

**Supplementary Table 1.** Characteristics of the SGLT2i initiator and non-SGLT2i initiator (comparison) cohorts at the start of follow-up.

<b>Variable</b>	<b>SGLT2i initiator N=12,978 n (%)</b>	<b>Non-SGLT2i initiator N=44,286 n (%)</b>
<b>Age (years)</b>		
18–39	380 (2.9)	975 (2.2)
40–59	6,179 (47.6)	20,117 (45.4)
60–79	6,233 (48.0)	22,477 (50.8)
≥80	186 (1.4)	717 (1.6)
Mean (SD)	59.6 (10.2)	60.4 (10.0)
<b>Sex</b>		
Male	7,900 (60.9)	27,557 (62.2)
Female	5,078 (39.1)	16,729 (37.8)
<b>BMI (kg/m<sup>2</sup>)</b>		
<20	26 (0.2)	215 (0.5)
20–24	541 (4.2)	3,856 (8.7)
25–29	2,862 (22.1)	12,771 (28.8)
≥30	9,456 (72.9)	26,978 (60.9)
Missing	93 (0.7)	466 (1.1)
<b>Smoking</b>		
Non-smoker	4,929 (38.0)	17,059 (38.5)
Current smoker	1,830 (14.1)	7,232 (16.3)
Ex-smoker	6,215 (47.9)	19,976 (45.1)
Missing	4 (0.0)	19 (0.0)
<b>Alcohol use (units/week)</b>		
None	3,264 (25.2)	11,403 (25.7)
1–9	6,246 (48.1)	20,485 (46.3)
10–20	1,645 (12.7)	5,792 (13.1)
21–41	469 (3.6)	1,792 (4.0)
>41	236 (1.8)	992 (2.2)
Missing	1,118 (8.6)	3,822 (8.6)
<b>Comorbidities</b>		
Myocardial infarction	804 (6.2)	3,098 (7.0)
IHD	1,899 (14.6)	6,976 (15.8)
CeVD	744 (5.7)	2,974 (6.7)
Heart failure	323 (2.5)	1,576 (3.6)
History of ESRD	5 (0.0)	74 (0.2)
Hyperlipidaemia	4,120 (31.7)	14,148 (31.9)
Hypertension	7,881 (60.7)	27,142 (61.3)
Atrial fibrillation	563 (4.3)	2,225 (5.0)

Variable	SGLT2i initiator N=12,978 n (%)	Non-SGLT2i initiator N=44,286 n (%)
COPD	771 (5.9)	2,974 (6.7)
Cancer	1,430 (11.0)	5,617 (12.7)
Depression	4,524 (34.9)	14,720 (33.2)
Obesity	4,414 (34.0)	12,732 (28.7)
Acute pancreatitis	199 (1.5)	535 (1.2)
CKD	1,170 (9.0)	7,059 (15.9)
Chronic liver disease	762 (5.9)	2,399 (5.4)
Haemorrhagic stroke	52 (0.4)	257 (0.6)
Ischaemic stroke	389 (3.0)	1,727 (3.9)
TIA	369 (2.8)	1,345 (3.0)
Urogenital bleed	1,331 (10.3)	4,988 (11.3)
UGIB	253 (1.9)	1,016 (2.3)
LGIB	1,102 (8.5)	4,033 (9.1)
Liver disease	1,217 (9.4)	4,046 (9.1)
Pancreatic disease	234 (1.8)	713 (1.6)
Valvular disease	208 (1.6)	872 (2.0)
Tachycardia	867 (6.7)	3,332 (7.5)
PAD	375 (2.9)	1,552 (3.5)
Asthma	2,761 (21.3)	9,038 (20.4)
Rheumatoid arthritis	422 (3.3)	1,486 (3.4)
Osteoarthritis	3,590 (27.7)	12,425 (28.1)
Parkinson's disease	33 (0.3)	149 (0.3)
Dementia psychosis	67 (0.5)	416 (0.9)
Alcohol abuse	734 (5.7)	2,955 (6.7)
IBD	183 (1.4)	654 (1.5)
Gastrointestinal disease	9,266 (71.4)	31,192 (70.4)
Diabetic retinopathy	4,028 (31.0)	14,090 (31.8)
Diabetic neuropathy	272 (2.1)	986 (2.2)
DKD	291 (2.2)	1,062 (2.4)
<b>CHA<sub>2</sub>DS<sub>2</sub>VASc score</b>		
1	2,051 (15.8)	7,129 (16.1)
2	4,811 (37.1)	15,202 (34.3)
3	3,657 (28.2)	12,495 (28.2)
4	1,643 (12.7)	6,057 (13.7)
5	565 (4.4)	2,324 (5.2)
6	193 (1.5)	801 (1.8)
7	49 (0.4)	237 (0.5)

<b>Variable</b>	<b>SGLT2i initiator N=12,978 n (%)</b>	<b>Non-SGLT2i initiator N=44,286 n (%)</b>
≥8	9 (0.1)	41 (0.1)
<b>Frailty</b>		
Fit	3,999 (30.8)	13,971 (31.5)
Mild frailty	6,230 (48.0)	19,714 (44.5)
Moderate frailty	2,266 (17.5)	8,258 (18.6)
Severe frailty	483 (3.7)	2,343 (5.3)
<b>HbA1c</b>		
>8% (>64mmol/mol)	10,240 (78.9)	15,462 (34.9)
7–8% (53–64mmol/mol)	2,186 (16.8)	12,743 (28.8)
<7% (<53mmol/mol)	410 (3.2)	13,382 (30.2)
Missing	142 (1.1)	2,699 (6.1)
<b>ACR (mg/g)</b>		
Normal (≤30)	5,856 (45.1)	18,593 (42.0)
Microalbuminuria (>30–<300)	1,715 (13.2)	4,932 (11.1)
Macroalbuminuria (≥300)	211 (1.6)	842 (1.9)
Missing	5,196 (40.0)	19,919 (45.0)
<b>PCP visits*</b>		
0–12	2,807 (21.6)	11,068 (25.0)
13–24	6,607 (50.9)	21,499 (48.5)
25–34	2,242 (17.3)	7,198 (16.3)
≥35	1,322 (10.2)	4,521 (10.2)
<b>Referrals*</b>		
0–9	9,328 (71.9)	31,895 (72.0)
10–19	2,981 (23.0)	9,917 (22.4)
≥20	669 (5.2)	2,474 (5.6)
<b>Hospitalisations*</b>		
0	10,963 (84.5)	36,587 (82.6)
≥1	2,015 (15.5)	7,699 (17.4)
<b>eGFR (ml/min/1.73m<sup>2</sup>)</b>		
<15	0 (0.0)	3 (0.0)
15–29	1 (0.0)	148 (0.3)
30–44	75 (0.6)	1,262 (2.8)
45–59	550 (4.2)	3,648 (8.2)
60–89	5,711 (44.0)	17,701 (40.0)
≥90	6,339 (48.8)	18,216 (41.1)
Missing	302 (2.3)	3,308 (7.5)

Variable	SGLT2i initiator N=12,978 n (%)	Non-SGLT2i initiator N=44,286 n (%)
<b>Polypharmacy</b>		
0–10	8,837 (68.1)	33,495 (75.6)
11–15	3,046 (23.5)	8,025 (18.1)
≥16	1,095 (8.4)	2,766 (6.2)
<b>Previous use of other glucose-lowering drugs</b>		
SU, GLP1, DDP4 and Insulin	347 (2.7)	891 (2.0)
GLP1, DDP4 and Insulin	28 (0.2)	33 (0.1)
SU, GLP1 and DDP4	563 (4.3)	1,349 (3.0)
SU, DDP4 and insulin	404 (3.1)	1,214 (2.7)
SU, GLP1 and insulin	452 (3.5)	1,292 (2.9)
SU and Insulin	468 (3.6)	1,632 (3.7)
GLP1 and Insulin	102 (0.8)	179 (0.4)
GLP1 and DDP4	102 (0.8)	150 (0.3)
SU and DDP4	3,013 (23.2)	10,625 (24.0)
SU and GLP1	310 (2.4)	722 (1.6)
DDP4 and insulin	57 (0.4)	77 (0.2)
SU only	2,112 (16.3)	7,992 (18.0)
Insulin only	334 (2.6)	1,003 (2.3)
GLP1 only	90 (0.7)	137 (0.3)
DDP4 only	1,614 (12.4)	5,160 (11.7)
None	2,982 (23.0)	11,830 (26.7)
<b>Warfarin</b>		
Non-use	12,547 (96.7)	42,495 (96.0)
Current use	403 (3.1)	1,588 (3.6)
Past use	28 (0.2)	203 (0.5)
<b>Antiplatelets</b>		
Non-use	8,838 (68.1)	29,633 (66.9)
Current use	3,805 (29.3)	13,384 (30.2)
Past use	335 (2.6)	1,269 (2.9)
<b>Parenteral anticoagulants</b>		
Non-use	12,927 (99.6)	44,046 (99.5)
Current use	9 (0.1)	79 (0.2)
Past use	42 (0.3)	161 (0.4)
<b>Statins</b>		
Non-use	2,345 (18.1)	8,790 (19.8)
Current use	10,179 (78.4)	33,521 (75.7)
Past use	454 (3.5)	1,975 (4.5)
<b>Antihypertensive drugs</b>		

<b>Variable</b>	<b>SGLT2i initiator N=12,978 n (%)</b>	<b>Non-SGLT2i initiator N=44,286 n (%)</b>
Non-use	3,193 (24.6)	10,943 (24.7)
Current use	9,555 (73.6)	32,399 (73.2)
Past use	230 (1.8)	944 (2.1)
<b>Digoxin</b>		
Non-use	12,805 (98.7)	43,692 (98.7)
Current use	167 (1.3)	555 (1.3)
Past use	6 (0.0)	39 (0.1)
<b>Antiarrhythmic drugs</b>		
Non-use	12,522 (96.5)	42,591 (96.2)
Current use	375 (2.9)	1,400 (3.2)
Past use	81 (0.6)	295 (0.7)
<b>Aspirin</b>		
Non-use	9,274 (71.5)	31,233 (70.5)
Current use	3,330 (25.7)	11,652 (26.3)
Past use	374 (2.9)	1,401 (3.2)
<b>Cox-2 inhibitors</b>		
Non-use	12,858 (99.1)	43,959 (99.3)
Current use	61 (0.5)	177 (0.4)
Past use	59 (0.5)	150 (0.3)
<b>Paracetamol</b>		
Non-use	7,942 (61.2)	27,471 (62.0)
Current use	3,253 (25.1)	10,806 (24.4)
Past use	1,783 (13.7)	6,009 (13.6)
<b>tNSAIDs</b>		
Non-use	10,387 (80.0)	35,983 (81.3)
Current use	1,079 (8.3)	3,356 (7.6)
Past use	1,512 (11.7)	4,947 (11.2)
<b>PPIs</b>		
Non-use	7,660 (59.0)	26,998 (61.0)
Current use	4,297 (33.1)	14,033 (31.7)
Past use	1,021 (7.9)	3,255 (7.3)
<b>H2 blockers</b>		
Non-use	12,481 (96.2)	42,626 (96.3)
Current use	377 (2.9)	1,181 (2.7)
Past use	120 (0.9)	479 (1.1)
<b>Oral steroids</b>		
Non-use	11,967 (92.2)	40,671 (91.8)
Current use	387 (3.0)	1,449 (3.3)

Variable	SGLT2i initiator N=12,978 n (%)	Non-SGLT2i initiator N=44,286 n (%)
Past use	624 (4.8)	2,166 (4.9)
<b>Inhaled steroids</b>		
Non-use	12,016 (92.6)	40,961 (92.5)
Current use	687 (5.3)	2,476 (5.6)
Past use	275 (2.1)	849 (1.9)
<b>Injected steroids</b>		
Non-use	12,712 (98.0)	43,492 (98.2)
Current use	84 (0.6)	171 (0.4)
Past use	182 (1.4)	623 (1.4)
<b>Anti-infective drugs</b>		
Non-use	6,436 (49.6)	23,319 (52.7)
Current use	2,330 (18.0)	6,402 (14.5)
Past use	4,212 (32.5)	14,565 (32.9)
<b>Antidepressants</b>		
Non-use	9,051 (69.7)	31,387 (70.9)
Current use	3,248 (25.0)	10,764 (24.3)
Past use	679 (5.2)	2,135 (4.8)
<b>Antipsychotics</b>		
Non-use	11,848 (91.3)	40,296 (91.0)
Current use	734 (5.7)	2,527 (5.7)
Past use	396 (3.1)	1,463 (3.3)
<b>HRT</b>		
Non-use	12,819 (98.8)	43,851 (99.0)
Current use	104 (0.8)	304 (0.7)
Past use	55 (0.4)	131 (0.3)
<b>Oral contraceptives</b>		
Non-use	12,752 (98.3)	43,716 (98.7)
Current use	173 (1.3)	414 (0.9)
Past use	53 (0.4)	156 (0.4)

\*In the year before the start date (start of follow-up).

Note that medication use at start date was classified into current-use (less than 30 days from the end of the last available prescription), past-use (between 30 and 365 days from the end of the last available prescription), and non-use (more than 1 year since the end of the last prescription or no prior prescription).

ACR, albumin-to-creatinine ratio; BMI, body mass index; CeVD, cerebrovascular disease; CKD, chronic kidney disease; CLD, chronic liver disease; DDP4, dipeptidyl peptidase-4; DKD, diabetic kidney disease; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; GLP1, glucagon-like peptide-1; HRT, hormone replacement therapy; H2 blockers, histamine H2-receptor antagonists; IBD, inflammatory bowel disease; IHD, ischaemic heart disease; LGIB, lower gastrointestinal bleeding; PAD, peripheral artery disease; PCP, primary care practitioner; PPI, proton pump inhibitors; SD, standard deviation; SGLT2, sodium-glucose co-transporter-2; SU, sulfonylurea;

TIA, transient ischaemic attack; tNSAIDs, traditional nonsteroidal anti-inflammatory drug; UGIB, upper gastrointestinal disease bleeding