

**Semaglutide Added to Type 2 Diabetes Mellitus Treatment for Improvement in
Hemoglobin A1c**

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DNP Quality Improvement Project

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Abstract

Background: The Centers for Disease Control and Prevention has identified Type 2 diabetes mellitus (T2DM) as a leading cause of death in the United States. More than 37 million people in the United States currently carry this diagnosis. Metformin and a low carbohydrate diet are currently first-line treatments for T2DM. Glucagon-like peptide 1 receptor agonists, for example, semaglutide, can be introduced to reduce circulating levels of hemoglobin A1c (HbA1c). The goal of this quality improvement (QI) project is to add semaglutide to reduce HbA1c levels to below 7.5% in T2DM patients managed with metformin alone. After completing a ten-day assessment to evaluate my current practice, a review of the evidence-based literature was performed to identify opportunities to improve the care provided to my T2DM patients.

Approval by my employer was obtained. In my current practice, patients diagnosed with T2DM are provided with education on the importance of a low carbohydrate diet and weight loss and started on metformin. Results from the literature review suggested that semaglutide (0.25 mg subcutaneously delivered weekly) might be effective at reducing circulating HbA1c levels in these patients. The resulting eight-week QI project focused on reducing circulating HbA1c levels and improving overall health and quality of life in this patient population.

Methods: The Plan-Do-Study-Act (PDSA) model was used in the design of this QI project. The QI project was conducted over eight weeks at Village Medical in El Paso, Texas. Baseline assessments, including patient medical histories and HbA1c levels, were obtained before initiating the new intervention. HbA1c levels were re-evaluated in our office four weeks after initiating semaglutide therapy. The patients were also provided with education on low carbohydrate diets, portion control, and the importance of cardiovascular exercise. Reassessments and adjustments were made as appropriate.

Intervention: Based on evidence from the literature review, semaglutide was provided to patients diagnosed with T2DM to reduce circulating levels of HbA1c. The QI project utilized the RE-AIM framework because it promotes health and translates evidence into practice for the management of chronic diseases.

Results: Fifteen patients (five males and ten females, aged 43–69 years) met the inclusion criteria for this study with baseline HbA1c levels ranging from 7.5–10.7%. At the end of the four-week trial, all patients exhibited improvements in Hb1Ac levels. Eleven patients met the stated goal and achieved levels of HbA1c that were below 7.5% (i.e., at 6.8–7.4%). The three remaining patients also presented with reduced HbA1c levels but did not meet this specific goal. One patient reported that the medication was not used as directed. Patients also reported that they were more successful at following a low carbohydrate diet and increasing exercise than they had been previously.

Conclusions: In this QI project, semaglutide was added to a pre-existing metformin regimen to reduce HbA1c levels to <7.5% in patients with T2DM to improve their overall health.

Reductions in HbA1c levels may be associated with weight loss as well as reductions in blood pressure, cardiac risk factors, and the risk of kidney injury. Providing patients with evidence-based interventions and ongoing guidance will improve their overall health.

Keywords : Type 2 Diabetes Mellitus, Semaglutide, Ozempic®, Adult, Hemoglobin A1c

Semaglutide Added to Type 2 Diabetes Mellitus Treatment for Improvement in Hemoglobin A1c

The United States Centers for Disease Control and Prevention has identified Type 2 diabetes mellitus (T2DM) as a leading cause of death in the United States (US). More than 37 million people in the US currently carry this diagnosis (CDC, 2022). Individuals with this disease are at risk for developing ischemic heart disease, neuropathy, stroke, renal disease, and vascular problems that may lead to the need for a lower extremity amputation (Adults with diabetes, 2020). Early detection and management are critical for reducing T2DM-associated risks and disease complications. Metformin is currently considered the first-line treatment for T2DM. When added to this treatment regimen, glucagon-like peptide 1 (GLP-1) receptor agonists, including semaglutide, can lead to further reductions in hemoglobin A1c, promote weight loss, and reduce the risk of developing cardiovascular sequelae (Wexler, 2022).

In 2020, 16.9% of the adults (ages 45–75 years) in El Paso County carried a diagnosis of T2DM. El Paso has a large Hispanic population and a high poverty rate and generally lacks many critical resources. Taken together, these factors contribute to the prevalence of patients at risk and can have a profound effect on their health outcomes. Patients must have adequate education and resources available to them if they are to be successful in managing their own care. Services that offer classes focused on meal planning, exercise, and medication management are crucial for all patients diagnosed with T2DM (Adults with diabetes, 2020)

Problem Description

Village Medical is a primary care clinic in El Paso, Texas that focuses on providing value-based care. Providers and patients at this clinic work together to develop treatment plans, educational programs, and prevention strategies. In my practice, I provide primary care for

adolescents, adults, and seniors (i.e., geriatrics). A reflective evaluation highlighted uncontrolled T2DM as the most critical issue in my practice. The approved treatment plan, which included metformin and a low carbohydrate diet, was not effective at reducing circulating HbA1c levels in my patients. Results from a literature review highlighted an evidence-based intervention that featured the addition of semaglutide (0.25 mg subcutaneously [SQ] once each week) as an effective treatment for adult patients with T2DM.

Available Knowledge

A recent meta-analysis published by Zaazouee et al. (2022) assessed the safety and efficacy of semaglutide compared with placebo and other anti-hyperglycemic agents for the treatment of T2DM. The study followed the PRISMA guidelines and included results from 26 randomized controlled trials that evaluated the impact of subcutaneous semaglutide *versus* tirzepatide, liraglutide, sitagliptin, canagliflozin, empagliflozin, and placebo. Sample sizes ranged from 37 to 1231 patients treated with semaglutide (0.25 or 1 mg SQ weekly) with follow-ups ranging from 4 to 30 weeks in each study. The mean ages of these patient cohorts were 52.8–71 years with baseline HbA1c levels of 7.3–8.7%. Administration of SQ semaglutide (0.25 mg dose) resulted in a more substantial reduction in HbA1c levels (as much as 1.9%) and lower fasting blood glucose levels compared to those achieved in response to other agents. Semaglutide was also superior to other antihyperglycemic agents for controlling routine glucose levels and promoting weight loss. The adverse effects reported (gastrointestinal) were comparable to those resulting from placebo administration (Zaazouee et al., 2022).

Another study reviewed the SUSTAIN 2,3,8 and PIONEER 2 trials and compared the efficacy of once-weekly semaglutide (1 mg) to once-daily empagliflozin (25 mg) in T2DM patients who were inadequately controlled on metformin. Results of this study revealed that

once-weekly semaglutide led to significant reductions in mean HbA1c and body weight compared to empagliflozin, both with all P values < 0.0001. Furthermore, an indirect comparison of these two drugs suggested that once-weekly semaglutide (1 mg SQ) led to more profound reductions in HbA1c than once-daily empagliflozin (Lingvay et al., 2020). This study included 995 patients treated with once-weekly semaglutide and 410 patients on once-daily empagliflozin. The results of this study revealed that a significantly larger proportion of the patients treated with semaglutide achieved HgbA1c levels >1% and <7% compared to those treated with empagliflozin, with no severe hypoglycemia. Patients with disease that was not controlled with metformin alone responded to once weekly semaglutide (1 mg) with reductions in baseline HbA1c and body weight evaluated one year later. This regimen also led to reductions in body mass index, waist circumference, total cholesterol, and cardiovascular risk (Lingvay et al., 2020).

The next publication that was evaluated for this project was a meta-analysis that assessed the efficacy and safety of semaglutide that included the results of six placebo-controlled and seven active-controlled RCTs. The studies included a total of 9501 participants ranging in age from 52.7–65 years of age with HbA1c levels from 7.5–8.7% who received drug treatments for up to 12 weeks. Overall, semaglutide resulted in superior anti-hyperglycemic efficacy compared to other agents, including sitagliptin, exenatide, liraglutide, dulaglutide, and insulin glargine. Furthermore, semaglutide (0.5 mg SQ once weekly) reduced circulating HbA1c levels by 1.01–1.38% compared with placebo; no hypoglycemic events were reported. Semaglutide was more effective compared to sitagliptin, insulin glargine, or any other GLP-1 receptor agonists. Semaglutide also had beneficial effects on body weight and systolic blood pressure. Adverse effects that were reported included gastrointestinal events and acute pancreatitis in seven patients (Andreadis et al., 2018).

Another meta-analysis was conducted to assess the effects of SQ and oral (PO) semaglutide in patients with T2DM and to identify any improvements in glycemic control and weight management. The study analyzed results from 22,185 patients who participated in 24 clinical trials. The results revealed that treatment with SQ semaglutide led to reductions in HbA1c levels between 1.14–1.37% compared to placebo. Furthermore, more of the patients treated with SQ and PO semaglutide achieved their HbA1c goals (Zhong et al., 2021).

The final study reviewed for this QI project was REALISE-DM, which provided the first real-world evidence of the effectiveness of semaglutide in T2DM patients who were managed with other GLP-1 RA medications. A head-to-head comparison revealed that semaglutide was superior to both liraglutide and dulaglutide. In this study, reductions in HbA1c of 0.65% over six months were observed among a cohort of 164 patients that switched to semaglutide from another drug regimen (Jain et al., 2021).

Rationale

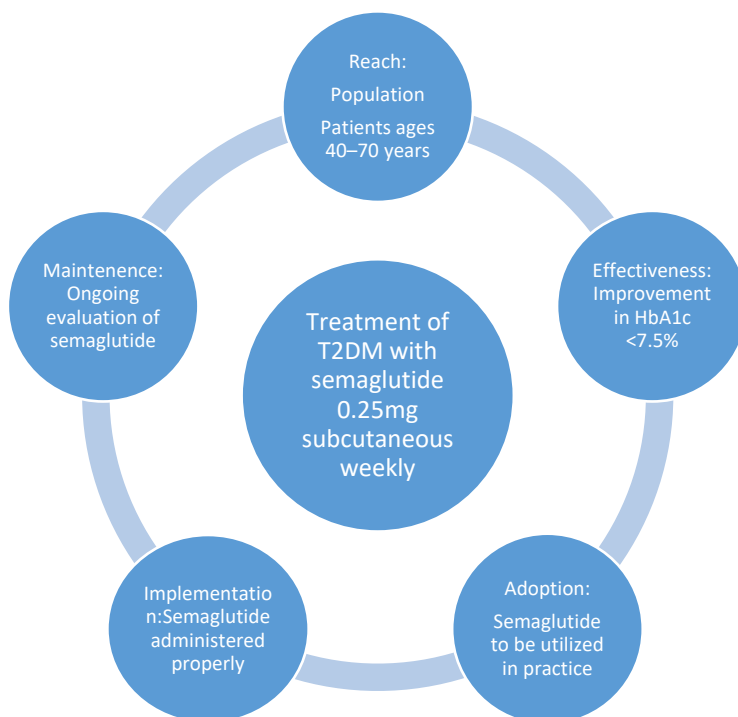
The Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) model is a framework that was developed by Glasgow, Voght, and Boles in 1999 that supports the QI project by promoting human health and translating science into practice in disease management. The RE-AIM model utilizes the nursing process when evaluating and applying a new intervention. The model focuses on a target population, assesses barriers, and allows providers to apply knowledge and develop a patient-specific plan (White et al., 2016).

The first step known as “Reach” allows the provider to screen patients diagnosed with T2DM to identify those who fulfill the inclusion criteria. The next step is “Effectiveness” which permits the provider to determine whether the new intervention is likely to make a positive change. For example, once the provider performs a literature review, evidence-based practice

will document the effectiveness of GLP-1 receptor agonists for the treatment of T2DM. This is followed by “Adoption” which focuses on how the new intervention will be utilized by the practice. Once the provider introduces the new intervention and HbA1c levels improve, the practice may consider the positive impact on patient outcomes. The next step is known as “Implementation”; in this step, the provider determines whether the intervention is being delivered properly. For example, in this case, the provider will work with the patients to ensure the appropriate administration of semaglutide. Tolerability will also be monitored. The final step is “Maintenance” in which the impact of the new intervention is evaluated over time. The provider will schedule follow-up appointments with their patients to determine whether the administration of semaglutide has resulted in improvements in circulating HbA1c levels and to address any adverse effects. The provider can also educate the patient on how to maintain the HbA1c at the goal level over the long term (Glasgow et al., 2019).

Figure 1

Adapted RE-AIM model: a Visual Framework for Treatment of Type 2 Diabetes Mellitus



Specific Aims

The QI project described in this manuscript was conducted to determine if the addition of semaglutide to the current treatment regimen for T2DM patients will reduce circulating HbA1c levels to <7.5%. Evidence-based practices described in the literature indicate that adding semaglutide (0.25 mg SQ once per week) will reduce HbA1c levels in patients who are already taking metformin and thus improve the treatment of T2DM for patients in my clinical practice. Superior HbA1c control will lead to an improved overall quality of life and may lead to reductions in body weight and associated risk factors.

Methods

Context

This quality improvement project was implemented at Village Medical in El Paso, Texas. The goal was to reduce circulating HbA1c levels by adding semaglutide (0.25 mg SQ weekly) to a pre-existing antidiabetic regimen as per evidence-based practice. The QI project received

approval from my workplace on October 27, 2022, and approval from the University of Texas at El Paso (UTEP) Institutional Review Board (IRB) on November 21, 2022. The QI project began on January 16, 2023, and ended on March 10, 2023. Patients who met the criteria described below were included in the study. The new intervention was initiated, and follow-up appointments were scheduled to address its safety and efficacy.

Interventions

The QI project began on Monday, January 16, 2023, with a ten-day practice improvement assessment. During this period, I assessed all the patients seen at my clinic at Village Medical and reviewed current diagnoses, laboratory results, and treatment plans. Data were collected and reviewed to determine what needed to be changed or improved. I decided to focus on improving protocols used for T2DM care because many of the patients in my practice remain uncontrolled. Many factors contribute to this observation, including problems with medication adherence, lack of education on the importance of medication, access, and cost, as well as poor diet and lack of exercise.

My review identified 79 patients who were seen at my clinic over the ten-day reflective practice period. These patients ranged from 20 to 94 years of age. Of this group, 15 patients were diagnosed with T2DM and other chronic conditions, including hypertension and hyperlipidemia. I reviewed their conditions, medications, laboratory results, and demographics, and identified three opportunities for improvement. As my practice includes both adult and geriatric patients who present for wellness visits with chronic conditions, including type 2 diabetes, hypertension, hyperlipidemia, and obesity, I developed three PICOT questions from the data I collected and presented them to my Doctor of Nursing Practice (DNP) chair. I chose the one PICOT question that I believed would have the largest impact on my practice:

Population: Patients 40–70 years of age diagnosed with T2DM with uncontrolled hemoglobin A1c (>7.5) despite daily metformin (500 mg ER)

Intervention: Add semaglutide 0.25 mg SQ once each week.

Current Practice: Provide handouts describing low carbohydrate diets, portion control, and cardiovascular exercise. Advise patients on strategies to promote weight loss and increase metformin and/or add semaglutide 0.25 mg SQ once per week.

Outcomes: Hemoglobin A1c levels <7.5%

Time: 30 days

I began my literature review with a search for the most up-to-date discussion of the treatment of adult T2DM. I searched the CINAHL, Medline, and PubMed databases for materials published from 2018–2022. The search terms used included type 2 diabetes mellitus, adult, semaglutide, Ozempic, and uncontrolled hemoglobin A1c. I identified 67 articles from my search of CINAHL, 43 from Medline, and 37 from PubMed. I reviewed the publications and narrowed the list down to the 16 with the highest quality of evidence, including randomized controlled trials, systematic reviews, and meta-analyses.

After collecting the relevant evidence-based literature, the QI Project underwent the following steps that were required to complete the process. As a first step, the project was approved by my work site supervisor on October 27, 2022. A practice improvement proposal was then submitted to the UTEP IRB and was approved as a non-research QI project on November 21, 2022. I was then able to proceed with my QI project which focused on the impact of adding semaglutide to treatment plans established for adults with T2DM with HbA1c levels > 7.5. The addition of semaglutide resulted in significant reductions in HbA1c with few adverse effects.

I used the Plan-Do-Study-Act (PDSA) cycle to implement the QI project. The four categories of the PDSA model are as follows: (1) Plan, i.e., describe the process; (2) Do, i.e., carry out the new intervention; (3) Study, i.e., assess and evaluate the results to identify specific improvements; and (4) Act, i.e., reflect on the outcomes (Harris et al., 2020). As part of this QI project, semaglutide (0.25 mg SQ weekly) was added to the current treatment regimens of patients with T2DM. The following depicts how this cycle was implemented (Figure 2):

Plan: I identified T2DM patients in my practice who were between 40–70 years of age with HbA1c levels >7.5.

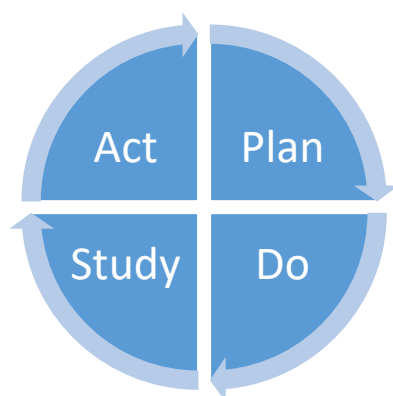
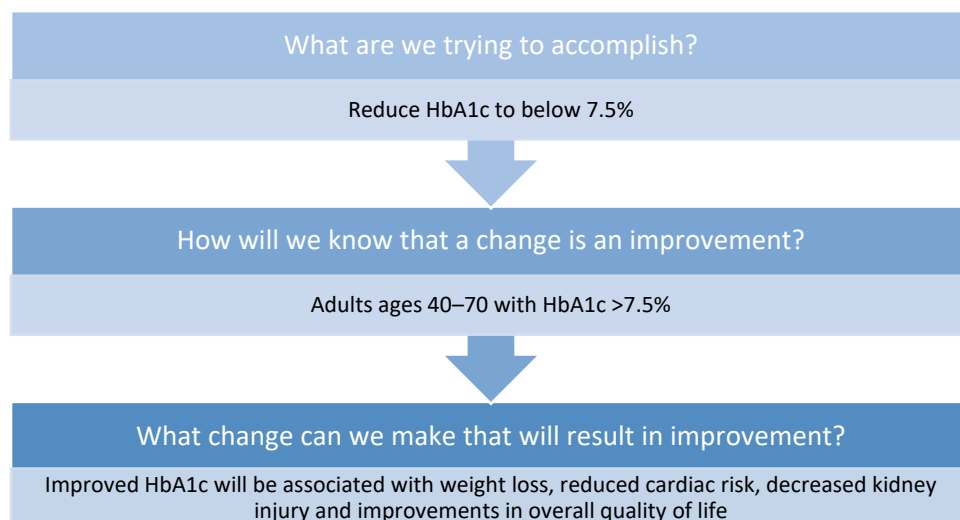
Do: From this cohort, I identified patients who were already taking metformin (500 mg ER). I added semaglutide (0.25 mg SQ weekly) to these patients' drug regimens, gave them drug samples, and scheduled follow-up visits in four weeks.

Study: I reviewed the HbA1c results at the four-week follow-up visit and compared them to the baseline results.

Act: I determined whether this intervention resulted in improved HbA1c levels and if patients exhibited any adverse effects in response to the new medication. Adjustments to the care plans were made as appropriate.

Figure 2

PDSA cycle: Developing New Interventions for T2DM (IHI, 2023).



Study of Interventions

This QI project was implemented in my office for a total of eight weeks starting on January 16, 2023. I screened all patients in my office over 20 days. The study included adults 40–70 years of age with T2DM and an HbA1c level >7.5% who were already on metformin. Fifteen of my patients met these criteria and were identified as part of the screening process. Each patient enrolled in the study was provided with a 0.25 mg sample of semaglutide together with instructions on how to administer medication. Patients were also advised regarding possible adverse effects. Each patient was also provided with instructions on following a low carbohydrate diet and advised regarding participation in cardiovascular exercise. Patients were

instructed to follow up in four weeks for a repeat HbA1c and all questions were addressed. Patients were urged to call the office if any issues with medications emerged. Once the follow-up review was completed, I evaluated each patient to assess tolerability and identify any adverse effects associated with medication. Patients were also provided with the results of the HbA1c test at that time. The impact of any dietary improvements was also evaluated. The RE-AIM framework was used to support this project to promote change and improve patient outcomes. The PDSA cycle was used to assess, implement, and evaluate the results and the need for future adjustments using the new evidence-based intervention.

Measures

Semaglutide was shown to be effective at reducing HbA1c levels after four weeks as an evidence-based intervention. Baseline HbA1c levels were monitored and then reevaluated four weeks after the implementation of the new intervention to ensure effectiveness. The second measurement was performed during the follow-up appointment, at which time any issues or problems with medication, cost, and the patient's overall experience with the new intervention were addressed.

Analysis

HbA1c levels measured both pre- and post-intervention were presented quantitatively. The data were analyzed using line graphs to evaluate potential improvements and compare the results after four weeks on a per-patient basis (Figure 3). The screening process identified fifteen patients (five males and ten females) between the ages of 43–69 years who met the inclusion criteria. At the end of the projected, 11 patients had met the goal of HbA1c levels <7.5%. By contrast, three patients exhibited reductions but did not meet the goal and one patient reported that medication had not been administered as directed.

Ethical Considerations

Careful monitoring of HbA1c levels at baseline and at follow-up appointments was essential to maintain a focus on the goal. Patients 40–70 years of age who were diagnosed with T2DM with HbA1c levels $>7.5\%$ were eligible to participate in the QI project. Patients who met these criteria were introduced and educated on the new intervention that was developed using evidence-based practice. The patients were also provided with information on the potential adverse effects of these medications and safety warnings. The goal of treatment was discussed, and all questions and concerns were addressed. Thus, patients were provided with the capacity to make informed decisions and were advised on alternative potential interventions.

No conflicts of interest or information arose during the performance of this QI project. All patient data for the project were collected and reviewed and were then used to update their electronic health records. De-identified patient data were collected and stored on my personal computer which was kept in a locked drawer in my office.

Results

Fifteen patients who were 43–69 years of age met the inclusion criteria for this QI project. Baseline HbA1c levels were determined and reviewed with each patient. Semaglutide therapy was initiated, and each patient was provided with instructions on following a low carbohydrate diet. Four-week follow-up appointments were scheduled for repeat HbA1c assessments. At the follow-up appointment, patients' questions were answered and they were informed of the second HbA1c result. Adverse effects and/or concerns with medications were also addressed at that time. Eleven of the original 15 patients met the goal, which was an HbA1c level $<7.5\%$. (Figure 3). The average HbA1c levels determined before and after the intervention were 8.1% and 7.3%, respectively. Three patients who did not achieve the target goal did exhibit

reduced HbA1c levels. One patient did not take the medication as directed. After completing the project, all patients who took semaglutide exhibited reductions in HbA1c levels, although not all got below the goal. Thus, the results of the QI project revealed that this medication is effective at reducing HbA1c levels. If they were provided with a longer timeframe, more patients would most likely reach this goal.

The PDSA cycle and RE-AIM model were used during the QI process. The PDSA cycle is an effective tool for this project because it permits a new intervention to be introduced using evidence from the literature and adjusted as needed in response to quantitative findings and feedback from the patient. The cycle can be repeated once the data is analyzed, and adjustments are made. At the end of the project, 73% of patients exhibited reductions in HbA1c levels to <7.5% as shown in Figure 4. A full 93% of patients who started the medication as instructed exhibited reductions in HbA1c levels (Figure 5). Thus, semaglutide was shown to be effective at reducing circulating HbA1c levels of T2DM patients in this setting when added to a preexisting metformin-based treatment plan.

Figure 3 *Circulating levels of HbA1c at Baseline and Follow-up*

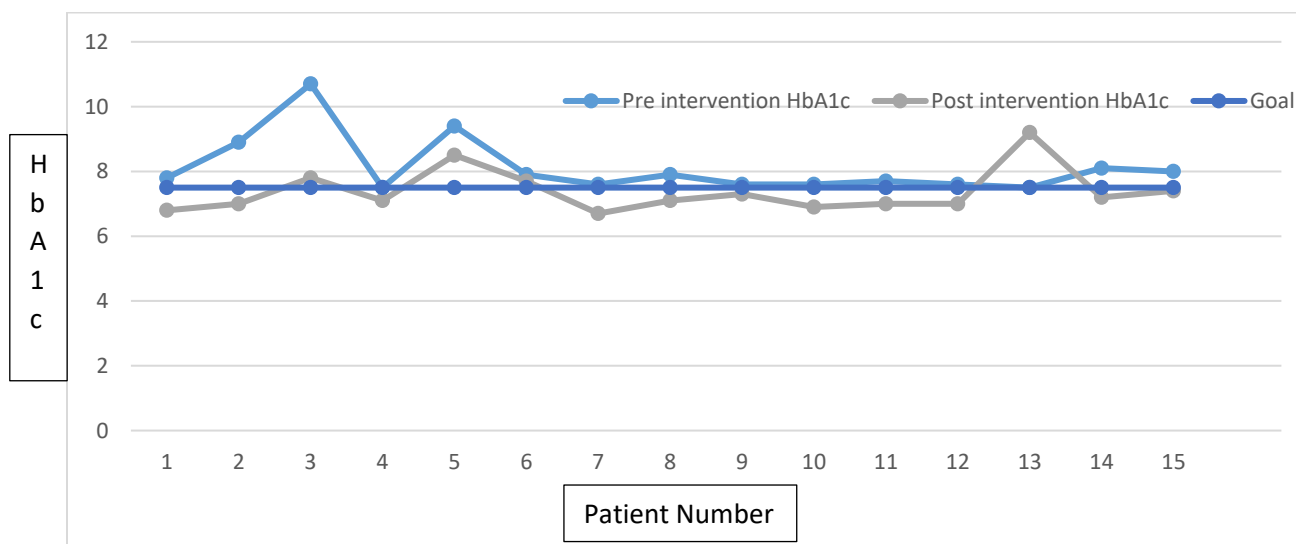
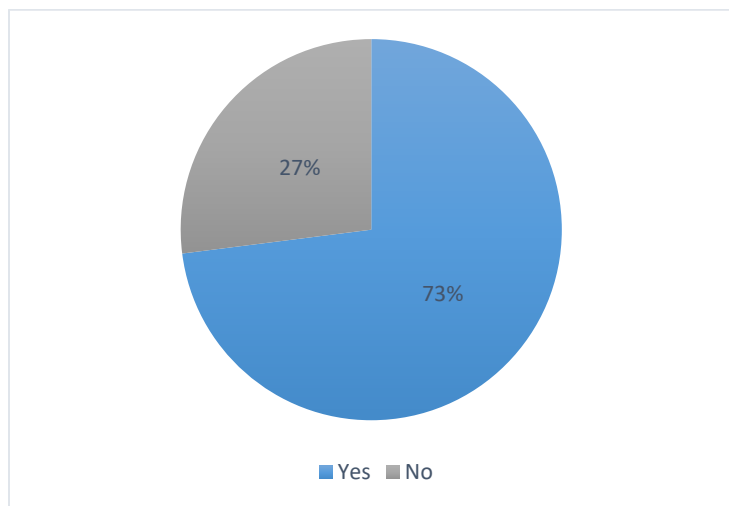


Figure 4

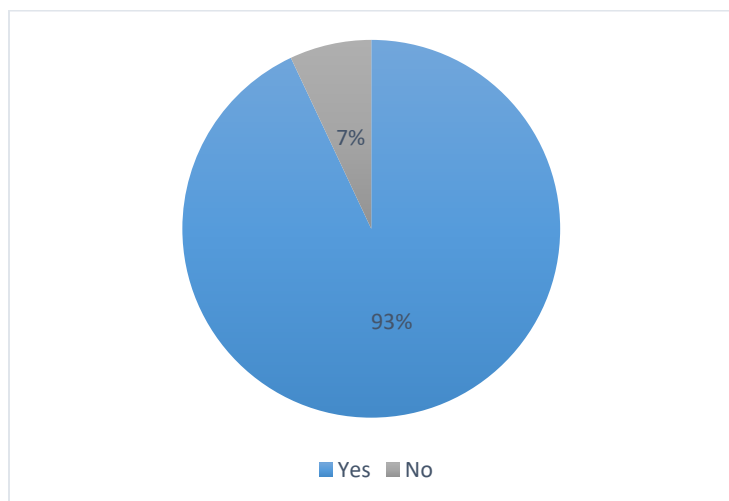
Percentages of Patients Who Responded to Semaglutide Treatment with Reductions in Circulating HbA1c to <7.5%



Note. N=15 patients

Figure 5

Percentages of Patients Who Responded to Semaglutide Treatment with Reductions in Circulating HbA1c



Note. N=14 patients.

Discussion

Summary

The results of this QI project revealed that semaglutide was effective at reducing HbA1c levels among patients in my practice. The introduction of semaglutide also resulted in weight loss, fewer cardiovascular events, and a reduced risk of developing kidney disease. The findings from this QI project support the evidence-based effectiveness of semaglutide and its role in improving patient outcomes and overall quality of life.

Interpretation

Patients who began taking semaglutide as directed exhibited reductions in circulating levels of HbA1c. The patients treated with semaglutide also reported improvements in home blood glucose monitoring and were more conscientious with respect to dietary decisions, notably intake of carbohydrates and sugar. They reported several medication-associated adverse effects, including nausea and upset stomach that improved over time. I was able to supply most of the patients with samples of semaglutide to reduce costs. Overall, the patients showed initiative in their efforts to become more healthy and were pleased with the results of the new evidence-based intervention.

Limitations

The QI project was implemented at Village Medical primary care clinic in El Paso, Texas. The intervention requires follow-up visits to evaluate data to maintain consistency and sustainability. Thus, these findings may not be generalizable to an inpatient setting. This intervention might be effective in other specialties and different settings if follow-up can be maintained. Another limitation is the timeframe used in this QI project. Semaglutide may require 90 days to demonstrate full effectiveness at reducing circulating HbA1c. Implementing this

intervention and evaluating the results over a longer time frame may permit all patients to reach target HbA1c levels.

Conclusions

The QI project was conducted to improve treatments for T2DM patients in my practice using an evidence-based intervention. Results from a literature review revealed that semaglutide was superior to other GLP-1 RA-type medications at reducing circulating levels of HbA1c. This new intervention can be maintained with frequent follow-up appointments to review patient data, address issues, and make adjustments as necessary. Ongoing efforts to work collaboratively with these patients will improve outcomes and overall quality of life.

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