HIGH FRUCTOSE CORN SYRUP and SUGAR SUBSTITUTES: HEMOGLOBIN A1C IMPLICATIONS in DIABETES?

A Scholarly Project

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By

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Abstract

Diabetes mellitus type 2 (DMt2) is an increasing health concern of epidemic proportion in the United States. High fructose corn syrup (HFCS) and artificial sweeteners (AS) have been implicated as contributory factors to DMt2. This project seeks to demonstrate elimination of daily consumption of HFCS and AS in DMt2 patients can contribute to lower hemoglobin A1C (HgbA1C) levels by comparing two groups of patients receiving two differing diabetes education programs. A reduction of HgbA1C levels by 0.2-0.5% is expected in DMt2 patients instructed to eliminate HFCS and AS, and no change is expected in HgbA1C levels in DMt2 patients receiving ADA standards diabetes education alone.

Keywords: High fructose corn syrup, artificial sweeteners, diabetes mellitus type two, hemoglobin A1C, sucralose, sucralose-6-acetate, gut microbiota.

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List of Abbreviations

American Diabetes Association (ADA)

Artificial sweeteners (AS)

Body Mass Index (BMI)

Centers for Disease Control and Prevention (CDC)

Diabetes mellitus type two (DMt2)

Deoxyribonucleic acid (DNA)

Glycosylated hemoglobin (HgbA1C)

Hemoglobin A1C (HgbA1C)

High fructose corn syrup (HFCS)

International Classification of Diseases (ICD)

Internal Review Board (IRB)

Kilogram (kg)

National Health and Nutrition Examination Survey (NHANES)

Nurse Practitioner (NP)

Regression point displacement (RPD)

World Health Organization (WHO)

HIGH FRUCTOSE CORN SYRUP and SUGAR SUBSTITUTES: HEMOGLOBIN A1C IMPLICATIONS in DIABETES?

Type 2 diabetes (DMt2) is a chronic disease that has proven to be one of the costliest to manage in the United States and presents as the seventh leading cause of death among populations (Boakye et al., 2023). Estimated median costs of care for Medicare individuals living with diabetes type 2 age sixty-five and older is approximately $5, 876 a year. Annually $327 billion dollars is spent on health care for individuals living with diabetes and diabetic related complications (Centers for Disease Control and Prevention (CDC), 2022). Diabetic education, standardized by the American Diabetes Association (ADA) and utilized by most primary care and endocrinology providers has not led to a reduction in DMt2 in the United States.

In fact, DMt2 has continued to rise annually in both children, adolescents, and adult populations. Research concerning the dangers of consuming HFCS was first published by Bocarsly et al. in 2010 known as the Princeton study. In this study male Sprague-Rawley rats were fed a 12 -hour diet consisting of 8% HFCS and *ad libitum* rat chow over an 8-week period while a control group of male Sprague-Rawley rats were fed a diet of *ad libitum r*at chow and 10% sucrose over the same 8 weeks. Rats consuming HFCS were found to have significant obesity in comparison to those consuming sucrose after only a period of 8 weeks.

In a second phase study also conducted by Bocarsly et al in 2010 male and female rats were fed a diet of 8% HFCS over an extended 6–7-month period with a control group being fed 10% sucrose over the same period with findings of obesity, elevated triglyceride levels, weight gain, and greater body fat in only the HFCS consumption rats. These studies read by an internal medicine nurse practitioner in 2013 influenced her to change how she educated DMt2 diabetic patients using existing standard ADA diabetes education guidelines. In addition to ADA standard

diabetes education, she began to incorporate education asking patients to eliminate daily consumption of high fructose corn syrup in their diets.

Research conducted in 2018 by Harpaz et al. led to additional findings of AS causing altered gut microbiota through toxicity of Escherichia coli and changed induction and inhibition of bioluminescent gut microbiota signaling. This led the same nurse practitioner to educate her DMt2 population concerning elimination of daily consumption of AS and HFCS. This education, in addition to ADA diabetes education was deemed necessary to aide in the reduction of hemoglobin A1C levels for patients living with type 2 diabetes and potentially delay or prevent the development of type 2 diabetes in other patients at risk of developing DMt2. Notably, DMt2 patients adhering to this additional education began to experience a reduction in hemoglobin A1C levels in her patient population. Ultimately this practitioner and this scholarly project author decided to design a study project to determine if elimination of daily consumption of high fructose corn syrup and artificial sweeteners would affect HbgA1C levels in DMt2 patient populations.

Stakeholders are defined as individuals, groups, or organizations that have an interest or concern in an organization making the chronic care of diabetes a focus priority defined by the four Ps of healthcare, patients, payors, providers, and policymakers (Lübbeke et al., 2019). Diabetes should be of major concern for all stakeholders as there was an estimated 96 million adults, ages eighteen and older, living with the diagnosis of diabetes in the United States in 2019 (Centers for Disease Control and Prevention, 2022). In addition, World Health Organization (WHO) just published recommendations that AS be eliminated as a source of weight loss for individuals secondary to AS's non-nutritive value, inability to contribute to weight loss or reduce risk of contracting noncommunicable disease, and inability to aid in reduction of body fat in

adults, children, or adolescents. WHO also reports systematic review findings suggestive of long-term use of AS contributing to development of DMt2, cardiovascular disease, and loss of life in adults. Thus, it is theorized that educating patients to eliminate daily consumption of HFCS and AS can aid in the prevention and control of type 2 diabetes for populations.

BACKGROUND

Diabetes has increased over the past century with the United States leading all North American countries in diabetes prevalence. Among those diagnosed with diabetes Type 2 DMt2 has the greatest prevalence at a rate of 90%-95% percent of all cases diagnosed, and approximately 37.3 million people are living with diabetes and chronic disease complications associated with this diagnosis (Boakye et al., 2023). Stress and traumatic experiences appear to be influencers in the development of type 2 diabetes (Boakye et al., 2023). High fat diets are thought to be contributory factors facilitating development of type 2 diabetes because of altered lipid metabolism. Lipid metabolism is controlled by several factors including substrate-level regulation, transcription, and translation leading to catabolism and fat storage (Moody et al., 2019). Moody et al., 2019 determined high fat diets in early years of life and adulthood contribute to alteration of gene expression within the brain, liver, and other organs and alters metabolic profile causing postnatal adiposity and changes in body weight. Contributory factors of increased fat intake remain under investigation with the effects of high fructose corn syrup and artificial sweeteners continuing to be poorly understood.

PROBLEM STATEMENT

There is no clear knowledge concerning the effect of high fructose corn syrup and artificial sweeteners on glycosylated hemoglobin (HgbA1C) levels in individuals diagnosed with diabetes mellitus type 2. Despite multiple studies concerning high fructose corn syrup and

artificial sweetener consumption in diabetes, findings have provided conflicting results with few studies being conducted in human subjects diagnosed with type 2 diabetes. Most research conducted concerning high fructose intake and sweeteners has involved administration of these substances in laboratory mice and rats (Ando et al., 2022, Chakraborti et al., 2021, Hattori et al., 2021, Moody et al., 2019, Wali et al, 2021). Human studies have been relatively obsolete concerning daily consumption of HFCS and AS and their effects on hemoglobin A1C levels in individuals with DMt2 (Alsunni, 2020, Bhat et al., 2021, Boakye et al., 2023, Briones-Avila et al., 2021, Jensen et al., 2019, Mathur et al., 2020, Sigala et al., 2022). Clearer understanding of the impact of HFCS and AS on HgbA1C levels in DMt2 is needed.

In an internal medicine clinic located in rural Virginia it was noted that patients's HgbA1C levels remained elevated above American Diabetes Association recommended levels of 5.7 and despite patient education and compliance to undergo dietary changes and exercise. Patient education was changed to include educating patients to eliminate daily consumption of HFCS and AS in addition to ADA diabetic teaching guidelines. It was then noted that HgbA1C levels within this population of DMt2 patients instructed to eliminate HFCS and AS in addition to traditional ADA recommended dietary changes and exercise began to lose weight and HgbA1C levels were successfully lowered with improved HgbA1C level control. Patients choosing to continue daily consumption of HFCS and AS were noted to continue to have elevated HgbA1C levels poorly controlled without weight loss.

PURPOSE OF THE PROJECT

The purpose of this project is to provide evidence-based education to DMt2 patients within the institution using ADA diabetes standards of care 2019 through 2023 guidelines teaching in addition to patient education concerning elimination of daily consumption of HFS

and AS while assessing institutional collected data to determine if A1C levels decrease by 0.2% to 0.5% in a 3 month period. A comparison of A1C levels before and after evidence-based teaching will be evaluated to determine if a decrease in HgbA1C levels is discovered. Patients educated to eliminated daily consumption of HFCS and AS in addition to ADA diabetes standards of care 2019 through 2023 teaching will be referred to as the HFCS/AS Elimination Group throughout the remainder of this paper. Patients receiving ADA diabetes standards of care 2019 thorugh 2023 education alone will be referred to as the Eucation Only Group throughout the remainder of this paper.

CLINICAL QUESTION

This project will ask the clinical question of whether additional teaching of daily elimination of high fructose corn syrup and artificial sweeteners consumption in addition to ADA standards of care diabetic teaching positively impact control of hemoglobin A1C levels.

SECTION TWO: LITERATURE REVIEW

Performing a literature review of research studies through the use of PubMed, CINAHL, Ebsco, and Cochran Database of Systematic Reviews with keywords artificial sweetener, high fructose corn syrup, and diabetes were used to search for journal articles published in English language over the past five years. Nineteen journal articles were found that met research criteria of use of consumption of high fructose corn syrup and use of artificial sweeteners. Three articles were elminated from the systematic review after determining one was based on expert opinion of effects of these agents in gastrointestinal diseases, another to be indeterminant of the effects of polyphenols in the treatment of type 2 diabetes and obesity. The third study found no correlation

between the consumption of diet sodas or non-caloric artificial sweeteners and the onset of diabetes in patients that participated in the Strong Heart study between 2007 and 2009.

CRITICAL APPRAISAL

In a review of articles the current standards of care in diabetes 2023 was reviewed as this information is applicable to current trends of patient education utilized by a majority of primary care providers when diagnosing pre-diabetes and diabetes mellitus type 2 in patient populations (American Diabetes Association, 2023). Another article determined the importance of information to discuss with individuals when diagnosing pre-diabetes and diabetes mellitus type 2, and the difficulties encountered by practitioners when diagnosing patients with pre-diabetes or type 2 diabetes and attempting to deliver educational information during this initial diagnostic encounter (Hattori et al., 2021).

One article examined the effects of HFCS dietary intake on hepatic lipid metabolism during pregnancy in an in vivo, randomized, non-blinded study finding hyperlipidemia and insulin resistance within mice consuming HCFS (Ando et al., 2022). An additionally similar randomized, controlled, unblinded study examined the effects of high fat dietary intake on hepatic metabolism in offspring rats (Moody et al., 2019) with long term consumption of a high fat diet determined to be contributory to alteration of transcriptional and oxidative hepatic environment and liver metabolism. Another study in in vivo, randomized, unblinded three week old mice examined the effects of HFCS beverage intake and glucose tolerance finding HCFS to cause impaired glucose tolerance secondary to defective insulin resistance (Hattori et al., 2021). Adolescent offspring mice were researched in another study to determine the effects of HFCS consumption on hepatic metabolism, liver disease, and gut microbiome finding short term

consumption of HFCS to contributory to fatty liver disease, alteration in hepatic metabolic pathways, and changes in gut microbe (Bhat et al., 2021).

In a study by Wali et al., 2021 seven hundred male mice were fed a 33 isocaloric diet to determine the how carbohydrates and protein quality impact diets. The researchers found the ability of the carbohydrate to be digested significantly impacted physiological and behavioral responses affecting how protein is diluted and how nutrients are broken down by the liver resulting in altered gut microbiota. These authors found diets consisting of ten percent protein, and seventy percent carbohydrates comprised of resistant starch promoted a healthier metabolic response. However, a diet consisting of 50:50 combination of monosaccharides, glucose, and fructose consistently produced poor health outcomes.

Eighteen to forty year old adults with body mass index (BMI) of 18/35 kg/m² were studied in a randomized, paralel double blinded trial of consumption of HFCS finding these sweet beverages to contribute to dysregulated metabolism resulting in the development of type 2 diabetes and non-alcoholic fatty liver disease (Sigala et al., 2022). A cross sectional study of artificial sweeteners on insulin resistance in type 2 diabetes mellitus patients determined those consuming artificially sweetened beverages on a regular basis to have higher insulin resistance as opposed to type 2 patients that did not consume beverages containing artificial sweeteners (Mathur et al. 2020). In a systematic review of clinical trials effects of artificial sweetener consumption and it's influence on glucose homeostasis in association with type 2 diabetes and obesity there was found no conclusive correlation although Alsunni et al., 2020 attributed these findings to lack of sizeable case studies examining correlation between artificial sweetener intake and diabetes mellitus type 2 glucose homeostasis (Jensen, 2019).

Daher et al., 2019 conducted a systemic review to determine if there exists a correlation between artificial sweetener consumption and type 2 diabetes mellitus. Their findings were also inconclusive secondary to a lack of interventional designed research studies examining the potential of contributing correlation of non-nutritive artificial sweeteners to onset of diabetes type2. In a qualitative study by Boakye et al. 2023 twenty-five newly diagnosed type 2 diabetic patients were questioned regarding disease information given to them during their initial diagnosis visit with their health care provider to determine what disease information is most beneficial when informing a patient of the diagnosis of type 2 diabetes. These researchers found that patients felt their emotional state and added stress at time of diagnosis greatly impacted their ability to comprehend disease information. Patients also felt provider reassurance concerning their diagnosis and a follow-up plan of action to manage their diabetes would be of greater benefit (Boakye et al., 2023).

Briones-Avila, 2021 performed a study of sweeteners used in dietary foods and beverages marketed to school aged children ages six to twelve years in Mexico. This study aimed to determine the effects of sweeteners on obesity in this population and was found to negatively impact gut microbiota, metabolism, cardiac, endocrinology, renal, bone, hepatic, dental, ocular, and cardiovascular systems in this population. They also discovered parents were not aware of the differences of each sweetener and had no understanding of how these agents would affect their children. The sweetener agents they investigated included HFCS, maltodextrins, sucrose, acesulfame K, sucralose, and fructose. In a systematic review by Glendinning, 2018 the author researched the effects of low-calorie sweeteners and their impact on the health of mice, rats, and humans. The author found existing studies concerning low calorie sweetener consumption to be

limited secondary to poor study designs conducted in rodents and humans with responses to treatment differing among trials.

In a recent research study by Schiffman et al., 2023 involving sucralose-6-acetate and sucralose these agents were introduced to human TK6 cells resulting in findings of altered cytochrome P450 members CYP1A2 and CYP2C19. More importantly sucralose-6-acetate was determined to be genotoxic causing breaks in deoxyribonucleic acid (DNA) strands within human intestinal lining. Both sucralose and sucralose-6-acetate cellular tight junctions within human intestinal epithelium impairing function of the intestinal barrier at mM concentrations. Sucralose-6-acetate was also found to increase genetic expression of inflammation, cancer, and oxidative stress. As other studies have demonstrated alteration in gut microbiota directly impacts glucose tolerance within the stomach and intestine of humans as well as mice and rats. This study demonstrated greater sucralose and sucralose-6-acetate intestinal epithelial lining impact in humans than found in rodents (Schiffman et al., 2023).

SYNTHESIS

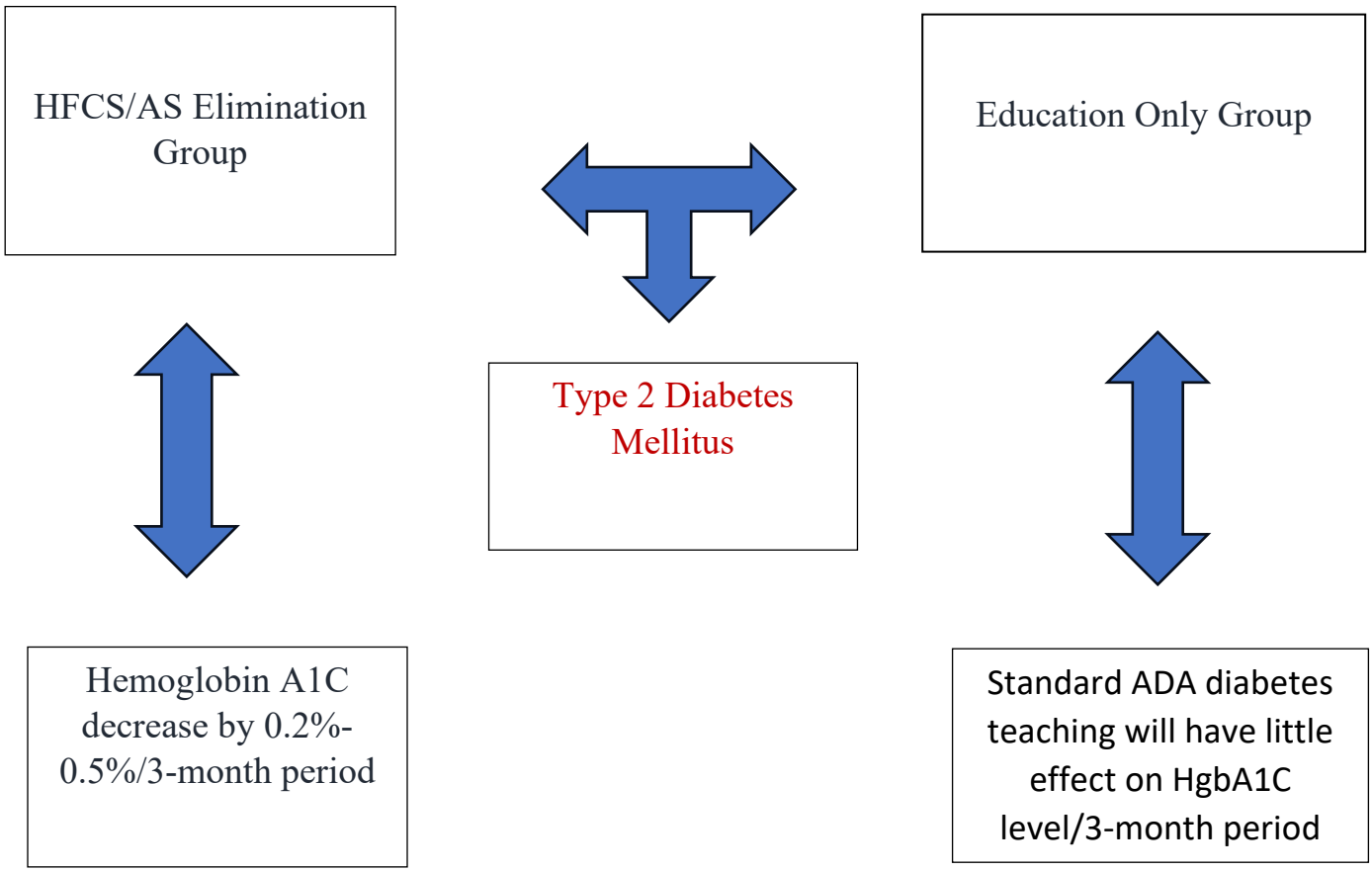
While research studies examining the correlation between HFCS and AS exists related to obesity, fatty liver disease, and glycemic effects most literature has studied the consumption of liquid containing HFCS or artificial sweetener beverages administered to mice or rats with little research involving human subjects. In human trials few studies have researched the effects of HFCS and AS in diabetic subjects versus intake among non-diabetic subjects. These studies have most often involved short weeks of intake of HFCS and AS beverages rather than over longer periods of time, and small subject populations have been selected to complete these human studies. What is known is that gut microbiota appears to be altered with increased ingestion of

HFCS and AS with most researchers stating larger study populations and longer trials are needed to determine whether HFCS and AS alter glucose levels in patients diagnosed with diabetes.

In more recent research finding significant intestinal epithelial lining alteration was determined as an effect of consuming sucralose and sucralose-6-acetate supporting altered gut microbiota as a potential trigger of elevated glycemic index in DMt2 patients. This scholarly project seeks to research the effects of HFCS and AS on HgbA1C levels in DMt2 patients to determine if limited intake of these dietary resources can aid in lowering glycemic levels and improve diabetic outcomes on a long-term basis.

CONCEPTUAL FRAMEWORK/MODEL

Figure 1



This conceptual framework involves the use of statistics and regression analysis. The independent variable, HFCS/AS Elimination Group was expected to decrease the dependent variable of HgbA1C levels by 0.2% to 0.5% in DMt2. This change, if followed by patients after receiving education, was expected to occur over a 3-month period of adherence. The Education Only Group, evaluated over a 3-month period of patient adherence, was expected to have no impact on the dependent variable of hemoglobin A1C levels (Gunzler et al., 2013).

SUMMARY

Conclusive correlation between consumption of artificial sweeteners and high fructose corn syrup and their effects on type 2 diabetics remains elusive and further research in humans is needed on a larger scale to determine their impact on hemoglobin A1C levels. This project used an evidence-based method utilizing education from the ADA standards of care 2019 through 2023 guidelines. It also used an additional education method asking one group of patients to eliminate daily consumption of HFCS and AS. Data concerning HgbA1C levels effects pre- and post-education was evaluated. Group 1, HFCA/AS Elimination Group was expected to produce a modest reduction of HgbA1C levels by 0.2-0.5% and HgbA1C levels were expected to have little to no change in the ADA Education Only Group 2.

SECTION THREE: METHODOLOGY

DESIGN

This quasi-experimental pilot project was conducted comparing a HFCS/AS Elimination Group to an Education Only Group. This project occurred within an internal medicine practice

setting to determine the effects of patient education on lowering of HgbA1C levels. Approval from the Liberty University Institutional Review Board (IRB) was given to complete this project.

MEASURABLE OUTCOME

Pre- and post-diabetes hemoglobin A1C levels will be compared in DMt2 patients, ages eighteen to ninety-five years old, involving a HFCS/AS Elimination Group and an Education Only Group. Pre- and post-education HgbA1C levels will be examined with an expected outcome of reduction in HgbA1C levels by 0.2%-0.5% within the HFCS/AS Elimination Group, and unchanged HgbA1C levels in the Education Only Group.

SETTING

This scholarly project occurred in a rural internal medicine practice in Virginia. Patients eighteen to one hundred plus years of age are seen for acute and chronic healthcare needs and followed by both nurse practitioners and physicians. The annual patient population in this facility is approximately 26,000 patients seen by five providers with about forty-five percent of these patients diagnosed with diabetes. Approximately 15%-20% of this population of patients have HgbA1C levels that are elevated above 6.5% where two nurse practitioners and four physician practitioners are employed.

POPULATION

Male and female patients diagnosed with DMt2 between ages eighteen through ninety-five years diagnosed with DMt2 will be assessed to determine the effects of HFCS and AS consumption have on HgbA1C levels. This population resides within a health district in the state

of Virginia. No project participant names, addresses, phone numbers, or personal identifiers other than ages and HgbA1C laboratory results will be examined during completion of this scholarly project.

ETHICAL CONSIDERATIONS

The scholarly project consists of two arms of patients diagnosed with DMt2 that are being cared for by a certified diabetes educator Nurse Practitioner (NP) or other non-certified diabetes educator providers. Each patient's initial HgbA1C level previously collected determining their diagnosis of DMt2 will be examined prior to their first diabetes education appointment with the diabetic NP educator or ADA standards of care 2019 through 2023 guidelines appointment with their primary care provider and three months later during their follow up appointment with their assigned providers.

Each groups three-month follow-up appointment post diabetes education HgbA1C level will be examined and compared to determine changes that may have occurred in HgbA1C levels post diabetes education with the NP diabetic educator or with their primary care provider. HgbA1C levels from pre-education and three-month post education primary care visits will be compared between both groups to determine the effects of certified diabetic educator nurse practitioner educated DMt2 patients eliminating daily HFCS and AS consumption versus DMt2 patients following ADA standards of diabetes care 2019 through 2023 guidelines education from their primary care provider.

DATA COLLECTION

Pre- and post-diabetic education HgbA1C levels were obtained by running a crystal report using a CompuGroup Medical program known as eMD. This electronic medical record system is used by the internal medicine practice where this project was completed. Hemoglobin A1C levels were compared to determine effects of HFCS and AS on HgbA1C levels in the HFCS/AS Only Group in comparison to the Elimination Only Group. Hemoglobin A1C levels were compared to aide in understanding potential effects of daily consumption of HFCS and AS in DMt2. A decrease in HgbA1C levels by 0.2% to 0.5% or greater was determined to be present in the HFCS/AS Elimination Group. Patients in the Education Only Group were found to have elevated HgbA1C levels post education in comparison to their pre-education HgbA1C levels.

TOOLS

A regression point displacement (RPD) design was used comparing pre-education HgbA1c results and post-education HgbA1C results, and a variable representing patients educated to eliminate daily consumption of HFCS and AS in addition to ADA standards of care 2019 through 2023 guidelines. In this RPD, where Ø = comparison and 1 = program, this design was used to demonstrate the x- value of rates in Hgb1Ac levels in daily elimination of HFCS and AS and ADA diabetes standards educated patients, and y- value of rates in HgbA1C levels among patients receiving ADA standards education alone (Conjointly, n.d.):

$$y_i = B_0 + B_1X_i + B_2Z_i + e_i$$

The x-axis served as the pre-education HgbA1C results, and the y-axis served as the post-education HgbA1C results. The internal medicine-based certified diabetic educator nurse practitioner educated teaching program of eliminating daily intake of HFCS and AS consumption along with ADA standards of care 2019 through 2023 guidelines teaching w compared to

patients receiving ADA diabetes standards of care 2019 through 2023 provider-based education alone. This allowed a regression line to be applied to the HFCS and AS daily elimination DMt2 patients and tested the burden of departure of this group of patients from the regression line (Trochim & Campbell, 2023). In RPD design the null group, ADA standards of care 2019 through 2023 guidelines group was not expected to deviate beyond chance levels from the regression level of the population of DMt2 patients in this internal medicine practice. Posttest demonstrated a displacement of patients in the HFCS/AS Elimination Group over that of patients in the Education Only Group along the regression line. This presented plausible evidence of elimination of daily consumption of HFCS and AS resulting in lowered HgbA1C levels clearly indicating need for formal research studies. Structured randomized control studies of larger populations would permit further evaluation of HFCS and AS consumption and their effect on HgbA1C levels in DMt2 and should be considered. Other causes of lowered HgbA1C should also be considered in future research studies.

INTERVENTION

In a cross-sectional study by DeChristopher et al. 2017 the National Health and Nutrition Examination Survey (NHANES) assessed adults, ages 45-59, consuming HCFS soft drinks, apple juice, and fruit drinks. The researchers determined consumption of these beverages directly correlated to an increase in coronary heart disease among this population of study participants and that it could potentially contribute to in-situ intestinal formation of pro-inflammatory advanced glycation end products which, in turn, may directly contribute to increased incidence of asthma, rheumatoid arthritis, chronic bronchitis, and DMt2 (DeChristopher et al., 2017).

In another study by Sigala et al., 2022 consumption of HFCS in individuals ages 18-45 years with mass body indexes of 18/35 kilograms (kg/m^2) was determined to lead to dysregulation of metabolism contributing to the development of fatty liver disease and DMt2. Reduction of HgbA1C levels by 0.5% or greater, if determined through the findings of this research in daily elimination of HFCS and AS consumption, will allow added education intervention that will complement current ADA 2022 DMt2 diabetes education guidelines.

Standards of care in diabetes 2023 call for inclusion of care systems that implement in-person and virtual patient care to include individuals knowledgeable and experienced in management of diabetes, use of support tools based on decision-making, patient registries, community involvement, and systematic approaches of support encouraging behavior changes and self-management education among diabetic patients. Person-centered goals enlisted in the current standards of care in diabetes also include addressing goals of preventing weight gain, championing weight loss, preventing increased cardiovascular risks, and slowing the progression of hyperglycemia with a recommendation to consider varietal dietary patterns to treat and prevent diabetes and reduce cardiovascular disease (American Diabetes Association, 2023).

It was theorized, by the diabetic educator nurse practitioner at an internal medicine practice, having DMt2 patients eliminate daily consumption of HFCS and AS would result in lowered HgbA1C levels. Because of this theory a research project was designed to collect pre-education HgbA1C levels from patients initially diagnosed with DMt2 and compare these results to post education HgbA1C levels after patients received diabetic management education from providers within this practice. Five providers within this practice standardly educated DMt2 patients using ADA diabetes standards of care guidelines. The diabetic educator nurse

practitioner used ADA diabetes standards of care guidelines in addition to teaching elimination of daily consumption of HFCS and AS.

For this scholarly project a crystal report using CompuMed eMD, the electronic health system utilized by the internal medicine practice, was used with a search entry using International Classification of Diseases (ICD) 10 code e119 was completed for periods January 1, 2019, through May 16, 2023. Data collection was reviewed by the nurse practitioner diabetic educator and me beginning on May 20, 2023. Pre- and post-education HgbA1C results were randomly collected from each provider's charts with compilation completed June 10, 2023. All data was compiled using SPSS to determine statistical findings and statistical results were obtained June 12, 2023. Statistical findings were analyzed, and results recorded in this article June 13, 2023.

DATA ANALYSIS

The outcomes-based performance measures obtained from this scholarly project were used to determine the effects of HFCS and AS on HgbA1C levels in patients diagnosed with DMt2. It was anticipated that HgbA1C levels would decrease by 0.2%-0.5% or greater within the 3-month study period. Findings implied negative influences of HFCS and AS on HgbA1C levels in patients with DMt2 indicating the need for further, well designed research studies examining larger bodies of participants to fully comprehend these negative effects. Diabetic teaching as determined by current American Diabetes Association standards will also require adaptation to include elimination of daily intake of HFCS and AS as part of an education regimen for practitioners and diabetic educators to include in patient management and teaching for those individuals diagnosed with DMt2. Diabetes education is an essential part of improving the care

of individuals diagnosed with this chronic disease and must also include recognition of health inequities including financial inability to provide adequate, healthy food sources and housing insecurities (American Diabetes Association, Fall 2023).

Section Four: Results

Descriptive Statistics

Preliminary analysis was conducted by use of a crystal report through use of a CompuMed eMD search using ICD 10 billing code e119 searching all male and female patients with this diagnosis of DMt2 between the periods of January 01, 2019, and May 16, 2023, within a rural internal medicine practice in Virginia. Crystal reports were completed by nursing personnel employed by the family practice office. Hemoglobin A1C results were randomly selected from 20 charts of the five providers teaching standard ADA diabetic teaching from ADA 2019 through 2023 guidelines were enrolled into the study. Hemoglobin A1C results from 20 charts of the diabetic educator nurse practitioner providing ADA 2019 through 2023 guidelines teaching and elimination of daily consumption of HFCS and AS were also collected.

Hemoglobin A1C levels collected at times of diagnosis of DMt2 were collected from charts of each patient seen by the five ADA diabetic teaching providers, and from the diabetic educator nurse practitioner teaching ADA diabetic standards and elimination of daily consumption of HFCS and AS. Each chart was reviewed to confirm that diabetic teaching using either ADA 2019, 2021, or 2023 diabetes standards of care education was given to each of the providers patients. Charts from patients seen by the diabetic educator nurse practitioner were also

examined to determine ADA 2019, 2021, or 2023 diabetes standards of care education, and elimination of daily consumption of HFCS and AS teaching was given to each patient.

Hemoglobin A1C levels collected from each chart 3-5 months after initial diabetic teaching to assess diabetes disease progression were collected for this project. Results of 3-month follow-up HgbA1C levels status post teaching was not fully obtainable as some patients did not return for assessment of HgbA1C levels until 5-months after diagnosis. These charts were not eliminated as HgbA1C levels were determined to be of value despite 1-2 additional months of diabetes education adherence or avoidance. All HgbA1C levels from each randomly selected chart were first follow-up HgbA1C values post diabetes education. Pre and post diabetes education HgbA1C values were entered into an Excel spreadsheet in SPSS to determine provider diabetic education influence on HgbA1C levels of newly diagnosed DMt2 patients (Table 1).

Measurable Outcome

Pre-diabetes education HFCS/AS Elimination group patients were found to have higher HgbA1C levels with an average level of 10.3%, mean of 8.43%, and standard deviation of 2.72 (Table 3). Pre-diabetes Education Only Group patients were found to have lower HgbA1C levels with an average level of 9.37%, mean of 8.29%, and standard deviation of 1.61 (Table 4).

Post-diabetes education HgbA1C levels in the HFCS/AS Elimination group patients were determined to average 7.75%, mean level of 7.005, and standard deviation of 1.18 (Table 6). Post-diabetes education HgbA1C levels in the Education Only Group were determined to average 9.3%, with a mean level of 8.71, and a standard deviation of 1.77 (Table 7).

SECTION FIVE: DISCUSSION

Implications for Practice

Based on recent findings from Schiffman et al., 2023 consumption of sucralose and sucralose-6-acetate can alter human cytochrome P450 members CYP1A2 and CYP2C19. In addition, sucralose-6-acetate was found to cause breakage of DNA strands through genotoxicity, and to increase genetic expression of inflammation, oxidative stress, and cancer. Wali et al, 2021 also found a diet consisting of 50% carbohydrate and 50% protein resistant starches affected metabolic health detrimentally. Sigala et al. 2021 also found that consumption of HFCS resulted in dysregulated metabolism which can contribute to DMt2.

Findings of this scholarly project concur with other research findings indicating consumption of HFCS and AS can contribute to negative alteration of gut microbiota which may result in glycemic index changes causing elevated glycated hemoglobin levels. Educating DMt2 patients to eliminate HFCS and AS daily consumption in addition to current 2023 diabetes standards teaching from the ADA may contribute to decreased HgbA1C levels and better overall control of diabetes contributing to reduction in comorbidities, thus reducing financial burden of disease in the Three Rivers district of the Northern Neck of Virginia.

Sustainability

American Diabetes Association diabetes standards of education (Appendix F) are currently offered by each provider within the internal medicine practice located in Virginia where this scholarly project was conducted. To provide additional information concerning

elimination of daily consumption of HFCS and AS would add approximately 10-15 additional minutes of education. The board-certified diabetic educator nurse practitioner schedules a 45–60-minute educational appointment with a newly diagnosed DMt2 patient. However, all other providers in this practice provide approximately 10-15 minutes of ADA diabetic standards education to newly diagnosed DMt2 patients under their care.

Teaching was provided to all providers concerning education of all newly diagnosed DMt2 patients concerning ADA diabetes standards and additional teaching about elimination of daily consumption of HFCS and AS. This would require an additional 45-60-minutes of appointment time and providers were made aware of the need to schedule a diabetic education meeting for this length of time. Providers were also informed scheduling each newly diagnosed DMt2 patient for a 45-60-minute diabetic teaching appointment would add no additional effort from the provider and would potentially contribute to lowering of HgbA1C percentages within this patient population through valuable education.

A buy in from providers would be needed to promote patient buy in and improved patient self-management of diabetes. This 30-minute educational session was held for providers during a weekly provider meeting presenting scholarly study results and required education to improve provider DMt2 patient teaching. Evidence-based practices contributing to improved patient outcomes are sustainable through evidence provided by this scholarly project and would be further supported through randomized clinical research trials.

Dissemination Plan

A planned thirty-minute educational in-service disseminating findings of this scholarly project was presented to the provider staff of this internal medicine practice located in Virginia

and supported by critical appraisal of evidence-based best practices regarding consumption of HFCS and AS in type two diabetes mellitus. Practice providers, nurse educators, patients, patient families, health care systems, and policy makers are all stakeholders affected by diabetes. Changes in how patients living with DMt2 are educated concerning diabetes management provide an opportunity for improved patient outcomes. Dissemination of evidence from this scholarly project can aide providers in the fight to control DMt2 and prevent long-term effects of this disease. This additional diabetes management education has the potential to positively impact all stakeholders.

Conclusion

This scholarly project provides supportive evidential findings demonstrating patient education concerning elimination of daily consumption of HFCS and AS in DMt2 populations can contribute to reduced HgbA1C levels if used in addition to standard diabetic ADA provider-based teaching. Further research is indicated to fully understand the effects of HFCS and AS on glycemic indexes and HgbA1C levels through advanced clinical research trials. Limitations of this project include no randomization of patient race or ethnicity, length of time of project being limited to 3-months duration, and no method of determining patient adherence to provider group education instructions. It is also unknown as to whether length of time of provider-patient education has a direct or indirect effect on patient HgbA1C levels.

Further clinical research studies should be designed with these limitations being addressed. What is known is sucralose and sucralose-6-acetate are now evidenced to contribute to altered gut microbiota through alteration of DNA strands indicating a clearer pathway as contributors to DMt2 (Schiffman et al., 2023). This project and Schiffman et al., 2023 findings

support need for further human research and larger clinical trials concerning the effects of HFCS and AS in diabetes.

REFERENCES

Alsunni, A. A. (2020). Effects of artificial sweetener consumption on glucose homeostasis and it's association with type 2 diabetes and obesity. *International Journal of General Medicine, 13,* 775-785. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7547772/

American Diabetes Association (Fall, 2023). Standards of care in diabetes-2023 abridged for primary care providers. *Clinical Diabetes, 41*(1), 4-34. https://doi.org/10.2337/cd23-as01

Ando, Y., Yamada, H., Munetsuna, E., Yamazaki, M., Kageyama, I., Teshigawara, A., Nouchi, Y., Fuji, R., Mizuno, G., Sadamoto, N., Ishikawa, H., Suzuki, K., Hashimoto, S., & Ohashi, K. (2022). Maternal high-fructose corn syrup consumption causes insulin resistance and hyperlipidemia in offspring via dna methylation of the ppara promoter region. *Journal of Nutrition Biochemistry, 103(*108951). https://doi.org/10.1016/j.jnutbio.2022.108951

Boakye, M. D. S. (2022). What individuals want to hear at the point of type 2 diabetes diagnosis. *Clinical Diabetes, 41*(1), 110-119. https://doi.org/10.2337/cd21-0151

Bocarsly, M. E., Powell, E. S., Avena, N. M., & Hoebel, B. G., (2010). High-fructose corn syrup causes characteristics of obesity in rats: increased body weight, body fat, and triglyceride levels. *Pharmacology biochemistry and Behavior, 97*(1), 101-106. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3522469/pdf/nihms189182.pdf

Bhat, S. F., Pinney, S. E., Kennedy, K. M., McCourt, C. R., Mundy, M. A., Surette, M. G., Sloboda, D. M., & Simmons, R. A. (2021). Exposure to high fructose corn syrup during adolescence in the mouse alters hepatic metabolism and the microbiome in a sex-specific manner. *The Journal of Physiology, 599*(5), 1487-1511. https://doi.org/10.1113/JP281388

Briones-Avila, L. S., Moranchelo-Hernandez, M. A., Moreno-Riolobos, D., Silva Pereira, T. S., Ortega Regules, A. E., Villasenor Lopez, K., Islas Romero, L. M., (2021). Analysis of caloric and noncaloric sweeteners present in dairy products aimed at the school market and their possible effects on health. *Nutrients, 13*(2994), 1-21. https://doi.org/10.3390/nu13092994

Centers for Disease Control and Prevention (September30, 2022). Prevalence of diabetes among adults. https://www.cdc.gov/diabetes/data/statistics-report/prevalence-of-prediabetes.html

Centers for Disease Control and Prevention (December 21, 2022). Health and economic benefits of diabetes interventions. https://www.cdc.gov/chronicdisease/programs-impact/pop/diabetes.htm

Chakraborti, A., Graham, C., Chehade, S., Vashi, B., Umfress, A., Kurup, P., Vickers, B., Chen, A., Telange, R., Berryhill, T., Van Der Pol, W., Powell, M., Barnes, S., Morrow, C., Smith Jr., D. L., Mukhtar, M. S., Watts, S., Kennedy, G., & Bibb, J. (2021). High fructose corn syrup-moderate fat diet potentiates anxio-depressive behavior and alters ventral striatal neuronal signaling. *Frontiers in Neuroscience, 15,* 1-16. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8187874/

Conjointly (n.d.). *Regression Point Displacement Analysis.* https://conjointly.com/kb/Regression-point-displacement-analysis/

Daher, M. J., Matta, J. M., & Abdel Nour, A. M. (2019). Non-nutritive sweeteners and type 2 Diabetes: Should we ring the bell? *Diabetes research and Clinical Practice, 155,* 1-11. https: //doi.org/10.1016/j.diabres.2019.107786

DeChristopher, L. R., Uribarri, J., & Tucker, K. L. (2017). Intake of high corn syrup sweetened soft drinks, fruit drinks, and apple juice is associated with prevalent coronary

heart disease, in u. s. adults, ages 45-59 y. *BMC Nutrition, 3*(51), 1-12. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7050890/

Glendinning, J. I. (2018). Oral and post-oral actions of low-calorie sweeteners: A tale of contradictions and controversies. *Obesity, 26,* S9-S17. https://pubmed.ncbi.nlm.nih.gov/30290077/

Goldhaber, S. (2021). The long, tortured history of artificial sweeteners. *American Council On Science And Health.* https://www.acsh.org.news/2021/08/18/long-tortured-history-artificial-sweeteners-15738

Gunzler, D., Chen, T., Wu, P., & Zhang, H. (2013). Introduction to mediation analysis with structural equation modeling. *Shanghai Archives of Psychiatry, 25*(6), 390-394. doi: 10.3969/j.issn.1002-0829.2013.06.009

Hattori, H., Hanai, Y., Oshima, Y., Kataoka, H., & Eto, N. (2021). Excessive intake of high-fructose corn syrup drinks induces glucose tolerance. *Biomedicines, 9,*541. https://doi.org/10.3390/biomedicines9050541

Harpaz, D., Yeo, L. P., Cecchini, F., Koon, T. H. P., Kushmaro, A., Tok. A. I. Y., Marks, R. S., & Eltzov, E. (2018). Measuring artificial sweeteners toxicity using a bioluminescent bacterial panel. *Molecules, 23*(10), 2454. DOI: https://www.mdpi.com/1420-3049/23/10/2454

Iizuka, K. (2021). The roles of carbohydrates response element binding protein in the relationship between carbohydrate intake and diseases. *International Journal of Molecular Sciences, 22,* 1-15. https://doi.org/10.3390/ijms222112058

Jensen, P. N., Howard, B. V., Best, l. G., O'Leary, M., Devereux, R. B., Cole, S. A., MacCluer, J. W., Ali, T., Lee, E. T., Yeh, F. L., Umans, J. G., & Fretts, A. M. (2019).

Associations of diet soda and non-caloric artificial sweetener use with marks of glucose and insulin homeostasis and incident diabetes: the strong heart family study. *European Journal of Clinical Nutrition, 74,* 322-327. https://doi.org/10.1038/s41430-019-0461-6

Johnson, D. A. (2021). "Sickeningly sweet"….high-fructose corn syrup-caveat emptor!. *American Journal of Gastroenterology,116,* 1970-1971. https://doi.org/10.14309/ajg.0000000000001335

Kim. Y., Keogh, J. B., & Clifton, P. M. (2020). Consumption of a beverage containing aspartame and acesulfame k for two weeks does not adversely influence glucose metabolism in adult males and females: A randomized crossover study. *International Journal of Environmental Research and Public Health, 17*(9049), 1-9. https://doi:10.3390/ijerph17239049

Loureiro, G., & Martel, F. (2019). The effect of dietary polyphenols on intestinal absorption of glucose and fructose: Relation with obesity and type 2 diabetes. *Food Reviews International, 35*(4), 390-406. https://www.tandfonline.com/doi/epdf/10.1080/87559129.2019.1573432?needAccess=true&role=button

Lübbeke, A., Carr, A. J., & Hoffmeyer, P. (2019). Registry stakeholders. *Effort Open Reviews, 4*(6), 330-336. file:///C:/Users/rache/Downloads/eor-2058-5241.4.180077.pdf

Mathur, K., Agrawal, R. K., Nagpure, S., & Deshpande, D. (2020). Effect of artificial sweeteners on insulin resistance among type-2 diabetes mellitus patients. *Journal of Family Medicine and Primary Care, 9,* 69-71. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7014832/pdf/JFMPC-9-69.pdf

Pacini, G., Tura, A., Sirlin, C. B., Chaudhari, A. J., Havel, P. J., & Stanhope, K. L. (2022). The dose-response effects of consuming high fructose corn syrup-sweetened beverages on hepatic lipid content and insulin sensitivity in young adults. *Nutrients, 14,* (1648). https://doi.org/10.3390/nu14081648

Parker, K., Salas, M., & Nwosu, V. C. (2010). High fructose corn syrup: Production, uses and public health concerns. *Biotechnology and Molecular Biology Review, 5*(5), 71-78. https://academicjournals.org/article/article1380113250_Parker%20et%20al.pdf

Schiffman, S. S., Scholl, E. H., Furey, T. S., & Nagle, H. T. (2023). Toxicological and pharmacokinetic properties of sucralose-6-acetate and its parent sucralose: *in vitro* screening assays. *Journal of Toxicology and Environmental Health,* Part B, 3-34. https://doi.org/10.1080/10937404.2023.2213903

Sigala, D. M., Hieronimus, B., Medici, V., Lee, V., Nunez, M. V., Bremmer, A. A., Cox, C. L, Price, C. A., Benyam, Y., Abdelhafez, Y., McGahan, J. P., Keim, N. L., Goran, M. I.,

Sud, A., Hodgson, K., Bloch, G., & Upshur, R. (2022). A conceptual framework for continuing medical education and population health. *Teaching and Learning in Medicine, 34*(5), 541-555. DOI: 10.1080/10401334.2021.1950540

Takeuchi, M. (2020). Toxic ages (tage) theory: a new concept for preventing the development of diseases related to lifestyle. *Diabetology & Metabolic Syndrome,12*(105), 1-12. https://doi.org/10.1186/s13098-020-00614-3

Trochim, W. M. K., & Campbell, D. T. (2023). The regression point displacement design for evaluating community-based pilot programs and demonstration projects. https://www. https://billtrochim.net/research/RPD/RPD.pdf

Wali, J. A., Milner, A. J., Luk, A. W., Pulpitel, T. J., Dodgson, T., Facey, H. J. W., Kebede, M. A., Senior, A. M., Sullivan., M. A., Brandon, A. E., Yau, B., Lockwood, G. P., Koay, Y. C., Ribeiro, R., Solon-Biet, S. M., Bell-Anderson, K. S., O'Sullivan, J. F., Marcia, L., Forbes, J. M., Cooney, G. J., Cogger, V. C., Holmes, A., Raubenheimer, D., Le Couteur, D. G., & Simpson, S. J. (2021). Impact of dietary carbohydrate type and protein-carbohydrate interaction on metabolic health. *Nature Metabolism, 3*, 810-828. https://www.nature.com/articles/s42255-021-00393-9

World Health Organization, (May 15, 2023). *WHO advises not to use non-sugar sweeteners for weight control in newly released guideline*. https://www.who.int/news/item/15-05-2023-who-advises-not-to-use-non-sugar-sweeteners-for-weight-control-in-newly-released-guideline

Appendix A
ARTICLE CRITIQUE and LEVELING MATRIX

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
1. Ando, Y., Yamada, H., Munetsuna, E., Yamazaki, M., Kageyama, I., Teshigawara, A., Nouchi, Y., Fuji, R., 1. Mizuno, G., Sadamoto, N., Ishikawa, H., Suzuki, K., Hashimoto, S., & Ohashi, K. (2022). Maternal high-fructose corn syrup consumption causes insulin resistance and hyperlipidemia in offspring via dna methylation of the ppara promoter region. *Journal of Nutrition Biochemistry, 103(*108951). https://doi.org/10.1016/j.jnutbio.2022.108951	To determine if increased maternal fructose intake adversely effects on the liver of their offspring causing resistance of insulin and lipid disorders	8-week-old & 9-week-old male and female rats and offspring of these rats were researched in a laboratory setting	In vivo randomized, non-blinded animal study	Maternal ingestion of HFCS resulted in hyperlipidemia and insulin resistance in offspring rats of mothers fed HFCS diets	Level II	Study conducted in laboratory rats and not in humans; limited control group sizes of 4 rats in each control cohort	Yes; the results of this study, albeit an animal study and small study sample, were conclusive without question of results indicating hyperlipidemia and insulin resistance with HFCS diet consumption during pregnancy
2. Hattori, H., Hanai, Y., Oshima,	To	3-week-	In vivo	Increased	Level II	Male mice	

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Y., Kataoka, H., & 2. Eto, N. (2021). Excessive intake of high-fructose corn syrup drinks induces glucose tolerance. *Biomedicines, 9,*541. https://doi.org/10.3390/biomedicines9050541	determine if HFCS beverages results in impaired glucose tolerance	old male mice were randomized into two study groups in a laboratory study	randomized, unblinded animal study	HFCS liquid intake causes impaired glucose tolerance because of defect in insulin-secretion in oral glucose tolerance test		only were studied; no human studies were conducted; small groups of randomized study mice used; only short term HFCS intake was studied	
3. Sigala, D. M., Hieronimus, B., Medici, V., Lee, V., Nunez, M. V., Bremmer, A. A., Cox, C. L, Price, C. A., Benyam, Y., Abdelhafez, Y., McGahan, J. P., Keim, N. L., Goran, M. I., Pacini, G., Tura, A., Sirlin, C. B., Chaudhari, A. J., Havel, P. J., & Stanhope, K. L. (2022). The dose-response effects of	To study ingestion of HFCS sweetened beverages to determine metabolic effect/ contributio	Healthy eighteen- to forty-year-old adults with body mass index (BMI) of 18/35	Parallel double blinded study	Evidence contributes to similar findings in other studies of consumption of HFCS sweetened beverages	Level III	DM	Yes; Although not a randomized study this trial was conducted on a younger adult population which is

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
consuming high fructose corn syrup-sweetened beverages on hepatic lipid content and insulin sensitivity in young adults. *Nutrients, 14,* (1648). https://doi.org/10.3390/nu14081648	n to type 2 diabetes and non-alcoholic fatty liver disease (NAFLD)	kg/m²		to dysregulation of metabolism leading to development of DM type 2 and NAFLD			more likely to consume HFCS beverages. The findings of this study support other study findings concerning consumption of HFCS contributing to DM type 2
4. Bhat, S. F., Pinney, S. E., Kennedy, K. M., McCourt, C. R., Mundy, M. A., Surette, M. G., Sloboda, D. M., & Simmons, R. A. (2021). Exposure to high fructose corn syrup during adolescence in the mouse alters hepatic metabolism and the microbiome in a sex-specific manner. *The Journal of*	To determine if high intake of HFCS during adolescence contributes to impaired hepatic	Adolescent offspring mice of C57bl/6J male and female bred mice were studied in a laboratory	A randomized, controlled, unblinded animal study	Limited, short-term consumption of HFCS during adolescence resulted in fatty liver disease, altered metabolic	Level II	Calories from HCFS intake in mice results in a greater total energy intake in mice than human subjects. HCFS in	Yes; although more human studies of HFCS beverage intake are grossly needed this study is supportive of

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Physiology, 599(5), 1487-1511. https://doi.org/10.1113/JP281388	metabolic signaling paths and composition of gut microbe resulting in sex specific effects secondary to altered energy metabolism	setting		pathways, and change in gut microbiome		water, as used in this experiment may modify rate of absorption of monosaccharides resulting in a higher glycemic effect in the mice in this experiment versus HFCS beverage intake in human subjects	the effects of HFCS on the liver, gut microbe, and metabolic pathways. Mice research studies commonly mirror research conducted in human subjects and have been used to guide further research in humans for centuries
5. Loureiro, G., & Martel, F. (2019). The effect of dietary polyphenols on intestinal	To determine if altering	This is a clinical review of	Evidence-based clinical	Intestinal absorption of sugar is	Level V	There are limited polyphenol	No; this research article does

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
absorption of glucose and fructose: Relation with obesity and type 2 diabetes. *Food Reviews International, 35*(4), 390-406. DOI: 10.1080/87559129.2019.1573432	of glycemic index within foods resulting in decreased BMI through inhibition of fructose and intestinal glucose absorption resulting in phenol reduction of postprandial glycemia will have implications in further research to	multiple research studies examining the effect of dietary phenols and their relationship to obesity and DM type 2	review article	affected by multiple polyphenols and might aide in prevention of minimal weight gain during overfeeding occurrence, but were not found to contribute to significant prevention of obesity or DM type 2		human clinical studies limiting findings concerning their use in treatment or prevention of obesity and DM type 2 which limits the known value of polyphenol diets to obesity and DM type 2 treatment or prevention	not support use of phenols in the treatment or prevention of DM type 2 or obesity and is not supportive of limiting HFCS or artificial sweeteners in the prevention or treatment of DM type 2

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
	treat and reduce DM type 2 and obesity						
6. Mathur, K., Agrawal, R. K., Nagpure, S., & Deshpande, D. (2020). Effect of artificial sweeteners on insulin resistance among type-2 diabetes mellitus patients. *Journal of Family Medicine and Primary Care, 9,*69-71. DOI10.4103/fmpc_329_19	To determine correlation between artificial sweeteners consumption and their effects on resistance of insulin	DM type 2 patients grouped into two groups, those who regularly consume artificially sweetened beverages, and those who never consume artificially sweetened beverages	A cross-sectional study	Study participants in group A consuming artificially sweetened beverages on a regular basis were found to have higher insulin resistance than study participant in group B which consumed no artificially sweetened	Level IV	These authors of this study failed to identify how many study participants were enrolled into each arm of the study, and this study was conducted over a short-term period of two weeks	Yes; although this study protocol is not accurately reported in writing it does demonstrate that insulin resistance was present after only researching two weeks of use of artificially sweetened beverages in patients with

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				beverages			DM type 2 versus DM type 2 patients never consuming artificially sweetened beverages; a larger, randomized, controlled study would offer better evidence as to the use of artificial sweeteners and insulin resistance
7. Jensen, P. N., Howard, B. V., Best, l. G., O'Leary, M., Devereux, R. B., Cole, S. A., MacCluer, J. W., Ali, T., Lee, E. T., Yeh, F. L., Umans, J. G.,	To determine associations of non-caloric	Strong heart study participants with no	A single qualitative research study	There was no finding of correlation between	Level VI	Study participants lived in rural areas as opposed	No; while the Strong heart study was conducted on a large

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
& Fretts, A. M. (2019). Associations of diet soda and non-caloric artificial sweetener use with marks of glucose and insulin homeostasis and incident diabetes: the strong heart family study. *European Journal of Clinical Nutrition, 74,* 322-327. https://doi.org/10.1038/s41430-019-0461-6	artificial sweeteners and diet sodas on diabetes and insulin and glucose stability	cardiovascular disease or diabetes that participated in the Strong heart study 2007-2009 with participants followed through 2017 for onset of incident diabetes		diet soda intake or use of non-caloric artificial sweetener and increased incidence of diabetes mellitus in this patient population		to metropolitan areas, and there was limited assessment of risk factors for diabetes in by researchers in this study group of participants. Study participants were asked to self-report NAS or diet soda intake and may have inaccurately reported,	population of human subjects this study used questionnaires years after study participant had completed the Strong study. A better designed/controlled study researching the use of NAS and diet sodas would be more beneficial

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
						or altered intake of these beverage types because of knowledge of possible correlation of these beverages to incidence of diabetes	
8. Alsunni, A. A. (2020). Effects of artificial sweetener consumption on glucose homeostasis and it's association with type 2 diabetes and obesity. *International Journal of General Medicine, 13,* 775-785. https://www.dovepress.com/terms.php	This review was to research articles that have studied the influences of artificial sweeteners (AS) on glucose	Sample patients ranging in ages 12 years to 65 years of age	Systematic review of clinical trials research studies	There is lacking evidence currently to correlate AS consumption with glucose stability, obesity, and	Level I	Current AS consumption studies lack case and cohort studies that are of useful sample sizes	Yes; this case review study is evidence for the need of ongoing research that is of better study design and of larger sample sizes that reflect

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
	stability, obesity, and DM type 2			DM type 2			true use of AS in human subjects
9. American Diabetes Association (2023). Standards of care in diabetes-2023 abridged for primary care providers. *Clinical Diabetes, 41*(1), 4-34. https://doi.org/10.2337/cd23-as01	To establish practitioner standards of care for individuals with diabetes	A multi-disciplinary expert committee conducting systematic reviews of clinical research studies	Systematic review	Standards of care to be utilized by practitioners in the treatment of diabetes mellitus type I, DM type II, and diabetes type 1.5 patients	Level I	Utilizes supportive evidence form poorly controlled or uncontrolled studies, and expert consensus or clinical experience that may not be evidence-based	Yes; standards of care are based on systematic review of research conducted and reviewed by a convened panel of expert clinicians in the management of diabetes
10. Daher, M. J., Matta, J. M., & Abdel Nour, A. M. (2019). Non-nutritive sweeteners and type 2 Diabetes: Should we	To investigate if artificial sweeteners	Systematic review	Systematic review	Results inconclusive for association	Level IV	Level IV studies were systematica	Yes: This study would support further

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
ring the bell?. *Diabetes research and Clinical Practice, 155,* 1-11. https://doi.org/10.1016/j.diabres.2019.107786	correlate as a contributor to diabetes mellitus type 2 (DM type 2)			between non-nutritive sweeteners (NNS) and DM type 2 secondary to limited interventional designed studies on isolated users of NNS and no long term users of NNS; study identified need for better designed studies of relationship between		lly reviewed without any review of levels I-III research studies	research concerning artificial sweeteners as contributors to type 2 DM. This evidence-based consensus of standards of care will be compared against research concerning the consumption of artificial sweeteners and of high fructose corn syrup in the management and

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				NNS and DM type 2			prevention of DM type 2
11. Moody, L., Xu, G. B., Chen, H., & Pan, Y-X. (2019). Epigenetic regulation of carnitine palmitoyltransferase 1 (cpt1a) by high fat diet. *BBA-Gene Regulatory Mechanisms, 1862,* 141-152. https://doi.org/10.1016/j.bbagrm.2018.12.009	Altered epigenetic marks and transcription binding factor were measured to determine hepatic effects of high fat intake	21 male offspring rat pups of Pregnant Sprague Rawley rat dams in a laboratory setting	A randomized, controlled, unblinded animal study	Beta oxidation of transcriptional hepatic environment was altered in life long HFDs causing increased *Cpt1a* mRNA expression, lowered DNA methylation, and H3K4Me2 enhancement	Level II	In this study only lifelong consumption of a HFD resulted in hepatic metabolism alterations, and it is not known if cellular changes in rats can translate to cellular changes in human study subjects exposed to similar HFDs	Yes; this study does demonstrate hepatic alterations that occur with lifelong consumption of diets rich in high fat intake. This is thought to be a contributory factor in altered metabolism of individuals diagnosed as pre-diabetic or with diabetes mellitus type

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
							2 indicating the need for human research of intake of high fructose corn syrup diets and artificial sweetener diets
12. Boakye, M. D. S., Myamoto, S., & Greenwood, D. (2023). What individuals want to hear at the point of type 2 diabetes diagnosis. *Clinical Diabetes, 41,* 110-117. https://doi.org/10.2337/cd21-0151	To determine what information t should be shared with patients by their health care providers at the time of diagnosis with type 2	25 individuals diagnosed with new onset diabetes mellitus type 2 over a twelve-month period	Qualitative study	Surge of emotions at time of diagnosis delays patient comprehension of important information concerning diagnosis and management;	Level VI	This is a qualitative research study with a small sample size and of higher educational level, and may not be re-applied in those with lower degrees of	Yes; this study can be used to explain the importance of diabetic education by health care providers when diagnosing individuals with pre-diabetes and type 2

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	diabetes mellitus			individuals diagnosed with diabetes type 2 would prefer reassurance from their provider and a follow-up plan of action		educational understanding	diabetes mellitus
13. Briones-Avila, L. S., Moranchelo-Hernandez, M. A., Moreno-Riolobos, D., Silva Pereira, T. S., Ortega Regules, A. E., Villasenor Lopez, K., Islas Romero, L. M. (2021). Analysis of caloric and noncaloric sweeteners present in dairy products aimed at the school market and their possible effects on health.	To determine effects of fifteen dairy sweeteners, present in Mexican foods aimed at school	A survey was administered to 36 parents of school aged children ages 6-12 years	Qualitative and systematic research methods were utilized	HFCS, maltodextrins, sucrose, fructose, sucralose, and acesulfame K were all found to have negative	Level VI	This is a qualitative research study design that does not randomize and reviewed the ingredients	Yes; this study went ot great lengths to research all findings on each sugar source and non-sweetener source in children's'

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
Nutrients, 13(2994), 1-21. https://doi.org/10.3390/nu13092994	children's consumption			effects on gut microbiome, metabolic, endocrinology, renal, osseous, hepatic, dental, ocular, and cardiovascular systems in school age children		of dietary sources for school aged children limiting ages from 6-12 years; in addition, this study took place in Mexico although this country has a record high obesity rate and onset of diabetes; this was not a specific research study to determine effects of HFCS or	foods and beverage and to determine the effects of these sweeteners on end organ systems in children. The study also confirmed child consumption of these products and educated parents concerning what each of these sugar sources contained and this could be beneficial to

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
						AS on HgbA1C levels	population health education, including individuals diagnosed with diabetes
14. Glendinning, J. I. (2018). Oral and post-oral actions of low-calorie sweeteners: A tale of contradictions and controversies. *Obesity, 26,* S9-S17. doi:10.1002/oby.2253	To determine low-calorie sweetener effects on gastrointestinal and metabolic systems, taste, and glucose homeostasis	A systematic critical review of research literature concerning low-calorie sweetener consumption	Systematic review	There is difficulty in formulating results of low-calorie sweetener effects in rats, mice, and humans secondary to inter-species taste differences and post-oral actions; also investigator	Level V	This was a systematic review from 2018 of research studies concerning low-calorie sweeteners use and determined more research is needed because of poor study designs between	Yes; I think this article serves to demonstrate the need for further, quality research concerning the metabolic effects of AS and HFCS and supports our study of the effects of these agents in DMt2 and HgbA1C

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				s use differing measures of response in mice, rats, and humans; because of confounding studies more research is needed to establish a clear understanding of metabolic effects of low-calorie sweeteners		rodents and humans with differing measures of response recorded	levels

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
15. Chakraborti, A., Graham, C., Chehade, S., Vashi, B., Umfress, A., Kurup, P., Vickers, B., Chen, A., Telange, R., Berryhill, T., Van der Pol, W., Powell, M., Barnes S., Morrow, C., Smith, Jr., D. L., Mukhtar, S., Watts, S., Kennedy, G., & Bibb. J., (2021). High fructose corn syrup-moderate fat diet potentiates anxio-depressive behavior and alters ventral striatal neuronal Signaling. *Frontiers in Neuroscience, 15*(689410), 1-16. doi: 10.3389/fnins.2021.669410	To evaluate effects of long-term consumption of HFCS and moderate fat diet on gut microbiome, neuronal signaling, and serum metabolism of mice	4-week-old male mice	Randomized, controlled trial	Diminished ventral striatal neuronal signaling was found, behavioral despair, anxiogenesis, and altered gut microbiota along with reduced glycogen phosphorylation that may contribute to neurobehavioral alteration that may induce	Level II	This study was conducted on 4-week-old male mice, is not a human study	Yes; this study utilized a 12 hour darkness and 12 hour light exposure similar to that of humans, fed a moderate fat diet along with HFCS to mice, and administered swim test, social interaction test, maze test, glucose and insulin tolerance tests, measured body composition,

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				obesity and metabolic syndrome co-morbidities			and performed behavioral assessments on study participants prior to dissection studies; many of these tests could be repeated in human HFCS and moderate fat diet intake research studies to determine the effects of these agents on gut microbiome and metabolism, along with neuronal

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
							signaling effects
16. Wali, J. A., Milner, A. J., Luk, A. W. S., Pulpitel, T. J., Dodgson, T., Facey, H. J. W., Wahl, D., Kebede, M. A., Senior, A. M., Sullivan, M. A., Brandon, A. E., Yau, B., Lockwood, G. P., Koay, Y. C., Ribeiro, R., Solon-Biet, S. M., Bell-Anderson, K. S., O'Sullivan, J. F. Marcia, L.,…Simpson, S. J. (2021). Impact of dietary carbohydrate type and protein-carbohydrate interaction on metabolic health. *Nature Metabolism, 3*, 810-	To determine the impact on health of differing carbohydrate source diets consisting of variable protein and carbohydrate sources	700 male mice	Non-randomized, non-blinded animal study	Low protein diets consisting of 70% high-carbohydrate and 10% low protein intake resulted in healthy metabolic results while diets consisting	Level II	This caloric intake study was conducted in male mice and there were no human subjects or female subjects	Yes; this study determined a diet consisting of 50% protein and 50% carbohydrates made up of resistant starches of monosaccharide fructose and glucose to be

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
838. https://www.nature.com/articles/s42255-021-00393-9				of 50% carbohydrate and 50% protein consisting of resistant starches resulted in poor health outcomes			detrimental to the metabolic health of mice. This study could potentially be conducted in human subjects producing a similar metabolic health outcome
17. Bocarsly, M. E., Powell, E. S., Avena, N. M., & Hoebel, B. G., (2010). High-fructose corn syrup causes characteristics of obesity in rats: increased body weight, body fat, and triglyceride levels. *Pharmacology biochemistry and Behavior, 97*(1), 101-106. doi: 10.1016/j.pbb.2010.02.012	To determine if HFCS consumption in rats over short- and long-term periods results in	Weight matched male Sprague-Rawley rats in 1st study; weight matched male and	Controlled trial without randomization	Diets consisting of excessive HFCS may result in obesity in rats and may result in obesity in humans	Level III	The first study was conducted on male rats only for an 8 wk period; the second study was conducted	Yes; The first study demonstrated rats consuming HFCS consumed less beverage and caloric intake than

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
	obesity.	female Sprague-Rawley rats in 2nd study				on both male and female rats without human studies being conducted	rats consuming sucrose and the HFCS rats developed obesity; the second study demonstrated male and female rats developed obesity, weight gain, elevated triglyceride levels, and increased fat accrual with HFCS intake as opposed to rats consuming sucrose which did not

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
							develop these effects
18. Schiffman, S. S., Scholl, E. H., Furey, T. S., & Nagle, H. T. (2023). Toxicological and pharmacokinetic properties of sucralose-6-acetate and its parent sucralose: *in vitro* screening assays. *Journal of Toxicology and Environmental Health,* Part B. https://doi.org/10.1080/10937404.2023.2213903	To discover toxicological and pharmacokinetic impetus of sucralose-6-aceteate	8 different studies were used with exposure of *in vitro* assays of Human TK6 cells to 20 different concentrations of sucralose-6-acetate or 20 concentrat	A well-controlled trial without randomization, quasi-experimental	Sucralose-6-acetate was found to increase greatly increased expressive genes of correlated to oxidative stress, cancer, and inflammation; integrity of the human intestinal	Level III	This study was conducted *in vitro* with human TK6 cells rather than in human subjects	Yes; the evidence form this study demonstrates clearly the effects of sucrose-6-acetate and sucrose on human cells within the intestinal lining and appear to have a greater affect

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
		ions of suscralose		barrier was also found to be impacted by both sucralose-6-acetate and sucrose; sucralose-6-acetate was additionally found to be genotoxic to a mutagenic agent (clastogen) MoA resulting in DNA breakage within the human intestinal barrier;sucr			on human intestinal cell than mouse intestinal cell. Altered gut DNA indicates both substances can affect gut microbiota which in turn can result in elevated human glycemic index range

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
				alose-6-acetate was also found to inhibit two agents of the human cytochrome P450 system, CYP1A2 and CYP2C19			
Harpaz, D., Yeo, L. P., Cecchini, F., Koon, T. H. P., Kushmaro, A., Tok. A. I. Y., Marks, R. S., & Eltzov, E. (2018). Measuring artificial sweeteners toxicity using a bioluminescent bacterial panel. *Molecules, 23*(10), 2454. DOI: https://www.mdpi.com/1420-3049/23/10/2454	To assess the effects of AS (aspartame, sucralose, saccharine, neotame, advantame, acesulfame potassium-k) used in sport	Genetically modified bioluminescent bacteria from Escherichia coli were studied	Luminescent signals and bacterial growth were measured status post exposure of gut microbiota to each	Artificial sweeteners were found to produce altered gut microbiota by causing toxicity of Escherichia coli and changed induction	Level III	Genetically modified biolumines cent bacteria were used in a laboratory setting to imitate biolumines cent	Yes; alteration in gut microbiota and it's affect on disease presentation is at the forefront of health research today and

Article Title, Author, etc. (Current APA Format)	Study Purpose	Sample (Characteristics of the Sample: Demographics, etc.)	Methods	Study Results	Level of Evidence (Use Melnyk Framework)	Study Limitations	Would Use as Evidence to Support a Change? (Yes or No) Provide Rationale.
	drinks and other beverages were examined to determine their toxicity on gut mocrobiota		AS	and inhibition of bioluminescent gut microbiota signaling		bacteria found in surface waters (drinking, surface, ground aquifers)	this early study contributes to the foundation of gut microbiota research proving how AS influences alteration in gut bacteria

Appendix B

Liberty University IRB Approval Letter

LIBERTY UNIVERSITY.
INSTITUTIONAL REVIEW BOARD

April 21, 2023

Rachelle Glover
Candi Payne

Re: IRB Application - IRB-FY22-23-1369 High Fructose Corn Syrup and Sugar Substitutes: Hemoglobin A1C Implications in Diabetes?

Dear Rachelle Glover and Candi Payne,

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 that your study does not meet the definition of 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 project is not considered human subjects research because evidence-based practice projects are considered quality improvement activities, which are not "designed to develop or contribute to generalizable knowledge" according to 45 CFR 46.102(l).

Please note that this decision only applies to your current application. 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.

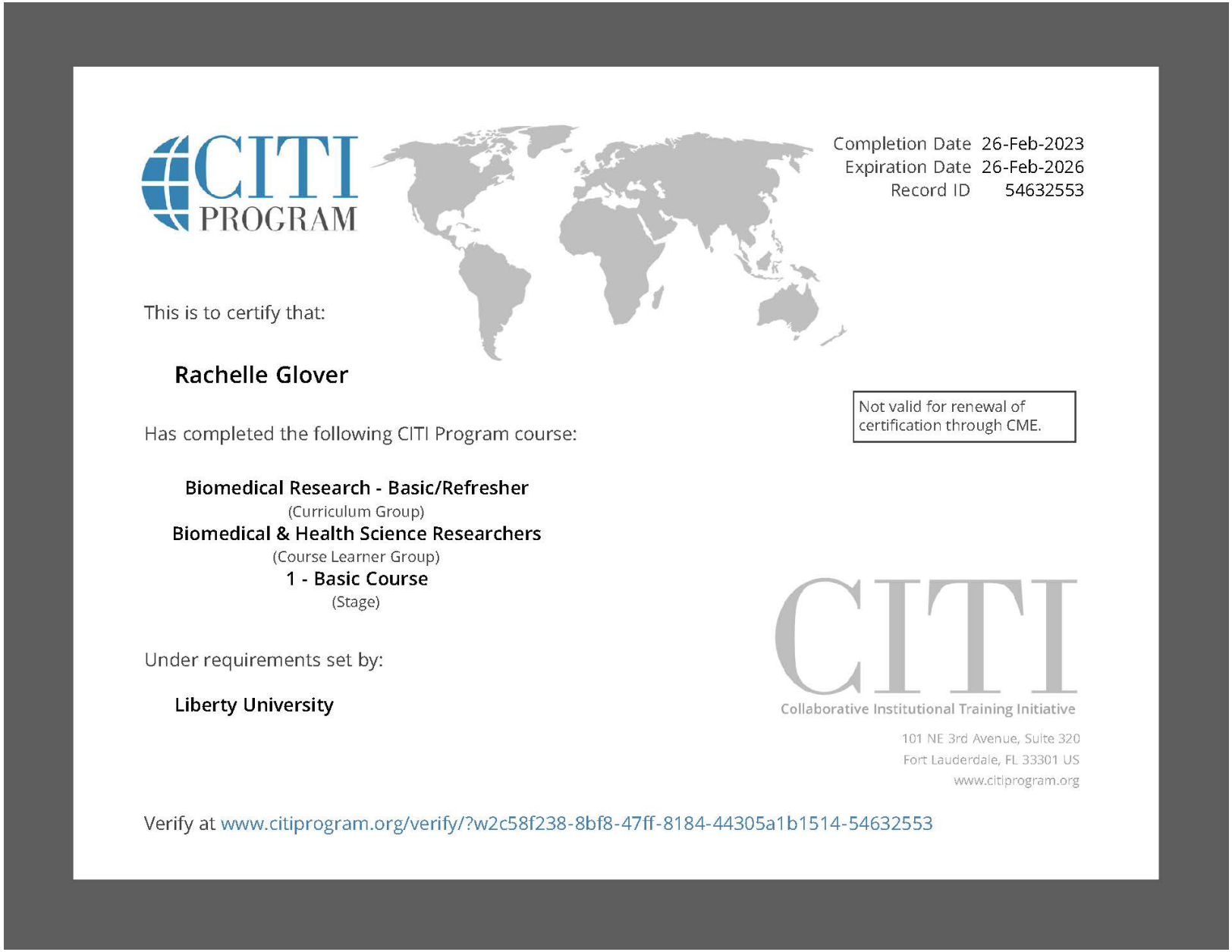
Also, although you are welcome to use our recruitment and consent templates, you are not required to do so. **If you choose to use our documents, please replace the word *research* with the word *project* throughout both documents.**

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, PhD, CIP
Administrative Chair
Research Ethics Office

Appendix C



CITI PROGRAM

Completion Date 26-Feb-2023
Expiration Date 26-Feb-2026
Record ID 54632553

This is to certify that:

Rachelle Glover

Not valid for renewal of certification through CME.

Has completed the following CITI Program course:

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
101 NE 3rd Avenue, Suite 320
Fort Lauderdale, FL 33301 US
www.citiprogram.org

Verify at www.citiprogram.org/verify/?w2c58f238-8bf8-47ff-8184-44305a1b1514-54632553

Appendix D

Project Site Letter

Date: 2/26/2023

To whom it may concern:

My name is [redacted] and I am a Nurse Practitioner working in an Internal Medicine clinic in [redacted], VA. I am an Acute Care NP and have recently obtained Board Certification in Advanced Diabetes Management. I give permission to [redacted] conduct a research study on the effects of eliminating daily intake of high fructose corn syrup and artificial sweetener consumption in Diabetic patients with me at [redacted].

[redacted]

[redacted] ACNP-BC, BC-ADM

Appendix E
Iowa Permission

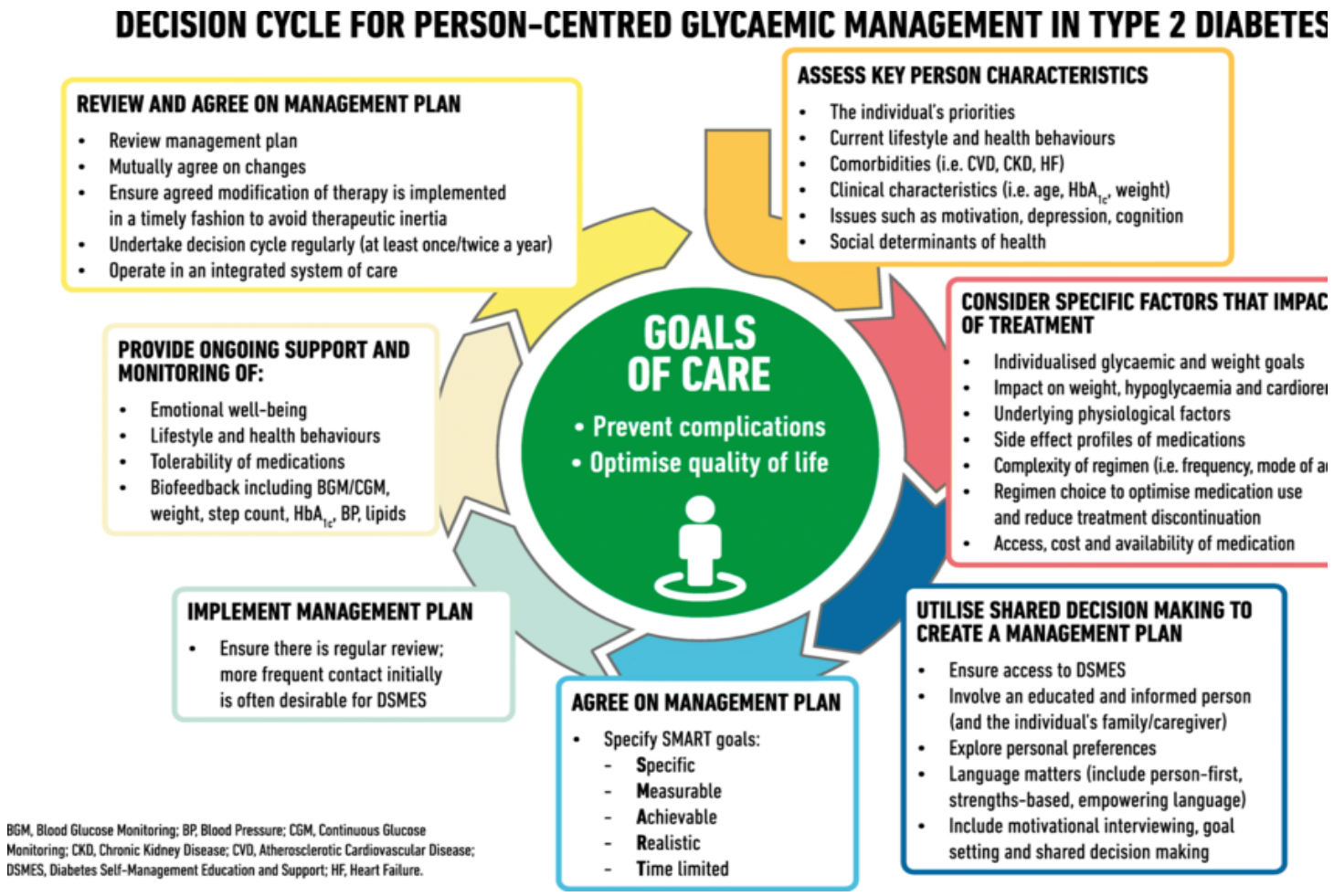
You have permission, as requested today, to review and/or use the Iowa Implementation for Sustainability Framework©. Click the link below to open.

[redacted]

Reference: Cullen, L., Hanrahan, K., Edmonds, S. W., Reisinger, H., & Wagner, M. (2022). Iowa implementation and sustainability framework. *Implementation Science, 17,* 1-20. https://doi.org/10.1186/s13012-021-01157-5

Please contact UIHCNursingResearchandEBP@uiowa.edu or 319-384-9098 with questions.

Appendix F



(American Diabetes Association, Fall 2022)

Table 1

HgbA1C Results Pre-/Post- Provider-Patient Education

Date	HFCS /AS Elimination HgbA1C Pre-Ed	Date2	HFCS /AS Elimination HgbA1C Post-Ed	HFCS /AS Elimination Post Education HgbA1C % Reduction/Increase
6/10/2020	7.40%	9/10/2020	6.10%	1.3
2/22/2019	10.90%	6/10/2019	8.10%	2.8
9/11/2019	12.50%	12/12/2019	10.10%	2.4
8/7/2020	7.40%	11/10/2020	6.70%	0.7
6/14/2022	7.30%	12/1/2022	7.00%	0.3
11/29/2021	7.00%	6/1/2022	6.50%	0.5
12/30/2020	6.12%	3/30/2021	5.74%	0.38
7/28/2022	7.80%	10/28/2022	6.90%	0.9
3/10/2022	11.10%	6/13/2022	8.60%	2.5
12/1/2021	7.10%	2/21/2022	5.90%	1.2
9/7/2022	8.90%	12/7/2022	7.70%	1.2
12/8/2021	8.50%	3/9/2022	7.80%	0.7
6/29/2021	9.62%	9/29/2021	6.40%	3.22
9/9/2021	13.00%	11/2/2021	8.80%	4.2
4/7/2022	7.50%	8/11/2022	6.20%	1.3
11/21/2019	7.10%	3/27/2020	5.70%	1.4
3/7/2019	7.50%	3/27/2020	6.70%	0.8
11/28/2021	8.25%	4/30/2021	5.67%	2.58
4/18/2022	103%	7/11/2022	6.90%	3.4
12/15/2022	8.30%	3/15/2023	6.50%	1.8

Date3	Education Only Group HgbA1C Pre-Ed	Date4	Education Only Group HgbA1C Post-Ed	Education Only Group HgbA1C Post Education % Reduction/Increase
10/11/2022	9.10%	1/24/2023	8.70%	0.4
1/6/2021	9.44%	3/15/2022	10.10%	+ 0.66
6/1/2021	9.00%	10/20/2021	8.40%	0.6
11/18/2022	9.70%	3/9/2023	8.90%	0.8
4/28/2022	7.10%	7/28/2022	7.80%	+0.7
7/1/2021	8.89%	10/28/2021	9.00%	+0.11
9/16/2021	10.50%	1/18/2021	9.00%	1.5
9/6/2022	9.30%	12/15/2022	9.60%	+0.3
08/26/20219	7.60%	12/10/2019	8.30%	+1.3
3/23/2022	7.00%	7/1/2022	7.10%	+0.1
8/12/2022	8.00%	11/15/2022	8.20%	+0.2
8/9/2022	7.40%	11/15/2022	7.70%	+0.3
7/6/2022	6.80%	11/29/2022	8.40%	+1.6
9/23/2022	6.90%	3/16/2023	7.20%	+0.3
6/6/2022	6.60%	9/8/2022	6.80%	+0.2
8/23/2022	7.40%	12/12/2022	8.00%	+0.6
4/20/2022	12.60%	5/22/2023	14.50%	+1.9
1/6/2021	9.44%	3/15/2022	10.10%	+0.66
8/5/2022	6.10%	11/22/2022	7.30%	+1.2
2/3/2023	9.00%	1/4/2023	7.10%	1.9

Table 2

File Information

Codebook

File Information

File Name		HgbA1C Levels Scholarly Project.sav
Location		C:\Users\rache\OneDrive\Documents
Label		
Number of Cases	Unweighted	20
	Weighted	20

Table 3

HFCS/AS Elimination Group Pre-Education HgbA1C Levels

VAR00001

		Value
Standard Attributes	Position	2
	Label	HFCS/AS Elimination Pre-Education HgbA1C Levels
	Type	Numeric
	Format	F4.3
	Measurement	Scale
	Role	Input
N	Valid	20
	Missing	0
Central Tendency and Dispersion	Mean	8.42950
	Standard Deviation	2.720409
	Percentile 25	7.25000
	Percentile 50	8.02500
	Percentile 75	10.30000

Table 4

Elimination Only Group Pre-Education H gbA1C Levels

VAR00003

		Value
Standard Attributes	Position	4
	Label	ADA Standard Teaching Pre-Education HgbA1C Levels
	Type	Numeric
	Format	F4.3
	Measurement	Scale
	Role	Input
N	Valid	20
	Missing	0
Central Tendency and Dispersion	Mean	8.29200
	Standard Deviation	1.612532
	Percentile 25	6.98500
	Percentile 50	7.80000
	Percentile 75	9.37000

Table 5

File Information

File Information

File Name		HgbA1C Levels Scholarly Project.sav
Location		C:\Users\rache\OneDrive\Documents
Label		
Number of Cases	Unweighted	20
	Weighted	20

Table 6

FCS/AS Elimination Group Post-Education HgbA1C Levels

VAR00002

		Value
Standard Attributes	Position	3
	Label	HFCS/AS Elimination Post-Education HgbA1C Levels
	Type	Numeric
	Format	F4.3
	Measurement	Scale
	Role	Input
N	Valid	20
	Missing	0
Central Tendency and Dispersion	Mean	7.00550
	Standard Deviation	1.179337
	Percentile 25	6.15000
	Percentile 50	6.70000
	Percentile 75	7.75000

Table 7

Education Only Group Post Education HgbA1C Levels

VAR00004

		Value
Standard Attributes	Position	5
	Label	ADA Standard Teaching Post-Education HgbA1C Levels
	Type	Numeric
	Format	F4.3
	Measurement	Scale
	Role	Input
N	Valid	20
	Missing	0
Central Tendency and Dispersion	Mean	8.71400
	Standard Deviation	1.765376
	Percentile 25	7.50000
	Percentile 50	8.35000
	Percentile 75	9.30000