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Key Messages:

- The uptake of glucagon-like peptide 1 receptor agonists has been low in patients who may benefit the most
- The use of diabetes medications lacking cardiovascular benefits remains higher amongst those populations
- Older age, A1C > 9%, and higher income quintile are associated with a greater odds of receiving glucagon-like peptide 1 receptor agonists

Keywords: type 2 diabetes; obesity; cardiovascular disease; glucagon-like peptide 1 receptor agonist; medication exposure

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MF was a consultant for ProofDx, a start-up company creating a point of care diagnostic test for COVID-19; is an advisor for SIGNAL1, a start-up company deploying machine learned models to improve inpatient care; and is recipient of the PSI Foundation Graham Farquharson Knowledge Translation Fellowship.

Abstract

Introduction: Glucagon-like peptide 1 receptor agonists (GLP-1RA) are effective medications for type 2 diabetes mellitus (T2DM) and obesity, yet their uptake among patients most likely to benefit has been slow.

Methods: We conducted a cross-sectional analysis of medication exposure in adults hospitalized at 16 hospitals in Ontario, Canada between 2015 and 2022. We estimated the proportion with T2DM, obesity, and cardiovascular disease. We identified the frequency of GLP-1RA use, and conducted multivariable logistic regression to identify factors associated with their use.

Results: Across 1,278,863 hospitalizations, 396,084 (31%) had T2DM and approximately 327,844 (26%) had obesity. GLP-1RA use (n=1,274) was low among those with a diagnosis of T2DM (0.3%) or obesity (0.7%), despite high prevalence of cardiovascular disease (36%). In contrast, use of diabetes medications lacking cardiovascular benefits was high during inpatient hospitalizations related to diabetes: 60% (n=236,612) received insulin and 14% (n=54,885) received a sulfonylurea. Apart from T2DM (OR=29.6, 95% CI 23.5, 37.2), characteristics associated with greater odds of receiving GLP-1RA were age 50-70 years (OR=1.71, 95% CI 1.38, 2.11) compared to age < 50 years, hemoglobin A1C > 9% (OR=1.83, 95% CI 1.36, 2.47) compared to < 6.5%, and highest income quintile (OR=1.73, 95% CI 1.45, 2.07) compared to lowest income quintile.

Conclusion: Knowledge translation interventions are needed to address the low adoption of GLP-1RA among hospitalized patients with T2DM and obesity, who are the most likely to benefit.

Introduction

Glucagon-like peptide 1 receptor agonists (GLP-1RA) are effective medications for adults with obesity or type 2 diabetes mellitus (T2DM).[1–4] Multiple randomized controlled trials (RCTs) have shown that GLP-1RA reduce the relative risk of cardiovascular events (i.e., myocardial infarction, stroke, and cardiovascular death) by approximately 15% in adults with T2DM, and by 20% in adults with cardiovascular disease and obesity but without T2DM.[3,5] GLP-1RA lead to reductions in body weight of approximately 5-10% in adults with T2DM and approximately 15% in adults without T2DM who are overweight or living with obesity.[2,6] Semaglutide, the most commonly prescribed GLP1-RA, was recently shown to reduce the risk of end-stage renal disease and cardiovascular disease in adults with T2DM and chronic kidney disease compared to placebo.[7] GLP-1RA lead to a two-fold reduction in heart-failure symptoms in people with heart failure with preserved ejection fraction, for those with either T2DM and obesity, or obesity alone.[8] Clinical guidelines now recommend GLP-1RA as one of the two recommended second-line treatments for adults with T2DM.[9] For adults with obesity and obesity-related co-morbidities, GLP-1RA are the first-line pharmacotherapy treatment.[10]

Despite guidelines consistently recommending their use, uptake of GLP-1RA among patients most likely to benefit from them remains low. This is concerning given the high prevalence of diabetes and obesity in North America.[11,12] Systematic reviews have identified common barriers to prescribing newer medications for chronic disease, including both patient and provider-level barriers.[13,14] Patients may be hesitant because of potential side effects, costs, and route of administration, all of which are directly relevant to GLP-1RA. In Canada, the cost of a one-month supply for adults without medication coverage is approximately $200 USD; in the United States, it can cost up to $1000 USD per month.[15] Ideally, preferential use should be

for patients who are most likely to benefit, rather than those most likely to afford the medications. The available clinical trials demonstrate that the patients most likely to benefit from GLP-1RA are older adults with cardiovascular disease and either T2DM or obesity.[1–3,5,7,8] However, the high out-of-pocket cost of GLP-1RA for adults without insurance has led to their preferential use among individuals with higher socioeconomic status.[16]

Hospitalized adults are one of the highest risk groups for subsequent cardiovascular events, because inpatients have a median age of 73 years, have a median of six underlying chronic medical conditions, and the reason for the hospitalization can directly (e.g., hospitalization for myocardial infarction) or indirectly (e.g., influenza, COVID-19) increase their risk of subsequent cardiovascular events.[17–19] Starting a new medication for a chronic disease in-hospital, including at the time of discharge, leads to better medication adherence compared to deferring the decision to the outpatient setting.[20,21] Medication adherence is especially important for T2DM and obesity because both are chronic diseases requiring long-term treatment. Therefore, the inpatient setting presents a valuable opportunity to start patients on medications such as GLP-1RA. Our primary objective was to determine the frequency of, and factors associated with, GLP-1RA use among hospitalized adults, who represent a high-risk population poised to benefit from GLP-1RA.

Methods

Data Source

We conducted a cross-sectional analysis to determine the frequency of GLP-1RA use across 16 hospitals in Ontario, Canada, using retrospective data from the General Medicine Inpatient Initiative (GEMINI) cohort. GEMINI represents the largest repository of inpatient data in Canada, and data within GEMINI have an accuracy of > 98%.[22] Data within GEMINI are

reported at the hospitalization level, and this approach was retained for the majority of our results. Within GEMINI, patients' medical records are linked to administrative datasets including Canadian Institute for Health Information (CIHI) and Discharge Abstract Database (DAD). GEMINI includes data on discharge diagnosis, patient demographics (e.g., age, sex, place of residence), laboratory results (e.g., HbA1C), imaging reports, vital status at discharge (e.g., death), medications, and other administrative data (e.g., length of stay). GEMINI also includes a proxy for socioeconomic status (SES), determined through postal code, which can be used to assess neighbourhood-level SES through linkage with Canadian census data (i.e., household income levels). Quintile 1 is the lowest income range while quintile 5 is the highest income range.[23] Data not available within GEMINI include physician-level data (e.g., specialty, gender), nursing notes, or daily charting notes.

Study Population

We identified hospitalizations of patients over 18 years of age who were admitted to general internal medicine between 2015 to 2022 (most recent available data). Of these hospitalizations, we identified those in which a GLP-1RA was administered. Within GEMINI, medication data is available in the aggregate and includes continuation of home medications, initiation of new medications in hospital not given at home, and medications prescribed on the day of discharge (i.e., "discharge medications"). We identified hospitalizations with T2DM using International Classification of Diseases, Tenth Revision (ICD-10) diagnosis codes for T2DM in any of the following fields: current or past admission; main responsible diagnosis; pre-admit, secondary, admitting, or transfer diagnosis. The ICD-10 codes for T2DM were recently validated within GEMINI (e.g., PPV and sensitivity > 95%).[24] We identified hospitalizations with obesity using previously validated ICD-10 codes which are specific but not sensitive (specificity > 99%,

sensitivity = 9%).[25] We report the prevalence of medical conditions (e.g. T2DM, obesity, cardiovascular disease) and medication use (e.g. frequency of GLP-1RA administration) during each hospitalization.

Study Objectives

Our primary objective was to identify the frequency of GLP-1RA use in hospital and the factors associated with their use. Given the cardioprotective benefits of GLP-1RA, we also reported the proportion of hospitalizations with T2DM and the following comorbidities using ICD-10 codes which have been previously validated in administrative databases: coronary artery disease (CAD), stroke or transient ischemic attack (TIA), peripheral vascular disease (PVD), heart failure, and renal disease.[9,26–29] We were unable to estimate the number of hospitalizations with obesity and cardiovascular disease because of the low sensitivity of ICD-10 codes for obesity. Our study received Research Ethics Board approval from the participating hospitals.

Sensitivity Analysis

We conducted a sensitivity analysis of GLP-1RA use in the last complete calendar year of our study (i.e., January 1, 2021 - January 1, 2022). This was done to assess the robustness of our study findings, because there may be time-varying factors (e.g., availability of GLP-1RA in hospital) contributing to GLP-1RA use between the 2015-2022 study period which were not accounted for in our primary analysis. The analysis was performed at both the hospitalization-level and the patient-level and included all patients with T2DM who were admitted to the hospital from January 1 2021 to January 1 2022. Among those who did not receive GLP-1RA, we identified the number of times they were hospitalized in the preceding six years and reported the mean count of hospitalizations.

Statistical Analysis

Descriptive statistics were used to compare the characteristics of hospitalizations with a GLP-1RA to those without. We reported the standardized mean difference (SMD) between the two groups. An SMD above 0.10 indicates an imbalance between the two groups for a given characteristic.[30] We identified hospitalizations with T2DM and obesity using ICD-10 codes. Given the low sensitivity of ICD-10 codes for obesity (i.e., 9%), we multiplied the number of hospitalizations with an ICD-10 code for obesity by 100%/9% to estimate the total number of patients with obesity within GEMINI.[25]

To identify factors associated with GLP-1RA use, we built a multivariable logistic regression model. The model included the following variables, which were selected based on content expertise and prior literature: demographics (i.e., age, sex, postal code [as a proxy for SES]), comorbidities (i.e., T2DM, obesity, cardiovascular disease, dementia, hypertension, dyslipidemia, renal disease), and results from inpatient laboratory tests (i.e., HbA1C, creatinine).[7] We also included the number of years since 2015, and each individual hospital (anonymized through identification numbers) as variables in this model.[13] Odds ratio estimates and 95% Wald confidence intervals were reported. All statistical analyses were performed using the R Statistical Software v4.0.5 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Study Population

We identified a total of 1,278,863 hospitalizations between 2015 and 2022. The median age was 70 years (IQR 56.0-82.0), 47% were female, and the three most common discharge diagnoses were heart failure, pneumonia, and chronic obstructive pulmonary disease/asthma

(Table 1). We identified 1274 (0.1%) hospitalizations in which a GLP-1RA was administered or ordered. These hospitalizations consisted of patients who were younger (66 years vs 70 years), more likely to be male (58%), and had a higher prevalence of T2DM (94% vs 31%) or obesity (16% vs 2%) compared to hospitalizations in which a GLP-1RA was not administered or ordered. (Table 1). There was also a higher prevalence of hypertension (56% vs 40%), CAD (37% vs 22%), and dyslipidemia (16% vs 8%) compared to hospitalizations in which a GLP-1RA was not administered or ordered.

Type 2 Diabetes Mellitus

One-third of all hospitalizations (n=396,084) involved patients with T2DM. Of these, 1,191 hospitalizations (0.3%) included administration or ordering of a GLP-1RA. Results for other diabetes medications were as follows: metformin (36%, n=143,914), insulin (60%, n=236,612), sulfonylurea (14%, n=54,885), dipeptidyl peptidase 4 inhibitor (DPP-4i, 26% n=101,890), and sodium-glucose co-transporter-2 inhibitor (SGLT2i, 5%, n=21,304). Among hospitalizations with T2DM, 31% (n=123,708) had CAD, 6% (n=24,003) had stroke or TIA, 3% (n=10,063) had PVD, 17% (n=66,366) had heart failure, and 22% (n=88,494) had renal disease (Table 2).

Obesity

Overall, 2% (n=29,506) of all hospitalizations had an ICD-10 diagnosis code for obesity and a GLP1-RA was administered or ordered for 0.7% of these hospitalizations. Weight data were available for 4% (n=51,154) of patients. The median weight for patients on GLP-1RA was 87 kg (IQR 80-104) and the median weight for patients not on GLP-1RA was 73 kg (IQR 61-88). Because the ICD-10 codes for obesity have a sensitivity of 9%, we estimated that the true

prevalence of obesity was 327,844 (i.e., 29,506 x 100%/9%), corresponding to approximately 26% of all hospitalizations. We did not report comorbidities among patients with obesity because the number of hospitalizations in our data with an ICD-10 code for obesity was low. Our point prevalence study of 35 patients on the general inpatient wards at one hospital identified that 26% (n=9) of patients had a BMI $\geq$ 30 kg/m^2.

Multivariable Logistic Regression Model

In our multivariable logistic regression model, the factor most strongly associated with receiving a GLP-1RA was T2DM (Odds Ratio (OR)=29.6, 95% Confidence Interval (CI) 23.5, 37.2) (Table 3). The following factors were also associated with higher odds of receiving GLP-1RA: obesity (OR=2.4, 95% CI 2.04, 2.83), age 50-70 years (OR=1.71, 95% CI 1.38, 2.11) compared with age less than 50 years, and dyslipidemia (OR=1.28, 95% CI 1.07, 1.54). Those with HbA1c between 6.5-9% (OR=1.67, 95% CI 1.28, 2.18) and HbA1c above 9% (OR=1.83, 95% CI 1.36, 2.47) were more likely to be prescribed GLP-1RA, compared with individuals with HbA1c less than 6.5%. Creatinine levels between 100-200 μmol/L (OR=1.18, 95% CI 1.04, 1.35) were associated with increased odds of receiving GLP-1RA compared to creatinine levels < 100 μmol/L.

GLP-1RA use in hospital was also increasingly likely each year since 2015 (OR=1.6, 95% CI 1.54, 1.67), and patients had a higher odds of receiving GLP-1RA if they were admitted to certain institutions: hospital "B" (OR=3.05, 95% CI 2.45, 3.79), hospital "I" (OR=5.67, 95% CI 4.63, 6.94), hospital "L" (OR=4.91, 95% CI 3.8, 6.35), and hospital "N" (OR=3.76, 95% CI 2.84, 5). Patients belonging to a higher income quintile had higher odds of receiving GLP-1RA compared to patients in the lowest income quintile: quintile 3 (OR=1.24, 95% CI 1.05, 1.47), quintile 4 (OR=1.3, 95% CI 1.1, 1.54), and quintile 5 (OR=1.73, 95% CI 1.45, 2.07). Variables

associated with lower odds of receiving GLP-1RA included older age (i.e., ≥ 91 years of age) (OR=0.24, 95% CI 0.13, 0.44) compared to younger age (i.e., < 50 years), dementia (OR=0.65, 95% CI 0.53, 0.79), renal disease (OR=0.85, 95% CI 0.72, 1), stroke or TIA (OR=0.60, 95% CI 0.45, 0.81), and creatinine greater than 200 μmol/L (OR=0.66, 95% CI 0.54, 0.81) compared to creatinine levels below 100 μmol/L.

Sensitivity Analysis

Between January 1, 2021 to January 1, 2022, there were 38,040 unique patients with T2DM among 54,647 hospitalizations (Table 4). Among these 38,040 patients, use of GLP-1RA was 1% (n=407). In comparison, 62% (n=23,529) of patients received insulin and 13% (n=4,834) received a sulfonylurea. Among the 99% (n=37,633) of patients with T2DM who did not receive GLP-1RA, they had a mean number of three hospitalizations since 2015. Of these 37,633 patients, 24,197 had at least two hospitalizations during the previous six years, and 15,802 had at least three admissions since 2015.

Discussion

In our multicentre retrospective study of over 1.2 million hospitalizations, use of GLP-1RA was rare (n=1,274) despite T2DM (n=396,084) and obesity (n=327,844) being common. Data from our study demonstrate a distinct gap between clinical evidence and clinical practice.

GLP-1RA are a preferred second-line medication for T2DM, but we found that use of sulfonylureas was 43-fold higher and use of insulin was 186-fold higher than GLP-1RA use. Sulfonylureas and insulin have no cardiovascular benefits, and cause weight gain and hypoglycemia.[31] While SGLT2i have established cardiovascular benefits for adults with T2DM,

use of SGLT2i was also low in our study. Starting GLP-1RA while a patient is acutely unwell is not advised, but this does not preclude its use before discharge when the patient has recovered, especially if the reason for the hospitalization is due to worsening glycemic control.[32] Starting medications in hospital or prescribing them at discharge instead of deferring the decision to the outpatient setting leads to improved medication adherence and better management of chronic conditions.[20,21] Deferring the decision to a patient's family doctor is particularly fanciful in Canada, because over 10% of Canadians don't have a family doctor. Such patients can be followed up by the internist or hospitalist who cared for them during their inpatient stay while the patient awaits being seen in a sub-specialty clinic (e.g., endocrinology, obesity clinic).

The 99% of patients with T2DM who were not on GLP-1RA in 2021 had an average of three hospitalizations in the past six years, indicating that despite multiple interactions with the healthcare system, they did not receive a GLP-1RA. While T2DM was the strongest factor associated with GLP-1RA use, the specific hospital to which a patient was admitted was strongly associated with both higher and lower odds of a patient receiving GLP-1RA. This finding is concerning, as care should ideally be consistent across hospitals, and patient-level characteristics should be the strongest factors associated with GLP-1RA use. Our study showed that comorbidities such as heart failure were not associated with GLP-1RA use in hospital, and stroke was paradoxically associated with lower odds of receiving GLP-1RA.

Explanations for the low use of GLP-1RA are likely multifactorial and related to clinician-level, patient-level, and system-level factors. Prescribing inertia is a common reason for slow uptake of new medications for chronic disease.[33–35] Cost is also a likely factor limiting the broad uptake of GLP-1RA. In our study, patients living in areas of higher SES were more likely to receive a GLP-1RA compared to those living in lower SES areas, a finding consistent with

studies of GLP-1RA use in the United States.[16,36] In 2019, semaglutide was included in Ontario's public coverage for T2DM treatment.[37] For patients between the ages of 25-64 years who are not covered by the Ontario Drug Benefit program and do not have private insurance plans, paying out of pocket for GLP-1RA is a clear potential barrier.[38] System-level factors, such as delays in adding GLP-1RA to the hospital formulary, may also have contributed to slow GLP-1RA uptake; each hospital in Ontario has its own decision-making process when adding medications to the hospital formulary.[39]

Limitations

The GEMINI database lacks data on whether patients had private insurance. However, because the average age of patients in our study was 70 years, and adults over 65 years in Ontario have medication coverage through the provincial government, cost alone is unlikely to explain the low uptake we observed. Our classification of obesity was limited due to the low sensitivity (9%) of ICD-10 codes and the lack of data on BMI in GEMINI. To address these limitations, in addition to ICD-10 codes, we included a point prevalence study where we collected height and weight data. This combined approach yielded prevalence estimates for obesity that were consistent with provincial averages for Ontario. We lacked data on when GLP-1RA were added to the hospital formulary at each hospital, affecting our interpretation of the factors that drove low use of GLP-1RA. However, GLP-1RA use in 2021 was low overall, which suggests against hospital-level formulary coverage being the primary reason for low use, since most hospitals in Ontario had added GLP-1RA to their formulary by 2021. We did not exclude individuals with contraindications for GLP-1RA, which include a history of medullary thyroid carcinoma (prevalence: 1 in 150,000 in Canada) or multiple endocrine neoplasia syndrome type 2 (prevalence: 1 in 30,000 - 50,000 in North America).[40] Given their low prevalence, these

contraindications are unlikely to significantly contribute to the low use of GLP-1RA. Comorbidities such as gastroparesis and a history of pancreatitis may also limit GLP-1RA use which we did not consider in our study. We did not report on GLP-1RA side effects, which include nausea and vomiting, and it is possible patients were not prescribed a GLP-1RA in hospital because they were acutely unwell. However, that does not preclude its use before discharge when the patient has recovered.

Conclusion

Clinical guidelines recommend GLP-1RA as a second-line agent for people with T2DM and a first-line agent for people with obesity, but their use among patients who stand to benefit is low. Among over 1.2 million hospitalized adults in Ontario between 2015 and 2022, the prevalence of T2DM, obesity, and cardiovascular disease was high. Hospitalized adults are at high risk for subsequent cardiovascular events, making the inpatient setting an important opportunity to optimize treatment for T2DM and obesity. Our study demonstrates the gap between clinical evidence and clinical practice, and lays the foundation for knowledge translation interventions—including those implemented for hospitalized patients—to improve the uptake of GLP-1RA among those who stand to benefit most.

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Table 1. Demographic and clinical characteristics associated with hospitalizations

	GEMINI 2015-2022	Receiving GLP-1RA	Not Receiving GLP-1RA	SMD*
Sample size				
N (hospitalizations)	1,278,863	1,274	1,277,589	
Age				
Years [IQR]	70.0 [56.0, 82.0]	66.0 [59.0, 73.8]	70.0 [56.0, 82.0]	0.127*
< 40	120,751 (9.4)	38 (3.0)	120,713 (9.4)	0.624
40–60	280,538 (21.9)	357 (28.0)	280,181 (21.9)	
61–80	525,034 (41.1)	769 (60.4)	524,265 (41.0)	
81–100	350,526 (27.4)	110 (8.6)	350,416 (27.4)	
> 100	2,012 (0.2)	0 (0.0)	2,012 (0.2)	
Sex				
Male	680,343 (53.2)	739 (58.0)	679,604 (53.2)	0.105*
Female	598,480 (46.8)	534 (41.9)	597,946 (46.8)	
Income				
1st (lowest)	297,441 (23.3)	313 (24.6)	297,128 (23.3)	0.076
2nd	233,700 (18.3)	210 (16.5)	233,490 (18.3)	
3rd	254,690 (19.9)	256 (20.1)	254,434 (19.9)	
4th	243,272 (19.0)	251 (19.7)	243,021 (19.0)	
5th (highest)	225,132 (17.6)	228 (17.9)	224,904 (17.6)	
Missing	24,628 (1.9)	16 (1.3)	24,612 (1.9)	
Chronic Disease				
T1DM	19,619 (1.5)	29 (2.3)	19,590 (1.5)	0.054
T2DM	396,084 (31.0)	1,191 (93.5)	394,893 (30.9)	1.689*
Diabetes mellitus, other	4,235 (0.3)	9 (0.7)	4,226 (0.3)	0.052
Gestational Diabetes	440 (0.0)	0 (0.0)	440 (0.0)	0.026
Obesity	29,506 (2.3)	201 (15.8)	29,305 (2.3)	0.484*
Hypertension	516,457 (40.4)	718 (56.4)	515,739 (40.4)	0.324*
Coronary Artery Disease	283,229 (22.1)	473 (37.1)	282,756 (22.1)	0.333*
Peripheral Vascular Disease	30,863 (2.4)	34 (2.7)	30,829 (2.4)	0.016
Retinopathy	16,390 (1.3)	21 (1.6)	16,369 (1.3)	0.031

Neuropathy	26,582 (2.1)	60 (4.7)	26,522 (2.1)	0.146*
Diabetic Foot Infection	219,912 (17.2)	690 (54.2)	219,222 (17.2)	0.837*
Dyslipidemia	101,587 (7.9)	206 (16.2)	101,381 (7.9)	0.255*
COPD/Asthma	149,200 (11.7)	145 (11.4)	149,055 (11.7)	0.009
Dementia	201,924 (15.8)	120 (9.4)	201,804 (15.8)	0.193*
Liver Disease	32,608 (2.5)	51 (4.0)	32,557 (2.5)	0.082
Renal Disease	169,338 (13.2)	245 (19.2)	169,093 (13.2)	0.163*
Stroke or TIA	52,951 (4.1)	47 (3.7)	52,904 (4.1)	0.023
Heart Failure	125,023 (9.8)	211 (16.6)	124,812 (9.8)	0.202*
Most responsible diagnosis for the hospitalization				
Heart Failure	63,007 (4.9)	74 (5.8)	62,933 (4.9)	0.039
Pneumonia	43,805 (3.4)	42 (3.3)	43,763 (3.4)	0.007
Dementia	28,126 (2.2)	11 (0.9)	28,115 (2.2)	0.109*
COPD/Asthma	46,733 (3.7)	26 (2.0)	46,707 (3.7)	0.097
UTI	32,779 (2.6)	42 (3.3)	32,737 (2.6)	0.044
In-hospital medications				
Metformin	143,914 (11.3)	676 (53.1)	143,238 (11.2)	1.002*
DPP4i	101,890 (8.0)	172 (13.5)	101,718 (8.0)	0.180*
Sulfonylurea	54,885 (4.3)	220 (17.3)	54,665 (4.3)	0.428*
Insulin	236,612 (18.5)	1,041 (81.7)	235,571 (18.4)	1.634*
SGLT2i	21,304 (1.7)	292 (22.9)	21,012 (1.6)	0.685*
Statin	505,957 (39.6)	1,033 (81.1)	504,924 (39.5)	0.938*
In-hospital GLP-1RA				
Semaglutide	910 (0.1)	910 (71.4)	0 (0.0)	2.236*
Liraglutide	307 (0.0)	307 (24.1)	0 (0.0)	0.797*
Lixisenatide	19 (0.0)	19 (1.5)	0 (0.0)	0.174*
Dulaglutide	36 (0.0)	36 (2.8)	0 (0.0)	0.241*
Insulin degludec + liraglutide	< 7 (0.0)	< 7 (0.5)	0 (0.0)	0.079
Insulin glargine + lixisenatide	20 (0.0)	20 (1.6)	0 (0.0)	0.179*
Baseline labs (% of patients missing lab value)				
Creatinine (μmol/L)	87.0 [68.0, 123.0] (12.3%)	97.0 [73.0, 149.0] (1.02%)	87.0 [68.0, 123.0] (12.3%)	0.088
Glucose (mmol/L)	6.8 [5.7, 8.9] (16.6%)	9.6 [7.2, 13.5] (6.28%)	6.8 [5.7, 8.9] (16.6%)	0.504*

HbA1c	6.1 [5.5, 7.4] (82.7%)	7.6 [6.5, 9.1] (68.0%)	6.1 [5.5, 7.4] (82.7%)	0.458*
Hemoglobin (g/L)	124.0 [107.0, 139.0] (12.2%)	127.0 [110.0, 142.0] (0.8%)	124.0 [107.0, 139.0] (12.2%)	0.117*
Vitals (% of patients missing value)				
Weight (kg)	73.0 [60.5, 88.0] (96.1%)	86.9 [80.0, 104.4] (98%)	73.0 [60.5, 88.0] (96.1%)	0.628*
Note: values < 7 are suppressed				

Legend: GEMINI=General Medicine Inpatient Initiative, SMD=standardized mean difference, T1DM=type 1 diabetes mellitus, T2DM=type 2 diabetes mellitus, COPD=chronic obstructive pulmonary disease, TIA=transient ischemic attack, UTI=urinary tract infection, DPP4i=dipeptidyl peptidase 4 inhibitor, GLP-1RA=glucagon-like peptide 1 receptor agonist, SGLT2i=sodium glucose transporter 2 inhibitor, HbA1c=hemoglobin A1C. Obesity prevalence is based on ICD 10 diagnosis codes.

SMD: Standardized mean difference comparing patients in the "Receiving GLP-1RA" and "Not receiving GLP-1RA" groups. *Variables with a SMD > 0.1 indicate unbalanced baseline characteristic between the two groups.

Categorical variables are expressed as counts and proportion N (%). Age (years) expressed as median [IQR]. Baseline labs are expressed as median [IQR] (% missing). Lab summary values are given as mean ± standard deviation (% missing). Vitals are expressed as median [IQR] (% missing).

Table 2. Number of patients with Type 2 Diabetes Mellitus who would benefit from GLP-1RA.

Comorbidity	**N encounters (%) in Hospitalizations with T2DM**
Coronary Artery Disease (CAD)	123,708 (31.2%)
Stroke or Transient Ischemic Attack (TIA)	24,003 (6.1%)
Peripheral Vascular Disease (PVD)	10,063 (2.5%)
Heart Failure	66,366 (16.8%)
Renal Disease	88,494 (22.3%)
CAD, Stroke, or TIA	138,689 (35.0%)
CAD, Stroke, TIA, or PVD	143,547 (36.2%)
CAD, Stroke, TIA, PVD, or heart failure	170,419 (43.0%)
CAD, Stroke, TIA, PVD, heart failure, or renal disease	201,586 (50.9%)

Legend: This represents the number of hospitalizations associated with the above conditions. There were a total of 396,084 hospitalizations with Type 2 Diabetes Mellitus.

Table 3. Multivariable logistic regression model identifying factors associated with GLP-1RA use in hospital.

Variable	Odds Ratio for GLP-1RA	95% CI*
Age (Ref < 50)		
50-70	1.71	1.38, 2.11*
71-90	0.81	0.65, 1.02
≥ 91	0.24	0.13, 0.44*
Sex (Male)	0.94	0.84, 1.06
Institutes (Ref. Hospital A)		
Hospital B	3.05	2.45, 3.79*
Hospital C	1.42	1.08, 1.86*
Hospital D	0.15	0.05, 0.39*
Hospital E	3.61e-7	0, Inf
Hospital F	0.24	0.11, 0.53*
Hospital G	2.87e-7	0, Inf
Hospital H	0.05	0.02, 0.13*
Hospital I	5.67	4.63, 6.94*
Hospital J	0.19	0.13, 0.27*
Hospital K	0.02	0.00, 0.14*
Hospital L	4.91	3.80, 6.35*
Hospital M	0.53	0.36, 0.80*
Hospital N	3.76	2.84, 5.00*
Hospital O	0.04	0.01, 0.09*
Hospital P	0.17	0.10, 0.30*
Number of Years Since 2015	1.60	1.54, 1.67*
Income Quintile (Ref. Quintile 1)		
Quintile 2	1.04	0.87, 1.24
Quintile 3	1.24	1.05, 1.47*
Quintile 4	1.30	1.10, 1.54*
Quintile 5 (highest)	1.73	1.45, 2.07*

Quintile Missing	0.99	0.59, 1.64
Type 2 Diabetes Mellitus	29.60	23.5, 37.2*
Obesity	2.40	2.04, 2.83*
Dementia	0.65	0.53, 0.79*
Coronary Artery Disease (CAD)	1.14	1.00, 1.29
Peripheral Vascular Disease	0.97	0.68, 1.37
Stroke or Transient Ischemic Attack (TIA)	0.60	0.45, 0.81*
Heart Failure	1.08	0.91, 1.29
Hypertension	0.98	0.86, 1.11
Dyslipidemia	1.28	1.07, 1.54*
Renal Disease	0.85	0.72, 1.00
Hemoglobin A1C (Ref. Normal)**		
Moderate	1.67	1.28, 2.18*
Severe	1.83	1.36, 2.47*
Missing	1.20	0.94, 1.52
Creatinine* (μmol/L) (Ref. Normal)**		
Moderate	1.18	1.04, 1.35*
Severe	0.66	0.54, 0.81*
Missing	0.08	0.04, 0.14*

** Confidence intervals that do not cross 1*
***For hemoglobin A1C, values were categorized as normal (< 6.5%), moderate (6.5-9%), severe (> 9%), or missing.*
****For creatinine (μmol/L**),** values were categorized as normal (< 100), moderate (100-200), severe (> 200), or missing.*

Table 4. Number of patients with Type 2 Diabetes Mellitus between January 1, 2021 to January 1, 2022.

	Hospitalizations Jan 1, 2021 - Jan 1, 2022 with T2DM	Number of unique patients Jan 1 2021 - Jan 1, 2022 with T2DM
Sample size	54,647	38,040
In-hospital medications		
Metformin	20,485 (37.5%)	16,463 (43.3%)
DPP4i	16,627 (30.4%)	12,487 (32.8%)
Sulfonylurea	5,889 (10.8%)	4,834 (12.7%)
Insulin	31,181 (57.1%)	23,529 (61.9%)
SGLT2i	6,159 (11.3%)	5,218 (13.7%)
Statin	34,794 (63.7%)	25,590 (67.3%)
GLP-1RA	480 (0.9%)	407 (1.1%)

Legend: T2DM=type 2 diabetes mellitus, DPP4i=dipeptidyl peptidase 4 inhibitor, GLP-1RA=glucagon-like peptide 1 receptor agonist, SGLT2i=sodium glucose transporter 2 inhibitor. Any hospitalization without a valid patient ID was excluded (n = 603).