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FULL RESEARCH PAPER
Diabetes and metabolic disorders

Use of sodium–glucose co-transporter 2 inhibitors and glucagon-like peptide-1 receptor agonists according to the 2019 ESC guidelines and the 2019 ADA/EASD consensus report in a national population of patients with type 2 diabetes

Carl-Emil Lim [1]*, Björn Pasternak [1,2], Björn Eliasson[3,4], Goodarz Danaei[5], and Peter Ueda [1]

[1]Clinical Epidemiology Division, Department of Medicine, Solna, Karolinska Institutet, Maria Aspmans Gata 16, 17176 Stockholm, Sweden; [2]Department of Epidemiology Research, Statens Serum Institut, Artillerivej 5, 2300 Copenhagen, Denmark; [3]Department of Medicine, Sahlgrenska University Hospital, Blå stråket 5, 413 45 Gothenburg, Sweden; [4]The Swedish National Diabetes Register, Center of Registers, Medicinaregatan 18 G, 413 45 Gothenburg, Sweden; and [5]Department of Global Health and Population, Harvard TH Chan School of Public Health, 665 Huntington Avenue, Boston, MA 02115, USA

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See the editorial comment for this article 'The role of cost-effectiveness in the use of sodium–glucose co-transporter 2 inhibitors and glucagon-like peptide-1 receptor agonists', by M. Liu and G. Hao, https://doi.org/10.1093/eurjpc/zwad032.

Aims To assess treatment eligibility for, and received treatment with, sodium–glucose co-transporter 2 inhibitors (SGLT2) and glucagon-like peptide-1 (GLP-1) receptor agonists according to the 2019 the American Diabetes Association (ADA)/European Association for the Study of Diabetes (EASD) consensus report and the 2019 European Society of Cardiology (ESC) guidelines in a nationwide sample of patients with type 2 diabetes.

Methods and results Both sets of guidelines included the treatment indications of heart failure, chronic kidney disease, and atherosclerotic cardiovascular disease while only the 2019 ESC guidelines also recommended treatment based on high or very high cardiovascular risk. The analyses included 435 000 patients with type 2 diabetes identified from the Swedish National Diabetes Register (2020–21). According to the 2019 ESC guidelines, 79.5% were recommended any of the two drugs (SGLT2 inhibitors: 37.2%; SGLT2 inhibitors or GLP-1 receptor agonists: 40.9%; GLP-1 receptor agonists: 1.4%). According to the 2019 ADA/EASD consensus report, 48.8% were recommended any of the two drugs (SGLT2 inhibitors: 37.2%; GLP-1 receptor agonists: 11.6%). Of those who had been recommended any of the two drugs, 33.7% had received the recommended treatment according to the 2019 ESC guidelines and 25.4% according to the 2019 ADA/EASD consensus report.

Conclusions In this nationwide study, the proportion of patients with type 2 diabetes who were recommended treatment with an SGLT2 inhibitor or a GLP-1 receptor agonist was approximately 80% according to the 2019 ESC guidelines and around half according to the 2019 ADA/EASD consensus report. Uptake of these recommendations in routine clinical practice was limited.

Lay summary We investigated the proportion of patients with type 2 diabetes in Sweden who were recommended treatment with two types of diabetes drugs, SGLT2 inhibitors, and GLP-1 receptor agonists, according to two European clinical guidelines.

- Depending on the guideline used, between half and 80% of the patients with type 2 diabetes were recommended treatment with an SGLT2 inhibitor or a GLP-1 receptor.
- Of those who had been recommended any of the two drugs, one in three or one in four, depending on the guideline used, had received the recommended treatment.

* Corresponding author. Tel: +46739727490, Email: carlemil.lim@ki.se

Structured Graphical Abstract

Key Question

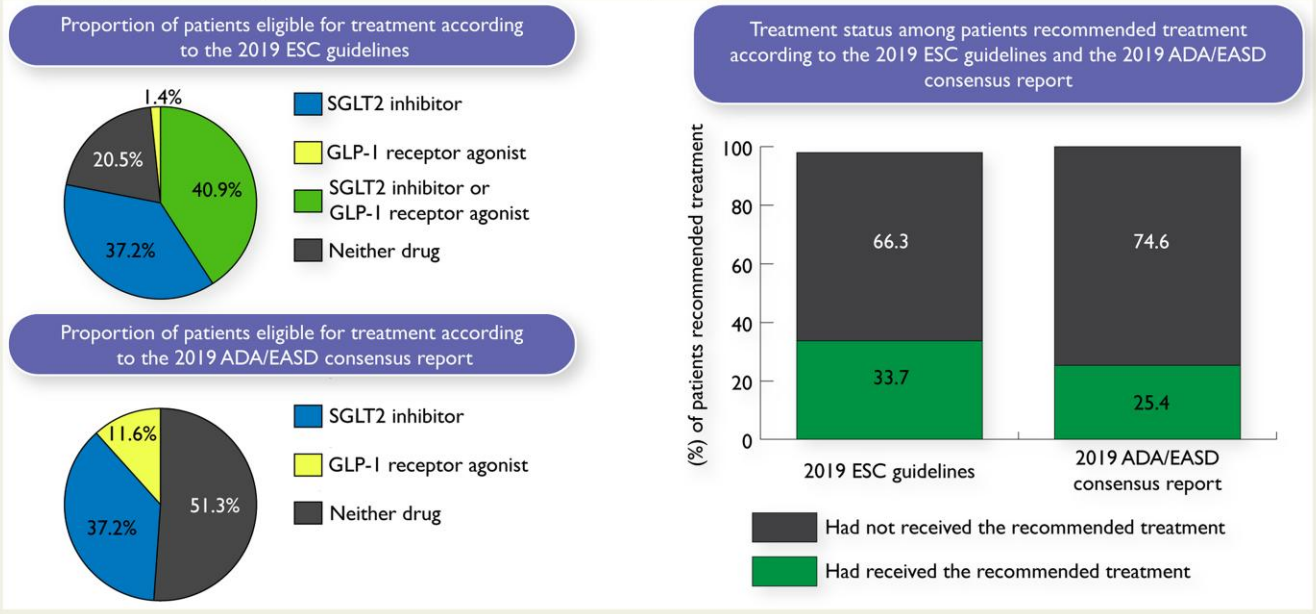
What proportion of patients with type 2 diabetes are eligible for treatment with SGLT2 inhibitors or GLP-1 receptor agonists according to the 2019 ESC guidelines and the 2019 ADA/EASD consensus report, and to what extent have the guidelines been implemented in routine clinical practice?

Key Finding

In this nationwide study, the proportion of patients with type 2 diabetes who were recommended treatment with an SGLT2 inhibitor or a GLP-1 receptor agonist was approximately 80% according to the 2019 ESC guidelines and around half according to the 2019 ADA/EASD consensus report. Of those who had been recommended any of the two drugs, 33.7% had received the recommended treatment according to the 2019 ESC guidelines and 25.4% according to the 2019 ADA/EASD consensus report.

Take Home Message

According to the latest European guidelines, most patients with type 2 diabetes are recommended treatment with an SGLT2 inhibitor or a GLP-1 receptor agonist. Uptake of guideline recommendations in routine clinical practice was limited.



ADA, American Diabetes Association; EASD, European Association for the Study of Diabetes; ESC, European Society of Cardiology; GLP-1, glucagon-like peptide-1; SGLT2, sodium–glucose co-transporter 2.

Keywords guidelines • guideline uptake • cardiovascular disease • chronic kidney disease • heart failure • treatment gaps

Introduction

In the past decade, large cardiovascular outcome trials have shown that sodium–glucose co-transporter 2 inhibitors (SGLT2) and glucagon-like peptide-1 (GLP-1) receptor agonists improve cardiovascular and renal outcomes in patients with type 2 diabetes and atherosclerotic cardiovascular disease (ASCVD), heart failure, or chronic kidney disease (CKD).[1–7] These data have led to substantial changes in medication recommendations for patients with type 2 diabetes.

Two sets of guidelines for the treatment of type 2 diabetes, both released in 2019, are currently under use in Europe: The European Society of Cardiology (ESC) guidelines, which were developed in collaboration with the European Association for the Study of Diabetes (EASD),[8] and the American Diabetes Association (ADA)/EASD consensus report.[9,10] The 2019 ESC guidelines recommend the use of SGLT2 inhibitors or GLP-1 receptor agonists for type 2 diabetes patients with established ASCVD or with very high or high cardiovascular risk according to the ESC risk categories.[8] The 2019 ADA/EASD consensus report recommends primarily GLP-1 receptor agonists to patients with established ASCVD, or ASCVD risk (coronary, carotid, or lower extremity artery stenosis >50%, or left ventricular hypertrophy among those aged ≥55 years).[10] Both the 2019 ESC guidelines and 2019 ADA/EASD consensus report recommend SGLT2 inhibitors before GLP-1 receptor agonists for type 2 diabetes patients with CKD or heart failure.[8,10]

Important knowledge gaps remain regarding the uptake of the two European guidelines among patients with type 2 diabetes. While the differences in the recommendations of the two guidelines have been subject to concern and debate,[11] the proportion of patients with type 2 diabetes who are eligible for treatment with SGLT2 inhibitors and GLP-1 receptor agonists according to each set of guidelines has not been investigated in a large population-based sample. Moreover, the extent to which they have been implemented in routine clinical practice is not known. Such data are important for planning health care delivery, assessment of costs associated with guideline implementation and identifying treatment gaps that indicate the potential for improvement in patient outcomes.

In this study, we used nationwide registers in Sweden to assess the eligibility for and treatment with SGLT2 inhibitors and GLP-1 receptor agonists in patients with type 2 diabetes according to the 2019 ESC guidelines and the 2019 ADA/EASD consensus report.

Methods

Data sources

We obtained information about diabetes type, glycated haemoglobin level (HbA1c), blood pressure, body mass index (BMI), albuminuria, estimated glomerular filtration rate (eGFR), and smoking status from the Swedish National Diabetes Register. This is a nationwide register including data, collected by trained physicians and nurses during patient visits to outpatient and primary care clinics, for patients with type 1 or type 2 diabetes in Sweden. During the study period (2020–21), 85–88% of all patients receiving drugs for diabetes in Sweden were included in the register.[12,13]

From the National Patient Register, we obtained data on procedure codes and diagnoses according to the International Classification of Diseases, tenth revision (ICD-10), assigned by physicians during hospital admissions and outpatient visits in Sweden.[14] Information about the use of glucose-lowering drugs and comedications was obtained from the Swedish National Prescription Drug register, which contains individual-level data based on anatomical therapeutic chemical (ATC) codes of all drug prescriptions filled at all pharmacies in Sweden since July 2005.[15] Data on age, sex, vital status, educational level, and income were obtained from Statistics Sweden.

Study population

We included patients who had filled a prescription for a glucose-lowering drug between 2005 and 2021 and who had been registered as a type 2 diabetes patient in The Swedish National Diabetes Register from 2020 through 2021. The latest registration date in the Swedish National Diabetes Register was defined as the index date.

Statistical analyses

We categorized patients based on their recommended treatment according to the 2019 ESC guidelines (SGLT2 inhibitor, GLP-1 receptor agonist, SGLT2 inhibitor or GLP-1 receptor agonist, and neither drug) and according to the 2019 ADA/EASD consensus report (SGLT2 inhibitor, GLP-1 receptor agonist, and neither drug). Patients were categorized according to mutually exclusive treatment indications in a hierarchical manner according to the order in which the indications are presented in *Table 1*. Treatment indications were prioritized to reflect the recommendations given in the evaluated guidelines. For example, a patient with both heart failure and ASCVD was categorized as being recommended an SGLT2 inhibitor based on the indication of heart failure.

For each set of guidelines, we described the proportions and characteristics (Supplementary material online, *Table S1*) of patients by their recommended treatment. Among patients who were recommended an SGLT2 inhibitor or GLP-1 receptor agonist, we assessed the proportion of patients by treatment indication categories, as presented in *Table 1* (detailed definitions are provided in Supplementary material online, *Table S2*). Across groups of patients categorized according to their recommended drug and treatment indication, we assessed the proportion of patients who had received an SGLT2 inhibitor, a GLP-1 receptor agonist, both an SGLT2 inhibitor and a GLP-1 receptor agonist, or neither drug. For these analyses, we considered prescriptions filled at any time before the index date and up to 30 days after the index date. We used this definition of treatment status to account for patients who had previously received the recommended drug but stopped due to potential adverse effects or limited adherence and to capture drugs that were prescribed during the healthcare visit at the index date. Among treated patients, we also assessed the proportions receiving treatment by types of SGLT2 inhibitors (empagliflozin, dapagliflozin, canagliflozin, and ertugliflozin) and GLP-1 receptor agonists (semaglutide, liraglutide, dulaglutide, lixisenatide, and exenatide). We performed the analyses in the total population and subgroups by age (≥65 and <65 years) as treatment decisions may be influenced by patient frailty and life expectancy.[16,17]

Given the proportion of missing data for variables used for assessing treatment eligibility, including eGFR (7.0%), albuminuria (25.4%), blood pressure (5.6%), dyslipidemia (19.5%), smoking (14.8%), and BMI (15.4%) (Supplementary material online, *Table S1*), we used multiple imputations (Markov chain Monte Carlo method) to handle missing data. In addition to variables used for assessing treatment eligibility, we imputed data for glycated haemoglobin levels (2.1% missing), place of birth (0.1%), educational level (3.2%), and income (1·5%). We imputed 10 data sets by predictive mean matching for continuous variables, logistic regression for dichotomous variables, and multinomial logistic regression for polytomous variables.

Table 1 Criteria for recommendation of SGLT2 inhibitors or GLP-1 receptor agonists according to the 2019 ESC guidelines and 2019 ADA/EASD consensus report

Indication	Recommended drug	
	2019 ESC guidelines	2019 ADA/EASD consensus report
Heart failure	SGLT2 inhibitor	SGLT2 inhibitor
CKD: eGFR 30 to <60 mL/min/1.73 m^2	SGLT2 inhibitor	SGLT2 inhibitor
CKD: Macro- or microalbuminuria	SGLT2 inhibitor	SGLT2 inhibitor
CKD: with eGFR 15 to <30 mL/min/1.73 m^2[a]	GLP-1 receptor agonist	GLP-1 receptor agonist
ASCVD[b]	SGLT2 inhibitor or GLP-1 receptor agonist	GLP-1 receptor agonist
Very high or high cardiovascular risk[c]	SGLT2 inhibitor or GLP-1 receptor agonist	Neither drug
None of the above	Neither drug	Neither drug

In accordance with the guideline recommendations, we categorized patients by mutually exclusive treatment indications in a hierarchical manner with priority given according to the order in which they are presented in this table. For example, all patients with heart failure (with eGFR ≥30), regardless of the status of other indication categories, were categorized as being recommended an SGLT2 inhibitor. Patients with end-stage kidney disease/renal replacement therapy were categorized as being recommended neither drug.

ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GLP-1, glucagon-like peptide-1; SGLT2, sodium–glucose co-transporter 2.

[a]All patients with eGFR 15 to <30 mL/min/1.73 m^2, regardless of the status of other indication categories, were categorized as being recommended a GLP-1 receptor agonist.

[b]Including previous ischaemic heart disease, ischaemic stroke, and arterial disease. Data on coronary, carotid, or lower extremity artery stenosis >50% (2019 ADA/EASD consensus report), or left ventricular hypertrophy (both investigated guidelines) used as treatment indications in the investigated guidelines were not available.

[c]Defined as having three or more major risk factors (age >50 years, hypertension, dyslipidemia, smoking, obesity), retinopathy, or having a time since first diabetes drug (substitute of diabetes duration) of 10 years or more and any additional major risk factor (detailed definitions are provided in supplementary material online, *Table S2*).

For each set of guidelines separately, we performed logistic regression analyses to assess the association of selected variables (Supplementary material online, *Table S1*) with the likelihood of having received treatment as defined earlier with either an SGLT2 inhibitor or a GLP-1 receptor agonist among patients recommended any of the drugs and for patients recommended neither drug. The models included all variables in Supplementary material online, *Table S1* as independent variables and were run across all imputed data sets and then pooled in accordance with Rubin's Rules.[18]

Individual consent is not required for patients to be included in national health registries such as the National Diabetes Register (but opt-out is possible), or this study, according to Swedish law. The Swedish Ethical Review Authority approved the study.

Results

Study population

The analyses included 435 000 patients. Median (IQR) age was 70 (61, 77) years, and 41.1% were women. Overall, 9.2% had heart failure,

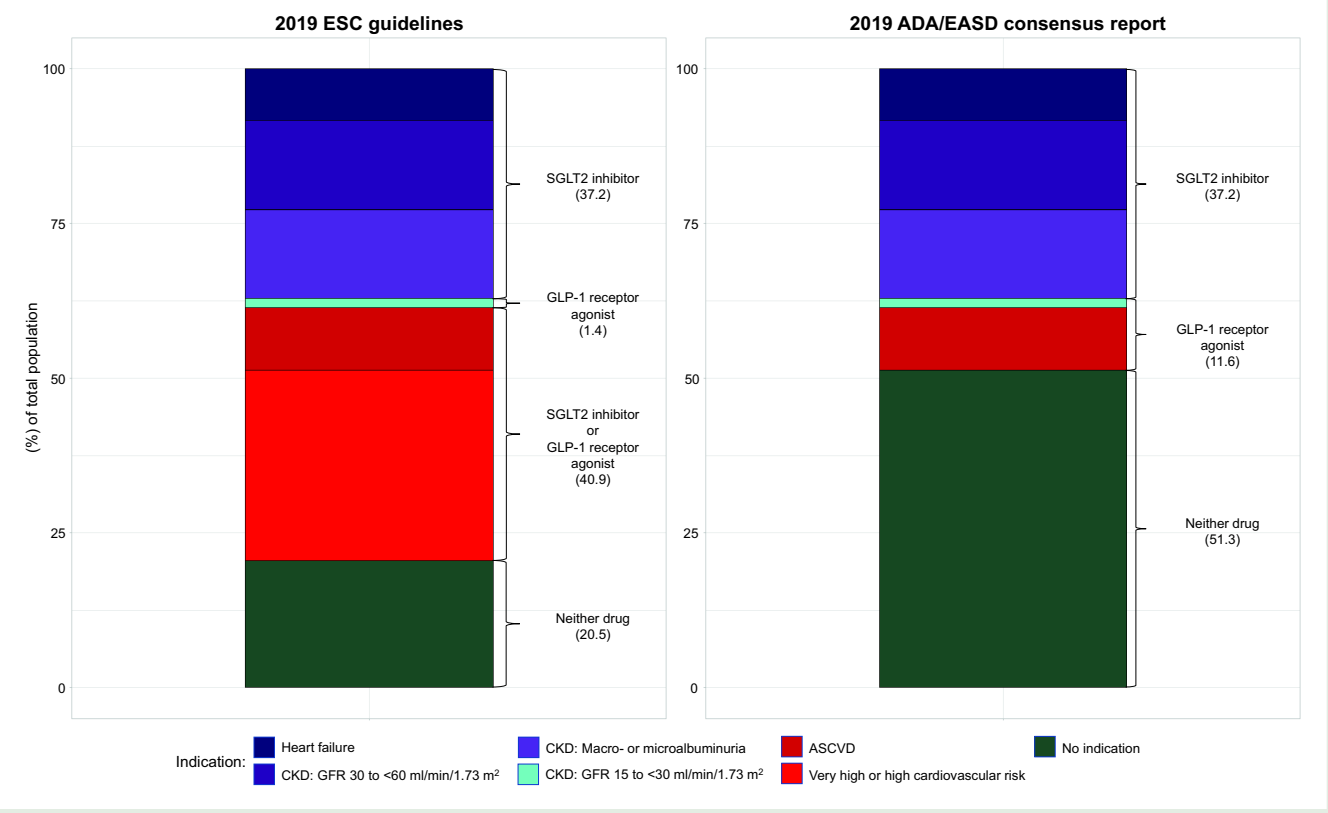


Figure 1 Proportion of patients recommended an sodium–glucose co-transporter 2 inhibitor or a glucagon-like peptide-1 receptor agonist by recommended drug and treatment indication according to the 2019 ESC guidelines and the 2019 ADA/EASD consensus report.

35.6% had CKD (including eGFR < 60, micro- or macroalbuminuria but not end-stage kidney disease), and 24.5% had ASCVD, with many patients having more than one condition. Moreover, 43.4% had no ASCVD but a very high cardiovascular risk, and 10.0% had a high cardiovascular risk according to the ESC criteria. (Supplementary material online, *Tables S3 and S4*).

Eligibility for treatment with sodium–glucose co-transporter 2 inhibitors and glucagon-like peptide-1 receptor agonists

Figure 1 shows that according to the 2019 ESC guidelines, 79.5% of the patients were recommended any of the drugs (SGLT2 inhibitors: 37.2%; SGLT2 inhibitors or GLP-1 receptor agonists: 40.9%; GLP-1 receptor agonists: 1.4%). According to the 2019 ADA/EASD consensus report, 48.8% were recommended any of the drugs (SGLT2 inhibitors: 37.2%; GLP-1 receptor agonists: 11.6%).

Received treatment with sodium–glucose co-transporter-2 inhibitors and glucagon-like peptide-1 receptor agonists

In total, 69 058 (15.9%) of the patients had received an SGLT2 inhibitor (but not a GLP-1 receptor agonist), 47 019 (10.8%) had received a GLP-1 receptor agonist (but not an SGLT2 inhibitor), and 44 483 (10,2%) had received both an SGLT2 inhibitor and a GLP-1 receptor agonist (*Figure 2*).

Most of the patients who had received an SGLT2 inhibitor had received empagliflozin (82.8%) or dapagliflozin (16.3%) while the most common GLP-1 receptor agonists were semaglutide (52.1%) and liraglutide (35.4%; Supplementary material online, *Table S5*).

In total, 33.7% of those who had been recommended treatment according to the 2019 ESC guidelines had received the recommended treatment (*Figure 2*). The corresponding proportion for the 2019 ADA/EASD consensus report was 25.4% (*Figure 3*).

Of the patients who were recommended treatment with SGLT2 inhibitors (according to both sets of guidelines), 27.0% had received an SGLT2 inhibitor (*Figures 2* and *3*). Of the patients who were recommended an SGLT2 inhibitor or a GLP-1 receptor agonist according to the 2019 ESC guidelines, 40.1% had received at least one of the drugs (*Figure 2*). Among patients recommended a GLP-1 receptor agonist according to the 2019 ADA/EASD consensus report (based on ASCVD or CKD with eGFR 15 to <30), 20.0% had received this treatment (*Figure 3*).

Among those who recommended neither drug, the proportion who had received at least one of the drugs was 28.1% according to the 2019 ESC guidelines and 34.9% according to the 2019 ADA/EASD consensus report (*Figures 2* and *3*).

Subgroup analyses by age

Figure 4 shows that, according to the 2019 ESC guidelines, 68.9% of the patients aged <65 years were recommended any of the drugs (SGLT2 inhibitors: 21.4%; SGLT2 inhibitors or GLP-1 receptor agonists: 47.2%; GLP-1 receptor agonists: 0.3%). Of patients aged ≥65.years, 84.9% were recommended any of the drugs (SGLT2 inhibitors: 45·2%; SGLT2 inhibitors or GLP-1 receptor agonists: 37.7%; GLP-1 receptor agonists: 2.0%).

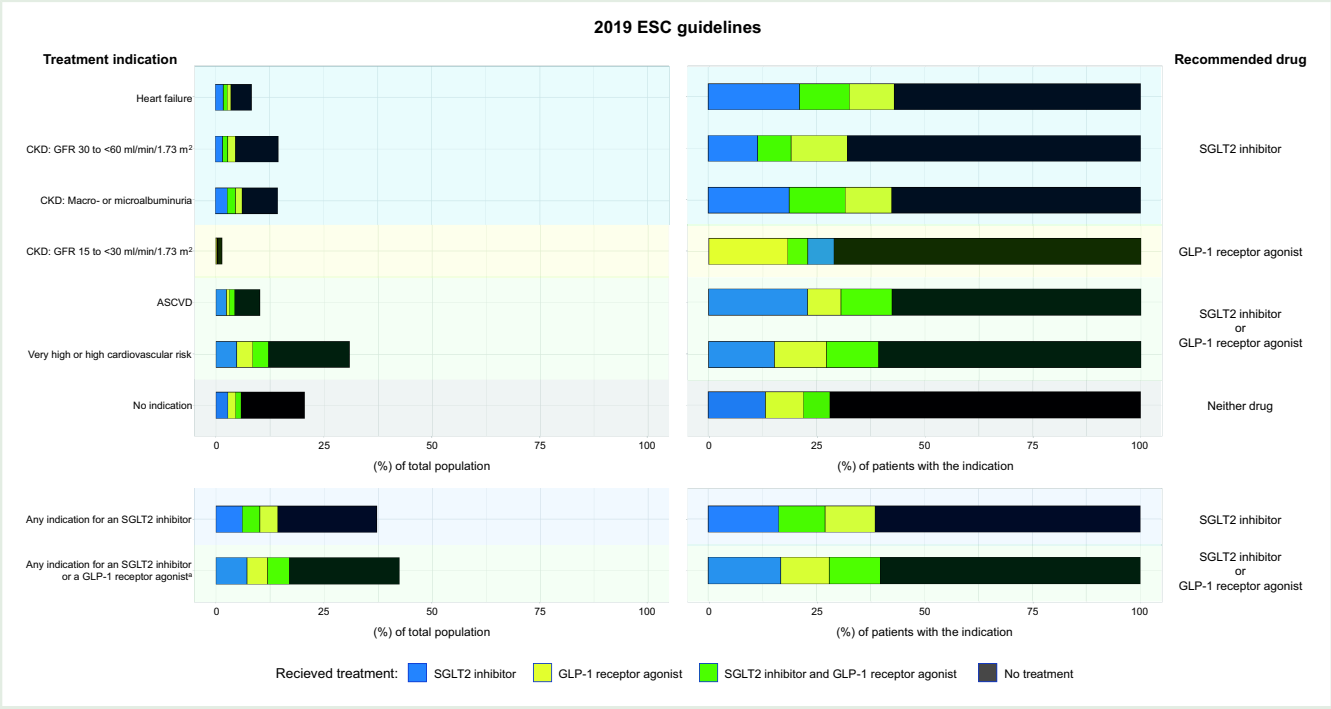


Figure 2 Received treatment by treatment indication according to the 2019 ESC guidelines. *Note*: Superscript 'a' denotes including patients recommended treatment with a glucagon-like peptide-1 based on chronic kidney disease with estimated glomerular filtration rate 15 to <30 mL/min/1.73 m^2.

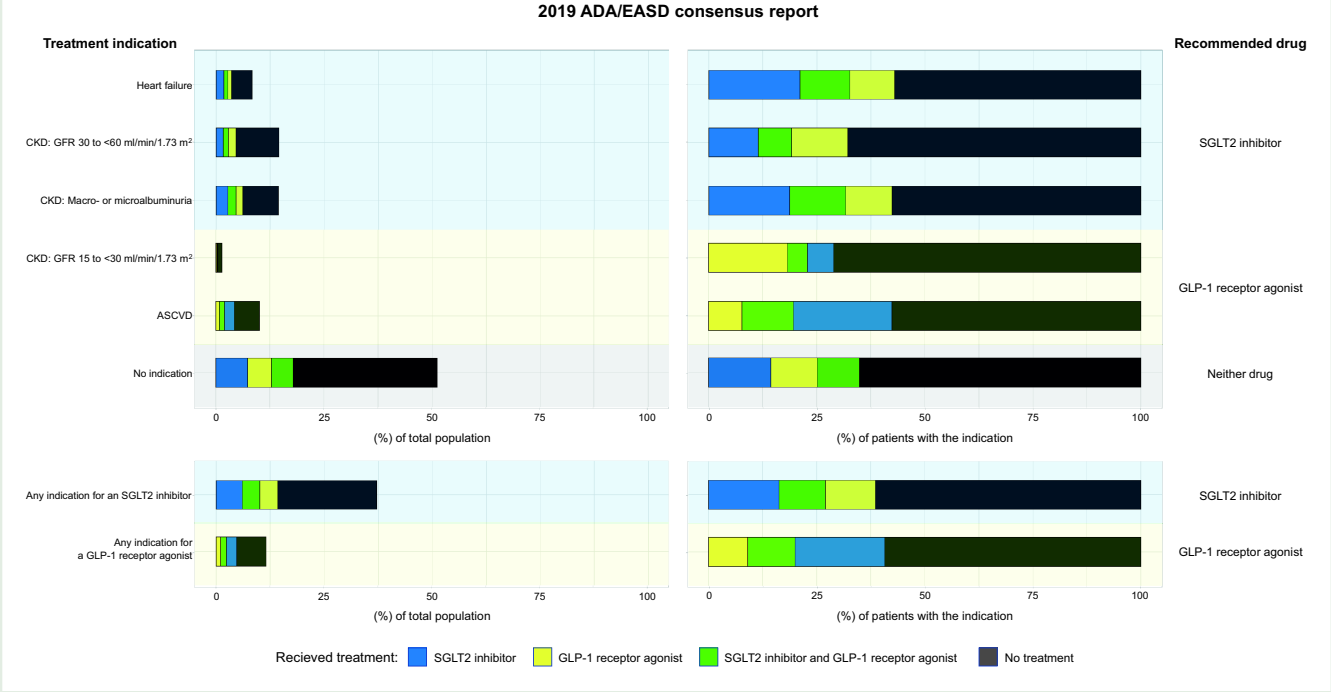


Figure 3 Received treatment by treatment indication according to the 2019 ADA/EASD consensus report.

Figure 4 also shows that, according to the 2019 ADA/EASD consensus report, 29.0% of patients aged <65 years were recommended any of the drugs (SGLT2 inhibitors: 21.4%; GLP-1 receptor agonists: 7.6%). Of patients aged ≥65 years, 58.8% were recommended any of the drugs (SGLT2 inhibitors: 45.2%; GLP-1 receptor agonists: 13.6%).

The proportion of treatment-eligible patients who had received the recommended treatment according to the 2019 ESC guidelines was

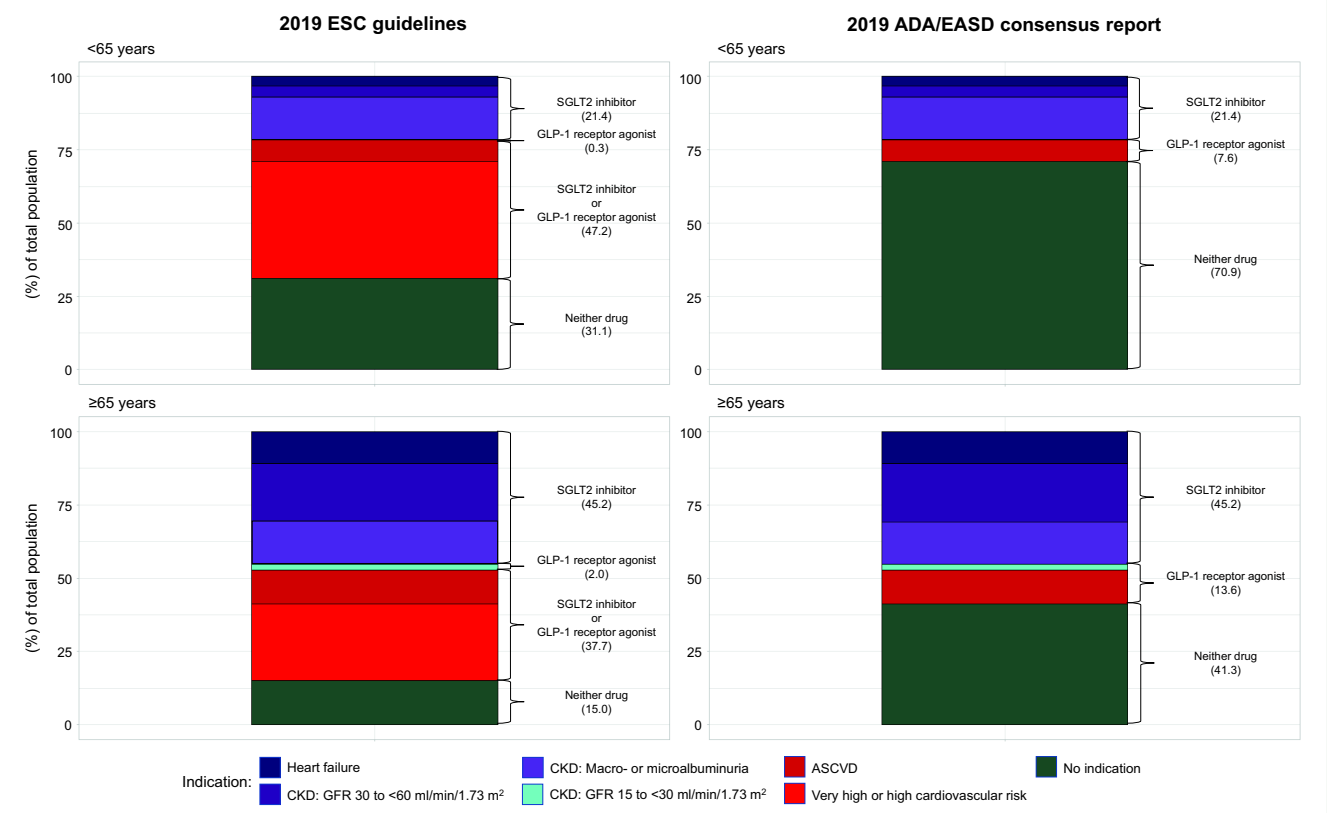


Figure 4 Proportion of patients by recommended drug and treatment indication according to the 2019 ESC guidelines and the 2019 ADA/EASD consensus report in subgroup analyses by age.

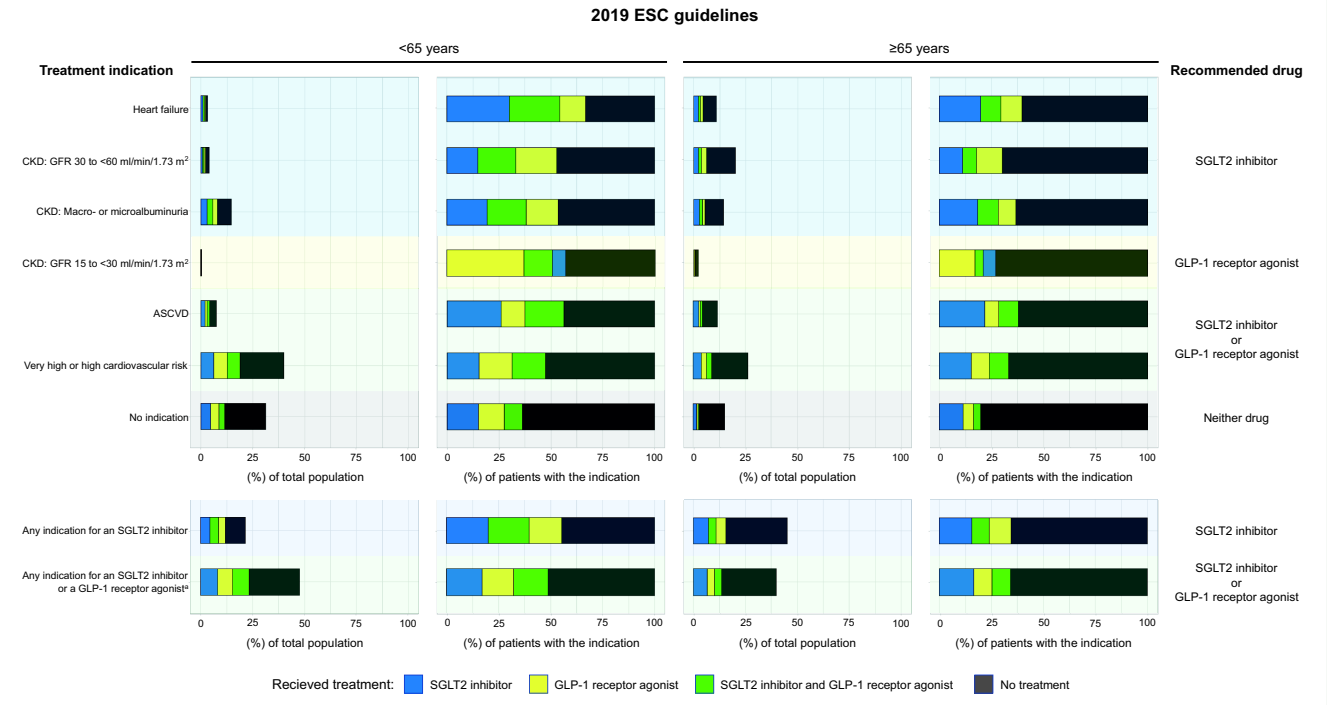


Figure 5 Received treatment by treatment indication according to the 2019 ESC guidelines in subgroup analyses by age. *Note*: Superscript 'a' denotes Including patients recommended treatment with a glucagon-like peptide-1 based on chronic kidney disease with estimated glomerular filtration rate 15 to <30 mL/min/1.73 m^2.

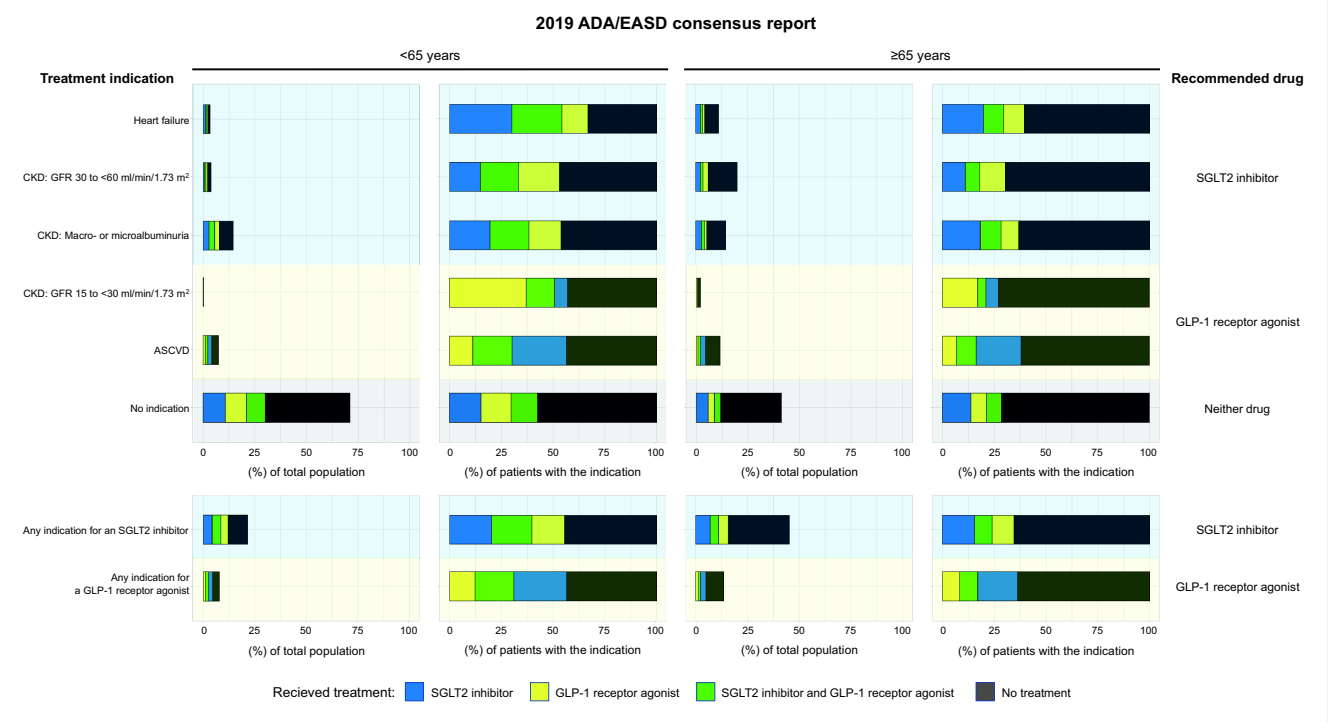


Figure 6 Received treatment by treatment indication according to the 2019 ADA/EASD consensus report in subgroup analyses by age.

45.9% for those aged <65 years and 28.6% for those aged ≥65 years (*Figure 5*). The corresponding numbers for the analyses of the 2019 ADA/EASD consensus report were 37·4% for those aged <65 years and 22·3% for those aged ≥65 years (*Figure 6*).

Factors associated with receiving the recommended treatment

Supplementary material online, *Tables S6* and *S7* show that several variables were associated with a higher or lower likelihood of having received an SGLT2 inhibitor or a GLP-1 receptor agonist. For example, among those who were recommended any of the drugs according to the 2019 ESC guidelines, older age (e.g. adjusted OR for 60–69 years vs. <40 years: 0.74 (95% CI, 0.66–0.84)), was associated with a lower likelihood of having received an SGLT2 inhibitor or a GLP-1 receptor agonist. Examples of variables associated with a higher likelihood of having received treatment included higher income (e.g. adjusted OR for highest income quartile vs. lowest income quartile: 1.28 (95% CI, 1.23–1.32)), higher education (e.g. adjusted OR for medium or long tertiary education vs. primary school and high school education: 1.09 (95% CI 1.05–1.13)), higher levels of HbA1c (e.g. adjusted OR for HbA1c 53–63 mmol/mol (7.0–7.9%) vs. HbA1c ≤ 48 mmol/mol (≤6.5%): 2.44 (95% CI 2.37–2.51)) and higher BMI (e.g. adjusted OR for obese class I/II vs. normal weight 2.11 (95% CI, 2.03–2.19)).

The directions and magnitude of the associations were similar in analyses using the 2019 ADA/EASD consensus report and among patients recommended neither drug in analyses of both sets of guidelines.

Discussion

In this nationwide study using Swedish register data, we found that around 80% of patients with type 2 diabetes would be recommended an SGLT2 inhibitor or a GLP-1 receptor agonist according to the 2019 ESC guidelines and that around half of the patients would be recommended such treatments by the 2019 ADA/EASD consensus report. In 2020–21, the proportion of treatment-eligible patients who had received the recommended treatment was 33.7% according to the 2019 ESC guidelines and 25.4% according to the 2019 ADA/EASD consensus report, with the proportion treated showing little variation across groups of patients by treatment indication and recommended drug.

Strengths of this study include the use of nationwide registers that contained information about a large study population comprising almost all patients with type 2 diabetes in Sweden, their patient characteristics, and prescription drug use.

Previous studies have assessed clinical guidelines from other parts of the world in smaller samples or selected populations of patients with type 2 diabetes.[19–21] In an analysis of 13 350 patients with type 2 diabetes identified from 18 primary care practices in MA, USA, 33% of the patients were eligible for an SGLT2 inhibitor or a GLP-1 receptor agonist according to the 2021 guidelines.[20] The 2019 ADA/EASD consensus report is largely similar to the 2021 ADA guidelines, although the 2019 ADA/EASD consensus report recommends treatment with SGLT2 inhibitors to a broader range of CKD patients, including those with microalbuminuria, which does not constitute a treatment indication in the 2021 ADA guidelines. This difference between the guideline recommendations may partly explain the larger proportion of treatment-eligible patients in our analysis.

In another analysis of 56 411 type 2 diabetes patients identified from primary care networks across Canada, approximately 60% were eligible for an SGLT2 inhibitor or a GLP-1 receptor agonist according to the Diabetes Canada guidelines.[21] The Canadian guidelines are comparable to the 2019 ESC guidelines as they recommend the use of SGLT2 inhibitors or GLP-1 receptor agonists for primary prevention in patients at high cardiovascular risk. The larger proportion of treatment-eligible patients found in our analysis as compared to the Canadian analysis could

potentially be explained by the broader criteria used for high or very high cardiovascular risk in the 2019 ESC guidelines. Moreover, our study population was older and had a higher prevalence of comorbidities constituting treatment indications compared with the Canadian study population.

We found that a substantial proportion of the patients who were recommended treatment according to the 2019 ESC guidelines or the 2019 ADA/EASD consensus report had not received the recommended treatment. The proportion untreated ranged between 57.5% and 80% across groups of patients categorized according to treatment indications and recommended treatment. These findings are in line with smaller studies from other countries indicating that a large proportion of patients with guidelines-based indications for SGLT2 inhibitors or GLP-1 receptor agonists do not receive those treatments.[19,21–25] As Sweden provides universal healthcare with very low patient costs for healthcare visits and prescription drugs, it could be hypothesized that fewer patients receive the recommended treatment in some other countries.

In 2022, updated clinical guidelines for the management of type 2 diabetes were released by the ADA and the EASD.[26,27] The 2022 ADA/EASD consensus report is identical to the 2019 ESC guidelines except for its use of a lower eGFR limit (20 vs. 30 mL/min/1.73 m^2) in the recommendation of SGLT2 inhibitor use and its slightly different definitions of some cardiovascular risk factors.[8,27] The 2022 ADA guidelines differ vs. the 2019 ESC guidelines mainly with respect to the lack of isolated albuminuria as an indication for SGLT2 inhibitors and slight differences in the definition of albuminuria.[8,26] Although our study focused on the European guidelines released in 2019, our analyses of treatment eligibility according to the 2019 ESC guidelines are therefore likely to be largely applicable to both the 2022 ADA/EASD consensus report and the 2022 ADA guidelines.

We found that among patients with any treatment indication for an SGLT2 inhibitor or a GLP-1 receptor agonist, higher HbA1c levels and higher BMI were associated with a higher likelihood of having received an SGLT2 inhibitor or a GLP-1 receptor agonist, indicating that many of the treatment decisions may be based on the need for glucose control and weight management rather than cardiovascular risk or renal function. In accordance with these findings, similar proportions of patients with and without treatment indications received an SGLT2 inhibitor or a GLP-1 receptor agonist. Moreover, partly in line with previous studies,[28–32] those with higher income and education, those born in Scandinavia, and men were more likely to have received an SGLT2 inhibitor or a GLP-1 receptor agonist, indicating that factors associated with lower socioeconomic status and sex could constitute barriers to receiving treatment.

In subgroup analyses by age, we found that the proportions of treatment-eligible patients were larger among those aged ≥65 years (almost 90% according to the 2019 ESC guidelines and around 60% according to the 2019 ADA/EASD consensus report) as compared to those aged <65 years (almost 70% according to the 2019 ESC guidelines and around 30% according to the 2019 ADA/EASD consensus report). Moreover, there was a strong association between higher age and a lower probability of having received treatment with an SGLT2 inhibitor or a GLP-1 receptor agonist. While the proportion of treatment-eligible patients who received the recommended treatment was also low among those aged <65 years (less than half according to both guidelines), these findings indicate that patient frailty or polypharmacy may be potential reasons for physicians' decision against treatment. The large proportion of treatment-eligible patients who did not receive the recommended treatment may be due to a combination of clinical inertia, limited uptake of guidelines as well as patient and physician preferences. Future studies need to provide health economic assessments that balance patient benefits and cost savings from improved cardiovascular and renal outcomes against the increased costs associated with following the guideline recommendations. In addition, a comparison of the cost-effectiveness of ADA/EASD vs. ESC guidelines would be needed, with a specific focus on the expanded eligibility criterion of high cardiovascular risk used by the ESC guidelines (and the 2022 EASD and ADA guidelines) to recommend the use of SGLT2 inhibitors and GLP-1 receptor agonists.

This study was not without limitations. First, we could not account for treatment indications based on coronary, carotid, or lower extremity artery stenosis of >50% (2019 ADA/EASD consensus report) and left ventricular hypertrophy (both sets of guidelines) and may therefore have underestimated the proportion of patients who were recommended treatment according to both sets of guidelines. Second, we could not distinguish between heart failure with reduced ejection fraction, which constitutes the treatment indication for SGLT2 inhibitors according to the evaluated guidelines, and heart failure with preserved ejection. Although SGLT2 inhibitors are also recommended (class II, level A) to patients with heart failure with preserved ejection fraction according to the US guidelines[33] for the management of heart failure, we may have overestimated the proportion of patients who were eligible for SGLT2 inhibitors according to the 2019 ESC guidelines and ADA/EASD consensus report. Lastly, although diagnoses registered in the Swedish Patient Register have high sensitivity and positive predictive value,[14] our findings might be affected by misclassification of diagnostic codes and variables used for defining treatment indications.

Conclusions

In this nationwide study, the proportion of patients with type 2 diabetes who were recommended treatment with an SGLT2 inhibitor or a GLP-1 receptor agonist was approximately 80% according to the 2019 ESC guidelines and around half according to the 2019 ADA/EASD consensus report. The uptake of these recommendations in routine clinical practice was limited.

Author contributions

C.E.L. and P.U. had full access to all the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis.

Concept and design: C.E.L., B.P., G.D., and P.U.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: C.E.L., B.P., and P.U.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: C.E.L.

Obtained funding: B.P. and P.U.

Study supervision: B.P., G.D., and P.U.

Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology*.

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Conflict of interest: *All authors have completed the Unified Competing Interest form at* www.icmje.org/coi_disclosure.pdf *(available on request from the corresponding author) and have the following declarations.* BE reports personal fees from Amgen, AstraZeneca, Boerhringer Ingelheim, Eli Lilly,

Merck Sharp & Dohme, Mundipharma, Navamedic, Novo Nordisk, and RLS Global outside the submitted work, and grants from Sanofi outside the submitted work.

Data availability

No additional data are available.

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