GLP-1 AGONISTS AND TYPE 2 DIABETES HEALTH OUTCOMES AMONG RURAL PATIENTS

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Doctor of Nursing Practice
by
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GLP-1 AGONISTS AND TYPE 2 DIABETES HEALTH OUTCOMES AMONG RURAL PATIENTS

The increasing prevalence of type 2 diabetes in developed countries is a predominant chronic health issue for more than 34 million Americans, with an annual cost in the United States of $327 billion dollars and mortality rate of around 103,000 (Centers for Disease Control and Prevention, 2023; CDC, 2022). Many of these patients find the rigorous treatment regimen for type 2 diabetes difficult to follow. The complexity of diabetes treatment often translates into many patients having poor adherence to the medication regimen and resulting in multi-organ/system complications (Rezaei et al., 2019). For patients with type 2 diabetes, medication adherence ranges anywhere from 36% to 93%, with compliance being influenced by a wide variety of factors (Aloudah et al., 2018). These factors include the complexity of the medication regimen, social influences, changes to lifestyle, level of knowledge regarding diabetes and its management, and self-management strategies including the use of digital health tools (Aloudah et al., 2018). As a whole, in type 2 diabetics, poor medication compliance results in poorer health outcomes which directly relates to increased morbidity and mortality rates. High rates of medication adherence however, relate to positive outcomes for patients with type 2 diabetes such as improved HgbA1c, reduced weight, and improved quality of life (Patel et al., 2019; Aloudah et al., 2018).

Many patients in the rural setting have adverse health outcomes associated with type 2 diabetes related to poor medication adherence due to complex medication regimens, cost of medications, and lack of knowledge regarding medications; or failure of the medication regimen to accurately manage their condition. For patients in the rural setting, a potential solution for poor patient outcomes related to inadequate treatment and disease management would be the integration of Glucagon-like Peptide-1 (GLP-1) agonists, such as dulaglutide and semaglutide. Weekly dosing with GLP-1 agonists has been associated with better adherence as opposed to other medication regimens dosed daily (Weeda et al., 2021). GLP-1 agonists also have the potential to provide cardiovascular benefits and lower HgbA1c and weight, all while having a lower risk of hypoglycemic events (Trujillo et al., 2021; Weeda et al., 2021).

Statement of Purpose

The purpose of this quality improvement (QI) project was to evaluate the relationship between GLP-1 agonist use and health outcomes in rural patients who are currently being treated for type 2 diabetes. The project objectives relate to the following PIOT question: In rural patients with type 2 diabetes (P) how does an existing medication program using GLP 1 agonists (I), affect HgbA1c levels, weight, and blood pressure (O) over the course of a year (T)?

The primary objectives of this project are:
1. 10% decrease in mean HgbA1c from T1 to T2
2. 5% decrease in mean weight from T1 to T2
3. 2.5% decrease in mean systolic blood pressure from T1 to T2
4. 2.5% decrease in mean diastolic blood pressure from T1 to T2

Review of Literature

A literature review was performed to identify how GLP-1 agonists affect health outcomes for patients with type 2 diabetes in rural settings. Primary research articles, published in peer-reviewed journals, in English, between the years 2013 and 2022, were searched through the following databases: PubMed, CINAHL, and Google Scholar. Medical Subject Heading (MeSH) search terms included type 2 diabetes and rural population. 8,480 studies were located, and 1,345
studies remained after merging duplicates. Exclusion criteria included: lack of screening tool reliability and validity, no discussion of barriers to type 2 diabetes care, and no mention of methods to overcome barriers to type 2 diabetes management. After exclusion, 13 studies were chosen for review. The critical review of the literature found the following themes: barriers and strategies to implementation of GLP-1 agonists, and GLP-1 agonist's effect on weight, blood pressure and HgbA1c levels. The reliability and validity of the study findings discussed should be highly regarded as the studies predominantly included in this appraisal are meta-analyses and randomized controlled trials (RCTs). The reliability and validity of the study findings discussed within this literature review should be considered with high regard as the studies predominantly included in this appraisal are meta-analyses and randomized controlled trials.

**Barriers and Strategies to Implementation of GLP-1 Agonists.** Six of the studies, three randomized control trials, two meta-analyses, and one qualitative study, in this review discussed barriers and strategies to GLP-1 agonists implementation. Glenn et al. (2019) and Polonsky et al. (2021) point out that barriers to type 2 diabetes management and GLP-1 agonists implementation include cost of treatment and disparities in healthcare associated with rural populations and patients with lower socio-economic status. Qin et al. (2017) and Thieu et al. (2019) state that patients consider many factors when deciding to initiate treatment with a GLP-1 agonist and that these factors include the effectiveness of the medication, side effects, frequency of dosing, and delivery device used. Bagepally et al. (2020) and Weeda et al. (2021) discussed strategies regarding implementation of GLP-1 agonists and concluded that patients preferred weekly dosing. They found that once weekly dosing was directly related to increased medication adherence.

**GLP-1 Agonists Effect on Weight and HgbA1c.** Four of the studies, two randomized control trials, one meta-analysis, and one cohort study, in this review addressed the effects of GLP-1 agonists on weight and HgbA1c. Hansen et al. (2021) and Seino et al. (2017) concluded that semaglutide use led to significant reductions in body weight and HgbA1c when used both independently and as compared to sitagliptin. Pasquel et al., (2021) noted that liraglutide compared to insulin glargine use, resulted in improved glycemic control and increased weight loss. Relating strictly to weight loss, Blundell et al. (2017) determined that semaglutide usage led to reductions in body fat, as well as overall weight, and was associated with decreased food-cravings, decreased preference for high fat foods, and increased control of eating.

**GLP-1 Agonists Effect on Blood Pressure.** Three of the studies in this review, two meta-analysis and one cohort study, examined the relationship between GLP-1 agonists and blood pressure. Leiter et al. (2020) and Longato et al. (2020) point out that GLP-1 agonists can reduce blood pressure as compared to insulin, sulfonylureas, and placebos and can help lead to improved cardiovascular outcomes for patients. Goldman (2020) found that dulaglutide, exenatide, and semaglutide all helped to lower mean systolic blood pressure, as compared to alternative medication regimens.

Type 2 diabetes is a very prevalent problem among rural populations and as the literature suggests, the health outcomes of these patients stand to greatly benefit from the implementation of GLP-1 agonists. As examined in this literature review, the current body of evidence details many of the potential beneficial effects of GLP-1 agonists for the treatment of type 2 diabetes. These health-related benefits are related to weight management, HgbA1c levels, and blood pressure readings.

**Methods**
**Project Design.** This project evaluated an existing treatment option for type 2 diabetes that is being utilized by a rural health clinic. In order to evaluate this treatment option, data concerning HgA1c, weight, and blood pressure was obtained from the electronic medical record for adult patients with type 2 diabetes pre and post taking a GLP-1 agonist. This data was collected over a period of time from January 2023 to June 2023 (T1) and from July 2023 to December 2023 (T2), in order to determine the effect of GLP-1 agonists on health outcomes for patients in a rural setting.

**Intervention.** A rural health clinic began utilizing GLP-1 agonists as a treatment option for patients in 2020. GLP-1 agonists have many potential benefits for patients with type 2 diabetes and have been more frequently prescribed at the clinic with the hope of improving health outcomes. Evaluation as to the actual effectiveness of GLP-1 agonists in relation to health outcomes for patients with type 2 diabetes had not previously been formally conducted, however data regarding these factors existed within the electronic medical record (EMR) and was obtained to determine the advantages/disadvantages to implementing GLP-1 agonists for patients in a rural area, as they pertain to HgA1c, weight, and blood pressure.

**Setting.** The setting is a Mid-Western rural primary care health clinic located in Potosi, Missouri.

**Participants.** The target population of this project is a purposive convenience sample of adult patients seen at the rural health clinic. Inclusion criteria includes being 18 years of age or older and having a diagnosis of type 2 diabetes. Exclusion criteria includes being younger than 18 years of age, not having a diagnosis of type 2 diabetes, or contraindications for GLP-1 use. Demographic information that was collected includes the patient’s gender and age.

**Sampling.** For the project’s chart review, a report was generated from the facility that included a list of all patients that meet the inclusion criteria. A confidence interval of 95%, a maximum margin of error of 5%, a population size of 25, and a response distribution of 50 was utilized to review a minimum of 20 charts at each time point (Raosoft, 2004). These 20 charts were chosen by simple random sampling from a list of eligible patients at T1 and T2.

**Measurement Tools and Data Analysis.** Data analysis and chart review consisted of a random selection of patients meeting inclusion criteria during the expected timeframe. Data from the charts to be reviewed was entered into a Statistical Package for Social Sciences (SPSS) database. Additionally, 5% of the data was used by the project investigator for verification of data.

The chi-squared was utilized to analyze nominal level data, while the independent t-test and paired sample t-test were employed to analyze ratio level. Measures of clinical significance, such as odds ratio, effect size, and 95% confidence interval, were also computed. Statistical significance was defined as $p \leq .05$.

The main objectives of the project were measured as follows:

- Descriptive statistics will calculate different percentage rates regarding mean HgbA1c, mean weight, mean systolic blood pressure, and mean diastolic blood pressure as they pertain to patients prior to and after taking a GLP-1 agonist.

**Ethical Considerations.** Ethical considerations for this project include the protection of patient’s personal health information in accordance with the Health Insurance Portability and Accountability Act (HIPAA). University of Missouri institutional review board (IRB) and project site approval were obtained prior to initiating the project. Preservation of patient confidentiality and privacy was accomplished through only accessing EMR data from a secure
workstation at the facility, utilizing existing EMR patient protection software within the facility, and entering only nonidentifying data into the project record. Aggregate form was used for project information and patient identifiers were excluded. This project poses little risks to patients in that it seeks to evaluate an existing measure within the facility. The numerous benefits of the project outweigh potential risks, as they include the potential to improve the health outcomes of patients with type 2 diabetes and the quality of care that is provided.

Results

Demographics

This project had 22 participants that met all of the inclusion criteria and for which data was available for T1 and T2. All 22 participants were included in the demographic analysis. Of the 22 participants, five were male (23%) and 17 were female (77%). The predominant age group for participants was 40-49 years old with five subjects (23%) falling into this category. This was followed by 20-29 with four subjects (18%), 30-39 with four subjects (18%), 50-59 with four subjects (18%), 60-69 with four subjects (18%), and finally 70-79 with one subject (5%). The predominant insurance carried by participants was United Healthcare with seven subjects (32%) utilizing this company. This was followed by Medicaid with five subjects (23%), no insurance carrier with four subjects (18%), Anthem Blue Cross Blue Shield with two subjects (9%), Medicare with two subjects (9%), and Cigna with two subjects (9%). The participants were split equally between type of GLP-1 agonist with 11 subjects (50%) utilizing dulaglutide and 11 subjects (50%) utilizing semaglutide.

Statistics

**Pre and Post GLP-1 Agonist Use.** A paired-samples T test was utilized to analyze differences between HgbA1c, weight and blood pressure both pre and post taking a GLP-1 agonist at T1 and T2 respectively. A statistically significant decrease was found for weight from T1 ($M = 213, SD = 54.23$) to T2 ($M = 202.4, SD = 53.02$) ($t(21) = 3.39, p = .003, d = 0.7$). A statistically significant decrease was also found for systolic blood pressure from T1 ($M = 125, SD = 13.94$) to T2 ($M = 120.3, SD = 13.47$) ($t(21) = 2.08, p = .05, d = 0.4$). While not statistically significant, there was a small to moderate decrease in HgbA1c from T1 ($M = 7.1, SD = 2.07$) to T2 ($M = 6.6, SD = 1.80$) ($p = .08, d = 0.4$). No differences were noted for diastolic blood pressure from T1 ($M = 75.2, SD = 9.89$) to T2 ($M = 75.6, SD = 10.23$) ($p = .84, d = 0.04$).

**Comparison Between Dulaglutide and Semaglutide.** An independent-samples T test was utilized to analyze differences between HgbA1c, weight and blood pressure both pre and post taking dulaglutide and semaglutide at T1 and T2 respectively. A statistically significant decrease in mean BP was found for diastolic blood pressure at T1 between participants prior to starting dulaglutide ($M = 79.3, SD = 11.43$) and semaglutide ($M = 71.1, SD = 6.16$), with those in the semaglutide group having a lower mean diastolic blood pressure prior to starting the medication ($t(20) = 2.09, p = .05, d = 0.9$). While not statistically significant, there was a small to moderate increase in mean HgbA1c between participants prior to starting dulaglutide at T1 ($M = 6.8, SD = 2.06$) and participants prior to starting semaglutide at T1 ($M = 7.5, SD = 2.12$), with those in the semaglutide group having a higher mean HgbA1c prior to starting the medication ($p = .48, d = 0.3$). A small to moderate increase in mean HgbA1c, that was not statistically significant, was present for participants taking dulaglutide at T2 ($M = 6.4, SD = 1.43$) and participants taking semaglutide at T2 ($M = 6.8, SD = 2.16$), with those in the semaglutide group having a higher mean HgbA1c after taking the medication ($p = .54, d = 0.3$). There was also a small to moderate decrease that was not statistically significant for mean weight between
participants taking dulaglutide at T2 \((M = 209.6, SD = 30.04)\) and participants taking semaglutide at T2 \((M = 195.3, SD = 69.92)\), with those in the semaglutide group having a lower mean weight after taking the medication \((p = .54, d = 0.3)\). Additionally, albeit it not statistically significant, a small decrease was noted for mean systolic blood pressure between participants prior to starting dulaglutide at T1 \((M = 126.2, SD = 14.25)\) and participants prior to starting semaglutide at T1 \((M = 123.0, SD = 14.12)\) \((p = .61, d = 0.2)\), as well as a small increase for mean diastolic blood pressure for participants taking dulaglutide at T2 \((M = 74.7, SD = 10.40)\) and participants taking semaglutide at T2 \((M = 76.6, SD = 10.48)\) \((p = .69, d = 0.2)\), with those in the semaglutide group having a lower mean systolic blood pressure prior to starting the medication and higher diastolic blood pressure after taking the medication.

**Comparison Between Gender.** An independent-samples T test was utilized to analyze differences between HgbA1c, weight and blood pressure for males and females, both pre and post taking a GLP-1 agonist at T1 and T2 respectively. No statistically significant differences were found based on gender however, there was a large increase between males and females relating to mean HgbA1c at T1 \((p = .15, d = 0.8)\), mean HgbA1c at T2 \((p = .20, d = 1.1)\), mean weight at T1 \((p = .33, d = 0.9)\), and mean weight at T2 \((p = .35, d = 0.8)\), with males having a higher mean HgbA1c prior to and after taking a GLP-1 agonist as well as having a higher mean weight prior to and after taking a GLP-1 agonist. While not statistically significant, a small to moderate decrease was also noted between males and females for mean systolic blood pressure at T2 \((p = .35, d = 0.4)\) as well as a small to moderate increase for mean diastolic blood pressure at T1 \((p = .43, d = .0.4)\), with females having a lower mean systolic blood pressure after taking a GLP-1 agonist and a higher mean diastolic blood pressure prior to starting a GLP-1 agonist.

**Conclusions**

The purpose of this quality improvement (QI) project was to evaluate the relationship between GLP-1 agonist use and health outcomes in rural patients who are currently being treated for type 2 diabetes. The first objective of a 10% decrease in mean HgbA1c from T1 to T2 was not met, as there was only a 7% decrease in mean HgbA1c observed from T1 to T2. While this decrease was not found to be statistically significant, it did have a small to moderate effect size. The second objective of a 5% decrease in mean weight from T1 to T2 was met with an observed 5% decrease in mean weight from T1 to T2. The third objective of a 2.5% decrease in mean systolic blood pressure from T1 to T2 was met with an observed 4% decrease in mean systolic blood pressure from T1 to T2. The fourth objective of a 2.5% decrease in mean diastolic blood pressure from T1 to T2 was not met, as there was a 0% change in diastolic blood pressure from T1 to T2.

**Future Research**

By demonstrating statistically significant decreases in weight and systolic blood pressure for rural patients with type 2 diabetes following a medication program with a GLP-1 agonist, this project presents a basis for future research to further explore the relationships between GLP-1 agonists and relevant health outcomes for rural patients with type 2 diabetes.

**Recommendations**

This project demonstrates that GLP-1 agonists can be a valuable consideration for the treatment of type 2 diabetes in rural patients. Future research is necessary to help better establish this relationship and the potential benefits that GLP-1 agonists may offer patients with type 2 diabetes in the rural population. The relationships noted by this project may lead to more rural providers considering treatment regimens with a GLP-1 agonist for their type 2 diabetic patients.
References
GLP-1 AGONISTS


Appendix A: D1

DNP Residential Project Committee
Appointment Request

Student’s Name: Hunter Wadlow
Student’s Number: 14338355
Date Submitted: 07/07/2022

I request that the faculty members listed below be appointed to serve as my Residential Project committee.

Dr. Shelby Thomas
Name of Chair*
Signature, Chair of Committee

Dr. Kelli Cash
Member*
Signature, Member

Sarah Trokey
Member*
Signature, Member

Member*
Robin Harris
Signature, Member
Signature of Director of DNP Program, School of Nursing

To be completed during the semester enrolled in:
N9080 Section 1 DNP Residency Project

SON Approved 7/2012
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Appendix B: D3

Approval of DNP Residency Project Proposal and the Institutional Review Board Protocol

Candidate's name: Wadlow, Hunter  
Mizzou ID number: 14338365

Project Title: GLP-1 AGONISTS AND TYPE 2 DIABETES HEALTH OUTCOMES AMONG RURAL PATIENTS

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<tr>
<th>Signatures of review members</th>
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<th>Unacceptable</th>
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<tr>
<td>Chair: Dr. Shelby Thomas</td>
<td>✓</td>
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<td>Dr. Kelli Cash</td>
<td>✓</td>
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<td>Sarah Rion</td>
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The clinical project is: ☐

The Program Committee has explained the decision regarding the acceptability of my project proposal.

Student Signature: Wadlow  
Date: 11/27/23

Miriam D. Butler, DNP, NP-C, FNP-BC
Digitally signed by Miriam D. Butler, DNP, NP-C, FNP-BC
Date: 2023.12.18 11:15:43 -06'00'

Director, DNP Program in Nursing
Date