A Real-World Examination of HbA1c Reduction and Target Achievement Comparing SGLT2 Inhibitors and GLP1 Receptor Agonists as Second-Line Augmentation to Metformin for Treating Type II Diabetes

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BACKGROUND

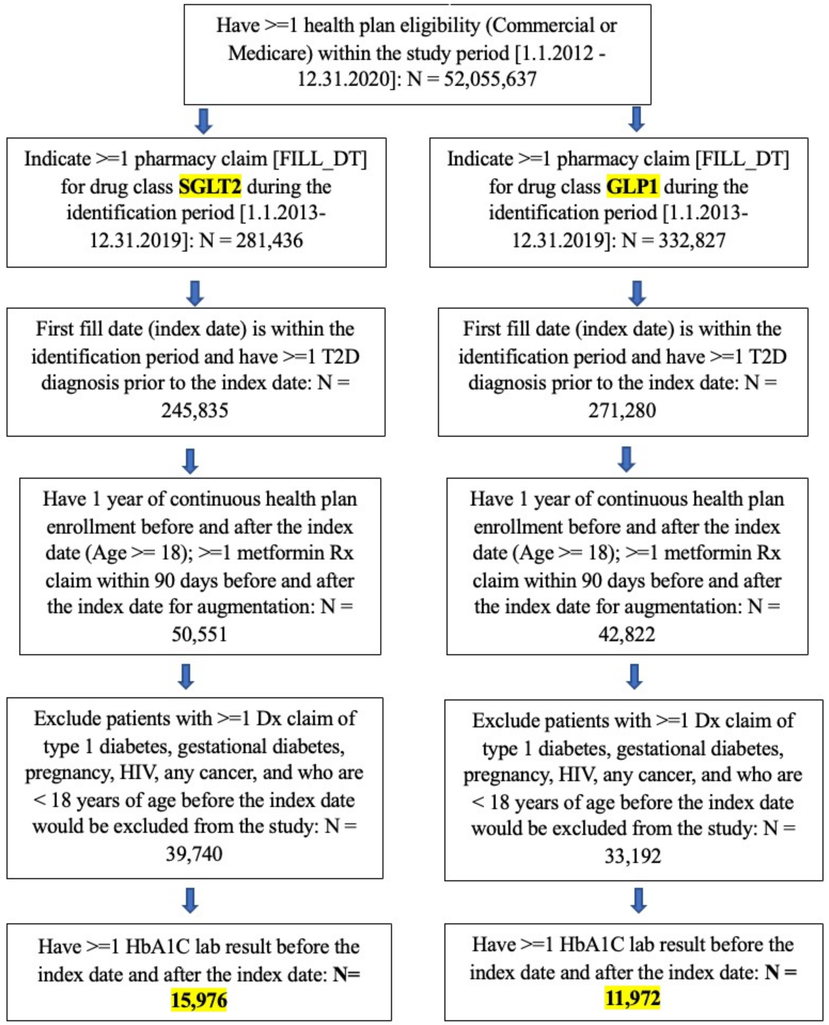
- Type II diabetes is caused by the malfunction of body cells to respond normally to insulin as well as the inability of pancreas to produce sufficient insulin, a hormone that is necessary to control glucose level (HbA1C) in blood. Poor management of A1C can lead to various complications such as strokes, cardiovascular diseases (CVD), retinopathy, neuropathy, and chronic kidney diseases (CKD).
- Though contraindicated among patients with severe renal disease, metformin is the most prescribed first-line oral treatment of T2D due to its mild side effects and multifunction to increase lifespan.
- However, as the disease progresses, metformin alone often becomes inadequate in controlling HbA1c level, and second-line drugs are often added to augment the initial treatment.
- Besides metformin and insulin, the current antihyperglycemic agents (AHAs) in the market include sulfonylureas (SUL), meglitinides (MEG), thiazolidinediones (TZD), dipeptidyl peptidase-4 enzyme inhibitors (DPP-4), sodium-glucose transport protein 2 inhibitors (SGLT2), and glucagon-like peptide-1 receptor agonists (GLP-1). Each drug class varies by antihyperglycemic mechanisms and potential benefits and side effects.
- Two newer pharmacologic drug classes include SGLT2 inhibitors, which are available as oral drugs that lower blood sugar by causing the kidneys to remove sugar from the body through the urine, and GLP1 receptor agonists, injectable medications (except for the oral drug semaglutide) that inhibit glucose formation and stimulate glucose uptake by cells, thus lowering the amount of glucose in the blood.
- According to the American Diabetes Association (ADA), both SGLT2 and GLP-1 have clinical benefits with respect to adverse cardiovascular and renal outcomes. They also show similar clinical outcomes in terms of hypoglycemic events and weight loss, with relatively higher costs compared with other medications.

OBJECTIVES

- SGLT2 and GLP1 are increasingly used as second-line augmentation therapies added after metformin. We conducted an observational study to examine and compare the real-world performance of SGLT2 and GLP1 in terms of HbA1c reduction and target achievement.

METHODS

Figure 1. Patient Selection



- Using claims from Optum's Clinformatics® Data Mart, we selected metformin users who initiated SGLT2 or GLP1 between 01/01/2013 and 12/31/2019, in which the initiation date was the index date, with a 12-month baseline and follow-up period, respectively.
- The explanatory variable in the study was the indication of the index treatment cohort as SGLT2 or GLP1.
- The pre-period of the study was set to be the 1 year prior to the index date. Demographic information including gender, age, region, insurance type, and plan type were collected. Baseline average HbA1C value, diabetic and non-diabetic comorbidities and finally, baseline concomitant non-AHA medications, blood-pressure-lowering medications, and other commonly prescribed medications were included as baseline covariates.
- Post-Period was set to be the 1 year after the index date and the study presented two outcomes of interest. The first outcome was to account for the proportion of patients with three criteria of HbA1c attainment: HbA1c < 7% (ADA target), < 8% (HEDIS target), and > 9% (HEDIS poor control) by the end of the 1-year follow-up period. The second outcome was designed to compare the relative change of HbA1c level from pre-period to post-period, comparing the two cohorts.
- Ordinary least square and logistic regressions were conducted to examine HbA1c reduction and target achievement between the two cohorts, controlling for baseline demographics and health status.

RESULTS

- A total of 15, 976 and 11, 972 patients were identified in the SGLT2 and GLP1 cohorts. The average HbA1c before and closest to the index date was 8.56% for the SGLT2 cohort and was 8.51% for the GLP1 cohort.

Table 1. HbA1c Descriptive Statistics

	Cohort SGLT2 N= 15,976		Cohort GLP1 N= 11,972		
	N or mean	%, or sd	N or mean	%, or sd	p-value
Baseline HbA1c %, mean (sd)	8.56	1.84	8.51	2.04	<0.0001
<7%, n(%)	1,991	12.46	2,199	18.37	
<8%, n(%)	4,394	27.50	2,670	22.31	
<=9%, n(%)	4,371	27.36	2,923	24.42	
>9%, n(%)	5,220	32.68	4,178	34.90	
Post-period HbA1c %, mean (sd)	7.58	45.33	7.50	1.79	

- SGLT2 users were more likely to attain the American Diabetes Association (ADA) target of HbA1c < 7% [OR: 1.324, CI: (1.254, 1.398), p < 0.0001], slightly less likely to achieve the Healthcare Effectiveness Data and Information Set (HEDIS) target of HbA1c < 8% [OR: 0.951, CI: (0.899, 1.005), p = 0.0747], and more likely to fall within the HEDIS standard of poor control of HbA1c > 9% [OR: 1.235, CI: (1.149, 1.327), p < 0.0001], compared with GLP1 takers by the end of the study period.
- Slightly less HbA1c reduction was estimated for the SGLT2 cohort, compared with the GLP1 cohort (0.045, p = 0.0183), where 0.043 was the estimated difference of reduction level (follow-up HbA1c minus index HbA1c) by being in the SGLT2 cohort.

CONCLUSIONS

- The study results suggested that SGLT2 showed better achievement in the ADA target of HbA1c < 7%, while GLP1 was more efficacious in the rest of targets and HbA1c reduction by the end of the study period.

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