Supplementary material:

Glycaemia status at admission and cardiovascular complications in patients hospitalised with COVID-19

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Supplementary Text

Supplementary text 1. ISARIC4C investigators

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Supplementary text 2. Variable definitions

Cardiovascular and renal complications:

Stroke was based on a clinical diagnosis, with or without supportive radiological findings. Heart failure was defined as failure of the heart to pump a sufficient amount of blood to meet the needs of the body tissues, resulting in tissue congestion and oedema. Cardiac arrhythmia was defined as presence of arrhythmia in those without a previous record of it. Cardiac ischaemia was defined as diminished blood and oxygen supply to the heart muscle, also known as myocardial ischemia and was confirmed by an electrocardiogram (showing ischaemic changes, e.g. ST depression or elevation) and/or cardiac enzyme elevation. Cardiac arrest referred to the sudden cessation of cardiac activity. Coagulation disorder was defined as abnormal coagulation identified by abnormal prothrombin time or activated partial thromboplastin time. Acute renal injury was defined as urine volume <0.5 mL/kg/hour for 6 hours or as a creatinine rise which corresponded to the Kidney Disease Improving Global Outcomes (KDIGO) stage I or above definition (increase in serum creatinine by ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours; increase in serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days)[1].

1. Kellum JA, Lameire N, Aspelin P, Barsoum RS, Burdmann EA, Goldstein SL, Herzog CA, Joannidis M, Kribben A, Levey AS. Kidney disease: improving global outcomes (KDIGO) acute kidney injury work group. KDIGO clinical practice guideline for acute kidney injury. Kidney international supplements 2012;2(1):1-138.

Supplementary Table 1. Characteristics of those included in the final sample (n=36 269) vs those excluded for having incomplete exposure, covariate or outcome data (n=80 790)

	Included in final sample (n=36 269)		**Excluded due to incomplete data (n=80 790)**		***Standardised difference*†**
	total n		*total n*		
Sex (male, n (%))	36 269	20 591 (56.8)	80 790	43 243 (53.5)	0.07
Age (years, mean (SD))	36 269	68.6 (16.9)	80 790	70.8 (17.4)	0.13
Ethnicity (n (%))					
White British		29 580 (81.6)		69 153 (85.6)	
South Asian	36 269	2 637 (7.3)	80 790	4 158 (5.2)	0.12
Black		1 285 (3.5)		2 017 (2.5)	
Other		2 767 (7.6)		5 462 (6.8)	
Glucose level on admission (mmol/l, mean (SD))	36 269	8.1 (4.3)	11 587	8.7 (4.9)	0.13
In-hospital cardiovascular/renal complications (yes, n (%))	36 269	10 421 (28.7)	69 365	17 545 (25.3)	0.08
Obesity (yes, n (%))	36 269	5 680 (15.7)	60 305	7 502 (12.4)	0.09
Pre-existing diabetes (yes, n (%))	36 269	9 202 (25.4)	66 221	12 651 (19.1)	0.15

*Chi^2 was used for proportions; Student's t test/Wilcoxon rank sum for continuous variables.† Standardized difference = difference in means or proportions divided by standard error; imbalance defined as absolute value greater than 0.10

Supplementary Table 2. Characteristics of those whose 28 day outcome status was discharged vs remaining in hospital/transferred (n=26 643)

	Status at 28 days		
	Discharged (n= 24 152)	**Remaining in hospital or transferred to another facility (n= 2 491)**	**Standardised difference†**
Sex (male, n (%))	13 163 (54.5)	1 460 (58.6)	0.08
Age (years, mean (SD))	65.0 (17.4)	70.0 (16.1)	0.29
Ethnicity (n (%))			
White British	19 360 (80.2)	2 000 (80.3)	
South Asian	1 898 (7.9)	172 (6.9)	0.04
Black	913 (3.8)	100 (4.0)	
Other	1 981 (8.2)	219 (8.8)	
Glucose level on admission (mmol/l, mean (SD))	7.9 (4.1)	8.3 (4.5)	0.11
(mg/dL, mean (SD))	142.2 (73.8)	149.4 (81)	
In-hospital cardiovascular/renal complications	4 708 (19.5)	1 021 (41.0)	0.48
Obesity (yes, n (%))	3 897 (16.1)	427 (17.1)	0.03
Pre-existing diabetes (yes, n (%))	5 687 (23.6)	661 (26.5)	0.07

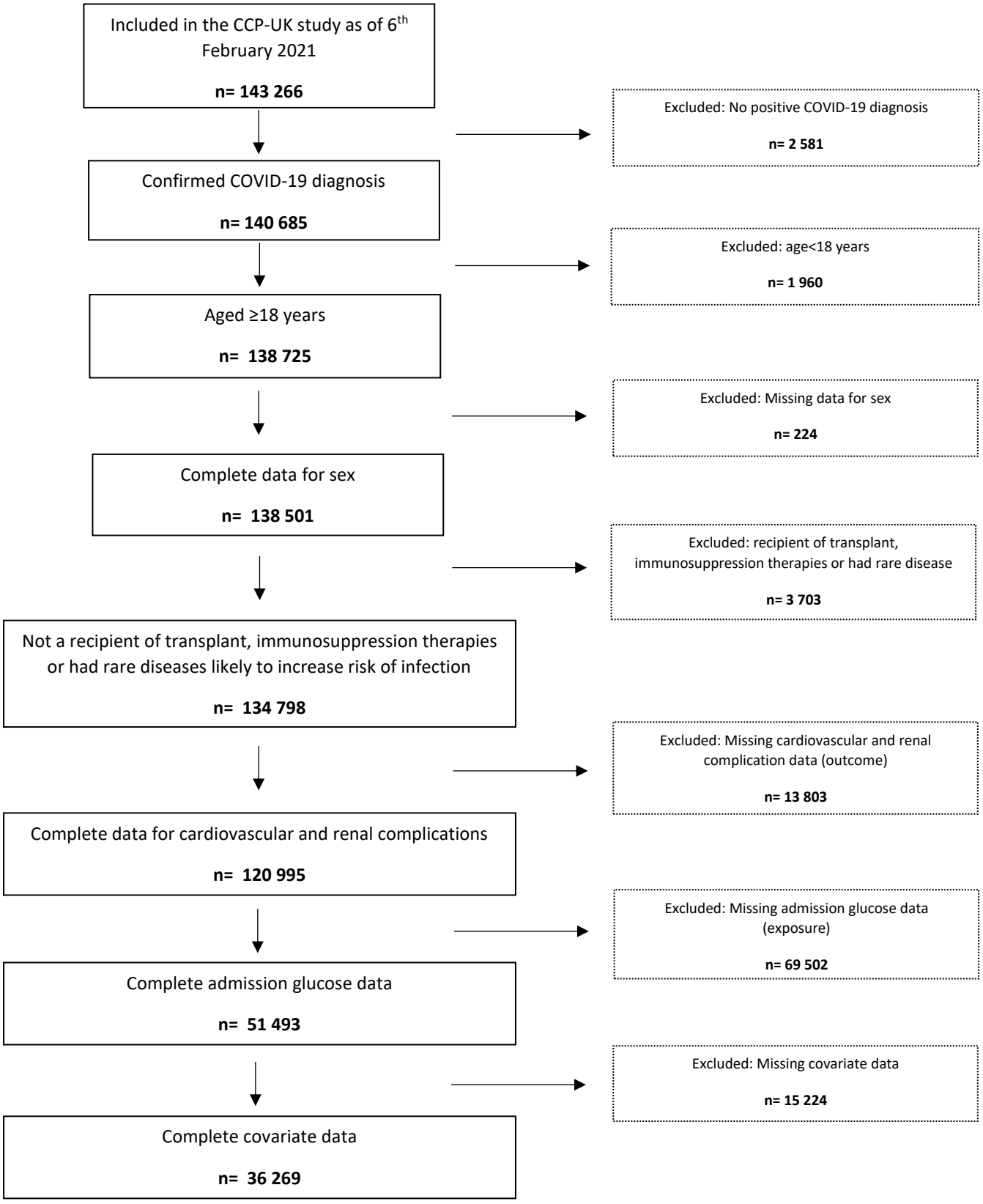
†Standardised difference = difference in means or proportions divided by standard error; imbalance defined as absolute value greater than 0.1

Supplementary Table 3. Patient characteristics, stratified by glycaemia status (n=36 269)

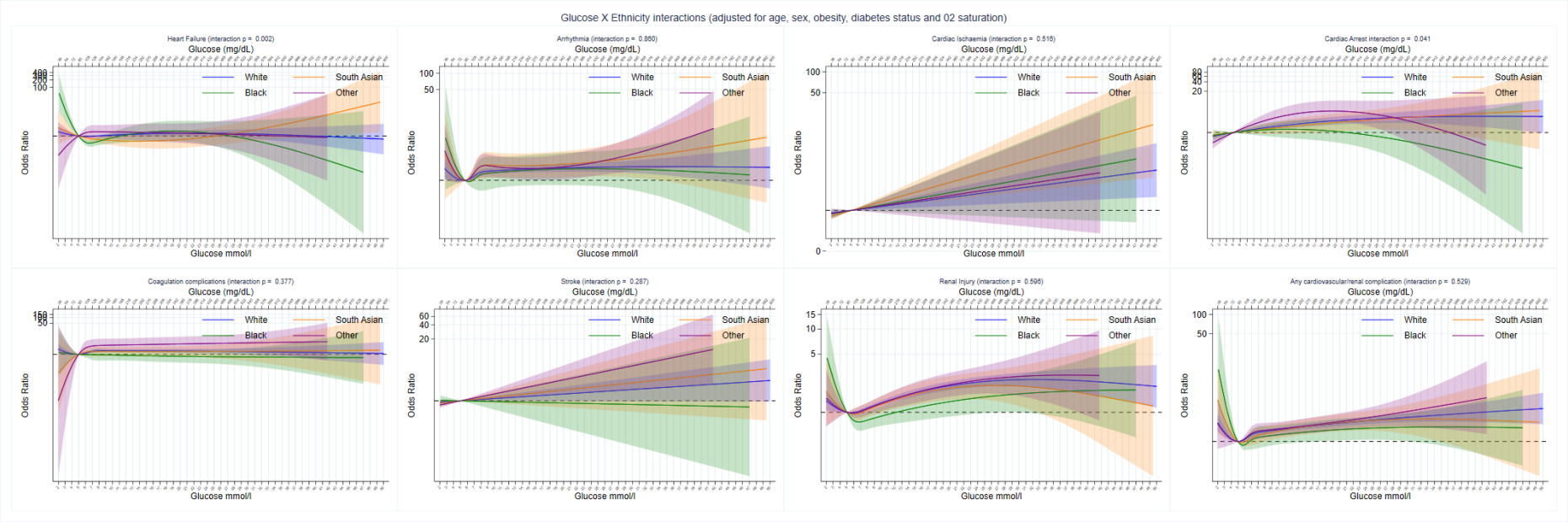
	Patients with admission glucose <3.9 mmol/l (n=450)	**Patients with admission glucose ≥3.9 & <11.1 mmol/l (n=30 760)**	**Patients with admission glucose ≥11.1 mmol/l (n=5 059)**
Sex			
Male	232 (51.6)	17 194 (55.9)	3 165 (62.6)
Female	218 (48.4)	13 566 (44.1)	1 894 (37.4)
Age on admission (years)	75 (63, 84)	72 (57, 83)	68 (56, 79)
Ethnicity			
White	375 (83.3)	25 554 (83.1)	3 651 (72.2)
South Asian	29 (6.4)	2 032 (6.6)	576 (11.4)
Black	12 (2.7)	946 (3.1)	327 (6.5)
Other	34 (7.6)	2 228 (7.2)	505 (10.0)
In-hospital cardiovascular/renal complications			
Arrhythmia	35 (7.8)	2 422 (7.9)	510 (10.1)
Cardiac ischaemia	10 (2.2)	415 (1.4)	126 (2.5)
Cardiac arrest	12 (2.7)	709 (2.3)	199 (3.9)
Coagulation complications	18 (4.0)	1 342 (4.4)	265 (5.2)
Stroke	-	378 (1.2)	88 (1.7)
Heart failure	25 (5.6)	1 042 (3.4)	215 (4.3)
Renal injury	97 (21.6)	5 023 (16.3)	1 338 (26.5)
Glucose on admission (mmol/l)	3.3 (2.7, 3.6)	6.5 (5.7, 7.6)	14.7 (12.5, 18.5)
mg/dL	59.4 (48.6, 64.8)	117.0 (102.6, 136.8)	264.6 (225.0, 333.0)
Obesity	65 (14.4)	4 505 (14.7)	1 110 (21.9)
Pre-existing diabetes	203 (45.1)	5 535 (18.0)	3 464 (68.5)

Data are reported as n(%) for categorical variables and median(IQR) for continuous variables

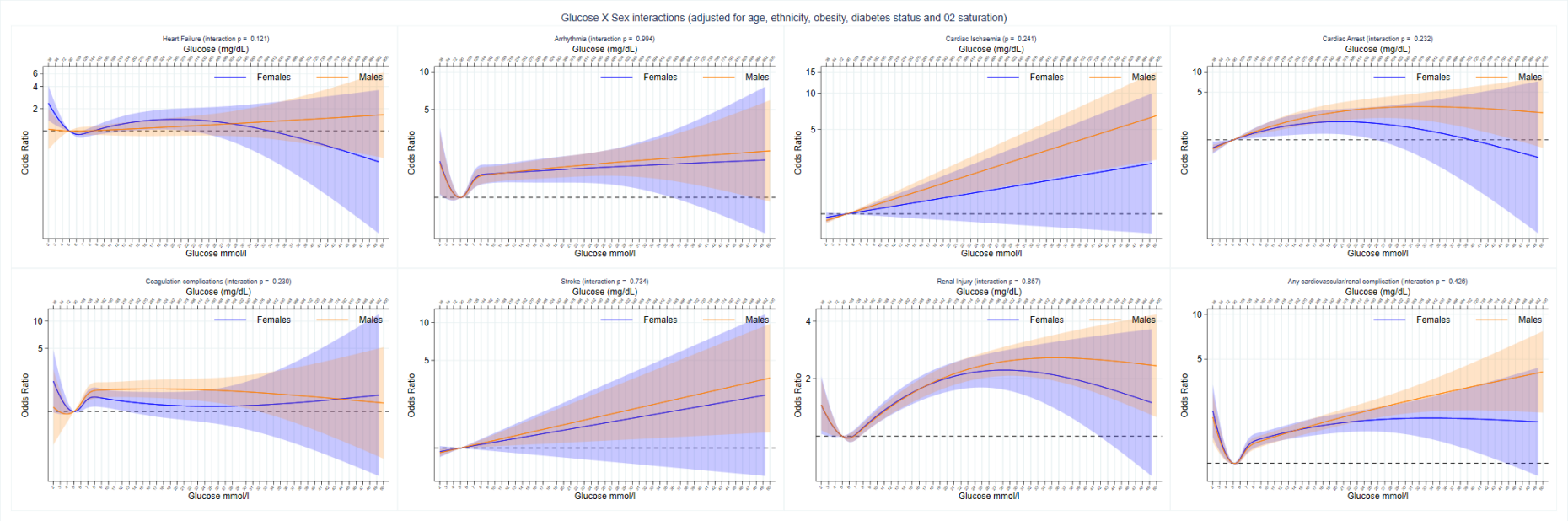
Supplementary Figure 1. Flow diagram outlining how final sample was derived



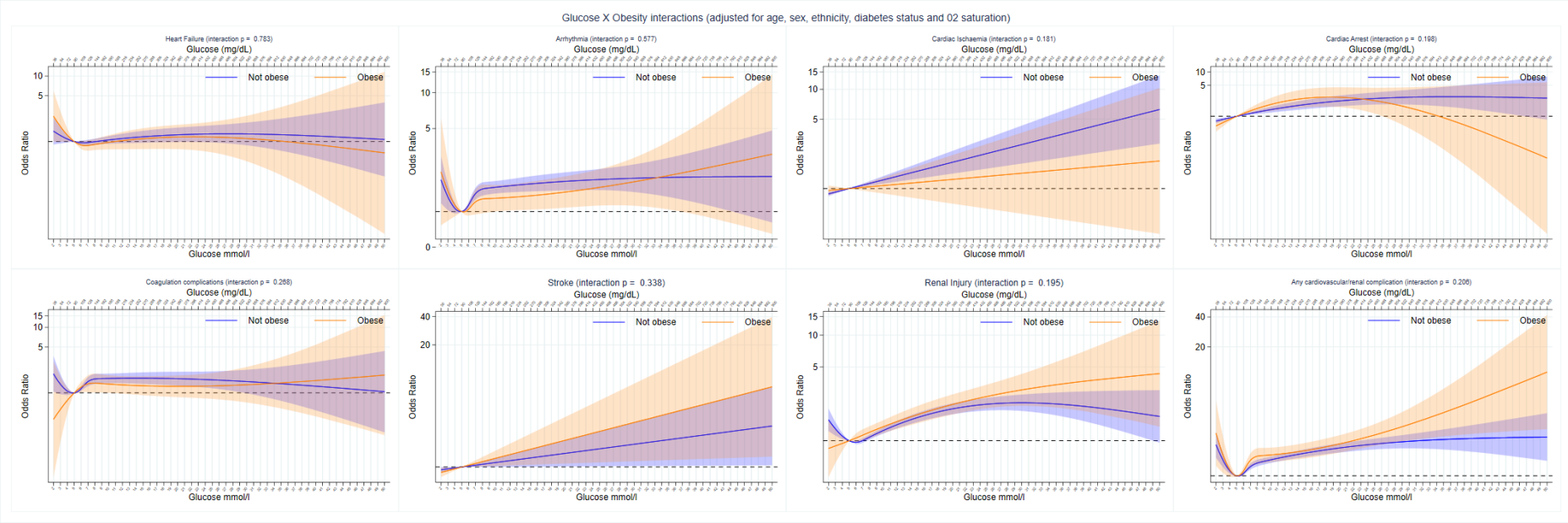
Supplementary Figure 2. Associations between glucose level at admission and cardiovascular/renal complications: by ethnicity (adjusted for sex, age, obesity, diabetes status and oxygen saturation)



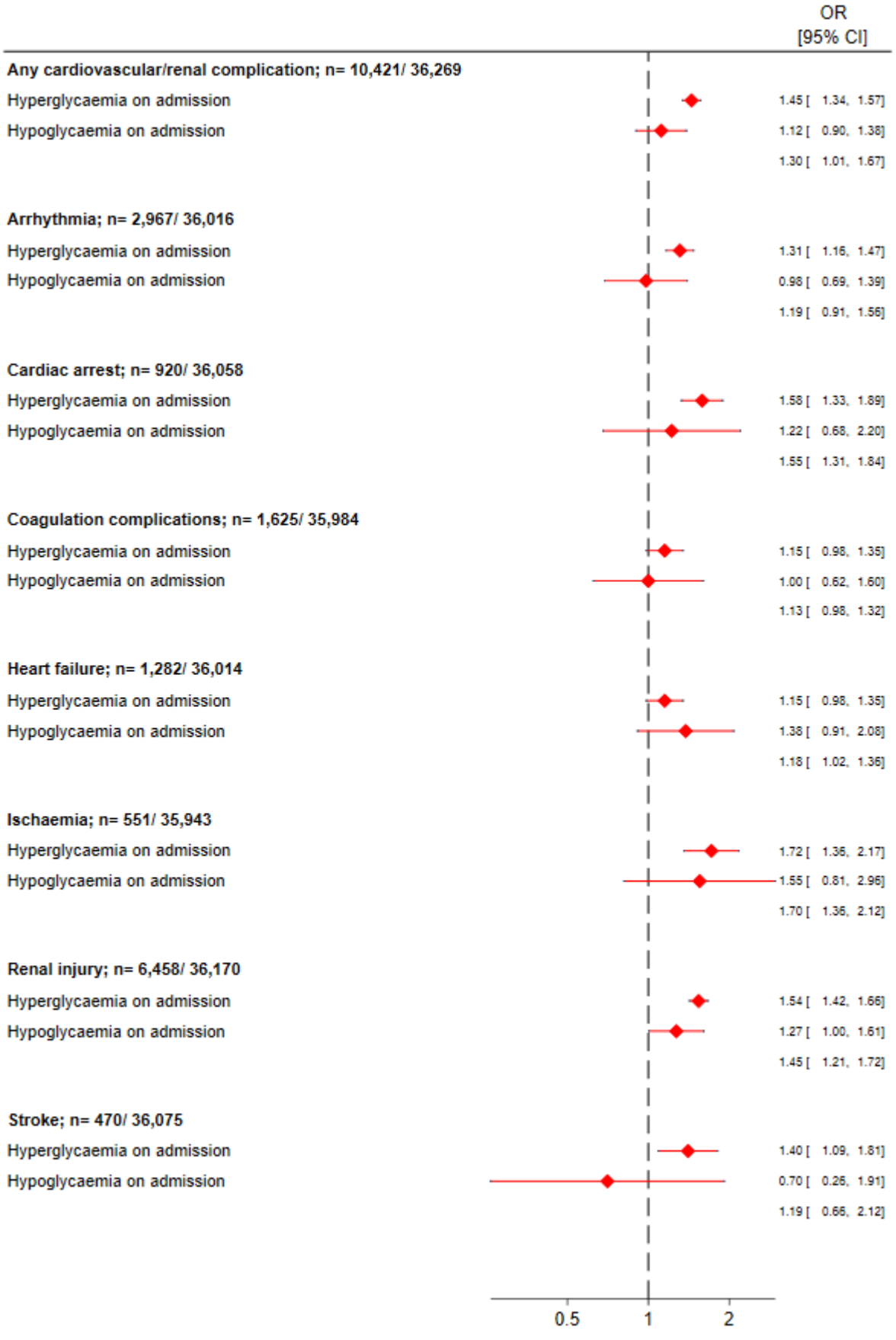
Supplementary Figure 3. Associations between glucose level at admission and cardiovascular/renal complications: by sex (adjusted for ethnicity, age, obesity, diabetes status and oxygen saturation)



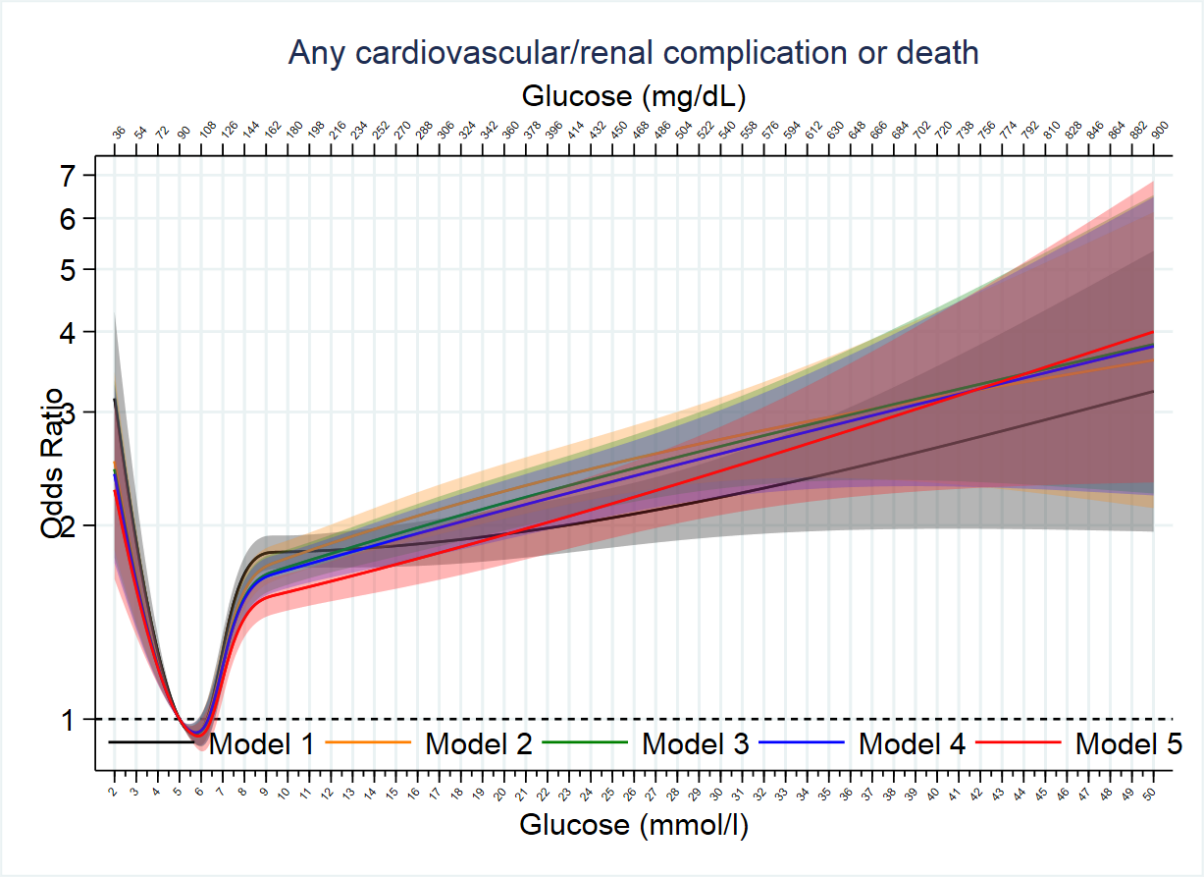
Supplementary Figure 4. Associations between glucose level at admission and cardiovascular/renal complications: by obesity status (adjusted for sex, age, ethnicity, diabetes status and oxygen saturation)



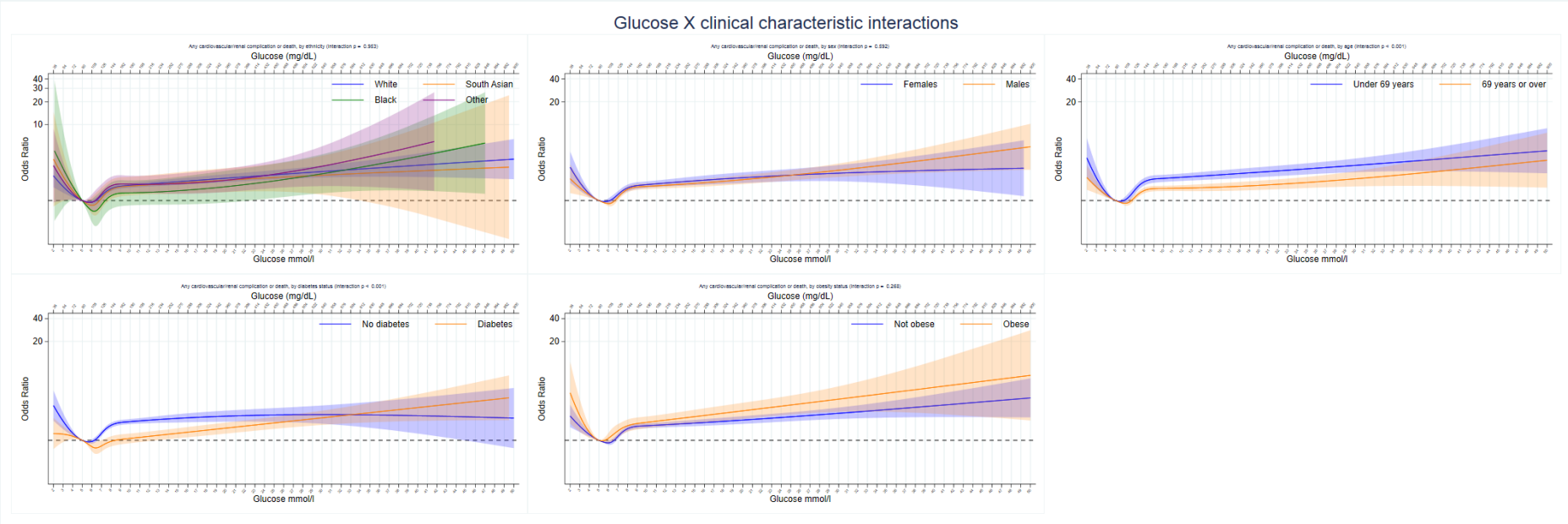
Supplementary Figure 5. Associations between hypo- and hyperglycaemia and cardiovascular/renal complications (adjusted for sex, age, ethnicity, obesity, diabetes status and oxygen saturation)


OR
[95% CI]
Any cardiovascular/renal complication; n= 10,421/ 36,269
Hyperglycaemia on admission
1.45 [1.34, 1.57]
Hypoglycaemia on admission
1.12 [0.90, 1.38]
1.30 [1.01, 1.67]
Arrhythmia; n= 2,967/ 36,016
Hyperglycaemia on admission
1.31 [1.16, 1.47]
Hypoglycaemia on admission
0.98 [0.69, 1.39]
1.19 [0.91, 1.56]
Cardiac arrest; n= 920/ 36,058
Hyperglycaemia on admission
1.58 [1.33, 1.89]
Hypoglycaemia on admission
1.22 [0.68, 2.20]
1.55 [1.31, 1.84]
Coagulation complications; n= 1,625/ 35,984
Hyperglycaemia on admission
1.15 [0.98, 1.35]
Hypoglycaemia on admission
1.00 [0.62, 1.60]
1.13 [0.98, 1.32]
Heart failure; n= 1,282/ 36,014
Hyperglycaemia on admission
1.15 [0.98, 1.35]
Hypoglycaemia on admission
1.38 [0.91, 2.08]
1.18 [1.02, 1.36]
Ischaemia; n= 551/ 35,943
Hyperglycaemia on admission
1.72 [1.36, 2.17]
Hypoglycaemia on admission
1.55 [0.81, 2.96]
1.70 [1.36, 2.12]
Renal injury; n= 6,458/ 36,170
Hyperglycaemia on admission
1.54 [1.42, 1.66]
Hypoglycaemia on admission
1.27 [1.00, 1.61]
1.45 [1.21, 1.72]
Stroke; n= 470/ 36,075
Hyperglycaemia on admission
1.40 [1.09, 1.81]
Hypoglycaemia on admission
0.70 [0.26, 1.91]
1.19 [0.66, 2.12]
0.5
1
2

Supplementary Figure 6. Associations between glucose level at admission and ‘any cardiovascular/renal complication or death’



Supplementary Figure 7. Associations between glucose level at admission and ‘any cardiovascular/renal complication or death’, by ethnicity, sex, age, obesity and diabetes status



Supplementary Figure 8. Associations between hypo- and hyperglycaemia and ‘any cardiovascular/renal complication or death’ (adjusted for sex, age, ethnicity, diabetes status, obesity and oxygen saturation)