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Morning Brief :
Scientific Review

8 June 2020

The purpose of the Morning Brief is to summarize and present key information, research articles and other relevant publications pertaining to critical care and COVID-19.

Stellenbosch University Research Response Team

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Content

Covid-19 statistics
Diabetes and Covid-19

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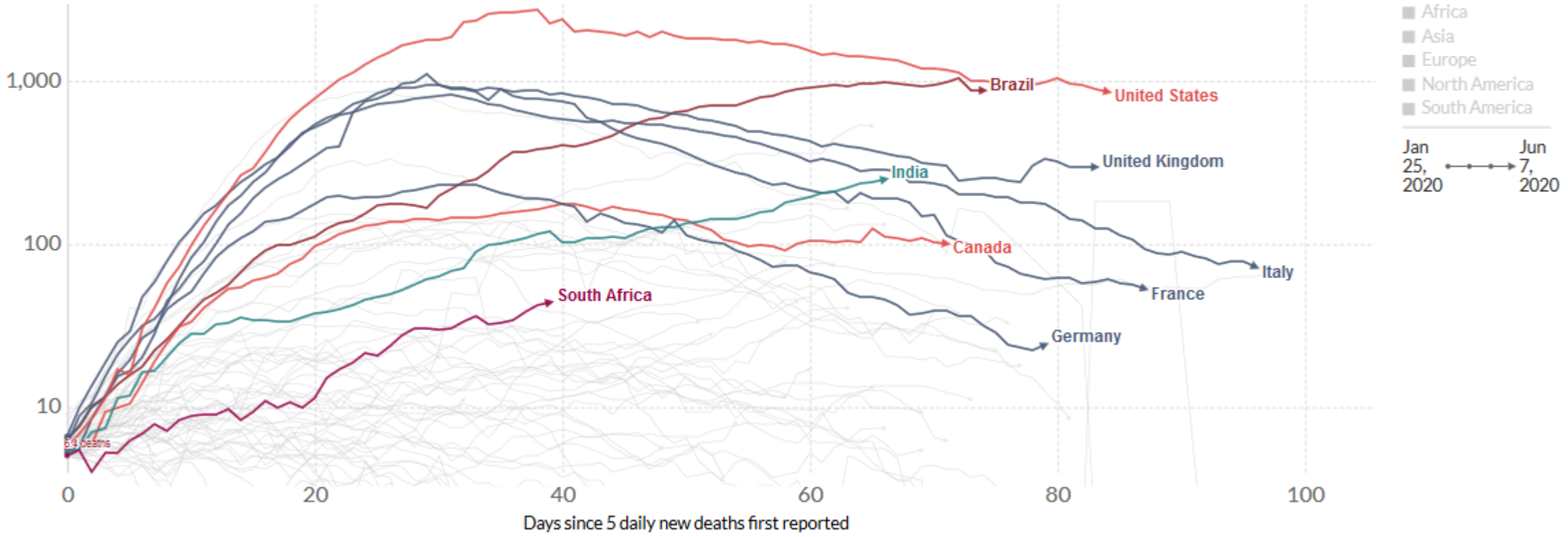
Daily new confirmed COVID-19 deaths

Our World in Data

Shown is the rolling 7-day average. Limited testing and challenges in the attribution of the cause of death means that the number of confirmed deaths may not be an accurate count of the true number of deaths from COVID-19.

LINEAR LOG



Source: European CDC – Situation Update Worldwide - Data last updated 7th Jun, 15:32 (GMT+02:00), European CDC – Situation Update Worldwide

▶ Jan 25, 2020 Jun 7, 2020

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COVID-19 STATISTICS IN SA

TESTS CONDUCTED	POSITIVE CASES IDENTIFIED	RECOVERIES	DEATHS	NEW CASES
891668	45973	24258	952	2539

SATURDAY
06
JUNE
2020

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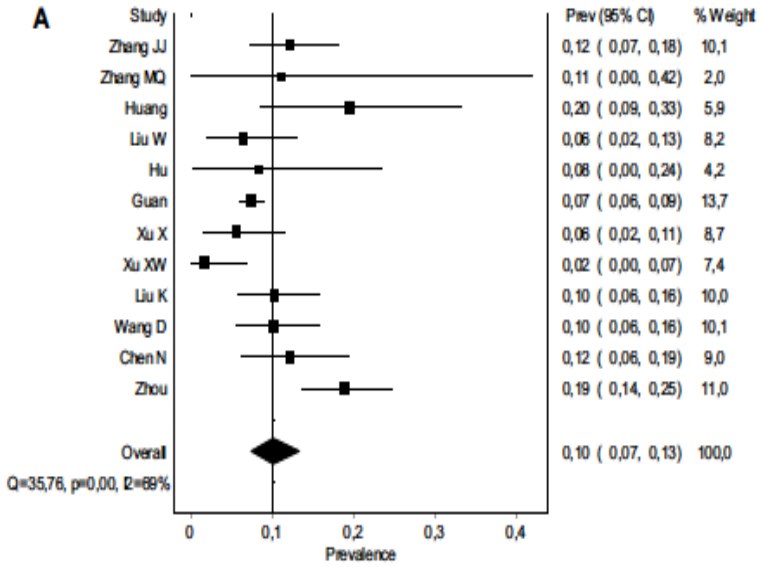
Diabetes Mellitus and Covid-19

- Are people living with Diabetes (PLWD) more susceptible to Covid-19?
- Are PLWD at increased risk of severe infection?
- Are all types of Diabetes at increased risk for severe Covid-19?
- Changes in insulin requirements during admission for severe Covid-19?
- Can SARS-CoV-2 cause DM?
- Modifiable factors in DM – Does glucose control alter the outcome?
    - Prior to admission
    - During admission
- What is the phenotype associated with adverse outcome in PLWD?

Are people with Diabetes Mellitus more susceptible to Covid-19?

- China (Figure A)
  - Prevalence DM + Covid-19 10.3%
  - Nationwide DM prevalence 10.9%-12.3%

- Italy
  - Prevalence DM + Covid-19 8.9% (95% CI 5.3–14.6)
  - Regional DM prevalence 6.2% -11.0%

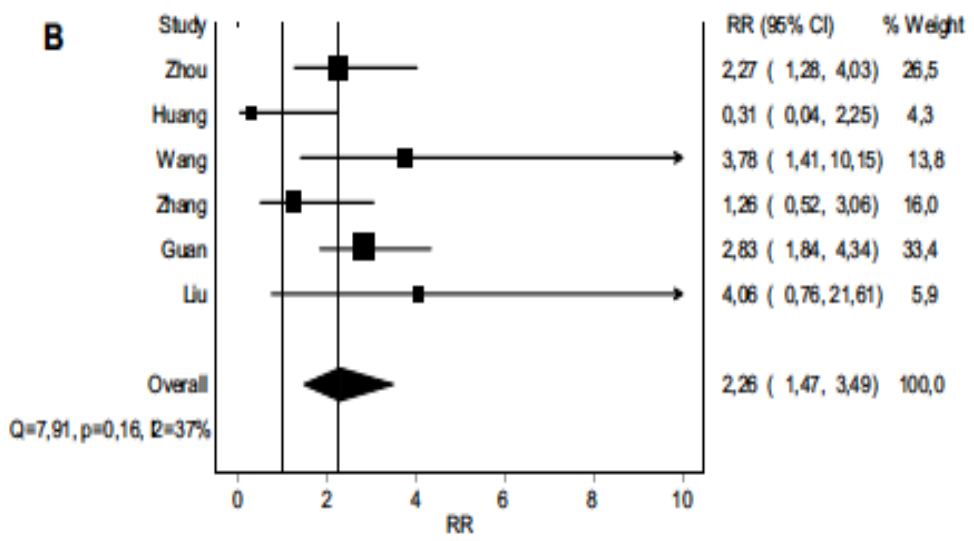


Conclusion

- Background prevalence of DM reflected
- People with DM not more susceptible

Fadini GP, Morieri ML, Longato E, Avogaro A. Prevalence and impact of diabetes among people infected with SARS-CoV-2. Journal of Endocrinological Investigation. 2020 Mar 28:1.

Are people with DM at risk of severe Covid-19?



RR 2.26 (95% CI 1.47–3.49)

Risk for Covid-19 mortality

- 2.3% in general population
- 7.3% in DM

PLWD have a more adverse outcome

Fadini GP, Morieri ML, Longato E, Avogaro A. Prevalence and impact of diabetes among people infected with SARS-CoV-2. Journal of Endocrinological Investigation. 2020 Mar 28:1.

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Glycemic Characteristics and Clinical Outcomes of COVID-19 Patients Hospitalized in the United States

Journal of Diabetes Science and Technology
1–9

DOI: 10.1177/1932296820924469
journals.sagepub.com/home/dst
SAGE

Bruce Bode, MD[1], Valerie Garrett, MD, MPH[2],
Jordan Messler, MD, SFHM, FACP[2], Raymie McFarland, CSSBB[2],
Jennifer Crowe, MHA, CPHQ, ASQ-SSBB[2],
Robby Booth, BS, LSSMBB, PSPO[2],
and David C. Klonoff, MD, FACP, FRCPE[3]

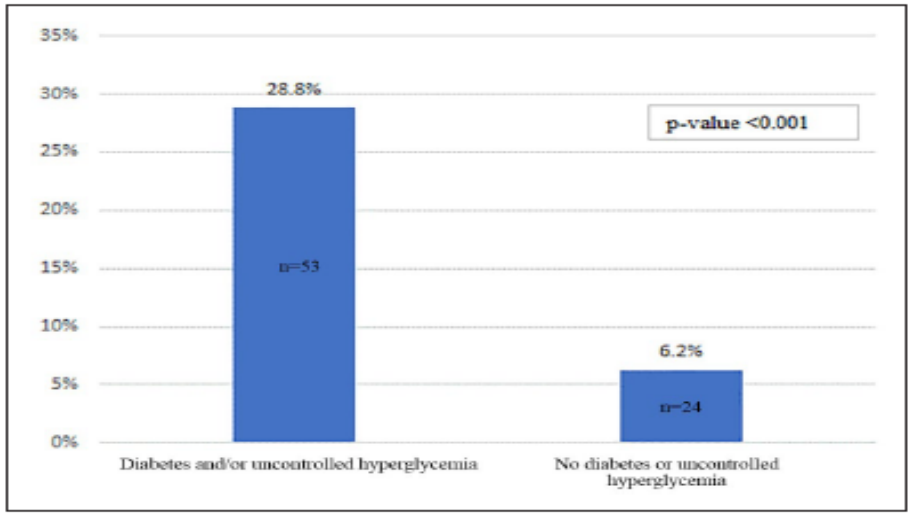

Figure 3. Mortality rates among patients who were discharged or died comparing diabetes and/or uncontrolled hyperglycemia (n = 184) with patients without diabetes or hyperglycemia (n = 386).

Table 4. Clinical Outcomes Among Patients Who Were Discharged or Died Comparing Diabetes and/or Uncontrolled Hyperglycemia (n=184) with Patients without Diabetes or Hyperglycemia (n=386).

Variable	+ Diabetes and/or Uncontrolled Hyperglycemia (n=184)	- Diabetes or Uncontrolled Hyperglycemia (n=386)	p-value
Patients, n (%)	184 (32.3)	386 (67.7)	
Died in hospital, n (%)	53 (28.8)	24 (6.2)	<0.001
Mean duration from admission to death (SD)	8.7 (±4.6)	7.9 (±4.4)	0.494
Median duration from admission to death (IQR)	7.5 (2.0-20.1)	6.9 (1.3-20.4)	0.560
Discharged Alive From hospital, n (%)	131 (71.2)	362 (93.8)	
Mean LOS in days (SD)	6.2 (±3.7)	5.0 (±3.3)	<0.001
Median LOS in days (IQR)	5.7 (1.1-24.6)	4.3 (1.0-21.2)	<0.001

DM associated with increased mortality & length of stay in hospital if alive

All types of Diabetes are independently associated with a significant increased risk of death with Covid-19

Table S2: COVID-19 related hospital deaths in England between 1st March 2020 and 11th May 2020; an alternative method of defining type of diabetes based on the NDA care processes and treatment targets report, multivariate logistic regression

	Death	Odds ratio	95% CI lower	95% CI upper	P value
Age	<40	0·01	0·01	0·01	<0·001
	40-49	0·11	0·10	0·12	<0·001
	50-59	0·36	0·34	0·39	<0·001
	60-69	1·00			
	70-79	2·63	2·51	2·75	<0·001
	80+	9·14	8·77	9·52	<0·001
Sex	Female	1·00			
	Male	1·94	1·89	1·99	<0·001
Deprivation quintile	IMD 1 (most deprived)	1·89	1·81	1·98	<0·001
	IMD 2	1·54	1·48	1·61	<0·001
	IMD 3	1·26	1·21	1·32	<0·001
	IMD 4	1·14	1·09	1·19	<0·001
	IMD 5 (least deprived)	1·00			
	Unknown	2·20	1·54	3·16	<0·001
Region	London	1·00			
	South West	0·23	0·22	0·25	<0·001
	South East	0·48	0·46	0·51	<0·001
	Midlands	0·57	0·54	0·59	<0·001
	East of England	0·60	0·58	0·63	<0·001
	North West	0·65	0·62	0·68	<0·001
	North East and Yorkshire	0·49	0·47	0·51	<0·001
Diabetes status	No diabetes	1·00			
	Type 1	3·30	2·91	3·74	<0·001
	Type 2	2·04	1·99	2·10	<0·001
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Ethnic group	White	1·00			
	Asian	1·36	1·29	1·43	<0·001
	Mixed	1·43	1·23	1·66	<0·001
	Black	1·72	1·62	1·82	<0·001
	Other Ethnic Groups	1·11	1·02	1·22	0·02
	Unknown	0·33	0·31	0·35	<0·001

Type 1 and Type 2 diabetes and COVID-19 related mortality in England: a cohort study in people with diabetes

Naomi Holman PhD[1,2,3], Peter Knighton MPhysc[2], Partha Kar MD[1,4], Jackie O'Keefe MSc[2], Matt Curley BA[2], Andy Weaver MSc[1], Emma Barron MSc[5], Chirag Bakhai MBA[1], Kamlesh Khunti MD[6], Nick Wareham PhD[7], Naveed Sattar MD[3], Bob Young MD[8], Jonathan Valabhji MD[1,9,10]

MPhysc PK, Partha Kar MD, BA MC, Chirag Bakhai MB, Kamlesh Khunti MD, Naveed Sattar MD, Bob Young MD, Jonathan Valabhji MD. Type 1 and Type 2 diabetes and COVID-19 related mortality in England: a cohort study in people with diabetes.

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Changes in insulin requirements during admission for severe Covid-19?

	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	2	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

29% Increase in insulin requirements in-hospital

37.5% Initiate insulin in-hospital

12.5% ~ 1/10 DKA

Guo et al Diabetes Metab Res Rev. 2020;e3319.

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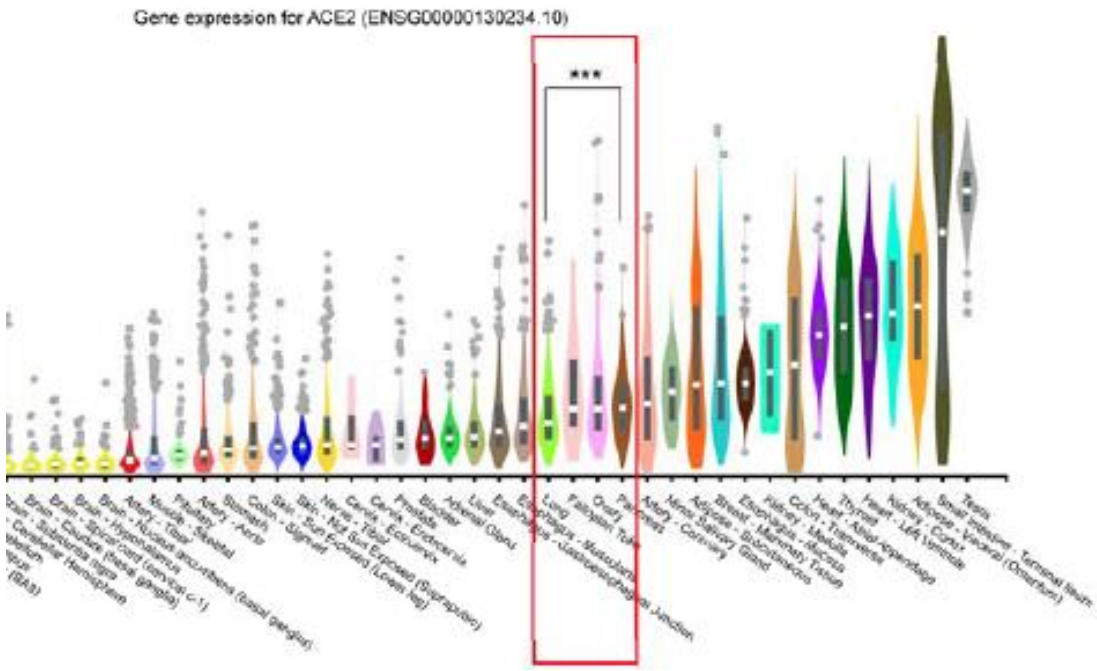
Can SARS-CoV-2 cause Diabetes?

Highly ACE2 Expression in Pancreas May Cause Pancreas Damage After SARS-CoV-2 Infection

Furong Liu[1,2], Xin Long[1,2], Wenbin Zou[3], Minghao Fang[4], Wenjuan Wu[5], Wei Li[6], Bixiang Zhang[1,2], Wanguang Zhang[1,2], Xiaoping Chen[1,2], Zhanguo Zhang[1,2*]



Acta Diabetol (2010) 47:193–199
DOI 10.1007/s00592-009-0109-4

ORIGINAL ARTICLE

Binding of SARS coronavirus to its receptor damages islets and causes acute diabetes

Jin-Kui Yang · Shan-Shan Lin · Xiu-Juan Ji · Li-Min Guo

medRxiv preprint doi: https://doi.org/10.1101/2020.02.28.20029181

Cell Metabolism

Clinical and Translational Report

Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes

Lihua Zhu,[1,2,28] Zhi-Gang She,[1,2,28] Xu Cheng,[1,2,28] Juan-Juan Qin,[1,2,28] Xiao-Jing Zhang,[1,2,28] Jingjing Cai,[3] Haitao Wang,[4] Jing Xie,[1] Wenxin Wang,[1,2] Haomiao Li,[1,2] Peng Zhang,[2,5] Xiaohui Song,[2] Xi Chen,[4] Mei Xiang Chaozheng Zhang,[2] Liangjie Bai,[2] Da Xiang,[2] Ming-Ming Chen,[1,2] Yanqiong Liu,[2] Youqin Yan,[7] Mingyu Liu,[8] Weiming Mao,[9] Jinjing Zou,[10] Liming Liu,[11] Guohua Chen,[12] Pengcheng Luo,[13] Bing Xiao,[14] Changjiang Zhan Zixiong Zhang,[15] Zhigang Lu,[16] Junhai Wang,[17] Haofeng Lu,[18] Xigang Xia,[19] Daihong Wang,[20] Xiaofeng Liao Gang Peng,[22] Ping Ye,[6] Jun Yang,[23] Yufeng Yuan,[4] Xiaodong Huang,[24,*] Jiao Guo,[25,*] Bing-Hong Zhang,[26,*] and Hongliang Li[1,2,5,27,29,*]

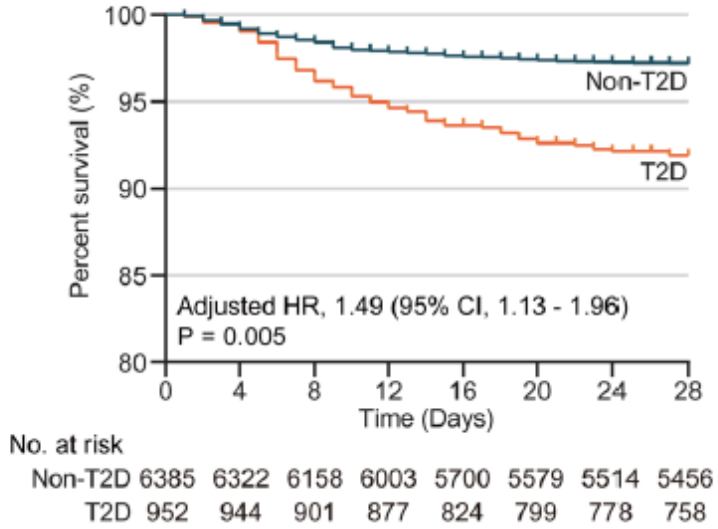


Table S3. Incidence for primary and secondary outcomes in T2D and non-T2D groups

Outcomes	Total (N=7337)	T2D (n=952)	Non-T2D (n=6385)	*P* value[a]
All-cause mortality, n (%)	248(3.4%)	74(7.8%)	174(2.7%)	<0.001
Septic shock, n (%)	76(1.3%)	27(3.8%)	49(1.0%)	<0.001
ARDS, n (%)	622(8.5%)	161(16.9%)	461(7.2%)	<0.001
DIC, n (%)	18(0.3%)	5(0.5%)	13(0.2%)	0.074
Acute kidney injury, n (%)	86(1.2%)	37(3.9%)	49(0.8%)	<0.001
Acute heart injury, n (%)	260(3.5%)	69(7.3%)	191(3.0%)	<0.001

Abbreviations: ARDS, Acute respiratory distress syndrome; DIC, disseminated intravascular coagulation.

a, The P value was calculated by Fisher's exact test or $\chi 2$ test.

Can outcome be altered with glucose control?

BMI T2D 24.7 (22.0–26.4) vs 23.4 (21.0–26.0) no T2DM

Adjusted for age, gender and indicators of severity of Covid-19 infection

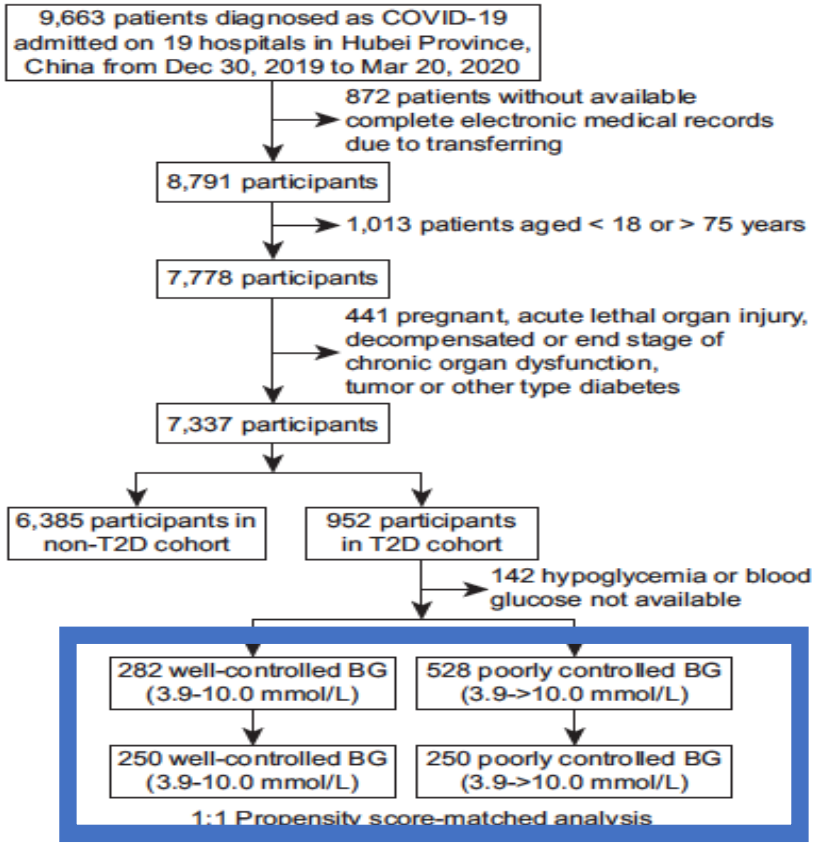


Table S5. Incidence for primary and secondary outcomes of patients in the well-controlled or poorly-controlled BG group.

Outcome	Total (N=810)	Well-controlled (n=282)	Poorly-controlled (n=528)	*P* value[a]
All-cause mortality, n (%)	61(7.5%)	3(1.1%)	58(11.0%)	<0.001
Septic shock, n (%)	19(3.1)	0(0.0%)	19(4.7%)	0.004
ARDS, n (%)	133(16.4%)	20(7.1%)	113(21.4%)	<0.001
DIC, n (%)	3(0.4%)	0(0.0%)	3(0.6%)	0.555
Acute kidney injury, n (%)	22(2.7%)	2(0.7%)	20(3.8%)	0.019
Acute heart injury, n (%)	56(6.9%)	4(1.4%)	52(9.9%)	<0.001

Improved in hospital glucose control = improved outcome in severe Covid-19

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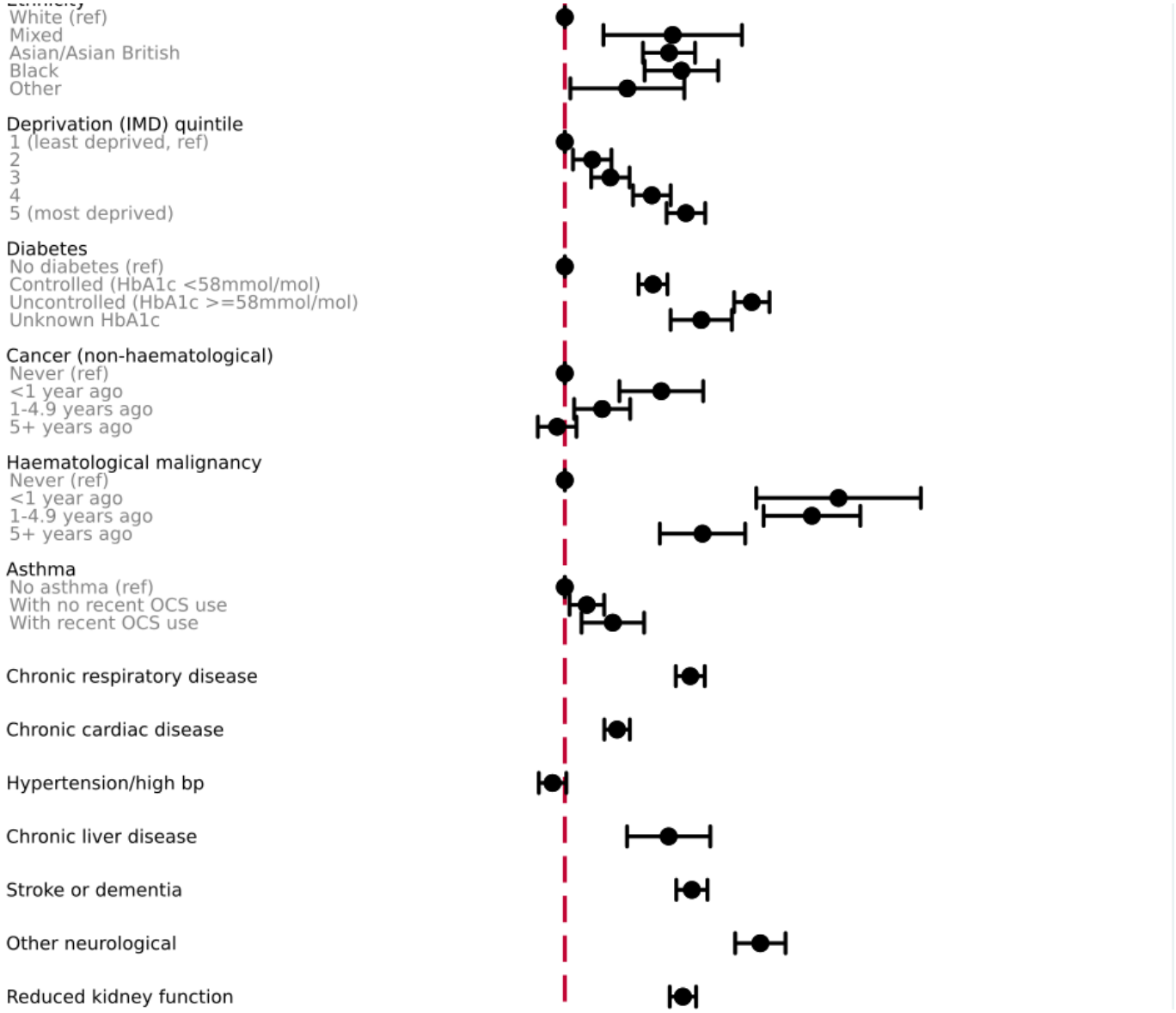
OpenSAFELY: factors associated with COVID-19-related hospital death in the linked electronic health records of 17 million adult NHS patients.

he OpenSAFELY Collaborative; Elizabeth Williamson[2*], Alex J Walker[1*], Krishnan Bhaskaran Seb Bacon[1*], Chris Bates[3*], Caroline E Morton[1], Helen J Curtis[1], Amir Mehrkar[1], David Evans Peter Inglesby[1], Jonathan Cockburn[3], Helen I McDonald[2,5], Brian MacKenna[1], Laurie Tomlinson[2], Ian J Douglas[2], Christopher T Rentsch[2], Rohini Mathur[2], Angel Wong[2], Richard Grieve[2], David Harrison[4], Harriet Forbes[2], Anna Schultze[2], Richard Croker[1], John Parry[3], Frar Hester[3], Sam Harper[3], Raf Perera[1], Stephen Evans[2], Liam Smeeth[2,5]†, Ben Goldacre[1]†‡

The DataLab, Nuffield Dept of Primary Care Health Sciences, University of Oxford, OX2 6GG
London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT
TPP, TPP House, 129 Low Lane, Horsforth, Leeds, LS18 5PX
ICNARC, 24 High Holborn, Holborn, London WC1V 6AZ
NIHR Health Protection Research Unit (HPRU) in Immunisation

Fully adjusted
HR 2.36 (2.18-2.56) HbA1c > 7.5%
HR 1.50 (1.40-1.60) HbA1c < 7.5%



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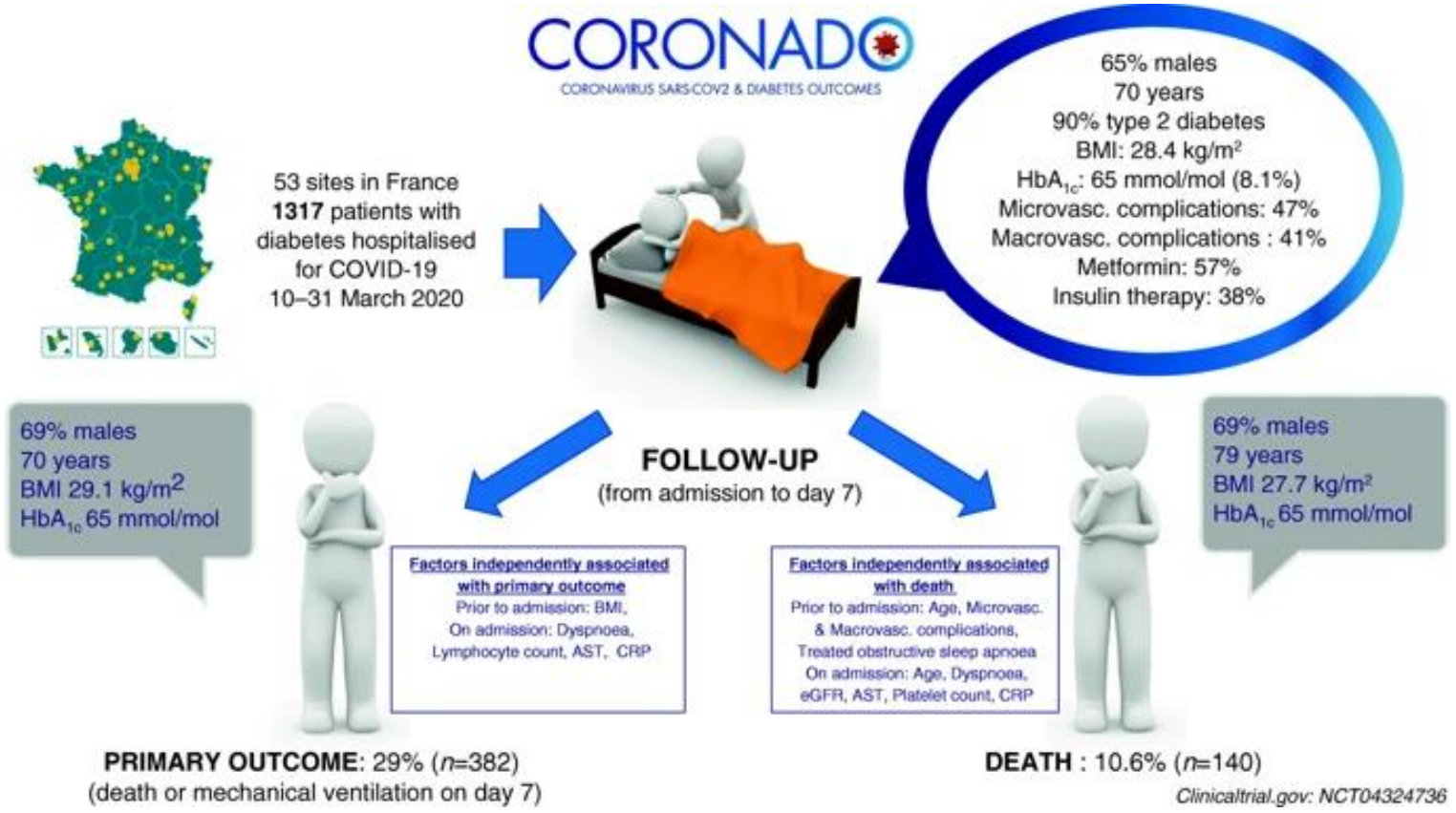
What is the T2DM phenotype associated with Covid-19 severity?



Cariou B, Hadjadj S, Wargny M, Pichelin M, Al-Salameh A, Allix I, Amadou C, Arnault G, Baudoux F, Bauduceau B, Borot S. Phenotypic characteristics and prognosis of inpatients with COVID-19 and diabetes: the CORONADO study. Diabetologia. 2020 May 29:1.

This summary was prepared by Dr Ankia Coetzee as part of the daily brief to the TBH ICU team.