

## **Supplemental Material**

- I.** **Page 2** – List of ISIC sites and investigators
- II.** **Page 3** – Supplemental Table 1. Associations between DM and thrombo-inflammation biomarkers in COVID-19
- III.** **Page 4** – Supplemental Table 2. Multivariable risk model for the primary outcome among COVID-19 individuals with DM
- IV.** **Page 6** – Supplemental Table 3. Multivariable risk model for individual outcomes among COVID-19 individuals with DM
- V.** **Page 7** – Supplemental Table 4. Correlation between thrombo-inflammatory biomarkers, glucose coefficient of variation, and insulin in COVID-19
- VI.** **Page 8** – Supplemental Figure 1. Associations between glucose, insulin, and combined outcome stratified by DM among M2C2
- VII.** **Page 9** – Supplemental Table 5. Associations between glucose, insulin, and combined outcome with suPAR among individuals with DM in M2C2

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**Supplemental Table 1. Associations between DM and thrombo-inflammation biomarkers in COVID-19**

	SuPAR	C-reactive protein	Biomarker, standardized $\beta$ (95%CI)				
			Lactate dehydrogenase	Interleukin-6	Procalcitonin	Ferritin	D-dimer
Diabetes mellitus	<b>0.10 (0.05-0.15)</b>	0.04 (-0.01, 0.09)	-0.02 (-0.07, 0.04)	0.05 (-0.04, 0.13)	0.00 (-0.06, 0.05)	0.03 (-0.02, 0.08)	0.04 (-0.02, 0.09)
Age, per 10 years	0.05 (-0.01-0.11)	0.00 (-0.06, 0.06)	-0.06 (-0.12, 0.00)	-0.06 (-0.15, 0.04)	0.03 (-0.03, 0.09)	0.02 (-0.04, 0.08)	0.00 (-0.06, 0.06)
Male sex	0.00 (-0.05, 0.05)	0.03 (-0.02, 0.08)	0.08 (0.03, 0.14)	0.06 (-0.02, 0.14)	0.01 (-0.04, 0.06)	0.12 (0.07, 0.17)	0.03 (-0.02, 0.08)
Body-mass index, per 5 kg/m <sup>2</sup>	0.08 (0.03-0.13)	0.06 (0.01, 0.12)	0.08 (0.03, 0.14))	0.00 (-0.09, 0.09)	-0.02 (-0.08, 0.03)	0.02 (-0.04, 0.07)	-0.02 (-0.08, 0.03)
Black race	0.00 (-0.05, 0.05)	0.06 (0.01, 0.10)	0.10 (0.05, 0.15)	-0.02 (-0.08, 0.05)	-0.01 (-0.04, 0.06)	0.08 (0.03, 0.13)	-0.03 (-0.08, 0.02)
Hypertension	0.05 (-0.00, 0.11)	-0.01 (-0.07, 0.05)	-0.03 (-0.09, 0.03)	0.04 (-0.05, 0.14)	-0.04 (-0.10, 0.02)	0.00 (-0.06, 0.06)	0.03 (-0.03, 0.09)
Coronary artery disease	0.02 (-0.03, 0.07)	0.00 (-0.05, 0.05)	-0.03 (-0.09, 0.03)	-0.03 (-0.11, 0.05)	-0.01 (-0.06, 0.05)	-0.04 (-0.10, 0.01)	-0.02 (-0.08, 0.03)
Heart failure	0.10 (0.05, 0.15)	-0.01 (-0.07, 0.04)	0.03 (-0.03, 0.08)	0.01 (-0.06, 0.08)	0.00 (-0.05, 0.05)	-0.02 (-0.07, 0.03)	0.00 (-0.05, 0.05)

Values in bold are statistically significant at P<0.05

**Supplemental Table 2. Multivariable risk model for the composite outcome among COVID-19 individuals with DM**

	Composite Outcome			
	Univariable	P-value	Multivariable*	P-value
	OR (95% CI)		OR (95% CI)	
<b>Clinical risk factors</b>				
Age, per 10 years	1.00 (0.89, 1.11)	0.961	0.99 (0.85, 1.15)	0.93
Male sex	1.17 (0.85, 1.60)	0.339	1.32 (0.92, 1.89)	0.10
Black race	1.43 (1.02, 2.01)	<b>0.041</b>	1.27 (0.87, 1.85)	0.16
BMI, per 5 kg/m <sup>2</sup>	1.15 (1.06, 1.26)	<b>0.001</b>	1.18 (1.06, 1.31)	<b>0.002</b>
History of smoking	1.35 (0.99, 1.85)	<b>0.05</b>	1.29 (0.91, 1.83)	0.15
Hypertension	1.58 (1.04, 2.38)	<b>0.032</b>	1.35 (0.84, 2.18)	0.28
Coronary artery disease	0.88 (0.61, 1.26)	0.49	0.91 (0.59, 1.40)	0.53
Heart failure	1.06 (0.71, 1.60)	0.76	0.97 (0.60, 1.56)	0.67
Chronic kidney disease	1.02 (0.72, 1.44)	0.93	0.73 (0.47, 1.13)	0.15
Admission eGFR, per 5 units lower	1.05 (1.02, 1.08)	<0.001	1.07 (1.03, 1.10)	<0.001
<b>Diabetes type</b>				
Type 1	0.69 (0.31, 1.54)	0.37	-	-
Insulin use	0.94 (0.64, 1.29)	0.71	-	-
<b>Diabetes medications</b>				
Metformin	0.96 (0.70, 1.30)	0.78	-	-
SGLT-2 inhibitor	0.90 (0.43, 1.92)	0.79	-	-
GLP-1 agonist	1.80 (0.94, 3.43)	0.08	-	-
Sulfonylurea	1.30 (0.84, 2.02)	0.24	-	-
DPP-4	1.40 (0.83, 2.37)	0.21	-	-
Thiazolidinediones	1.66 (0.33, 8.27)	0.54	-	-
<b>Inflammatory biomarkers<sup>†</sup></b>				
SuPAR, ng/mL	1.89 (1.44, 2.47)	<0.001	1.75 (1.26, 2.42)	<0.001
C-reactive protein, mg/dL	1.51 (1.31, 1.73)	<0.001	1.55 (1.30, 1.84)	<0.001
Lactate dehydrogenase, IU/L	3.14 (2.46, 4.75)	<0.001	3.36 (2.32, 4.84)	<0.001
Interleukin-6, pg/mL	1.47 (1.27, 1.71)	<0.001	1.50 (1.27, 1.78)	<0.001
Procalcitonin, ng/mL	1.97 (1.55, 2.49)	<0.001	1.94 (1.49, 2.54)	<0.001
Ferritin, ng/mL	1.36 (1.22, 1.53)	<0.001	1.37 (1.20, 1.56)	<0.001
D-dimer, FEU mg/L	1.40 (1.26, 1.56)	<0.001	1.58 (1.38, 1.81)	<0.001

**Glucose range (mg/dL) at admission, n (%)**

< 54 – 69	1.11 (0.20, 6.15)	0.91	1.32 (0.23, 7.51)	0.84
70 – 180	1.0 [reference]		1.0 [reference]	
181 – 250	1.63 (1.09, 2.44)	<b>0.018</b>	1.85 (1.20, 2.83)	<b>0.012</b>
> 250	2.49 (1.64, 3.78)	<b>&lt;0.001</b>	2.51 (1.60, 3.94)	<b>&lt;0.001</b>

\*Multivariable risk model adjusted for age, sex, race, BMI, smoking, history of hypertension, coronary artery disease, congestive heart failure, and chronic kidney disease, admission eGFR (estimated glomerular filtration rate), and glucose categories. †Each biomarker added to multivariable risk model separately; each biomarker is log<sub>2</sub> transformed.

**Supplemental Table 3. Multivariable risk model for the primary outcome among COVID-19 individuals with DM**

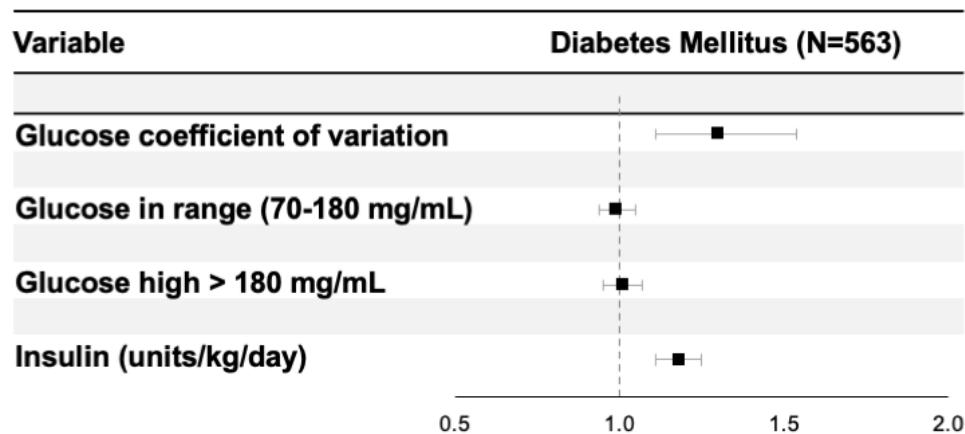
	In-hospital death		Mechanical ventilation		Renal replacement therapy	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
<b>Clinical risk factors</b>						
Age, per 10 years	1.44 (1.17, 1.77)	<b>&lt;0.001</b>	0.87 (0.74, 1.01)	0.07	0.81 (0.65, 1.01)	0.06
Male sex	1.15 (0.72, 1.84)	0.55	1.31 (0.90, 1.91)	0.15	<b>2.33 (1.31, 4.12)</b>	<b>0.004</b>
Black race	0.93 (0.56, 1.53)	0.78	1.40 (0.95, 2.06)	0.09	1.62 (0.96, 2.76)	0.07
BMI, per 5 kg/m <sup>2</sup>	1.06 (0.92, 1.22)	0.41	<b>1.22 (1.10, 1.36)</b>	<b>&lt;0.001</b>	<b>1.20 (1.04, 1.39)</b>	<b>0.011</b>
History of smoking	1.24 (0.79, 1.95)	0.35	1.44 (1.00, 2.07)	0.05	1.29 (0.76, 2.27)	0.34
Hypertension	1.07 (0.56, 2.05)	0.83	1.39 (0.84, 2.29)	0.20	1.42 (0.64, 3.17)	0.39
Coronary artery disease	0.98 (0.58, 1.66)	0.94	0.95 (0.60, 1.50)	0.83	0.85 (0.43, 1.67)	0.64
Heart failure	1.08 (0.60, 1.93)	0.80	0.59 (0.35, 0.99)	<b>0.045</b>	0.75 (0.38, 1.51)	0.42
Chronic kidney disease	0.89 (0.52, 1.52)	0.67	0.83 (0.53, 1.32)	0.44	0.84 (0.46, 1.54)	0.58
Admission eGFR, per 5 units lower	0.96 (0.92, 1.01)	0.10	<b>0.95 (0.92, 0.98)</b>	<b>0.004</b>	<b>0.87 (0.82, 0.91)</b>	<b>&lt;0.001</b>
<b>Inflammatory biomarkers**</b>						
SuPAR, ng/mL	1.12 (0.73, 1.70)	0.61	<b>1.94 (1.36, 2.75)</b>	<b>&lt;0.001</b>	<b>2.06 (1.21, 3.51)</b>	<b>0.008</b>
C-reactive protein, mg/dL	1.17 (0.96, 1.43)	0.11	<b>1.71 (1.41, 2.07)</b>	<b>&lt;0.001</b>	<b>1.41 (1.08, 1.82)</b>	<b>0.010</b>
Lactate dehydrogenase, IU/L	1.51 (1.00, 2.29)	0.05	<b>4.18 (2.82, 6.20)</b>	<b>&lt;0.001</b>	<b>1.83 (1.16, 2.90)</b>	<b>0.009</b>
Interleukin-6, pg/mL	1.12 (0.96, 1.29)	0.14	<b>1.37 (1.18, 1.60)</b>	<b>&lt;0.001</b>	<b>1.50 (1.25, 1.81)</b>	<b>&lt;0.001</b>
Procalcitonin, ng/mL	1.42 (1.12, 1.81)	<b>0.004</b>	<b>1.90 (1.48, 2.44)</b>	<b>&lt;0.001</b>	<b>1.50 (1.15, 1.95)</b>	<b>0.002</b>
Ferritin, ng/mL	1.19 (1.00, 1.40)	<b>0.045</b>	<b>1.44 (1.25, 1.66)</b>	<b>&lt;0.001</b>	<b>1.55 (1.25, 1.91)</b>	<b>&lt;0.001</b>
D-dimer, FEU mg/L	1.24 (1.07, 1.43)	<b>0.005</b>	<b>1.50 (1.32, 1.71)</b>	<b>&lt;0.001</b>	<b>1.32 (1.12, 1.56)</b>	<b>0.001</b>
<b>Glucose range (mg/dL) at admission, n (%)</b>						
< 54 – 69	1.01 (0.11, 9.38)	0.99	0.74 (0.08, 6.69)	0.79	2.30 (0.25, 21.5)	0.47
70 – 180	1.0 [reference]	-	1.0 [reference]	-	1.0 [reference]	-
181 – 250	1.60 (0.93, 2.76)	0.09	<b>1.67 (1.08, 2.60)</b>	<b>0.021</b>	1.56 (0.82, 2.97)	0.18
> 250	2.13 (1.22, 3.72)	<b>0.008</b>	<b>2.28 (1.45, 3.57)</b>	<b>&lt;0.001</b>	1.59 (0.85, 2.97)	0.14

**Supplemental Table 4. Correlation between thrombo-inflammatory biomarkers, glucose coefficient of variation, and insulin in COVID-19**

	<b>Glucose Coefficient of Variation</b>	<b>Insulin</b>
SuPAR, ng/mL	0.14 (P=0.007)	0.23 (P<0.001)
C-reactive protein, mg/dL	0.11 (P=0.015)	0.23 (P<0.001)
Lactate dehydrogenase, IU/L	0.01 (P=0.87)	0.22 (P=0.15)
Interleukin-6, pg/mL	0.08 (P=0.22)	0.03 (P=0.005)
Procalcitonin, ng/mL	0.21 (P<0.001)	0.09 (P<0.001)
Ferritin, ng/mL	0.10 (P=0.028)	0.15 (P=0.044)
D-dimer, FEU mg/L	0.05 (P=0.26)	0.18 (P=0.46)

FEU, fibrinogen-equivalent units

**Supplemental Figure 1. Associations between glucose, insulin, and combined outcome among individuals with DM in M2C2.** Forest plot depicting the odds ratio and 95% confidence intervals for the association between glucose, insulin, and the composite outcome of in-hospital death, need for mechanical ventilation, and need for renal replacement therapy among those with DM in the M2C2 cohort (n=563). All odds ratios for glucose represent a 10-unit difference; 0.1-unit difference for insulin. The glucose coefficient of variation is calculated as the standard deviation divided by the mean of all glucose measurements taken during hospitalization and then multiplied by ten. The percentage in glucose range and high glucose is expressed as the percentage of all glucose measurements within each category during hospitalization. Insulin is calculated as the average insulin dose administered. Models were adjusted for age, sex, race, BMI, and history of hypertension, coronary artery disease, and congestive heart failure.



**Supplemental Table 5. Associations between glucose, insulin, and combined outcome with suPAR and corticosteroids among individuals with DM in M2C2**

	SuPAR		Corticosteroids	
	OR* (95% CI)	P-value	OR† (95% CI)	P-value
Glucose coefficient of variation	1.33 (1.07, 1.66)	0.011	1.36 (1.09, 1.71)	0.008
% in glucose range (70-180 mg/dL)	0.99 (0.91, 1.07)	0.73	0.98 (0.90, 1.06)	0.61
% in high glucose range (> 180 mg/dL)	1.02 (0.94, 1.10)	0.63	1.03 (0.95, 1.11)	0.50
Insulin (units/kg/day)	1.17 (1.08, 1.27)	<0.001	1.18 (1.09, 1.29)	<0.001

Both models were adjusted for age, sex, race, BMI, and history of hypertension, coronary artery disease, and congestive heart failure. \*Model adjusted for log-transformed suPAR. †Model adjusted for use of corticosteroid use.