

# 2020 WRITING CONTEST POST-GRADUATE WINNER

## Impact of Pharmacists in Therapeutic Optimization Relative to the 2020 American Diabetes Association Standards of Medical Care in Diabetes Guidelines in Patients with Clinical Atherosclerotic Cardiovascular Disease

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His winning manuscript, "Impact of pharmacists in therapeutic optimization relative to the 2020 American Diabetes Association Standards of Medical Care in Diabetes Guidelines in patients with clinical atherosclerotic cardiovascular disease," examines the role of the ambulatory pharmacist in optimizing patient therapy. Under the mentorship of Dr. Jarred Prudencio, Associate Professor of Pharmacy Practice at The Daniel K. Inouye College of Pharmacy, this research evaluated the therapeutic regimens of patients with both type II diabetes and atherosclerotic cardiovascular disease at a rural clinic in East Hawai'i. The data analysis showed statistically significant differences in therapeutic optimization between patients who had a pharmacist involved in their care versus those patients without a pharmacist involved in their care. This research not only reinforced the value of the ambulatory pharmacist as a member of the healthcare team but also allowed for an examination of potential factors associated with the differential prescribing practices of practitioners.

### Abstract

In 2020, the American Diabetes Association (ADA) Standards of Medical Care in Diabetes Guidelines newly recommended adding a sodium-glucose cotransporter-2 (SGLT-2) inhibitor or a glucagon-like peptide 1 (GLP-1) receptor agonist in patients with both type 2 diabetes and atherosclerotic cardiovascular disease, regardless of hemoglobin A1c (HbA1c) levels. In this study, the primary objective was to assess the pharmacist's role in the therapeutic optimization of patients with both type 2 diabetes and atherosclerotic cardiovascular disease relative to the new recommendations. The secondary objectives were to assess other factors affecting therapeutic optimization and clinician familiarity with the recommendations. This study, conducted at the East Hawai'i Health Clinic, included 60 patients with type 2 diabetes and atherosclerotic cardiovascular disease. Anonymous surveys were sent to clinicians at the clinic to assess recommendation familiarity. Patients seen by a pharmacist were significantly more likely to be therapeutically optimized per the 2020 ADA guidelines than those not seen by a pharmacist. HbA1c and age also influenced SGLT-2/GLP-1 therapy use. All clinicians were more likely to prescribe SGLT-2/GLP-1 therapy for patients with uncontrolled HbA1c but were less likely to prescribe additional therapy for patients with controlled HbA1c, even in patients with previous atherosclerotic events.

### Abbreviations and Acronyms

ADA = American Diabetes Association  
ASCVD = atherosclerotic cardiovascular disease  
CVOT = cardiovascular outcome trial  
EHR = electronic health record  
FDA = US Food and Drug Administration  
GLP-1 = glucagon-like peptide 1  
HbA1c = hemoglobin a1c

SGLT-2 = sodium glucose transporter-2  
TZD = thiazolidinediones

### Introduction

In the Centers for Disease Control and Prevention's 2020 National Diabetes Statistics Report, it is estimated that 10.2% of American adults were diagnosed with type 2 diabetes mellitus in 2018.<sup>1</sup> Atherosclerotic cardiovascular disease (ASCVD), which is collectively defined as coronary heart disease, myocardial infarction, stroke, and peripheral artery disease of atherosclerotic origin, is 1 of the leading causes of morbidity and mortality in patients with diabetes.<sup>2</sup> Other risk factors associated with ASCVD include dyslipidemia and hypertension, both of which are comorbidities commonly afflicting patients with diabetes.<sup>3</sup>

Before 2008, antihyperglycemic effects were the sole focus in the development and study of antidiabetic drugs. Improvements in hemoglobin A1c (HbA1c) values served as surrogate markers for improved microvascular outcomes, and cardiovascular risk assessment was based on investigator-reported adverse events. At this time, clinical trials were relatively short, ranging from 6 to 12 months.<sup>4</sup> These trials were also often performed in patients with newly onset diabetes; given the decreased duration of time with the disease, patient risk for adverse cardiac events was generally low.<sup>4,5</sup> In 2008, concerns with rosiglitazone, a medication belonging to the class of thiazolidinediones (TZDs), was found to be associated with a significant increase in the risk of

myocardial infarction and heart failure in patients and prompted the US Food and Drug Administration (FDA) to reevaluate the process through which it determines cardiovascular safety for antihyperglycemic medications.<sup>5,6</sup> In response, the FDA set forth a Guidance for Industry, specifying cardiovascular risk evaluation criteria in new antidiabetic therapies.<sup>4</sup> Drug developers would be required to demonstrate that the treatment does not result in an unacceptable increase in cardiovascular risk in patients. Specific recommendations outlined in the guidance include a recommendation for establishing an independent cardiovascular endpoints committee and the inclusion of patients deemed high-risk for cardiovascular events in phase 2 and 3 trials.<sup>4</sup> In 2018, the guidance was further modified, detailing specific durations that therapy must be studied in patients to assess safety and requiring more stringent patient criteria. At least 1500 patients should be exposed to the drug for at least 1 year, and at least 500 patients should be exposed to the new drug for at least 2 years to assess safety.<sup>7</sup>

The collection of trials for new medications developed following the FDA guidance are collectively referred to as cardiovascular outcomes trials (CVOTs). As a result of these trials, specific agents in 2 classes of medications, sodium-glucose cotransporter-2 (SGLT-2) inhibitors, and glucagon-like peptide 1 (GLP-1) agonists, demonstrated not only cardiovascular safety but also cardiovascular risk reduction. As the evidence supporting these findings increased, the value of SGLT-2 inhibitor and GLP-1 agonist therapy for more than just HbA1c lowering became more apparent. Currently, some medications are being examined in alternative therapeutic avenues outside of antidiabetic treatment, including to treat heart failure.<sup>8</sup>

GLP-1 receptor agonist medications are injectable (except for 1 oral formulation currently available) peptides that mimic the effects of incretin in the body. Incretins are released in response to the ingestion of food and regulate insulin secretion, glucagon inhibition, and gastric emptying, among other mechanisms.<sup>9</sup> Incretins generally have a short half-life in the body due to being broken down quickly by an enzyme called dipeptidyl peptidase-4, but the addition of exogenous incretin-mimetics allows for an increased duration of effect. The increase in insulin and decrease in glucagon serve to decrease blood sugar levels, while the delay in gastric emptying helps patients feel full longer and can lead to weight loss.<sup>9</sup>

SGLT-2 inhibitors are a class of oral medications that function in the kidney to prevent glucose reabsorption. These medications inhibit the sodium-glucose transport protein 2, which would generally reabsorb glucose and sodium, resulting in a net decrease of glucose in the body. SGLT-2 inhibitors have also been shown to promote weight loss and natriuresis, which may reduce blood pressure.<sup>10</sup>

The 2019 American Diabetes Association (ADA) Standards of Medical Care in Diabetes Guidelines recommend metformin

as the first-line treatment for patients with type 2 diabetes, and a GLP-1 receptor agonist or SGLT-2 inhibitor as a second-line option if the patient's HbA1c is not sufficiently controlled on metformin and they have a history of clinical ASCVD. In 2020, the ADA updated this recommendation, given the new evidence from various CVOTs. Metformin remains first-line therapy, but in patients with indicators of high-risk or established ASCVD, regardless of HbA1c, a GLP-1 receptor agonist or SGLT-2 inhibitor is recommended to be added to their regimen for cardiovascular risk reduction.<sup>11</sup>

These recommendations are relatively new, and the concept of adding therapy when HbA1c is already controlled is also novel in type 2 diabetes. For these reasons, this research project sought to identify if patients at the East Hawai'i Health Clinic were appropriately prescribed SGLT-2 inhibitor or GLP-1 agonist therapy as recommended by the 2020 ADA guidelines, and specifically the pharmacist's role in therapeutic optimization.

## Methods

This retrospective study was conducted at the East Hawai'i Health Clinic, a primary care clinic where clinical pharmacists from the University of Hawai'i work as part of the interdisciplinary team alongside medical residents, nurse practitioners, and faculty physicians to provide comprehensive medication management; clinical pharmacists work under a progressive, collaborative practice agreement. Patients are referred to the clinical pharmacists' care by their primary care provider for more complex and comprehensive medication management of chronic conditions. Institutional review board approval was procured under protocol ID 2020-00041.

Patient data were examined via the institution's electronic health record (EHR) and visit information between May 2017 and April 2020 was assessed. Patients were included in the study if they were diagnosed with type 2 diabetes and a confirmed clinical atherosclerotic event: coronary artery disease, peripheral artery disease, myocardial infarction, or stroke. There were no exclusion criteria.

The primary objective of this study was to evaluate the pharmacist's role in therapy optimization for patients with type 2 diabetes and ASCVD relative to the 2020 ADA guideline. This objective was assessed by comparing the prescribing rates of SGLT-2 inhibitors and GLP-1 agonists for patients managed by a clinical pharmacist versus those without a pharmacist involved in their care in this sample population.

The secondary outcomes included assessing other factors affecting the use of SGLT-2/GLP-1 therapy in the described patient populations and examining prescriber familiarity with the most recent ADA guidelines. Demographic information, including age, sex, weight, and laboratory values such as HbA1c, estimated glomerular filtration rate, and urine albumin-to-creatinine ratio,

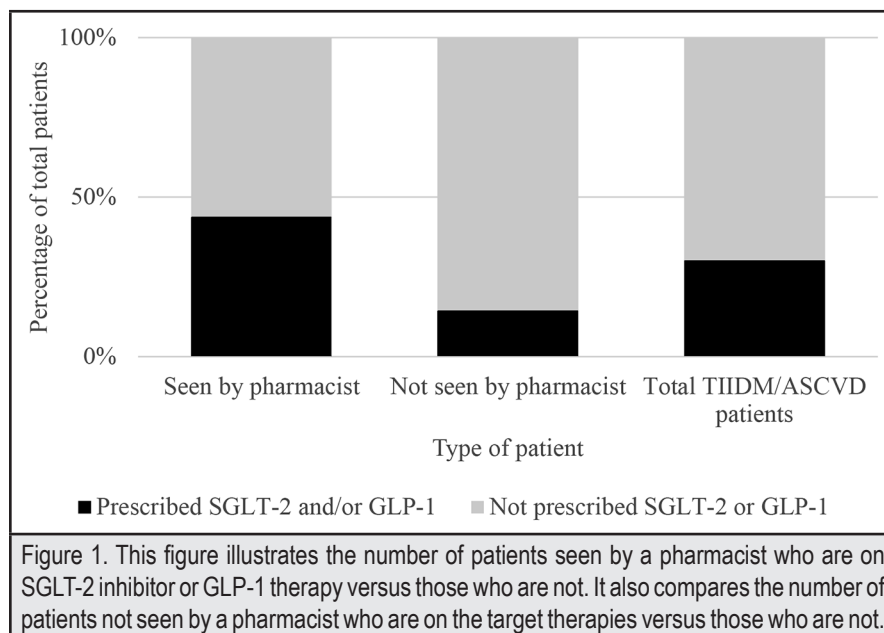
were examined. Other factors assessed include the number of clinic visits and additional medication regimen components: other antihyperglycemic medications, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, HMG-CoA reductase inhibitors, beta-blockers, and aspirin. Continuous variables were analyzed using a *t*-test, and categorical variables were examined using Fisher's exact test.

A 10-question, anonymous survey was disseminated by email via SurveyMonkey to assess clinician likelihood of implementing the 2020 ADA guidelines into general practice. All 29 clinicians were sent the survey, including ambulatory care pharmacists, medical residents, and faculty physicians employed at the East Hawai'i Health Clinic. The questions were developed by the primary author and reviewed by the supervising pharmacist who is credentialed in diabetes management. Questions in the survey addressed respondent demographics, including professional position and time spent practicing as a medical professional, self-rated familiarity with current and previous ADA recommendations, familiarity with the diabetes CVOTs, and general prescribing practices relative to critical scenarios. Respondents ranked their familiarity via a 5-point Likert scale and ranked drug prescribing preferences given scenarios on a 4-point Likert scale.

## Results

A total of 60 patients were identified with type 2 diabetes and ASCVD and included in the analysis (Figure 1). Of these, 32 patients had been seen by a clinical pharmacist at the East Hawai'i Health Clinic as part of their healthcare team, while a clinical pharmacist had not seen the remaining 28. Of the 32 patients, 14 (44%) were appropriately prescribed SGLT-2/GLP-1 therapy, as recommended by the 2020 ADA Guidelines compared to 4 of the 28 (14%) patients prescribed SGLT-2/GLP-1 therapy who had not been seen by a pharmacist ( $P=.02$ ).

In assessing secondary outcomes, significance was also detected when examining the difference in age of patients prescribed SGLT-2/GLP-1 therapy (Table 1). The mean age of patients prescribed the target medications was 57.67 years, while the age of those not prescribed SGLT-2/GLP-1 therapy averaged 66.79 years ( $P=.006$ ). Significance was also detected when examining baseline HbA1c as a factor associated with differential SGLT-2/GLP-1 therapy use (Table 2). For the patients who would eventually be placed on SGLT-2/GLP-1 therapy, their pre-SGLT-2/GLP-1 HbA1c values averaged 9.62%, while the patients who were not on SGLT-2/GLP-1 therapy averaged 7.14% ( $P<.001$ ). The most recent mean HbA1c of the patients seen by the pharmacist was 7.64%, while the mean HbA1c for patients who the pharmacist did not see was roughly 6.86% ( $P=.05$ ). This difference of approximately 0.8%, although not statistically significant, is trending towards significance and is clinically relevant.



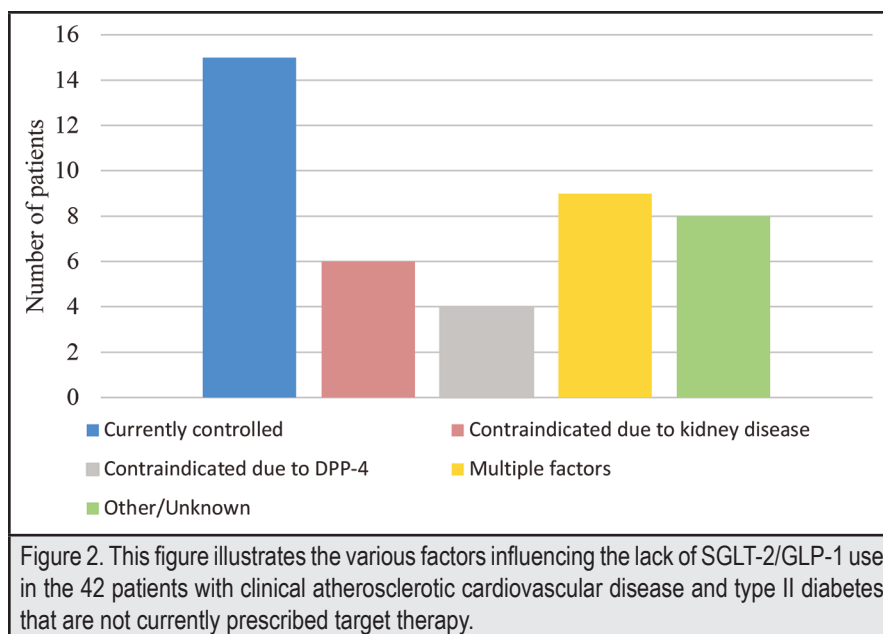
	Mean age (years)	P value
Total	64.04	
SGLT-2 patients	56.83	.73
GLP-1 patients	58.53	
SGLT-2 and/or GLP-1 patients	57.67	.006
Non-SGLT-2/GLP-1 patients	66.79	
Pharmacy patients	64.06	.99
Non-pharmacy patients	64.04	

	Mean HbA1c (%)	P value
Total (most recent)	7.27	
SGLT-2 and/or GLP-1 patients (Pre-SGLT-2/GLP-1)	9.62	.001
Non-SGLT-2/GLP-1 patients (most recent)	7.14	
SGLT-2 and/or GLP-1 patients (most recent)	7.85	.07
Non-SGLT-2/GLP-1 patients (most recent)	7.14	
Pharmacy patients (most recent)	7.64	.054
Non-pharmacy patients (most recent)	6.86	

Finally, of the 60 patients with type 2 diabetes and ASCVD, a total of 42 were not on target therapy (Figure 2). There were various reasons for this, the most common being that the patients were currently controlled (defined here as HbA1c < 7%) on their regimen. Fifteen patients (36%) were considered controlled on their current regimen. Other reasons include contraindication to target therapy due to chronic kidney disease, contraindication due to current therapeutic interactions, combinations of the reasons above, or there may have been no apparent reason that the patient was not on the targeted therapy.

Of the emailed surveys, a total of 15 responses were received out of 29 target recipients. Among those that responded were 3 faculty physicians, 8 medical residents, and 4 clinical pharmacists (Table 3). All respondents rated themselves as “somewhat familiar” or greater with the 2019 ADA Guidelines, and the majority, 73%, were “somewhat familiar” with the 2020 ADA Guidelines. Overall, pharmacists were more likely to self-assess as “very familiar” or “extremely familiar” with the material regarding guidelines and trials than other respondents. In contrast, medical residents were more likely to self-assess as “somewhat familiar” or “not so familiar.”

Given a patient case with a patient diagnosed with diabetes with an uncontrolled HbA1c of 8.5% and a past myocardial infarction who is already prescribed a maximum metformin dose, all respondents were either “likely” or “extremely likely” to introduce a second therapeutic agent, with SGLT-2 inhibitors or GLP-1 agonists most chosen (Figure 3). Pharmacists preferred SGLT-2/GLP-1 therapy relative to other practitioners, with all pharmacists surveyed “extremely likely” to add a GLP-1 agonist. When given a patient with a controlled HbA1c of 6.5%



and a past myocardial infarction or a patient with HbA1c of 6.5% with no history of but at high risk for ASCVD, the likelihood of adding SGLT-2/GLP-1 therapy was much lower than in the uncontrolled patient for all practitioners (Figures 4 and 5). The likelihood of prescribing additional therapy was also similar between the controlled patient with a history of ASCVD and the controlled patient without a history of ASCVD for all practitioners.

Table 3. Responses to Survey Background Information		
Survey Question	Response	Number of Respondents
Which best describes you as a medical professional?	Faculty physician	3
	Medial resident	8
	Pharmacist	4
How long have you practiced as a medical professional?	3 years or less	7
	Between 3 and 10 years	5
	10 years or more	3

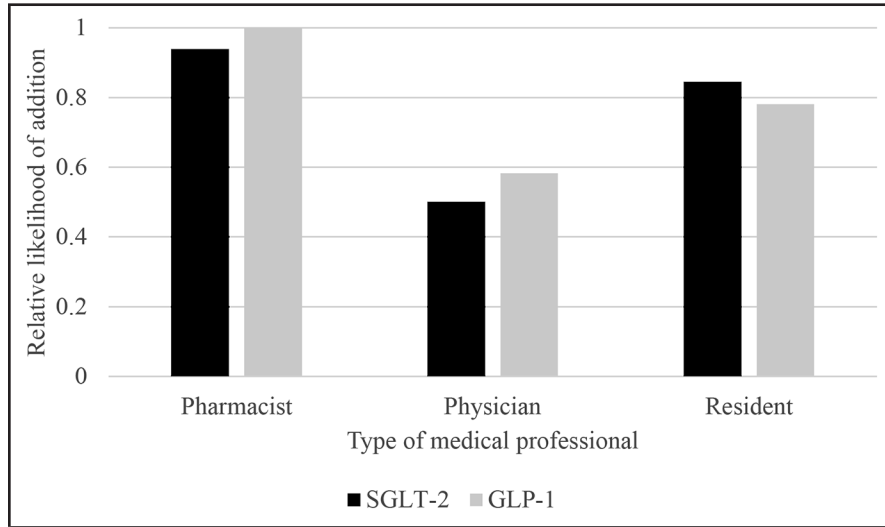


Figure 3. The figure illustrates the relative likelihood of prescribing an SGLT-2 inhibitor or GLP-1 agonist in a 60-year-old patient with a hemoglobin A1c of 8.5% currently maxed on metformin with a history of myocardial infarction but otherwise healthy.

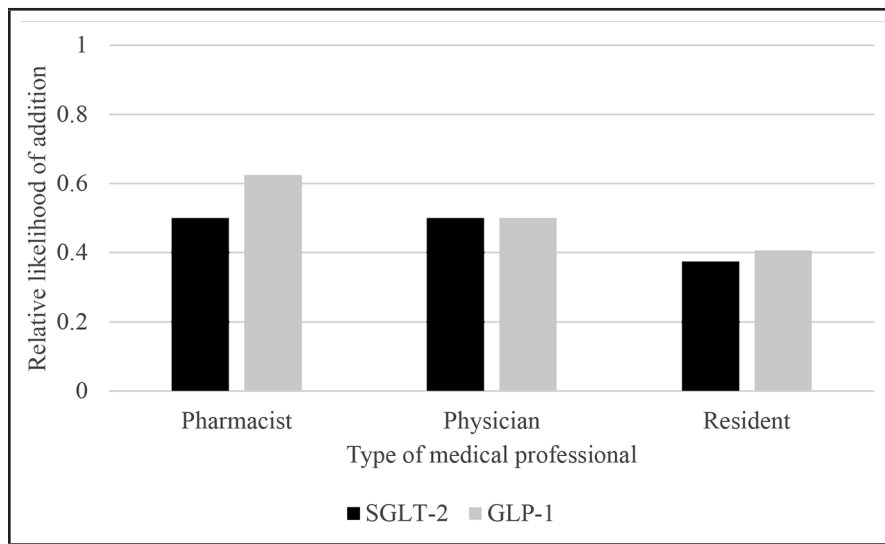
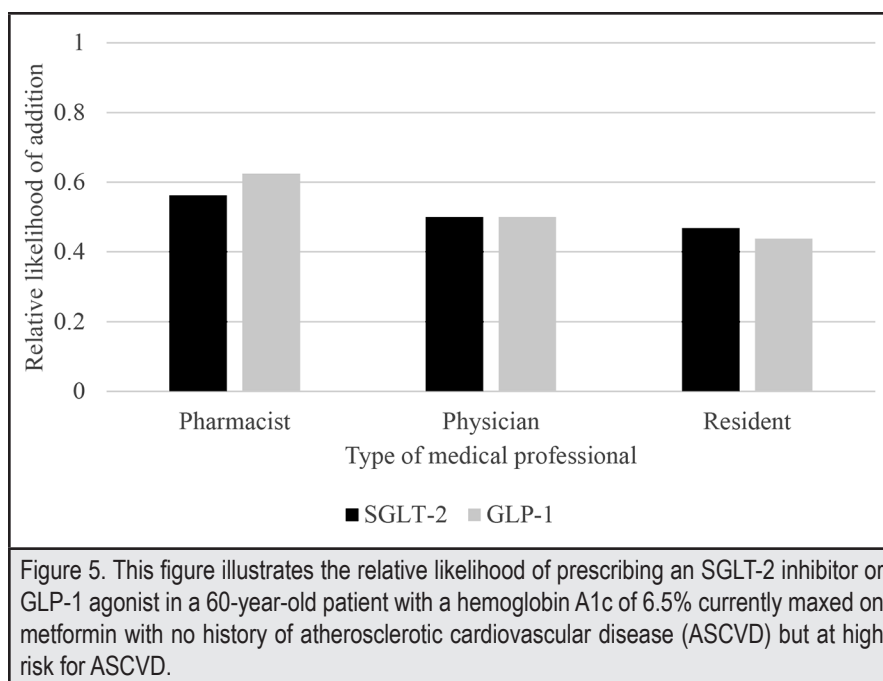


Figure 4. This figure illustrates the relative likelihood of prescribing an SGLT-2 inhibitor or GLP-1 agonist in a 60-year-old patient with a hemoglobin A1c of 6.5% currently maxed on metformin with a history of myocardial infarction but otherwise healthy.



## Discussion and Conclusion

Patients with both type 2 diabetes and ASCVD with a pharmacist involved in their care at the East Hawai'i Health Clinic are significantly more likely to be placed on SGLT-2/GLP-1 therapy as recommended by the 2020 ADA Guidelines. The ADA annually updates its recommendations and given that diabetes management is primarily medication-based, the pharmacist can play a vital role in managing this disease state. Multiple factors may contribute to the disparity between therapeutic optimization between patients seen versus not seen by a pharmacist.

At the East Hawai'i Health Clinic, patients are referred to a pharmacist's care by their primary care provider. These patients are generally more complex and require intense medication management for their chronic conditions. They may present with significant adherence barriers, varying degrees of treatment resistance, or other factors. It could be that clinically, these patients require SGLT-2 or GLP-1 therapy as part of their HbA1c lowering regimen regardless of ASCVD benefit. The propensity for more complex patients may also contribute to the difference in HbA1c seen in patients with a pharmacist involved in their care versus those without a pharmacist involved in their care.

Looking at age as a factor influencing SGLT-2/GLP-1 therapy, patients with the target therapies have a mean age of 58 years while patients without have a mean age of 67 years. There may be multiple factors influencing this result, the first of which may be the guidelines themselves. As patients age, they develop more comorbidities, and the benefit of aggressive diabetes treatment begins to lessen as the risk of hypoglycemia becomes

more prevalent. The 2020 ADA Guidelines recommend a less stringent HbA1c goal of less than 8% in older patients. Alternatively, more aggressive treatment may be warranted in younger individuals to prevent complications associated with diabetes. These patients typically have HbA1c goals lower than 7%, as long as they may be achieved with minimal hypoglycemic risk. Additionally, SGLT-2 inhibitors carry common side effects such as urinary tract infections or dizziness, and GLP-1 agonists have gastrointestinal upset, appetite suppression, and weight loss as common side effects. Some clinicians may view these risks as outweighing the benefits in some patients, especially older adults.

The HbA1c values for the SGLT-2/GLP-1 patients before initiating their therapy were significantly higher than the current HbA1c value of patients not on SGLT-2/GLP-1 therapy. This finding suggests again that SGLT-2 inhibitors and GLP-1 agonists may be utilized primarily for their HbA1c lowering potential with an added benefit of ASCVD risk lowering.

Of the 60 patients at the clinic with type 2 diabetes and ASCVD, 42 were not on the target SGLT-2/GLP-1 therapy. Fifteen of these 42 were considered controlled on their current therapy and did not require additional therapeutics. Patients with a controlled HbA1c in previous guidelines had not been recommended additional medications, but the 2020 ADA Guidelines newly recommend SGLT-2 or GLP-1 therapy in patients, regardless of HbA1c, with type 2 diabetes and a history of ASCVD. Although these patients' HbA1c levels were considered controlled, there may have been other factors influencing the lack of SGLT-2/GLP-1 use.

Most of the prescribers at the clinic are unlikely to prescribe an additional medication to patients with both type 2 diabetes and ASCVD with a currently controlled HbA1c. Although some of these prescribers are familiar with the new recommendations and associated trials, the evidence may not be compelling enough to justify the addition in every situation. There may also be situations where patients are not amenable to additional therapy, especially injectable therapy such as a GLP-1 agonist; insurance issues may prevent the addition of SGLT-2/GLP-1 therapy as well.

Ten of the patients had a contraindication to one of the two therapeutic options. Patients with severe chronic kidney disease have a contraindication to SGLT-2 inhibitors. Patients currently being treated with a drug in a class of medications known as dipeptidyl peptidase-4 inhibitors should not be placed on GLP-1 agonists due to overlap in the mechanism of action. Eight of the patients not currently on SGLT-2 inhibitor or GLP-1 agonist therapy had no clear indication in their chart for the lack of medication. There may be patient-specific factors at play, such as a refusal to inject themselves or insurance issues. These eight patients are critical patients to follow up with for medication management.

This analysis does carry limitations. Since this was a retrospective EHR review and patients were not contacted or interviewed as part of this study, there may be pieces of the clinical picture that were not depicted in the analysis. Another limitation would be the relatively small number of survey responses in examining clinician familiarity and prescriptive preferences.

In conclusion, the clinical pharmacist plays an important role in optimizing patient care at the East Hawai'i Health Clinic; there were significantly more patients on ADA-recommended therapies when a pharmacist was directly involved in patient care. However, there are other factors that may influence the use of SGLT-2/GLP-1 therapy in the target population. It is vital to understand that although the ADA 2020 guidelines are evidence-based recommendations, healthcare providers must adjust medication regimens according to patient-specific factors. The next steps in this research project include follow-up of the individual patients identified and discussion with the clinicians to identify if medication adjustments following the 2020 ADA guidelines would be appropriate.

### Conflict of Interest

None of the authors identify any conflict of interest.

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### Appendix

#### Survey

##### Question 1.

Which of the following best describes you as a medical professional?

- A. Faculty Physician
- B. Medical Resident
- C. Pharmacist

##### Question 2.

How long have you practiced as a licensed medical professional?

- A. 3 years or less
- B. Between 3 and 10 years
- C. 10 years or more

##### Question 3.

How would you rate your familiarity with the 2019 American Diabetes Association Standards of Medical Care in Diabetes, Pharmacologic Treatment Guidelines?

- A. Extremely familiar
- B. Very familiar
- C. Somewhat familiar
- D. Not so familiar
- E. Not at all familiar

##### Question 4.

How would you rate your familiarity with the 2020 American Diabetes Association Standards of Medical Care in Diabetes, Pharmacologic Treatment Guidelines?

- A. Extremely familiar
- B. Very familiar
- C. Somewhat familiar
- D. Not so familiar
- E. Not at all familiar

Question 5.

How would you rate your familiarity with the cardiovascular outcomes trials (CVOTs) relating to diabetes medications?

- A. I have read the majority of the CVOTs
- B. I have read a few of the CVOTs
- C. I have listened to presentations or completed CE's on this topic
- D. I have heard the general outcomes
- E. I have not heard of these trials

Question 6.

How often do you prescribe the following drug classes as second-line therapy (after metformin) in patients diagnosed with uncontrolled type II diabetes mellitus:

SGLT-2 Inhibitors?

- A. Greater than 75% of the time
- B. Between 50% and 75% of the time
- C. Between 25% and 50% of the time
- D. Less than 25% of the time

DPP-4 Inhibitors?

- A. Greater than 75% of the time
- B. Between 50% and 75% of the time
- C. Between 25% and 50% of the time
- D. Less than 25% of the time

GLP-1 Agonists?

- A. Greater than 75% of the time
- B. Between 50% and 75% of the time
- C. Between 25% and 50% of the time
- D. Less than 25% of the time

TZDs?

- A. Greater than 75% of the time
- B. Between 50% and 75% of the time
- C. Between 25% and 50% of the time
- D. Less than 25% of the time

Sulfonylureas?

- A. Greater than 75% of the time
- B. Between 50% and 75% of the time
- C. Between 25% and 50% of the time
- D. Less than 25% of the time

Question 7.

Given a 60 year old patient currently taking metformin ER 1000mg BID with an A1c of 8.5% and a history of myocardial infarction but otherwise healthy, rate the likelihood with which you would prescribe the following:

SGLT-2 Inhibitors?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

Sulfonylureas?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

GLP-1 Agonists?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

DPP-4 Inhibitors?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

TZDs?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

No additional medications?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

Question 8.

Given a 60 year old patient currently taking metformin ER 1000mg BID with an A1c of 6.5% and a history of myocardial infarction but otherwise healthy, rate the likelihood with which you would prescribe the following:

SGLT-2 Inhibitors?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

DPP-4 Inhibitors?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

GLP-1 Agonists?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

TZDs?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

Sulfonylureas?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

No additional medications?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

Question 9.

Given a patient currently taking metformin ER 1000mg BID with an A1c of 6.5% at high risk for ASCVD (age 55 or older with coronary, carotid, or lower extremity artery stenosis) but otherwise healthy, rate the likelihood with which you would prescribe the following:

SGLT-2 Inhibitors?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

GLP-1 Agonists?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

Sulfonylureas?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

TZDs?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

DPP-4 Inhibitors?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

No additional medications?

- A. Extremely likely
- B. Likely
- C. Unlikely
- D. Extremely unlikely

10. Thank you very much for taking the time to complete the survey. Please enter any general comments you have on the medications, survey questions, or cases.