Diabetes Ther (2022) 13:1499–1510
https://doi.org/10.1007/s13300-022-01289-x

ORIGINAL RESEARCH

An Early Assessment of the Real-World Treatment Patterns of Type 2 Diabetes: A Comparison to the 2018 ADA/EASD Consensus Report Recommendations

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Received: April 25, 2022 / Accepted: June 9, 2022 / Published online: June 29, 2022

ABSTRACT

Introduction: Using the American Diabetes Association (ADA) Hyperglycemic Pharmacotherapy Guidelines for type 2 diabetes, we evaluated the medication use patterns in real-world patients with type 2 diabetes in the USA.
Methods: Health care claims among patients with type 2 diabetes were analyzed (IBM® MarketScan® 2007 to 2019 Commercial and Medicare Databases). Diabetes treatment patterns were evaluated for the total patient sample of 580,741 during the year 2019. Prior years' claims data were used to construct patient history and determine clinical groups per the 2018 ADA/EASD consensus statement: atherosclerotic cardiovascular disease (ASCVD), chronic kidney disease (CKD), heart failure (HF), hypoglycemia (hypo), and obesity. The recommended therapy use rates (RTUR) were calculated for clinical groups. Univariate chi-square tests were performed to compare RTUR within and outside clinical groups. Multivariate logistic regression was used to identify variables associated with recommended therapy use.
Results: A large proportion of patients belonged to multiple clinical groups; this was more common in the Medicare cohort. Each clinical group in the Commercial cohort had a substantially higher RTUR than in the Medicare cohort. However, no clinical group achieved > 40% RTUR. The RTUR was the highest in the CKD and obesity groups in the Commercial cohort and in the hypo and obesity groups in the Medicare cohort, but lowest in hypo and HF groups in the Commercial and Medicare cohorts, respectively.
Conclusion: Prevalence of guideline-aligned treatment use in 2019 was low, particularly since many patients fit into multiple risk groups with established treatment benefits.

Keywords: Glucose-lowering agents; Medication use; Treatment guidelines; Type 2 diabetes

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s13300-022-01289-x.

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Key Summary Points

Why carry out this study?

Recent trials demonstrated significant benefits of glucagon-like peptide-1 receptor agonist (GLP-1 RA) and sodium-glucose co-transporter 2 inhibitor (SGLT-2i) drug classes in type 2 diabetes patients with specific clinical characteristics

The type 2 diabetes treatment guidelines have been updated by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) recommending new preferred agents for different clinical groups

An early evaluation of adherence to the guidelines recommendations is informative regarding uptake of guideline-driven therapy

What was learned from the study?

This retrospective study using claims data reveals that recommended therapies, such as SGLT-2is and GLP-1RAs, evaluated in the first year after guideline publication, are underutilized in most of the targeted clinical groups and are only partially aligned with current treatment recommendations

This study identified factors that influence adherence to the guidelines, which can help inform where to target efforts to improve guideline adherence

Since many patients fit into multiple risk groups with established treatment benefits, improving adherence would represent significant opportunities to make meaningful improvement in the care for patients with type 2 diabetes

INTRODUCTION

Recent studies of drugs in the glucagon-like peptide-1 receptor agonist (GLP-1 RA) and sodium-glucose co-transporter 2 inhibitor (SGLT-2i) classes provided evidence of glycemic efficacy and safety, along with strong evidence of benefits for cardiovascular outcomes and improved outcomes in patients with heart failure (HF) or renal disease [1, 2]. Key SGLT-2i cardiovascular outcomes trials (CVOTs) showed that treatment with this drug class reduced major adverse cardiovascular events (MACE) by up to 20% and reduced the incidence of hospitalization for HF by up to 39% [3–5]. Key GLP-1 RA CVOTs showed that treatment with this drug class reduced MACE by up to 26% [6–9]. Significant benefits of these drug classes on renal outcomes, obesity, and minimizing hypoglycemia were also observed in numerous clinical trials [1].

These studies prompted changes in the type 2 diabetes treatment guidelines from major diabetes associations, such as The American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Together, these organizations released a consensus report in December 2018, which identified targeted clinical groups of interest where GLP-1 RA and SLGT-2i were the preferred agents for treatment [10, 11]. These clinical groups included patients with high risk or history of atherosclerotic cardiovascular disease (ASCVD), chronic kidney disease (CKD), history of HF, a need to minimize hypoglycemia, and/or a need to minimize weight gain or to promote weight loss. These recommendations were later adopted by the official guidelines.

Evaluating RTUR in the year of publication of the guideline allows an assessment of the cumulative adoption in prior years and provides a baseline for future evaluations of guideline alignment. The guideline is based on accumulating data that may have driven adoption prior to the actual publication. The current data likely reflect primarily this early adoption rather

than guideline-driven changes in the pattern of treatment. Knowledge about the degree of guideline alignment can motivate efforts to improve it. Furthermore, evaluating factors associated with treatment choices can help guide interventions to improve guideline alignment. Therefore, we set out to provide a description of the use rates and the factors associated with utilization (or not) of guideline-aligned therapy in real-world data derived from Commercial- and Medicare-supported practices.

Based on these recommendations, we retrospectively investigated the medication use patterns in real-world patients with type 2 diabetes in the US. Data were drawn from a large health insurance claims database, evaluating medication utilization patterns and alignment with these clinical groupings.

METHODS

This was a retrospective observational study of patients with type 2 diabetes in a large health insurance claims database (IBM® MarketScan®, including Commercial and Medicare Supplemental Databases). The objectives of this study were to provide an early post-guideline update of patterns of medication use among patients with type 2 diabetes using the latest healthcare claims data available from 2019 and to examine how different classes of diabetes treatments are used in clinical groups defined in the ADA Pharmacotherapy Prescribing Guidelines [2].

The database provided information on patient enrollment, demographic characteristics, inpatient and outpatient services, and prescription drug use over time. The Commercial cohort contained data from 475,613 patients and the Medicare cohort contained data from 105,128 patients with type 2 diabetes. Inclusion criteria for this study were patients identified as having type 2 diabetes by two separate diagnoses during the study period, were at least 18 years of age in midyear 2019, and filled diabetes prescription claims in 2019. All patients were required to have continuous enrollment for medical and pharmacy coverage during the immediate year before (2018) and the year (2019) of prescribing pattern analysis.

This study utilized the full calendar year 2019 data to evaluate treatment utilization patterns. Prior data from 2007 to 2018 were used to establish disease history and comorbidities of each patient. Laboratory data, such as hemoglobin A1c (HbA1c), estimated glomerular filtration rate (eGFR), and lipid levels, were incorporated for a small proportion of patients based on availability.

All database records used in the study are de-identified and fully compliant with the US Health Insurance Portability and Accountability Act (HIPAA) of 1996. This study was exempted from Institutional Review Board approval as it did not involve collection, use, or transmittal of individually identifiable data. Eli Lilly has the User License with the owner of the data for a fee. This is an enterprise-wide license, which gives Lilly the right to access and analyze data while the license is in effect.

Five clinical groups based on the ADA/EASD consensus statement were identified and defined using the following criteria. Corresponding recommended therapies in the consensus statement are noted in parentheses:

1. High risk or history of ASCVD, identified by the presence of current or past diagnostic codes for ASCVD. (GLP-1 RA or SGLT-2i) Supplementary Table 1 in the supplementary material lists all of the codes used for ASCVD.
2. CKD, identified by CKD diagnosis codes or by abnormal eGFR test results (SGLT-2i or GLP-1 RA).
3. History of HF, through HF diagnosis from 2007 to 2018 (SGLT-2i or GLP-1 RA).
4. Need to minimize hypoglycemia was identified through history of hospitalizations or emergency department visits for hypoglycemia as primary diagnosis (DPP-4, GLP-1RA, SGLT-2i or TZD).
5. Obesity, through diagnosis coding (GLP-1 RA or SGLT-2i).

Data from the Commercial and Medicare insurance cohorts were analyzed separately.

Univariate chi-square tests were performed to compare 2019 recommended therapy utilization rates (RTUR) as recommended by the guidelines within and outside a given clinical

Table 1 Patient baseline characteristics and demographics

Demographics	Commercial cohort (*N* = 475,613)	Medicare cohort (*N* = 105,128)
Age (mean [SD]), years	53.6 (8.0)	74.2 (7.0)
Sex (*n* [%])		
Female	207,986 (43.7)	49,449 (47.0)
Male	267,627 (56.3)	55,679 (53.0)
Insurance plan type		
Preferred provider organization	250,447 (52.7)	68,017 (64.7)
Consumer-driven health plan	57,296 (12.0)	581 (0.6)
Health maintenance organization	63,299 (13.3)	17,315 (16.5)
High deductible health plan	48,292 (10.2)	708 (0.7)
Comprehensive	11,684 (2.5)	13,622 (13.0)
CCI score (mean [SD])	3.2 (2.4)	5.8 (3.3)

CCI Charlson Comorbidity Index; *N* total number of patients; *n* number of patients in the group; *SD* standard deviation

group. The comparisons with $p < 0.05$ were treated as statistically significant. Multivariate logistic regression was used to further evaluate adoption of the guideline recommendations at the patient level, and only patients with full data (i.e., no missing variables) were included in the modeling. The use of recommended therapy in 2019 was regressed as a logistic regression on a pre-selected set of patient demographics and clinical and treatment history recorded in 2018. Supplementary Table 2 in the supplementary material lists all selected/dropped variables. The odds ratios for the membership in the five clinical groups and for the 20 most important explanatory variables are presented. The importance was assessed via Wald chi-square statistics.

RESULTS

Patient Characteristics

Patient characteristics are shown in Table 1. The mean age of patients was approximately 54 years and 74 years in the Commercial and Medicare cohorts, respectively. Sex was generally well distributed in both cohorts, with 56% and 53% males in the Commercial and Medicare cohorts, respectively. The Charlson Comorbidity Index (CCI) measures the burden of comorbid diseases [12]. The CCI mean score was 3.2 in the Commercial cohort but was higher in the Medicare cohort, with a CCI mean score of 5.8, suggesting greater health burdens associated with diabetes and other comorbidities at older age.

Clinical Groups

Patients with type 2 diabetes in the real world often have multiple comorbidities. Table 2 shows distribution of memberships across the clinical groups and how they overlap with other groups. The Medicare cohort has a higher rate of group membership than the Commercial cohort overall and in each clinical group except for obesity.

In the Commercial cohort, obesity was the most prevalent clinical group (59.7% of individuals met criteria), followed by ASCVD (23.3%) and then CKD (15.8%). Fewer patients had a history of HF and severe hypoglycemia, comprising 5.2% and 0.6% of Commercial patients, respectively.

In the Medicare cohort, ASCVD was the most prevalent clinical group (60.9%) and was followed closely by the obesity clinical group (55.5%). Patients with CKD in the Medicare cohort were also highly prevalent as they accounted for nearly 40% of patients. As in patients in the Commercial cohort, fewer patients in the Medicare cohort had a history of HF and severe hypoglycemia history, although the prevalence was higher in the latter (19.8% and 2.0% of Medicare patients, respectively).

Table 2 Proportion of patients belonging in each clinical group with overlaps

(%)	Commercial					Medicare				
	ASCVD	HF	CKD	Hypo	Obesity	ASCVD	HF	CKD	Hypo	Obesity
Overall membership	23.3	5.2	15.8	0.6	59.7	60.9	19.8	39.6	2	55.5
Clinical subgroups										
ASCVD	100	22.4	25.2	1.2	68.5	100	32.5	46.6	2.7	60.6
No ASCVD	0	0	13	0.4	57	0	0	28.7	0.9	47.5
HF	100	100	38.7	1.9	75.4	100	100	61.1	4.5	67.6
No HF	19	0	14.5	0.5	58.8	51.2	0	34.3	1.4	52.5
CKD	37.1	12.7	100	1.5	66.1	71.6	30.5	100	3.4	61.7
No CKD	20.7	3.8	0	0.4	58.5	53.8	12.7	0	1.1	51.4
Hypo	47.6	16.7	39.2	100	66.7	82.7	44.5	67.4	100	64
No hypo	23.1	5.1	15.7	0	59.7	60.4	19.3	39.1	0	55.3
Obesity	26.7	6.6	17.5	0.7	100	66.5	24.1	44.1	2.3	100
No obesity	18.2	3.2	13.3	0.5	0	53.9	14.4	34.1	1.6	0

ASCVD atherosclerotic cardiovascular disease; *CKD* chronic kidney disease; *HF* heart failure; *Hypo* hypoglycemia
Data in each cell represent the percentage of overlap between corresponding column and row

Treatment Utilization Rates

Treatment utilization rates by clinical group are shown in Table 3. In both cohorts, metformin was the most commonly used treatment across all clinical groups. Sulfonylurea (SU) was the second most frequently prescribed treatment, except for the hypoglycemia group where bolus insulin was the second most frequently prescribed treatment. In the overall Commercial cohort, SGLT-2i and GLP-1 RA were the third and fourth most commonly used diabetes treatments in 2019 and were very close in terms of overall utilization rates, that is, 21.1% and 20.8%, respectively. In all Commercial cohort clinical groups except ASCVD, the GLP-1 RA use rate was numerically higher than the SGLT-2i use rate. In the overall Medicare cohort, GLP-1 RA and SGLT-2i use rates were measurably lower in the Medicare cohort than in the Commercial cohort, with 11.6% and 10.5%, respectively, and ranked in fifth and sixth place after metformin, SU, dipeptidyl peptidase-4 inhibitor (DPP-4), and basal insulin classes. In the Medicare cohort, GLP-1 RA use was narrowly higher than SGLT-2i use in overall use rate, as well as in the ASCVD, HF, and obesity clinical groups; however, GLP-1 RA had a relatively larger proportion of use in the CKD and hypoglycemia groups.

ASCVD Groups

In the ASCVD groups, the RTUR was approximately 37% in the Commercial cohort and 19% in the Medicare cohort. In the Commercial cohort, the RTUR was higher in patients with ASCVD than in patients without ASCVD ($p < 0.0001$); however, no differences in RTUR were observed between patients with and without ASCVD in the Medicare cohort ($p = 0.28$) (Table 4).

CKD Groups

In the CKD clinical groups, the RTUR was approximately 39% in the Commercial cohort and 19% in the Medicare cohort. In the Commercial cohort, the RTUR was higher in patients with CKD than in patients without CKD

Table 3 Individual treatment utilization rates by clinical groups in 2019

Variables (%)	Overall	ASCVD	Commercial			
			CKD	HF	Hypo	Obesity
Metformin	85.3	80.3	74.1	71.5	60.4	84.5
SU	26.5	27.3	32.0	27.0	25.3	25.7
SGLT-2i	21.1	23.1	22.0	20.3	19.0	21.9
GLP-1 RA	20.8	23.0	26.5	22.8	25.0	24.5
DPP-4	18.0	19.1	20.5	17.7	16.7	17.2
Basal insulin	12.0	14.6	18.0	17.2	21.9	12.4
Bolus insulin	8.5	13.3	17.1	19.1	36.0	9.5
TZD	6.7	6.4	8.4	5.0	7.4	6.7
Pre-mixed insulin	1.4	2.0	2.7	2.7	5.2	1.5
Insulin/GLP-1 RA	0.9	1.0	1.3	1.1	1.4	1.0
Variables (%)	**Overall**	**ASCVD**	**Medicare**			
			CKD	HF	Hypo	Obesity
Metformin	74.5	69.8	60.7	58.2	43.0	72.4
SU	31.8	32.1	35.4	32.7	28.6	31.3
DPP-4	21.5	22.1	23.5	21.6	19.1	20.8
Basal insulin	12.9	14.2	16.5	16.5	22.3	14.4
GLP-1 RA	11.6	11.7	12.6	10.8	11.3	14.6
SGLT-2i	10.5	10.4	8.5	8.1	6.9	11.3
Bolus insulin	10.2	12.3	15.3	17.4	34.2	12.4
TZD	6.8	6.3	7.4	5.1	6.7	7.0
Pre-mixed insulin	2.0	2.4	3.0	3.4	6.5	2.5
Meglitinides	1.9	2.2	2.6	2.6	2.7	1.8

ASCVD atherosclerotic cardiovascular disease; *CKD* chronic kidney disease; *DPP-4* dipeptidyl peptidase-4 inhibitor; *GLP-1 RA* glucagon-like peptide-1 receptor agonist; *HF* heart failure; *Hypo* hypoglycemia; *SGLT-2i* sodium-glucose co-transporter 2 inhibitor; *SU* sulfonylurea; *TZD* thiazolidinedione

($p < 0.0001$). Conversely, patients without CKD had higher RTUR in the Medicare cohort ($p < 0.0001$) (Table 4).

Heart Failure Groups

In the HF clinical groups, the RTUR was approximately 35% in the Commercial cohort and 17% in the Medicare cohort. In the Commercial cohort, the RTUR was higher in patients with HF than in patients without HF ($p = 0.0003$). Conversely, patients without HF had a higher RTUR in the Medicare cohort ($p < 0.0001$) (Table 4).

Obesity Groups

In the obesity clinical groups, the RTUR was approximately 38% in the Commercial cohort and 22% in the Medicare cohort. In the

Table 4 Guideline recommended therapy utilization rates of SGLT-2i and GLP-1 RA by cohort and clinical group in 2019

	Commercial			Medicare		
	In clinical group	Not in clinical group	*p* value	In clinical group	Not in clinical group	*p* value
ASCVD	37.32%	33.34%	< 0.0001	19.03%	19.30%	0.28
CKD	39.22%	33.34%	< 0.0001	18.53%	19.54%	< 0.0001
HF	35.33%	34.21%	0.0003	16.57%	19.77%	< 0.0001
Obesity	37.59%	29.34%	< 0.0001	22.27%	15.23%	< 0.0001
Hypo	34.75%	32.82%	0.03	24.89%	24.87%	0.98
Hypo (receiving SU only)	10.60%	11.75%	0.06	16.37%	17.02%	0.44

ASCVD atherosclerotic cardiovascular disease; *CKD* chronic kidney disease; *GLP-1 RA* glucagon-like peptide-1 receptor agonist; *HF* heart failure; *Hypo* hypoglycemia; *SGLT-2i* sodium-glucose co-transporter 2 inhibitor; *SU* sulfonylurea

Commercial cohort, the RTUR was higher in patients with obesity than in patients without obesity ($p < 0.0001$). Similarly, the RTUR was higher in patients with obesity in the Medicare cohort ($p < 0.0001$) (Table 4).

Hypoglycemia Groups

In the hypoglycemia clinical groups, the RTUR was approximately 35% in the Commercial cohort and 25% in the Medicare cohort. In the Commercial cohort, the RTUR was higher in patients with severe hypoglycemia than patients without severe hypoglycemia ($p = 0.03$); however, in the Medicare cohort, the RTUR was similar in patients with and without severe hypoglycemia ($p = 0.98$) (Table 4). To further assess appropriateness of prescribing in this group, according to the guideline-directed treatments, we have calculated the rate of patients who receive SU as the only diabetes treatment. In the Commercial cohort, 10.6% of patients with severe hypoglycemia were receiving sulfonylurea only, while a significantly higher number of patients (11.8%) without severe hypoglycemia were receiving sulfonylurea only ($p = 0.06$). In the Medicare cohort, a higher number of patients with severe hypoglycemia (16.4%) and without severe hypoglycemia (17.0%) were receiving sulfonylurea only treatment, with no significant differences observed between these groups ($p = 0.44$).

Regression Analysis

The logistic regression analysis examined the likelihood of being on guideline-recommended therapy for the five clinical groups while controlling for patient characteristics (Figs. 1, 2). Supplementary Tables 3 and 4 in the supplementary material list the results for the 5 clinical groups, the most important 20 significant variables sorted by their decreasing importance, and their odds ratios and upper and lower confidence limits.

The results show that having obesity is strongly positively associated with RTUR. The fact that GLP-1 agonists induce weight loss, and that one of the GLP-1 RA products had been indicated for obesity at a higher dose at the time of analysis, may explain this finding. Among the rest of the clinical groups, ASCVD use rates were similar to those of the reference, but surprisingly, HF, CKD, and hypoglycemia groups were less likely to receive the recommended therapy than the reference. The same pattern was evident in both Commercial and Medicare data sets. Among patient characteristics, younger age, weight loss, medication use history, and prior DPP-4 or prior SU use were

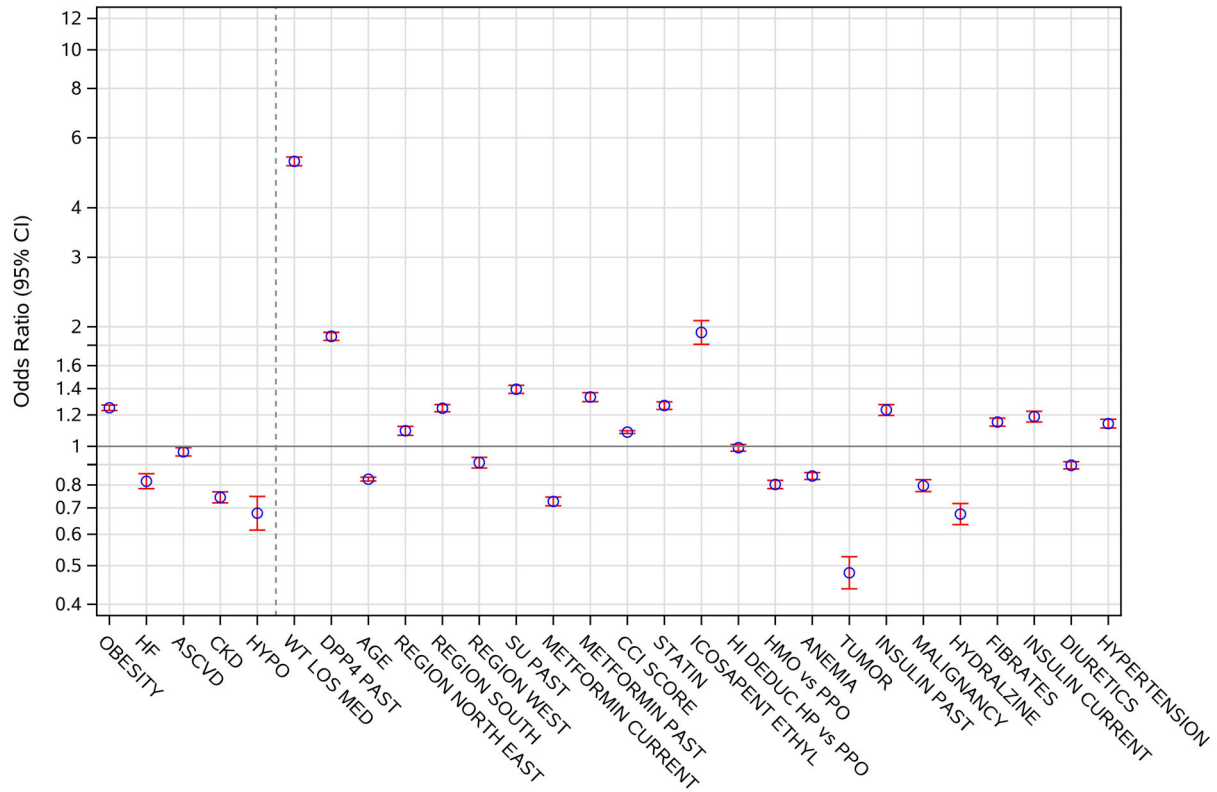

Fig. 1 Use of GLP-1 RA and/or SGLT-2i in 2019: odds ratio and 95% CIs for the Commercial cohort. *ASCVD* atherosclerotic cardiovascular disease; *CCI* Charlson Comorbidity Index; *CKD* chronic kidney disease; *DPP-4* dipeptidyl peptidase-4 inhibitor; *HF* heart failure; *HI DEDUC HP* high deductible health plan; *HMO* health maintenance organization; *Hypo* hypoglycemia; *PPO* preferred provider organization; *SU* sulfonylurea; *TZD* thiazolidinedione; *WT LOS MED* weight loss medications. For AGE, the odds ratio is for 10-year increase. The top 20 most important significant variables (on the right side of vertical dashed line) are sorted by their decreasing importance (Wald chi-square)

positive factors contributing to RTUR. Sex did not emerge as a strong predictor in either cohort.

DISCUSSION

The current study applied data from 2019 and attempted an early evaluation of utilization rates of guideline-recommended treatments for diabetes in relation to recommendations in the 2018 ADA/EASD consensus report on management of hyperglycemia and the subsequent 2019 guidelines update. The results showed that a large proportion of patients with type 2 diabetes in both the Commercial and Medicare cohorts had qualifying conditions for the recommendation, and this was more common in the Medicare cohort. Overall, GLP-1 RA and SLGT-2i were underutilized in several clinical groups.

At the end of the first year following the Management of Hyperglycemia in Type 2 Diabetes Consensus Report (2018), RTURs were < 40% in each clinical group. The Medicare cohort had a measurably lower RTUR in each clinical group (∼ 20%). This difference between cohorts could be due to demographic, clinical, economic, or other factors that are associated with Medicare coverage. For example, as evident in the higher CCI, patients in the Medicare cohort had more chronic comorbidities and therefore were likely require more medications, with the attendant medical and financial

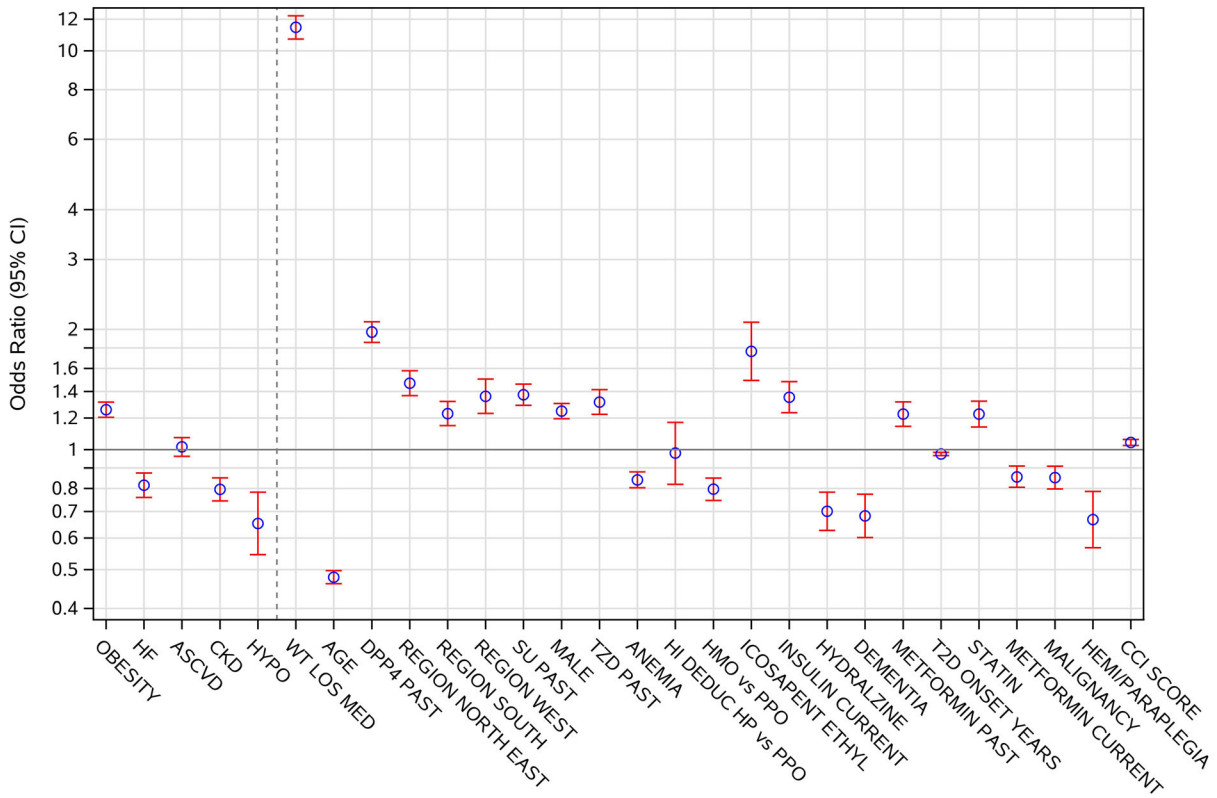

Fig. 2 Use of GLP-1 RA and/or SGLT-2i in 2019: odds ratio and 95% CIs for the Medicare cohort. *ASCVD* atherosclerotic cardiovascular disease; *CCI* Charlson Comorbidity Index; *CKD* chronic kidney disease; *DPP-4* dipeptidyl peptidase-4 inhibitor; *HF* heart failure; *HI DEDUC HP* high deductible health plan; *HMO* health maintenance organization; *Hypo* hypoglycemia; *PPO* preferred provider organization; *SU* sulfonylurea; *T2D* type 2 diabetes; *TZD* thiazolidinedione; *WT LOS MED* weight loss medications. For AGE, the odds ratio is for 10-year increase. The top 20 most important significant variables (on the right side of vertical dashed line) are sorted by their decreasing importance (Wald chi-square)

burdens. Features of Medicare coverage, such as formulary listings and copays for branded drugs like these new medication classes, may have also contributed.

Recent studies examined the clinical characteristics and prescribing preferences for SGLT-2is and GLP-1 RAs in the years prior to the release of the 2018 ADA/EASD consensus statement. Dave et al. [13] concluded that over 5 years between 2013 and 2018 for SGLT-2i, shifts in preference for an SGLT-2i with proven CV benefit did occur following changes in drug labels and guidelines, while for GLP-1 RAs, shifts in preference for GLP-1 RAs with proven CV benefit following changes in drug labels and guidelines were not evident, and other factors, such as price or ease of administration, may have been the cause. Ganz et al. [14] reported that despite recent increases, use of GLP-1 RA and SGLT-2i among patients with type 2 diabetes and CVD in the Optum claims database remained similar and low across 2014 to 2018.

Surprisingly, SGLT-2i utilization rate in the HF patient group was below the overall cohort average in 2019. There were several CV outcomes studies demonstrating clear benefits in HF for a period of time [3–5]; however, definitive trials with HF improvement as the primary endpoint have only recently been published [15, 16]. This may suggest delayed utilization pending availability of fully supportive data. Other considerations may include

comorbidities, polypharmacy, or renal dysfunction complicating medication decision making. The current available data provide stronger support for preferential utilization of SGLT-2i in HF, as reflected in the guideline. Our observed RTUR and differences in utilization between Medicare and Commercial cohorts represent an opportunity for meaningful improvement in care.

In patients with a history of severe hypoglycemia (prior hospitalization or emergency room visit for hypoglycemia), no preferential utilization of GLP-1 RA and SLGT-2i was evident in the Medicare cohort; however, there was a small preference for these drug classes in patients with a history of severe hypoglycemia in the Commercial cohort, and the utilization of SU only was comparable to that without severe hypoglycemic event history in both cohorts. The utilization rate of SU was also higher in the Medicare cohort than in the Commercial cohort, where both increased age and the declining renal status of this cohort point to greater risk of SU-related hypoglycemia events [17], magnifying the risk associated with prior hypoglycemic events. In patients with a compelling need to minimize hypoglycemia, with or without ASCVD, CKD or HF, secretagogues (e.g., SUs) are the least preferred therapy [2]. Our data highlight the persisting use of SU among patients with a history of severe hypoglycemia as an opportunity for meaningful improvement in care.

Interestingly, the obesity group in both cohorts achieved relatively favorable alignments with the guidelines. This may have been influenced by patients' desire for weight management and the physicians' perception of obesity as a risk modifier, which together might increase the likelihood of selecting an SGLT2i or GLP-1RA. The multivariate regression analysis also showed that only the obesity group achieved a higher guideline alignment; all other groups (ASCVD, HF, CKD, and hypo) lagged behind the reference group. The regression further revealed that many individual patient factors, including demographics, past and current type 2 diabetes treatment regimens, and comorbidities contribute to the RTUR in the real world.

There are some limitations to our study. Although studies demonstrating CV and renal benefits had been published in years prior, the recommendation that suggested preferential utilization of SGLT2i and GLP-1RA among specified clinical groups was first published in December 2018. The current evaluation was based on the first 12 months of prescription claims data following the release of the recommendation. Longer term evaluation is needed. The guidelines apply to patients who are not successfully managed by metformin and diet. However, actual and target HbA1c data were not available to determine whether first-line metformin and lifestyle therapy were sufficient, potentially contributing to an incorrect perception of treatment inertia. Although this study attempted to identify patients with specific risks using all available information and well-established algorithms in the database, the clinical groups may fail to accurately include all eligible patients. For example, patients with obesity or mild CKD may not have been diagnosed. It is also possible that the current prescriber may not be aware of relevant clinical history (e.g., prior hypo). Some covariates, such as race/ethnicity and socioeconomic status of the patients, were not available. This study was based on large samples of a relatively well-insured population (Commercial insurance and Medicare with supplemental insurance). Thus, patients may have fewer access problems. The results may not be extended to other special populations, such as the uninsured or those on Medicaid.

CONCLUSION

In conclusion, prevalence of guideline-aligned treatment use in 2019 was low, particularly since many patients fit into multiple risk groups with established treatment benefits. This research in the real world reveals that SGLT-2is and GLP-1RAs are underutilized and are only partially aligned with current treatment recommendations. Lower RTUR and larger alignment gaps were seen in the Medicare population. Utilization of recommended therapies are lagging in some clinical and

demographic groups, and they represent potential opportunities to make meaningful improvement in the care for patients with type 2 diabetes. Continued monitoring and evaluations of real-world use data will help inform and improve implementation of guideline-based treatment in actual prescribing practice and perhaps identify where further consensus is needed to enhance effectiveness in diabetes care.

ACKNOWLEDGEMENTS

Funding. Sponsorship for this study and the journal's Rapid Service Fee were funded by Eli Lilly and Company.

Medical Writing and Editorial Assistance. The authors thank Ciara O' Neill, PhD, Eli Lilly and Company, for writing and editorial support. The authors would also like to thank Era Seth, Eli Lilly and Company, for editorial assistance.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Author Contributions. Jay P. Bae, Chanadda Chinthammit, Kristina S. Boye, and Kieren J. Mather contributed to the design and conception of the study. Dongju Liu participated in the acquisition of the data. Jay P. Bae, Zbigniew A. Kadziola, Dongju Liu, Chanadda Chinthammit, Kristina S. Boye, and Kieren J. Mather contributed to the analysis and interpretation of the data. All authors participated in writing and revising the manuscript.

Disclosures. Jay Bae, Zbigniew Kadziola, Dongju Liu, Chanadda Chinthammit, Kristina Boye, and Kieren Mather are full-time employees and/or stockholders of Eli Lilly and Company. A portion of these findings was presented at ADA 2021 (Bae JP, Liu D, Chinthammit C, Kadziola ZA, Boye K, Mather KJ. 685-P: Medication Use Pattern in Type 2 Diabetes Patients: Commercial and Medicare Data. ADA 2021). Jay Bae is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Prior Presentation. A part of this study was previously presented as a poster at the American Diabetes Association Virtual Meeting, from June 25–29, 2021.

Compliance with Ethics Guidelines. All database records used in the study are de-identified and fully compliant with the US Health Insurance Portability and Accountability Act (HIPAA) of 1996. This study was exempted from Institutional Review Board approval as it did not involve collection, use, or transmittal of individually identifiable data. Eli Lilly has the User License with the owner of the data for a fee. This is an enterprise-wide license, which gives Lilly the right to access and analyze data while the license is in effect.

Data Availability. The datasets generated during and/or analyzed during the current study are not publicly available due to the proprietary nature of the source data, which was procured under a user license agreement with fee.

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