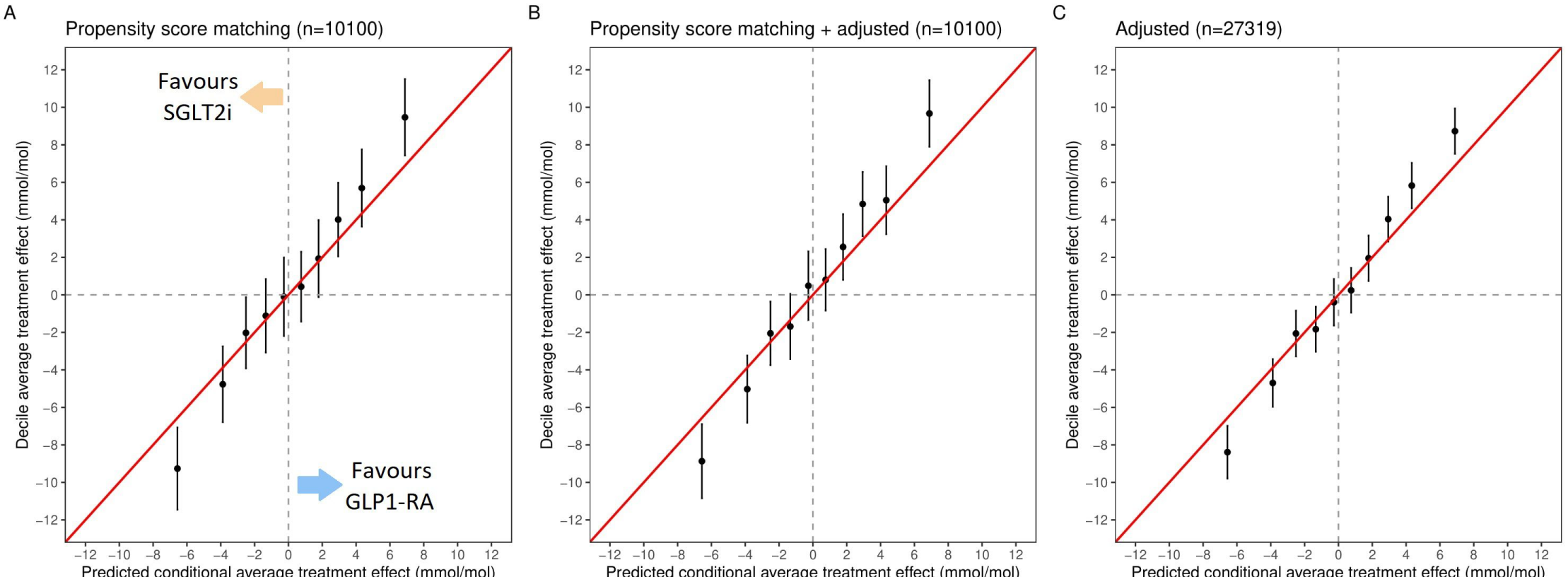
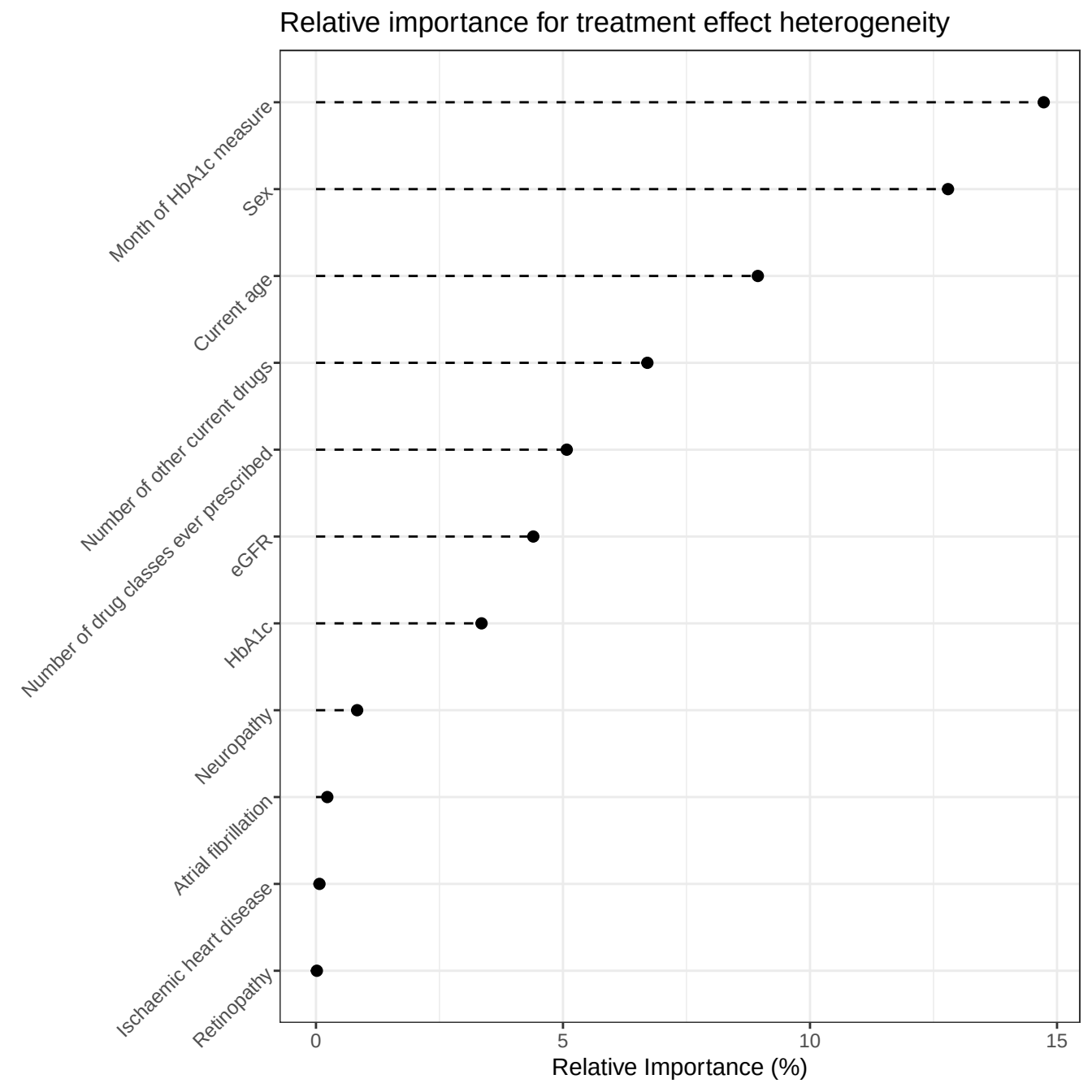
Full cohort: v2

	GLP-1 receptor agonists (n=28081)		SGLT2 inhibitors (n=84193)		SMDs	
		% missing		% missing		
Current age, years	57.8 [11.3]	-	58.4 [10.8]	-	0.064	*
Duration of diabetes, years	9.4 [6.4]	-	9.4 [6.6]	-	0.012	
Sex						
Male	14960 (53.3%)	-	51288 (60.9%)	-		*
Female	13121 (46.7%)	-	32905 (39.1%)	-	0.155	
Ethnicity						
White	24063 (85.7%)		64111 (76.1%)			
Asian	2144 (7.6%)	1.3%	12234 (14.5%)	2.1%		
Black	987 (3.5%)		3861 (4.6%)			
Other	262 (0.9%)		1316 (1.6%)			
Mixed	246 (0.9%)		885 (1.1%)		0.255	
SGLT2 inhibitor type						
Canagliflozin	-	-	14965 (17.8%)	-		
Dapagliflozin	-	-	36250 (43.1%)	-		
Empagliflozin	-	-	32860 (39.0%)	-		
Ertugliflozin	-	-	137 (0.2%)	-		
GLP-1 receptor agonist type					-	*
Dulaglutide	10337 (36.8%)	-	-	-		
Exenatide (short-acting)	1367 (4.9%)	-	-	-		
Exenatide (long-acting)	2377 (8.5%)	-	-	-		
Liraglutide	11258 (40.1%)	-	-	-		
Lixisenatide	2751 (9.8%)	-	-	-		
Index of multiple deprivation						
1 (Least deprived)	4568 (16.3%)		14143 (16.8%)			
2	4925 (17.5%)	0.1%	14836 (17.6%)	0.1%		
3	5393 (19.2%)		16194 (19.2%)			
4	6099 (21.7%)		18841 (22.4%)			
5 (Most deprived)	7078 (25.2%)		20132 (23.9%)		0.037	
Smoking status						
Active	4689 (16.7%)	4.4%	14265 (16.9%)	4.0%		
Ex-smoker	15543 (55.4%)		45283 (53.8%)			
Non-smoker	6605 (23.5%)		21311 (25.3%)		0.048	
Number of glucose-lowering drug classes ever prescribed						
2	2886 (10.3%)	-	18724 (22.2%)	-		*
3	6772 (24.1%)	-	25570 (30.4%)	-		
4	10536 (37.5%)	-	25217 (30.0%)	-		
5+	7887 (28.1%)	-	14682 (17.4%)	-	0.420	
Number of other current glucose--lowering drugs						
0	1616 (5.8%)	-	5155 (6.1%)	-		
1	9948 (35.4%)	-	34032 (40.4%)	-		*
2	12422 (44.2%)	-	35540 (42.2%)	-		
3	3862 (13.8%)	-	9187 (10.9%)	-		
4+	233 (0.8%)	-	279 (0.3%)	-	0.137	
Background therapy						
Metformin	24075 (85.7%)	-	73392 (87.2%)	-	0.042	
Sulfonylurea	13312 (47.4%)	-	23256 (27.6%)	-	0.237	
DPP-4 inhibitor	4595 (16.4%)	-	23256 (27.6)	-	0.274	
SGLT2 inhibitor	4019 (14.3%)	-	-	-	-	
Thiazolidinedione	1312 (4.7%)	-	2374 (2.8%)	-	0.098	
GLP-1 receptor agonist	-	-	4603 (5.5%)	-	-	

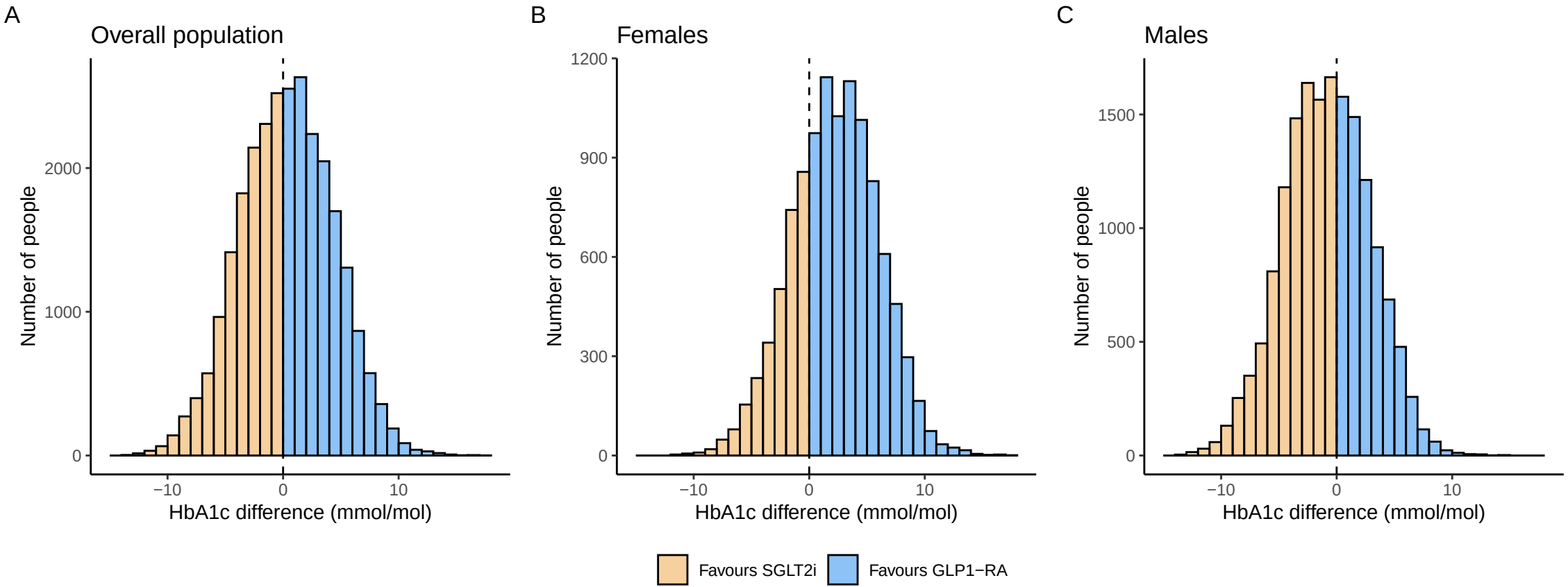
Biomarkers						
HbA_{1c}, mmol/mol	78.6 (17.1)	20.6%	76.9 (16.9)	12.2%	0.101	*
BMI, kg/m_2	37.3 (7.2)	2.7%	33.7 (6.9)	3.8%	0.522	
eGFR, mL/min per 1.3 m^2	92.0 (19.7)	0.2%	94.7 (15.5)	0.3%	0.152	*
HDL, cholesterol, mmol/L	1.1 (0.3)	4.8%	1.1 (0.3)	3.6%	0.083	
Alanine transaminase, IU/L	35.1 (20.6)	6.4%	34.5 (20.2)	5.7%	0.027	
Albumin, g/L	41.6 (3.9)	4.8%	42.0 (3.9)	4.4%	0.109	
Bilirubin, µmol/L	9.1 (4.7)	4.2%	9.5 (5.0)	4.0%	0.084	
Total cholesterol, mmol/L	4.4 (1.1)	0.6%	4.3 (1.1)	0.5%	0.039	
Mean arterial blood pressure, mm Hg	96.1 (9.0)	0.3%	96.2 (9.0)	0.3%	0.016	
Microvascular complications						
Nephropathy	730 (2.6%)	-	1623 (1.9%)	-	0.045	
Neuropathy	7942 (28.3%)	-	20161 (23.9%)	-	0.099	*
Retinopathy	10540 (37.5%)	-	31664 (37.6%)	-	0.002	*
Cardiovascular conditions						
Angina	3224 (11.5%)	-	8251 (9.8%)	-	0.055	
Atherosclerotic cardiovascular disease	6285 (22.4%)	-	16530 (19.6%)	-	0.068	
Atrial fibrillation	1737 (6.2%)	-	4129 (4.9%)	-	0.056	*
Cardiac revascularisation	1863 (6.6%)	-	5632 (6.7%)	-	0.002	
Heart failure	1662 (5.9%)	-	3654 (4.3%)	-	0.072	
Hypertension	16833 (59.9%)	-	46550 (55.3%)	-	0.094	
Ischaemic heart disease	4181 (14.9%)	-	11309 (13.4%)	-	0.042	*
Myocardial infarction	1943 (6.9%)	-	5655 (6.7%)	-	0.008	
Peripheral arterial disease	1703 (6.1%)	-	3836 (4.6%)	-	0.067	*
Stroke	1270 (4.5%)	-	3422 (4.1%)	-	0.023	
Transient ischaemic attack	766 (2.7%)	-	4129 (4.9%)	-	0.013	
Other conditions						
Chronic kidney disease	2684 (9.6%)	-	2962 (3.5%)	-	0.258	
Chronic liver disease	3754 (13.4%)	-	10241 (12.2%)	-	0.036	
HbA_{1c} outcome						
HbA_{1c}, mmol/mol	66.3 (18.3)	54.8%	64.2 (15.0)	47.5%	0.126	*
Month of HbA_{1c} measure	8.9 [3.5]	54.8%	9.2 [3.5]	47.5%	0.071	*

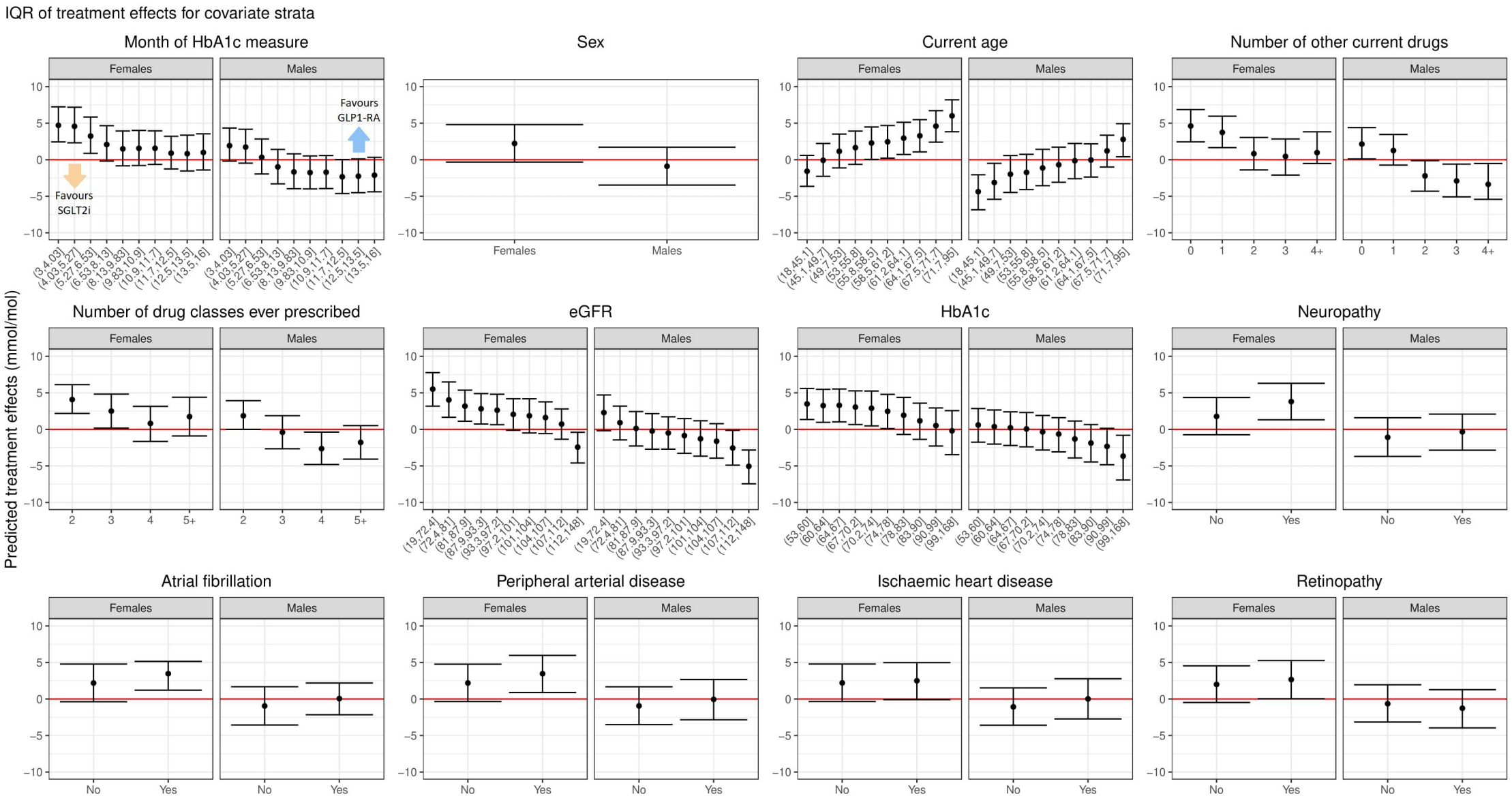
Validation of treatment effects for training cohort




Relative importance for treatment effect heterogeneity
Month of HbA1c measure
Sex
Current age
Number of other current drugs
Number of drug classes ever prescribed
eGFR
HbA1c
Neuropathy
Atrial fibrillation
Ischaemic heart disease
Retinopathy
0
5
10
15
Relative Importance (%)

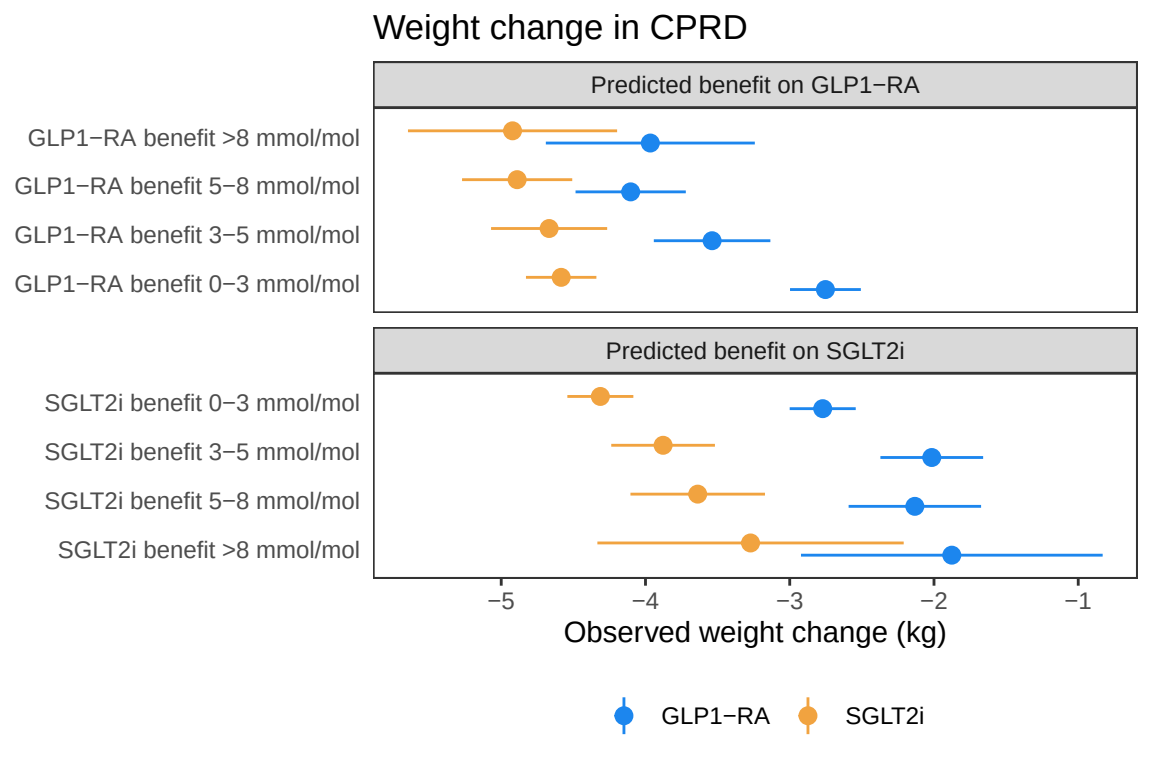
Heterogeneity of treatment effects

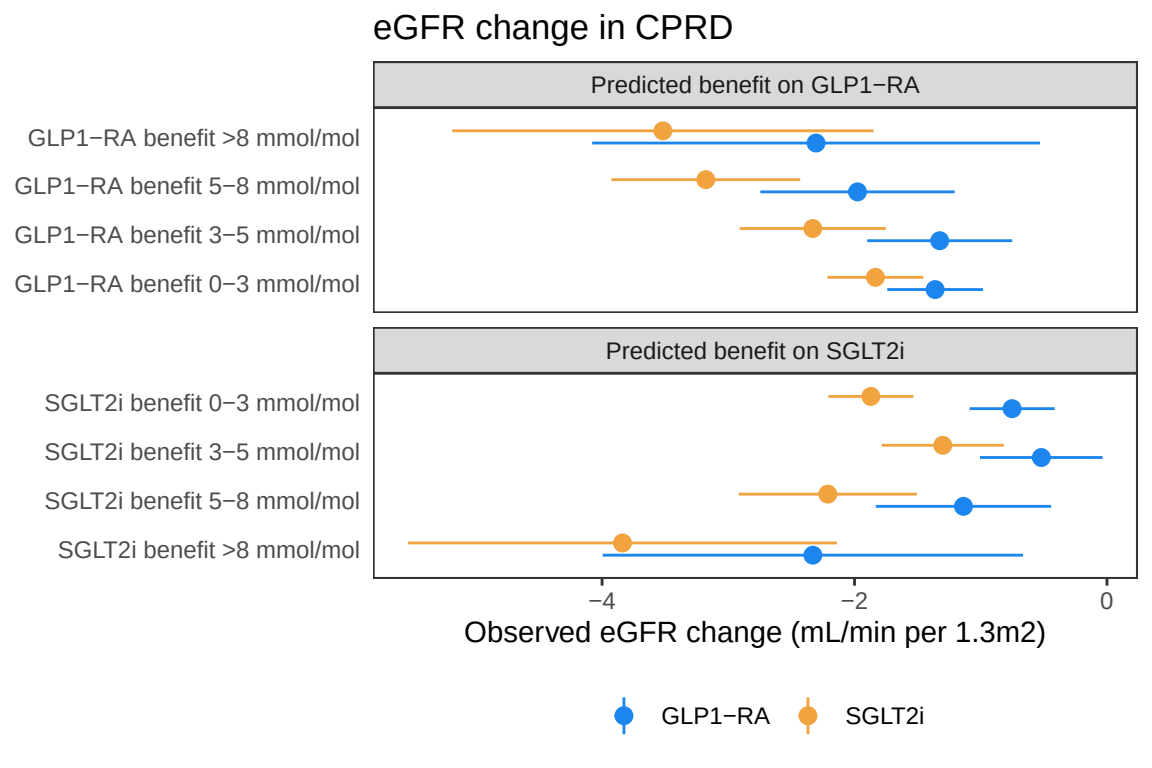


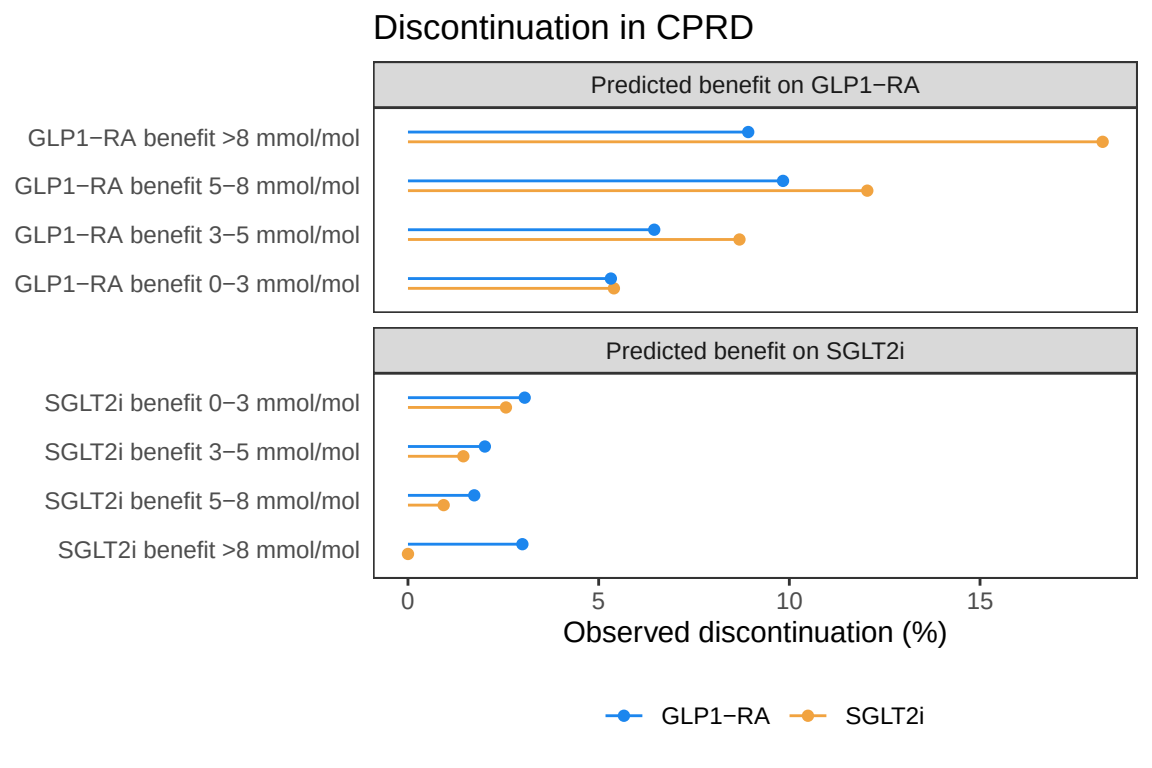

IQR of treatment effects for covariate strata
Month of HbA1c measure
Sex
Current age
Number of other current drugs
Number of drug classes ever prescribed
eGFR
HbA1c
Neuropathy
Atrial fibrillation
Peripheral arterial disease
Ischaemic heart disease
Retinopathy
Females
Males
Predicted treatment effects (mmol/mol)
Favours SGLT2i
Favours GLP1-RA
No
Yes

Patient benefit

	Predicted benefit on SGLT2i >8 mmol/mol (n=850)		Predicted benefit on GLP1-RA >8 mmol/mol (n=606)		SMDs
Current age, years	72.0 (8.0)	-	45.1 (8.3)	-	3.294
Duration of diabetes, years	11.6 (7.4)	-	8.3 (4.5)	-	0.536
Sex					
Male	131 (15.4%)	-	567 (93.6%)	-	2.532
Female	719 (84.6%)		39 (6.4%)		
Ethnicity					
White	757 (89.1%)	0.7	421 (69.5%)	2.3	
Asian	51 (6.0%)		127 (21.0%)		
Black	26 (3.1%)		25 (4.1%)		
Other	7 (0.8%)		13 (2.1%)		
Mixed	3 (0.4%)		6 (1.0%)		0.255
Biomarkers					
HbA_{1c}, mmol/mol	74.7 (17.5)	-	95.9 (12.9)	-	1.384
BMI, kg/m_2	34.3 (7.2)	-	34.7 (7.4)	-	0.059
eGFR, mL/min per 1.3 m^2	71.0 (18.3)	-	113.1 (10.4)	-	2.828
Cardiovascular conditions					
Atherosclerotic cardiovascular disease	204 (24.0%)	-	77 (12.7%)	-	0.295


Weight change in CPRD
Predicted benefit on GLP1−RA
GLP1−RA benefit >8 mmol/mol
GLP1−RA benefit 5−8 mmol/mol
GLP1−RA benefit 3−5 mmol/mol
GLP1−RA benefit 0−3 mmol/mol
Predicted benefit on SGLT2i
SGLT2i benefit 0−3 mmol/mol
SGLT2i benefit 3−5 mmol/mol
SGLT2i benefit 5−8 mmol/mol
SGLT2i benefit >8 mmol/mol
−5
−4
−3
−2
−1
Observed weight change (kg)
GLP1−RA
SGLT2i


eGFR change in CPRD
Predicted benefit on GLP1−RA
GLP1−RA benefit >8 mmol/mol
GLP1−RA benefit 5−8 mmol/mol
GLP1−RA benefit 3−5 mmol/mol
GLP1−RA benefit 0−3 mmol/mol
Predicted benefit on SGLT2i
SGLT2i benefit 0−3 mmol/mol
SGLT2i benefit 3−5 mmol/mol
SGLT2i benefit 5−8 mmol/mol
SGLT2i benefit >8 mmol/mol
−4
−2
0
Observed eGFR change (mL/min per 1.3m2)
GLP1−RA
SGLT2i


Discontinuation in CPRD
Predicted benefit on GLP1−RA
GLP1−RA benefit >8 mmol/mol
GLP1−RA benefit 5−8 mmol/mol
GLP1−RA benefit 3−5 mmol/mol
GLP1−RA benefit 0−3 mmol/mol
Predicted benefit on SGLT2i
SGLT2i benefit 0−3 mmol/mol
SGLT2i benefit 3−5 mmol/mol
SGLT2i benefit 5−8 mmol/mol
SGLT2i benefit >8 mmol/mol
0
5
10
15
Observed discontinuation (%)
GLP1−RA
SGLT2i