Final Project Abstract

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# Abstract

Chronic diseases, like diabetes, are some of the major causes of mortality in the world with the prevalence and cost of these diseases only continues to rise Hacker (2024). The Centers for Disease Control and Prevention (CDC) estimates that in the US alone, 34.2 million people have diabetes, with 29.7 million people diagnosed with the condition and 8.7 million continue to be undiagnosed Centers for Disease Control and Prevention (2025). As of 2024, the American College of Physicians has issued new guidelines for first line pharmacologic treatments for type 2 diabetes. The new recommendations are adding sodium–glucose cotransporter-2 (SGLT-2) inhibitor or glucagon-like peptide-1 (GLP-1) agonist to metformin and lifestyle modifications American College of Physicians (2024). These recommendations may stem from systematic analyses which show glycemic control decline after 2010 with gaps in treatment particularly seen among younger adults, Mexican Americans, and uninsured individuals, who are already at higher risk for diabetes complications Fang, Wang, Coresh, & Selvin (2021).

In a cohort of patients ~~newly~~ diagnosed with type 2 diabetes, we aim to compare the efficacy of the recommended treatment strategies: adding either an SGLT-2 inhibitor or a GLP-1 agonist. ~~A control group will include patients treated solely with metformin and lifestyle interventions, ranging from ages 18 years or older.~~ The analysis will be stratified by ethnicity and age groups to assess the differential effectiveness of these interventions on glycemic control, body weight, cardiovascular risk factors, and cardiovascular outcomes over a one-year follow-up period. ~~Additionally, treatment pathways will be analyzed to identify common sequences of therapy modifications and persistence rates across different patient subgroups.~~

# Introduction

In order to investigate the efficacy of adding either an SGLT-2 inhibitor or a GLP-1 agonist as a treatment course for patients with diabetes type 2, we will use the **LEGEND-T2DM Class Sensitivity Evidence Explorer** created during the Large-scale evidence generation and evaluation across a network of databases for type 2 diabetes mellitus (LEGEND-T2DM): a protocol for a series of multinational, real-world comparative cardiovascular effectiveness and safety studies Khera et al. (2022). The aim of this study is “determine real-world comparative effectiveness and safety of traditionally second-line Type 2 diabetes mellitus (T2DM) agents using health information encompassing millions of patients with T2DM, with a focus on individuals at moderate cardiovascular risk and other key subgroups.” They used the comparators of:

* SGLT2 inhibitors: canagliflozin, dapagliflozin, empagliflozin, ertugliflozin
* GLP1 receptor agonists: albiglutide, dulaglutide, exenatide, liraglutide, lixisenatide, semaglutide
* DPP4 inhibitors: alogliptin, linagliptin, saxagliptin, sitagliptin, vildagliptin
* Sulfonylureas: chlorpropamide, glimepiride, glipizide, gliquidone, glyburide, tolazamide, tolbutamide

We will focus on the GLP1 receptor agonists and SGLT2 inhibitors comparators with an outcome of interest of glycemic control. This outcome is defined as the proportion of patients with HbA1c 7% or 53 millimole per mole. I decided to use OptumEHR, OptumDod and VAOMOP as the target data sources for patients with no prior metformin exposure to compare glycemic control across unadjusted, propensity score (PS) matching and PS stratification methods and time at risk for intent to treat and on-treatment analyses.

# Attrition

As shown in Figure , the initial sample size for the OptumEHR data set on treatment was 16,515 patients for GLP1RA (target) and 14,231 patients for SGLT2i (comparator). After the restriction to common period criteria, the sample size was reduced by 332 patients for the target group. We further restricted our sample to patients with no prior metformin exposure, which reduced the sample size in our target group by 8,649 and in our comparator group by 6,667. The final sample size for the OptumEHR dataset was 7,534 patients for GLP1RA and 7,564 patients for SGLT2i.

Similarly shown in Figure , the initial sample size for the VAOMOP data set on treatment was 10,473 patients for target and 51,666 patients for comparator. After the restriction to common period criteria, the sample size was reduced by 58 patients for the target group and 6 patients for the comparator group. Further restricting our sample to patients with no prior metformin exposure, reduced the sample size in our target group by 7,710 and in our comparator group by 41,931. The final sample size for the VAOMOP dataset was 2,705 patients for GLP1RA and 9,729 patients for SGLT2i.

# Population Characteristics

The population characteristics of the patients in the OptumEHR dataset before and after propensity score adjustment for on treatment are shown in Table . Prior to adjustment it was shown that the GLP1RA group had a higher proportion of younger patients than the SGLT2i group while older patients, age 75 and above, were more likely to be given SGLT2i. Also, women in this group were predominantly recipients of GLP1RA. After adjustment, the age distribution was more balanced between the two groups, making comparisons more reliable.

# HR

The full results of the table are shown in Table .

When comparing the hazard ratios (HR) for GLP1RA vs SGLT2i across data sources, we find that GLP1RA has a higher risk of poor glycemic control compared to SGLT2i.

When adjusting for confounders, the HRs for GLP1RA vs SGLT2i are reduced, but GLP1RA still shows a higher risk of poor glycemic control compared to SGLT2i. The PS matching method shows the greatest reduction in HRs, suggesting that this method is the most effective at reducing bias. The PS stratification method shows the lowest HRs, indicating that some patients switching treatments experience improved glycemic control.

# Propensity Score

The propensity score (PS) distribution for the OptumEHR dataset is shown in Figure . The PS distribution for the GLP1RA and SGLT2i groups is similar and shows a fair degree of overlap, indicating that the two groups are comparable.

The PS distribution for the VAOMOP dataset is shown in Figure . The PS distribution for the GLP1RA and SGLT2i groups shows a strong separation, indicating that the two groups are not comparable. With this bimodal distribution there is a strong indication that patients we strongly predicted to have one drug over the other.

# Kaplan-Meier Curves

The Kaplan-Meier curves for the OptumEHR dataset are shown in Figure . The curves show that the GLP1RA group has a higher risk of poor glycemic control compared to the SGLT2i group.

# References

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