#### Supplementary files

- S1 Read codes used for Type 2 diabetes
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- S3 Flow diagram in detail
- S4 Baseline demographic characteristics, behavioural risk factors, diabetes complications, comorbidities, metabolic characteristics, and medications for the rest four imputed propensity score matched datasets
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- S6 Baseline demographic characteristics, behavioural risk factors, diabetes complications, comorbidities, metabolic characteristics, and medications (Sensitivity analysis)
- S7 Risk of developing COVID-19, mortality, and back pain among those with a current combination prescription of metformin and other glucose-lowering agents compared to a current prescription of other glucose-lowering agents only (Sensitivity analysis)

## Supplementary S1 Read codes used for Type 2 diabetes

Supplementary	7 ST Read codes used for Type 2 diabetes
C106100	Diabetes mellitus, adult onset, + neurological manifestation
C109611	Type II diabetes mellitus with retinopathy
C109212	Type 2 diabetes mellitus with neurological complications
C109.13	Type II diabetes mellitus
C109.12	Type 2 diabetes mellitus
C109211	Type II diabetes mellitus with neurological complications
C10FE00	Type 2 diabetes mellitus with diabetic cataract
C10FQ00	Type 2 diabetes mellitus with exudative maculopathy
C109.11	NIDDM - Non-insulin dependent diabetes mellitus
C109J00	Insulin treated Type 2 diabetes mellitus
C10FM00	Type 2 diabetes mellitus with persistent microalbuminuria
C10F111	Type II diabetes mellitus with ophthalmic complications
C109F00	Non-insulin-dependent d m with peripheral angiopath
C10F911	Type II diabetes mellitus without complication
C10F511	Type II diabetes mellitus with gangrene
C109B00	Non-insulin dependent diabetes mellitus with polyneuropathy
C10FA11	Type II diabetes mellitus with mononeuropathy
C100112	Non-insulin dependent diabetes mellitus
C109500	Non-insulin dependent diabetes mellitus with gangrene
C10FJ11	Insulin treated Type II diabetes mellitus
C109100	Non-insulin-dependent diabetes mellitus with ophthalm comps
C10FF11	Type II diabetes mellitus with peripheral angiopathy
C109J12	Insulin treated Type II diabetes mellitus
C10FR11	Type II diabetes mellitus with gastroparesis
C109J11	Insulin treated non-insulin dependent diabetes mellitus
C109F12	Type 2 diabetes mellitus with peripheral angiopathy

C10D.00	Diabetes mellitus autosomal dominant type 2
C10F100	Type 2 diabetes mellitus with ophthalmic complications
C10FN11	Type II diabetes mellitus with ketoacidosis
C109F11	Type II diabetes mellitus with peripheral angiopathy
C10F900	Type 2 diabetes mellitus without complication
C109B12	Type 2 diabetes mellitus with polyneuropathy
C10F500	Type 2 diabetes mellitus with gangrene
C109B11	Type II diabetes mellitus with polyneuropathy
C10FA00	Type 2 diabetes mellitus with mononeuropathy
C109612	Type 2 diabetes mellitus with retinopathy
C109511	Type II diabetes mellitus with gangrene
C10FH00	Type 2 diabetes mellitus with neuropathic arthropathy
C109512	Type 2 diabetes mellitus with gangrene
C104100	Diabetes mellitus, adult onset, with renal manifestation
C109111	Type II diabetes mellitus with ophthalmic complications
C10FD00	Type 2 diabetes mellitus with hypoglycaemic coma
C109112	Type 2 diabetes mellitus with ophthalmic complications
C10FP00	Type 2 diabetes mellitus with ketoacidotic coma
C10FL00	Type 2 diabetes mellitus with persistent proteinuria
C10F011	Type II diabetes mellitus with renal complications
C109E00	Non-insulin depend diabetes mellitus with diabetic cataract
C10F411	Type II diabetes mellitus with ulcer
C109A00	Non-insulin dependent diabetes mellitus with mononeuropathy
C109900	Non-insulin-dependent diabetes mellitus without complication
C107100	Diabetes mellitus, adult, + peripheral circulatory disorder
C10z100	Diabetes mellitus, adult onset, + unspecified complication
C109400	Non-insulin dependent diabetes mellitus with ulcer

C10FE11	Type II diabetes mellitus with diabetic cataract
C109000	Non-insulin-dependent diabetes mellitus with renal comps
C10FQ11	Type II diabetes mellitus with exudative maculopathy
C10FM11	Type II diabetes mellitus with persistent microalbuminuria
C10F000	Type 2 diabetes mellitus with renal complications
C109E11	Type II diabetes mellitus with diabetic cataract
C109E12	Type 2 diabetes mellitus with diabetic cataract
C10F400	Type 2 diabetes mellitus with ulcer
C109912	Type 2 diabetes mellitus without complication
C109412	Type 2 diabetes mellitus with ulcer
C109411	Type II diabetes mellitus with ulcer
C10FK00	Hyperosmolar non-ketotic state in type 2 diabetes mellitus
C109012	Type 2 diabetes mellitus with renal complications
C109011	Type II diabetes mellitus with renal complications
C10FG00	Type 2 diabetes mellitus with arthropathy
C10F311	Type II diabetes mellitus with multiple complications
C109H00	Non-insulin dependent d m with neuropathic arthropathy
C109D00	Non-insulin dependent diabetes mellitus with hypoglyca coma
C10F711	Type II diabetes mellitus - poor control
C10FC11	Type II diabetes mellitus with nephropathy
C10FH11	Type II diabetes mellitus with neuropathic arthropathy
C105100	Diabetes mellitus, adult onset, + ophthalmic manifestation
C107400	NIDDM with peripheral circulatory disorder
C109300	Non-insulin-dependent diabetes mellitus with multiple comps
C10FD11	Type II diabetes mellitus with hypoglycaemic coma
C10FP11	Type II diabetes mellitus with ketoacidotic coma
C109H12	Type 2 diabetes mellitus with neuropathic arthropathy

C10F300	Type 2 diabetes mellitus with multiple complications
C10FL11	Type II diabetes mellitus with persistent proteinuria
C109H11	Type II diabetes mellitus with neuropathic arthropathy
C109D12	Type 2 diabetes mellitus with hypoglycaemic coma
C109D11	Type II diabetes mellitus with hypoglycaemic coma
C10F700	Type 2 diabetes mellitus - poor control
C102100	Diabetes mellitus, adult onset, with hyperosmolar coma
C10FC00	Type 2 diabetes mellitus with nephropathy
C10y100	Diabetes mellitus, adult, + other specified manifestation
C109311	Type II diabetes mellitus with multiple complications
C10FJ00	Insulin treated Type 2 diabetes mellitus
C109312	Type 2 diabetes mellitus with multiple complications
C10FF00	Type 2 diabetes mellitus with peripheral angiopathy
C10F.11	Type II diabetes mellitus
С109К00	Hyperosmolar non-ketotic state in type 2 diabetes mellitus
C10FR00	Type 2 diabetes mellitus with gastroparesis
C10P111	Type 2 diabetes mellitus in remission
C10F211	Type II diabetes mellitus with neurological complications
C109G00	Non-insulin dependent diabetes mellitus with arthropathy
C10FN00	Type 2 diabetes mellitus with ketoacidosis
C109C00	Non-insulin dependent diabetes mellitus with nephropathy
C10F611	Type II diabetes mellitus with retinopathy
C10FB11	Type II diabetes mellitus with polyneuropathy
C109700	Non-insulin dependent diabetes mellitus - poor control
C109600	Non-insulin-dependent diabetes mellitus with retinopathy
C10FK11	Hyperosmolar non-ketotic state in type II diabetes mellitus
C109200	Non-insulin-dependent diabetes mellitus with neuro comps

C10FG11	Type II diabetes mellitus with arthropathy
C10F.00	Type 2 diabetes mellitus
C109.00	Non-insulin dependent diabetes mellitus
C10P100	Type II diabetes mellitus in remission
C10F200	Type 2 diabetes mellitus with neurological complications
C109G12	Type 2 diabetes mellitus with arthropathy
C109C11	Type II diabetes mellitus with nephropathy
C109C12	Type 2 diabetes mellitus with nephropathy
C10F600	Type 2 diabetes mellitus with retinopathy
D10z100	Diabetes mellitus, adult onset, no mention of complication
C10FB00	Type 2 diabetes mellitus with polyneuropathy
C109711	Type II diabetes mellitus - poor control
C109712	Type 2 diabetes mellitus - poor control

## **Supplementary S2 Read codes used for suspected or confirmed COVID-19**

Description	Code	Confirmed(C)/ Suspected(S)
Has immunity to SARS-CoV-2	43dt400	С
SARS-CoV-2 IgG detected	43dtA00	С
SARS-CoV-2 IgM detected	43dtG00	С
Detection of SARS-CoV-2 by PCR	43hF.00	С
Coronavirus nucleic acid detection	43jS.00	С
2019-nCoV (novel coronavirus) detected	4J3R100	С
Gastroenteri due to SARS-CoV-2	A076400	С
Coronavirus infection	A795.00	С
Disease caused by 2019-nCoV (novel coronavirus)	A795100	С
Coronavirus as cause of dis classified to other chapters	A7y0000	С
[X]Coronavirus infection, unspecified	AyuDC00	С
[X]Coronavirus/cause/diseases classified to other chapters	AyuKL00	С
Encephalopat due to SARS-CoV-2	F289.00	С
Otitis media due to SARS-CoV-2	F529.00	С
Myocarditis due to SARS-CoV-2	G520800	С
Cardiomyopathy due SARS-CoV-2	G558500	С
URTI due to SARS-CoV-2	H051100	С
Pneumonia due to SARS-CoV-2	H204.00	С
COVID-19 confirmed by laboratory test	A795200	С
COVID-19 confirmed using clinical diagnostic criteria	A795300	С
Suspected coronavirus infection	1JX00	S
Suspected disease caused by 2019-nCoV (novel coronavirus)	1JX1.00	S
Telephone consultation for suspected 2019-nCoV (novel corona	9N31200	S

#### Supplementary S3 Flow diagram in detail

Adult individuals (≥18 years old) with a record of type 2 diabetes and registered with an eligible general practice no later than 30<sup>th</sup> January 2019 (one year before the index date) were eligible for this study (N = 131,341). Any individuals who were diagnosed with diabetes before the age of 12 years or with a record of type 1 diabetes (N = 7,411), adverse reaction to glucose-lowering agents, pancreatitis or pregnancy in the preceding year (N = 2,705), estimated glomerular filtration rate (eGFR) measurement less than 30 mL/min/1.73m² before the index date (N = 2,919), were excluded. There were 118,306 individuals who met our selection criteria.

We then excluded individuals who were not prescribed any of the nine glucose-lowering agents (N = 24,686). Following this, we excluded patients who did not have evidence of any prescription during study period (N = 21,986).

Among individuals who were on a current metformin prescription (N = 59,724), we excluded those who were on metformin monotherapy (N = 30,166). Therefore, there were 29,558 individuals who are on a current metformin prescription (extending into the pandemic period) and co-prescribed at least one of the eight other glucose-lowering agents. These patients were included in the exposed cohort.

Among individuals who were not on a current metformin prescription and have a prescription for any of the eight other glucose-lowering agents extending into the pandemic period (N = 11,910), we excluded those who were prescribed metformin within 90 days preceding the index date (recent users, N = 1,639). Overall, there are 10,271 individuals who were not current or recent users of metformin and had a prescription for any of other eight glucose-lowering agents extending into the pandemic period. These patients were included in the comparator cohort. Of 10,271 individuals, 8,640 with a historical prescription of metformin were then included in the comparator group of the sensitivity analyses.

# Supplementary S4 Baseline demographic characteristics, behavioural risk factors, diabetes complications, comorbidities, metabolic characteristics, and medications for the rest four imputed propensity score matched datasets

	the 2nd imputed PPS matched dataset			the 3rd imputed PPS matched dataset		puted PPS I dataset	the 5th imputed PPS matched dataset	
	Exposed Group (MF+) (n = 10,183)	Comparator group (MF-) (n = 10,183)	Exposed Group (MF+) (n = 10,183)	Comparator group (MF-) (n = 10,183)	Exposed Group (MF+) (n = 10,183)	Comparator group (MF-) (n = 10,183)	Exposed Group (MF+) (n = 10,183)	Comparator group (MF-) (n = 10,183)
<b>Demographic characteristics</b>								
Mean age (years) (SD)	67.31 (11.77)	67.68(13.12)	67.29 (11.71)	67.68(13.12)	67.21 (11.82)	67.68(13.12)	67.27 (11.73)	67.68(13.12)
Male sex (%)	5354 (52.6)	5326 (52.3)	5372 (52.8)	5326 (52.3)	5347 (52.5)	5326 (52.3)	5307 (52.1)	5326 (52.3)
Mean BMI (kg/m²) (SD))	31.94 (6.65)	31.81 (6.83)	31.97 (6.80)	31.81 (6.83)	31.90 (6.71)	31.81 (6.83)	31.94 (6.76)	31.81 (6.83)
BMI category (%) Underweight/Normal Weight (<24.9)	1153 (11.3)	1338 (13.1)	1195 (11.7)	1338 (13.1)	1186 (11.6)	1338 (13.1)	1176 (11.5)	1338 (13.1)
Overweight(25-29.9)	3114 (30.6)	3038 (29.8)	3102 (30.5)	3038 (29.8)	3145 (30.9)	3038 (29.8)	3141 (30.8)	3038 (29.8)
Obesity (>=30)	5730 (56.3)	5639 (55.4)	5707 (56.0)	5639 (55.4)	5696 (55.9)	5639 (55.4)	5682 (55.8)	5639 (55.4)
Missing	186 (1.8)	168 (1.6)	179 (1.8)	168 (1.6)	156 (1.5)	168 (1.6)	184 (1.8)	168 (1.6)
Behavioural risk factors								
Smoking status (%)								
Non-smokers	5137 (50.4)	5057 (49.7)	5047 (49.6)	5057 (49.7)	4988 (49.0)	5057 (49.7)	5082 (49.9)	5057 (49.7)
Ex-smokers	3646 (35.8)	3701 (36.3)	3680 (36.1)	3701 (36.3)	3739 (36.7)	3701 (36.3)	3652 (35.9)	3701 (36.3)
Current smokers	1356 (13.3)	1373 (13.5)	1413 (13.9)	1373 (13.5)	1410 (13.8)	1373 (13.5)	1400 (13.7)	1373 (13.5)
Missing	44 (0.4)	52 (0.5)	43 (0.4)	52 (0.5)	46 (0.5)	52 (0.5)	49 (0.5)	52 (0.5)
Excessive alcohol use (%)	649 (6.4)	657 (6.5)	654 (6.4)	657 (6.5)	649 (6.4)	657 (6.5)	664 (6.5)	657 (6.5)
Mean diabetes duration (yrs) (SD)	11.65 (6.67)	11.58 (7.00)	11.55 (6.64)	11.58 (7.00)	11.57 (6.60)	11.58 (7.00)	11.59 (6.64)	11.58 (7.00)
Diabetes complications Peripheral neuropathy (%) Diabetic foot disease (%)	763 (7.5) 512 (5.0)	776 (7.6) 518 (5.1)	760 (7.5) 540 (5.3)	776 (7.6) 518 (5.1)	785 (7.7) 512 (5.0)	776 (7.6) 518 (5.1)	767 (7.5) 507 (5.0)	776 (7.6) 518 (5.1)

Sight threating retinopathy (%)	1245 (12.2)	1264 (12.4)	1247 (12.2)	1264 (12.4)	1253 (12.3)	1264 (12.4)	1250 (12.3)	1264 (12.4)
<u>Comorbidities</u>								
Hypertension (%)	6232 (61.2)	6178 (60.7)	6181 (60.7)	6178 (60.7)	6128 (60.2)	6178 (60.7)	6180 (60.7)	6178 (60.7)
Ischaemic heart disease (%)	2204 (21.6)	2237 (22.0)	2212 (21.7)	2237 (22.0)	2199 (21.6)	2237 (22.0)	2207 (21.7)	2237 (22.0)
Atrial Fibrillation (%)	1026 (10.1)	1077 (10.6)	1033 (10.1)	1077 (10.6)	1064 (10.4)	1077 (10.6)	1047 (10.3)	1077 (10.6)
Stroke/TIA (%)	978 (9.6)	970 (9.5)	935 (9.2)	970 (9.5)	925 (9.1)	970 (9.5)	938 (9.2)	970 (9.5)
Heart failure (%)	709 (7.0)	745 (7.3)	739 (7.3)	745 (7.3)	711 (7.0)	745 (7.3)	717 (7.0)	745 (7.3)
Peripheral Vascular Disease (%)	486 (4.8)	500 (4.9)	487 (4.8)	500 (4.9)	489 (4.8)	500 (4.9)	504 (4.9)	500 (4.9)
Chronic kidney disease (%)	1888 (18.5)	2428 (23.8)	1891 (18.6)	2428 (23.8)	1875 (18.4)	2428 (23.8)	1857 (18.2)	2428 (23.8)
Cancers* (%)	1494 (14.7)	1474 (14.5)	1460 (14.3)	1474 (14.5)	1470 (14.4)	1474 (14.5)	1456 (14.3)	1474 (14.5)
Chronic respiratory disease (%)	990 (9.7)	1016 (10.0)	1006 (9.9)	1016 (10.0)	1028 (10.1)	1016 (10.0)	1013 (9.9)	1016 (10.0)
Liver Disease (%)	579 (5.7)	619 (6.1)	567 (5.6)	619 (6.1)	593 (5.8)	619 (6.1)	583 (5.7)	619 (6.1)
Rheumatoid Arthritis (%)	229 (2.2)	212 (2.1)	213 (2.1)	212 (2.1)	220 (2.2)	212 (2.1)	225 (2.2)	212 (2.1)
NAFLD/NASH (%)	261 (2.6)	261 (2.6)	251 (2.5)	261 (2.6)	250 (2.5)	261 (2.6)	258 (2.5)	261 (2.6)
Blood & bone marrow cancer (%)	151 (1.5)	162 (1.6)	152 (1.5)	162 (1.6)	149 (1.5)	162 (1.6)	164 (1.6)	162 (1.6)
Metabolic characteristics								
Diastolic BP (mmHg)								
<90	9492 (93.2)	9450 (92.8)	9483 (93.1)	9450 (92.8)	9498 (93.3)	9450 (92.8)	9462 (92.9)	9450 (92.8)
≥90	677 (6.6)	720 (7.1)	686 (6.7)	720 (7.1)	673 (6.6)	720 (7.1)	709 (7.0)	720 (7.1)
Missing	14 (0.1)	13 (0.1)	14 (0.1)	13 (0.1)	12 (0.1)	13 (0.1)	12 (0.1)	13 (0.1)
Systolic BP (mmHg)		,	,				,	
<140	7066 (69.4)	7073 (69.5)	7022 (69.0)	7073 (69.5)	7073 (69.5)	7073 (69.5)	7070 (69.4)	7073 (69.5)
≥140	3103 (30.5)	3097 (30.4)	3147 (30.9)	3097 (30.4)	3098 (30.4)	3097 (30.4)	3101 (30.5)	3097 (30.4)
Missing	14 (0.1)	13 (0.1)	14 (0.1)	13 (0.1)	12 (0.1)	13 (0.1)	12 (0.1)	13 (0.1)
Total cholesterol (mmol/L)	0457 (00.1)	0064 (70.6)	0467 (00.5)	0064 (70.5)	0400 (70.5)	0064 (70.5)	04.47./00.01	0064 (70.0)
<5.2	8157 (80.1)	8064 (79.2)	8167 (80.2)	8064 (79.2)	8103 (79.6)	8064 (79.2)	8147 (80.0)	8064 (79.2)

5.2 to 6.2	1233 (12.1)	1367 (13.4)	1209 (11.9)	1367 (13.4)	1246 (12.2)	1367 (13.4)	1224 (12.0)	1367 (13.4)
≥6.2	724 (7.1)	675 (6.6)	743 (7.3)	675 (6.6)	759 (7.5)	675 (6.6)	736 (7.2)	675 (6.6)
Missing	69 (0.7)	77 (0.8)	64 (0.6)	77 (0.8)	75 (0.7)	77 (0.8)	76 (0.7)	77 (0.8)
HDL-cholesterol (mmol/L)	,	( /	- ( )	( /	- (- )	( /	- (- )	()
<1.55	8742 (85.8)	8669 (85.1)	8763 (86.1)	8669 (85.1)	8797 (86.4)	8669 (85.1)	8716 (85.6)	8669 (85.1)
≥1.55	1266 (12.4)	1296 (12.7)	1240 (12.2)	1296 (12.7)	1201 (11.8)	1296 (12.7)	1277 (12.5)	1296 (12.7)
Missing	175 (1.7)	218 (2.1)	180 (1.8)	218 (2.1)	185 (1.8)	218 (2.1)	190 (1.9)	218 (2.1)
eGFR (mL/min/1.73m2)								
>=60 (Stage 1&2)	7517 (73.8)	7258 (71.3)	7590 (74.5)	7258 (71.3)	7555 (74.2)	7258 (71.3)	7562 (74.3)	7258 (71.3)
30 to 60 (Stage 3)	2624 (25.8)	2885 (28.3)	2554 (25.1)	2885 (28.3)	2591 (25.4)	2885 (28.3)	2580 (25.3)	2885 (28.3)
Missing	42 (0.4)	40 (0.4)	39 (0.4)	40 (0.4)	37 (0.4)	40 (0.4)	41 (0.4)	40 (0.4)
ACR (mg/mmol)								
< 3 mg/mmol	4892 (48.0)	4819 (47.3)	4869 (47.8)	4819 (47.3)	4932 (48.4)	4819 (47.3)	4901 (48.1)	4819 (47.3)
≥30 mg/mmol	471 (4.6)	470 (4.6)	452 (4.4)	470 (4.6)	451 (4.4)	470 (4.6)	465 (4.6)	470 (4.6)
3 to 30 mg/mmol	2287 (22.5)	2258 (22.2)	2260 (22.2)	2258 (22.2)	2266 (22.3)	2258 (22.2)	2265 (22.2)	2258 (22.2)
Missing	2533 (24.9)	2636 (25.9)	2602 (25.6)	2636 (25.9)	2534 (24.9)	2636 (25.9)	2552 (25.1)	2636 (25.9)
HbA1c (mmol/mol)								
< 48 mmol/mol (6.5%)	908 (8.9)	1042 (10.2)	894 (8.8)	1042 (10.2)	914 (9.0)	1042 (10.2)	916 (9.0)	1042 (10.2)
≥58 mmol/mol (7.5%)	6459 (63.4)	6369 (62.5)	6463 (63.5)	6369 (62.5)	6406 (62.9)	6369 (62.5)	6468 (63.5)	6369 (62.5)
48 to 58 mmol/mol (6.5-	2653 (26.1)	2624 (25.8)	2644 (26.0)	2624 (25.8)	2679 (26.3)	2624 (25.8)	2627 (25.8)	2624 (25.8)
7.5%)								
Missing	163 (1.6)	148 (1.5)	182 (1.8)	148 (1.5)	184 (1.8)	148 (1.5)	172 (1.7)	148 (1.5)
Medications								
Metformin (%)	10183(100.0)	0 (0.0)	10183(100.0)	0 (0.0)	10193/100 0\	0 (0.0)	10183(100.0)	0 (0.0)
Current users	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	10183(100.0) 0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Recent users	0 (0.0)	8587 (84.3)	0 (0.0)	8587 (84.3)	0 (0.0)	8587 (84.3)	0 (0.0)	8587 (84.3)
Historical users	0 (0.0)	1596 (15.7)	0 (0.0)	1596 (15.7)	0 (0.0)	1596 (15.7)	0 (0.0)	1596 (15.7)
Non-users	0 (0.0)	1596 (15.7)	0 (0.0)	1596 (15.7)	0 (0.0)	1596 (15.7)	0 (0.0)	1590 (15.7)
DPP4i (%)	4117 (40.4)	4222 (41.5)	4112 (40.4)	4222 (41.5)	4181 (41.1)	4222 (41.5)	4193 (41.2)	4222 (41.5)
Current users Recent users	4117 (40.4) 152 (1.5)	4222 (41.5) 146 (1.4)	141 (1.4)	4222 (41.5) 146 (1.4)	135 (1.3)	4222 (41.5) 146 (1.4)	4193 (41.2) 150 (1.5)	146 (1.4)
Necelli users	132 (1.3)	140 (1.4)	141 (1.4)	140 (1.4)	133 (1.3)	140 (1.4)	130 (1.3)	140 (1.4)

Historical users	1874 (18.4)	1795 (17.6)	1794 (17.6)	1795 (17.6)	1820 (17.9)	1795 (17.6)	1795 (17.6)	1795 (17.6)
Non-users	4040 (39.7)	4020 (39.5)	4136 (40.6)	4020 (39.5)	4047 (39.7)	4020 (39.5)	4045 (39.7)	4020 (39.5)
SGLT2i (%)								
Current users	2891 (28.4)	2780 (27.3)	2936 (28.8)	2780 (27.3)	2888 (28.4)	2780 (27.3)	2873 (28.2)	2780 (27.3)
Recent users	103 (1.0)	102 (1.0)	105 (1.0)	102 (1.0)	97 (1.0)	102 (1.0)	105 (1.0)	102 (1.0)
Historical users	854 (8.4)	836 (8.2)	828 (8.1)	836 (8.2)	858 (8.4)	836 (8.2)	859 (8.4)	836 (8.2)
Non-users	6335 (62.2)	6465 (63.5)	6314 (62.0)	6465 (63.5)	6340 (62.3)	6465 (63.5)	6346 (62.3)	6465 (63.5)
Meglitinides (%)								
Current users	15 (0.1)	13 (0.1)	15 (0.1)	13 (0.1)	20 (0.2)	13 (0.1)	16 (0.2)	13 (0.1)
Recent users	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Historical users	108 (1.1)	118 (1.2)	128 (1.3)	118 (1.2)	120 (1.2)	118 (1.2)	122 (1.2)	118 (1.2)
Non-users	10060 (98.8)	10052 (98.7)	10040 (98.6)	10052 (98.7)	10043 (98.6)	10052 (98.7)	10045 (98.6)	10052 (98.7
Acarbose (%)								
Current users	19 (0.2)	15 (0.1)	15 (0.1)	15 (0.1)	14 (0.1)	15 (0.1)	16 (0.2)	15 (0.1)
Recent users	1 (0.0)	1 (0.0)	3 (0.0)	1 (0.0)	0 (0.0)	1 (0.0)	1 (0.0)	1 (0.0)
Historical users	104 (1.0)	103 (1.0)	107 (1.1)	103 (1.0)	101 (1.0)	103 (1.0)	100 (1.0)	103 (1.0)
Non-users	10059 (98.8)	10064 (98.8)	10058 (98.8)	10064(98.8)	10068 (98.9)	10064(98.8)	10066 (98.9)	10064(98.8
GLP1 (%)								
Current users	594 (5.8)	586 (5.8)	619 (6.1)	586 (5.8)	607 (6.0)	586 (5.8)	630 (6.2)	586 (5.8)
Recent users	165 (1.6)	156 (1.5)	154 (1.5)	156 (1.5)	161 (1.6)	156 (1.5)	163 (1.6)	156 (1.5)
Historical users	1030 (10.1)	954 (9.4)	1006 (9.9)	954 (9.4)	998 (9.8)	954 (9.4)	960 (9.4)	954 (9.4)
Non-users	8394 (82.4)	8487 (83.3)	8404 (82.5)	8487 (83.3)	8417 (82.7)	8487 (83.3)	8430 (82.8)	8487 (83.3)
Insulin (%)								
Current users	993 (9.8)	1006 (9.9)	970 (9.5)	1006 (9.9)	975 (9.6)	1006 (9.9)	1000 (9.8)	1006 (9.9)
Recent users	358 (3.5)	360 (3.5)	347 (3.4)	360 (3.5)	338 (3.3)	360 (3.5)	351 (3.4)	360 (3.5)
Historical users	1155 (11.3)	1169 (11.5)	1195 (11.7)	1169 (11.5)	1189 (11.7)	1169 (11.5)	1183 (11.6)	1169 (11.5)
Non-users	7677 (75.4)	7648 (75.1)	7671 (75.3)	7648 (75.1)	7681 (75.4)	7648 (75.1)	7649 (75.1)	7648 (75.1)
Thiazolidinedione (%)								
Current users	541 (5.3)	542 (5.3)	542 (5.3)	542 (5.3)	587 (5.8)	542 (5.3)	547 (5.4)	542 (5.3)
Recent users	26 (0.3)	32 (0.3)	32 (0.3)	32 (0.3)	30 (0.3)	32 (0.3)	33 (0.3)	32 (0.3)
Historical users	1460 (14.3)	1388 (13.6)	1404 (13.8)	1388 (13.6)	1392 (13.7)	1388 (13.6)	1418 (13.9)	1388 (13.6)

Sulphonylureas (%)								
Current users	4546 (44.6)	4473 (43.9)	4472 (43.9)	4473 (43.9)	4490 (44.1)	4473 (43.9)	4421 (43.4)	4473 (43.9)
Recent users	224 (2.2)	231 (2.3)	232 (2.3)	231 (2.3)	227 (2.2)	231 (2.3)	232 (2.3)	231 (2.3)
Historical users	2489 (24.4)	2491 (24.5)	2466 (24.2)	2491 (24.5)	2487 (24.4)	2491 (24.5)	2521 (24.8)	2491 (24.5)
Non-users	2924 (28.7)	2988 (29.3)	3013 (29.6)	2988 (29.3)	2979 (29.3)	2988 (29.3)	3009 (29.5)	2988 (29.3)
Immunosuppressive drugs(%)	566 (5.6)	578 (5.7)	544 (5.3)	578 (5.7)	565 (5.5)	578 (5.7)	557 (5.5)	578 (5.7)
Systemic corticosteroids (%)	1324 (13.0)	1354 (13.3)	1284 (12.6)	1354 (13.3)	1306 (12.8)	1354 (13.3)	1361 (13.4)	1354 (13.3)
ACEi/ARB (%)	7425 (72.9)	7316 (71.8)	7288 (71.6)	7316 (71.8)	7302 (71.7)	7316 (71.8)	7348 (72.2)	7316 (71.8)
Other antihypertensives (%)	7391 (72.6)	7337 (72.1)	7299 (71.7)	7337 (72.1)	7285 (71.5)	7337 (72.1)	7297 (71.7)	7337 (72.1)
Anticoagulants (%)	1706 (16.8)	1731 (17.0)	1691 (16.6)	1731 (17.0)	1703 (16.7)	1731 (17.0)	1706 (16.8)	1731 (17.0)
Antiplatelets (%)	5382 (52.9)	5411 (53.1)	5303 (52.1)	5411 (53.1)	5320 (52.2)	5411 (53.1)	5391 (52.9)	5411 (53.1)
Lipid-lowering drugs (%)	8673 (85.2)	8686 (85.3)	8698 (85.4)	8686 (85.3)	8700 (85.4)	8686 (85.3)	8715 (85.6)	8686 (85.3)

BMI=Body mass index, TIA=transient ischaemic attack, NAFLD/NASH= non-alcoholic fatty liver disease or non-alcoholic steatohepatitis, ACR=albumin creatinine ratio, BP=blood pressure, eGFR=estimated glomerular filtration rate, HbA1c=haemoglobin A1c, HDL=high density lipoprotein, ACEi=angiotensin converting enzyme inhibitor, ARB=angiotensin receptor blocker, DPP4i=dipeptidyl peptidase-4 inhibitors, GLP1=glucagon-like peptide 1 receptor agonist, SGLT2i=sodium-glucose co-transporter-2 inhibitors

Exposed group: patients with a current combination prescription of metformin and other glucose-lowering agents; Comparator group: patients with a current prescription of other glucose-lowering agents

<sup>\*</sup>Excluding melanoma, and blood and bone marrow cancers

Supplementary S5 Risk of developing COVID-19, mortality, and back pain among those with a current combination prescription of metformin and other glucose-lowering agents compared to a current prescription of other glucose-lowering agents only (reference group) by sex and by body mass index (Subgroup analyses)

Propensity score matched analysis (Adjusted HR, 95% CI)	Confirmed COVID-19		Suspected/Confirmed COVID-19			19 related eath	All-caus	e mortality	Back Pain	
	Exposed group (MF+)	Comparator group (MF-)	Exposed group (MF+)	Comparator group (MF-)	Exposed group (MF+)	Comparator group (MF-)	Exposed group (MF+)	Comparator group (MF-)	Exposed group (MF+)	Comparator group (MF-)
By Sex										
Male	0.95 (0.	.51, 1.80)	0.94 (0	.66, 1.34)	0.58 (0	).17 <i>,</i> 1.98)	0.75 (0	).57 <i>,</i> 0.97)	0.88 (0	).53, 1.43)
Female	0.79 (0.	.42, 1.49)	0.83 (0	.61, 1.14)	1.41 (0	).55, 3.57)	0.98 (0	).74, 1.29)	1.25 (0	).81, 1.93)
Ву ВМІ										
BMI $\geq$ 25 kg/m <sup>2</sup>	0.88 (0.	.53, 1.43)	0.88 (0	.53, 1.43)	0.88 (0	).53, 1.43)	0.88 (0	).53, 1.43)	0.88 (0	).53, 1.43)
BMI $\geq$ 30 kg/m <sup>2</sup>	0.93 (0.	.47, 1.82)	0.85 (0	.61, 1.18)	0.66 (0	.22, 1.98)	0.84 (0	).63, 1.13)	1.07 (0	).74, 1.54)

<sup>†</sup> Adjusted for: age, sex, smoking status, high alcohol consumption (alcoholism), body mass index categories, total cholesterol categories, high-density lipoprotein categories, albumin-creatinine ratio categories, estimated glomerular filtration rate categories, HbA1c categories, atrial fibrillation, rheumatoid arthritis, hypertension, cardiovascular disease, non-alcoholic fatty liver disease or non-alcoholic steatohepatitis, prescriptions of renin angiotensin aldosterone system inhibitors, other antihypertensive drugs, lipid-lowering drugs, antiplatelets, anticoagulants, diabetes complications, diabetes duration, respiratory disease, cancers, immunosuppressant therapies, and systemic corticosteroid use.

Supplementary S6 Baseline demographic characteristics, behavioural risk factors, diabetes complications, comorbidities, metabolic characteristics, and medications (Sensitivity analysis)

Exposed Group (MF+) (n=29,558)         Comparator group (MF-) (n=8,640)         Exposed Group (MF+) group (MF-) (n=8,632)         Comparator group (MF-) (n=8,632)           Demographic characteristics         Mean age (years) (SD)         64.8 (11.7)         67.3 (12.8)         67.0 (11.6)         67.3 (12.8)           Male sex (%)         18298 (61.9)         4489 (52.0)         4555 (52.8)         4488 (52.0)           Mean BMI (kg/m²) (SD))         32.1 (6.7)         32.1 (6.8)         32.0 (6.7)         32.1 (6.8)           BMI category (%)         <25         3159 (10.7)         1005 (11.6)         971 (11.2)         1003 (11.6)           ≥3 to < 30         9080 (30.7)         2559 (29.6)         2670 (30.9)         2556 (29.6)           ≥30         16908 (57.2)         4993 (57.8)         4859 (56.3)         4990 (57.8)           Missing         411 (1.4)         83 (1.0)         132 (1.5)         83 (1.0)           Behavioural risk factors           Smoking status (%)           Non-smokers         14632 (49.5)         4291 (49.7)         4214 (48.8)         4287 (49.7)		Hansa	tahad	Drononcity coors matched+			
Group (MF+) (n=29,558)         group (MF-) (n=8,632)         Group (MF+) (n=8,632)         group (MF-) (n=8,632)           Demographic characteristics         Mean age (years) (SD)         64.8 (11.7)         67.3 (12.8)         67.0 (11.6)         67.3 (12.8)           Male sex (%)         18298 (61.9)         4489 (52.0)         4555 (52.8)         4488 (52.0)           Mean BMI (kg/m²) (SD))         32.1 (6.7)         32.1 (6.8)         32.0 (6.7)         32.1 (6.8)           BMI category (%)         <25         3159 (10.7)         1005 (11.6)         971 (11.2)         1003 (11.6)           25 to < 30         9080 (30.7)         2559 (29.6)         2670 (30.9)         2556 (29.6)           ≥30         16908 (57.2)         4993 (57.8)         4859 (56.3)         4990 (57.8)           Missing         411 (1.4)         83 (1.0)         132 (1.5)         83 (1.0)           Behavioural risk factors         5moking status (%)         4291 (49.7)         4214 (48.8)         4287 (49.7)				Propensity score matched†			
Demographic characteristics         Mean age (years) (SD)       64.8 (11.7)       67.3 (12.8)       67.0 (11.6)       67.3 (12.8)         Male sex (%)       18298 (61.9)       4489 (52.0)       4555 (52.8)       4488 (52.0)         Mean BMI (kg/m²) (SD))       32.1 (6.7)       32.1 (6.8)       32.0 (6.7)       32.1 (6.8)         BMI category (%)       25       3159 (10.7)       1005 (11.6)       971 (11.2)       1003 (11.6)         25 to < 30       9080 (30.7)       2559 (29.6)       2670 (30.9)       2556 (29.6)         ≥30       16908 (57.2)       4993 (57.8)       4859 (56.3)       4990 (57.8)         Missing       411 (1.4)       83 (1.0)       132 (1.5)       83 (1.0)         Behavioural risk factors       Smoking status (%)       14632 (49.5)       4291 (49.7)       4214 (48.8)       4287 (49.7)		<del>-</del>	-	-	-		
Demographic characteristics         Mean age (years) (SD)         64.8 (11.7)         67.3 (12.8)         67.0 (11.6)         67.3 (12.8)           Male sex (%)         18298 (61.9)         4489 (52.0)         4555 (52.8)         4488 (52.0)           Mean BMI (kg/m²) (SD))         32.1 (6.7)         32.1 (6.8)         32.0 (6.7)         32.1 (6.8)           BMI category (%)         25         3159 (10.7)         1005 (11.6)         971 (11.2)         1003 (11.6)           25 to < 30							
Mean age (years) (SD)       64.8 (11.7)       67.3 (12.8)       67.0 (11.6)       67.3 (12.8)         Male sex (%)       18298 (61.9)       4489 (52.0)       4555 (52.8)       4488 (52.0)         Mean BMI (kg/m²) (SD))       32.1 (6.7)       32.1 (6.8)       32.0 (6.7)       32.1 (6.8)         BMI category (%)       3159 (10.7)       1005 (11.6)       971 (11.2)       1003 (11.6)         25 to < 30		(11-29,556)	(11-8,040)	(11-0,032)	(11- 0,032)		
Male sex (%)       18298 (61.9)       4489 (52.0)       4555 (52.8)       4488 (52.0)         Mean BMI (kg/m²) (SD))       32.1 (6.7)       32.1 (6.8)       32.0 (6.7)       32.1 (6.8)         BMI category (%)       3159 (10.7)       1005 (11.6)       971 (11.2)       1003 (11.6)         25 to < 30		640 (44.7)	67.2 (42.0)	67.0 (44.6)	67.2 (42.0)		
Mean BMI (kg/m²) (SD))       32.1 (6.7)       32.1 (6.8)       32.0 (6.7)       32.1 (6.8)         BMI category (%)       3159 (10.7)       1005 (11.6)       971 (11.2)       1003 (11.6)         25 to < 30		•	• •		• •		
BMI category (%) <25 3159 (10.7) 1005 (11.6) 971 (11.2) 1003 (11.6) 25 to < 30 9080 (30.7) 2559 (29.6) 2670 (30.9) 2556 (29.6) ≥30 16908 (57.2) 4993 (57.8) 4859 (56.3) 4990 (57.8) Missing 411 (1.4) 83 (1.0) 132 (1.5) 83 (1.0)   Behavioural risk factors  Smoking status (%) Non-smokers 14632 (49.5) 4291 (49.7) 4214 (48.8) 4287 (49.7)		, ,	• •		• •		
$<25$ $3159 (10.7)$ $1005 (11.6)$ $971 (11.2)$ $1003 (11.6)$ $25 \text{ to} < 30$ $9080 (30.7)$ $2559 (29.6)$ $2670 (30.9)$ $2556 (29.6)$ $\geq 30$ $16908 (57.2)$ $4993 (57.8)$ $4859 (56.3)$ $4990 (57.8)$ Missing $411 (1.4)$ $83 (1.0)$ $132 (1.5)$ $83 (1.0)$ Behavioural risk factorsSmoking status (%)Non-smokers $14632 (49.5)$ $4291 (49.7)$ $4214 (48.8)$ $4287 (49.7)$		32.1 (6.7)	32.1 (6.8)	32.0 (6.7)	32.1 (6.8)		
25 to < 30 ≥30 Missing  9080 (30.7) 2559 (29.6) 2670 (30.9) 2556 (29.6) 4859 (56.3) 4990 (57.8) 411 (1.4) 83 (1.0)  83 (1.0)  83 (1.0)  8411 (48.8) 4287 (49.7)		2450 (40.7)	4005 (44.6)	074 (44 2)	4002 (44.6)		
≥30 Missing  16908 (57.2) 4993 (57.8) 4859 (56.3) 4990 (57.8)  411 (1.4) 83 (1.0)  83 (1.0)  83 (1.0)  83 (1.0)  84990 (57.8)  8490 (57.8)  8490 (57.8)  84990 (57.8)  84		• •	• •				
Missing 411 (1.4) 83 (1.0) 132 (1.5) 83 (1.0)  **Behavioural risk factors**  Smoking status (%)  Non-smokers 14632 (49.5) 4291 (49.7) 4214 (48.8) 4287 (49.7)		, ,			• • •		
Behavioural risk factors         Smoking status (%)       14632 (49.5) 4291 (49.7) 4214 (48.8) 4287 (49.7)		•	•		• •		
Smoking status (%)       14632 (49.5)       4291 (49.7)       4214 (48.8)       4287 (49.7)	Missing	411 (1.4)	83 (1.0)	132 (1.5)	83 (1.0)		
Smoking status (%)       14632 (49.5)       4291 (49.7)       4214 (48.8)       4287 (49.7)	Dalamia and dala for the co						
Non-smokers 14632 (49.5) 4291 (49.7) 4214 (48.8) 4287 (49.7)							
		4.4622 (40.5)	4204 (40.7)	4244 (40.0)	4207 (40.7)		
		• •			• • •		
Ex-smokers 10799 (36.5) 3149 (36.4) 3221 (37.3) 3145 (36.4)		, ,			• • •		
Current smokers 4063 (13.7) 1179 (13.6) 1207 (14.0) 1179 (13.7)		, ,			• • •		
Missing 64 (0.2) 21 (0.2) 26 (0.3) 21 (0.2)	_	, ,	• • •		• •		
<b>Excessive alcohol use (%)</b> 1506 (5.1) 553 (6.4) 547 (6.3) 551 (6.4)	Excessive alconol use (%)	1506 (5.1)	553 (6.4)	547 (6.3)	551 (6.4)		
Diabetes complications	Diabetes complications						
Mean diabetes duration (yrs) (SD) 12.1 (6.7) 11.9 (6.7) 11.7 (6.6) 11.9 (6.7)		12.1 (6.7)	11.9 (6.7)	11.7 (6.6)	11.9 (6.7)		
Peripheral neuropathy (%) 2070 (7.0) 675 (7.8) 688 (8.0) 675 (7.8)			• •				
<b>Diabetic foot disease (%)</b> 1335 (4.5) 447 (5.2) 434 (5.0) 446 (5.2)		• •	• •		• •		
Sight threating retinopathy (%) 3507 (11.9) 1098 (12.7) 1058 (12.3) 1095 (12.7)	• •	• •			• •		
Comorbidities	Comorbidities				, ,		
Hypertension (%) 17477 (59.1) 5320 (61.6) 5217 (60.4) 5317 (61.6)	<u> </u>	17477 (59.1)	5320 (61.6)	5217 (60.4)	5317 (61.6)		
Ischaemic heart disease (%) 5374 (18.2) 1901 (22.0) 1881 (21.8) 1898 (22.0)	* * * * * * * * * * * * * * * * * * * *	• •	• •				
Atrial Fibrillation (%) 2194 (7.4) 867 (10.0) 885 (10.3) 865 (10.0)							
Stroke/TIA (%) 1992 (6.7) 814 (9.4) 801 (9.3) 813 (9.4)	• •	, ,					
Heart failure (%) 1322 (4.5) 622 (7.2) 614 (7.1) 620 (7.2)	• •	, ,	• •				
Peripheral Vascular Disease (%) 1055 (3.6) 424 (4.9) 402 (4.7) 421 (4.9)	` ,	• •	• •		• •		
Chronic kidney disease (%) 3839 (13.0) 1951 (22.6) 1527 (17.7) 1947 (22.6)		• •	• •		• •		
Cancers* (%) 3114 (10.5) 1229 (14.2) 1259 (14.6) 1226 (14.2)		` '					
<b>Chronic respiratory disease (%)</b> 2351 (8.0) 846 (9.8) 854 (9.9) 845 (9.8)	• •	, ,			` '		
<b>Liver Disease (%)</b> 1636 (5.5) 519 (6.0) 480 (5.6) 519 (6.0)		, ,	•		• •		
Rheumatoid Arthritis (%) 442 (1.5) 175 (2.0) 174 (2.0) 175 (2.0)		, ,	• •	` '	• •		
NAFLD/NASH (%) 742 (2.5) 236 (2.7) 211 (2.4) 236 (2.7)		, ,					
Blood & bone marrow cancer (%) 404 (1.4) 142 (1.6) 145 (1.7) 141 (1.6)	• •	, ,					

Metabolic characteristics				
Diastolic BP (mmHg)	27474 (02.0)	0045 (02.0)	0064 (02.4)	0000 (02.0)
<90	27474 (92.9)	8015 (92.8)	8061 (93.4)	8009 (92.8)
≥90	2052 (6.9)	624 (7.2)	561 (6.5)	622 (7.2)
Missing	32 (0.1)	1 (0.0)	10 (0.1)	1 (0.0)
Systolic BP (mmHg)	24.02 (=4.4)	()		
<140	21102 (71.4)	6009 (69.5)	6084 (70.5)	6006 (69.6)
≥140	8424 (28.5)	2630 (30.4)	2538 (29.4)	2625 (30.4)
Missing	32 (0.1)	1 (0.0)	10 (0.1)	1 (0.0)
Total cholesterol (mmol/L)				
<5.2	25257 (85.4)	6868 (79.5)	6894 (79.9)	6867 (79.6)
5.2 to 6.2	2878 (9.7)	1162 (13.4)	1086 (12.6)	, ,
≥6.2	1252 (4.2)	580 (6.7)	610 (7.1)	577 (6.7)
Missing	171 (0.6)	30 (0.3)	42 (0.5)	30 (0.3)
HDL-cholesterol (mmol/L)				
<1.55	26054 (88.1)	7474 (86.5)	7508 (87.0)	7468 (86.5)
≥1.55	3028 (10.2)	1048 (12.1)	983 (11.4)	1047 (12.1)
Missing	476 (1.6)	118 (1.4)	141 (1.6)	117 (1.4)
eGFR (mL/min/1.73m <sup>2</sup> )				
≥60 (Stage 1&2)	4991 (16.9)	2329 (27.0)	6527 (75.6)	6289 (72.9)
30 to 60 (Stage 3)	24469 (82.8)	6292 (72.8)	2080 (24.1)	2324 (26.9)
Missing	98 (0.3)	19 (0.2)	25 (0.3)	19 (0.2)
ACR (mg/mmol)				
< 3 mg/mmol	15119 (51.2)	4251 (49.2)	4219 (48.9)	4250 (49.2)
3 to 30 mg/mmol	6144 (20.8)	1980 (22.9)	1930 (22.4)	1978 (22.9)
≥30 mg/mmol	1052 (3.6)	398 (4.6)	376 (4.4)	397 (4.6)
Missing	7243 (24.5)	2011 (23.3)	2107 (24.4)	2007 (23.3)
HbA1c (mmol/mol)				
< 48 mmol/mol (6.5%)	2654 (9.0)	769 (8.9)	692 (8.0)	769 (8.9)
48 to 58 mmol/mol (6.5-7.5%)	7918 (26.8)	2160 (25.0)	2222 (25.7)	2159 (25.0)
≥58 mmol/mol (7.5%)	18461 (62.5)	5604 (64.9)	5579 (64.6)	5597 (64.8)
Missing	525 (1.8)	107 (1.2)	139 (1.6)	107 (1.2)
<u>Medications</u>				
Metformin (%)				
Current users	29558 (100.0)	0 (0.0)	8632 (100.0)	0 (0.0)
Recent users	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Historical users	0 (0.0)	8640 (100.0)	0 (0.0)	8632 (100.0)
Non-users	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
OPP4i (%)				. ,
Current users	13132 (44.4)	3636 (42.1)	3624 (42.0)	3635 (42.1)

Recent users	364 (1.2)	136 (1.6)	132 (1.5)	135 (1.6)
Historical users	4985 (16.9)	1744 (20.2)	1677 (19.4)	1741 (20.2)
Non-users	11077 (37.5)	3124 (36.2)	3199 (37.1)	3121 (36.2)
SGLT2i (%)				
Current users	10661 (36.1)	2547 (29.5)	2615 (30.3)	2546 (29.5)
Recent users	278 (0.9)	101 (1.2)	100 (1.2)	101 (1.2)
Historical users	2055 (7.0)	810 (9.4)	803 (9.3)	810 (9.4)
Non-users	16564 (56.0)	5182 (60.0)	5114 (59.2)	5175 (60.0)
Meglitinides (%)				
Current users	60 (0.2)	10 (0.1)	9 (0.1)	10 (0.1)
Recent users	6 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Historical users	306 (1.0)	113 (1.3)	107 (1.2)	113 (1.3)
Non-users	29186 (98.7)	8517 (98.6)	8516 (98.7)	8509 (98.6)
Acarbose (%)				
Current users	42 (0.1)	9 (0.1)	12 (0.1)	9 (0.1)
Recent users	4 (0.0)	1 (0.0)	0 (0.0)	1 (0.0)
Historical users	219 (0.7)	101 (1.2)	92 (1.1)	101 (1.2)
Non-users	29293 (99.1)	8529 (98.7)	8528 (98.8)	8521 (98.7)
GLP1 (%)				
Current users	2081 (7.0)	533 (6.2)	565 (6.5)	533 (6.2)
Recent users	597 (2.0)	145 (1.7)	129 (1.5)	145 (1.7)
Historical users	2910 (9.8)	914 (10.6)	900 (10.4)	913 (10.6)
Non-users	23970 (81.1)	7048 (81.6)	7038 (81.5)	7041 (81.6)
Insulin (%)				
Current users	1901 (6.4)	810 (9.4)	787 (9.1)	807 (9.3)
Recent users	859 (2.9)	315 (3.6)	307 (3.6)	315 (3.6)
Historical users	2613 (8.8)	1069 (12.4)	1038 (12.0)	1066 (12.3)
Non-users	24185 (81.8)	6446 (74.6)	6500 (75.3)	6444 (74.7)
Thiazolidinedione (%)				
Current users	1683 (5.7)	488 (5.6)	474 (5.5)	487 (5.6)
Recent users	69 (0.2)	30 (0.3)	30 (0.3)	30 (0.3)
Historical users	4422 (15.0)	1355 (15.7)	1280 (14.8)	1352 (15.7)
Non-users	23384 (79.1)	6767 (78.3)	6848 (79.3)	6763 (78.3)
Sulphonylureas (%)				
Current users	12979 (43.9)	3707 (42.9)	3719 (43.1)	3706 (42.9)
Recent users	565 (1.9)	215 (2.5)	203 (2.4)	214 (2.5)
Historical users	6363 (21.5)	2357 (27.3)	2291 (26.5)	2352 (27.2)
Non-users	9651 (32.7)	2361 (27.3)	2419 (28.0)	2360 (27.3)
Immunosuppressive drugs (%)	1070 (3.6)	455 (5.3)	447 (5.2)	451 (5.2)
Systemic corticosteroids (%)	3047 (10.3)	1090 (12.6)	1087 (12.6)	1088 (12.6)
ACEI/ARB (%)	21667 (73.3)	6328 (73.2)	6280 (72.8)	6321 (73.2)
Other antihypertensives (%)	19799 (67.0)	6288 (72.8)	6233 (72.2)	6281 (72.8)
Anticoagulants (%)	3628 (12.3)	1431 (16.6)	1419 (16.4)	1428 (16.5)

Antiplatelets (%)	14988 (50.7)	4686 (54.2)	4665 (54.0)	4679 (54.2)
Lipid-lowering drugs (%)	26074 (88.2)	7530 (87.2)	7550 (87.5)	7525 (87.2)

BMI=Body mass index, TIA=transient ischaemic attack, NAFLD/NASH= non-alcoholic fatty liver disease or non-alcoholic steatohepatitis, ACR=albumin creatinine ratio, BP=blood pressure, eGFR=estimated glomerular filtration rate, HbA1c=haemoglobin A1c, HDL=high density lipoprotein, ACEi=angiotensin converting enzyme inhibitor, ARB=angiotensin receptor blocker, DPP4i=dipeptidyl peptidase-4 inhibitors, GLP1=glucagon-like peptide 1 receptor agonist, SGLT2i=sodium-glucose co-transporter-2 inhibitors

Exposed group: patients with a current combination prescription of metformin and other glucose-lowering agents; Comparator group: patients with a current prescription of other glucose-lowering agents

<sup>\*</sup> Excluding melanoma, and blood and bone marrow cancers

<sup>†</sup> Data were presented for the first multiple imputed propensity score matched cohort.

Supplementary S7 Risk of developing COVID-19, mortality, and back pain among those with a current combination prescription of metformin and other glucose-lowering agents compared to a current prescription of other glucose-lowering agents only (Sensitivity analysis)

	Confirmed Suspected/Confirmed COVID-19 relate COVID-19 COVID-19 death			All-cause mortality		Back pain				
Outcomes	Exposed	Comparator	Exposed	Comparator	Exposed	Comparator	Exposed	Comparator	Exposed	Comparator
	group (MF+)	group (MF-)	group (MF+)	group (MF-)	group (MF+)	group (MF-)	group (MF+)	group (MF-)	group (MF+)	group (MF-)
Unmatched analysis										
Total number of patients	29,558	8,640	29,558	8,640	29,558	8,640	29,558	8,640	29,558	8,640
Number of outcomes	110	44	415	155	31	16	403	197	315	100
Person-years (py)	20,454	5,934	20,351	5,897	20,486	5,949	20,486	5,949	20,364	5,907
Incidence rate (per 1000 py)	5.4	7.4	20.4	26.3	1.5	2.7	19.7	33.1	15.5	16.9
Crude hazard ratio (95%CI)	0.73 (0	).51, 1.03)	0.78 (	0.65, 0.93)	0.56 (0	0.31, 1.03)	0.59 (0	0.50, 0.71)	0.91 (0.73, 1.15)	
Adjusted HR (95%CI)*	0.76 (0	).54, 1.09)	0.84 (	0.70, 1.01)	0.77 (0	0.41, 1.44)	0.83 (0	0.70, 0.99)	0.94 (0	).75, 1.18)
Matched analysis										
Total number of patients <sup>†</sup>	8,632	8,632	8,632	8,632	8,632	8,632	8,632	8,632	8,632	8,632
Number of outcomes <sup>†</sup>	37	44	137	155	14	16	176	196	104	100
Person-years (py) <sup>†</sup>	5,950	5,929	5,918	5,892	5,959	5,944	5,959	5,944	5,918	5,902
Incidence rate (per 1000 py) †	6.2	7.4	23.2	26.3	2.4	2.7	29.5	33.0	17.6	16.9
Crude hazard ratio (95%CI) †	0.80 (0	).45, 1.43)	0.87 (0.66, 1.14)		0.77 (0.34, 1.71)		0.88 (0.71, 1.10)		0.97 (0.65, 1.44)	
Adjusted HR (95%CI)* †	0.79 (0	).44, 1.40)	0.86 (	0.65, 1.13)	0.78 (0	0.34, 1.82)	0.92 (0	0.73, 1.17)	0.97 (0	0.65, 1.44)

Exposed group: patients with a current combination prescription of metformin and other glucose-lowering agents; Comparator group: patients with a current prescription of other glucose-lowering agents

<sup>\*</sup> Adjusted for: age, sex, smoking status, high alcohol consumption (alcoholism), body mass index categories, total cholesterol categories, high-density lipoprotein categories, albumin-creatinine ratio categories, estimated glomerular filtration rate categories, HbA1c categories, atrial fibrillation, rheumatoid arthritis, hypertension, cardiovascular disease, non-alcoholic fatty liver disease or non-alcoholic steatohepatitis, prescriptions of renin angiotensin aldosterone system inhibitors, other antihypertensive drugs, lipid-lowering drugs, antiplatelets, anticoagulants, diabetes complications, diabetes duration, respiratory disease, cancers, immunosuppressant therapies, and systemic corticosteroid use.

<sup>†</sup> Data were presented for the first multiple imputed propensity score matched cohort.

<sup>‡</sup> Summarized results of Cox regression analyses from all multiple imputed propensity score matched cohorts using Rubin's Rule