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BRIEF REPORT

Type 2 diabetes pharmacotherapy trends in high-risk subgroups

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Abstract

Medication use trends among patients with type 2 diabetes from 2015 to 2019 were investigated in relation to the clinical group-specific recommendations from the 2018 American Diabetes Association (ADA)/European Association for the Study of Diabetes (EASD) consensus report. Data were drawn from a large health insurance claims database representing Commercial (total patient-year count: 2,379,704) and Medicare (total patient-year count: 845,823) insurance programmes (IBM® MarketScan®). The utilization of sodium-glucose co-transporter-2 inhibitors or glucagon-like peptide-1 receptor agonists increased over time but was lower in the Medicare cohort in every year evaluated. Patients diagnosed with obesity received recommended therapies at higher rates than those without obesity. Differences were more modest between those with versus without atherosclerotic cardiovascular disease (ASCVD) or chronic kidney disease, with greater treatment adoption in those without ASCVD in the Medicare cohort. Utilization of recommended treatments was paradoxically lower in those with versus without heart failure, and worse in the Medicare than in the Commercial cohort. Utilization of sulphonylureas was not different in those with versus without severe hypoglycaemia history. In conclusion, utilization of therapies recommended in the guidelines is increasing overall, which is not preferentially guided by ADA/EASD-defined clinical groups, and there exists a persistent gap in utilization between Commercial and Medicare populations.

KEYWORDS
observational study, type 2 diabetes

1 | INTRODUCTION

During their preapproval development and testing, studies of drugs in the sodium-glucose co-transporter-2 inhibitor (SGLT2i) and glucagon-like peptide-1 receptor agonist (GLP-1 RA) classes provided evidence of glycaemic efficacy and safety,[1] followed by robust evidence of benefits for cardiovascular outcomes and improved outcomes in patients with heart failure (HF) or renal disease.[2] These data prompted changes in the type 2 diabetes (T2D) treatment guidelines from major diabetes associations worldwide. For example, the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) released a consensus report in 2018,[3] subsequently

adopted in the official guidelines,[4] which identified targeted groups of interest where SGLT2is and GLP-1 RAs were preferred agents and where sulphonylureas (SUs) were no longer preferred. These groups included patients with a history of atherosclerotic cardiovascular disease (ASCVD), chronic kidney disease (CKD), a history of HF, a need to minimize hypoglycaemia, and/or a need to minimize weight gain or to promote weight loss. Recommendations for hypoglycaemia considerations also include dipeptidyl peptidase-4 inhibitors and thiazolidinediones. Based on these recommendations, the medication utilization was retrospectively investigated in the real world among patients with T2D. Data were drawn from a large health insurance claims database evaluating medication utilization patterns and alignment with these clinical groupings.

2 | METHODS

This was a retrospective observational study of patients with T2D in a large health insurance claims database (IBM® MarketScan®, including Commercial and Medicare supplemental databases). All patients were aged at least 18 years, had a minimum of one diagnosis of T2D, were using diabetes treatment, with continuous enrolment for the year of inclusion and a minimum of 1-year follow-up. In cases where patients had both T1D and T2D diagnoses, those who had more T1D than T2D diagnoses were excluded. The database provided information on patient enrolment, demographic characteristics, inpatient and outpatient services, and prescription drug use.

Five clinical groups based on the ADA/EASD consensus statement were identified and defined using the following criteria:

1. History of ASCVD identified by the presence of current or past diagnostic codes for ASCVD;
2. CKD identified by CKD diagnosis codes or by estimated glomerular filtration rate test results;
3. History of HF through HF diagnosis coding;
4. A need to minimize hypoglycaemia, identified through a history of hypoglycaemia-related hospitalization or emergency department visits in prior years; and
5. Obesity through diagnosis coding.

The data period used for evaluating treatment utilization was from January 2015 to December 2019 (each calendar year was evaluated individually). Data from 2007 until the year preceding evaluation were used to establish disease history and co-morbidities. Data from the Commercial and Medicare cohorts were handled separately to assess utilizations in both employment-based private insurance for the working-age population (Commercial cohort) and the government-sponsored plus private retiree supplemental insurance (Medicare cohort). Univariate chi-square tests were performed to assess the statistical significance of comparisons between the proportion of patients utilizing specific therapies with and without a given clinical diagnosis. To test overall trends within clinical groups and the difference in trends between the groups, linear probability regression models (using generalized estimating equations) were executed with clinical group, calendar year, and interaction between them as independent variables.

3 | RESULTS

3.1 | Patient characteristics

The mean age of patients was approximately 54 and 74 years in the Commercial and Medicare cohorts, respectively (Table S1). Sex was generally evenly distributed in both cohorts, with 52%-56% male. The Charlson–Quan co-morbidity index (CCI)[5] score (mean) ranged from 2.8 to 3.2 in the Commercial cohort but it was higher in the Medicare cohort with a range of 5.2-5.8 (Table S1).

3.2 | Clinical groups

Obesity and ASCVD were the most prevalent clinical groups, with all clinical groups except obesity present at greater frequencies in the Medicare cohort (Table S2). There was significant overlap among the clinical groups, such that individuals were more probable to belong to more than one clinical group (Table S2).

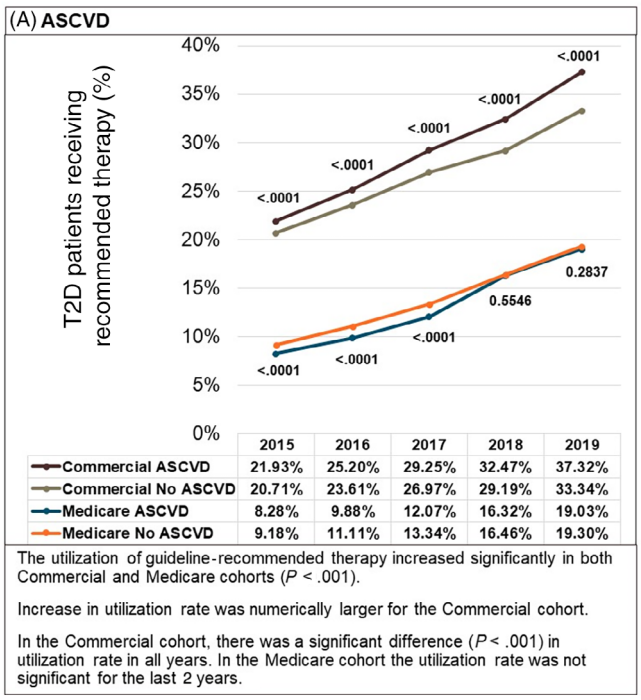
3.3 | Trends in recommended therapy

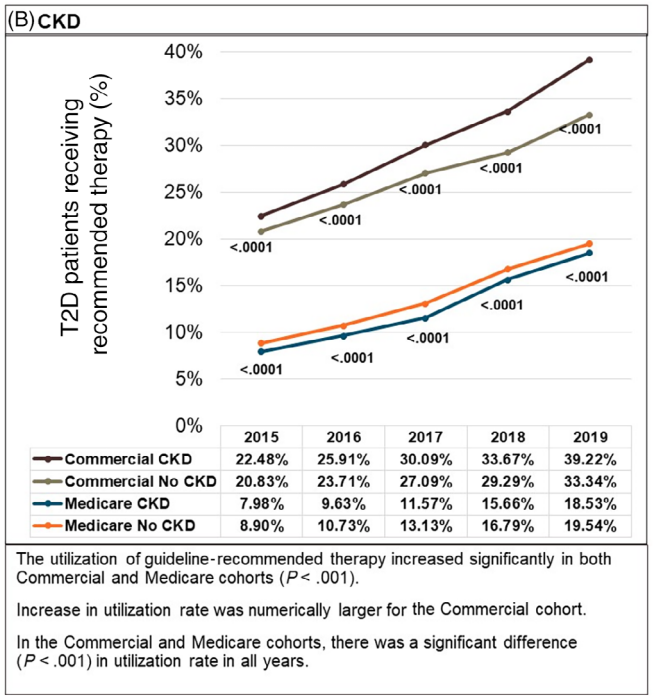
Overall, the trend in utilization of guideline-recommended therapy showed a significant increase ($P < .001$) in all clinical groups (ASCVD, CKD, HF, and obesity) over the years. In each of these clinical groups, a larger numerical increase in the utilization of recommended therapy was observed in the Commercial cohort than in the Medicare cohort over time (Figure 1A–D).

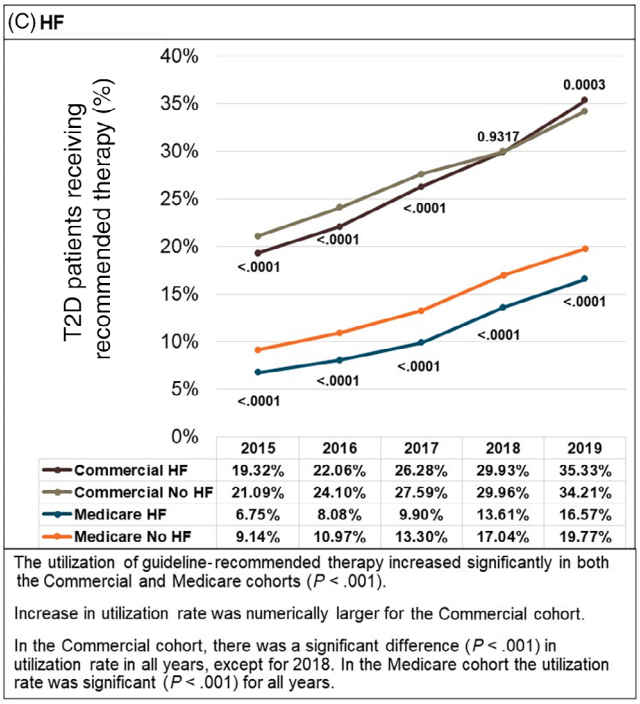
The hypoglycaemia group results also show a similar pattern for the Commercial and Medicare cohorts (Figure 2A,B). The rate of SU monotherapy treatment showed a significant decrease ($P < .001$) in both cohorts; however, there was no statistical difference of use rates between those with and without a risk of hypoglycaemia, except for 2016 in the Medicare cohort ($P = .04$) (Figure 2A,B).

3.3.1 | ASCVD groups

In the ASCVD clinical groups, the utilization of guideline-recommended therapy increased in both cohorts over time (Figure 1A). In the Commercial cohort, the utilization of SGLT2is or GLP-1 RAs among those with ASCVD reached 37.3% in 2019. The group without ASCVD also showed an increase in utilization of these medication classes over time. In the Medicare cohort, the utilization rates were lower overall. The magnitude of difference between those with and without ASCVD was smaller than the Commercial cohort and was no longer statistically different in 2018 and 2019 (Figure 1A).







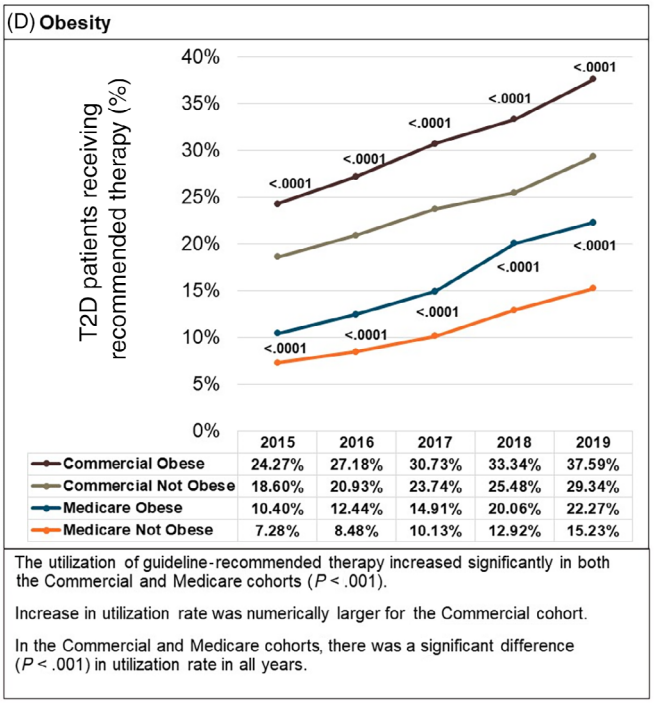


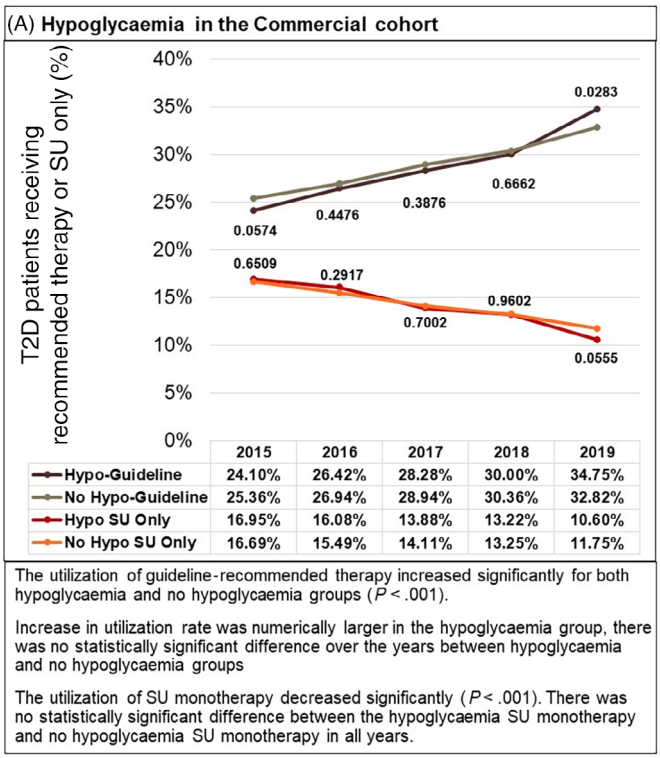
FIGURE 1 Trends in patients receiving guideline-recommended therapy by clinical group. A, ASCVD; B, CKD; C, HF; D, Obesity. ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; HF, heart failure; T2D, type 2 diabetes

3.3.2 | CKD groups

In the CKD clinical groups, the utilization rate of guideline-recommended therapy showed a similar increasing trend in both cohorts (Figure 1B), with greater utilization in those with CKD versus without CKD. The utilization rate of SGLT2is and GLP-1 RAs also increased in those without CKD. In the Medicare cohort, the utilization rates were lower overall but similar patterns were observed, with numerically small but significant differences between those with CKD versus without CKD (Figure 1B).

3.3.3 | HF groups

In the HF clinical groups, the utilization rates of the guideline-recommended therapies increased over time in both cohorts



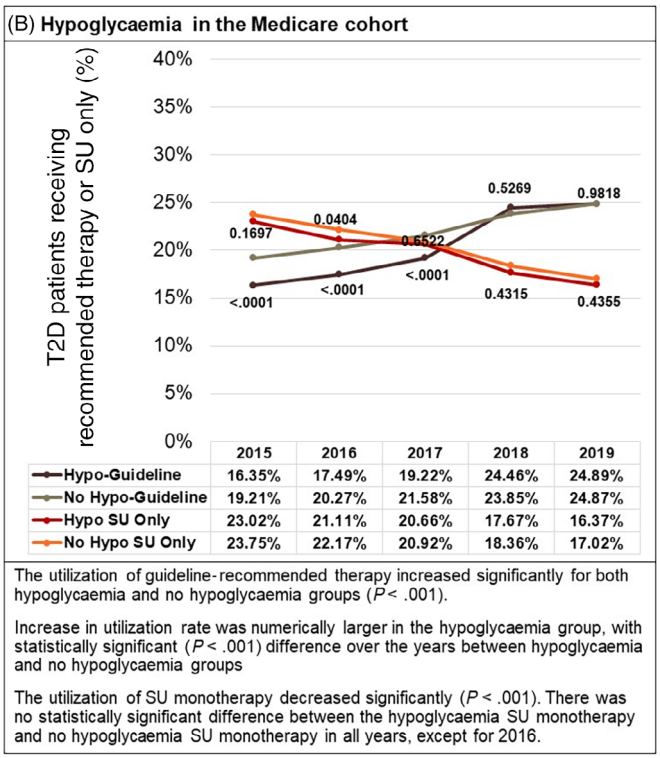


FIGURE 2 Hypoglycaemia risk and treatment: patients receiving guideline-recommended therapy or an SU only per cohort. A, Commercial cohort; B, Medicare cohort. Hypo, hypoglycaemia; SU, sulphonylurea; T2D, type 2 diabetes

(Figure 1C). However, in both cohorts, the utilization rate of SGLT2is or GLP-1 RAs was paradoxically lower in those with HF versus without HF observed from 2015 to 2017 in the Commercial cohort and for all the years evaluated in the Medicare cohort (Figure 1C). The overall utilization of SGLT2is or GLP-1 RAs was lower in the Medicare cohort.

3.3.4 | Obesity groups

For the obesity clinical groups, both cohorts had an overall notable increase in utilization of guideline-recommended therapies (Figure 1D). Large numerical differences were seen in utilization rates between those with and without obesity in both cohorts, favouring those with obesity. In the Medicare cohort, the overall utilization rates were lower. In both cohorts, the utilization of SGLT2is or GLP-1 RAs increased over time in those without a diagnosis of obesity (Figure 1D).

3.3.5 | Hypoglycaemia groups

In the Commercial cohort, the utilization rate of guideline-recommended therapy among patients with a hypoglycaemia history increased from 2015 to 2019 (Figure 2A). However, similar utilization rates, and utilization trends, were also observed in those without a hypoglycaemia history. In the Medicare cohort, hypoglycaemia was paradoxically associated with a lower utilization of recommended therapies in patients with a hypoglycaemia history from 2015 to 2017 (Figure 2B). We further investigated what proportion of patients used an SU as the only diabetes treatment in the hypoglycaemia group and compared this with patients without a hypoglycaemia history. Although SU use decreased over time in both cohorts, still approximately one in 10 in the Commercial cohort and one in six in the Medicare cohort continued to receive SUs as the only diabetes treatment, which was not different from the control group (Figure 2A,B).

4 | DISCUSSION

Increasing the adoption of newer medications for the treatment of T2D, particularly SGLT2i and GLP-1 RA class agents, has been described.[6,7] The current report applied historical data to extract diagnostic group information, allowing evaluation of utilization rates in relation to ADA/EASD-defined clinical groups. As previously reported, increasing utilization of agents was observed in these classes, particularly for those with underlying diagnoses of obesity, ASCVD, and CKD. However, these salutary trends in utilization rates were also seen in those without diagnoses, perhaps diluting the notion that treatment choices were based upon these diagnostic groups. Further, the utilization rates of SGLT2is or GLP-1 RAs were paradoxically lower among those with HF compared with those without HF in both cohorts, with some reversal in 2018 and 2019 in the Commercial cohort. Among those with a history of hospitalization or emergency

room visits for hypoglycaemia, no preferential utilization of these agents was evident, and the utilization of SUs persisted without difference according to this diagnosis.

For all the years evaluated, the utilization of SGLT2is or GLP-1 RAs was lower in the Medicare cohort than in the Commercial cohort across all the clinical groups, and the utilization of SUs was conversely higher in the Medicare cohort, although the Medicare cohort shared the favourable overall time trends seen in the Commercial cohort. This difference between cohorts could be because of demographic, clinical, economic, or other factors that are associated with Medicare coverage. For example, as was evident in the higher CCI, patients in the Medicare cohort had more chronic co-morbidities and therefore were more probable to require more medications. Features of Medicare coverage such as formulary listings and co-pays for branded drugs like these new medication classes may also have contributed.[8-10]

The observation of paradoxically lower utilization of SGLT2is or GLP-1 RAs among those with HF is notable. The fact that this occurred in both cohorts suggests different causes are at work other than the factors of lower utilization rates among those with Medicare coverage. The studies showing clear benefits in HF included the earliest of the guideline-changing cardiovascular outcomes trials,[11,12] although definitive trials with HF improvement as the primary endpoint have only recently been published.[13,14] This may suggest delayed utilization, pending availability of fully supportive data. Other considerations could include co-morbidities, polypharmacy, or renal dysfunction that complicate medication decision-making. The available data provide convincing support for preferential utilization of SGLT2is or GLP-1 RAs in HF, as reflected in the guidelines, and this represents an opportunity for meaningful improvement in care.

Another important observation was the persistent utilization of SU class medications among patients with a significant hypoglycaemia history. The utilization rate of SUs was higher in the Medicare cohort, where both the increased age and declining renal status of this cohort indicated a greater risk of SU-related hypoglycaemia events, magnifying the risk associated with prior hypoglycaemic events.[15] The EASD/ADA consensus report recommends an SU as the last choice of drug in patients with or without established ASCVD or CKD and/or HF. Furthermore, in patients without ASCVD or CKD with a compelling need to minimize hypoglycaemia, secretagogues (e.g. SUs) are recommended as the last-choice therapy.[3] However, our analysis revealed that this guideline is not followed, and still too many patients with a risk of hypoglycaemia are solely treated with an SU. This represents another opportunity for meaningful improvement in care.

In conclusion, we note that with the emergence of newer treatment options for T2D and evidence of their clinical benefits, real-world data reveal that the utilization of SGLT2is and GLP-1 RAs is increasing and is partially aligned with current treatment recommendations.[16] A persistent gap between Commercial and Medicare populations exists, with lower utilization rates in the Medicare population. The utilization of recommended therapies by some ADA/EASD-defined clinical groups is lagging, particularly those with HF or a history of hypoglycaemia, representing opportunities to make meaningful improvements in the care for patients with diabetes. This study found positive trends towards the implementation of the guidelines in real-world T2D prescribing. However, we also observed suboptimal adherence in prescribing for some subgroups of patients, possibly because of prescribing inertia and access challenges. Although we cannot ascertain the effect because of the lack of individual patients' economic data, out of pocket costs, and insurance coverage details, access challenges may be an important driver of the observed trends. Overall, further improvement in guideline adherence and management of diabetes care should be possible through better-targeted prescribing practice.

4.1 | Limitations

Because of the limitations in claims data, HbA1c data were not available to examine the treatment effects on glycaemic control. This study was performed at the drug class-level, and we have not checked for individual drug's limitations of use language to identify ineligible patients for specific drugs. Because some drugs are inappropriate for patients with kidney disease, our reported use rate in the overall T2D population may underestimate the use rate in the appropriate population. We report the proportion of patients with end-stage renal disease in Table S1. The study was based on large samples of US-based insured populations (Commercial and Medicare); hence, the results may not be extended to other populations such as the uninsured or those on Medicaid.

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CONFLICT OF INTEREST

JB, DL, CC, ZK, KB, and KM are employees of Eli Lilly and Company.

AUTHOR CONTRIBUTIONS

Jay Bae contributed towards study design, conduct data analysis, drafting and critical review of the manuscript; Dongju Liu contributed to conduct data analysis and critical review of the manuscript; Zbigniew Kadziola contributed to the study design, data analysis and critical review of the manuscript; Chanadda Chinthammit, Kristina Boye and Kieren Mather contributed to study design and critical review of the manuscript.

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1111/dom.14678.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the present study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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