NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Epidemiological report

Uptake of sodium-glucose cotransporter-2 inhibitors in patients with type 2 diabetes: a report for NICE committee members

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0. Executive Summary

NICE guideline committees are prompted to consider health inequalities at throughout guideline development. When informed by evidence on the extent of health inequalities in the populations in scope of a guideline, committees have previously made recommendations for commissioners and clinicians to identify and engage with underserved populations, and for research into the acceptability and cost-effectiveness of interventions in different populations.

We present results on the uptake of sodium-glucose cotransporter-2 (SGLT-2) inhibitors in the populations recommended them in the February 2022 type 2 diabetes (T2DM) guideline update. There is evidence in the literature of variable and unequal uptake of NICE guideline recommendations for other diseases. This analysis seeks to establish if this is also an issue for T2DM. Our objective is to support the committee to consider if recommendations or actions are needed to encourage uptake of T2DM treatments in primary care, and reduce inequalities.

In February 2022 GPs were recommended to offer an SGLT-2 inhibitor to T2DM patients with comorbid atherosclerotic cardiovascular disease (ASCVD) or comorbid chronic heart failure (CHF). They were recommended to consider offering an SGLT-2 inhibitor to patients with high ASCVD risk. Using data from a representative sample of 24% of GP practices in the UK, we report the percentage of T2DM patients with a current prescription for an SGLT-2 inhibitor in September 2023, 18 months after that guideline was published. We report uptake in subgroups of T2DM patients with comorbid ASCVD, CHF, and at high ASCD risk; and according to age, gender, ethnicity, and socioeconomic status.

We found that uptake of SGLT-2 inhibitors was relatively low: 19.9% of patients with comorbid ASCVD had a current prescription for one, compared to 27.4% of patients with CHF. Uptake in patients at high risk of ASCVD was 18.6%. Inequalities in uptake by age and gender were observed. Compared to men aged 18-39 with ASCVD, men aged 70-79 had a third the odds of a current prescription; men aged 80-99 had less than a fifth, and women had

2/3rds the odds of men. Differences in uptake were also observed by ethnicity and socioeconomic status, with prescribing being less common in people of Black or Black British ethnicity and people living in areas of higher deprivation.

Mean eGFR was 1-5 ml/min/1.73m2 higher in the patients with a current SGLT-2 inhibitor prescription compared to those without one. Considering just patients without a current prescription, in those with ASCVD the mean eGFR was 67.9 ml/min, and in those with CHF it was 58.2 ml/min. These results imply that eGFR differences are unlikely to explain the low uptake observed.

Where comparable data are available, other studies have returned similar results to ours. However, to our knowledge, no previous studies have evaluated uptake of SGLT-2 inhibitors for T2DM in the UK up to 2023. Evidence from the literature is that uptake of NICE guidelines for other diseases in primary care is variable, and can be low.

Using this report and the other evidence available, the committee may wish to consider:

- Whether they judge that uptake of SGLT-2 inhibitors is too low overall, or too low in specific subgroups of patients. Alternatively, whether uptake is in line with expectations, given prescribing considerations and/or time for NICE recommendations to become practice.

- If further information is needed to reach a conclusion on whether uptake of SGLT-2 inhibitors is acceptable in the populations recommended them, and what information would be most useful.

- Whether recommendations, research recommendations, or other actions specifically on uptake of the guideline-recommended drugs should be made as part of or following the 2024 guideline update.

1. Background

The 2021-2026 National Institute for Health and Care Excellence (NICE) Strategy sets an ambition for greater use of real-world evidence in NICE guidance development [1]. It also reaffirms an ambition for NICE guidance to support reductions in health inequalities. This report is intended to support the type 2 diabetes (T2DM) guideline committee to consider and address health inequalities in the 2024 medicines update. We report an analysis of uptake of sodium-glucose cotransporter-2 (SGLT-2) inhibitors in populations recommended them in the 2022 guideline, based on an analysis of real-world GP records. We evaluate inequalities in uptake according to patient characteristics and socioeconomic status, and describe the clinical characteristics of the patients taking SGLT-2 inhibitors and those not taking them.

1.1 Guidelines and reducing inequalities

NICE committees are required to consider health inequalities throughout the guideline development process. The equality and health inequalities assessment (EHIA) is carried out at several stages during development, and the issues identified at each stage are documented. Health Inequalities Briefings support this process [2]. The briefings report on inequalities between patients with different protected characteristics, socioeconomic status, geography, and inclusion groups [3]. Where possible, guidance should support reductions in inequalities in these domains.

Key findings in the current NICE T2DM Health inequalities briefing are of higher prevalence of T2DM in ethnic minorities and people living in areas of higher deprivation; lower completion of T2DM care processes and treatment targets in these populations; and a recent increase in prevalence of T2DM in younger patients, also disproportionately in areas of higher deprivation. [4].

Evidence on inequalities has supported previous recommendations of NICE committees to help reduce them. One example is recommendations on arm and shoulder problems following breast cancer treatment [5]. Evidence of

differing levels of engagement with cancer services and physical activity according to ethnicity influenced two committee recommendations. The first was a recommendation for support for exercises to be made available in a variety of different mediums, as face-to-face support may be more beneficial for patients at a higher risk or with additional needs, including patients from ethnic minorities. The second was a recommendation for research on the cost effectiveness and acceptability of arm and shoulder interventions in different groups with protected characteristics.

For the T2DM guideline update in 2022 [6], evidence of inequalities informed recommendation 1.6.26: that commissioners, providers and healthcare professionals should address inequalities in continuous glucose monitoring access and uptake by identifying groups with lower uptake, and planning engagement with those groups.

1.2 Analysing uptake of the 2022 Type 2 diabetes medicines guideline recommendations

This analysis aims to evaluate uptake of the treatments recommended in the February 2022 T2DM guideline update [6]. The following recommendations were made regarding prescribing of SGLT-2 inhibitors according to patient's cardiovascular comorbidities:

- Patients with T2DM and atherosclerotic cardiovascular disease (ASCVD): Offer an SGLT-2 inhibitor.
- Patients with T2DM and chronic heart failure (CHF): Offer an SGLT-2 inhibitor.
- Patients with high risk of ASCVD: Consider an SGLT-2 inhibitor.
- Patient with low risk of ASCVD: Only consider an SGLT-2 inhibitor for some patients if Metformin is contraindicated.

In each of the first three groups the SGLT-2 inhibitor should be offered or considered respectively in addition to metformin immediately after metformin tolerability is confirmed, or instead of metformin if it is contraindicated. The recommendations apply equally for first-line treatment of new T2DM in

patients with pre-existing conditions, and at treatment review for patients who developed them after T2DM. The prescribing information for SGLT-2 inhibitors states that in general they should be avoided if estimated glomerular filtration rate (eGFR) is < 60 ml/min; that they should be prescribed with caution in people of older age; and that empagliflozin should not prescribed in patients aged over 85 [7].

Using real-world data from a representative sample of 24% of GP practices in the UK, obtained from the Clinical Practice Research Datalink (CPRD), we report uptake of these treatment recommendations. We report on the percentage of patients with a current prescription for an SGLT-2 inhibitor on 1st September 2023, 18 months after the recommendations were published. Differences in uptake between the different subgroups the recommendations were made for, and inequalities within these subgroups by age, gender, deprivation, and ethnicity, are described. Characteristics of patients including renal function and prescribing of other medicines, are reported, stratified by whether they have current SGLT-2 inhibitor prescription.

2 Methods

2.1 Data sources

The cohort and outcomes for analysis were extracted from CPRD Aurum. CPRD Aurum is a database of GP records from practices using the EMIS GP IT system. It includes recorded symptoms, diagnoses, test results, and drug issues for patients at participating practices from 1995 to present, with approximately 24% coverage of the UK population as of December 2023 [8]. The patients in CPRD Aurum are broadly representative of the wider English population with respect to geographic distribution, deprivation, age, and gender [9].

Records of patients extracted from CPRD were linked to their Hospital Episode Statistics (HES) records to retrieve diagnoses and procedures recorded in any hospital inpatient admissions they had [10], and also to their Index of Multiple Deprivation (IMD). The IMD ranks small areas in England

from most to least deprived based on 7 components including income, employment, education, health, crime, barriers to housing and services, and living environment. These factors are compiled into a single score to measure overall deprivation [11]. The linkages were done using an algorithm managed by NHS England [12].

Diagnoses, measurements and test results are recorded in CPRD with SNOMED codes. Diagnoses and procedures in HES are recorded with ICD-10 and OPCS-4 codes respectively. Lists of codes from these libraries were collated to select demographics, comorbidities, risk factors, and current medicines from the CPRD-HES datasets. Where relevant code lists were already available from the Primary Care Domain Set maintained by NHS England [13], the Open Code Lists website maintained by the Bennett Institute [14], or the CVDPrevent audit [15], these were used. Otherwise, code lists were taken from the literature, or created using the World Health Organisation ICD-10 codes library [16] or free-text searches in the CPRD code browser. Each code list was reviewed by a member of the HE team, a guideline committee member, or both. The full code lists with details of the origin and derivation of each is available on request as supplementary documents (Appendix 2).

2.2 Cohort selection, stratification, exposure and outcome definitions

The cross-sectional analysis of treatment uptake was done on the most recent date data data were available: 1 September 2023 (the “index date”). Cohort selection was done as follows. Within CPRD, all patients who had any record of T2DM and no record of another form of diabetes between 1st January 2000 and the index date were selected. Of these, those whose records could be linked to both HES and IMD datasets and who were judged by CPRD to have a ‘research-quality’ record, and who were aged 18 or over on the index date, were retained [17]. Patients were excluded if they died or de-registered prior to the index date, or if they had less than one year registration on the index date.

The selected patients were stratified into the following cohorts: with ASCVD, with CHF, at high CVD risk, and at low CVD risk. Presence of ASCVD and CHF was based on any record of these in CPRD or HES between January 2000 and the index date. Patients at high risk of CVD were identified using QRISK2 scores [18], with a score >10% indicating high risk. Most patients did not have a recent QRISK2 recorded in CPRD Aurum, so these were instead estimated using an algorithm developed by researchers at the London School of Hygiene and Tropical Medicine [19]. Appendix 1 describes the implementation and validation of the algorithm for the present analysis. The ASCVD, high CVD risk, and low CVD risk subgroups were defined to be mutually exclusive and exhaustive, whilst the CHF cohort could overlap with the others.

Patients' IMD scores were grouped into quintiles from least (5) to most (1) deprived. Presence of a comorbidity was defined based on any record of it in either CPRD or HES from January 2000 to the index date. For CVD risk factors, including laboratory results and BMI, the most recent measurement within 24 months prior to the index date was used; if none were available in this window the value was set to missing. Presence of a current prescription of any medication was defined using the algorithm developed by Farmer *et al,* which uses available information on quantities, daily doses, or typical prescription length, to estimate the length of any prescription [20]. Patients were categorised as having a current prescription of an SGLT-2 inhibitor if they had a current prescription for either Dapagliflozin, Empagliflozin, Canagliflozin, or Ertugliflozin.

2.3 Descriptive and statistical analysis

The demographic and clinical characteristics of the prevalent population with Type 2 diabetes were summarised with counts, percentages, means, and reported stratified by patient's deprivation status (IMD 1 – 5) and cohort subgroup (ASCVD, CHF, high CVD risk, low CVD risk).

Uptake of SGLT-2 inhibitors in each subgroup was defined based on the proportion of the population with a current prescription on the index date,

without reference to any other current prescriptions the patient was taking or none. Uptake was calculated overall and by patient characteristics: age, gender, ethnicity, deprivation status, and recency of diagnosis. Detailed statistics on demographics, comorbidities, risk factors, and current medicines were also reported separately for the patients with and without a current prescription for an SGLT-2 inhibitor within each of the subgroups.

For each of the ASCVD and CHF cohorts, a logistic regression model was fitted to estimate the adjusted association between patient characteristics and SGLT-2 inhibitor uptake. In each case the model included all the patient characteristics as categorical variables, and additional variables for presence of co-morbid CKD and ASCVD (for the CHF model) or CHF (for the ASCVD model).

3 Results

3.1 Characteristics of the cohort and cohort subgroups.

In total 642,788 patients with prevalent T2DM on 1st September 2023 met all the study inclusion criteria. The T2DM patients were more likely to live in areas of high deprivation compared to the whole population: 151,690 were living in the most deprived quintile in England compared to 105,121 living in the least deprived (Table 1). Cardiovascular disease was common: 28.1% of the cohort had pre-existing ASCVD; 63.8% of patients were at high CVD risk; 8% had low CVD risk, and 8.0% had comorbid CHF. Most patients were aged over 60 (71.7%), 56.5% were male, 75.6% were white, and 75.6% had a diagnosis of T2DM for over 5 years on the index date.

A higher proportion of patients in the most deprived quintile were of Asian or Asian British or Black or Black British ethnicity compared to the whole cohort. Patients in the most deprived quintile were also younger than those in the least deprived: the average age was 59.6 compared to 65.3, with 16.6% aged under 50 compared to 5.9%. Despite these age differences, the prevalence of comorbid conditions and recency of T2DM diagnosis were very similar.

Uptake of SGLT-2 inhibitors in primary care was relatively low (Table 2). In the cohorts with low and high risk of CVD 18.6% of the patients had a current SGLT-2 inhibitor prescription in September 2023; in the cohort with ASCVD 19.9% did; and in the cohort with CHF 27.4% did.

Table 1. Characteristics of patients in CPRD with prevalent T2DM, overall and by index of multiple deprivation quintile, September 2023.

	All patients	IMD 5 (least deprived)	IMD 4	IMD 3	IMD 2	IMD 1 (most deprived)
All patients						
	642,788 (100%)	105,121 (100%)	118,076 (100%)	124,730 (100%)	143,171 (100%)	151,690 (100%)
Comorbid conditions*						
Atherosclerotic CVD	180,874 (28.1%)	29,421 (28.0%)	33,852 (28.7%)	34,786 (27.9%)	39,457 (27.6%)	43,358 (28.6%)
Heart Failure	54,090 (8.4%)	8,795 (8.4%)	10,144 (8.6%)	10,469 (8.4%)	11,752 (8.2%)	12,930 (8.5%)
Low CVD risk	51,529 (8.0%)	5,615 (5.3%)	6,834 (5.8%)	9,142 (7.3%)	13,399 (9.4%)	16,539 (10.9%)
High CVD risk	410,385 (63.8%)	70,085 (66.7%)	77,390 (65.5%)	80,802 (64.8%)	90,315 (63.1%)	91,793 (60.5%)
Age						
Mean age	61.9	65.3	64.3	62.7	60.6	59.6
18-39	14,909 (2.3%)	1,294 (1.2%)	1,774 (1.5%)	2,603 (2.1%)	3,826 (2.7%)	5,412 (3.6%)
40-49	46,713 (7.3%)	4,905 (4.7%)	6,264 (5.3%)	8,245 (6.6%)	12,092 (8.4%)	15,207 (10.0%)
50-59	121,019 (18.8%)	15,384 (14.6%)	18,841 (16.0%)	22,139 (17.7%)	29,765 (20.8%)	34,890 (23.0%)
60-69	170,100 (26.5%)	25,389 (24.2%)	29,777 (25.2%)	32,859 (26.3%)	39,351 (27.5%)	42,724 (28.2%)
70-79	168,948 (26.3%)	32,111 (30.5%)	34,786 (29.5%)	33,965 (27.2%)	34,780 (24.3%)	33,306 (22.0%)
80-89	100,754 (15.7%)	21,323 (20.3%)	22,224 (18.8%)	20,673 (16.6%)	19,537 (13.6%)	16,997 (11.2%)
90+	20,345 (3.2%)	4,715 (4.5%)	4,410 (3.7%)	4,246 (3.4%)	3,820 (2.7%)	3,154 (2.1%)
Sex						
Male	363,240 (56.5%)	61,885 (58.9%)	68,662 (58.2%)	71,250 (57.1%)	79,561 (55.6%)	81,882 (54.0%)
Female	279,548 (43.5%)	43,236 (41.1%)	49,414 (41.8%)	53,480 (42.9%)	63,610 (44.4%)	69,808 (46.0%)
Ethnicity						
White	486,046 (75.6%)	90,974 (86.5%)	99,782 (84.5%)	96,091 (77.0%)	96,920 (67.7%)	102,279 (67.4%)
Mixed	7,873 (1.2%)	1,040 (1.0%)	1,106 (0.9%)	1,390 (1.1%)	2,087 (1.5%)	2,250 (1.5%)
Asian or Asian British	93,129 (14.5%)	9,291 (8.8%)	12,283 (10.4%)	18,343 (14.7%)	26,014 (18.2%)	27,198 (17.9%)
Black or Black British	40,573 (6.3%)	1,385 (1.3%)	2,430 (2.1%)	5,908 (4.7%)	14,384 (10.0%)	16,466 (10.9%)
Chinese or Other	9,962 (1.5%)	1,371 (1.3%)	1,425 (1.2%)	1,957 (1.6%)	2,682 (1.9%)	2,527 (1.7%)
Not stated/known	5,205 (0.8%)	1,060 (1.0%)	1,050 (0.9%)	1,041 (0.8%)	1,084 (0.8%)	970 (0.6%)
Recency of diagnosis						
<1 year	47,928 (7.5%)	8,143 (7.7%)	8,909 (7.5%)	9,249 (7.4%)	10,567 (7.4%)	11,060 (7.3%)
1-2 years	40,358 (6.3%)	6,690 (6.4%)	7,213 (6.1%)	7,777 (6.2%)	9,081 (6.3%)	9,597 (6.3%)
2-3 years	38,738 (6.0%)	6,046 (5.8%)	6,743 (5.7%)	7,263 (5.8%)	8,993 (6.3%)	9,693 (6.4%)
4-5 years	29,565 (4.6%)	4,573 (4.4%)	5,206 (4.4%)	5,817 (4.7%)	6,776 (4.7%)	7,193 (4.7%)
>5 years**	486,199 (75.6%)	79,669 (75.8%)	90,005 (76.2%)	94,624 (75.9%)	107,754 (75.3%)	114,147 (75.3%)

* Atherosclerotic CVD risk, low CVD risk, and high CVD risk are mutually exlcusive; CKD and heart failure are not, either to each other or CVD status.

** Includes 116 patients whose date of diagnosis was unknown but assumed to be >5 years.

There were marked differences in uptake of SGLT-2 inhibitors by patient characteristics within each cohort. Age was strongly negatively associated with uptake, with higher age group associated with a lower percentage of patients with a current SGLT-2 inhibitor prescription. In the subgroup with ASCVD, 30.0% of the patients aged 50-59 had a current prescription

compared with only 11.2% of the patients aged 80-89 (Table 2). Similar age gradients in uptake were observed in the other subgroups.

Gender, ethnicity, and recency of diagnosis were also associated with uptake of the SGLT-2 inhibitors. Consistent patterns in the percentage with current prescriptions were present for the ASCVD, CHD, and high CVD risk subgroups: approximately 2/3rds as many women as men had one; a higher percentage of White people than Black or Black British people had one; and a lower percentage of patients with a more recent diagnosis of T2DM had one. In contrast, the percentage of patients with a current prescription varied little between deprivation quintiles.

Table 2. Proportion of patients with prevalent T2DM and a current prescription for an SGLT-2 inhibitor, by cardiovascular disease status, September 2023.

	Atherosclerotic CVD		Heart Failure		High CVD risk		Low CVD risk	
	Count patients	Taking SGLT2i (%)	Count patients	Taking SGLT2i (%)	Count patients	Taking SGLT2i (%)	Count patients	Taking SGLT2i (%)
All patients								
	180,874	36,082 (19.9%)	54,090	14,829 (27.4%)	410,385	76,370 (18.6%)	51,529	9,591 (18.6%)
Age								
18-39	358	90 (25.1%)	147	65 (44.2%)	2,402	474 (19.7%)	12,149	1,675 (13.8%)
40-49	3,415	1,008 (29.5%)	864	368 (42.6%)	21,495	4,566 (21.2%)	21,803	4,116 (18.9%)
50-59	18,176	5,455 (30.0%)	3,882	1,538 (39.6%)	86,579	20,363 (23.5%)	16,264	3,567 (21.9%)
60-69	42,974	11,856 (27.6%)	10,001	3,756 (37.6%)	125,815	28,635 (22.8%)	1,311	233 (17.8%)
70-79	59,777	12,087 (20.2%)	17,177	5,297 (30.8%)	109,169	17,701 (16.2%)	<10	<10
80-89	45,665	5,124 (11.2%)	17,169	3,377 (19.7%)	55,089	4,330 (7.9%)	-	-
90+	10,509	462 (4.4%)	4,850	428 (8.8%)	9,836	301 (3.1%)	-	-
Gender								
Men	114,044	25,986 (22.8%)	32,924	10,499 (31.9%)	229,202	47,735 (20.8%)	19,994	3,534 (17.7%)
Women	66,830	10,096 (15.1%)	21,166	4,330 (20.5%)	181,183	28,635 (15.8%)	31,535	6,057 (19.2%)
Ethnicity								
White	147,335	28,463 (19.3%)	45,613	12,305 (27.0%)	312,859	58,902 (18.8%)	25,852	5,289 (20.5%)
Mixed	1,562	336 (21.5%)	404	131 (32.4%)	4,694	777 (16.6%)	1,617	257 (15.9%)
Asian or Asian British	22,306	5,515 (24.7%)	5,175	1,592 (30.8%)	59,315	11,517 (19.4%)	11,508	2,068 (18.0%)
Black or Black British	7,047	1,226 (17.4%)	2,288	600 (26.2%)	23,562	3,576 (15.2%)	9,964	1,566 (15.7%)
Chinese or Other	2,065	457 (22.1%)	472	160 (33.9%)	6,013	1,000 (16.6%)	1,884	313 (16.6%)
Not stated/known	559	85 (15.2%)	138	41 (29.7%)	3,942	598 (15.2%)	704	98 (13.9%)
Deprivation								
5 (least deprived)	29,421	5,638 (19.2%)	8,795	2,387 (27.1%)	5,615	1,102 (19.6%)	70,085	12,937 (18.5%)
4	33,852	6,686 (19.8%)	10,144	2,849 (28.1%)	6,834	1,400 (20.5%)	77,390	14,444 (18.7%)
3	34,786	6,776 (19.5%)	10,469	2,761 (26.4%)	9,142	1,721 (18.8%)	80,802	14,843 (18.4%)
2	39,457	8,019 (20.3%)	11,752	3,278 (27.9%)	13,399	2,446 (18.3%)	90,315	17,003 (18.8%)
1 (most deprived)	43,358	8,963 (20.7%)	12,930	3,554 (27.5%)	16,539	2,922 (17.7%)	91,793	17,143 (18.7%)
Recency of diagnosis								
<1 year	8,831	846 (9.6%)	2,510	657 (26.2%)	7,848	445 (5.7%)	31,249	1,719 (5.5%)
1-2 years	8,264	958 (11.6%)	2,481	625 (25.2%)	5,618	602 (10.7%)	26,476	2,387 (9.0%)
2-3 years	8,395	1,129 (13.4%)	2,475	650 (26.3%)	5,565	706 (12.7%)	24,778	2,740 (11.1%)
4-5 years	6,814	1,003 (14.7%)	2,034	524 (25.8%)	3,784	584 (15.4%)	18,967	2,385 (12.6%)
>5 years*	148,570	32,146 (21.6%)	44,590	12,373 (27.7%)	28,714	7,254 (25.3%)	308,915	67,139 (21.7%)

* Includes 116 patients whose date of diagnosis was unknown but assumed to be >5 years.

Similar proportions of patients taking SGLT-2 inhibitors had CKD stage 1-3 (64.6% and 64.1% and in patients with and without a current SGLT-2 inhibitor prescription, respectively) and CKD stage 4 (2.5% and 1.9% respectively, Appendix Table 3). Albuminuria was more common in the patients with a current SGLT-2 inhibitor prescription compared to those without, at 30.5% compared 23.3% in the patients with ASCVD, and 33.7% compared to 26.8% in the patients with HF. Mean recorded eGFR was slightly higher in patients with a current SGLT-2 inhibitor prescription compared to those without: 72.0 ml/min compared to 67.9 in patients with ASCVD; 60.8 compared to 58.2 in patients with HF; and 82.8 compared to 78.0 in patients at high CVD risk (Appendix Table 4). Of the patients not taking an SGLT-2 inhibitor, 42-46% were also not currently taking any other glucose modifying therapy either (Appendix Table 5).

3.2 Modelling analysis of association between patient characteristics and treatment uptake.

The associations between patient characteristics and SGLT-2 inhibitor uptake were also observed in the adjusted logistic regression models for the ASCVD and CHF subgroups (Table 3, Appendix Table 6). In the ASCVD subgroup, the odds of having a current prescription were lower in the patients aged 80-89 compared to patients aged 18-39 (Odds ratio: 0.16 (95% CI: 0.13, 0.21)). Women had lower odds of a current prescription than men (Odds ratio: 0.68 (0.66, 0.69)), and Black and Black British people had lower odds than White people (OR: 0.77 (0.72, 0.82)).

A deprivation gradient was observed in the adjusted analysis: patients in the most deprived quintile had lower odds of a current prescription than those in the least deprived (OR: 0.86 (0.83, 0.89)).

Similar results were observed in the logistic model fitted in the CHF subgroup (Appendix Table 6). Similarly to the model for the ASCVD subgroup, there was evidence of a deprivation gradient in uptake, with patients in the most deprived quintile having approximately 15% lower odds of a current

prescription than those in the least deprived (OR: 0.85 (0.77, 0.90)) in the model where age, gender, and other differences were adjusted for.

Table 3. Logistic regression model estimates of odds ratios for association between a current SGLT-2 inhibitor prescription and patient characteristics and comorbidities in patients with T2DM and comorbid atherosclerotic cardiovascular disease, September 2023.

	Odds ratio (95% CI)	P-value
Age group		
18-39	1.00	
40-49	1.03 (0.79, 1.33)	0.84
50-59	0.92 (0.71, 1.18)	0.49
60-69	0.67 (0.52, 0.86)	<0.01
70-79	0.36 (0.28, 0.46)	<0.01
80-89	0.16 (0.13, 0.21)	<0.01
90+	0.06 (0.04, 0.07)	<0.01
Gender		
Men	1.00	
Women	0.68 (0.66, 0.69)	<0.01
Ethnicity		
White	1.00	
Mixed	1.02 (0.89, 1.15)	0.81
Asian or Asian British	1.14 (1.10, 1.18)	<0.01
Black or Black British	0.77 (0.72, 0.82)	<0.01
Chinese or Other Ethnic Group	1.04 (0.93, 1.16)	0.48
Not stated/known	0.81 (0.63, 1.03)	0.08
Deprivation		
1 (Least deprived)	1.00	
2	0.98 (0.94, 1.02)	0.37
3	0.92 (0.88, 0.96)	<0.01
4	0.90 (0.86, 0.94)	<0.01
5 (most deprived)	0.86 (0.83, 0.89)	<0.01
Diagnosis recency		
0-1 years	1.00	
1-2 years	1.18 (1.06, 1.30)	<0.01
3-4 years	1.41 (1.28, 1.56)	<0.01
4-5 years	1.60 (1.44, 1.77)	<0.01
>5 years	3.16 (2.93, 3.40)	<0.01
Comorbid conditions		
Neither CHF nor CKD	1.00	
With comorbid CHF	2.09 (2.03, 2.14)	<0.01
With comorbid CKD 1-3	1.71 (1.66, 1.77)	<0.01
With comorbid CKD 4	2.65 (2.48, 2.83)	<0.01

4 Discussion

4.1 Principal findings

Uptake of SGLT-2 inhibitors in primary care patients with T2DM and ASCVD or CHF was relatively low, despite the February 2022 NICE guideline recommendations that they should be offered to these patients. The percentage of patients with a current prescription for an SGLT-2 inhibitor was 19.9% and 27.4% respectively in patients with T2DM and comorbid ASCVD and CHF. Uptake was equal between patients with T2DM and high and low risk of CVD, at 18.6%, despite the guideline recommending that that GPs should consider offering an SGLT-2 inhibitor only to the former group.

Age and gender were strongly associated with uptake of SGLT-2 inhibitors, with lower proportions of older patients and women having a current prescription for one. Smaller ethnicity and deprivation gradients were also observed, the latter only evident in the multivariable model which adjusted for age and gender. Mean eGFR was slightly higher in patients taking an SGLT-2 inhibitor. Mean eGFR in patients with ASCVD not taking an SGLT-2 inhibitor was 67.9 ml/min, and in patients with CHF not taking an SGLT-2 inhibitor it was 58.2 ml/min.

Our results suggests that if (uniformly) increased uptake of SGLT-2 inhibitors could be safely achieved, the greatest net benefit would be for people living in deprived areas and ethnic minorities, given the higher prevalence of T2DM in these populations.

4.2 Comparison to other research on CVD risk and uptake of T2DM recommendations

To our knowledge ours is the first analysis of uptake of SGLT-2 inhibitors for T2DM in the UK which is current to 2023. Farmer *et al* evaluated current prescriptions of patients with T2DM with and without CVD, using CPRD GOLD, in a period up to 31st December 2019 [20]. They reported that, in people without CVD, the percentage of patients with a current SGLT-2 inhibitor prescription increased from 6.7% to 13.8% between end-2016 and

end-2019. In patients with CVD it increased from 4.3% to 9.8%. These results are compatible with our findings, but imply a smaller increase in SGLT-2 inhibitor prescribing in patients without CVD and a much larger increase in patients with CVD, between 2019 and 2023.

Wilkinson *et al* evaluated uptake of first-intensification treatments for T2DM between 2014 and 2017, at a time when guidelines did not present evidence of superiority for the first-stage intensification treatments sulfonylureas, DPP-4 inhibitors, and SGLT-2 inhibitors, using the CPRD [21]. They reported that SGLT-2 inhibitors were more commonly prescribed to younger people, in patients who were overweight and obese, and in patients who were white and of higher socioeconomic status.

One non-peer reviewed study of aggregated data from the National Diabetes Audit (NDA), reported that in 2017-18, adherence to NICE recommendations on HbA1c monitoring, blood pressure monitoring, and cholesterol monitoring was over 90% [22]. In contrast, the proportion of patients with meeting the target HbA1c <=7.5% was 65.4%, and the percentage with cholesterol <5mmol/l was 76.1%.

Young *et al* assessed the population eligibility for SGLT-2 inhibitors based on the 2022 NICE recommendations using CPRD [23]. Using data from February 2020, they estimated that 59.6% of T2DM patients had high risk of CVD and 6.9% had low risk; compared to our estimates of 63.8% and 8% respectively in 2023 in the present study.

4.3 Uptake and inequalities in uptake of other NICE guidelines

There is evidence that inclusion of NICE process-of-care quality standards in the Quality and Outcomes Framework has resulted in improved adherence to guidelines [24]. Otherwise, however, there is evidence that adherence to NICE guideline recommendations in primary care is frequently low.

In 2016 Smith *et al* conducted a survey of GP attitudes towards and awareness of the 2013 NICE guidelines on Tamoxifen for prevention of breast cancer [25]. They found that only approximately half of GPs knew tamoxifen

can reduce breast cancer risk, and fewer than a quarter were aware of the 2013 NICE guideline. With respect to the same guideline, Curtis *et al* examined trends in Tamoxifen and Raloxifene prescribing following the 2013 guideline publication. They concluded there was only a modest impact of the guideline on trends in prescribing, and that uptake of the recommended treatments was low [26].

Several small studies in primary care settings have evaluated uptake of NICE recommendations in areas including heart failure [27], hypertension [28], T2DM and comorbid hypertension [29], and osteoarthritis [30]. They have reported variable and low uptake. Uptake of guidelines for HbA1c assessment in suspected heart failure was 59.3% after an education intervention; adherence to hypertension guidelines was <50% in one survey of GPs from 2006; NICE recommended combination treatment of T2DM and comorbid hypertension in people of African origin was 36.3%, and uptake of non-pharmaceutical interventions for osteoarthritis was low at <10%.

4.4 Limitations

This analysis has two key limitations which may bear on the interpretation of the results. Firstly, the differentiation of “high risk of CVD” and “low risk of CVD” patients is approximate. Evaluation of the QRISK2 algorithm we applied indicated that up to 20% of patients we classified as low risk may be high risk (Appendix 1). Additionally, in the present study we selected patients as high-risk based solely on QRISK2, whereas the 2022 guideline update also includes patients under 40 with at least one cardiovascular disease risk factor in this group [6]. The percentage of patients aged under 40 in our cohort is 2.3%, so the overall impact of this is expected to be small. However, the imprecision in our QRISK2 scoring indicates our “low risk” cohort will include many patients the GP considered high risk. This may partly explain the similarity in uptake of SGLT-2 inhibitors between patients and low- and high-risk.

Secondly, in our cohort 34.0% of patients with a diagnosis of T2DM had no record of a current prescription for glucose-lowering medication. If any of

these patients were in remission, or were receiving T2DM treatment elsewhere, then our estimates of uptake of SGLT-2 inhibitors in the populations recommended them may be low. Excluding the patients not taking any glucose-lowering medication results in higher estimates of SGLT-2 inhibitor uptake, ranging from 28% to 41% in the different subgroups (Appendix Table 5).

4.5 Interpretation and committee options for action

Using this report and other evidence they have reviewed, the committee may wish to consider:

- Whether they judge that uptake of SGLT-2 inhibitors that is too low overall, or in specific subgroups of patients. Alternatively, whether uptake is in line with expectations, given the considerations around prescribing these drugs and/or time for NICE recommendations to become practice.

- If further information is needed to reach a conclusion on whether uptake of SGLT-2 inhibitors is acceptable in the populations recommended them, and what information would be most useful.

- Whether recommendations, research recommendations, or other actions specifically on uptake of the guideline-recommended drugs should be made as part of or following the 2024 guideline update.

The information provided in this report on uptake in different subgroups of patients, and according to demographics within each subgroup, may support committee discussion. The information in appendices 3-5 on patients' comorbidities, risk factors, and prescribing of other glucose-modifying therapies in each subgroup, further stratified into whether the patient has current SGLT-2 inhibitor prescription or not, may also provide insights into reasons for uptake.

The committee may conclude that uptake is too low. If so, they may wish to consider actions which can support uptake of the treatments which will be

recommended in the 2024 guideline. Actions could include: recommendations for commissioners and clinicians to take steps to increase uptake; recommendations for research to understand barriers or concerns that may limit prescribing; or other activities to raise awareness of the new guideline recommendations. There is currently a NICE quality standard for prescribing of SGLT-2 inhibitors in patients with T2DM and ASCVD or CHF, but it is not part of 2023/24 the Quality and Outcomes Framework.

Alternatively, the committee may conclude that SGLT-2 inhibitor uptake is broadly in line with expectations, or that it is not possible to tell from these results alone if uptake is unacceptably low. If the latter, the committee may wish to consider what further evidence would be helpful: for example, further stratification of patient subgroups and detail on these; insights into GP concerns and rationale for not prescribing SGLT-2 inhibitors; or evidence on the cost-effectiveness of the drugs for certain populations where prescribing is lower i.e. older patients and women. The committee could make a research recommendation, or request that additional analysis be done at NICE to investigate using CPRD, if appropriate.

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Appendices

Appendix 1: Identification of type 2 diabetes patients at low and high risk of cardiovascular disease (CVD) using the CPRD primary care database

The QRISK2 algorithm is used in primary care in the UK to estimate patient's 10-year CVD risk as part of CVD primary prevention [18], with a score over 10% indicating high risk. Initial analysis of CPRD indicated that a timely (within 2 months either way) QRISK2 was only recorded for 28% of newly diagnosed patients in 2023, with a smaller percentage expected for the prevalent population on 1st September 2023.

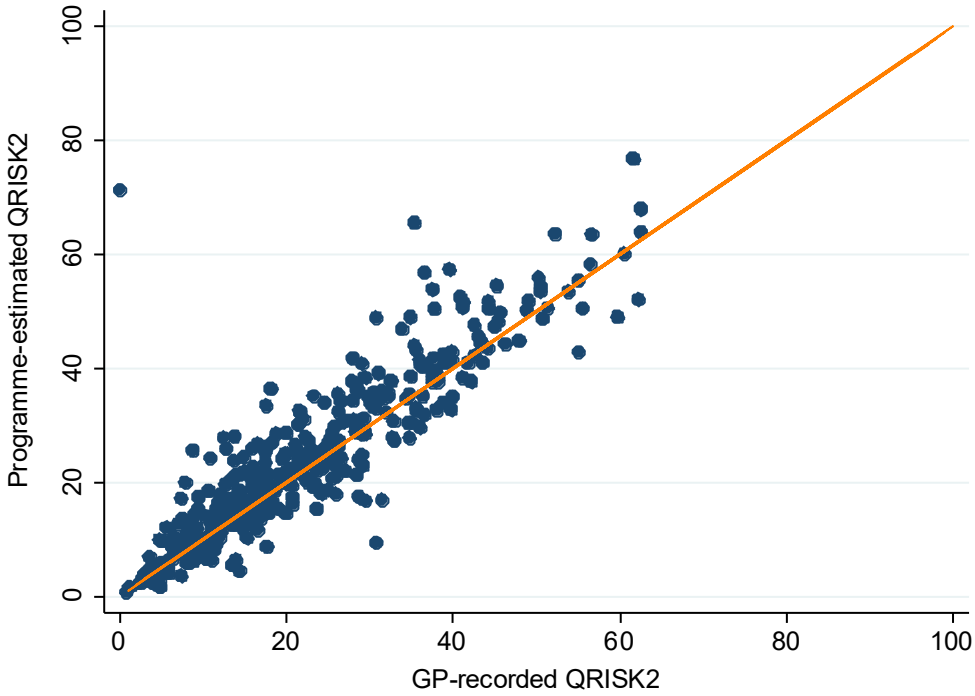
After discussion with the committee, it was determined the best approach for cohort selection was to directly estimate QRISK2 at 1st September 2023 for all patients without a timely QRISK2 record, using records of relevant clinical information in patient's primary care records, and identify high and low risk patients from this. Herrett *et al* at LSHTM previously created a STATA programme to estimate QRISK2 using CPRD Aurum records [19], and published the programme code on GitHub [31]. In brief, the programme searches for relevant diagnoses and most recent clinical measurements in CPRD, and estimates QRISK2 using these. Where an item needed to calculate QRISK2 for a patient is missing, population-average results are substituted. We applied this programme to our CPRD Aurum extracts. All CPRD drug issue and observation records prior to September 2023 were used for the calculation, but patient's Townsend scores were not available.

We evaluated the concordance of programme-estimated QRISK2 on 1st September 2023 and actual recorded scores for 387 patients who also had GP-recorded QRISK2 on 1st September 2023 (Figure 1). Concordance in risk category (low (<10%) or high (>10%)) between programme-estimated and GP-recorded QRISK2 scores was 92.0% (Table 1). However, people with GP-recorded low risk were more likely to be categorised differently by the programme: the programme classified only 77.0% of these patients as also

being low risk, whereas it classified 95.5% of patients with GP-recorded high risk as high risk.

The QRISK2 programme gave a higher mean QRISK2 than GP entered QRISK2: 24.0% compared to 22.4%. These results mirror the report from Herrett *et al* on an equivalent evaluation in CPRD GOLD: they reported the average programme QRISK2 was 0.4% higher than the GP-recorded, but notably, it was 1% higher for people with type 2 diabetes and 4.5% higher for people with CKD [31]. With our sample, in those instances where the GP recorded QRISK2 was <10% whilst the programme estimated was >10%, the median programme-estimated QRISK2 was 12.9% and the mean was 14.3%, indicating that whilst these patients were above the high risk threshold, they were typically also close to it.

Appendix Figure 1. Concordance of GP-recorded and programme estimated QRISK2 scores on 1st September 2023 (line at x=y).



Appendix Table 1. Concordance of CVD risk categorisation from GP-recorded and programme-estimated QRISK2 scores on 1st September 2023.

	GP-recorded < 10%	GP recorded > 10%	Total
Programme estimated < 10%	57 (80.3%)	14 (19.7%)	71 (100.0%)
Programme estimated > 10%	17 (5.3%)	299 (94.6%)	316 (100.0%)
Overall misclassification: 31/387 (8.0%)			

Appendix 2. Two Excel files are available which include the full code lists and details of their provenance: one for clinical concepts and another for medicines. If you would like to receive a copy of the code lists, please email the development team at diabetesupdate@nice.org.uk.

Appendix Table 3 Prevalence of T2DM-related comorbidities in patients with T2DM, stratified by cardiovascular disease status and whether the patient has a current SGLT-2 inhibitor prescription, September 2023.

		CVD risk status				CKD status	
	All	ASCVD	HF	High risk	Low risk	CKD 1-3	CKD 4
Without a current SGLT2i prescription							
N	518,484 (100.0%)	144,623 (27.89%)	39,254 (7.57%)	333,216 (64.27%)	40,645 (7.84%)	332,154 (64.06%)	9,818 (1.89%)
Cardiovascular comorbidities							
Angina	78,226 (15.1%)	77,235 (53.4%)	18,344 (46.7%)	972 (0.3%)	19 (0.0%)	58,322 (17.6%)	2,999 (30.5%)
Atrial fibrillation	58,338 (11.3%)	34,335 (23.7%)	19,361 (49.3%)	23,904 (7.2%)	99 (0.2%)	45,654 (13.7%)	2,972 (30.3%)
Myocardial infarction	38,662 (7.5%)	38,662 (26.7%)	11,825 (30.1%)	-	-	28,015 (8.4%)	1,605 (16.3%)
Peripheral arterial disease	25,085 (4.8%)	25,085 (17.3%)	5,369 (13.7%)	-	-	18,194 (5.5%)	1,219 (12.4%)
Stroke	31,270 (6.0%)	31,148 (21.5%)	5,508 (14.0%)	117 (0.0%)	<10	23,119 (7.0%)	1,250 (12.7%)
Diabetes-related comorbidities							
Albuminuria*	95,931 (18.5%)	33,749 (23.3%)	10,533 (26.8%)	57,622 (17.3%)	4,560 (11.2%)	89,773 (27.0%)	4,850 (49.4%)
Lower limb amputation	5,798 (1.1%)	3,463 (2.4%)	1,063 (2.7%)	2,198 (0.7%)	137 (0.3%)	3,757 (1.1%)	284 (2.9%)
Lower limb ulcer	38,379 (7.4%)	17,359 (12.0%)	7,065 (18.0%)	19,935 (6.0%)	1,085 (2.7%)	26,658 (8.0%)	1,705 (17.4%)
Renal failure	5,457 (1.1%)	3,000 (2.1%)	1,721 (4.4%)	2,379 (0.7%)	78 (0.2%)	1,496 (0.5%)	618 (6.3%)
Diabetic retinopathy	53,684 (10.4%)	21,426 (14.8%)	7,165 (18.3%)	30,300 (9.1%)	1,958 (4.8%)	36,934 (11.1%)	2,618 (26.7%)
With a current SGLT2i prescription							
N	122,406 (100.0%)	36,194 (29.57%)	14,859 (12.14%)	76,579 (62.56%)	9,633 (7.87%)	79,057 (64.59%)	3,031 (2.48%)
Cardiovascular comorbidities							
Angina	20,930 (17.1%)	20,615 (57.0%)	7,047 (47.4%)	293 (0.4%)	22 (0.2%)	15,802 (20.0%)	1,057 (34.9%)
Atrial fibrillation	13,748 (11.2%)	8,463 (23.4%)	7,143 (48.1%)	5,246 (6.9%)	39 (0.4%)	11,274 (14.3%)	1,018 (33.6%)
Myocardial infarction	12,657 (10.3%)	12,657 (35.0%)	5,252 (35.3%)	-	-	9,386 (11.9%)	644 (21.2%)
Peripheral arterial disease	6,048 (4.9%)	6,048 (16.7%)	1,911 (12.9%)	-	-	4,616 (5.8%)	412 (13.6%)
Stroke	6,264 (5.1%)	6,238 (17.2%)	1,735 (11.7%)	25 (0.0%)	<10	4,741 (6.0%)	342 (11.3%)
Diabetes-related comorbidities							
Albuminuria*	31,972 (26.1%)	11,051 (30.5%)	5,004 (33.7%)	19,131 (25.0%)	1,790 (18.6%)	30,135 (38.1%)	1,736 (57.3%)
Lower limb amputation	1,444 (1.2%)	818 (2.3%)	375 (2.5%)	582 (0.8%)	44 (0.5%)	1,029 (1.3%)	103 (3.4%)
Lower limb ulcer	9,771 (8.0%)	4,205 (11.6%)	2,331 (15.7%)	5,207 (6.8%)	359 (3.7%)	6,902 (8.7%)	536 (17.7%)
Renal failure	546 (0.4%)	313 (0.9%)	201 (1.4%)	225 (0.3%)	<10	271 (0.3%)	99 (3.3%)
Diabetic retinopathy	18,053 (14.7%)	6,827 (18.9%)	2,846 (19.2%)	10,342 (13.5%)	884 (9.2%)	12,678 (16.0%)	908 (30.0%)

Definitions: HF, heart failure; CKD, chronic kidney disease; ASCVD, atherosclerotic cardiovascular disease; SD, standard deviation; N, number of observations. * Recorded in the 24 months prior to the cross-sectional date. Otherwise recorded at any point prior to cross-sectional date.

Appendix Table 4 Prevalence of T2DM-related cardiovascular risk factors in patients with T2DM, stratified by cardiovascular disease status and whether the patient has a current SGLT-2 inhibitor prescription, September 2023.

	Without a current SGLT2i prescription				With a current SGLT2i prescription			
	ASCVD	HF	High risk	Low risk	ASCVD	HF	High risk	Low risk
N	144,623	39,254	333,216	40,645	36,194	14,859	76,579	9,630**
Smoking status*								
Smoker	19,723 (13.6%)	4,017 (10.2%)	47,094 (14.1%)	3,500 (8.6%)	5,256 (14.5%)	1,737 (11.7%)	10,748 (14.0%)	579 (6.0%)
Ex-smoker	79,453 (54.9%)	22,702 (57.8%)	147,453 (44.3%)	11,659 (28.7%)	20,323 (56.2%)	8,819 (59.4%)	34,723 (45.3%)	3,081 (32.0%)
Never smoked	45,388 (31.4%)	12,513 (31.9%)	138,499 (41.6%)	25,386 (62.5%)	10,599 (29.3%)	4,293 (28.9%)	31,092 (40.6%)	5,966 (61.9%)
Not known	59 (0.0%)	22 (0.1%)	170 (0.1%)	100 (0.2%)	16 (0.0%)	10 (0.1%)	16 (0.0%)	<10
Systolic blood pressure (mmHG)								
Mean (SD)	131.83 (15.39)	130.07 (16.99)	133.06 (13.84)	125.17 (12.63)	127.84 (14.92)	124.72 (16.69)	130.39 (12.95)	123.61 (11.92)
Missing (%)	13,342 (9.2%)	3,993 (10.2%)	35,688 (10.7%)	5,131 (12.6%)	322 (0.9%)	102 (0.7%)	1,230 (1.6%)	218 (2.3%)
Heart rate (beats per minute)								
Mean (SD)	74.54 (12.89)	73.88 (13.16)	78.61 (12.68)	81.92 (12.64)	74.90 (12.71)	73.43 (13.15)	80.02 (12.55)	83.33 (12.30)
Missing (%)	30,756 (21.3%)	7,727 (19.7%)	90,020 (27.0%)	11,993 (29.5%)	4,611 (12.7%)	1,328 (8.9%)	14,636 (19.1%)	1,980 (20.6%)
Estimated glomerular filtration rate (ml/min/1.73m^2)								
Mean (SD)	67.88 (22.06)	58.24 (23.30)	77.97 (20.29)	100.66 (16.67)	71.98 (23.16)	60.84 (23.42)	82.77 (20.07)	100.97 (16.08)
Missing (%)	13,077 (9.0%)	3,861 (9.8%)	34,584 (10.4%)	5,051 (12.4%)	228 (0.6%)	54 (0.4%)	880 (1.1%)	177 (1.8%)
Haemoglobin (g/L)								
Mean (SD)	131.77 (17.22)	127.98 (18.36)	136.67 (16.13)	136.98 (15.88)	139.15 (17.81)	136.31 (19.16)	143.45 (16.05)	141.54 (15.53)
Missing (%)	21,426 (14.8%)	5,347 (13.6%)	67,118 (20.1%)	8,997 (22.1%)	2,405 (6.6%)	531 (3.6%)	9,190 (12.0%)	1,149 (11.9%)
Glycosylated haemoglobin (%)								
Mean (SD)	7.23 (1.43)	7.23 (1.48)	7.28 (1.46)	7.54 (1.85)	7.94 (1.48)	7.70 (1.53)	8.08 (1.45)	8.14 (1.62)
Missing (%)	13,945 (9.6%)	4,333 (11.0%)	34,283 (10.3%)	4,646 (11.4%)	319 (0.9%)	135 (0.9%)	876 (1.1%)	149 (1.5%)
High-density lipoprotein (mmol/L)								
Mean (SD)	1.22 (0.35)	1.21 (0.36)	1.29 (0.36)	1.26 (0.35)	1.13 (0.31)	1.14 (0.33)	1.21 (0.32)	1.25 (0.33)
Missing (%)	19,594 (13.5%)	6,251 (15.9%)	45,979 (13.8%)	6,629 (16.3%)	1,169 (3.2%)	621 (4.2%)	2,491 (3.3%)	385 (4.0%)
Low-density lipoprotein (mmol/L)								
Mean (SD)	1.95 (0.87)	1.92 (0.87)	2.27 (0.95)	2.59 (0.94)	1.83 (0.83)	1.85 (0.85)	2.05 (0.87)	2.28 (0.92)
Missing (%)	62,160 (43.0%)	17,803 (45.4%)	142,983 (42.9%)	16,919 (41.6%)	13,051 (36.1%)	5,347 (36.0%)	28,380 (37.1%)	3,300 (34.3%)
White blood cell count (× 10^9/L)								
Mean (SD)	7.77 (2.20)	7.84 (2.28)	7.60 (2.12)	7.47 (2.20)	7.94 (2.14)	7.99 (2.19)	7.78 (2.06)	7.71 (2.15)
Missing (%)	21,961 (15.2%)	5,495 (14.0%)	68,180 (20.5%)	9,116 (22.4%)	2,513 (6.9%)	588 (4.0%)	9,457 (12.3%)	1,182 (12.3%)

* Smoking status was determined using records going back to '2001-01-01'. All other measures used the most recent plausible value recorded in the 24 months prior to the cross-sectional date. Definitions: HF, heart failure; CKD, chronic kidney disease; ASCVD, atherosclerotic cardiovascular disease; SD, standard deviation; N, number of observations ** Rounded to nearest 10 to ensure inferences about small numbers in cells are not possible.

Appendix Table 5 Currently prescribed glucose-modifying therapies in patients with T2DM, stratified by cardiovascular disease status and whether the patient has a current SGLT-2 inhibitor prescription, September 2023.

	Without a current SGLT2i prescription				With a current SGLT2i prescription			
	ASCVD	**HF**	**High risk**	**Low risk**	**ASCVD**	**HF**	**High risk**	**Low risk**
N	144,623	39,254	333,216	40,645	36,194	14,859	76,579	9,633
Number of glucose lowering therapies prescribed								
None	60,152 (41.6%)	17,876 (45.5%)	139,302 (41.8%)	18,257 (44.9%)	-	-	-	-
1	49,163 (34.0%)	12,287 (31.3%)	121,387 (36.4%)	14,573 (35.9%)	4,440 (12.3%)	3,358 (22.6%)	6,079 (7.9%)	718 (7.5%)
2	23,259 (16.1%)	6,233 (15.9%)	48,345 (14.5%)	5,381 (13.2%)	12,881 (35.6%)	5,361 (36.1%)	28,895 (37.7%)	4,136 (42.9%)
3	9,936 (6.9%)	2,355 (6.0%)	20,068 (6.0%)	1,972 (4.9%)	12,347 (34.1%)	4,068 (27.4%)	28,545 (37.3%)	3,414 (35.4%)
4+	2,113 (1.5%)	503 (1.3%)	4,114 (1.2%)	462 (1.1%)	6,526 (18.0%)	2,072 (13.9%)	13,060 (17.1%)	1,365 (14.2%)
Therapies								
Metformin	67,529 (46.7%)	14,587 (37.2%)	170,058 (51.0%)	20,010 (49.2%)	26,058 (72.0%)	8,479 (57.1%)	62,349 (81.4%)	8,040 (83.5%)
Sulfonylurea	15,208 (10.5%)	3,737 (9.5%)	33,387 (10.0%)	3,309 (8.1%)	8,197 (22.6%)	2,540 (17.1%)	18,842 (24.6%)	1,912 (19.8%)
Insulin	16,989 (11.7%)	5,781 (14.7%)	23,218 (7.0%)	2,491 (6.1%)	6,878 (19.0%)	3,024 (20.4%)	8,908 (11.6%)	879 (9.1%)
SGLT2 inhibitors								
Any	-	-	-	-	36,194 (100.0%)	14,860* (100.0%)	76,579 (100.0%)	9,633 (100.0%)
Dapagliflozin	-	-	-	-	20,924 (57.8%)	10,904 (73.4%)	39,709 (51.9%)	4,528 (47.0%)
Empagliflozin	-	-	-	-	12,376 (34.2%)	3,340 (22.5%)	28,800 (37.6%)	4,159 (43.2%)
Canagliflozin	-	-	-	-	2,959 (8.2%)	650 (4.4%)	8,109 (10.6%)	947 (9.8%)
Ertugliflozin	-	-	-	-	45 (0.1%)	<10	144 (0.2%)	34 (0.4%)
GLP1 receptor agonists								
Any	6,390 (4.4%)	1,680* (4.3%)	14,775 (4.4%)	2,550* (6.3%)	5,120 (14.1%)	1,710* (11.5%)	11,955 (15.6%)	1,700* (17.6%)
Liraglutide	993 (0.7%)	283 (0.7%)	1,940 (0.6%)	266 (0.7%)	694 (1.9%)	224 (1.5%)	1,507 (2.0%)	197 (2.0%)
Dulaglutide	3,036 (2.1%)	844 (2.2%)	6,925 (2.1%)	1,060 (2.6%)	2,416 (6.7%)	805 (5.4%)	5,610 (7.3%)	735 (7.6%)
Exenatide	154 (0.1%)	44 (0.1%)	368 (0.1%)	40 (0.1%)	111 (0.3%)	40 (0.3%)	278 (0.4%)	31 (0.3%)
Semaglutide (oral)	469 (0.3%)	113 (0.3%)	1,368 (0.4%)	260 (0.6%)	487 (1.3%)	149 (1.0%)	1,455 (1.9%)	209 (2.2%)
Semaglutide (injectable)	1,881 (1.3%)	424 (1.1%)	4,565 (1.4%)	1,007 (2.5%)	1,551 (4.3%)	534 (3.6%)	3,500 (4.6%)	568 (5.9%)
Lixisenatide	31 (0.0%)	<10	68 (0.0%)	<10	18 (0.0%)	<10	50 (0.1%)	<10
DPP4 inhibitors								
Any	20,174 (13.9%)	6,082 (15.5%)	37,538 (11.3%)	2,680* (6.6%)	8,123 (22.4%)	2,927 (19.7%)	17,169 (22.4%)	1,760* (18.2%)
Linagliptin	9,121 (6.3%)	3,631 (9.3%)	12,140 (3.6%)	572 (1.4%)	2,976 (8.2%)	1,527 (10.3%)	4,376 (5.7%)	354 (3.7%)
Alogliptin	4,446 (3.1%)	873 (2.2%)	10,412 (3.1%)	678 (1.7%)	2,007 (5.5%)	514 (3.5%)	5,373 (7.0%)	526 (5.5%)
Saxagliptin	373 (0.3%)	84 (0.2%)	697 (0.2%)	44 (0.1%)	182 (0.5%)	49 (0.3%)	408 (0.5%)	30 (0.3%)
Vildagliptin	81 (0.1%)	17 (0.0%)	199 (0.1%)	<10	42 (0.1%)	15 (0.1%)	98 (0.1%)	<10
Sitagliptin	6,208 (4.3%)	1,492 (3.8%)	14,185 (4.3%)	1,389 (3.4%)	2,948 (8.1%)	834 (5.6%)	6,969 (9.1%)	839 (8.7%)
Thiazolidinediones								
Pioglitazone	1,134 (0.8%)	87 (0.2%)	3,787 (1.1%)	256 (0.6%)	433 (1.2%)	47 (0.3%)	1,785 (2.3%)	188 (2.0%)

Note: All individuals prescribed a combination therapy have been excluded from the above table (1.33%). Definitions: HF, heart failure; CKD, chronic kidney disease; ASCVD, atherosclerotic cardiovascular disease; SD, standard deviation; N, number of observations. NOTE: identifying current medications was done using a modified version of the Farmer et al 2021 methodology. In our version we excluded implausible values before applying logic, and in the final step applied the most-common duration (per medicine) rather than subsituting missing values with 28 days. * Rounded to nearest 10 to ensure inferences about small numbers in cells are not possible.

Appendix Table 6. Logistic regression model estimates of odds ratios for association between a current SGLT-2 inhibitor prescription and patient characteristics and comorbidities in patients with T2DM and comorbid chronic heart failure, September 2023.

	Odds ratio (95% CI)	P-value
Age group		
18-39	1.00	
40-49	0.86 (0.59, 1.24)	0.42
50-59	0.64 (0.45, 0.91)	0.01
60-69	0.48 (0.34, 0.68)	<0.01
70-79	0.30 (0.21, 0.42)	<0.01
80-89	0.16 (0.12, 0.23)	<0.01
90+	0.07 (0.05, 0.10)	<0.01
Gender		
Male	1.00	
Female	0.62 (0.59, 0.64)	<0.01
Ethnicity		
White	1.00	
Mixed	1.22 (0.98, 1.52)	0.07
Asian or Asian British	1.12 (1.05, 1.20)	<0.01
Black or Black British	0.89 (0.80, 0.99)	0.03
Chinese or Other Ethnic Group	1.23 (1.01, 1.51)	0.04
Not stated/known	1.05 (0.71, 1.54)	0.81
Deprivation		
5 (Least deprived)	1.00	
4	1.01 (0.94, 1.08)	0.78
3	0.89 (0.83, 0.95)	<0.01
2	0.91 (0.85, 0.97)	<0.01
1 (most deprived)	0.85 (0.79, 0.90)	<0.01
Diagnosis recency		
0-1 years	1.00	
1-2 years	0.92 (0.80, 1.05)	0.22
3-4 years	0.96 (0.84, 1.10)	0.60
4-5 years	0.96 (0.83, 1.10)	0.52
>5 years	1.27 (1.15, 1.40)	<0.01
Comorbid conditions		
Neither CVD nor CKD	1.00	
With comorbid CVD	1.00 (0.96, 1.05)	0.93
With comorbid CKD 1-3	2.91 (2.73, 3.10)	<0.01
With comorbid CKD 4	4.18 (3.81, 4.58)	<0.01