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Revisions of a Clinical Practice Guideline for Diabetes Management Protocol

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This is to certify that the doctoral study by

Daniel Huston

has been found to be complete and satisfactory in all respects,
and that any and all revisions required by
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Walden University
2020

Abstract

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MS, Walden University, 2009

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Project Submitted in Partial Fulfillment

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Abstract

Management of type 2 diabetes mellitus (T2DM) is essential from cost and treatment perspectives. In 2017, costs associated with diabetes management in the United States amounted to approximately $327 billion. The treatment of T2DM has been in a dynamic state for the past several years with the arrival of new classes of medications and new data supporting the use of diabetes medications to reduce risks from cardiovascular disease and slow the decline of renal function. This project explored the current evidence on treatment of T2DM to support changing either the flow of the current protocol algorithm or the medications identified in the algorithm. Current evidence and guidelines for the treatment of T2DM were reviewed and critically appraised using the levels of evidence for prognostic studies guideline. Knowles's theory of adult learning guided this project. Current evidence supported the recommendation to maintain the current protocol algorithm. A 2-member expert panel AGREE II tool review revealed their support of the current protocol. The expert panel indicated strong agreement with 98% of the items and agreement with the remaining 2%. The recommendation to continue the protocol algorithm was presented to the diabetes council. Treating T2DM patients using the most current recommendations can support improved quality of life for patients and families. Decision-making authority by nurse-led groups such as the diabetes council will promote positive social change within the organization.

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Dedication

I dedicate this paper and project to all those who have diabetes and to those who manage patients with diabetes. To my professional and personal family, for all the diligent and challenging roles they play in their treatment of persons with diabetes.

Acknowledgments

Thank you to the Walden University staff and facility members for their patience and support through this entire program. Thank you specifically to Dr. Diane Whitehead, who, as my instructor, was so much more, serving as a mentor and supporter of my trials and tribulations. Lastly, thank you to my loving wife, Bonny, for being supportive of me when I lost faith and drive to complete this project and for being my driver for project completion.

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Section 1: Nature of the Project

Introduction

A local health care system developed an algorithm for use in management and treatment recommendations for type 2 diabetes mellitus (T2DM). Under U.S. Food and Drug Administration (FDA) guidelines, many T2DM medications have received approvals for the treatment of additional diseases other than T2DM. This project explored the present evidence related to T2DM medications and determined if they are appropriate for use while considering the new FDA recommendations. A revised algorithm was then presented to an expert panel.

Problem Statement

Obesity is one of the two most significant risk factors for the development of T2DM (Raghavan et al., 2016). Reported as between 30% and 35%, Pennsylvania's obesity rate places the state in the second-highest category of states ranked by obesity prevalence (Centers for Disease Control and Prevention [CDC], 2017). T2DM affects nearly 22 million people in the United States (CDC, 2018). T2DM has been identified as the seventh leading cause of death in the United States,with an expected cost of $327 billion in 2017 (American Diabetes Association [ADA], 2019). With approximately one-third of Pennsylvania residents at higher risk for developing T2DM, nurses in the state must be ready and prepared to treat this growing population with efficiency and efficacy to control diabetes. Nurses play an integral role in T2DM management (Essien et al., 2017).

The health care system involved with this project is a Magnet-level-designated hospital. As a requirement of Magnet status, each facility must show the use of evidence-based materials in its treatment plans (American Nurses Credentialing Center, n.d.). To meet this requirement, a standardized algorithm for the treatment and management of T2DM patients was developed by the health system's diabetes care committee. The committee included the heads of various departments in the hospital, so approval for the use of the algorithm stayed with the committee. The algorithm was designed to provide direction for staff who work in diabetes management. The algorithm serves as a resource to guide the suggested order of medication management in the treatment of T2DM. The current algorithm, based on data that are nearly two years old, does not include references or supporting evidence. A review of the literature was completed to identify whether the current flow remains the best flow based on the evidence found in the review. The review also served to provide proof of the quality of the information in the protocol. Lastly, the discussion served to help reintroduce the protocol to the nursing providers. Recommendations for any additions or changes were presented to the diabetes care committee and nursing educators.

Purpose

The members of the diabetes care committee identified through medication-use reports completed by the hospital that many practitioners were not using the algorithm to drive their thought processes in T2DM management. Given that T2DM management has changed dramatically over the past 5 to 10 years, it is imperative that practitioners not

only are aware of the most up-to-date medications and interventions, but also have an evidence-based tool to use to standardize and guide T2DM management.

The practice-focused question for this project was the following: Does the current evidence on treatment of T2DM support changing either the flow of the current algorithm or the medications identified in the algorithm? This project supported the use of the algorithm from both a quality standpoint and a quantity standpoint. Dissemination of this project will serve to assist in the improvement of the quality and quantity of T2DM care within the health care system.

Nature of the Doctoral Project

The Walden University Library was used to explore most of the data to be collected. The following databases were accessed:

- CINAHL
- MEDLINE
- ProQuest
- PubMed
- Annual Reviews
- Cochrane Database of Systematic Reviews
- CINAHL Plus
- Database of Abstracts of Reviews of Effects (DARE)

Keywords included but were not limited to *diabetes*, *obesity*, *education*, *outcomes*, *management*, and *treatment*. Additional relevant terms were included when

identified. Inclusion and exclusion criteria were identified. Literature was reviewed from 2014 to the present. Only literature written in English was reviewed. The project followed the guidelines defined in the Walden University Manual for Clinical Practice Guideline Development.

Active dissemination of this project served as a catalyst to bring the topic of diabetes management to the forefront and provide a standardized, evidence-based method of control for nurses when working with patients with T2DM. The system for which this project was developed is a Magnet hospital. Having evidence-based data will serve to support one of the requirements for Magnet status. Additionally, ensuring that nurse educators have current knowledge of diabetes medication management is expected to improve the quality of the nurses' education and patients' knowledge. Nursing education continues to grow in importance, and evidence-based data improve the quality of this education. With an increase in educational excellence, one can expect a community to become better educated. The premise is that better education leads to better health and lower health care costs (Odnoletkova et al., 2016).

Significance

Stakeholders in this project included hospital administrators, direct caregivers, patients, and families. Affecting nearly 10% of the population in the United States, T2DM has the potential to change almost every household. The effects of T2DM include financial treatment costs (e.g., for medications, copayments and deductibles, and transportation) as well as nonfinancial costs related to decreased quality of life resulting

from complications of diabetes. Use of the most effective drugs can promote the most effective management of this disease, decreasing hospitalization costs and loss of work time. Adherence to the most recent recommendations for treating T2DM has implications for positive social change, in that it promotes higher quality of life for patients and their families.

Summary

T2DM incurs significant costs to the U.S. healthcare system. Section 1 introduced the use of a standardized treatment algorithm that may reduce health care costs and improve the evidence-based care of patients with T2DM. The practice-focused question for this project was the following: Does the current evidence on treatment of T2DM support changing either the flow of the current algorithm or the medications identified in the algorithm? This algorithm will serve as the foundation for nursing education and medication management for persons with T2DM. Section 2 introduces the model supporting this project. Literature supporting the project's relevance to nursing practice is discussed. My role in the system is clarified, along with that of the project team.

Section 2: Background and Context

Introduction

The practice-focused question for this project was the following: Does the current evidence on treatment of T2DM support changing either the flow of the current algorithm or the medications identified in the algorithm? In this section, I define the methods as the basis for this project, including the reasoning to support the use of each method. An established algorithm provides a structured document to nurse educators to guide them in diabetes medication management and optimization. The leaders of a local health care system felt that it was necessary to devise such an algorithm to provide uniformity, direction, and support in medication use and management for T2DM patients. This project provided evidence-based support and background for reviewing the current algorithm and offering evidence-based recommendations for change. Ultimately, the goal was to improve the consistency and quality of nursing education for T2DM medication management.

Concepts, Models, and Theories

T2DM affects about 9.4% of the U.S. population (CDC, 2017). A recent report estimated the total cost of managing diabetes in the United States at $327 million, indicating a cost increase of 26% over the previous 5 years (ADA, 2019). These data support the importance of diabetes management to nursing and the need to provide evidence-based education to improve management efforts.

I applied Knowles's principles of andragogy in reviewing how this project meets the needs of adult learners. Table 1 aligns the project with Knowles's model.

Table 1

Knowles's Theory of Adult Learning

Principles	Relationship to project
1: Self-concept	The adults using this algorithm will exhibit self-confidence and show independent thought processes and teaching.
2: Adult learner experience	With each opportunity to use the algorithm, users will grow in their knowledge base and share this in their teaching.
3: Readiness to learn	As the material is presented, users will increasingly become more aware of their need to meet learners' needs.
4: Orientation to learning	Each time this material is used, users will learn the concepts behind the algorithm and work toward education for diabetes management with consideration of the patient's needs.
5: Motivation to learn	This provides the basis for diabetes management and allows users to promote self-reflection and self-growth in their knowledge base.

Relevance to Nursing Practice

Diabetes is a significant economic drain on the U.S. economy and health care system, not including only the cost of providing care to persons with diabetes but also the indirect health care costs. Nurses are in an ideal position to help control these costs with the use of evidence-based algorithms. This document will serve to either support the current algorithm or provide current evidence-based information to bring the algorithm current This project served as the catalyst to increase the dissemination of this material with both an evidence-based and nursing-based focus for use in diabetes educator sessions.

Multiple certifications are available for nurses to obtain as an indication of their level of competency in relation to diabetes education. One such certification is Certified Diabetes Educator (CDE) certification from the National Certification Board for Diabetes Educators (NCBDE). This certification requires a position as a diabetes educator and some level of licensure, such as that of a nurse, dietician, or pharmacist. The majority of the focus of the NCBDE is on the education of the patient, with a smaller focus on medication management (NCBDE, n.d.) Additionally, a Board Certification—Advanced Diabetes Management (BC-ADM) credential is available from the American Association of Diabetes Educators (AADE). This certification is for licensed individuals with master's degrees or higher who work in a diabetes education role. The focus of this certification program is stronger medication management during diabetes education, as

well as more in-depth, more global review of patients with diabetes and how to best meet their needs. However, in the local system, only a few CDEs also hold nursing licenses. There are currently three educators who hold the BC-ADM certification: two nurses and one pharmacist.

Terens et al. (2018) identified disparities within diabetes education and recommended the use of superior evidence-based material to educate patients with diabetes. The use of an evidence-based algorithm will undoubtedly work toward meeting this requirement.

Diabetes treatments date back some 3,500 years, but all current diabetes medications have been developed since the 1920s (White, 2014). As several new classes of drugs were developed within the past 15 years, it became apparent that many nurses and practitioners have not kept themselves current with the latest drugs. Therefore, older drugs continue to be used that do not have the additional benefits that many of the new drugs have been proven to offer.

In the subsections that follow, diabetes medications are listed in the order of recommended use. I review each medication's advantages, side effects, and contraindications and provide the cash price (using GoodRx) for a 30-day supply based on a single location in central Pennsylvania (GoodRx, n.d.).

Metformin (Biguanide)

Metformin was the first medication on the algorithm recommended for use as the initial medication. Metformin brings a slight reduction in the risk for colorectal cancer

(Higurashi et al., 2016). Studies have indicated a possible cardiovascular (CV) risk reduction, but data from multiple studies lack consistency in indicating a clear link to CV risk reduction (Griffin et al., 2017). Metformin was associated with approximately a 2-point decrease in A1c (Chung, Hartzler, Smith, Hatton, & Kelley, 2018).

Metformin carries a low risk of side effects, with the most common side effect being gastrointestinal upset. Blonde and colleagues (2004) found that the use of extended-release metformin was associated with nearly a halving of side effects as compared to the use of immediate-release metformin. An additional concern that has been raised regarding the use of metformin is that metformin is linked with an increased risk of acidosis. However, recent studies have indicated that there is no increased risk of acidosis as long as the estimated glomerular filtration rate (eGFR) remains above 30 ml/min (Lazarus et al., 2018).

In 2016, the FDA issued revised guidelines indicating that metformin use was safe in patients with decreased kidney function. This revised guideline allowed increased use of metformin for those patients with an eGFR between 30ml/min and 60ml/min.

The typical cash price for a 2,000-milligram daily dose of metformin is between $11.76 and $37.19 per month. This medication is taken as oral pills daily. Of note is that *metformin* is the generic name of this class of drugs. There are several brand names available at higher cost than the generic version.

Liraglutide (Victoza®; Glucagon-Like Peptide 1 Receptor Agonist [GLP1])

Liraglutide, the second-choice medication, brings several advantages with its use. The Liguratide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results (LEADER®) trial used a large cohort of subjects with established CV disease. The trial demonstrated a 22% reduction in death from CV causes, a 12% reduction in nonfatal myocardial infarctions (MI), and an 11% reduction in nonfatal stroke among its study group as compared to the control group (a total of 9,340 patients; Marso, Daniels, et al., 2016). Additionally, Victoza demonstrated A1c lowering at 1.8 after 26 weeks, as well as weight reduction of more than 7 pounds after the same 26-week period.

Victoza® has a relatively high rate of side effects (nausea, 20%; diarrhea, 12%) with its use, with gastrointestinal side effects representing the most significant percentage. Other side effects include headache, nasopharyngitis, vomiting, decreased appetite, dyspepsia, which occurred at rates of 7% to 10% among those in the study (NovoNordisk, 2017). The product also carries a pancreatitis warning. However, the raw data support that the incidence of pancreatitis was lower for those on Victoza than for those in the control group. This medication also carries a low risk of hypoglycemia (NovoNordisk, 2017). This medication is only available as a once-daily injection and as a brand-name medication. Generic versions are not yet available. There are several other GLP1 medications available, but they have not yet demonstrated any CV risk reduction in clinical trials.

Victoza® also carries a “black box” warning regarding the possible risk of thyroid C-cell tumors (NovoNordisk, 2017). The data support that increased incidence of tumors appeared only in rats during the medication’s original trial. There have not been reports of any human cases of C-cell tumors believed to have been caused by Victoza®. The cash price for Victoza® for the maximum dose of 1.8 mg injected daily is between $872.85 and $934.40 per month.

Empagliflozin (Jardiance®; Sodium Glucose Cotransporters [SGLT2 Inhibitor])

The third-choice medication also brings several advantages with its use. The EMPA-REG trial showed CV risk reduction not dissimilar to that seen in the Victoza trial. Empagliflozin showed a 38% reduction in CV death and a 35% reduction in hospitalization for heart failure (Zinman et al., 2015). A1c reduction and weight reduction were also evident in the EMPA-REG trial. A1c levels reduced by 0.6, and weight reduced by 2.1kg (Boehringer Ingelheim Pharmaceuticals, Inc., 2017a).

Side effects of Jardiance® include urinary tract infections and mycotic infections, particularly in females, with incidence ranging from 5.4% to 9.3% (Boehringer Ingelheim Pharmaceuticals, Inc., 2017a). The product information addresses the risk of developing diabetic ketoacidosis and volume depletion due to increased urination; however, this side effect is not listed in the side effects table (Boehringer Ingelheim Pharmaceuticals, Inc., 2017a). Jardiance® carries a low risk of hypoglycemia (Boehringer Ingelheim Pharmaceuticals, Inc., 2017a). Jardiance® is not approved for use in persons with an eGFR of < 45 ml/min (Boehringer Ingelheim Pharmaceuticals, Inc., 2017a); this may

limit the number of people with diabetes who can use this medication. Jardiance® is available as an oral tablet to be taken once daily. Typical costs range from $381.11 to $449.07 for a 1-month supply (GoodRx, n.d.).

Linagliptin (Tadjenta®; Dipeptidyl Peptidase-4 [DPP-4] Inhibitors)

This fourth class of medications, called DPP-4, includes three different medications. Of these three, linagliptin is the only one that is not renally excreted, such that no dose adjustment is necessary based on renal function (McKeage, 2014). Linaglipitin has not been shown to increase CV risks and is considered neutral for CV risk reduction. Linagliptin use has shown a decrease of 0.7points in their A1c..

Side effects listed include pancreatitis, the potential for heart failure (demonstrated in the other two medications in this class), severe joint pain, and bullous pemphigoid (Boehringer Ingelheim Pharmaceuticals, Inc., 2017b). As with many other medicines, linagliptin is contraindicated for persons with any hypersensitivity to it. Monthly costs for this medication range from $356 to $499 for a 30-tablet supply (GoodRx, n.d.).

Sulfonylureas

Sulfonylureas are an older class of medications with a broad base of users. This class of drugs is also associated with low cost, which makes the use of sulfonylureas even more attractive to many. Side effects include a higher risk of hypoglycemia than with nearly all other diabetic medications; additionally, sulfonylureas are associated with a small amount of weight gain with use (Costello & Shivkumar, 2018). Contraindications

are hypersensitivities to the medicines. It is a general belief that sulfonylureas should be avoided in persons with a severe sulfa allergy (Costello & Shivkumar, 2018). Of note, sulfonylureas are negatively associated with CV risk reduction (D. A. Smith, 2017).

The remaining two classes of medications on the algorithm are basal and bolus insulins. These are not reviewed because of the number of choices available for basal and bolus insulins; moreover, these medications are used when all of the other medications have not been effective in lowering blood sugars (ADA, 2018).

Thiazolidinediones

The last class of medications to be discussed is the thiazolidinediones (TZDs). This class of drugs has been found to have mixed CV risks. Of the two TZDs currently available, pioglitazone appears to reduce heart attack (19% reduction) and stroke (18% reduction) but increases the risk for heart failure (210% increase; Chi et al., 2017). They are contraindicated in persons with a high risk of or history of heart failure (Chi et al., 2017). In my practice as a BC-ADM, I see little to no use of the TZD class of medications. The cost of pioglitazone ranges from no cost to $90 per month (GoodRx, n.d.).

With the development and use of newer medications, T2DM management has become more complex. Currently, there is evidence that many of these medications have benefits in addition to their blood-sugar-lowering effects. Using evidence-based information and an evidence-based algorithm can serve as a useful basis to not only improve diabetes management, but also incorporate other disease-risk-reduction effects in

the treatment protocol. This has the potential to lower the cost of T2DM management more than just reducing blood sugar level.

Additional Medications

Medications not included in the algorithm include α-glucosidase inhibitors and thiazolidinediones. The α-glucosidase inhibitor to be discussed is Acarbose (Precose®). Acarbose has shown to reduce CV risk in all measures, including stroke and heart failure, by about 35%. Heart attack risk was reduced by about 65% (Chi, Snaith, & Gunton, 2017). The medication is associated with a low to moderate risk of gastrointestinal upset in many people (Standl et al., 2014). This medication is typically taken by mouth with the first bite of every meal (usually three times a day). A typical 1-month supply of tablets costs between $10 and $30 (GoodRx, n.d.).

Local Background and Context

Leaders at this health care system located in the northeastern United States found that diabetes continued to increase in prevalence, bringing increased costs. The diabetes management algorithm is one tool that the health care system has implemented to help control these costs. The current belief is to avoid using higher cost medications. Their thought is that this would control the cost of diabetes, and health care must control today's price of treatment. The leaders of the local health care system have taken this philosophy to the next level in that they are looking to use medications that will decrease the risks of CV and renal complications in the future. This algorithm uses current evidence-based drugs to achieve this goal.

Previously, research was conducted to evaluate efficacy and safety when medications were pending FDA approval. In 2008, the FDA mandated that all new applications for drug approvals must include CV data. As a result of this requirement, many of the newer diabetes medications now have CV data (R. J. Smith et al., 2016). Consequently, some diabetes medications are currently being considered for use for CV risk reduction in addition to diabetes control. This has introduced a new factor in diabetes management and, therefore, this is on reason for the health care system's development and use of their diabetes algorithm.

Role of the DNP Student

My role in this project was to review the current algorithm, verify evidence, and make recommendations. I presented the revised proposals to the health care system's administration and the diabetes care transformation committee (DCTC). Although not part of this project, once the revisions are approved, I will promote the distribution and use of the diabetes algorithm. Only when the algorithm is available and in use will it realize its potential to reduce long-term diabetes costs by reducing CV risks and slowing renal decline.

Role of the Project Team

The project team consisted of members of the DCTC committee, who served as an expert panel reviewing the proposed changes to the algorithm. Members included the medical director of the health care system, chair of the endocrinology department, and

outpatient and inpatient stakeholders for improving diabetes care and outcomes in the system.

Summary

The practice-focused question for this project was the following: Does the current evidence on treatment of T2DM support changing either the flow of the current algorithm or the medications identified in the algorithm? In Section 2, I discussed Knowles's theory of adult learning, evidence relevant to nursing practice, the local context for this project, and my role. In Section 3, I discuss the process for the revision of the clinical practice guideline.

Section 3: Collection and Analysis of Evidence

Introduction

The purpose of this project was to explore current evidence related to T2DM management. This evidence was used to update the current diabetes management algorithm used by a facility in the northeastern United States. Section 3 identifies the scope of the review of current recommendations and revision of the algorithm.

Practice-Focused Question

The practice-focused question for this project was: Does the current evidence on treatment of T2DM support changing either the flow of the current algorithm or the medications identified in the algorithm?

Evidence Generated for This Project

This project followed the steps in the Walden University Doctor of Nursing Practice (DNP) Manual for Clinical Practice Guideline Development. Sources of evidence reviewed from the Walden University online database included CINAHL, MEDLINE, ProQuest, PubMed, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (DARE), and Google Scholar. Inclusion criteria applied to sources of evidence from 2015-2019 that were written in English and published in peer-reviewed journals. Individual medications' product information (PI) sheets, as currently approved by the FDA, also served as resources for this project. Other sources of evidence included position statements by the ADA and the American Association of Clinical Endocrinologists (AACE). These sources are dynamic resources, in that they

undergo review each year, after which new or updated recommendations are published. The year 2018 marked the first time that the European Association for the Study of Diabetes (EADS) partnered with the ADA in releasing a consolidated recommendation, "Management of Hyperglycemia in Type 2 Diabetes (2018), a Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)" (Davies et al., 2018). New for 2019 was the American College of Cardiologists position endorsement of the 2019 ADA Standards of Medical Care (American College of Cardiology, 2019).

Search terms included *type 2 diabetes mellitus*, *medications and type 2 diabetes mellitus*, *atherosclerotic CV disease risk*, *atherosclerotic CV disease risk*, and *type 2 diabetes mellitus*, the individual names of currently approved drugs for type 2 diabetes mellitus treatments, and *Association of Clinical Endocrinologists and diabetes*.

Evidence Generated for the Doctoral Project

The project followed the steps outlined in the Walden University DNP manual for clinical practice guideline development, which I have summarized in the subsections that follow.

Step 1: Critically Appraise the Evidence

I used the following levels of evidence for prognostic studies to synthesize the level of evidence (American Society of Plastic Surgeons, 2020):

I High-quality prospective cohort study with adequate power or systematic review of these studies

II Lesser quality prospective cohort, retrospective cohort study, untreated controls from an RCT, or systematic review of these studies

III Case-control study or systematic review of these studies

IV Case series

V Expert opinion; case report or clinical example; or evidence based on physiology, bench research, or "first principles"

T2DM management has become more complicated during the past 20 years. During the past 10 years, there have been five new classes of diabetes medications approved by the FDA in the United States (White, 2014). This intake of new classes of treatment medications has created a challenge for health care providers to keep up. Further, over the past decade, the FDA has mandated that CV risk data be included in each medication's study trials. Many T2DM medications are now being prescribed and used based on CV risk reduction. No longer is lowering blood sugar the only concern when treating T2DM.

Metformin (biguanide). Nearly all of the literature supported using metformin as the initial drug in the management of T2DM for persons who have sufficient renal function (Practitioners, 2015). In addition to lowering blood sugars, metformin has been shown to reduce CV events in persons with T2DM and a CV history (Luo et al., 2019; Level III). The CV risk reduction is believed to derive from the pleiotropic effects of metformin on the body in multiple systems (Luo et al., 2019; Level II). Numerous studies have also shown that metformin has anticancer properties and can destroy cancer cells

(Saini & Yang, 2018; Level I). As pointed out earlier, the cost of metformin is reasonable and affordable for most patients.

Metformin is known to increase blood lactic acid levels; however, this is not a concern until a metformin overdose occurs or an outside force causes renal failure with increased lactic acidosis (DeFronzo et al., 2016; Level II). As a result, the FDA implemented new guidelines. Due to this action, the use of metformin has increased; however, the incidence of acidosis has not increased (DeFronzo et al., 2016; Level II). Another side effect is gastrointestinal distress (Siavash et al., 2017; Level II). Fortunately, digestive distress resolves when metformin is stopped.

Metformin works by decreasing glucose absorption in the intestines and by lowering the production of glucose by the liver (Chung et al., 2018; Level II). These actions, in addition to a low incidence of hypoglycemia, support making metformin an appropriate T2DM drug to use. The literature search supports keeping metformin as the initial drug of choice in T2DM management.

Victoza (liraglutide—GLP1). The entire GLP1 class of medications continues to evolve. As of today, there are different GLP1 medications available:

- Adlyxin® (lixisenatide) daily use
- Bydureon® (exenatide ER) weekly use
- Byetta® (exenatide) twice-daily use
- Ozempic® (semaglutide) injection weekly use
- Rybelsus® (semaglutide) oral daily use

- Trulicity® (dulaglutide) weekly use
- Victoza® (liraglutide) daily use

As a result of the newer entries into the class, there have been numerous studies completed showing CV data and therapeutic efficacy. These multiple studies make it difficult to determine which specific medication shows the best value for its cost (Schernthaner et al., 2017; Level II). Arguably, the most promising GLP-1 medicine to enter the market is Ozempic®. The results of the Sustain-6 trial showed a risk reduction in nonfatal CVA, non-fatal heart attack, and CV death rate (Marso, Bain, et al., 2016; Level I). Ozempic demonstrated a significant reduction in A1c and weight in an additional study (Petri, Ingwersen, Flint, Zacho, & Overgaard, 2018; Level I).

Liraglutide is the only GLP-1ra medication on the pathway. Liraglutide is known for several positive effects leading to improved diabetes health, such as reduction in weight, A1c, low-density lipoproteins (LDL), and more (Rizzo et al., 2016; Level I). At the time of the development of the algorithm, semaglutide had not been released. GLP1 is a hormone that is known as an incretin. Incretins increase insulin manufacture and insulin secretion, reduces glucagon generation and release, slows the emptying of the stomach, and help to rebuild beta cells (Chung et al., 2018; Level II). These advantages help to make the GLP1 class perhaps the most valuable class of medications for treating T2DM.

Jardiance (empagliflozin—SGLT2i). Jardiance is one of four medications in the SGLT2 class. Other medicines in this class include the following:

- Farxiga® (dapagliflozin)

- Invokana® (canagliflozin)
- Jardiance® (empagliflozin)
- Steglatro® (ertugliflozin)

Of these four, canagliflozin was the first approved for use in the United States in 2013. Since then, the other three have been released and approved by the FDA. Empagliflozin was the first SGLT2 released that had CV data. This CV data surprised many in the diabetes management community because of a significant reduction in death from all-cause mortality (32% reduction) and reduction in heart failure readmission by 35% (Inzucchi et al., 2018; Level I). Since then, the other SGLT2 drugs have been shown to reduce CV risks and to help protect the kidneys and slow renal function decline (Donnan et al., 2019; Level I). Following the introduction of empagliflozin, numerous other SGLT2 medications have completed CV risk studies, all of which have shown some level of CV risk decline and slowing of renal function decline.

A new paradigm has developed as the result of a dapagliflozin CV risk trial called Dapagliflozin in Patients With Heart Failure (DAPA-HF). This trial proved that dapagliflozin reduced CV risk, cardiac death, and heart failure decline regardless of whether the patient has diabetes or not (McMurray et al., 2019; Level I).

The SGLT2 class works by preventing the reabsorption of glucose in the proximal renal tubule (Schork et al., 2019, p. 2; Level II). This process then allows the glucose to be flushed out with the urine. The effects are glucose lowering and slight weight reduction due to not absorbing the calories lost in the urine.

Tradjenta (linagliptin—DPP4). Tradjenta is one of three medications in the DPP4 class approved for use in the United States. Additional drugs in this class included:

- Januvia (Sitagliptin)
- Onglyza (Saxagliptin)
- Tradjenta (Linagliptin)

The DPP4 class was approved in 2006. In 2015, the FDA released a drug safety communication warning of potential severe joint pain (FDA, n.d.). The DPP4 class has marginal A1c lowering, as shown in Figure 3. There are also limited CV data with this class; however, these agents do not appear to increase the risk of CV events (Gantz et al., 2017; Level II). These concerns, coupled with the relatively high cost of these medications, perhaps makes their use a lower priority on the algorithm.

Sulfonylureas. Sulfonylureas were first available in the United States in 1956, with second-generation sulfonylureas available in 1964 (see Table 2). First-generation sulfonylureas are not currently in use in the United States. However, second-generation sulfonylureas maintain their place in American diabetes management. One of the most significant advantages of using sulfonylureas is their low cost. They are available as generics and are inexpensive (see Table 3). They are known for a history of no CV benefit, weight gain, and reduced response with time (Chung et al., 2018; Level II). Other reviews have suggested an increase in CV risks (Azoulay & Suissa, 2017; Level I). This ambiguity supports that sulfonylureas should not be front-line medications for most persons with T2DM.

Thiazolidinediones (TZD—Pioglitazone [Actos]). TZD first appeared in the United States in 1996 (See Table 2). The first TZD, troglitazone, was short lived on the market due to increased liver toxicity (Temple, 2009; Level III). The use of the other TZDs dropped off, and their use has not become widespread, even though they are relatively inexpensive and can substantially reduce A1c levels (see Table 3). TZDs are noted for causing fluid retention leading to congestive heart failure, as well as osteoporosis (Rizos et al., 2016; Level II). These concerns perhaps limit the usefulness of this class of medications in the treatment of T2DM.

Step 2: Synthesize the Evidence From the Literature

Metformin remains the first-choice medication for several reasons. It is inexpensive, has been in the United States since the 1990s and in Europe since the 1950s, and has a known safety profile. These positive features, along with the pleiotropic benefits found, in addition to high A1c lowering, make metformin an excellent first-line medicine to use.

The second choice of medication is not as clear. GLP1 agents offer the best weight lowering and the nearly the best A1c lowering of all the options. There is a known CV risk reduction. However, their high cost and the fact that most in the class are currently available only as injections limit their use. If someone has an aversion to an injectable, then an SGLT2 could be the second choice. SGLT2s offer good A1c control and weight lowering while providing CV risk reduction and slowing of renal function decline. With either choice of drug, the GLP1 or the SGLT2, CV risk reduction, A1c

reduction, and weight reduction can be expected to occur, making either class an appropriate second choice with the other as a third-choice medication. TZDs could be an option for those in whom osteoporosis, congestive heart failure, or fluid retention is not a concern. Sulfonylureas remain an option for persons with low income or medication cost concerns.

The recent addition of CVD data to development trials has complicated the issue of choosing the most appropriate medication to treat T2DM. Ranking CVD risk reduction is beyond the scope of this paper and is not addressed.

Step 3: Develop the Revised Guideline

Based on the current evidence, the recommendation to continue the current protocol algorithm for T2DM was sent to the expert panel for review.

Step 4: Expert Panel Review

The panelists used the AGREE II instrument and made recommendations for revisions. Each panel member reviewed the proposed guideline in relation to the following domains (Brouwers et al., 2010):

1. Scope and purpose
2. Stakeholder involvement
3. Rigor of development
4. Clarity of presentation
5. Applicability
6. Editorial independence

See Section 4 for further details on this step.

Step 5: Finalize Guideline

See Section 4 for discussion of Step 5.

Step 6: Present to Organization

See Section 4 for discussion of Step 6.

Summary

Section 3 described the process and analysis for this project, following the guidelines outlined in the Walden University DNP Manual for Clinical Practice Guideline Development. The practice question was: Does the current evidence on treatment of T2DM support changing either the flow of the current algorithm or the medications identified in the algorithm? In Section 4, I discuss findings, implications, and recommendations to the organization.

Section 4: Findings and Recommendations

Introduction

The management of T2DM has become more complicated with the introduction of multiple medication classes over the past 10 years. The number of new medications in each category, along with research studies that provide CV risk reduction data, has had an impact on health care providers' decision making in several ways. The recent introduction of newer classes of medications such as the GLP1ra and the SGLT2i has presented new educational challenges for practitioners (Farahani, 2015). These dynamic medication changes have posed barriers for many currently practicing providers in terms of their ability to remain up to date concerning the latest options for diabetes management.

Findings and Implications

The literature search supported the current guideline and did not reveal any significant changes. The current classes of medications in the guideline remain available and are hierarchical in their use. The ADA's 2020 guidelines support the local algorithm. The AACE's 2019 guidelines also support the use of the local algorithm due to having many similarities.

I used the AGREE II tool to review the validity of the guideline. A three-person panel of local experts was provided the AGREE II tool and this paper to evaluate. The AGREE II tool consisted of 23 questions using six domains and two overall rating assessments. The results of the panel's use of the tool are documented in Table 2.

Table 2

AGREE II Expert Panel Results

Criteria	Reviewer 1	Reviewer 2	Comments
1. The overall objectives of the guidelines were specifically described.	7	7	Objective was clear, concise, and articulated nicely.
2. Health questions read the guideline are specifically described.	7	7	Health question covered by guideline was described in detail.
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	7	7	T2DM is becoming an epidemic in our rural community. The prevalence of such was identified as well as compared at a national level.
4. The guideline development group includes individuals from all relevant professional groups.	7	7	It is apparent that much thought and research went to the stated population.
5. The views and preferences of the target population (patients, public, etc.) have been sought.	7	7	Subject matter experts in the field of diabetes management were well represented and utilized appropriately.
6. The target users of the guideline are clearly identified.	7	7	Target users were clearly identified and defined.
7. Systematic methods were used to search for evidence.	7	7	Algorithms noted throughout paper.
8. The criteria for selecting the evidence are clearly described.	7	7	Strong correlation noted.
9. The strengths and limitations of the body of evidence are clearly described.	7	7	Strengths and limitations were called out in professional document.
10. The methods for formulating the recommendations are clearly described.	7	7	Recommendations were clear and concise.
11. The health benefits, side effects, and risk have been considered in formulating the recommendations.	7	7	All noted.
12. There is an explicit link between the recommendations and the supporting evidence.	7	7	Supporting evidence was found as well as referenced throughout professional document.
13. The guideline has been externally reviewed by experts prior to its publication.	7	7	Reviewed and recommendations provided prior to submission.
14. A procedure for updating the guideline is provided.	7	7	As noted in diagram.
15. The recommendations are specific and unambiguous.	7	7	

(*table continues*)

16. The different options for management of the condition or health issue are clearly presented.	7	7	
17. Key recommendations are easily identified.	7	7	
18. The guideline describes facilitators and barriers to its application.	7	7	
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	7	7	
20. The potential resource implications of applying the recommendations have been considered.	7	6	
21. The guideline presents monitoring and/or auditing criteria.	7	7	
22. The views of the funding body have not influenced the content of the guideline.	7	7	
23. Competing interests of guideline development group members have been recorded and addressed.	7	7	
Supplemental questions			
Rating of overall quality of this guideline.	7	7	Very well written. It is clear a considerable amount of research went into this project. A well-rounded approach using the latest references assisted in the paper's solid foundation. Extensive process including utilizing national best practices to create a well-designed helpful guideline for a high-volume diagnosis. great work
I would recommend this guideline for use.	Yes	Yes	

Recommendations

The result of the AGREE II tool clearly demonstrated that the expert panel strongly agreed with the results and the process. Out of 46 responses, there were 45 ratings of 7 and a single rating of 6, for a 9.8% *strongly agree* rating. The expert panel nearly unanimously supported the tool in its current state. The current guideline and the supporting information in this paper will be presented to the DCTC group for consideration and review at its next meeting slated for February. This committee is the group that is charged with overall diabetes management and policy within the health care system. This committee has the power and the potential to implement change in the organization and is the ideal group to use as the catalyst for change.

Strengths and Limitations of the Project

Strengths

Review of the studies in my literature review indicated that each study was powered and designed to prove non-inferiority or superiority against a lesser agent or no agent. The studies used varied population groups and different methodologies, with similar outcomes measured in A1c lowering. Most of the studies used large population numbers, lending additional support to their validity. These variabilities included a diverse population with large numbers, all sharing a common outcome of A1c measurement. Many studies also used a placebo-controlled trial, leading to a higher quality of information (Möller, 2011). The panel of experts unanimously supported this tool, providing a level of agreement and support within the organization.

Limitations

Lack of participation by one of the members of the expert panel diluted the use of the AGREE II tool; however, the experts nearly 100% agreed with the protocol and gave their support, as evidenced by the comments at the end of the AGREE II table. All of the studies compared the medication against a placebo or a drug in another class. No reviews compared medicines within the same type. This methodology did not allow direct comparison of drugs within a category. This lack of having a direct comparison between medications in a class, prevents knowing which medication in the class is expected to provide the most A1c reduction, weight reduction, and possibly the most CV risk reduction.. Without this information, it is a challenge to determine which medication is the most appropriate one to use. Moreover, lack of specific information means that practitioners do not have the educational support they need to use the most effective medication. This same lack of direct comparison also posed a challenge to the effort to compare drugs for use in this review for the guideline.

An additional limitation is that newer diabetes medications continue to be in the development stage and in clinical trials. Additionally, studies are currently in process to show CVD risk reduction as well as other benefits such as fatty liver reduction, slowing of renal function decline, and lower risk of other diseases and conditions.

Perhaps the most challenging limitation is that new research is frequently released that provides new insights into the benefits of diabetes medications. This dynamic activity further complicates diabetes management.

Summary

The determination to choose the most appropriate medication to manage and treat T2DM remains a challenge for providers. First, newer medications and newer study outcomes are both in a dynamic state, and second, limited data allow direct comparison of the medications within a class. This paper, now finished, is nearly outdated. This situation makes diabetes management even more challenging than in the past. However, even with these limitations, this protocol allows a single resource to assist practitioners in making more appropriate choices for medication use and titration.

Section 5: Dissemination Plan

In this paper, I have reviewed a current algorithm/protocol to assist practitioners in treating T2DM patients. I conducted literature searches to review the medications in the current protocol to determine current information regarding their use, safety, side effects, and cost. I assembled an expert panel of providers, provided them with the current draft of this paper, and used the AGREE II tool to systematically review the literature as presented herein and to determine whether the current protocol tool should be modified and, if so, how. These results led to the determination that the current tool remains appropriate and current.

Using this information, I will present the results to the members of the DCTC group at their February 2020 monthly meeting. As a member of this committee, I also personally tasked myself with staying current with diabetes management and will present new information at future meetings. With this new information, the committee has the authority to revise the protocol. The DCTC group is also challenged with the dissemination of diabetes management to the entire healthcare system.

Analysis of Self

This project assisted my professional growth and my personal growth in many ways. Professionally, I worked with the medical director of the health care system. This led to an increase in our respect for each other. This interaction also supported me in proving my value as a member of the DCTC. In our most recent email exchange, the medical director signed with his first name. He also said that he is “appreciative of all I

do" in providing diabetes education. This paper's completion was also a goal for my professional growth toward my personal goals as an employee of this healthcare system.

I came to realize that when I look at a project, I tend to look at the entire project and see a mass of smaller sections. As a result of this paper, I recognize the need to take a whole project and break it down into smaller, more manageable tasks. Then, when a task is completed, I can feel a sense of accomplishment and can feel energized to take on the next smaller task. This revelation has already moved over into my professional life. I see more positive responses from my coworkers and family than I have ever received in the past.

Summary

Diabetes management has become a complicated process with the advent of new classes and new medications within classes. The protocol described in this document is helpful in assisting providers with a one-page resource to support them in diabetes management. This review determined that the current protocol remains current and appropriate for use. The health care system has a process in place for dissemination. As a member of the committee that is charged with diabetes oversight for the system, I will be able to influence and drive changes if and when these changes are published in evidence-based professional journals and other information sources.

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