DOES THE USE OF HOME-BASED CONTINUOUS GLUCOSE MONITORING DEVICES IN ADULTS WITH DIABETES MELLITUS IMPROVE HEMOGLOBIN A1C LEVELS? AN INTEGRATIVE REVIEW

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ABSTRACT

The prevalence of diabetes continues to rise, but patients' ability to obtain and maintain glycemic control remains a challenge. In 2017, complications from diabetes resulted in over $300 billion expenditures in lost productivity and medical costs. The nation's approach to addressing this problem starts with acknowledging the benefits that continuous glucose monitoring (CGM) as an adjunct intervention could change the trajectory of both diabetic care outcomes and the national expenditures associated with poor glycemic control, which leads to the destruction of other cells such as those found in the heart, eyes, and kidneys. Moreover, CGM use has been associated with reductions in glycated hemoglobin A1c (HbA1c) levels. Lower HbA1c levels in diabetes patients translate to better glycemic control. If diabetes patients can improve glycemic levels, they could prevent the severe complications associated with poor glycemic control. This integrative review involved a detailed search, review, and analysis of the literature to further evaluate the relationship between CGM use and HbA1c levels, reliability of CGM data, and patients' acceptance of CGM use for glycemic management.

Keywords: diabetes, adult diabetics, diabetes self-monitoring blood sugar tools, home-based continuous glucose monitoring, HbA1c,

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List of Abbreviations

Centers for Disease Control and Prevention (CDC)

Continuous glucose monitoring (CGM)

Diabetes mellitus (DM)

Estimated HbA1c (eHbA1c)

Glucometer (GM)

Glycosylated hemoglobin A1c (HbA1c)

Integrative review (IR)

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)

Randomized controlled trial (RCT)

Real-time continuous glucose monitor (rtCGM)

Self-monitoring blood glucose (SMBG)

Time-above range (TAR)

Time-below range (TBR)

Time-in-range (TIR)

Type 1 DM (T1DM)

Type 2 DM (T2DM)

SECTION ONE: FORMULATING THE REVIEW QUESTION

Introduction

Chronic diseases are a common phenomenon responsible for various health crises suffered by millions residing in the United States (U.S.). Chronic diseases are a known leading cause of death and disability nationally. Additionally, they are a driving force behind the country's $3.8 trillion yearly healthcare-related costs, which account for 90% of the nation's healthcare expenditures (National Center for Chronic Disease Prevention and Health Promotion [NCCDPHP], 2021). Among the list of chronic illnesses, diabetes mellitus (DM) is one of seven problematic health challenges existing alone or as a comorbidity for many Americans. The most recent statistics indicate that six in ten adults have a chronic disease, and four in ten suffer from two or more chronic illnesses (NCCDPHP, 2021, p. 1).

Diabetes directly impacts over 34.2 million Americans and prediabetes, a condition that predisposes a person to develop diabetes, dwells in the shadows of 88 million adults, roughly 10% of the adult population residing in the U.S. (Gill et al., 2018). Type 2 diabetes mellitus (T2DM), a preventable disease, accounts for 90−95% of all diabetes patients, and in 2017, complications from diabetes resulted in over $300 billion expenditures in lost productivity and medical costs. Consequently, diabetes ranked number seven of the top 15 leading causes of death nationally, increasing from 1999 death rates (Centers for Disease Control and Prevention [CDC]: Centers for Disease Control and Prevention, 2019). While prevention is key to reducing such costs, successfully managing symptoms that curtail disease progression is the next best alternative. Further, successful disease self-management is more likely to occur if patients have access to improved management tools that can provide improved accurate health data (Lameijer et al., 2021).

Defining Concepts and Variables

The interest for this integrative review (IR) stemmed from a desire to understand adult diabetes patients' use of continuous glucose monitoring (CGM) and its relationship to HbA1c levels. Therefore, the population of interest comprises adults with diabetes and the intervention is defined as the use of a CGM and its relationship to the outcome variable of HbA1c levels. According to Toronto and Remington (2020), establishing this criterion is required. Patients with chronic diabetes are generally separated into two main groups, type 1 DM (T1DM) and T2DM. The type of diabetes diagnosed determines a patient's treatment plan. According to the American Association of Endocrinology (2021), T2DM represents 90−95% of all diagnosed diabetes patients. It represents a group of individuals with a metabolic condition where they either cannot produce enough insulin, lack the ability to effectively use the insulin produced by the cells in their own bodies, or exhibit a combination of both deficiencies. This challenge causes blood glucose (blood sugar, glycemia) levels to become elevated, which causes preventable damage to other critical organs. Glycated hemoglobin A1c (HbA1c) is the gold standard metric used to determine how well diabetes patients manage their diabetes. It is a measurement obtained through a blood sample that measures the average sugar level circulating on the blood's hemoglobin protein over the preceding 3 months (CDC, 2019). To reduce the risk of complications from diabetes, the desired HbA1c level is < 7% (National Institute of Diabetes and Digestive and Kidney Diseases [NIDDK], 2021).

T1DM represents approximately 5% of all diagnosed diabetes patients and is the second most common type of diabetes. T1DM falls under the category of an autoimmune medical condition, which means that the person's body makes antibodies against the cells that are responsible for making insulin, eventually destroying the beta cells of the pancreatic islets of

Langerhans. This destruction results in these patients having to self-administer insulin for the rest of their lives (NIDDK, 2021).

A glucose meter or glucometer (GM) is a portable electronic device that allows users to test blood glucose levels using a lancet finger stick. Each blood sample obtained requires the user to retrieve a sample by administering a finger stick with a lancet. The glucometer measures the blood glucose level at one moment in time. It does not inform the user whether the blood glucose level decreases or increases; therefore, the device does not provide directional glucose levels. The GM is the traditional self-monitoring blood glucose (SMBG) tool used by patients with diabetes to self-monitor and manage their blood glucose levels. The glucometer is a key glucose monitoring tool used by patients with diabetes.

The at-home CGM is a portable electronic blood glucose monitoring device that allows users to retrieve blood glucose levels via a sensor affixed to the user's skin and stays in place 10−14 days, depending on the device's manufacture. It allows users to view their blood sugar levels anytime at-a-glance. It is sometimes called a real-time continuous glucose meter (rtCGM) (Gill et al., 2018). Commonly used among patients with T1DM, these devices utilize technology that offers users blood glucose levels delivered without additional finger sticks and with results available within 1 to 5 min of each other (Azhar et. al., 2020). In addition, some CGM devices inform the user of blood glucose trend direction. The technology has recently improved, and these devices are currently being marketed to patients with T2DM due to the enhanced blood glucose control benefits available and experienced by device users.

To avoid micro and macrovascular complications associated with poorly controlled diabetes, successful glycemic control is required. A general international consensus when using CGMs has determined that a percent time-in-range (%TIR) equates glucose values of 70−180

mg/dL (approx. 3.9−10.0 mmol/L), time-above range (TAR) > 180 mg/dL (> 10.0 mmol/L) and > 250 mg/dL, and time-below range (TBR) < 70 mg/dL and < 54 mg/dL (< 3.0 mmol/L) (Vigersky and McMahon, 2019). When diabetes patients spend more time in TIR, HbA1c levels improve (Advani, 2019).

Rationale for Conducting the Review

Complications due to diabetes are known to cause serious health problems like heart disease, kidney failure, and blindness (CDC: Centers for Disease Control and Prevention, 2019). When diabetes has been diagnosed, successful control of blood glucose levels is key in preventing further complications and disease progression. Traditional self-care management regimens include daily episodic blood glucose monitoring using a traditional GM device, which could include one−three daily finger sticks required to obtain blood glucose level measurements. Patients and healthcare providers use these measurements to help determine the patient's daily progress. The use of CGM technology has been reported to impact HbA1c levels (Azhar et al., 2020). Currently, CGMs are not routinely covered by health insurance benefits for all diabetes patients. Patients with T1DM generally enjoy the use of CGMs as a covered insurance benefit, but this health care service is not generally experienced by patients diagnosed with T2DM. However, in 2017 T2DM accounted for more than 90−95% of all diabetes patients and associated U.S. healthcare costs (CDC: Centers for Disease Control and Prevention, 2019). During the same year, the Advanced Technologies and Treatments for Diabetes Congress convened an international panel of expert researchers and physicians to define specific metrics information used to assess CGM data (Martin et al., 2019). Therefore, the rationale for conducting this IR was to search, review, critique, and analyze relevant data that adds insight to the relationship between CGM use and HbA1c levels in diabetes patients.

Problem Statement

The U.S. healthcare economic burden due to complications associated with diabetes needs to improve. Successful disease management is required to achieve positive patient outcomes when disease prevention has not prevailed. When blood sugar levels of diabetes patients are not well controlled, other organs such as the heart, the kidneys, and the eyes are negatively impacted, resulting in less-than-optimal patient outcomes and increased U.S. expenditures (CDC: Centers for Disease Control and Prevention, 2019). Patient studies have proven that optimal glycemic control aids in the reduction of morbidity from diabetes (Kieu et al., 2021). Traditional SMBG efforts have fallen short with helping to reduce national cost expenditures of healthcare-associated complications resulting from progressive diabetes, which classifies as a chronic disease. HbA1c levels have continued to trend upward among this population (CDC, 2019). As discussed earlier, traditional episodic glucose measuring devices provide patients with blood glucose levels at a given time, but these devices do not provide trend information. Since most CGM devices have built-in technology with the capacity to deliver blood glucose directional trend data as often as every 5 mins, the use of CGMs could prove more beneficial (Advani, 2019). Trend data provides information to patients that could yield a more accurate treatment response when compared with a treatment plan that lacks this type of detailed information. When diabetes patients use CGM devices, patients have been found to experience better glycemic control with lowered mean blood glucose levels (Beck et al., 2017). The use of CGMs has also been associated with lowered HbA1c levels, and when compared with episodic GMs, CGMs has proven more favorable among patients (Kropff et al., 2017).

Purpose of this Scholarly Project: IR

In general, the purpose of IR is to provide a comprehensive summary of past empirical or theoretical literature of what is known about a particular subject area and to share the synthesis of literature regarding a healthcare topic or phenomenon to the interested groups (Whittemore & Knafl, 2005). The purpose of this IR was to search, collect, review, analyze, and synthesize relevant literature published from 2016−2021 to determine if the use of CGM devices in home setting is a reliable, cost-effective, and user-friendly alternative over traditional episodic (SMBG) devices used among adult diabetes patients, in lowering HbA1c levels. Preliminary literary research for this IR suggested favorable evidence that supports this inverse relationship. If the lowering of HbA1c levels is consistently found with the use of CGMs, this could benefit all diabetes patients, especially those with T2DM, by improving success with diabetes management and support for optimal health (Azhar et al., 2020). Furthermore, clinical information gleaned from IRs can potentially impact healthcare practice and policy (Whittemore & Knafl, 2005).

Findings from this IR will be shared with clinicians in the primary care setting and any other interested parties, such as insurance companies. This evidence-based information can be used to assist clinicians with guiding patients on the use of diabetic self-management tools like CGMs. The ability of the family practitioner to assist diabetes patients in lowering their HbA1c levels could positively impact this population group, the overall health of the community where they reside and aid in lowering national expenditures associated with care rendered to diabetes patients, especially those with T2DM.

Clinical IR Question

Does the use of home-based CGM devices in adults with diabetes improve HbA1c levels?

Data Collection Process

The reviewer completed the required CITI training (Appendix E) according to Liberty University policy. Although this IR did not involve the participation of human participants, approval from Liberty University's Institutional Review Board (IRB) was sought and obtained (See Appendix F) (IRB approval letter). The IRB approval was followed by a well-defined literature search strategy that included clearly defined parameters to conduct a literature search. According to Whittemore and Knafl (2005), this was necessary to obtain enhance rigor and a comprehensive collection of data that was challenged for relevancy to the clinical question. The reviewer of this IR used computerized databases with more than two strategies or filters with clearly defined eligibility criteria. The use of electronic databases was effective and efficient (Whittemore and Knafl, 2005).

Formulation of Inclusion and Exclusion Criteria of the Literature

A clinical question must be clearly defined to establish a comprehensive literary research method to initiate a literature review (Toronto and Remington, 2020). After a clinical question has been formalized, inclusion and exclusion criteria must be identified to help guide the data search. Inclusion criteria for this project were peer-reviewed studies and journal articles that evaluated the relationship between home-based CGM use and HbA1c levels in adult diabetes patients. Exclusion criteria were newspaper articles, dissertation/thesis, trade publication articles, and journal studies that were narrowly focused, such as those that solely studied children or pregnant women with diabetes.

The study selection search included consultation with the school librarian and use of electronic databases to identify full text, peered reviewed articles written in the English language that covered published years of 2016−2021 and targeted the subject area of CGM as an

intervention to monitor blood glucose levels in patients with diabetes (Table 1). Research efforts were further refined with the specificity of search terms and keywords: *adults' diabetes self-management tools, home-based continuous glucose monitors, home-based continuous glucose monitors* and *hemoglobin A1c levels, home-based CGM and costs,* using six databases (Cochran Database, MEDLINE, CINAHL, Plus, PubMed, ProQuest, and government websites). The disciplines used in the initial search included nursing, medicine, education, and public health.

Literature Search Results

Initial results using general terms of *diabetes management tools* yielded 56,133 articles. With narrowing the data criteria to include *home-based CGMs,* the database search yielded 111 articles. When the search criteria included both terms *home-based CGM and HbA1c*, the database search yielded 100 articles. When the term *cost* was added to *portable CGM*, 112 journals were yielded, and when the terms *home-based CGM and patients with T2DM* were used, 162 journals were populated. With further examination, removal of duplicates, 103 articles remained. Following inclusion and exclusion criteria (Table 1), 50 full-text articles were assessed for eligibility which rendered a total of 26 journals that were collected using the article title, abstract, purpose, findings, and conclusions to establish topic relevancy to the IR clinical question. The 24 articles excluded from this IR contained studies that solely focused on children, hospitalized patients, or the study did not include information regarding HbA1c levels. The selected articles were reviewed and examined for participant clarity and rigor (See Appendix A) (Melnyk and Fineout-Overholt, 2015) and literature categorized by theme (See Appendix B).

The 26 articles selected for this IR provided information relevant to the clinical question (Toronto and Remington, 2020) of CGM use by adult diabetes patients and HbA1c level reduction (Advani et al., 2019; Al Hayek et al., 2017; Azhar et al., 2020; Beck et al., 2017; Chan

et al., 2018; Eleftheriadou et al., 2019; Gilbert et al., 2021; Kropff et al., 2017; Lameijer et al., 2021; Martin et al., 2019; Rivera-Ávila et al., 2021; Schlüter et al., 2020; Valenzano et al., 2021;) Other articles were chosen because they support CGM data reliability by demonstrating a linear relationship between TIR and HbA1c or estimated HbA1c (eHbA1c) and asymptomatic hypoglycemia (Al Hayek et al., 2017; Beck et al., 2019; Fabris et al., 2020; Gabby et al., Hirsch and Verderese, 2017; Kropff et al., 2017; Martin et al., 2019; Mattishent & Loke, 2018; Ushigome et al., 2020; Vigersky & McMahon, 2019; Xu et al., 2020; Yamada et al., 2020). Patient acceptance or satisfaction with CGM use was supported in the selected articles (Barnard et al., 2018; Edelman, 2017; Gilbert et al., 2021; Martin et al., 2019; Mattishent and Loke, 2018; Schlüter et al., 2020). In addition, the article that gave insight into CGM use and cost was also selected (Gill et al., 2018). Other articles whose studies were not yet complete were added because they included foundational information on the importance of CGM use for all diabetes patients challenged with unsuccessful glycemic control (Kieu et al., 2021; Lind et al., 2021). Non-journal information obtained from the United States CDC, American Association of Clinical Endocrinology (AACN), and NIDDK, was used to provide relevant statistical data used to define the importance of glycemic control in diabetes patients.

The data rendered for this IR included eight systematic reviews, six randomized controlled trials (RCTs), seven controlled cohort studies, two uncontrolled cohort studies, one qualitative study, and two expert opinions. The latter was included because one of the expert opinions provided an overview of the international consensus for the metrics TIR, which strengthens CGM data reliability (Gabby et al., 2020). The other journal referenced increased patient satisfaction with CGM use (Edelman, 2017). Overall, the articles selected for this IR

addressed the clinical question using comprehensive methodologies or provided valuable insight into CGM use's practicality.

Conceptual Framework

The conceptual framework used for this IR is a version of Whittemore and Knafl's constant comparison method (2005). This process required and involved a methodical rigor evaluation of primary literature data in evaluating each article's relativeness to the research question and each other. Each article obtained for this IR was evaluated, analyzed (reduced, displayed, compared, and categorized), and conclusions were drawn based on recurring themes in the findings (Toronto & Remington, 2020). The scientific underpinning framework for this IR was based on the premise that a relationship between diabetes and HbA1c levels exists. Understanding how this relationship is affected by glycemic management tools like CGMs can help improve patient outcomes by improving the blood glucose level control. The research was initiated using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guidelines (Moher et al., 2009) and Melnyk and Fineout-Overholt's (2015) pyramid levels of hierarchy tool. The methodology of IRs provided by Whitmore and Knafl (2005) provided the framework umbrella for this IR. Using the constant comparative method, each piece of data was compared and contrasted using the clinical question *Does home-based CGMs use by diabetes patients decrease HbA1c* as the umbrella and principal guide to categorize each piece of data into an appropriate category based on the article's findings. In this IR, evidence was arranged in a logical building order reflective of the clinical question (Whittemore and Knafl, 2005) and formulated results. Appendix A shows a visual display of the literary matrix and reduction analysis using the hierarchy levels by Melnyk and Fineout-Overholt (2015) and Appendix B for formulated categories and themes created based on the data. According to

Whittemore and Knafl (2005), an IR should present its findings logically and methodically based on the evidence presented.

SECTION TWO: COMPREHENSIVE AND SYSTEMATIC SEARCH

Search Organization Reporting Strategy

Sources for this IR were obtained using a thorough systematic search approach (Toronto and Remington, 2020) of six databases (Cochran Database, MEDLINE, CINAHL, Plus, PubMed, ProQuest, and government websites). As described in the inclusion and exclusion section, data were collected, reviewed, analyzed, and sorted. Based on Melnyk and Fineout-Overholt's (2015) pyramid levels of hierarchy tool, data for this IR was categorized first based on its data type strength (Melnyk and Fineout-Overholt, 2015). The Melnyk and Fineout-Overholt (2015) evidence tool qualifies literature sources based on defined hierarchy levels. Level I is rated the highest and level VI the lowest in terms of rigor. Level I is assigned to literature that includes a systematic review and meta-analysis of randomized controlled clinical trials (p. 92), to which eight articles were assigned. Level II is assigned to literature that includes one or more RCTs (p. 92), to which six articles were assigned. Level III is reserved for studies that include controlled cohort and non-randomized studies (p. 92), to which seven articles were assigned. Level IV includes studies that are uncontrolled cohort in nature (p. 92). Two of the 26 articles retained for this review project met this level of evidence. Hierarchy Level V is reserved for literature that describes a review of descriptive and qualitative case studies or series, evidenced-based project implementations, or quality improvement projects (p. 92). This review identified one article that met this level of evidence. Level VI, the last and lowest level of the Melnyk and Fineout-Overholt (2015) hierarchy of evidence, is reserved for an expert opinion presented by someone who is believed to have a high level of knowledge regarding a topic. This

IR contained two articles assigned to this level. This IR presents an analysis covering the literature from the highest priority level (level I) of evidence to the lowest (level VI).

An IR requires a cohesive reporting method. The PRISMA tool is used to systematically and in a categorical way, organize literature findings (Moher et al., 2009). The PRISMA tool was adapted for this IR to provide a logistical visual flow of research data analyzed throughout this IR to assist in the minimization of bias while increasing rigor of the review (Toronto and Remington, 2020). The flow chart demonstrates the literary flow of topics: diabetes, CGM, HbA1c, patient CGM use and costs, and the associated number of data that resulted from the search.

Terminology

To minimize confusion in this IR, the word *database* when used refers to a searchable electronic collection of published materials that include professional peer-reviewed journals and publicly available government statistical data (Toronto and Remington, 2020). Furthermore, the term *search engine* used in this IR describes an electronic library search of multiple databases using the Jerry Falwell library located at Liberty University (Toronto and Remington, 2020).

SECTION III: METHODS: MANAGING THE COLLECTED DATA

The design method aligns with the activities associated with an evidenced-based IR process that requires enhanced rigor and analysis (Whittemore and Knafl, 2005). The process was initiated with a preliminary literature review, evaluation, appraisal, and synthesis of the best available scientific evidence (Melnyk and Fineout-Overholt, 2015) relevant to adult patients with diabetes, home-based CGM use, and HbA1c levels. Abstracts of the articles were read and evaluated for topic relevancy, followed by a thorough evaluation for result relevancy. An evidence-based literature synthesis matrix can be observed in Appendix A and was completed by

one reviewer. The studies were evaluated for quality, bias, and clinical question relevancy using the constant comparison method (Toronto and Remington, 2020). The PRISMA flowchart was used to visually screen the article selection process (Moher et al., 2009) (see Appendix C and Appendix E).

SECTION FOUR: QUALITY APPRAISAL

Sources of Bias

Any information that distorts study findings systematically that results from the study methodology causes bias (Melnyk and Fineout-Overholt, 2015). Scholarly research requires methods that ensure internal validity and that reduce bias (Toronto and Remington, 2020). Reduction of bias in this IR article database was established using the PRISMA framework (Moher et al., 2009) and Melnyk and Fineout-Overholt's levels of hierarchy tool, which involved the review, evaluation, analysis, and sorting of each article. (Melnyk and Fineout-Overholt, 2015). This analysis was completed to establish topic relevancy for use in this IR (Melnyk and Fineout-Overholt, 2015). This effort yielded no findings of bias.

Internal Validity

When the study results are obtained using proper scientific methods, validity can be established. Internal validity is important to establish because it relates the believability of research results when the findings are obtained using appropriate scientific methods without bias (Toronto and Remington, 2020). If internal validity is not established, external validity will not be applicable. If external validity or generalizability cannot be established, the usefulness and applicability of the findings in this IR to populations outside of this review are unlikely (Melnyk and Fineout-Overholt, 2015).

Appraisal Tools (Literature Matrix)

Critical appraisal of the evidence is highly recommended, but the appraisal tools and methods used should align with the type of literature being reviewed (Toronto and Remington, 2020). With over 100 appraisal tools available for use, no gold standard appraisal tool has been established to confirm quality ratings (Toronto and Remington, 2020). For this IR proposal, empirical and theoretical data was evaluated first for topic relevancy and second for rigor of methodology (Whittemore and Knafl, 2005). Diverse primary data collected was appraised for relevance and quality using the Melnyk and Fineout-Overholt framework. The evidence was placed into a matrix and categorized using the Melnyk and Fineout-Overholt's levels of evidence that ranks data from I to VI (Melnyk and Fineout-Overholt, 2015) as previously described. Article themes was an additional categorical method used to categorize and synthesize articles based on their theme trend (See Appendix B).

Applicability of Results

The 26 articles selected for this IR proposal were critically appraised and relevant to the clinical topic of home-based CGM use and the lowering of HbA1c levels. The literary data was organized and placed in the matrix by title, study purpose, sample size, methodology, results, and limitations (Melnyk and Fineout-Overholt, 2015). Following a thorough review and categorization of data based on themes observed in the literature reviewed, the data suggests that CGMs used in the outpatient setting are useful self-monitoring tools that can aid in the reduction of HbA1c levels for diabetes patients.

Reporting Guidelines

IRs are a data reporting method that allows for methodologies of diverse foundations that offer varied perspectives of a phenomenon and are important to nursing science and practice (Whittemore and Knafl, 2005). Each article in this IR was evaluated for the applicability of

CGMs used in the out-patient setting and the lowering of HbA1c levels. To minimize bias and increase transparency, PRISMA reporting and Melnyk and Fineout-Overholt's (2015) appraisal tools were used to arrange and report data (Toronto and Remington, 2020).

SECTION FIVE: DATA ANALYSIS AND SYNTHESIS

Data Analysis Methods

According to Whittemore and Knafl (2005), the analysis of data in the research of a phenomenon requires that the primary data sources be "ordered, coded, categorized, and summarized" and meshed into a unified conclusion (p. 550). The primary goal is to provide additional insight to the IR clinical question, which is CGMs use and lowered HbA1c levels in diabetes patients. Therefore, each article was placed in the Melnyk and Fineout-Overholt's (2015) level of evidence categorizing system, which allowed for repeated comparisons of primary sources for topic relationship and then synthesized based on the themes observed during the evaluation process. Moreover, study design, purpose, and data results were key evidence information used to compare data for topic relevance and applicability.

Data Reduction

Determining a classification system that supports subgroups for the primary data is a primary step for data reduction (Whittemore and Knafl, 2005). Logical placement of primary data into subgroups aids in further data analysis (p. 550). For this IR, the evidence matrix used was Melnyk and Fineout-Overholt (2015) literature classification system. Each article was alphabetized by title and author and categorized into columns that divided and identified the literature by study purpose, sample size, methods, study results, level of evidence (I-VI), study limitations, and whether the study should be included in this IR study sample. Once categorized, the articles were further coded, and information was extracted based on to what degree the

clinical question was addressed or supported. This step increased the manageability of the framework allowing for systematical comparison of the primary data (p. 550).

Data Display

The data display allows for further data extracted into subgroups or themes based on the article concentration or focus related to the study question, according to Whittemore and Knafl (2005). In this IR, there are two data display tables. First, one categorized all 26 articles individually with categorical information, which separated the data (See Appendix A, the Evidence Matrix Table). Second, data displayed has been presented in a table form with a thematic display, where the articles were placed in categories based on the theme(s) presented, which was derived using the constant comparison method (See Appendix B, the CGM Article Matrix Table). Some articles were reflected in more than one theme. The thematic matrix allows for data visualization related to the clinical question (p. 551).

Data Comparison

Whittemore and Knafl (2005) resolve the stance that sequential data analysis involves the process of data comparison where the data display of the primary data requires the IR project leader to order the data based on "identified patterns themes or relationships" (p. 551). The data comparison phase sets the platform for the discernment of a conceptual map that shows the relationship between the clinical question variables and themes presented in the data. In this IR, the data comparison and visualization helped bring clarity which allowed for early interpretation of the data (p. 551). In addition, this phase resulted in identifying meaningful higher-order clusters of information that has been presented in the CGM article matrix table (See Appendix B). The first and key relationship identified answered the clinical question concerning the relationship between CGMs used in the out-patient setting by diabetes patients and the lowering

of HbA1c levels. The second theme identified was the verification and reliability of the data produced using CGMs, confirmed by demonstrating the inverse linear relationship between TIR and HbA1c levels and hypoglycemia. This theme supports the first higher theme. The third theme that surfaced was the diabetes patient's acceptance and satisfaction with CGMs used in the out-patient setting. The fourth theme represented was the value in reducing overall healthcare costs associated with CGMs, and the last theme identified was the importance of CGM use with dedicated plans for future studies.

Conclusion Drawing and Verification

According to Whittemore and Knafl (2005), this phase allows for IR in its entirety to be displayed with a presentation of the subsets generalized in a format that allows for checks and balances of the clinical question, variables, themes, and subsets to be reverified using the primary sources for accuracy and final confirmation. This process was used and increased correctness in drawing accurate IR conclusions that reflect the primary data. It must also be noted that some themes were represented in more than one data set. This aids theme strength.

Article Themes Discussion

CGM use and HbA1c Reduction

Of the 26 articles evaluated, CGM use and reduction on HbA1c levels were found in 13 articles. Advani (2019) found that when TIR (a key GCM matrix) was greater than 70%, diabetes patients experienced lowered HbA1c levels. Azhar et al. (2020), in their systemic review of 17 studies purposed to report CGM implications, found that two studies reported CGM use was associated with lowered HbA1c levels and that T2DM users who commonly have less glycemic variability than patients with T1DM had a higher significant reduction in their HbA1c levels than in patients with T1DM. Beck et al. (2017), Eleftheriadou et al. (2019), and Gilbert et al. (2021),

in their RCTs, reported reductions of HbA1c levels in patients with T2DM from 8.0% to 7.7%. Eleftheriadou et al. (2019) found reductions from 8.0% to 7.6% and 7.6% to 7.1% in patients with T1DM. When they evaluated patient responses to CGM use, Gilbert et al. (2021) found reductions from 8.1% to 7.0% and 8.5% to 7.1% in patients with T1DM and T2DM, respectfully. Chan et al. (2018) reported that CGM use was associated with lowered HbA1c levels in young adults with cystic fibrosis. Al Hayek et al. (2017) found that when comparing SMBG and CGM use, HbA1c levels were further reduced with the use of CGM device. Kropff et al. (2021) found in their observational study to assess patient response to CGM use that HbA1c levels dropped from 7.54% to 7.19%. Lameijer et al. (2021) evaluated data extracted from 16,331 analyzable readers over 6-month and reported lowered eHbA1c levels. Martin et al. (2019), in their review of six RCTs of advanced technologies of insulin pumps and CGMs, found that CGM use was favored over the use of insulin pumps and HbA1c levels were reduced with CGM use when the technologies were compared. Rivera-Ávila et al. (2021) evaluated the effects of CGM use in a controlled study with 302 patients with T2DM whose HbA1c levels were above 8%. At the end of 3 months, the intervention group experienced a mean difference of 0.439 lower HbA1c level than the control group. Schlüter et al. (2020), in their evaluation of the SPECTRUM training program for CGMs, found that patients experienced a reduction of HbA1c levels from 12% down to 9%. Valenzano et at. (2021), in their study of 70 white patients with T1DM, first-time CGMs users, found that in patients who experienced an increasingly higher percent of TIR, their HbA1c levels lowered from 7.5% to 7.0%.

CGM Data Reliability: Linear Relationship Between TIR, HbA1c. and Hypoglycemia Detection

In a study to better understand the relationship between TIR, HbA1c, and hypoglycemia, Beck et al. (2019), in a review of four RCTs involving 545 adult patients with T1DM, found that TIR of 70% and 50% correlated to HbA1c levels of 7% and 8%, respectively. Hypoglycemia and hyperglycemia are more accurately detected when TIR is > 70%. Fabris et al. (2020) desired to bridge the gap between laboratory measured HbA1c levels. In 125 patients with T1DM, they set out to determine the relationship between HbA1c levels and estimated HbA1c (eHbA1c) (CGM obtained). They discovered that eHbA1c levels were 10% from reference HbA1c levels of 97.6% and 96.3%. They concluded that HbA1c and TIR are reflections of the same underlying process of glycemic fluctuation and that eA1c is an intermediate metric that can be used to assess glycemic control with CGM use. These findings support the reliability of data provided using the CGM devices. Gabby et al. (2020) conducted a technical review that provided insight and overview of the international consensus in TIR. An expert opinion that recommends TIR use as a new metric to evaluate glycemic control in diabetes patients. Al Hayek et al. (2017), in their study described above, identified the inverse linear relationship between CGM use and HbA1c levels and that CGM use was also associated with a reduction of hypoglycemic episodes, which equated to less fear of hypoglycemia expressed by patients. Hirsch and Verderese (2017), in their exploration of literature to assess the use of an ambulatory glucose profile reporting to supplement current diabetic management tools, found that CGM use by diabetes patients helped this population identify glycemic targets by identifying symptomatic hypoglycemia that could be corrected. Kropff et al. (2017), also described above, found in their observational 180-days study that 99.2 % of the participants experienced clinically acceptable error zones with hypoglycemic events detected 81% of the time. Martin et al. (2019), in their review of six RCTs of patient response to insulin pumps and CGM use, found that patients using CGMs experienced an

increase in the detection of hypoglycemia. Mattishent et al. (2018), in their review of nine CGM studies with 898 older diabetics, found that participants experienced a higher rate of detection of asymptomatic hypoglycemic episodes. Ushigome et al. (2020), in their RCT study involving 18 patients with T2DM undergoing hemodialysis, aimed to evaluate if blood glucose control can be evaluated using eHbA1c levels (obtained from the CGM device). The study helped determine that eHbA1c obtained from CGM devices can be a reliable indicator for evaluating glycemic control and avoiding hypoglycemia episodes in patients undergoing hemodialysis. Vigersky and McMahon (2019), in their review of 18 articles and 1,137 participants over 10-years, found that there were excellent correlations between HbA1c and % TIR in a linear relationship, which confirms the reliability of CGM data. Xu et al. (2020), in their effort to evaluate the degree of discrepancy of (eHbA1c) from CGM and laboratory HbA1c levels, found that the glycemic marker eHbA1c accurately reflects laboratory HbA1c may provide a tool for assessing glycemia over a variable time period using the CGM device. Finally, Yamada et al. (2020) also aimed to evaluate the relationship between HbA1c and mean glucose levels in 59 patients with T1DM and T2DM in the out-patient setting found a significant correlation between HbA1c and mean glucose levels using the CGM. This relationship was stronger in patients with T2DM than in patients with T1DM.

CGM Use, Patient Acceptance and Increased Patient Satisfaction

Barnard et al. (2018), in their systemic review on the implications of CGM involving 51 adult diabetes patients, found that new and old users prefer CGM use over traditional SMBG tools. Both groups reported improved glycemic control with CGM use and favored continued CGM use at the end of the study. Edelman (2017) provides an expert opinion regarding the Dexcom 5 CGM where he reports patient acceptance and satisfaction of this newer CGM

currently being marketed to all diabetes patients. In their study previously described, Gilbert et al. (2021) also evaluated the psychosocial changes among patients with T1DM and T2DM regarding CGM use. They found that patients were satisfied or very satisfied with CGM use. Martin et al. (2019), with representation in the first two themes, also reported increased patient satisfaction with CGM use. Mattishent et al. (2019), also represented in the theme above, reported CGM use associated with patient acceptability and improved health-related wellness. Schlüter et al. (2020), represented in previous themes, reported that in addition to the 3% improvement in HbA1c levels, a secondary endpoint of their study included patient satisfaction for CGM use, which was rated high.

CGM Use and Cost Reductions

Gill et al. (2018), in their retrospective cross-sectional analysis study of health care costs and CGM, found in their review of 1,027 patients whose insurance pays for CGM use, spent on approximately $4,200 less in total health care costs when compared with patients not using CGMs. They also found that CGM user patients experienced fewer hospitalizations and better glycemic control.

CGM Importance and Future Studies

Kieu et al. (2021) share plans of a future hierarchy level 1 study that provides a systematic review protocol on the benefits of the addition of CGM use in the primary care setting versus standard SMBG and HbA1c levels. Lind et al. (2021) have plans for a future RCT trial to evaluate CGM use and patients with T2DM. The study was set to start from August 2020 to August 2022 and aims to examine the effectiveness of CGM versus standard SMBG in patients with insulin treated T2DM.

Descriptive Results

This integrative review examined 26 articles from diverse data sources with variable design styles enhancing a holistic understanding of CGM use, HbA1c levels, and their value to diabetes patients (Whittemore and Knafl, 2005). The articles covered a recent time period of 2016−2021 with the interests of capturing studies that reflect the current state of the problem. Themes and visual aids (see Appendices A−D) have been included to improve the logistics in the presentation of this IR data. This IR has presented a literature analysis that answered the clinical question surrounding the relationship between CGM use and lowered HbA1c levels. The data presented support the phenomenon of an inverse linear relationship between CGM use among diabetes patients and HbA1c levels. This relationship has been strengthened with the data reliability demonstrated in CGM use and TIR. Hypoglycemia, a life-threatening situation, has also been detected as a health benefit with CGM use. Some studies even indicated that CGM linear relationship with HbA1c data in patients with T2DM was more strongly correlated than results found in T1DM. This IR also provided insight into patients' personal experiences and increased satisfaction with CGM use. Gill et al. provided insight into the cost savings of insurance covered CGM use. As CGM use increases, more studies ensue. This will add to the body of knowledge of CGM use and benefits.

Synthesis

The 26 articles presented in this IR have provided information that answered the clinical question (Toronto and Remington, 2020) of CGM use by adult diabetes patients and HbA1c level reduction (Advani et al., 2019; Azhar et al., 2020; Beck et al., 2017; Chan et al., 2018; Eleftheriadou et al., 2019; Gilbert et al., 2021; Al Hayek et al., 2017; Kropff et al., 2017; Lameijer et al., 2021; Martin et al., 2019; Rivera-Ávila et al., 2021; Schlüter et al., 2020;

Valenzano et al., 2021;) Other articles presented supported CGM data reliability by demonstrating a linear relationship between TIR and HbA1c or eHbA1c and symptomatic and asymptomatic hypoglycemia detection (Al Hayek et al., 2017; Beck et al., 2019; Fabris et al., 2020; Gabby et al., Hirsch and Verderese, 2017; Kropff et al., 2017; Martin et al., 2019; Mattishent and Loke, 2018; Ushigome et al., 2020; Vigersky and McMahon, 2019; Xu et al., 2020; Yamada et al., 2020). Patient acceptance or satisfaction with CGM use was supported in the selected articles (Barnard et al., 2018; Edelman, 2017; Gilbert et al., 202; Martin et al., 2019; Mattishent and Loke, 2018; Schlüter et al., 2020). In addition, the article discussed that it gave insight into CGM use and decreased health care cost was provided (Gill et al., 2018). Other articles whose studies were not yet complete were discussed in the IR because they added foundational information on the importance of CGM use for all diabetes patients challenged with unsuccessful glycemic control (Kieu et al., 2021; Lind et al., 2021).

Ethical Considerations

This was an IR, and the IR project leader did not have direct contact with human participants or exposure to identifiable participants' data. Therefore, ethical concern was not applicable to this study. Successful electronic submission and approval for this IR was received by the Liberty University IRB and status of exemption was given (See Appendix C).

SECTION SIX: DISCUSSION

Implications for Practice/Future Work

Additional research is needed to further explain the hesitancy toward CGM use becoming a covered insurance benefit by health plans. This IR has provided data to show that CGM use is associated with many health benefits for diabetes patients and the U.S. healthcare economy. U.S. Statistics have shown that current management tools such as SMBG have fallen short in helping

diabetes patients improve glycemic control and prevent the development of cellular damage that translates into increased co-morbidities, premature death and increased national expenditures, and diabetes patients' health care costs. When new knowledge of advanced technology demonstrates improved patient outcomes and a reduction in overall health care costs for a group of patients, healthcare policy changes should be considered. This IR has presented data that can be used in the clinical guidelines for needed policy changes for diabetes patients, when using CGM as an intervention management tool.

Dissemination

The intended audience for this IR is anyone interested in CGM use and its relationship to HbA1c levels in diabetes patients in the community. It applies to clinicians who manage diabetes patients and those who advocate for improved health care services and policy changes for this population. Diverse methodologies were used in this IR to present the topic in a clear, systematic way that answered the clinical question. With rising healthcare costs and an aging population, improved ways to manage and improve glycemic control in diabetes patients should be a national priority. This IR has presented data that demonstrated an alternative to standard SMBG and that CGM use is associated with lowered HbA1c levels, CGM data have been deemed reliable, CGM use is approved by the patients, and associated with health care cost savings. Dissemination of information in this IR can be presented in a publication, poster format, or presented in its current format.

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TABLES

Table 1

Inclusion and Exclusion Criteria

Inclusion	Exclusion
Publication from 2016−2021	Publication prior to 2016
Adult diabetes patients > 18 y	Pediatric population < 18 y Pregnant women
Publications written in the English language	Publications written in a foreign language
Peer-reviewed journals	Non-peer-reviewed articles
Full-text articles	Abstract only articles
Out-patient setting	Hospital setting

Appendix A

Evidence Matrix Table

Article Title, Author	Study Purpose	Sample	Methods	Study Results	Level of Evidence: Melnyk Framework	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale
Positioning TIR in diabetes management (Advani, A., 2019)	To summarize guidance for healthcare professional in helping patient interpret TIR goals	*n = 64* resources	Systematic Review	TIR is a key metric for CGM use in determining glucose control and inversely correlates with HbA1c	Level I	None discussed	Yes: Provides descriptive data which helps with clarifying TIR and TBR
Evaluation of FreeStyle Libre Flash glucose monitoring system on glycemic control, health-related quality of life, and fear of hypoglycemia in patients with T1DM. (Al Hayek et al., 2017)	To evaluate patient experience with the FreeStyle Libre a CGM device compared with traditional finger-pricking blood glucose monitoring	*n* = 47 (aged 13–19) patients at a diabetic treatment center in Riyadh, Saudi Arabi. 64% of the participants were ages (17-19)	A prospective study conducted between Jan 2021 and May 2017	*Patients preferred the CGM over the finger-pricking method. *Increasing scanning was observed *HbA1c levels significantly decreased. Hypoglycemia frequency decreased. *Patient fear of hypoglycemia decreased	Level III: Controlled cohort study	Small sample size and the inclusion of only one center for study	Yes. The study adds to the body of knowledge regarding the benefits of CGM and lowering of HbA1c levels

A systematic review on clinical implication of CGM (Azhar, Gillani, Mohiuddin, & Majeed, 2020)	To report clinical implications of CGM use in patients with diabetes, HbA1c, estimated A1c, and glucose variability	*n = 17* articles from years 2017−2019	PRISMA guidelines were used to study and analyze data	When compared with non-CGM users, T1DM and T2DM CGM users had a decrease in HbA1c levels of a significant levels	Level I	Lack of internationally accepted standards for CGMs	Yes: CGM use in patients with T2DM is still in its infancy and this systematic review adds to the body of knowledge surrounding support for validity of results obtained from CGMs
Acceptability of implantable CGM sensor. (Barnard et al. 2018)	Assess benefits of CGM including psychosocial	51 T1DM (*n = 46*). T2DM (*n = 5*) 18 yrs. + patients across the United Kingdom and Germany	A non-experimental, descriptive survey. PRECISE trial.	CGM devices were favorable to users, helped to improve glucose management, Both groups, first-time users and previous users would like to continue CGM devices	Level V	Lack of psychosocial baseline data. None listed by researchers	Yes. Descriptive data is helpful. Aids in understanding patient experiences with CGMs use
The relationships between TIR, hyperglycemia metrics, and HbA1c. (Beck et al. 2019)	To understand the relationship between CGM use, TIR (70−180 mg/dL) of metric and patterns, hyperglycemia, and HbA1c levels	545 adults with T1DM (from four random trials) were obtained from a database with centralized laboratory HbA1c results and CGM metrics	Analyses from datasets from four RCT Cross-sectional and longitudinal (6-months)	TIR levels averages correlated in the following way: 70% and 50% corresponded with HbA1c levels approximately 7% and 8%, respectively. A noted considerable	Level I	Study data are reflective of individuals who participated in clinical trials, which might not be representative of the full population of adults with T1DM	Yes. Data adds insight to CGMs use and benefits. It supports the reliability of data obtained from CGMs and its correlation to HbA1c levels

				spread of change in HbA1c for a given change in time-in-change levels			
CGM versus usual care in patients with T2DM receiving multiple daily insulin injections. (Beck et al. 2017)	To evaluate the effectiveness of CGM use in adults with T2DM receiving multiple daily injections of insulin	25 endocrinology practices in North American 158 participants with T2DM, randomly assigned to CGM: *n* = 79; control group (usual care) *n* = 79	RCT: 158 participants with T2DM, randomly assigned to CGM: *n* = 79; control group (usual care) *n* = 79	Mean HbA1c levels decreased to 7.7% in the CGM group and 8.0% in the control group at 24 weeks	Level II	There was no 6-month follow-up	Yes. The data offers helpful information to describe the beneficial outcomes with CGMs use and the lowering of HbA1c levels
HbA1c accurately predicts CGM-derived average glucose in youth and young adults with cystic fibrosis. (Chan et al. 2018)	To assess and compare glucose markers: HbA1c and an average sensor glucose (ASG) in patients with cystic fibrosis with CGM use	39 patients with cystic fibrosis (CF) and 29 control group; aged 6−25 years with CGM use	Controlled cohort study	HbA1c levels did not underestimate ASG as previously assumed. No other glycemic marker correlated more strongly with ASG than HbA1c levels	Level III	Study estimates for average glucose were generated from 1 week of CGM use, while HbA1c represents a weighted measure of average glucose over the preceding 3 to 4 months. Uncertainty of comparisons of	Yes

						diabetes patients and CF	
Regulation catches up to reality: Nonadjunctive use of CGM data (Edelman, S. 2017)	Commentary regarding the DEXCOM 5 and Food and Drug Administration (FDA) approval	N/A	N/A	N/A	Level VI	N/A	Yes. Commentary on patient experience using the DEXCOM 5 CGM device is helpful
Improvement of metabolic control after 3-months rtCGM use in patients with T1DM: A multicenter study in Greece (Eleftheriadou et al., 2019)	To evaluate the efficacy of rtCGM added to insulin pump therapy for 3-months	43 adult patients with T1DM on insulin pump therapy and HbA1c > 7%	Data analysis of participants' HbA1c at the start of the program and 3-months post	At 3-months, participants' baseline HbA1c levels decreased from 8.0 to 7.6 and from 7.1 to 6.7 % ($P <$ 0.001). Nineteen (44.2%) of the sample had HbA1c level drop to $\leq$ 7%	Level III	Not discussed	Yes. The study validates CGM use with the reduction of HbA1c levels
Estimation of HbA1c from CGM data in individuals with T1DM: Is TIR all we need? (Fabris, Heinemann, Beck, Cobelli, & Kovatchev, 2020)	To bridge the gap between laboratory-measured HbA1c and CGM-derived TIR, introducing TIR-driven estimated A1c (eA1c)	125 individuals with T1DM, and HbA1c at 3 months; and 168 individuals, and HbA1c at 3, 6, and 9 months	Data from Protocol 1 (training data set) and Protocol 3 (testing data set) of the International Diabetes Closed-Loop Trials were used	Mean absolute differences between HbA1c and eA1c 3- and 6-months post calibration were 0.25% and 0.24%; Pearson's correlation coefficients were 0.93 and	Level II	Not discussed	Yes. The information helps to bridge the knowledge gap of HbA1c and TIR

				0.93; percentages of eA1c within 10% from reference HbA1c were 97.6% and 96.3%, respectively. HbA1c and TIR are reflections of the same underlying process of glycemic fluctuation			
TIR: A new parameter to evaluate blood glucose control in diabetes patients (Gabby et al., 2020)	To provide an overview of the International Consensus in TIR	Diabetics using CGM	Technical review commentary	Recommendation of use of TIR as a new and useful metric to evaluate glycemic control	Level VI: Expert Opinion	Limitations not discussed	Yes: The information shared provides additional insight that supports CGM use and data reliability
Change in HbA1c and quality of life with rtCGM use by people with insulin-treated diabetes in Landmark's study (Gilbert,	To evaluate glycemia and psychosocial changes in T1DM and T2DM during their first few months of CGM use	*n = 248* (182 with T1DM and 66 with T2DM)	Real-world prospective study from nationwide callers who placed orders for the Dexcom G6 CGMs. Baseline and	Mean HbA1c levels for patients with T1DM decreased from 8.1% to 7.0% and for patients with T2DM HbA1c	Level IV	1. Lack of a control group and the absence of baseline blinded CGM data. 2. Possible heterogeneity in HbA1c measurement	Yes: Provides data that CGM use is associated with lowered HbA1c levels in patients with T1DM and T2DM

Noar, Blalock, & Polonsky, 2021)			12+ weeks post HbA1c levels were compared	decreased from 8.5% to 7.1%. 93% of patients were either satisfied or very satisfied with the device. 73% (70% of T1DM and 80% of T2DM) found it very easy to use		method (point-of-care) vs. laboratory reporting	
Health care costs, hospital admissions, and glycemic control using a standalone, rtCGM system in commercially insured patients with T1DM. (Gill et al., 2018)	To compare health care spending, hospital admissions, and HbA1c levels of patients using rtCGM to that of patients not using rtCGM	rtCGM patients; *n = 1,027* non-users, *n = 32,583*	retrospective, cross-sectional analysis that used a large repository of health plan administrative data to compare average health care costs	Patients using rtCGM spent an average of approximately $4200 less in total health care costs when compared with patients not using rtCGM ($P < .05$). They also experienced fewer hospital admissions ($P < .05$) and lower HbA1c ($P < .05$) during the post-index year	Level II	1. Optum database does not include actual allowed amounts for claims, which caused the researcher to determine the actual effect of rtCGM on spending. 2. Optum database includes only direct costs; thus, we were unable to evaluate the impact of rtCGM on indirect costs, such as days missed from work. 3. the sample size for	Yes. Links other health benefits to CGM use

						the subgroup of patients for whom HbA1c data were available was relatively small	
Professional flash CGM with ambulatory glucose profile reporting to supplement HbA1c: Rational and practical implementation. (Hirsch & Verderese, 2017)	To determine if the use of a standardized report form called the ambulatory glucose profile (AGP) supplemented with CGM and HbA1c levels is a helpful management tool for diabetes patients	The exact number of medical literatures, professional guidelines, and real-world evidence of CGM use was used to build an integrative practice framework to examine AGP use was not given	An exploration of literature, professional guidelines, and information obtained from CGM users and AGP use to create comprehensive data that reflects practical CGM use and its relationship to HbA1c levels	CGM use helps diabetes patients to safely meet glycemic targets by identifying symptomatic hypoglycemia that can be corrected. AGP use and HbA1c monitoring can aid clinicians with translating to patients the long-term benefits of diligent glycemic control	Level 1	No limitations were discussed	Yes. The study supports reliability of CGM data and linkage to HbA1c levels
Benefits of the addition of continuous or flash glucose monitoring versus standard practice using self-monitored	To compare usual care use of SMBG and HbA1c and if adding CGM in primary care patients improves	This study was planned from February 2021 to December 2021	Systematic Review of RCT	To be determined	Level 1	Not applicable	Yes. Preliminary information validates the seriousness and need for improvements in glucose

blood glucose and HbA1c in the primary care of DM: a systematic review protocol. (Kieu et al., 2021)	glycemic control, decrease rates of hypoglycemia, and improve patient and physician satisfaction?						management for diabetes patients
Accuracy and longevity of an implantable continuous glucose sensor in the PRECISE Study: A 180-day, prospective, multicenter, pivotal trial. (Kropff et al., 2017)	To assess patient response to the use of the Eversense implantable CGM device, device accuracy, and whether its use increased patient glycemic control	Patients with T1DM and T2DM; *n = 71*, aged 18 years and older multinational	An observational, 180-day multicenter pivotal trial	99.2% of sample clinically acceptable error zones with hypoglycemic events detected 81% of the time within 30 mins. Improved HbA1c from 7.54 to 7.19.	Level III	No limitations were shared by researchers	Yes. Helpful information regarding comparable CGM devices
Flash glucose monitoring in the Netherlands: Increased monitoring frequency is associated with improvement of glycemic parameters. (Lameijer et al., 2021)	To evaluate the association between flash glucose monitoring (FLASH) frequency and glycemic parameters during real-life circumstances in the Netherlands	20 equally sized rank ordered groups (*n = 817*)	Data extracted from 16,331 analyzable readers between September 2014 and March 2020 were analyzed	Increased scans rates were associated with *a higher % of TIR (3.9−10 mmol/L) (better glycemic control). *Less time in hyperglycemia (> 10 mmol/L) *Improvement with eHbA1c	Level IV: Uncontrolled cohort study	1. Cross-sectional study design precludes conclusions regarding causality. 2. Detailed information about the FLASH users was not available.	Yes. The study results support improved glycemic control with FLASH CGM system use

						3.Lack of information regarding carbohydrate intake was not available. 4. Sub-groups not identified. 5. eHbA1c does not always closely approximate laboratory measured HbA1c	
rtCGM versus self-monitoring of blood glucose in adults with insulin-treated T2DM: a protocol for a center trial. (Lind et al., 2021)	This is a future study aimed to examine the effectiveness of CGM use compared with SMBG	Recruitment of adults with T2DM for this study started in August 2020 and ended in July 2021 with a follow-up planned for August 2022. The target aim for participants was 100	Planned for a single-center, prospective, randomized, open-labeled, three-armed	To be determined	Level II: RCT	Researchers discussed the study's possible limitation with generalizability due to exclusion criteria. The unblinded methods of the trial and unforeseen rates of participant dropout, which could bias the results	Yes. The study introduction highlights the significance and need for change with addressing glycemic control in patients with T2DM
Advanced technology in the	The review of RCTs of advanced	Review of six RCT	Summary of reported	CGM use favored over insulin pump.	Level 1 Systematic	Article did not discussed limitations	Yes, the article reports inverse relationship

management of diabetes: which comes first – CGM or insulin pump? (Martin et al., 2019)	technologies, including the CSII insulin pump and CGM for the management of diabetes in patients with T1DM		published findings	With CGM use there was an increased with patient satisfaction, an increased in hypoglycemia detection and a reduction of HbA1c levels	review of RCTs		between CGM use and HbA1c, and increase patient satisfaction
Detection of asymptomatic drug-induced hypoglycemia using CGM in older people – a systematic review (Mattishent & Loke 2018)	A systematic review of CGM use in older patients and hypoglycemia	9 studies with 898 older diabetes patients	Searched Web of Science, Ovid SP MEDLINE, and EMBASE from January 2010 to June 2017 for observational studies and RCT of CGM in older patients (mean age 65 or older) with diabetes	Asymptomatic Hypoglycemic episodes codes observed, CGM acceptable and experienced improved health-related wellness	Level 1	Data included heterogenous information, which limits the generalizability to the general older population with diabetes	Yes. Level 1
The effects of professional CGM as an adjuvant educational tool for improving glycemic	To evaluate the effects of CGM as an adjuvant educational tool for improving glycemic control in	*n = 302* patients with T2DM: Intervention group *n = 150*, control group; *n = 152*	A 3-month quasi-experimental study with an intervention and control group in one family	At the end of the 3-month follow-up, study found a 0.439 mean HbA1c difference between the groups (*P* =	Level III: Non-randomized quasi-experimental study with the intervention	1.This design is "quasi-experimental" because assignment into the intervention and control groups were not random. 2.	Yes. Study supports CGM use and inverse relationship to HbA1c

control in patients with T2DM (Rivera-Ávila et al., 2021)	patients with T2DM		medicine clinic with T2DM with HbA1c levels > 8% who attended a comprehensive diabetes program involving CGM use	0.004), with an additional decrease in HbA1c levels in the intervention group compared with the control group (Diff-in-Diff HbA1c mean of − 0.481% points, *P* = 0.023). *Compared with the baseline, the 3-month CGM patterns showed a significant increase in the percentage of time in glucose range (+ 7.25; *P* = 0.011); a reduction in the percentage of time-above 180 mg/dL (− 6.01; *P* = 0.045), a decrease in glycemic variability (− 3.94, *P* = 0.034); and improvements in dietary patterns, shown by a reduction in total caloric	and control group in one family medicine clinic	Study did not document study participants' adherence to pharmacological and non-pharmacological recommendations 3. Due to logistical restrictions, the dietary and glucose patterns were only measured in the intervention group. 4. The dietary patterns were assessed through self-reporting, which potentially risks over- or under-estimating the effect of the intervention	

				intake (− 197.66 Kcal/day; *P* = 0.0001)			
Evaluation of the SPECTRUM training program for real-time CGM: A real-world multicenter prospective study in 120 adults with T1DM. (Schlüter et al., 2020)	To evaluate acceptance and efficacy of a training program using CGM among patients with T1DM 6-months post training	*n = 120* T1DM adult German patients from 19 different diabetes clinics across Germany. Full study completion *n = 108*	Evaluation of seven core competencies and patient satisfaction using questionnaire using (Students *t* test, Mann-Whitney *U* test, ANOVA, and Kruskal-Wallis test). Wilcoxon signed-rank tests were used for longitudinal analysis	Primary endpoint: rtCGM knowledge increase by 43%. Secondary endpoint: Patient satisfaction: High for CGM use. Also, HbA1c levels reduced from 12% to 9%	Level III: Controlled cohort study	1. A missing controlled group. Reasons justified. CGM use without training would be unethically justifiable due to potential therapeutic risks. 2. Efficacy comparable data on other training programs not available	Yes. Although the study purpose was specific to researcher study question for this IR, results in study answers important questions related to IR question regarding CGM and HbA1c. The study results also aligned with IR findings related to trend themes, such as patient usability, satisfaction with CGM use, reliability of CGM data, and early detection of asymptomatic hypoglycemia
Critical discrepancy in blood glucose control levels evaluated by GA and estimated HbA1c levels determined from a flash CGM system	To investigate if eHbA1c levels obtained from a flash CGM could be used to indicate glycemic control status in diabetes patients	*n = 18* patients with T2DM undergoing hemodialysis	RCT	The study helped to determine eHbA1c obtained from a CGM device can be used as a reliable indicator for evaluating glycemic	Level II	FGM (flash glucose monitoring) might be underestimate when blood glucose levels are low. GA levels were measured within 1 week	Yes

in patients with T2DM undergoing hemodialysis. (Ushigome et al., 2020)	undergoing hemodialysis			control and avoiding hypoglycemic episodes in diabetes patients undergoing hemodialysis		before or after FGM, which could be a source of bias	
TIR-HbA1c relationship with CGM to T1DM: A real-world study. (Valenzano et al., 2021)	To assess and compare CGM of patients with T1DM, TIR, and HbA1c levels	70 adult Caucasian raced patients with T1DM ages 20−60 with no previous use of CGM usage at one diabetic care center in Toronto	12-month observation. Statical data evaluation using linear regression models and multivariate OLS	0.5% decrease in HbA1c levels from 7.5% to 7.0% with a mean improvement of the predicted TIR percentages	Level III	Not discussed.	Yes. Offers help insight to this population
The Relationship of HbA1c to TIR in patients with diabetes. (Vigersky & McMahon, 2019)	To evaluate the relationship between CGM use among diabetes patients and HbA1c levels	*n = 18* articles which includes 1,137 participants: CGM-HbA1c and 1,140 participants: SMBG-HbA1c	Evaluation of 18 articles from over a 10-year period using linear regression analysis and Pearson's correlation coefficient	Excellent correlations between HbA1c and %TIR. The presence of a linear relationship between CGM use and HbA1c levels	Level I: Systematic review of the literature	1. Only four of the 18 articles included patients with T2DM. 2. The mean was based on the mean from multiple studies. 3. Most of the patients were categorized as white or non-Hispanic	Yes. This data validates the reliability of metrics data obtained CGM. Helps to establish data reliability. Data that can be used to clinically manage patients
A kinetic model for glucose levels	To evaluate the degree of discrepancy	120 diabetes patients	Collection of qualified clinical data	Glycemic marker cHbA1c accurately	Level II	Limitations not discussed	Yes: Level II and articles offer helpful information

and HbA1c provides a novel tool for individualized diabetes management. (Xu, Dunn, & Ajjan, 2020)	between estimated HbA1c (eHbA1c) levels created with the use of CGM and laboratory HbA1c		obtained from previous studies	reflects laboratory HbA1c and may provide a tool for assessing glycemia over a variable time period			regarding the estimated HbA1c levels and laboratory HbA1c levels
Evaluation of the relationship between HbA1c and mean glucose levels derived from the professional continuous FGM system. (Yamada et al., 2020)	To evaluate the relationship between glycated HbA1c and mean glucose levels derived from the professional continuous FGM system	*n* = 59: T1DM *n* = 28 T2DM *n* = 31	Out-patients using CGM device FreeStyle Libre Pro between December 2016 and August 2017. Data evaluated using mean and standard deviation	Statistically significant correlation between HbA1c and mean glucose levels using the CGM device, (r = 0.7248, *P* < 0.0001). This relationship was stronger in patients with T2DM than in T1DM	Level II	1. CGM data was collected for only 14 days (10.7 +/- 3.7). 2. The study had a cross-sectional design and was conducted by recruiting patients within a single center	Yes. The study adds to the reliability of data obtained from CGMs and validates the consistent relationship between CGM use usable data regarding HbA1c level interpretation when managing patient care

Appendix B

CGM Article Matrix Table

CGM use and HbA1c Reduction ***n*** **= 13**	**CGM Data Reliability: Linear Relationship Between TIR and HbA1c and Hypoglycemia Detection** ***n*** **= 12**	**CGM Use, Patient Acceptance and Increased Patient Satisfaction** ***n*** **= 6**	**CGM Use and Cost Reduction** ***n*** **= 1**	**CGM Importance and Future Studies** ***n*** **= 2**
Advani A. (2019)	Beck RW, Bergenstal RM, Cheng P, Kollman C, Carlson AL, Johnson ML, & Rodbard D. (2019)	Barnard KD, Bromba M, de Lange M, Halbron M, Levy BL, Lippmann-Grob B, Walshe K, & Ziegler R. (2018)	Gill M, Zhu C, Shah M, & Chhabra H. (2018)	Kieu A, Govender R, Östlundh L, & King J. (2021)
Al Hayek, Robert, & Al Dawish (2017)				
Azhar, A., Gillani, S., Mohiuddin, G., & Majeed, R. A. (2020)	Fabris, C., Heinemann, L., Beck, R., Cobelli, C., & Kovatchev, B. (2020)	Edelman, S. V. (2017)		Lind, N., Lindqvist Hansen, D., Sætre Rasmussen, S., & Nørgaard, K. (2021)
Beck RW, Riddlesworth TD, Ruedy K, Ahmann A, Haller S, Kruger D, Janet B, McGil, JB, & Polonsky, W. (2017)	Gabbay, M., Rodacki, M., Calliari, L., Vianna, A., Krakauer, M., Pinto, M., Reis, J., Puñales, M., Miranda, L., Ramalho, A., Franco, D., & Pedrosa, H. (2020)	Gilbert, T. R., Noar, A., Blalock, O., & Polonsky, W. H. (2021)		

Chan CL, Hope E, Thurston J, Vigers T, Pyle L, Zeitler PS, & Nadeau KJ. (2018)	Al Hayek, Robert, & Al Dawish (2017)	Martin CT, Criego AB, Carlson AL, & Bergenstal RM. (2019)		
Eleftheriadou I, Didangelos T, Pappas AC, Anastasiou E, Vasilopoulos C, Zoupas C, Manes C, Tsatsoulis A, Benroubi M, Pangalos E, Thomakos P, Gerasimidi-Vazeou A, & Tentolouris N. (2019)	Hirsch IB, & Verderese CA. (2017)	Mattishent K, & Loke Y. (2018)		
Gilbert, Noar, Blalock, Polonsky (2021)	Kropff J, Choudhary P, Neupane S, Barnard K, Bain S C, Kapitza C, Forst T, Link M, Dehennis A, & DeVries J. (2017)	Schlüter S, Freckmann G, Heinemann L, Wintergerst P, & Lange K. (2020)		
	Martin, C. T., Criego, A. B., Carlson, A. L., & Bergenstal, R. M. (2019)			
Kropff J, Choudhary P, Neupane S, Barnard K, Bain SC, Kapitza C, Forst T, Link M, Dehennis	Mattishent, K, & Loke Y. (2018)			

A, & DeVries J. (2017)				
Lameijer A, Lommerde N, Dunn TC, Fokkert MJ, Edens MA, Kao K, Xu Y, Gans R, Bilo HJ, & van Dijk PR. (2021).	Ushigome E, Matsusaki S, Watanabe N, Hashimoto T, Nakamura N, & Fukui M. (2020)			
Martin CT, Criego AB, Carlson AL, & Bergenstal RM. (2019)	Vigersky RA, & McMahon C. (2019)			
Rivera-Ávila D, Esquivel-Lu A, Salazar-Lozano C, Jones K, & Doubova SV. (2021)	Xu Y, Dunn TC, & Ajjan RA. (2020)			
Schlüter S, Freckmann G, Heinemann L, Wintergerst P, & Lange K. (2020)	Yamada M, Okada S, Oda H, Nakajima Y, C. Bastie C, Kasai Y, Osaki A, Shimoda Y, Shibusawa R, Uehara R, Saito T, Ozawa A, & Yamada E. (2020)			
Valenzano M, Cibrario Bertolotti, I, Valenzano A, & Grassi, G. (2021)				

Appendix C

PRISMA 2020 Checklist Reference

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	

PRISMA 2020 Checklist

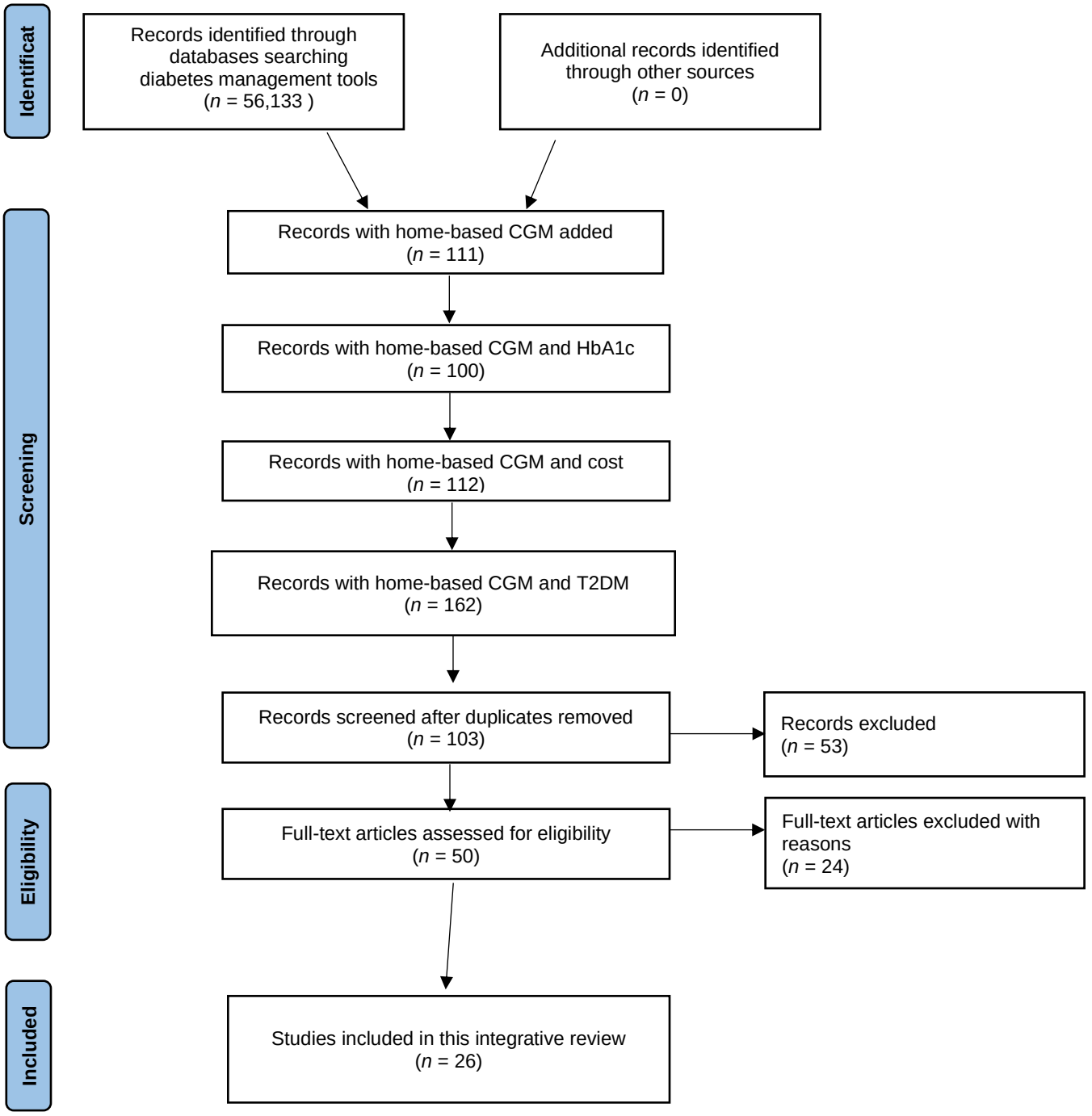
Section and Topic	Item #	Checklist item	Location where item is reported
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	
Study characteristics	17	Cite each included study and present its characteristics.	
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	
	23b	Discuss any limitations of the evidence included in the review.	
	23c	Discuss any limitations of the review processes used.	
	23d	Discuss implications of the results for practice, policy, and future research.	
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	
Competing interests	26	Declare any competing interests of review authors.	
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Appendix D

PRISMA 2020 Flow Diagram Systematic Review



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Appendix E

CITI Training Certificate

CITI PROGRAM

Completion Date 14-May-2021
Expiration Date 13-May-2024
Record ID 41808222

This is to certify that:

Ophelia Ansari

Has completed the following CITI Program course:

Not valid for renewal of certification through CME.

Biomedical Research - Basic/Refresher
(Curriculum Group)
Biomedical & Health Science Researchers
(Course Learner Group)
1 - Basic Course
(Stage)

Under requirements set by:

Liberty University

CITI
Collaborative Institutional Training Initiative

Verify at www.citiprogram.org/verify/?w7c6a48d6-4271-43d4-bcc9-20f9deaa1cf6-41808222

Appendix F

Liberty University IRB Approval

Wednesday, January 26, 2022 at 17:32:32 Eastern Standard Time

Subject: [External] IRB-FY21-22-421 - Initial: Non-Human Subjects Research
Date: Thursday, December 16, 2021 at 10:15:18 AM Eastern Standard Time
From: do-not-reply@cayuse.com <do-not-reply@cayuse.com>
To: Ansari, Ophelia <oansari@liberty.edu>, Kopis, Sharon Jean (Doctoral Nursing) <skopis@liberty.edu>
Attachments: ATT00001.png

[EXTERNAL EMAIL: Do not click any links or open attachments unless you know the sender and trust the content.]

LIBERTY UNIVERSITY.
INSTITUTIONAL REVIEW BOARD

December 16, 2021

Ophelia Ansari
Sharon Kopis

Re: IRB Application - IRB-FY21-22-421 Does the use of home-based continuous glucose monitoring devices in adults with Diabetes Mellitus (DM) improve glycosylated hemoglobin (HbA1) levels? An Integrative Review

Dear Ophelia Ansari and Sharon Kopis,

The Liberty University Institutional Review Board (IRB) has reviewed your application in accordance with the Office for Human Research Protections (OHRP) and Food and Drug Administration (FDA) regulations and finds your study does not classify as human subjects research. This means you may begin your project with the data safeguarding methods mentioned in your IRB application.

Decision: No Human Subjects Research

Explanation: Your study is not considered human subjects research for the following reason:

(1) It will not involve the collection of identifiable, private information from or about living individuals (45 CFR 46.102).

Please note that this decision only applies to your current application, and any modifications to your protocol must be reported to the Liberty University IRB for verification of continued non-human subjects research status. You may report these changes by completing a modification submission through your Cayuse IRB account.

Also, although you are welcome to use our recruitment and consent templates, you are not required to do so. If you choose to use our documents, please replace the word *research* with the word *project* throughout both documents.

If you have any questions about this determination or need assistance in determining whether possible modifications to your protocol would change your application's status, please email us at irb@liberty.edu.

Sincerely,

G. Michele Baker, MA, CIP
Administrative Chair of Institutional Research
Research Ethics Office