34	652 (3.4)	446 (3.2)	206 (3.8)
35-44	1,152 (6.0)	695 (5.0)	457 (8.4)
45-54	2,468 (12.8)	1,331 (9.6)	1,137 (20.9)
55-64	3,662 (19.0)	1,900 (13.8)	1,762 (32.3)
65-74	3,850 (20.0)	2,550 (18.5)	1,300 (23.9)
75-84	4,052 (21.0)	3,551 (25.7)	501 (9.2)
85+	3,248 (16.9)	3,202 (23.2)	46 (0.8)
Sex			
Female	7,683 (39.9)	6,084 (44.1)	1,599 (29.4)
Male	11,573 (60.1)	7,725 (55.9)	3,848 (70.6)
Ethnicity			
White	11,439 (73.0)	8,413 (76.9)	3,026 (63.9)
Asian	2,036 (13.0)	1,204 (11.0)	832 (17.6)
Black	1,097 (7.0)	727 (6.6)	370 (7.8)
Mixed	211 (1.3)	72 (0.7)	139 (2.9)
Other	895 (5.7)	523 (4.8)	372 (7.8)
Obesity			
Non-obese	7,543 (65.3)	5,467 (75.8)	2,076 (47.9)
Obese	4,004 (34.7)	1,742 (24.2)	2,262 (52.1)
Comorbidity			
Type 2 diabetes	3,524 (18.3)	2,139 (15.5)	1,385 (25.4)
Chronic respiratory disease	1,673 (8.7)	1,166 (8.4)	507 (9.3)
Asthma	1,628 (8.5)	929 (6.7)	699 (12.8)
Hypertension	5,657 (29.4)	3,602 (26.1)	2,055 (37.7)
Chronic heart disease	2,662 (13.8)	2,034 (14.7)	628 (11.5)
Chronic renal disease	1,827 (9.5)	1,426 (10.3)	401 (7.4)
Chronic liver disease	390 (2.0)	244 (1.8)	146 (2.7)
Chronic neurological disease	1,408 (7.3)	1,174 (8.5)	234 (4.3)
Immunosuppressive disease	468 (2.4)	274 (2.0)	194 (3.6)
Time in hospital			
Days from hospital to ICU admission per day increase (Mean [SD])	NA	NA	2 (5.62)

SFigure 1: Kaplan-Meier plots for in-hospital COVID-19 death in 19,256 patients admitted to critical care (HDU or ICU) in CHESS by time since hospital admission, with type 2 diabetes status coded as Yes, No, and Not recorded. Plots show the proportion of individuals at risk who were still alive at regular intervals up to 30 days from admission. People discharged from hospital prior to 30 days were assumed to survive to 30 days and are included in the number at-risk until 30 days, in keeping with the standard practice for time-to-event modelling in analysis of critical care patients.
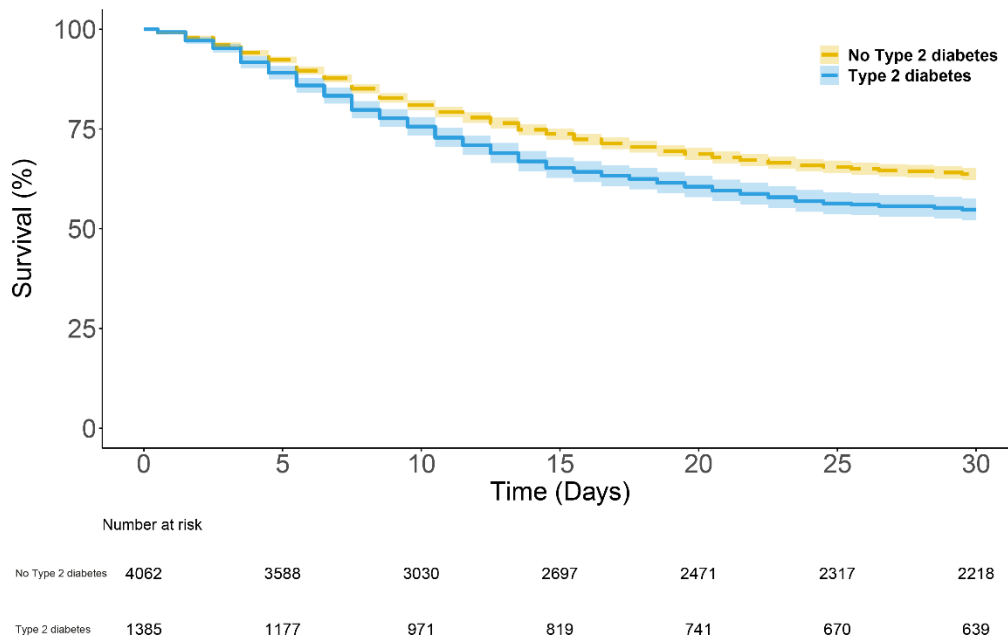

Number at risk							
Diabetes not recorded	5723	5340	4817	4474	4257	4122	4025
No type 2 diabetes	10009	9240	8326	7757	7329	7045	6867
Type 2 diabetes	3524	3154	2741	2455	2293	2159	2089

SFigure 2: Kaplan-Meier plots for in-hospital COVID-19 death over time, by diabetes status for:

a) HDU only cohort, n=13,809)

Number at risk						
No type 2 diabetes	11670	10809	9919	9375	8987	8768	8617
Type 2 diabetes	2139	1896	1684	1563	1498	1448	1421

a) ICU cohort, n=5,447)

Number at risk						
No Type 2 diabetes	4062	3588	3030	2697	2471	2317	2218
Type 2 diabetes	1385	1177	971	819	741	670	639

sTable 2: Hazard ratios for full covariate set in multivariable analysis of the primary outcome of 30 day all-cause in-hospital mortality for each study cohort. Data in brackets are 95% confidence intervals.

	HDU/ICU cohort (n=19,256)	HDU only cohort (n=13,809)	ICU cohort (n=5,447)
Type 2 diabetes			
No type 2 diabetes	1.00 (ref)	1.00 (ref)	1.00 (ref)
Type 2 diabetes	1.23 (1.14;1.32), p<0.001	1.19 (1.08;1.31), p<0.001	1.24 (1.11;1.38), p<0.001
Age			
Age spline	1.06 (1.06;1.07), p<0.001	1.10 (1.09;1.11), p<0.001	1.04 (1.03;1.05), p<0.001
Age spline'	0.97 (0.96;0.98), p<0.001	0.96 (0.95;0.97), p<0.001	1.00 (0.99;1.01), p=0.699
Sex			
Female	1·00 (ref)	1·00 (ref)	1·00 (ref)
Male	1.33 (1.25;1.41), p<0.001	1.30 (1.21;1.39), p<0.001	1.08 (0.98;1.20), p=0.121
Ethnicity*			
White	1.00 (ref)	1.00 (ref)	1.00 (ref)
Asian	1.32 (1.20;1.46), p<0.001	1.24 (1.07;1.45), p=0.005	1.27 (1.11;1.44), p<0.001
Black	1.19 (1.04;1.35), p=0.010	1.19 (0.99;1.44), p=0.065	1.33 (1.11;1.59), p=0.002
Mixed	1.74 (1.34;2.25), p=0.000	1.52 (0.90;2.58), p=0.119	1.24 (0.92;1.67), p=0.157
Other	1.00 (0.85;1.17), p=0.964	0.83 (0.63;1.08), p=0.165	0.99 (0.81;1.20), p=0.887
Missing	1.10 (1.01;1.18), p=0.020	1.16 (1.06;1.27), p=0.001	1.03 (0.90;1.19), p=0.645
Obesity**			
Non-obese (BMI<30)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Obese (BMI≥30)	1.06 (0.99;1.15), p=0.113	0.84 (0.74;0.95), p=0.007	0.95 (0.86;1.06), p=0.393
Missing	0.94 (0.88;1.01), p=0.089	0.89 (0.82;0.97), p=0.005	1.51 (1.35;1.70), p<0.001
Comorbidity (versus No/Missing)			
Chronic respiratory disease	1.29 (1.18;1.41), p<0.001	1.35 (1.21;1.51), p<0.001	1.11 (0.96;1.28), p=0.175
Asthma	1.02 (0.92;1.13), p=0.755	0.99 (0.85;1.14), p=0.862	0.92 (0.79;1.06), p=0.253
Hypertension	1.04 (0.97;1.11), p=0.237	0.91 (0.83;0.99), p=0.024	1.01 (0.91;1.12), p=0.846
Chronic heart disease	1.11 (1.03;1.20), p=0.009	1.11 (1.01;1.22), p=0.026	1.10 (0.97;1.26), p=0.146
Chronic renal disease	1.17 (1.07;1.27), p<0.001	1.24 (1.11;1.37), p<0.001	1.29 (1.11;1.50), p=0.001
Chronic liver disease	0.99 (0.81;1.21), p=0.924	1.21 (0.93;1.58), p=0.162	0.91 (0.67;1.23), p=0.540
Chronic neurological disease	1.12 (1.02;1.23), p=0.022	1.20 (1.07;1.33), p=0.001	1.13 (0.91;1.39), p=0.276
Immunosuppressive disease	1.23 (1.05;1.44), p=0.009	1.20 (0.97;1.49), p=0.095	1.01 (0.80;1.27), p=0.938
Time in hospital			
Days from hospital to ICU admission (per day increase)	NA	NA	1.00 (0.99;1.01), p=0.722

*Ethnicity not recorded for HDU/ICU 3,578 patients; HDU 2,870; ICU 708. **Obesity not recorded for HDU/ICU 7,709 patients; HDU 6,600; ICU 1,109.

sTable 3: Hazard ratios for additional subgroup and sensitivity analysis. Data in brackets are 95% confidence intervals.

Subgroup and sensitivity analysis. All adjusted for the full covariate set.	HDU/ICU cohort	HDU only cohort	ICU cohort
Admitted to hospital in March 2020 (All n=5606, HDU n=3,725, ICU n=1881)	1.34 (1.18, 1.51), p<0.001	1.39 (1.18, 1.64), p<0.001	1.30 (1.09, 1.54), p=0·003
Admitted to hospital in April 2020 (All n=9440, HDU n=6,666, ICU n=2774)	1.13 (1.02, 1.26), p=0.02	1.05 (0.92, 1.21), p=0.47	1.19 (1.02, 1.39), p=0.03
Admitted to hospital in May-July 2020 (All n=4210, HDU n=3418, ICU n=792)	1.24 (1.01, 1.52), p=0.04	1.24 (0.96, 1.60), p=0.10	1.19 (0.84, 1.69), p=0.34
Calendar week of hospital admission added as an addition covariate (All n=19,256, HDU n=13,809, ICU n=5,447)	1.21 (1.13, 1.31), p<0.001	1.18 (1.07, 1.30), p<0.001	1.22 (1.10, 1.36), p<0.001
Exclude transferred patients and patient who remain in hospital (All n=17,044, HDU n=13,033, ICU n=4,483)	1.22 (1.14, 1.31), p<0.001	1.17 (1·06, 1·29), p=0·002	1·24 (1.11, 1.38), p<0·001
Include only patients with PCR swab positive result during admission (All n=17,606, HDU n=12,550, ICU n=5056)	1.23 (1.14, 1.32), p<0.001	1.22 (1.11, 1.35), p<0.001	1.18 (1.06, 1.32), p=0.004
NHS Trust as additional random effect (All n=19,256, HDU n=13,809, ICU n=5,447)	1·19 (1·11, 1·29), p<0·001	1.20 (1.09, 1.32), p<0.001	1.18 (1.06, 1.32), p=0·003
Multiple imputation model (All n=19,256, HDU n=13,809, ICU n=5,447)	1.25 (1.15, 1.36), p<0.001	1.16 (1.03, 1.31), p=0.02	1.31 (1.16, 1.49), P<0.001
Include patients from all hospitals, assuming non-coded comorbidity represents the absence of a comorbidity (All n=21452 , HDU n=15,637, ICU n=5,815)	1.26 (1.17, 1.35), p<0·001	1.24 (1.13, 1.36), p<0·001	1.25 (1.12, 1.39), p<0·001
Include patients only from hospitals with <25% missing comorbidity coding (All n=13,995, HDU n=8,8981, ICU n=4,482)	1·25 (1·16, 1·35), p<0·001	1·25 (1·12, 1·39), p<0·001	1·27 (1·13, 1·42), p<0·001

sTable 4: Recorded characteristics of patients in hospitals included and excluded from study cohorts. Data are N (%) unless stated.

	Hospitals excluded (hospital n= 15, patient n=1,993)	Hospitals included (hospital n=91, patient n=19,256)
Age in years (Mean [SD])	70 (16.26)	67 (16.88)
Age Group		
18-24	14 (0.7)	172 (0.9)
25-34	39 (2.0)	652 (3.4)
35-44	91 (4.6)	1,152 (6.0)
45-54	235 (11.8)	2,468 (12.8)
55-64	282 (14.1)	3,662 (19.0)
65-74	398 (20.0)	3,850 (20.0)
75-84	509 (25.5)	4,052 (21.0)
85+	425 (21.3)	3,248 (16.9)
Sex		
Female	827 (41.5)	7,683 (39.9)
Male	1,166 (58.5)	11,573 (60.1)
Ethnicity		
White	735 (36.9)	11,439 (59.4)
Asian	80 (4.0)	2,036 (10.6)
Black	11 (0.6)	1,097 (5.7)
Mixed	7 (0.4)	211 (1.1)
Other	14 (0.7)	895 (4.6)
Not recorded	1,146 (57.5)	3,578 (18.5)
Obesity		
Non-obese	61 (3.1)	7,543 (39.1)
Obese	36 (1.8)	4,004 (20.8)
Not recorded	1,896 (95.1)	7,709 (40.0)
Comorbidity (recorded yes)		
Diabetes	80 (4.0)	3,524 (18.3)
Chronic respiratory disease	66 (3.3)	1,673 (8.7)
Asthma	27 (1.4)	1,628 (8.5)
Hypertension	123 (6.2)	5,657 (29.4)
Chronic heart disease	70 (3.5)	2,662 (13.8)
Chronic renal disease	38 (1.9)	1,827 (9.5)
Chronic liver disease	3 (0.2)	390 (2.0)
Chronic neurological disease	40 (2.0)	1,408 (7.3)
Immunosuppressive disease	15 (0.8)	468 (2.4)
Time in hospital		
Admitted to ICU	294 (14.8)	5,447 (28.2)