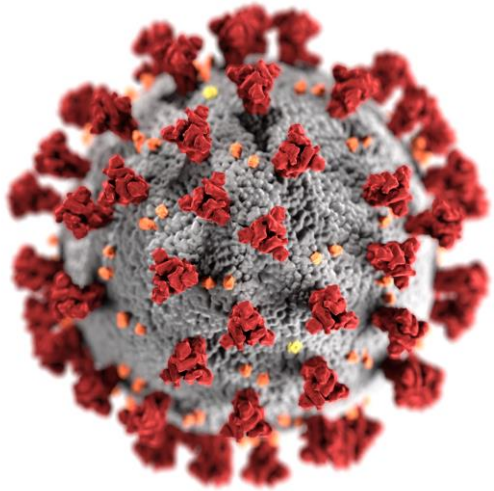
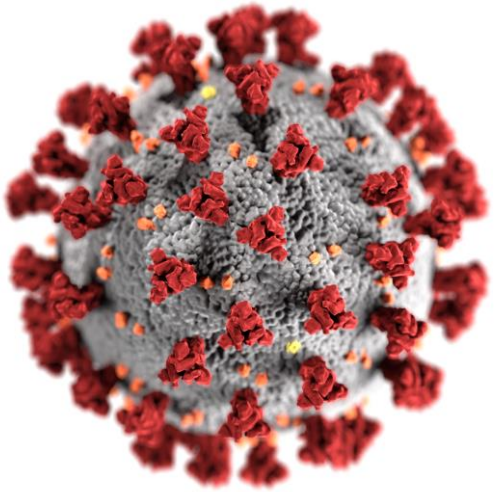
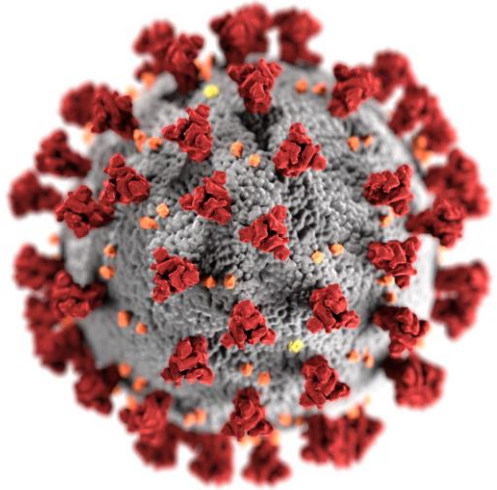


Diabetes and COVID-19



Leonor Corsino, MD, MHS

Alyson Myers, MD



Duke University School of Medicine

North Shore University Hospital
Northwell Health℠

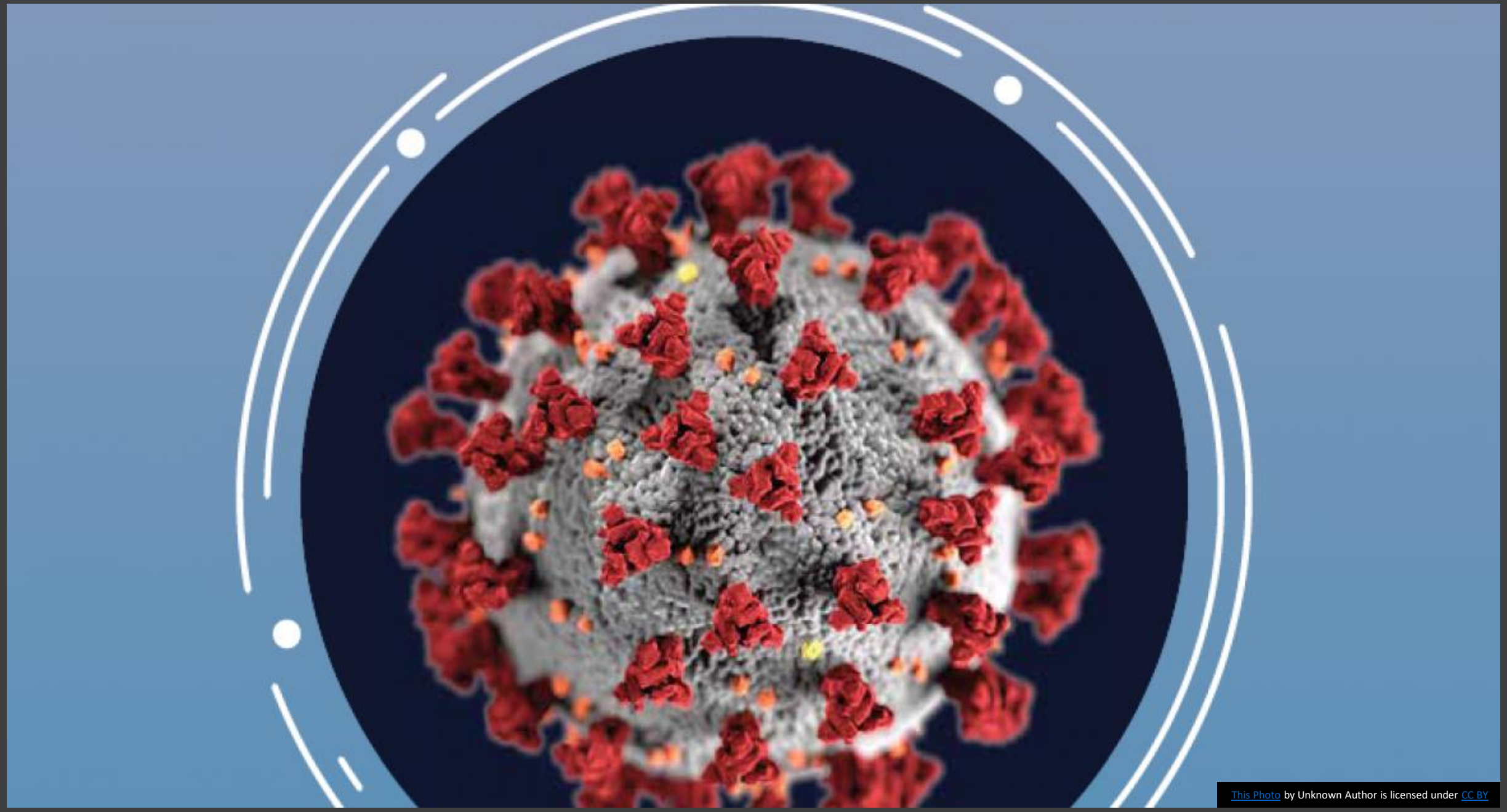
Disclosure

- Dr Corsino reports support from Novo Nordisk for her role as advisor on the health disparities virtual advisory board.

- Dr Myers has no disclosures.

Objectives

- To review the relationship between diabetes and COVID-19
- To describe the outcomes of patients with diabetes and COVID-19
- To describe diabetes management of patients with COVID-19



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Comorbidities	
Total No.	5700
Cancer	320 (6)
Cardiovascular disease	
Hypertension	3026 (56.6)
Coronary artery disease	595 (11.1)
Congestive heart failure	371 (6.9)
Chronic respiratory disease	
Asthma	479 (9)
Chronic obstructive pulmonary disease	287 (5.4)
Obstructive sleep apnea	154 (2.9)
Immunosuppression	
HIV	43 (0.8)
History of solid organ transplant	55 (1)
Kidney disease	
Chronic[c]	268 (5)
End-stage[d]	186 (3.5)
Liver disease	
Cirrhosis	19 (0.4)
Chronic	
Hepatitis B	8 (0.1)
Hepatitis C	3 (0.1)
Metabolic disease	
Obesity (BMI ≥30)	1737 (41.7)
No.	4170
Morbid obesity (BMI ≥35)	791 (19.0)
No.	4170
Diabetes[e]	1808 (33.8)

Presenting Characteristics, Comorbidities, and Outcomes Among 5700Patients Hospitalized With COVID-19 in the New York City Area

- A total of 5700 patients in New York
- Median age, 63 years
- 33.8% of admitted patients had diabetes

JAMA. 2020;323(20):2052-2059.

Diabetes is a risk factor for the progression and prognosis of COVID-19

Retrospective study of 174 patients (37 with diabetes) with SARS-Cov-2 infection who were admitted to Wuhan Union hospital from 10 February 2020 to 29 February 2020.

TABLE 1 Demographics and baseline characteristics of patients infected with SARS-CoV-2

	No. (%) Total (n = 174)	Non-diabetes (n = 137)	Diabetes (n = 37)	*P*-value[a]
Age, median (IQR), y	59 (49-67)	58 (47-66)	61 (55-69)	.054
Gender				
Male	76 (43.7)	56 (40.9)	20 (54.1)	.152
Female	98 (56.3)	81 (59.1)	17 (45.9)	
Comorbidities				
Hypertension	43 (24.7)	33 (24.1)	10 (27)	.713
Cardiovascular disease	32 (18.4)	20 (14.6)	12 (32.4)	.013
Malignancy	17 (4.6)	16 (11.7)	1 (2.7)	.187
Pulmonary disease	14(9.7)	12 (8.7)	2 (5.4)	.745
Cerebrovascular disease	13 (7.5)	12 (8.7)	1 (2.7)	.373
Chronic kidney disease	13 (7.5)	12 (8.7)	1 (2.7)	.373
Chronic liver disease	8 (4.6)	8 (5.8)	0	.288
Immunodeficiency	4 (2.3)	4 (2.9)	0	.294
Hepatitis B infection	2 (1.1)	2 (1.5)	0	.461
Signs and symptoms				
Fever	136 (78.2)	114 (83.2)	22 (59.5)	.002
Highest temperature, °C				
<37.3	38 (21.8)	23 (16.8)	15 (40.5)	.002
37.3 to 38.0	36 (20.7)	28 (20.4)	8 (21.6)	.875
38.1 to 39.0	73 (42)	62 (45.3)	11 (29.7)	.089
>39.0	27 (15.5)	24 (17.5)	3 (8.1)	.161
Fatigue	47 (27)	36 (26.3)	11 (29.7)	.675
Chill	119 (68.4)	98 (71.5)	21 (56.8)	.086
Cough	56 (32.2)	48 (35)	8 (21.6)	.121

Diabetes Metab Res Rev. 2020;36:e3319.

Diabetes is a risk factor for the progression and prognosis of COVID-19

TABLE 5 Treatments and complications of diabetic COVID-19 patients without other comorbidities

	No. (%) Yes	No	*P*-value[a]
Insulin therapy pre-hospital	7 (29.2)	17 (70.8)	
Mortality	1	3	1
Insulin dose increased in hospital	7 (29.2)	17 (70.8)	
Mortality	1	3	1
Start insulin therapy after admission	9 (37.5)	15 (62.5)	
Mortality	3	1	.13
Diabetic complications	3 (12.5)	21 (87.5)	
Mortality	2 (66.7)	2 (9.5)	.045
Diabetic ketoacidosis	2 (12.5)	22 (87.5)	
Mortality	1 (50)	3 (13.6)	.31
Infectious shock	1 (4.2)	23 (95.8)	
Mortality	1 (100)	3 (13)	.17

[a]*P* values indicate differences between the two groups. $P < .05$ was considered statistically significant.

Having diabetes related complications increases mortality

Diabetes Metab Res Rev. 2020;36:e3319.

- Single-center, retrospective, observational study comparing 145 patients with severe COVID to 48 patients with severe COVID and diabetes
- Persons with diabetes were older (mean age 70 vs 64)

- The survival duration in patients with severe COVID-19 with diabetes is shorter than in those without diabetes

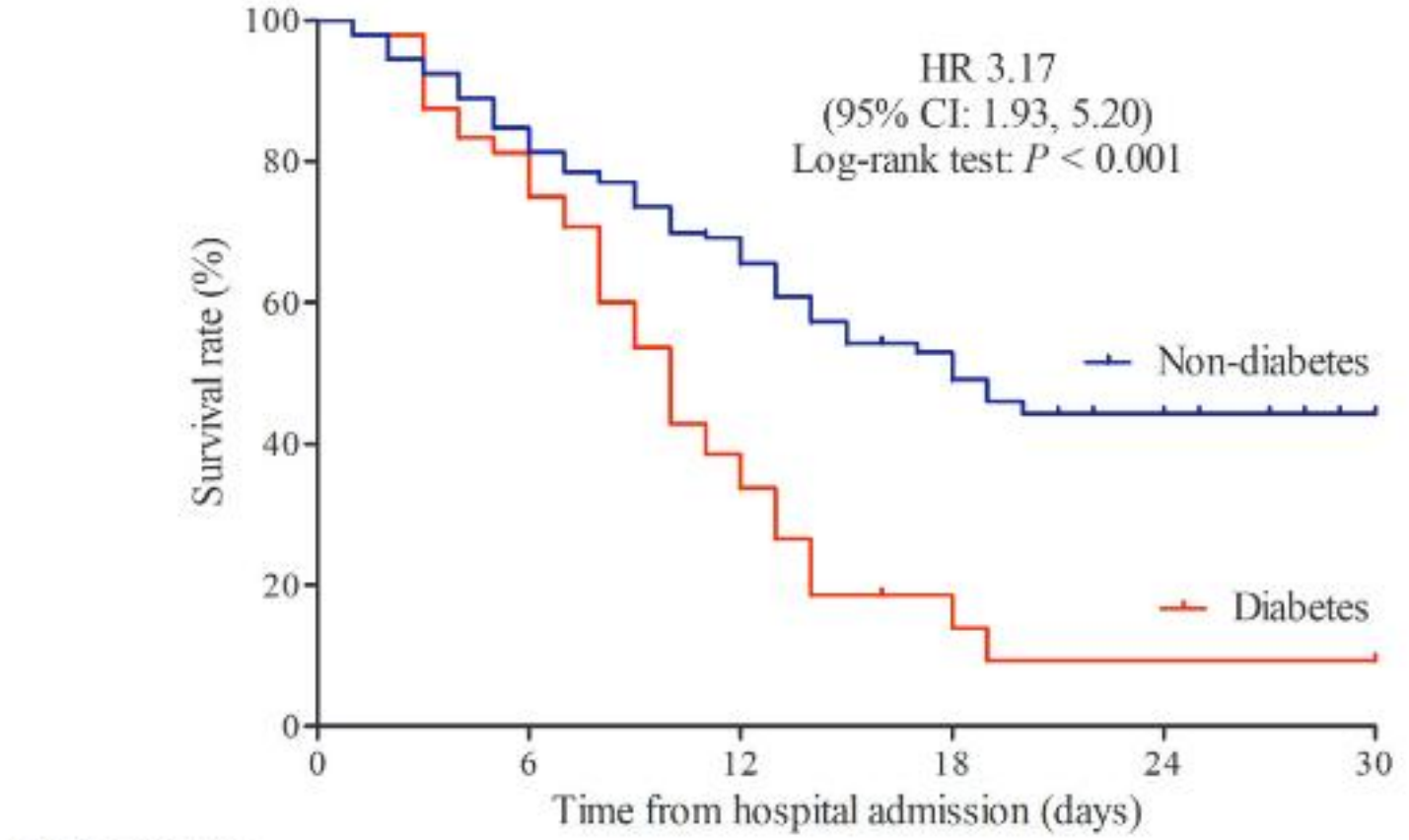


Figure 1 Kaplan-Meier survival curve for patients with severe covid-19 with and without diabetes.

BMJ Open Diab Res Care 2020;8:e001343

Cohort of Persons with Diabetes and COVID-19 at Montefiore Hospital

- 98.4% T2D
- Average Age 67.9 + 13.7 years
- 50.7% Women
- 74.5% Black/African-American
- 40.4% Hispanic Ethnicity
- Average BMI 30.1
- Average HbA1c 7.5%

Table 2—Mortality odds ratios of preadmission clinical characteristics in hospitalized patients with diabetes and COVID-19 (*N* = 1,126)

	Unadjusted OR	Unadjusted 95% CI	Adjusted OR*	Adjusted 95% CI*
Glycemic control: HbA_{1c}†	1.02	0.96, 1.08	1.01	0.94, 1.09
Treatment regimen (Ref: no treatment)				
Noninsulin only	1.45	1.00, 2.10	1.30	0.89, 1.91
Insulin + noninsulin	1.68	1.15, 2.45	1.74	1.13, 2.68
Insulin only	1.98	1.20, 3.26	2.30	1.32, 4.01
Comorbidity or long-term diabetes complication				
Hypertension	0.84	0.44, 1.58	0.54	0.28, 1.05
Cardiovascular disease	1.57	1.21, 2.04	1.18	0.88, 1.57
Chronic kidney disease	1.34	1.05, 1.72	1.11	0.84, 1.45
Chronic obstructive pulmonary disease	1.63	1.16, 2.29	1.46	1.02, 2.08

Ref, reference. *Adjustment: each variable was adjusted for age, sex, BMI, insurance, and the other variables in the table. †Most recent HbA_{1c} within 3 years prior to or 1 week after hospitalization was used for analyses.

Diabetes Care 2020;43:2339–2344

Clinicaltrial.gov: NCT 04324736

CORONADO

CORONAVIRUS SARS-COV2 & DIABETES OUTCOMES

68 sites in France
2796 patients with diabetes
hospitalised for COVID-19
10 March to 10 April 2020

64% males
70 years
BMI: 28.4 kg/m^2
HbA_{1c}: 61 mmol/mol (7.7%)
Microvasc. complications: 44%
Macrovasc. complications: 39%
Metformin: 56%
Insulin therapy: 37%

Hospital discharge: 50.2%

- Routine metformin use
- Longer time between symptom onset and admission
- Higher age
- History of microvasc. complications
- Routine anticoagulation therapy
- Dyspnoea on admission
- ↗ AST, ↗ white cell count, ↗ CRP

FOLLOW-UP:
From admission to day 28

Factors independently associated

\+ Protective

− Deleterious

Death: 20.6%

- Routine metformin use
- Longer time between symptom onset and admission
- Higher age
- History of microvasc. complications
- Routine insulin use
- Dyspnoea on admission
- ↗ AST, ↗ white cell count, ↗ CRP
- ↘ platelets

CORONADO study. Diabetologia (2021)

Persons with T2D and COVID-19 admitted to Northwell between January 1st and May 31st

Table 1. Baseline characteristics of COVID-19 patients with diagnosis of T2DM

	Total		Alive		Expired		P value
Characteristics	3846		2893		953		
Age, years							
Median(IQR)	68	(59,77)	66	(58,75)	73	(64,81)	<.0001
Gender (No. [%])							
Male	2291	59.57%	1657	57.28%	634	66.53%	<0.001
Race(No.[%])							0.057
African American/Black	943	27.10%	718	24.82%	225	23.61%	
Asian	361	10.40%	247	8.54%	114	11.96%	
Declined	14	0.40%	10	0.35%	4	0.42%	
Native American/Alaskan	23	0.70%	19	0.66%	4	0.42%	
Native Hawaiian/Pacific Islander	5	0.10%	5	0.17%	0	0.00%	
Other/Multiracial	867	24.90%	656	22.68%	211	22.14%	
Unknown	146	4.20%	111	3.84%	35	3.67%	
White	1127	32.30%	817	28.24%	310	32.53%	
Ethnicity							0.205
Declined	253	6.58%	187	6.46%	66	6.93%	
Hispanic or Latino	662	17.21%	510	17.63%	152	15.95%	
Not Hispanic or Latino	2438	63.39%	1793	61.98%	645	67.68%	
Unknown	133	3.46%	93	3.21%	40	4.20%	
Insurance							0.081
Private	1671	43.45%	1266	43.76%	405	42.50%	
Public	1792	46.59%	1299	44.90%	493	51.73%	
Self-Pay	23	0.60%	18	0.62%	5	0.52%	
Smoking Status							p<.001
Former smoker	111	2.89%	15	0.52%	96	10.07%	
Non Smoker	2904	75.51%	2307	79.74%	597	62.64%	
Smoker	261	6.79%	218	7.54%	43	4.51%	

Journal of diabetes. 2021 Jan 23

Persons with T2D and COVID-19 admitted to Northwell between January 1st and May 31st

Conclusions

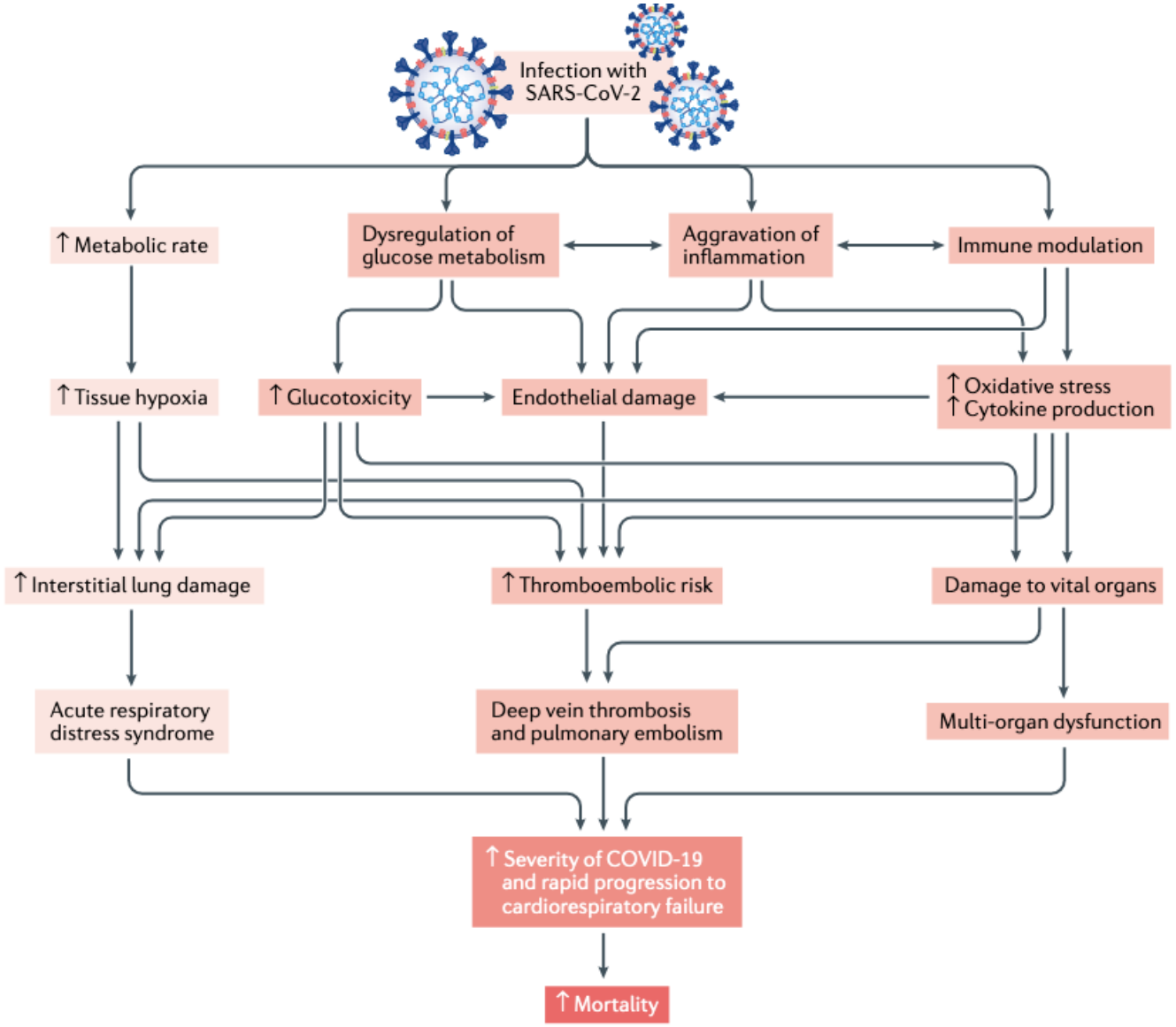
- -Admission serum or point of care glucose (not HbA1c) is a predictor of mortality in persons with Type 2 Diabetes and COVID-19.
- -Those with diabetes and COVID-19 who were intubated had a higher mortality than those who were not intubated.
- -Older age, male gender, or comorbid COPD or MI increased the risk of mortality.
- Race, insurance type had no impact on mortality.

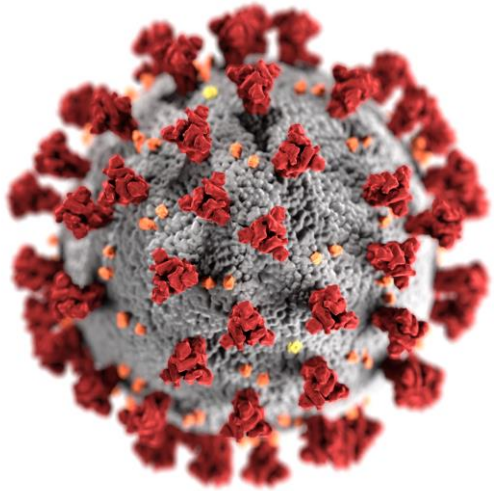
Table 1 | **Clinical characteristics and outcomes in patients with diabetes mellitus and COVID-19**

Region	Study design	Age (years; mean or median)	Number (women/men)	Glycaemic status, HbA_{1c} (%) (proportion)	Comorbidities (%)	Main findings
Diabetes mellitus						
France	Nationwide observational cohort study	69.8 ± 13.0	1,317 (462/855)	8.1 ± 1.9	HTN (77) CVD (41) HF (12) CKD (33) COPD (10)	Primary outcome (MV, death on day 7): 29% Risk factors for primary outcome: BMI Risk factors for mortality: older age, microvascular and macrovascular complications
China	Retrospective cohort study	64.0 (56.2–72.0)	153	<7.0 (16%) 7.0–8.0 (13%) 8.0–9.0 (12%) >9.0 (24%)	HTN (57) CVD (21) CKD (4) COPD (5)	ICU admission: 18% (non-DM 8%) In-hospital death: 20% (non-DM 11%) Risk factors for mortality: age ≥70 years, HTN
USA	Retrospective cohort study	66.7 ± 14.2	178 (68/110)	8.1 ± 2.0	HTN (75) CHD (25) HF (16) CKD (26) COPD (26)	ICU admission: OR 1.59 (95% CI 1.01–2.52)[a] MV: OR 1.97 (95% CI 1.21–3.20)[a] Mortality: OR 2.02 (95% CI 1.01–4.03)[a]
USA	Retrospective cohort study	67.9 ± 13.7	1,276 (649/630)	7.5 ± 2.0	HTN (91) CVD (59) CKD (43) COPD (14)	Death: 33% Risk factors for mortality: insulin treatment before admission, COPD, male sex, older age, higher BMI
T1DM						
UK (England)	Population-based cohort study	46.6 ± 19.6	264,390 (114,710/149,680)	<6.5 (7%) 6.5–7.0 (8%) 7.1–9.9 (50%) ≥10.0 (12%)	HTN (SBP >140 mmHg (17); antihypertensive agents (44)) CKD (10) MI (1) Stroke (1) HF (3)	COVID-19-related deaths: 464 Risk factors for mortality: male sex, older age, renal impairment, non-white ethnicity, socioeconomic deprivation, previous stroke, previous HF, HbA_{1c} ≥10.0% (reference range 6.5–7.0%) BMI (U-shaped, reference range 25.0–29.9 kg/m^2)
UK (England)	Whole population study	46.6 ± 19.5	263,830 (114,495/149,330)	No glycaemic data	CHD (10) CeVD (4) HF (3)	COVID-19-related deaths: 364 72-day mortality: 138 (95% CI 124–153) per 100,000 people Mortality[a]: OR 3.51 (95% CI 3.16–3.90)
France	Nationwide observational cohort study	56.0 ± 16.4	56 (25/31)	8.4 (7.6–9.5)	Microvascular complications (49) Macrovascular complications (33) CKD (29) COPD (4)	Primary outcome (MV, death on day 7): 23% (age <55 years 12%; 55–74 years 24%; ≥75 years 50%)
T2DM						
China	Retrospective cohort study	62 (55–68)	952 (442/510)	Glucose 8.3 mmol/l (6.2–12.4 mmol/l)	HTN (53) CHD (14) CeVD (6) CKD (5) COPD (1)	Well-controlled versus poorly controlled T2DM All-cause mortality: HR 0.14 (95% CI 0.03–0.60) ARDS: HR 0.47 (95% CI 0.27–0.83) Acute kidney injury: HR 0.12 (95% CI 0.01–0.96) Acute heart injury: HR 0.24 (95% CI 0.08–0.71)

Region	Study design	Age (years; mean or median)	Number (women/men)	Glycaemic status, HbA_{1c} (%) (proportion)	Comorbidities (%)	Main findings	Ref.
T2DM (cont.)							
UK (England)	Population-based cohort study	67.5 ± 13.4	2,874,020 (1,267,590/1,606,430)	<6.5 (25%) 6.5–7.0 (21%) 7.1–7.5 (13%) 7.6–9.9 (25%) ≥10.0 (11%)	HTN (SBP >140 mmHg (67); antihypertensive agents (76)) CKD (18) MI (2) stroke (2) HF (5)	COVID-19-related deaths: 10,525 Risk factors for mortality: male sex, older age, renal impairment, non-white ethnicity, socioeconomic deprivation, previous stroke, previous HF, HbA_{1c} ≥7.5% or <6.5% (reference range 6.5%–7.0%), BMI (U-shaped, reference range 25.0–29.9 kg/m^2)	11
UK (England)	Whole population study	67.4 ± 13.4	2,864,670 (1,263,615/1,601,045)	No glycaemic data	CHD (19) CeVD (7) HF (6)	COVID-19-related deaths: 7,434 72-day mortality: 260 (95% CI 254–264) per 100,000 people Mortality[b]: OR 2.03 (95% CI 1.97–2.09)	19
China	Retrospective cohort study	63.0 (56.0–69.0)	1,213 (632/581)	Glucose 8.6 (6.5–12.5) mmol/l	CHD (15) HF (0.2) CeVD (4)	Metformin versus non-metformin Acidosis: HR 2.73 (95% CI 1.04–7.13) Lactic acidosis: HR 4.46 (95% CI 1.11–18.00) Mortality: HR 1.65 (95% CI 0.71–3.86) ARDS: HR 0.85 (95% CI 0.61–1.17) DIC: HR 1.68 (95% CI 0.26–10.90) Acute kidney injury: HR 0.65 (95% CI 0.19–2.24) Acute heart injury: HR 1.02 (95% CI 0.62–1.66)	214

Potential accentuated clinical processes after SARS-CoV-2 infection in people with diabetes mellitus



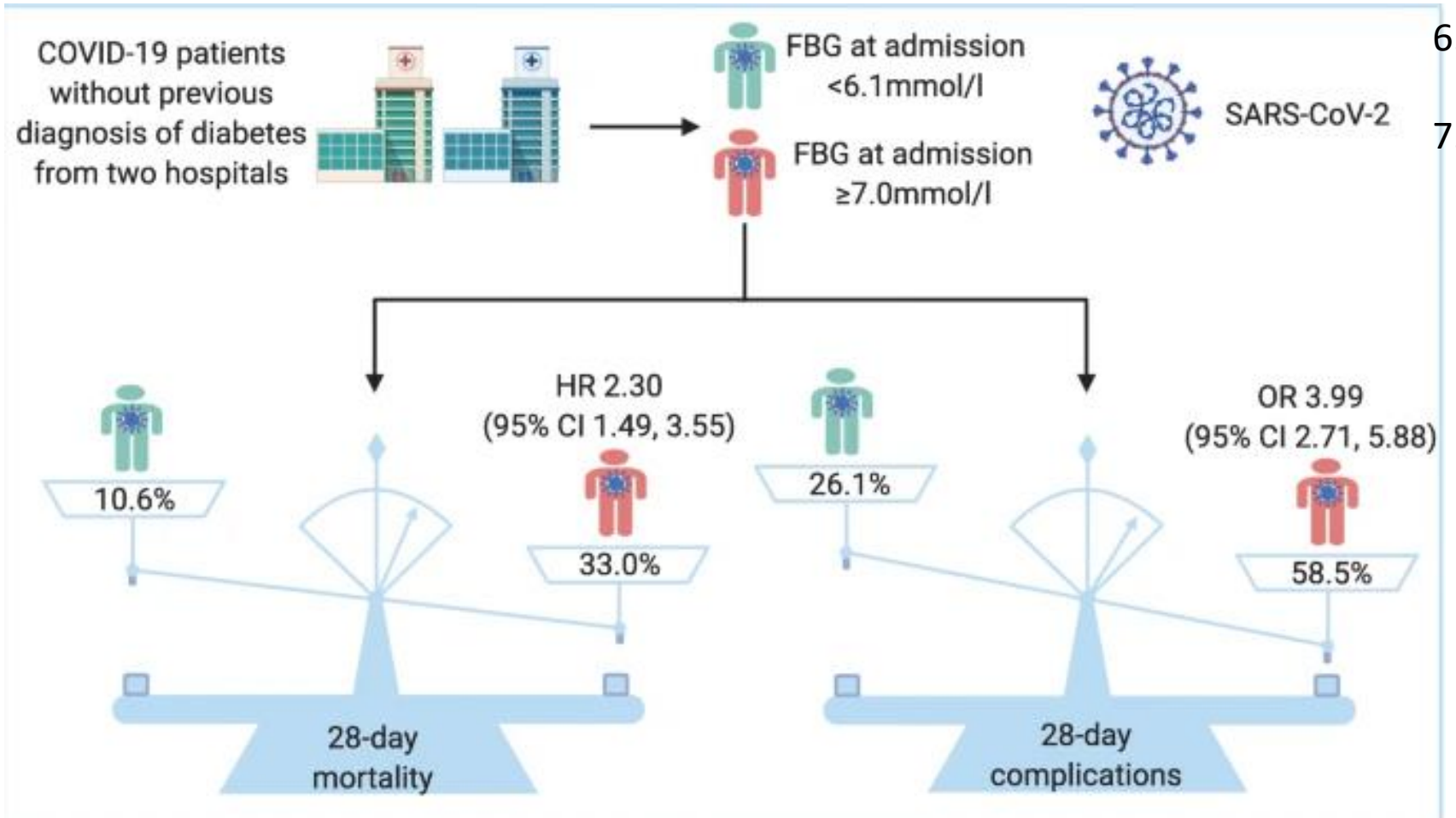


Summary

- In patients admitted to the hospital with COVID-19, diabetes was a major comorbidity

- The rate of admission to intensive care unit (ICU), need for mechanical ventilation, and mortality of patients with diabetes is greater than that of patients without diabetes.

Fasting blood glucose at admission is an independent predictor for 28-day mortality in patients with COVID-19 without previous diagnosis of diabetes: a multi-centre retrospective study

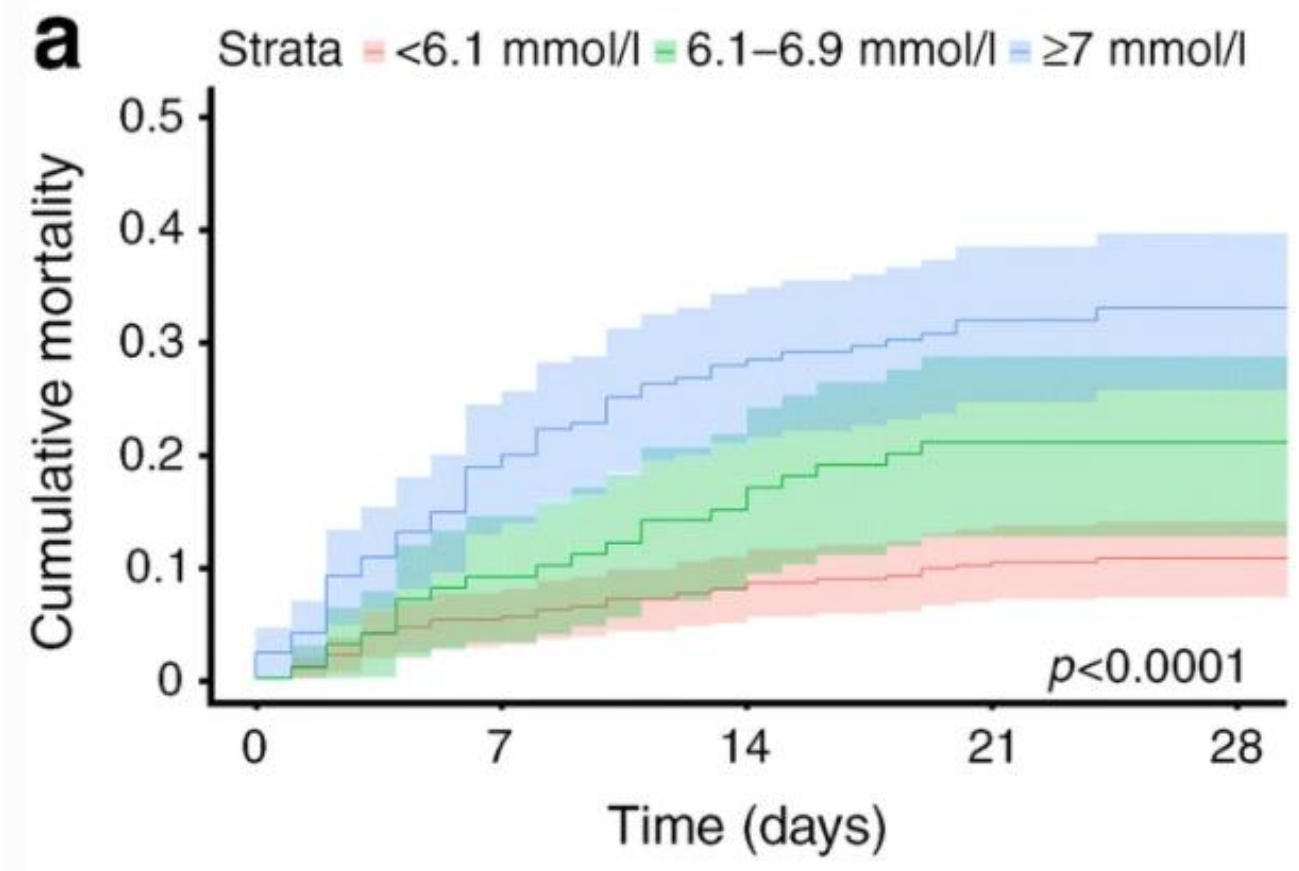


6.1mmol/l = 110mg/dL

7.0mmol/L =126mg/dL

Diabetologia volume 63, pages2102–2111(2020)

Fasting blood glucose at admission is an independent predictor for 28-day mortality in patients with COVID-19 without previous diagnosis of diabetes: a multi-centre retrospective study

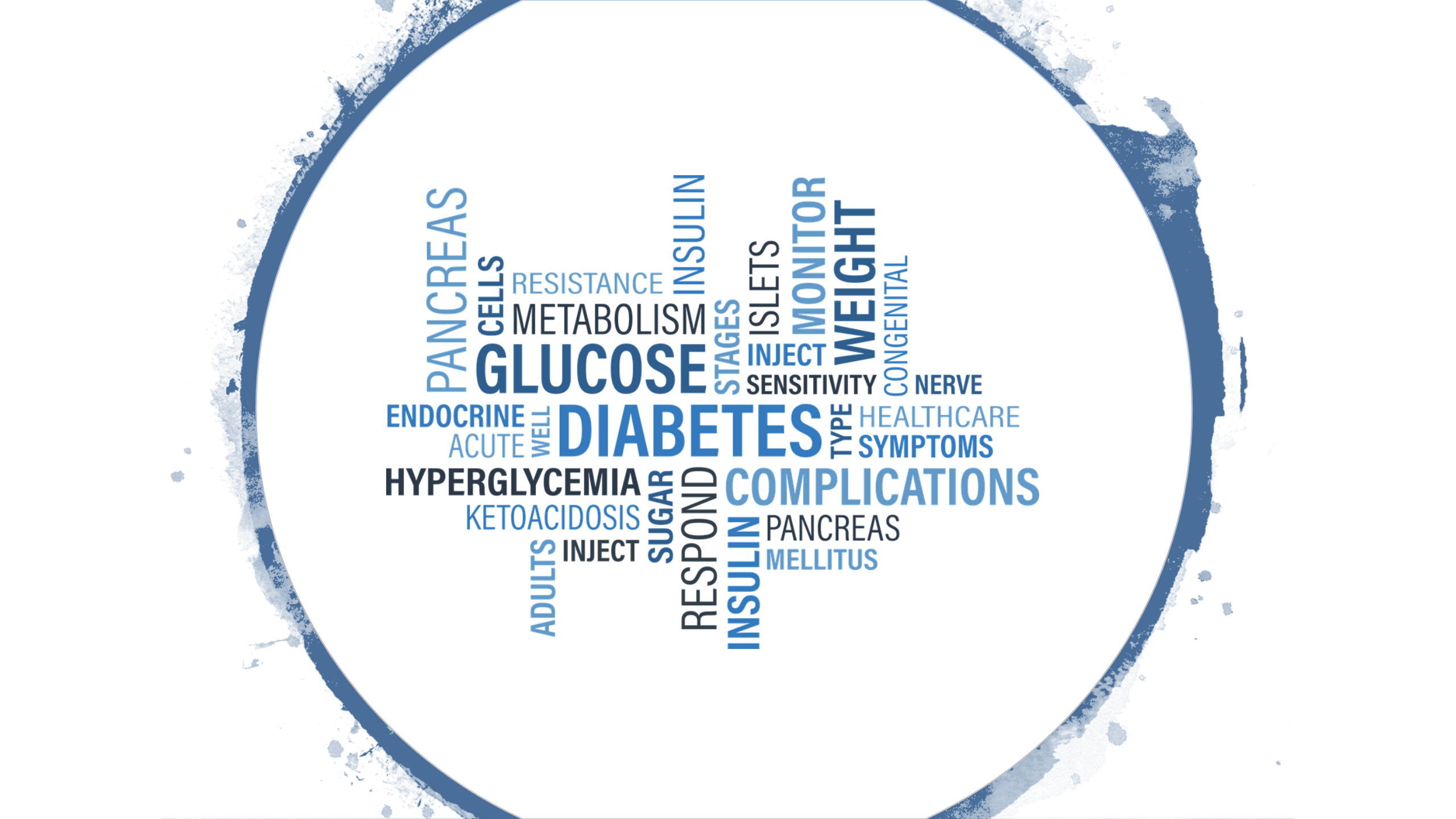


6.1mmol/l = 110mg/dL

7.0mmol/L =126mg/dL

(**a**) Kaplan–Meier survival curves of all COVID-19 patients stratified by FBG

Diabetologia volume 63, pages2102–2111(2020)


PANCREAS
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ENDOCRINE
ACUTE
WELL
DIABETES
TYPE
HEALTHCARE
SYMPTOMS
HYPERGLYCEMIA
COMPLICATIONS
KETOACIDOSIS
SUGAR
RESPOND
INSULIN
PANCREAS
MELLITUS
ADULTS
INJECT

Management of diabetes in the time of COVID-19

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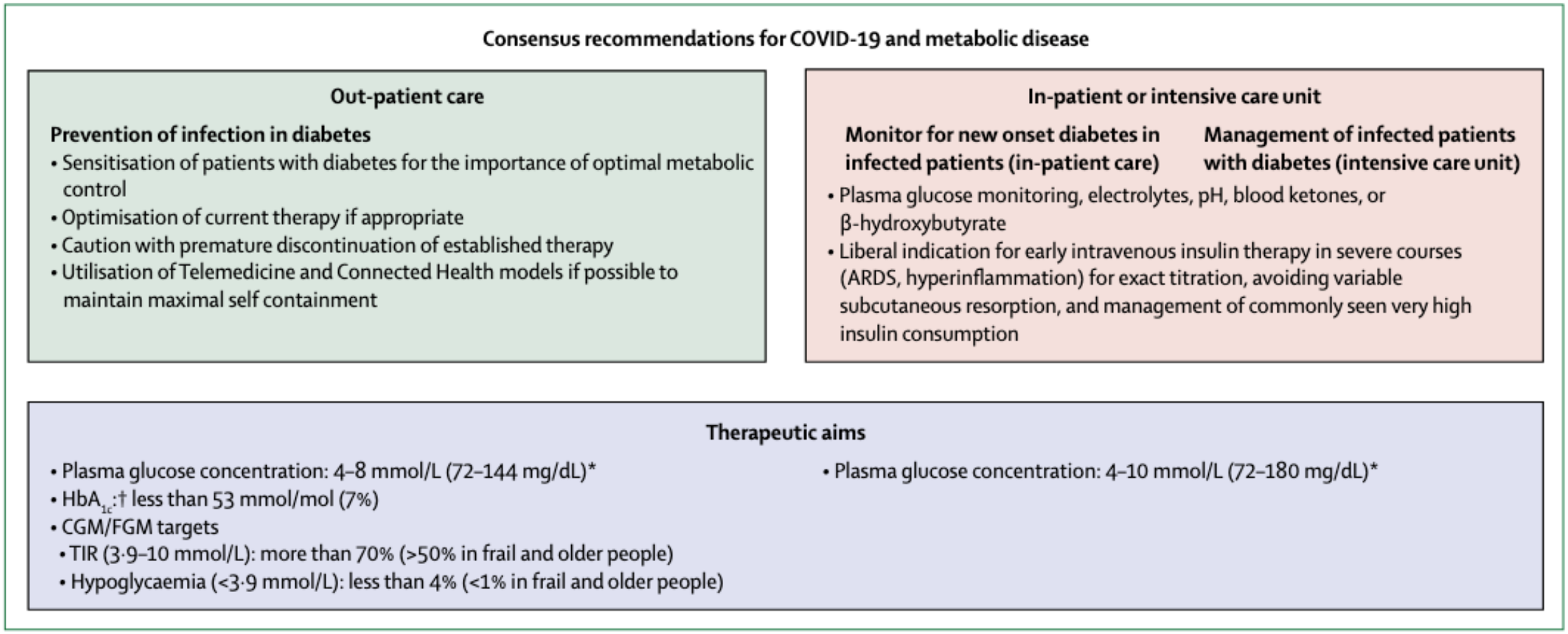
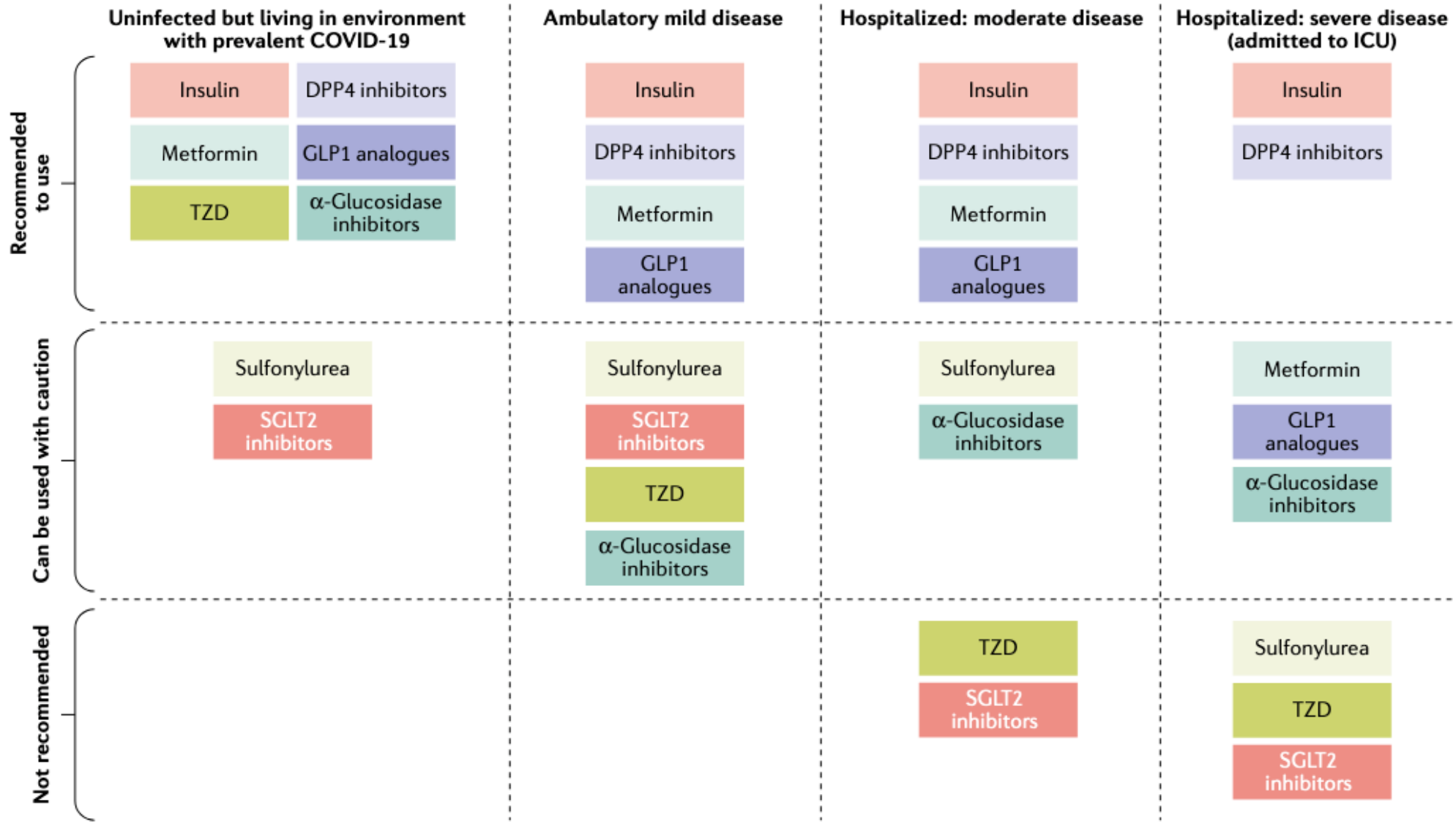


Figure: **Flowchart for metabolic screening and type 1 and 2 diabetes management of patients with COVID-19**

Older patients refers to those aged 70 and above. ARDS=Acute Respiratory Distress Syndrom. CGM=Continous Glucose Measurement. FGM=Flash Glucose Measurement. HbA_{1c}=haemoglobin A_{1c}. TIR=time in range. *Target concentrations for lower plasma glucose can be adjusted to 5 mmol/L (90 mg/dL) in frail patients. †HbA_{1c} testing might not be possible at the time, but previous measurements if available allow for differentiation of chronic and acute decompensation.

Lancet Diabetes Endocrinol2020; 8: 546–50

Use of antidiabetic medications in patients with T2DM and COVID-19



Nature Reviews Endocrinology **volume 17**, pages11–30(2021)

***Panel:* Consideration of potential metabolically interfering effects of drugs in suspected or COVID-19 positive patients with type 2 diabetes**

Metformin

- Dehydration and lactic acidosis will probably occur if patients are dehydrated, so patients should stop taking the drug and follow sick day rules
- During illness, renal function should be carefully monitored because of the high risk of chronic kidney disease or acute kidney injury

Sodium-glucose-co-transporter 2 inhibitors

- These include canagliflozin, dapagliflozin, and empagliflozin
- Risk of dehydration and diabetic ketoacidosis during illness, so patients should stop taking the drugs and follow sick day rules
- Patients should avoid initiating therapy during respiratory illness
- Renal function should be carefully monitored for acute kidney injury

Glucagon-like peptide-1 receptor agonists

- These include albiglutide, dulaglutide, exenatide-extended release, liraglutide, lixisenatide, and semaglutide
- Dehydration is likely to lead to a serious illness so patients should be closely monitored
- Adequate fluid intake and regular meals should be encouraged

Dipeptidyl peptidase-4 inhibitors

- These include alogliptin, linagliptin, saxagliptin, and sitagliptin
- These drugs are generally well tolerated and can be continued

Insulin

- Insulin therapy should not be stopped
- Regular self-monitoring of blood-glucose every 2–4 hours should be encouraged, or continuous glucose monitoring
- Carefully adjust regular therapy if appropriate to reach therapeutic goals according to diabetes type, comorbidities, and health status

Connected Health models and Telemedicine should be used to continue regular reviews and self-management education programmes virtually and ensure patients are adherent to therapy.

Lancet Diabetes Endocrinol2020; 8: 546–50

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