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Increasing Awareness of Hereditary Fructose Intolerance: An Evidence-Based Practice Implementation Project

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By Jacqueline Bridge, FNP-BC, RN

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A DNP project submitted in partial fulfillment of the requirements for the degree of Doctor of Nursing Practice at Davis & Henley College of Nursing

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Without the support of the faculty and my colleagues at Sacred Heart University This would not be possible. I'd like to thank the staff and faculty that were so kind, understanding, and accommodating when life threw curve balls during my time in the program.

I would especially like to thank my project advisor, Dr. Goddard, for all the support and guidance during this project.

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Dedication

I would like to dedicate this my family- they are the reason I do what I do every day.

I'd like to dedicate this to my family, especially my children, Zachary and Eliza, who helped me to understand the importance (and fear) that parents of these children must encounter when they have a sick child.

Most of all, this is dedicated to my mother.

As a child with a rare disease she trusted her instincts and fought tooth and nail to figure out what was wrong with me.

Without her love and persistence, I have no doubt that I would not be here today to do what I can for others with Hereditary Fructose Intolerance.

Abstract

Background: Hereditary Fructose Intolerance (HFI) is an inborn error of metabolism which results in the absence of an effective Aldolase B enzyme. Without this enzyme, ingestion of fructose and metabolic precursors leads to acute illness, multiorgan damage, and possible death. The increased presence of these sugars results in earlier onset of symptoms and more difficulty for those with HFI.

Purpose: The project's aim is to increase awareness of HFI in healthcare providers using a learning module and assessments of knowledge at three different points in time.

Methods: The IOWA model for evidence-based practice projects was applied during the development and completion of this project. A learning module was used, and knowledge was assessed before, after, and one month after following completion of the module.

Results: Self-reported awareness of HFI increased on a 4-point Likert Scale from 1.6 to 3.06 from preassessment to post-assessment and from 1.5 to 2.8 for awareness of FM. The average amount of symptoms identified as being related to HFI increased from 1.95 to 3.76 (preassessment and post-assessment). Choice of genetic testing increased from 31.3% of participants to 90% in the post-assessment. The selection of dangerous diagnostic tests (IV fructose challenge and hydrogen breath test) decreased from preassessment (24.4% and 35.6%) to post-assessment (23.3% and 16.7%).

Discussion: Education focused on HFI had a significant impact on participants' knowledge base as seen by the pre and post-test responses. As this project was conducted during the COVID-19 pandemic, significant attrition from the post-evaluation to the follow-up assessment was seen. Therefore, it is unclear whether the knowledge would be sustained over time. Future reiterations

of this project should consider the requirements of all completion of the module within a specified timeframe and should include follow-up post-assessment items.

Keywords: Hereditary Fructose Intolerance, Aldolase B, Fructose Intolerance, Inborn Errors of Metabolism

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Chapter 1: Problem Identification, Clinical Question, and Evidence Review

Background and Introduction to the Problem

Inborn errors of metabolism are rare individually, but overall, occur once in every 1,500 to 5,000 births (Pourfarzam & Zadhoush, 2013). The early screening and diagnosis of genetic mutations in newborns can lead to earlier identification and intervention. This often will significantly impact the health and well-being of the infant, allowing for current best practices to guide patient care. While many disorders are screened for during elective carrier screenings and on "Baby's First Test" newborn screening, the autonomy in a parent's decision to undergo a carrier screening and the absence of many genetic disorders during the newborn screenings can result in children going undiagnosed (Baby's First Test, 2018).

Presentation of these autosomal recessive metabolic disorders is often challenging to identify and differentiate from other disease processes. The cause of this is twofold. First, it is due to the rarity of individual disorders. Second, the presentation of patients with metabolic disorders varies greatly. The patient presentation will vary based on factors, including the gene impacted by the mutation, the type of mutation that occurred, and the effect on the individual. Inborn errors of metabolism can affect any metabolic pathway in the body.

Increased awareness of these disorders will likely result in earlier diagnosis and appropriate interventions. It is more likely that practitioners can help patients with these disorders avoid acute illness and avoid long complications and damages based on their specific error of metabolism through early diagnosis and recommendation of appropriate interventions.

Description of Problem: Need for Awareness of Hereditary Fructose Intolerance (HFI)

Incredible progress in genetic testing and newborn screenings is evident in the successful early identification of patients with Phenylketonuria (PKU) (Bosch et al., 2105). Phenylketonuria

(PKU) is an inborn error of metabolism resulting in decreased metabolism of the amino acid phenylalanine. If PKU is left untreated, intellectual disability, seizures, behavioral problems, and mental disorders result. Hereditary fructose intolerance (HFI) also occurs from an inborn error of metabolism caused by the absence of an enzyme called aldolase B. In people with HFI, ingestion of fructose (fruit sugar) and sucrose (cane or beet sugar, table sugar) causes severe hypoglycemia (low blood sugar), a build-up of substances in the liver, and can result in death.

While both HFI and PKU are autosomal recessive metabolic disorders, both are treated by avoiding substances that rely on a certain enzyme for metabolism. In PKU, a deficiency in phenylalanine hydroxylase inhibits the metabolism of the amino acid phenylalanine (Foreman et al., 2021). In HFI, the genetic mutation results in either the absence of or the production of ineffective aldolase B enzyme, which is necessary for the metabolism of fructose and the metabolic precursors. In both disorders, complications can be avoided with early diagnosis, family and patient education, and strict adherence to diets avoiding phenylalanine and fructose, respectively. Unlike PKU, which is found in newborn genetic screening, HFI is often not diagnosed until a patient is experiencing possibly life-threatening complications that could have been avoided (Aldámiz-Echevarría et al., 2019; Bosch et al., 2015; Cox, 1993; Steinmann et al., 2006).

Until HFI is screened more universally, it is necessary to increase awareness among healthcare providers for many reasons discussed further in this chapter. This project aims to increase the awareness of Hereditary Fructose Intolerance (HFI) among current and future healthcare providers.

Confusion Between Hereditary Fructose Intolerance and Fructose Malabsorption

Healthcare providers need increased knowledge about HFI and the difference between HFI and fructose malabsorption (FM). Anecdotal evidence is often noted through online medical advice columns where providers, including physicians, confuse HFI and fructose malabsorption, which can be fatal. For instance, one said medical advice column notes a health care provider is giving "advice" on HFI, noting that HFI is serious in children but not adults. Additionally, inappropriate dietary interventions were recommended that may be appropriate for an FM diagnosis but deadly for an individual with HFI. While a subject matter expert caught this error and issued a redaction, readers had already absorbed this information. Unfortunately, this is common in online forums, where HFI patients sometimes go for medical information. This confusion between HFI and FM is one example of the lack of awareness and confusion between the two pathologies (Roach, 2019a; Roach, 2019b). Confusing the diagnoses is extremely dangerous for HFI patients and is a documented occurrence in the peer-reviewed literature. (Gaughan et al., 2015; Usai, 2014). Furthermore, testing, and dietary recommendations for patients with FM can be hazardous and create mortalities for those with HFI. See Appendix A for the differences between FM and HFI.

Dietary Changes in Western Society

The increased number of sugars in our foods and drinks, especially in western societies, puts individuals with HFI at greater risk for mortality and morbidity (Ali et al., 1998). The consumption of high fructose corn syrup in foods and beverages has increased by more than 100% between 1970 and 1990 (Akram & Hamid, 2012). The increased presence of various sugars in foods and beverages is linked to the increase in the number of patients identified as having HFI due to difficulty avoiding the dangerous sugars (Akram & Hamid, 2012; Ali et al., 1998; Cox, 1991).

The presence of sugars in food is a potential danger anyone with HFI. The most notable and dangerous example is the inclusion of fructose and other sugars in infant formula—many examples of infants presenting with significant hepatic and renal damage. In the past, the initial presentation of HFI was children with gastrointestinal complaints accompanied by a distaste for sweets when fruit was first introduced. However, now that sugar has been added to formula, this led to the initial production of a much younger patient with more severe complications (Li et al., 2018).

Dangers Related to Routine and Diagnostic Medical Care

Undiagnosed patients as well as individuals with HFI but unable to communicate such as infants, are susceptible to the dangers associated with the medical care they may receive. Routine medical procedures can be dangerous, if not deadly, for patients of any age who have HFI. This is due partially to the lack of knowledge about HFI by healthcare providers as well as the lack of understanding of the severity of HFI if sugars are not entirely avoided (Ali & Cox, 1995; Ali, Rellos, & Cox, 1998; Cox, 1993; Cox, 1995; Gaughan et al., 2015).

Of further concern are individuals with undiagnosed HFI being admitted to hospitals. For patients with HFI, routine medical procedures can be dangerous if not deadly. This is due possibly due to the lack of knowledge about HFI in providers or a lack of understanding or appreciation of the severity of the metabolic disorder. Patients have died or have been significantly harmed, such as developing hepatorenal failure, from medications, parenteral fluids, diagnostic testing, or other treatments performed as part of diagnostics performed with undiagnosed HFI presentations (Ali & Cox, 1995; Cox, 1993; Cox, 1995).

Infants presenting with complications from undiagnosed HFI can also be at risk during their hospitalization using the primary method for pain management (Gaughan et al., 2015;

Lefrak et al., 2006). This is a solution of sucrose and water, commonly known as “sweet-ease,” which is put in the baby’s mouth with a gloved finger or on a pacifier and used as an analgesic (Gaughan et al., 2015; Lefrak et al., 2006). Although some hospital policies list fructose intolerance as a contraindication to use, there is no information guiding clinicians and nurses in how to identify a patient with HFI (Melbourne, 2019). Without prompt identification of this disorder and exclusion of offending sugars, these infants are essentially being poisoned with sugar that their bodies are unable to digest, putting them at risk for further mortality during hospital diagnostic procedures using this method (Gaughan et al., 2015; Li et al., 2018).

In patients of any age, routine medical care can result in death or multiorgan failure as well. For example, the presence of sugars in medication formulations can be poisonous to individuals with HFI due to the inability to break down these sugars. Inactive ingredients and buffers to stabilize medications are not commonly found in food and drinks but can be added to medication formulations, causing additional risk for these individuals (Ali & Cox, 1995; Ali et al., 1998; Arthur & Burgess, 2017; Gaughan et al., 2015; Brooks & Tolan, 1993; Cox, 1993).

Early diagnosis and appropriate patient education emphasizing the importance of strict adherence to a diet that avoids fructose, sucrose, sorbitol, and other precursors of fructose can result in an individual leading a life free of complications or acute illness related to HFI (Aldámiz-Echevarría et al., 2019; Ali & Cox, 1995; Ali et al., 1998; Cox, 1993; James et al., 1996). Furthermore, early diagnosis and intervention can save a patient from illness, multi-organ damage, and unnecessary suffering. However, healthcare providers need to be able to recognize and diagnosis HFI, including understanding the differences between HFI and FM. This scholarly project will aim to increase awareness and education on HFI and FM diagnoses and differences, therefore, decreasing the time to identification, diagnosis, and intervention for HFI patients.

Chapter 2: Development of Clinical Question and Evidence Review

Question Leading Project

In current and future healthcare providers (P), will a learning module about Hereditary Fructose Intolerance (I) increase knowledge about HFI (C) compared to baseline knowledge (O)?

Evidence Search

External Evidence

A review of the available research literature on HFI was completed. This was two-fold: to ensure that the learning module reflects the most recent research available and provide a critical appraisal of the available literature on HFI. Search terms included "Hereditary Fructose Intolerance," "Fructose Intolerance," and "Aldolase B Deficiency." Any material that was not relevant or was consistent with the diagnosis of Fructose Malabsorption was not included in analysis.

Internal Evidence

Sacred Heart University's APRN program has a comprehensive curriculum extensively covering diverse topics necessary for future practitioners to be well-rounded and knowledgeable. Currently the curriculum includes general knowledge of chromosomal disorders and inheritance patterns during the program. While there is mention of some genetic disorders throughout the program, these do not include HFI or FM. On further review of the textbooks utilized in the program through 2018-2022, HFI is only mentioned once in a chart of metabolic disorders without any associated discussion of symptoms, interventions, or diagnostic testing methods. Finally, when asking APRN faculty about HFI and FM, many admitted that they themselves were not aware of the differentiation between these disorders as well as the potential fatality with HFI being missed. Additionally, the state of Connecticut does not require HFI as part of the

regular newborn screening panel and providers may not be aware of the potential differences between PKU and HFI.

Review of the Literature and Practice Guideline Evidence

While there were several articles and case studies that discuss HFI, there was no literature found addressing the knowledge gap among providers, the frequency of misdiagnosis, the average age of diagnosis, or the cost of misdiagnosis. Available HFI literature included topics such as the associated genetic mutations, the pathophysiology, the clinical presentation, and individual case studies. Additionally, there are no guidelines discussing the best practice in diagnosing and treating individuals with HFI. Articles were evaluated and compared for information consistency. See Appendix B, C and D for critical appraisal of the literature and a synthesis of the results.

After reviewing many articles focusing on HFI, it was apparent that there was agreement regarding many aspects of the pathophysiology, necessary intervention, appropriate methods of testing of HFI. There was not, however, any practice guidelines appropriate for the treatment of an individual with or who is believed to have HFI. While research frequently discussed the danger of not adhering to a strict diet avoiding HFI, there are no recommendations to aid clinicians to manage these patients.

Evidence Appraisal and Recommendations

Articles found using the search terms listed previously were focused on for analysis and comparison. Through the analysis of multiple resources, there were many consistencies noted in the data and recommendations. In all articles analyzed, there was consistency in the cause, signs, and symptoms although some articles went into greater depth than others. The prevalence of HFI differed between different sources and ranged between 1:18,000 to 1:31,000 and variations were

noted to be due to geography (Steinmann et al., 2006; Aldámiz-Echevarría et al., 2019; Ali & Cox, 1995; Gaghan et al., 2015; Ali et al., 1994; James et al., 1996). Other similarities within the research included the signs and symptoms consistently seen in HFI including failure to thrive

Also of note, the research is largely focused on Caucasian populations of European descent. Lazarin et al., (2013) discusses those carriers of HFI occurring as frequently as 1:90 in their study but 1:81 in research. This finding contrasted with the frequency of 1:226 in African Americans and 1:97 Middle Eastern individual. These frequencies, unlike the Caucasian frequency, has not additional research to compare this finding to. There is a significant gap in research looking at the frequency of HFI in minority populations. Multiple studies state that the genetic mutation causing HFI varies within different ethnicities and geographical area therefore the lack of data regarding HFI in minority populations may be dangerous to these individuals. In studies of carrier screenings, HFI has been found in Northwestern European and African American to be among the top ten most frequently occurring heterozygous genetic mutation (Ali et al., 1998; Lazarin et al., 2013).

Through the literature review, patterns emerged regarding the presentation of patients with HFI. The most frequently mentioned included:

- Distaste or aversion to sweet tastes (Ali & Cox, 1995; Ali, Rellos, & Cox, 1998; Ali, Rosien & Cox, 1992; Ali, Tuncman et al., 1994; Brooks & Tolan, 1993; Cox, 1991; Cox, 1990a; Cox, 1990b; Cox, 1993; Cross & Cox, 1990; Gaughan et al., 2015; James et al., 1996; Kim et al., 2020; Kim et al., 2021; Li et al., 2018; Mock et al., 1983; Steinmann & van den Berghe, 2006).
- Postprandial hypoglycemia (Akram & Hamid, 2013; Aldámiz-Echevarría et al., 2019; Ali & Cox, 1995; Ali, Rellos, & Cox, 1998; Ali, Rosien & Cox, 1992; Ali,

Tuncman et al., 1994; Brooks & Tolan, 1993; Cox, 1991; Cox, 1990a; Cox, 1990b; Cox, 1993; Cross & Cox, 1990; Gaughan et al., 2015; James et al., 1996; Kim et al., 2020; Kim et al., 2021; Li et al., 2018; Mock et al., 1983; Steinmann & van den Berghe, 2006).

- Failure to thrive or growth retardation (Aldámiz-Echevarría et al., 2019; Ali & Cox, 1995; Ali et al., 1998; Ali et al., , 1992; Ali et al., 1994; Brooks & Tolan, 1993; Cox, 1991; Cox, 1990a; Cox, 1990b; Cox, 1993; Cross & Cox, 1990; Gaughan et al., 2015; James et al., 1996; Kim et al., 2020; Kim et al., 2021; Li et al., 2018; Mock et al., 1983; Steinmann & van den Berghe, 2006).
- Abdominal complaints such as nausea, vomiting and abdominal pain (Akram & Hamid, 2013; Aldámiz-Echevarría et al., 2019; Ali & Cox, 1995; Ali et al., 1998; Ali et al., 1992; Ali et al., 1994; Brooks & Tolan, 1993; Cox, 1991; Cox, 1990a; Cox, 1990b; Cox, 1993; Cross & Cox, 1990; Gaughan et al., 2015; James et al., 1996; Kim et al., 2020; Kim et al., 2021; Li et al., 2018; Mock et al., 1983; Steinmann & van den Berghe, 2006).

These symptoms that are frequently reported in patients with undiagnosed HFI or those who are not adherent to an appropriate diet avoiding fructose and its precursors. Of these symptoms, the aversion to sweets has been discussed as indicator to consider HFI regardless of the presence of other symptoms (Kim et al., 2020).

Research also varies in the recommendations regarding diagnostic methodologies. Articles published prior to 1990 recommended the use of an intravenous fructose challenge in a controlled setting for the diagnosis of HFI (Cox, 1990a; Cox, 1990b; Cross & Cox, 1990; Mock et al., 1983). Research after this point stated that intravenous fructose challenges were dangerous

and should not be used for diagnosis (Ali & Cox, 1995; Ali et al., 1998; Ali et al., 1992; Ali et al., 1994; Brooks & Tolan, 1993; Cox, 1993; Gaughan et al., 2015; James et al., 1996; Kim et al., 2021; Steinmann & van den Berghe, 2006).

Most recently, the recommended diagnostic method is diagnostic testing for a mutation in the gene responsible for Aldolase B production (Aldámiz-Echevarría et al., 2019; Ali et al., 1998; Ali et al., 1992; Ali, Tuncman et al., 1994; Brooks & Tolan, 1993; Cox, 1991; Cox, 1990a; Cox, 1990b; Cox, 1993; Gaughan et al., 2015; James et al., 1996; Kim et al., 2020; Kim et al., 2021; Li et al., 2018; Mock et al., 1983; Steinmann & van den Berghe, 2006). Many of these sources also introduce liver biopsy to assess Aldolase B activity as less ideal due to the associated risks but able to confirm a diagnosis of HFI (Ali et al., 1998; Ali at al., 1992; Ali et al., 1994; Brooks & Tolan, 1993; Cox, 1990b; Cox, 1993; Gaughan et al., 2015; James et al., 1996; Kim et al., 2021; Steinmann & van den Berghe, 2006). Further, use of a Hydrogen Breath test indicated for diagnosis of FM is contraindicated in HFI as all these sources state that the most important intervention in HFI is the minimization or avoidance of fructose and its precursors (Akram & Hamid, 2013; Aldámiz-Echevarría et al., 2019; Ali et al., 1998; Ali at al., 1992; Ali et al., 1994; Brooks & Tolan, 1993; Cox, 1991; Cox, 1990a; Cox, 1990b; Cox, 1993; Cross & Cox, 1990; Gaughan et al., 2015; James et al., 1996; Kim et al., 2020; Kim et al., 2021; Li et al., 2018; Mock et al., 1983; Steinmann & van den Berghe, 2006). Analysis of the research in regards to the symptoms and diagnostic methods discussed can be seen in Appendix E.

More recent research has been looking at the use of Carbohydrate- Deficient Transferrin levels as an indicator of undiagnosed HFI or nonadherence with dietary restrictions (Aldámiz-Echevarría et al., 2019; Cano et al., 2022; DiDato et al., 2019; Gaughan et al., 2015; Pronicka et al., 2007). This finding could serve as a helpful addition to confirm diagnosis in patients who

may not have a previously identified pathogenic mutation which it believed to lead to inability to diagnose some individuals using genetic testing (Ali et al., 1998; Ali at al., 1992; Ali et al., 1994; Brooks & Tolan, 1993; Gaughan et al., 2015).

Within the research, there are two sources that serve as clinical guidelines for patients and providers but there is no single source that includes a comprehensive review of all the data (Ali, Rellos & Cox, 1998; Gaughan et al., 2015). These clinical guidelines are thorough but there is a need for more straight forward recommendations for the care and management of patients with HFI about normal management and dietary recommendations.

Summary

As demonstrated in Appendices B, C, and D a synthesis of available literature was conducted and summarized for this project. The evidence reviewed for this project revealed two key components. 1) While there are various pieces of research discussing HFI, there is no exhaustive review of the disease process. 2) Also, in the studies reviewed, there were no clinical guidelines available to guide best practices for the care of patients with HFI. These findings illuminate a gap in current research that must be addressed in the future. This scholarly project focused on providing the most up to date knowledge base of HFI for current and future health care providers, attending Sacred Heart University's advanced practice provider programs. Future recommendations will be summarized at the conclusion of this work.

Chapter 3: Project Plans and Methods

Introduction

This evidence-based practice project was developed to increase awareness of HFI. While the goal was to increase awareness in healthcare providers for this project, increasing awareness can continue indefinitely through the creation of an easily accessible educational module within a website focused on HFI. While the author ‘s immediate goal is to increase awareness to HFI, the long-term goal is to sustain the knowledge and continue to spread awareness.

To simplify completion of the components of this project and for the long-term sustainment of this project, a website was created through using Wix. This website is home to the learning module and assessments for the convenience of participants. In addition, the website contains data about HFI. Screenshots of the website and the contents within it can be seen in Appendix F and G. This website will remain active and will reflect the questions and concerns commonly heard within the HFI community.

This project was launched during the advent of COVID-19, therefore a virtual, online setting for this education was modified and a targeted population to pilot the educational module within an online environment. This format for the project provided simplicity of completion as all components of the project. This format also allowed for sustainment of the project for future use and a resource for individuals who have or are curious about HFI. The project measures and outcomes shifted to an exploration of increasing HFI awareness overall. By using this form that work will occur continuously if the website is active.

Purpose and Global Aim

This project aimed to increase awareness and understanding of HFI in current and future clinicians. The overall goal of this project is to: 1) Provide a baseline of knowledge related to

HFI in current and future health care providers; 2) Identify a potential gap in the curriculum for APRN and PA students with recommendations on HFI diagnosis inclusion for program directors; and 3) Increase awareness of HFI, patient presentation, and diagnostic methods.

Specific Aims

The global aim for this scholarly project was to increase awareness of HFI with health care providers, specifically those who diagnose and treat patients such as APRNs, PAs, and physicians. By providing increased awareness and education for health care providers, this will additionally help identify and provide more rapid intervention for patients with undiagnosed HFI. Additional specific aims of this project include: 1) education on the differences between HRI and FM; 2) increase the knowledge of appropriate diagnostic testing in HFI patients; 3) increase the ability to recognize HFI as a genetic inborn error metabolic disorder with students currently enrolled at Sacred Heart University.

Framework

The Iowa Model

The IOWA Model for evidence-based practice improvement was utilized for the overall development of this project plan (Cullen et al., 2018). This model consists of twelve steps as seen in Appendix H. Each step included actions while allowed foe the completion of the next step. Individual steps will be discussed in the following sections.

Identify Triggering Issues/ Opportunities

The need for increased awareness of HFI was identified as an issue. As discussed previously, the risk of misdiagnosis and lack of diagnosis is dangerous, and potentially fatal. Factors such as the increased use of high fructose corn syrup in foods, beverages and infant formulas emphasized the need for increased awareness in healthcare providers (Li et al., 2019).

This in conjunction with the absence of education on this topic in the APRN curriculum at SHU, an opportunity was found with a goal of increasing awareness in future healthcare providers.

State the Question or Purpose

In current and future healthcare providers (P), will a learning module about Hereditary Fructose Intolerance (I) increase knowledge about HFI (C) compared to baseline knowledge (O)?

Is This Topic a Priority?

This topic is a priority. This is due to the increased risks associated with having HFI without an increase in awareness of the disorder and the potential for a life free of symptoms of complications. The increased awareness, diagnosis, and introduction of appropriate interventions are crucial for patients.

Form a Team

Completion of this project was done with a great deal of assistance from the faculty at Sacred Heart University's DNP-FNP program. Dr. Anna Goddard served as a mentor in the completion of this project.

Assemble, Appraise, Synthesis Body of Evidence and Is There Sufficient Evidence

Evidence review and related discussion can be seen within the section entitled 'Evidence Search.'

Design and Pilot the Practice Change

The design of this project included the development of a website, learning module, and three learning assessments. The rationale for the creation of a website was for the convenience of participants as well as to serve as a resource for future use by practitioners and patients.

Is Change Appropriate for Adoption in Practice?

A gap in the curriculum highlighted a need for the adoption of this project at SHU. Based on this finding it was believed that there may be a similar gap in other educational programs for clinicians from various background's pursuing different degrees.

Integrate, Sustain the Practice Change

Integration, sustainment, and dissemination of this project will be discussed in detail in following sections. Integration will include sharing the address of the website that includes the learning module and assessments. Completion will be done at the participant's convenience. Responses to the survey will be the sections will be done automatically using Google forms. Sustainment of knowledge was assessed by the follow-up assessment. Also, sustainment will be possible by maintaining the website, learning modules and assessments for future use.

Disseminate Results

The dissemination plan for this project will involve sharing the results in a poster presentation at Sacred Heart and at upcoming conferences. Also, findings related to this project will be submitted as an abstract or for presentation at upcoming conferences. Dissemination will be discussed in further detail in the relevant section.

Design

The initial setup of this project included the development of a website (http://aldolasebhfi.com). This website has information about HFI from the articles reviewed during this project. It also includes separate links to the assessments and learning modules. A screenshot of this website can be seen in Appendix F. By putting all items on a single website, participants were quickly able to find the components of the project. The project was developed and intended for participants to complete a preassessment, a learning module, a post-assessment, and a follow-up assessment at least one month after completing the initial portion.

Sample

Originally, practicing health care providers were targeted as participants by mailing introductory letters of interest in the mail and as PDF documents to practice emails. This occurred in the Fall of 2020 and this initial letter can be seen in Appendix I.

However, as indicated in the project deviation section, this project shifted to pilot the educational module website to Sacred Heart University APRN and PA students. The SHU APRN and PA program directors were contacted in the Fall of 2020 with an introductory letter to the project (Appendix J). With the aid and support of the APRN faculty, Carrie Sauer, a program administrator at Sacred Heart University, sent an email to the members of the APRN program periodically between January 2022 and February 2022 to encourage student and faculty participation. These emails were sent to the current students in the hybrid APRN-DNP program between January 4th 2022, and February 3rd 2022. These emails were sent to 102 individuals on three different occasions during that time span.

Setting

Due to the convenience of participants for completion and the increased ability to allow for future use of this project, the setting was decided to be a virtual/online format. This decision to be virtual was further reinforced by the fact that implementation of this project was during the height of the COVID-19 pandemic. All components of this project can be found at https://www.aldolasebhfi.com.

Project Team Members and Key Stakeholders

The key stakeholders for this project included the patients with potential HFI diagnoses. However, this project aimed at increasing awareness in practicing and future providers in order to by-proxy reach pediatric patients who may be presenting with these symptoms in the

community currently and in the future. The DNP project director and DNP student led the creation and implementation of this project. Other project team members included Anna Goddard, Ph.D., APRN, CPNP-PC, fulfilled the role of DNP Project Faculty Advisor. She served an integral part in developing the project and supplying guidance throughout the process. Susan DeNisco DNP, APRN, FNP-BC, FAANP served as the practice mentor as the FNP-DNP director and provided additional advice, expertise, and encouragement throughout the project, particularly in deviations of the original aims pre-COVID-19.

Data Collection

Project Measures

The specific aims of this project include: 1) education on the differences between HFI and FM; 2) increase the knowledge of appropriate diagnostic testing in HFI patients; 3) increase the ability to recognize HFI as a genetic inborn error metabolic disorder with students currently enrolled at Sacred Heart University. Therefore, the key project measures included data related to education on HFI and FM from a pre-post evaluation survey. Demographic questions were additionally collected.

Data Collection Plan

The project included three separate assessments for data collection throughout the educational module. The assessments including a pre-assessment prior to taking the HFI educational module (for baseline data on knowledge related to HFI), an immediate post-assessment prior to finishing the HFI educational module, and a 1-month follow-up for the educational module to assess knowledge sustainment.

The data collected for these assessments are Google Forms which are embedded into the website. Google Forms were chosen for use in this project due to their ability to collect data and

transform the data into a spreadsheet for analysis. Each assessment contains the same knowledge-based questions except for the preassessment which had additional items related to participant demographics. Individuals were assigned participant numbers to assess for completion of various portions of the project in a separate document.

Data collection aimed at participant answers to knowledge-based questions surrounding HFI at three different points in time. The preassessment data would reflect individual baseline knowledge. The post learning module responses would reflect the knowledge gained from the learning module. The follow-up assessment would determine whether the knowledge gained from this project was retained. The assessments after the learning module attempted to assess for an increase the practitioners' awareness of HFI both short term and long term. The data collection assessments can be seen in Appendices J, K and L.

Demographic questions addressed the frequency with which individuals from various groups (current clinical, APRN students, and PA students) completed the project and their levels of experience in clinical practice. A screenshot of this section can be found in Appendix K and are listed individually below. These questions will be answered on a nominal and ordinal scale.

The questions asked in assessments attempted to address the following questions to determine the impact of the learning module on the participant's knowledge of HFI. Participants are asked to report their familiarity with HFI at three different points in time to determine the impact of the learning module on their self-reported familiarity in a 4-point Likert scale from "no, not at all; I am not sure; Yes, somewhat familiar; Yes, very familiar." Participants were then asked, "What symptoms could a patient with HFI present with (Select all that apply)." To determine how many symptoms participants, identify as occurring with HFI, a select all that apply question was used. The choices were based on the symptoms most frequently discussed in

the literature as discussed previously (Appendix E). Post module and follow-up assessments can be found in Appendix L and M, respectively.

Identification of patient presentation and diagnostic test selection. This question item was meant to look at the choice of diagnostic test selection by the participant when presented with a patient with possible HFI. The question assessed how often participants selected the safest and most appropriate diagnostic testing methods before and after the learning module (genetic testing), and diagnostic testing that would confirm a diagnosis of HFI (liver biopsy for Aldolase B activity). This item also assessed the frequency participants selected dangerous diagnostic testing methods before and after the learning module (intravenous fructose challenge and hydrogen breath test). Answer options in this question also included neutral options which would not be diagnostic or detrimental (Hemoglobin A1C and Endoscopy).

Demographics

Before reading the learning module, participants were asked to complete a preassessment to collect demographic information and assess their baseline knowledge of HFI. The appearance of the demographic questions can be seen in Figure 1. The questions asked to participants included:

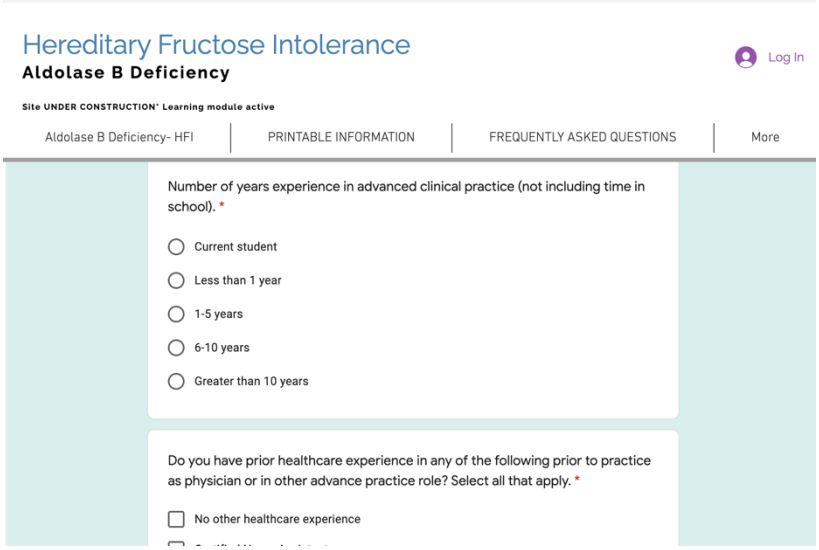
1. What is your email address?
2. What is your current discipline? (Medical Doctor, Doctor of Osteopathic Medicine, Practicing PA, Practicing APRN or NP, PA student, APRN or NP student, other)
3. Number of years of experience in advanced clinical practice (not including time in school). (Current student, less than one year, 1-5 years, 6-10 years, more significant than ten years)
4. Do you have healthcare experience before practicing as a physician or in other advanced practice roles? Select all that apply. (No different healthcare experience,

Certified Nurse Assistant, Medical Assistant, Licensed Practical Nurse, Emergency Responder (Emergency Medical Technician/ Paramedic), Registered Nurse, or Other).

5. If you had prior healthcare-based experience, how many years of experience do you have? (Current student/ no other healthcare experience, less than one year, 1-5 years, 6-10 years, more significant than ten years)
6. What was your specialty/focus in your past healthcare experience (i.e., emergency medicine, pediatrics, long-term care, etc.) (open-ended question)?
7. *Sacred Heart Students Only* Please select your program (Physician Assistant Program- year 1, full time, Physician Assistant Program- year 1, part-time, Physician Assistant Program- year 2, full time, Physician Assistant Program- year 2, part-time, APRN Program- year 1, full time, APRN Program- year 1, part-time, APRN Program- year 2, full time, APRN Program- year 2, part-time, APRN Program- year 3, full time, APRN Program- year 3, part-time, Unsure, PA program, Unsure APRN program).

Figure 1

Demographics Section of Preassessment



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Measures (Pre-assessment)

The following questions were asked following the demographic questions in the preassessment. These four questions were also asked in the post-learning module and follow-up assessments. The goal of the repetition of the following four questions was asked to determine the participant's baseline knowledge of HFI, the ability learned from the learning module, and knowledge retention. The appearance of these questions can be seen in Figure 2. These questions included:

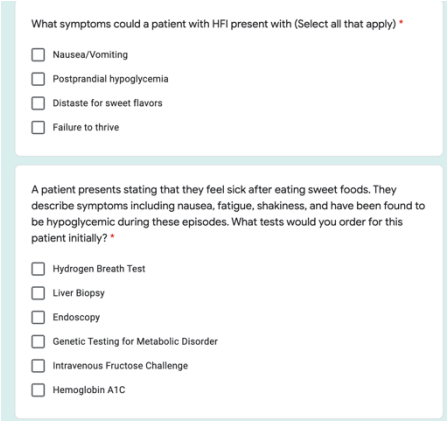
1. Are you familiar with Hereditary Fructose Intolerance?
    a. Yes, very familiar
    b. Yes, somewhat familiar
    c. I am not sure
    d. No, not at all
2. Are you familiar with Fructose Malabsorption?
    a. Yes, very familiar
    b. Yes, somewhat familiar
    c. I am not sure
    d. No, not at all
3. What symptoms differentiate HFI from FM (select all that apply)
    a. Nausea/vomiting
    b. Postprandial hypoglycemia
    c. Distaste for sweet flavors
    d. Failure to thrive

4. A patient presents, stating that they feel sick after eating sweet foods. During these episodes, they describe symptoms including nausea, fatigue, shakiness, and hypoglycemia. What test would you order for this patient initially? (Select all that apply)
    a. Hydrogen Breath Test
    b. Liver Biopsy
    c. Endoscopy
    d. Genetic testing for metabolic disorder
    e. Intravenous Fructose Challenge
    f. Hemoglobin A1c

The first two questions assessed participants for their self-reported familiarity with HFI and FM at three different points. Question three listed four symptoms often seen in patients presenting with HFI (Aldámiz-Echevarría, 2019; Cox, 1993; Kim et al., 2020; Li et al., 2019). Questions about HFI were developed based on the data found during the comprehensive review of literature discussed previously.

Figure 2

Questions in Assessment portion of Follow-up Assessment



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Project Learning Module

A learning module was created using Microsoft PowerPoint. The PowerPoint was transformed into a PDF document which was embedded into the website as shown in Figure 3 and 5. Topics covered in the learning module focused on the following:

- The rationale for implementing this project
- The cause and pathophysiology of HFI (Figure 4)
- The biochemistry of the alteration in fructose metabolism in the absence of Aldolase B
- Metabolic alterations and abnormal lab values seen in undiagnosed or uncontrolled HFI
- Symptoms of HFI
- Acute illness and effects of chronic ingestion of fructose and precursors
- Patient presentation
- Dietary management of patients with HFI
- Clarification on need for caution with anything ingested by individuals with HFI (oral, intravenous, medications etc.)
- Screening methods for HFI

All information included in the learning module is based on the data compilation an analysis discussed previously.

Figure 3

First Slide of Learning Module

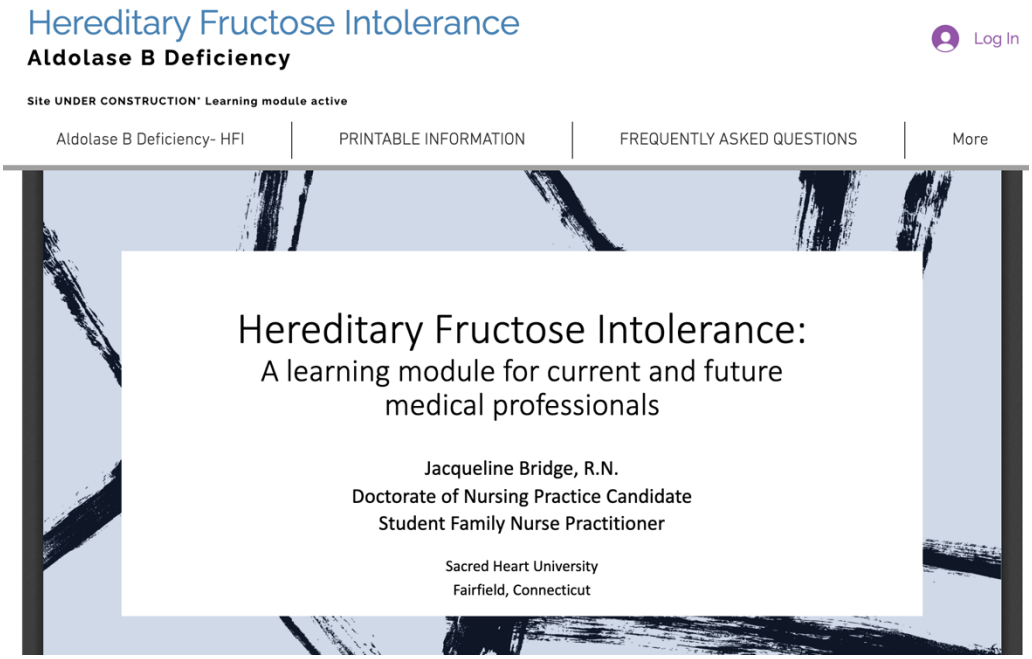

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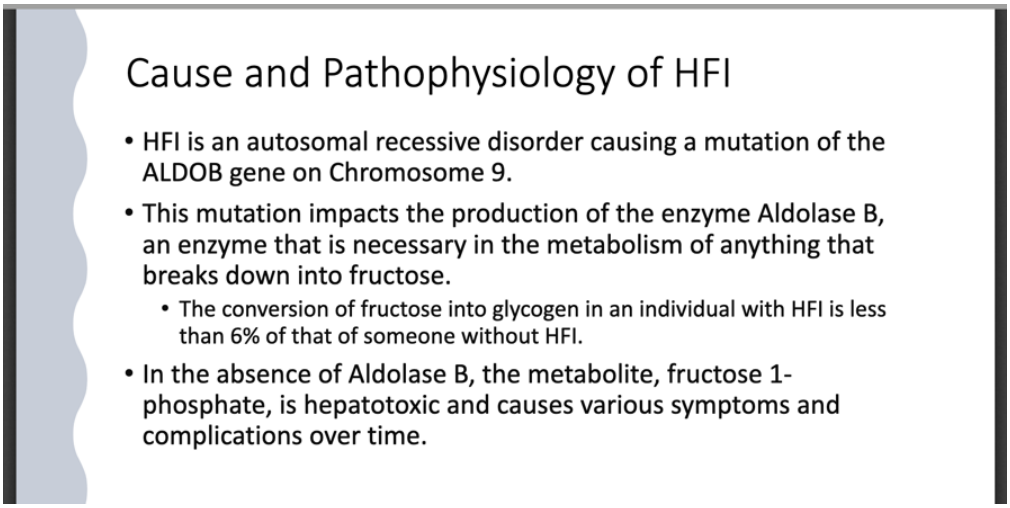
Figure 4

Pathophysiology Section of Learning Module



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Data Analysis Plan

Responses from each point in time would be collected and analyzed to look for changes indicating success in increasing and sustaining awareness of HFI. Changes indicative of increase in awareness of HFI include the following analyses:

- Increase in number of symptoms identified as being present in patients with HFI on sequential assessments.
- Increase in number of participants who select genetic testing as a diagnostic test on sequential assessments.
- Decrease in number of participants who selected IV fructose challenge or hydrogen breath test on sequential assessments.

Project Deviation

This project was initially intended to be implemented with two focal areas: to increase awareness of HFI for practicing pediatric clinicians and primary care physician assistant and family nurse practitioner graduate students. This project was prepared and conducted during the COVID-19 pandemic and subsequent variations to the original intended practice change intervention was made to support a 100% virtual environment. This revised plan included outreach to outpatient medical facilities that care for pediatric patients in the Fairfield County and New Haven County areas. Letters and email introductions were sent to practitioners to recruit clinicians to partake in this project. A personalized letter was written and sent to local pediatric clinicians to create buy-in and interest (Appendix H). A total of 14 letters and emails were sent with three responses: 2 provider practices agreed to participate in the educational module while one refused to participate. Eleven practices did not respond at all. A timeline gap of more than two semesters (or 9 months) created lost interest in project participation by clinical

providers, during a time of increased morbidity and case presentations during the COVID-19 pandemic. Therefore, it was decided to focus solely on the second intended setting and foci of this project: current faculty and students at Sacred Heart University in the APRN and PA advanced practice provider programs.

Ethical Merit and Project Approvals

This project was developed as an education-based evidence-based practice project aimed to act to increase awareness. Using the SHU DNP checklist clarifying whether a project was Quality Improvement or Research necessitating Institutional Review Board Approval (Foster, 2019). This worksheet can be found in Appendix N.

All responses form participants are password protected within the Google Forms document. Participants are given a participation number to determine completion of each section of the project was only done once. No other identifying information was collected. Based on the content of the project, there are no foreseeable risks to the participants partaking in this project.

Implementation Timeline

The timeline for the completion of this project can be seen in Appendix O

Resources

The costs associated with the completion of this project are $779.12 between February 2020 and March 2022. These costs include the costs associated with keeping the website, domain name, and any associated email. A breakdown of these expenses can be seen in Appendix P The author paid these costs. Future upkeep of this website is expected to be $357.33 annually based on the cost from previous years. Microsoft PowerPoint was used for the completion of the learning module and Microsoft Excel for the organization and analysis of the data. A Google Form was used for survey management and collection of responses

Barriers and Solutions

The completion of this project was met with many barriers to implementation. First, The COVID-19 pandemic made it challenging to discuss the implementation of this project with providers in the community. Further, practicing providers in the community as well as students in the DNP project were front-line staff during COVID-19 and had other clinical priorities related to the morbidity and mortality seen in our communities across Connecticut, and therefore, a DNP project based on genetic-knowledge base was not prioritized during these perilous times. Also, the author's timeline was suspended due to personal reasons. During this time, the faculty changes within the PA program occurred, resulting in the project not being implemented in this group. Another significant barrier to implementation was attrition. Of the participants asked to participate, a majority did not complete all project components.

Summary

The plan for completion of this project was to distribute the website for the completion of the preassessment. After completion, participants were to review the learning module and then the post module assessment. Last participants were to receive an email reminding them to return and complete the follow-up assessment one to three months after completion of the original portions of the project.

Chapter 4: Project Findings

Introduction

To increase awareness in providers, a learning module was created. To determine efficacy in increasing knowledge, a preassessment, post assessment and follow-up assessment were used. These assessments addressed the basic components necessary for the identification and diagnosis of HFI for clinicians. The learning modules includes more in-depth information about the pathophysiology, presentation, diagnosis, and interventions.

Results

After implementation of the HFI online module and pre and post data was collected, the data was analyzed using Microsoft Excel. Each item response was reviewed as an average pre-and-post, as individual participant log ins was not conducted to assure anonymity. As expected, a smaller sample size then expected resulted, most likely as a direct affect from COVID-19 and extraneous priorities during this time. There as a decrease in participants from pre-assessment (N=45) to post-assessment module (N=31). A follow-up at least 1-month post-module only had a returning six respondents.

The invitation to participate in the educational module was emailed directly to 3 program directors at Sacred Heart University. One of the directors agreed to introduce the project to students resulting in 102 participants from the APRN programs at Sacred Heart University receiving an email with an invitation to participate.

Additionally, letters were mailed to 14 local medical practices, however, while original agreement to participate was agreed upon, these medical practices did not respond to the later invitation.

The total invitations for participation included verbal or electronic communication to 18 additional physicians, 26 APRNs, 7 PA students, 8 APRN students and one medical student. Some participants shared the project to current or future medical practitioners.

Participant Demographics

Of the 177 individuals who received the invitation to participate, the pre-assessment questionnaire was completed by 45 individuals (25.4%). Of these, 31 (68.8%) reported being APRN students, 5 (11.1%) were PA students, and five (11.1%) reported being licensed APRNs. The remaining two participants included a practicing PA and a Certified Nurse Midwife (0.02%).

Of the 45 participants, 40 (88.9%) reported experience in healthcare while 16 (35.6%) reported more than 10 years, 11 (24.4%) reported 6-10 years, and 13 (28.9%) reported 1-5 years. Before working as a healthcare provider or pursuing a degree, participants reported healthcare experiences in roles including Registered Nurse (n=33, 73.3%), Emergency Medical Technician or Paramedic (n=7, 15.6%), Medical Assistant (n=5, 11.1%), and Certified Nurses Aid (n=3, 0.06%), and Licensed Practical Nurse (n=2, 0.04%). Of these individuals, six (0.13%) reported fulfilling two or more roles, and one (0.02%) said they had fulfilled three of these roles in the past.

Sacred Heart University Students

Of the 36 students that took part in the project, 32 (88.9%) reported pursuing a degree as an APRN or PA at Sacred Heart. Most participants within the sample of students who completed the project reported being in year 3 in the part-time track (n=13, 36.1%). When assessing the completion by SHU students, Table 1 illustrated the distribution of students with regards to their program and progress in that program.

Table 1

Progress within Sacred Heart APRN or PA Program

Progress	Total Participants (n)	Percentage
APRN Program- year 1, full time	2	6.25%
APRN Program- year 1, part-time	0	0%
APRN Program- year 2, full time	3	9.38%
APRN Program, year 2, part-time	2	6.25%
APRN Program- year 3, full time	3	9.38%
APRN Program- year 3, part-time	13	40.62%
APRN Program- modified schedule/unsure of the progress	4	12.5%
PA Program- year 1	0	0%
PA Program- year 2	5	15.62%
Total	**32**	**100%**

Familiarity with Hereditary Fructose Intolerance and Fructose Malabsorption.

The participants were asked to report their familiarity with HFI and FM before the learning module. Responses included "Yes, very familiar," "Yes, somewhat familiar," "I am not sure," and "No, not at all." Table 2 illustrates the frequency participants selected each response in each assessment, with the associated percentage due to the variation in sample size. By assigning the answer choices with the numbers based on their ordinal level (1=No, not at all; 2= I am not sure; 3= Yes, somewhat familiar; 4= Yes, very familiar) the mean response of all participants can be calculated. The preassessment mean in response to familiarity with HFI was 1.6; the post assessment familiarity average response was 3.06; follow-up assessment mean response was 3.

Table 2

Changes in Reported Familiarity with Hereditary Fructose Intolerance

	Preassessment	Post-assessment	Follow-up Assessment
	Choice (%)	Choice (%)	Choice (%)
No, not at all	30 (66.7%)	3 (10%)	0 (0%)
I am not sure	9 (20%)	1 (3.3%)	1 (16.7%)
Yes, somewhat familiar	6 (13.3%)	21 (70%)	4 (66.7%)
Yes, very familiar	0 (0%)	5 (16.7%)	1 (16.7%)
Total	**45 (100%)**	**30 (100%)**	**6 (100%)**

In a similar manner to the question about HFI, participants were asked about their familiarity with FM. While participants were not directly educated about FM in the learning module, FM was discussed in relation to HFI. Table 3 illustrates the reported familiarity with FM. Responses are also reported as percentages to account for the variation in sample size. By ranking the answer choices based on their ordinal level (1=No, not at all; 2= I am not sure; 3= Yes, somewhat familiar; 4= Yes, very familiar) the mean response of all participants was calculated. The preassessment mean in response to familiarity with FM was 1.56; the post assessment familiarity average response was 2.8; follow-up assessment mean response was 3.

Table 3

Changes in Reported Familiarity with Fructose Malabsorption

	Preassessment	Post-assessment	Follow-up Assessment
	Choice (Percentage)	Choice (Percentage)	Choice (Percentage)
No, not at all	29 (64.4%)	5 (16.7%)	0 (0%)
I am not sure	7 (15.6%)	0 (0%)	1 (16.7%)
Yes, somewhat familiar	9 (20%)	21 (70%)	4 (66.7%)
Yes, very familiar	0 (0%)	4 (13.3%)	1 (16.7%)
Total	**45 (100%)**	**30 (100%)**	**6 (100%)**

Symptoms Associated with HFI. Participants were asked to select symptoms they believed were associated with a patient presenting with HFI. Participants were asked to choose as many options as they felt appropriate from four choices; nausea and vomiting, postprandial hypoglycemia, distaste for sweets, and failure to thrive. Reporting of frequency and the mean number of options each participant selected is presented in Table 4. Also shown is the percentage of participants who chose this choice due to the discrepancy in participation between the sections.

Table 4

Presentation of Symptoms in HFI

	Pre-assessment (n=45)	Post-assessment (n=30)	Follow-up Assessment (n=6)
	N (%)	N (%)	N (%)
Nausea and Vomiting	25 (55.5%)	28 (96.7%)	6 (100%)
Postprandial Hypoglycemia	22 (48.9%)	28 (96.7%)	6 (100%)
Distaste for Sweet Tastes	17 (37.8%)	22 (76.7%)	4 (66.7%)
Failure to Thrive	24 (53.3%)	30 (100%)	5 (83.3%)
Mean	**1.95**	**3.76**	**3.5**

Choice of Diagnostic Test. Participants were presented with six options for diagnostic tests for a patient presenting symptoms of HFI. Participants were asked to select the choices they would want to order if they were the clinician. The options provided included genetic testing, the safest and most productive diagnostic test, and liver biopsy, which could diagnose HFI but has significant risks associated with the procedure. Unsafe diagnostic procedures included the Intravenous Fructose Challenge and the Hydrogen Breath Test. Other options were not dangerous, but they would not yield a diagnosis of HFI. Table 5 displays the frequency and percentage of participants who selected each option during each portion of the project.

Table 5

Choice of Diagnostic Test

	Preassessment (n=45)	Post-assessment (n=30)	Follow-up Assessment (n=6)
Hydrogen Breath Test	16 (35.6%)	5 (16.7%)	1 (16.7%)
Liver Biopsy	3 (6.7%)	6 (20%)	0 (0%)
Endoscopy	1(2.2%)	1 (3.3%)	0 (0%)
Genetic Testing	14 (31.1%)	27 (90%)	6 (100%)
IV Fructose Challenge	11 (24.4%)	7 (23.3%)	2 (33.3%)
Hemoglobin A1C	23 (51.1%)	7 (23.3%)	5 (83.3%)

Chapter 5: Discussion of Project Findings and Implications

Data analysis included examination of the pre- and post-assessment items given during the module. This information was then discussed in terms of alignment with the current, available literature on HFI.

Data collected from the three assessments attempted to determine if participants would report a change in their self-report of familiarity with HFI at three different points. Based on the results, there was an increase in participants who reported being somewhat familiar (13.3% to 70%) and very familiar (0% to 16.7%) after completing the assessment. There was also a decrease in participants who reported that they were not familiar (66.7% to 10%). Based on the significant difference in sample size and attrition at the 1-month follow-up evaluation, it was difficult to determine whether this change was substantial. However, the purpose of this project was to increase awareness of HFI. Based on these results, this overall global aim was met.

Symptom Identification

In Table 4, the participant selections for symptoms associated with HFI. In alignment with the goals of this project, participants identified more symptoms during the preassessment (the mean of symptoms selected was 1.95 in the preassessment to 3.76 in the post-assessment). Although representing only a portion of the original participants, the follow-up assessment still had a mean of 3.5 symptoms selected, which they believed were associated with HFI.

Choice of Diagnostic Test

Along with the identification of HFI in patients, the choice of the diagnostic test must be safe and sensitive in the ability to confirm the diagnosis. Participants selected the diagnostic tests that they would order for the presenting patient. As predicted, implementation of the learning

module led to a decrease in the choice of unsafe diagnostic tests (Hydrogen Breath Test and IV Fructose Challenge).

Also of note is the increase in the frequency and percentage of participants who chose genetic testing to diagnose HFI. As seen in Table 6, 31.1% of participants initially chose this option, and 90% of participants selected this option in the post-assessment. There was also an increase in participants who selected liver biopsy as a diagnostic test from the preassessment (6.7%) to the post-assessment (20%).

Table 6

Appropriateness of Choice of Diagnostic Test

	Diagnostic Test	Preassessment (n=45)	Post-assessment (n=30)	Follow-up Assessment (n=6)
Unsafe Diagnostic Tests	Hydrogen Breath Test	16 (35.6%)	5 (16.7%)	1 (16.7%)
	IV Fructose Challenge	11 (24.4%)	7 (23.3%)	2 (33.3%)
Inappropriate Choice of Tests	Endoscopy	1 (2.2%)	1 (3.3%)	0 (0%)
	Hemoglobin A1C	23 (51.1%)	7 (23.3%)	5 (83.3%)
Appropriate Diagnostic Test	Liver Biopsy	3 (6.7%)	6 (20%)	0 (0%)
Best Choice of Diagnostic Test	Genetic Testing	14 (31.1%)	27 (90%)	6 (100%)

Discussion

The findings from this project were consistent with the hypothesized lack of awareness of HFI. This hypothesis is consistent with the discussions in research regarding HFI being more prevalent than what is seen due to mutations still being unidentified (Ali & Cox, 1995; Ali et al., 1998; Ali et al., 1994; Brooks & Tolan, 1993; Gaughan et al., 2015).

While research does not specifically address the lack of awareness or need for more education about HFI, the research supports a danger in the increased amounts of sugars in food and beverages resulting in a need for increased vigilance and awareness of HFI (Akram & Hamid, 2012; Ali et al., 1998; Cox, 1991; Li et al., 2018).

The findings from this project show an increased average in the self-reported awareness in HFI from preassessment to post assessment (1.6 to 3.6) and preassessment to follow-up assessment (1.6 to 3) where 1 indicates no, not at all and four indicates yes, very familiar. Findings for FM familiarity from preassessment to post assessment (1.56 to 2.8) and preassessment to follow-up assessment (1.56 to 3) were not as drastic which was expected as FM was only discussed in contrast to HFI and not in depth in this module.

Regarding choice of symptoms related to HFI, there was an increase in the number of symptoms selected from preassessment to post assessment (1.95 to 3.76) and from preassessment to follow-up assessment (1.95 to 3.5). This indicated that the increased knowledge of symptoms associated with HFI from the baseline.

Similar results indicated an increased awareness of selection of diagnostic test from preassessment to post assessment and preassessment to follow-up assessment. Approximately 31% of participants selected genetic testing as a diagnostic test during the preassessment. This number increased to 90% and 100% (n=6) of participants in the post assessment and follow-up assessment. In contrast, 35.6% (n=16) of participants selected hydrogen breath test and 16.7% chose this option in both the post module (n=5) and follow-up assessments (n=1).

Contrary to the desired increase in awareness was the results surrounding the selection of intravenous fructose challenge. On the preassessment, 24.4% (n=11) of participants selected this choice followed by 23.3% (n=7) on the post assessment and 33.3% (n=2) on the follow up.

These findings, including the lack of change in the selection of intravenous fructose challenge is consistent with the findings in literature regarding the significant dangers for those with HFI undergoing medical treatments (Ali & Cox, 1995; Ali et al., 1998; Cox, 1993; Cox, 1995; Gaughan et al., 2015; Li et al., 2018).

Overall, of the three key aims discussed previously, these results supported an increased awareness of HFI and FM in this project, indicating these aims were met. The second aim of increasing knowledge of the appropriate diagnostic test in potential HFI patients can be seen in the increased selection of genetic testing by participants discussed previously. Lastly, as many participants were SHU students, the results of this project overall supported the increased awareness regarding symptom of HFI, and choice of diagnostic test indicated that this project was effective in increasing awareness within this population.

Strengths and Limitations of the Project

This project had may strengths and limitations which likely impacted the outcomes. As far as strengths of this project, the biggest strength was the virtual platform used for completion and sustainability of the project. This strength in design allowed for ease of use by participants and the flexibility for completion. As the project progressed, this virtual platform allowed for a continuation of this project due to the COVID-19 pandemic occurring during the implementation phase of this project.

The DNP student had immediate access to the APRN student population since she was an enrolled DNP student at Sacred Heart University. Since this project was developed for use within an APRN student population, this module fit nicely with this targeted population and setting. Further, the project was meant to assess basic knowledge and increase awareness of HFI to allow current and future practitioners to identify the differentials surrounding HFI. Therefore,

the information in this module was purposely intended to include basics information around specific symptom patterns indicative of HFI as well as appropriate, and safe diagnostic tests. This information was easy to read and easily accessible to students and a strength in the project design.

Limitations surrounding this project including the timing around implementation. COVID-19 occurred between the creation and planning of this project and was a worldwide pandemic during the project implementation phase. The original project plan including interaction with practicing healthcare providers and the COVID-19 environment did not allow for a safe, effective space for the original project plan to be conducted. Further, healthcare providers were faced with unprecedented stressors which did not allow for time to introduce a knowledge-based DNP scholarly project in the field. These limitations led to a shift in project design to focus on the targeted student population who were preparing to be future APRN providers. Despite this shift, significant attrition from the preassessment (n=45) to post-assessment (n=30) to the 1-month follow-up (n=6) was found.

Another potential recognized limitation to this project was a potential participant biases in the student population who participated. This DNP student was the author and presenter of many DNP assignments which also focused on HFI which could have given students baseline knowledge and recognition of some of the materials.

Project Implication for the Field

The results found in this project illustrated a gap in the education of a nurse practitioner and physician assistant programs regarding HFI and other inborn errors of metabolism. It also shows that a learning module with basic information about this diagnosis was sufficient in increasing knowledge in some current and future practitioners allowing for safer diagnosis and

initiation of care for these patients. Overall, increasing awareness of HFI will allow for progress toward closing the knowledge gap in healthcare providers. This will ultimately help clinicians in the diagnosis of current and future patients with HFI to allow for safer diagnosis and timelier introduction of safe interventions. Further, identification of the symptoms of HFI, knowledge of the safest diagnostic testing methodologies, awareness of the severity of lack of or inappropriate treatment may potentially increase awareness of the possibility that metabolic disorders other than HFI can cause.

Key Lessons Learned

During the implementation of this project, it became clear that inborn errors of metabolism are not covered in the current APRN curriculum at the College of Nursing at Sacred Heart University. Based on the similarity in the responses to self-reported familiarity with HFI and FM, there is likely a gap in education in other educational programs for APRNs and PAs. In conjunction with this finding, the discrepancy in the number of responses between students and clinicians showed that introducing this information would make the most significant impact when introduced within an educational setting.

Sustainability Plan

To ensure that the findings of this project are responded to appropriately, the continued use of the learning module and possibly the assessments will be presented to the faculty of SHU's APRN and PA programs. The sustainment of this project, whether as a learning module, a continuing education module, or an introduction to course material, would ideally lead to success in increasing Sacred Heart University student knowledge base of HFI. This project virtual platform (website) will remain active and up to date with the most recent evidence related to HFI

by a subject matter expert, currently a certified family nurse practitioner student in Connecticut and soon to be licensed upon graduation.

Summary

In HFI and many other metabolic disorders, early diagnosis and dietary intervention can often spare a patient from any possible illness, organ damage, and unnecessary suffering by strictly adhering to a diet free of fructose, sucrose, sorbitol, and other precursors of fructose. Timely diagnosis and intervention are key to avoid unnecessary medical costs and the diagnostic testing many patients often undergo before diagnosis. Increased awareness and understanding in clinicians will result in the best possible outcomes for patients with HFI.

Chapter 6: Dissemination and Sustainability

Dissemination

An overview of this student project as well as the use and availability of this module will be written and submitted to a nurse-led journal such as "*Nurse Education Today.*" Further, the website created for this project will be maintained for use by future students, clinicians, and the public as a professional, scholarship of this DNP student. Overall, the research related to HFI is lacking comprehensive guidelines for patients and providers and clinical guidelines are needed for the field. Potential submission of this material in the form of an integrative literature review or critical analysis of available literature will be considered in the future.

The results of this project will be disseminated in a poster presentation as a course requirement at Sacred Heart University in NU 820. The poster or abstract of this project will also be submitted to local conference, identified in the future. Additionally, this project overview will be submitted as a course requirement for NU 824 as well as uploaded to the DNP Repository online as a requirement for the Doctorate in Nursing Practice degree at Sacred Heart University, College of Nursing.

Sustainment

The future use of these project materials would be beneficial to students and clinicians alike. This DNP student will maintain the upkeep of this HFI virtual information platform as part of her own APRN scholarship.

It was found that the Family Nurse Practitioner curriculum at Sacred Heart University was limited in the discussions regarding genetic diseases with nearly no discussion of inborn errors of metabolism, such as HFI. While this is similar to that found on review and critical appraisal of available literature in the field, continued advancement requires recognition of

illness and disease that new and emerging APRNs need to know to safely practice in the community. Based on the experiences gained from this project, future use of this module would be more effective if incorporated into formal course curriculum such as SHU's APRN programs.

Sustainability of this project relies on further dissemination of these project materials in order to decrease the frequency of which HFI and other inborn errors of metabolism occur and go undiagnosed. Early identification of HFI leads to complication-free development and a future free from severe morbidity and mortality. Knowledge of HFI remains imperative and should be priority for incorporation into APRN curriculum and continuing education modules for current practicing practitioners.

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Appendix A

Comparison of Hereditary Fructose Intolerance and Fructose Malabsorption

	Hereditary Fructose Intolerance	Fructose Malabsorption
Pathophysiology	Autosomal recessive metabolic disorder in which individuals do not produce or produce ineffective Aldolase B. This enzyme is necessary for the metabolism of fructose, sucrose, sorbitol, and their precursors. Ingestion of these substances results in an accumulation of hepatic Fructose-1-Phosphate, which interferes with normal cellular function.	Metabolism of nutrients is impaired due to the problem of membrane transport systems in the epithelium of the small intestine. Individuals can be born with it (primary malabsorption), or it can be developed (acquired malabsorption)
Prevalence		
Age at time of presentation	Upon introduction to food or beverages with sugars or ingredients which metabolize into fructose. (Complications in infancy often occur due to sugars in infant formula)	Varies
Possible complications	Hepatic damage (hepatomegaly, jaundice, fatty liver), hepatorenal failure, seizures, coma, and death.	Malabsorption, diarrhea, weight loss
Symptoms	Aversion to sweet tastes, otherwise asymptomatic if all sugars that metabolize into fructose are avoided. Acute intoxication with fructose or other sugars: nausea, vomiting, abdominal pain, post-prandial hypoglycemia Long-term exposure: failure to thrive, hepatic damage, hepatorenal failure, seizures, coma, and death.	Bloating, abdominal pain, nausea, heartburn, gas, and diarrhea
The goal of treatment/ dietary modification	Implement dietary interventions and live a symptom-free life	Avoid symptoms associated with ingestion of fructose

Dietary intervention	Complete avoidance of food and beverages containing fructose, sucrose, sorbitol, and their precursors	Avoid foods with more fructose than glucose, items sweetened with fructose (including crystalline fructose or high fructose corn syrup or honey). Temporarily avoid fruits with high fructose concentration (apples, pears, prunes, dates). Reintroduce them if symptoms are not significantly better with exclusion. Limit beverages with high fructose corn syrup to 12 ounces per day. Minimal caffeine intake; avoid sorbitol and sugar alcohols.
Diagnosis	Genetic testing	Fructose Breath Test

American Gastroenterological Association, 2020; Mason, 2019

Appendix B

Data Organization Chart

Article	(See reference list below)	1	2	3	4	5	6	7	8	9
Information	Cause (in-depth)	X	X	X	X	X	X	X	X	X
	Symptoms	X	X	X	X	X	X	X	X	X
	Signs	X	X	X	X	X	X	X		X
	Alterations in Lab work	X	X	X		X				
	Case Studies						X			
Diagnosis	Genetic cause of HFI	X	X	X	X	X	X	X	X	X
	Prevalence		1: 20,000	Varies by population	1:20,000	1: 18,000-31,000	1: 20,000 in Switzerland			1: 23,000
	Prevalence with neonatal screening	1: 18,000 to 1: 29,600			~1.3 % of neonates in UK are carriers					
	More prevalent than we think			X	Different mutations based on ethnicity-most research on	X	85% of disease alleles have been identified in west	Not all mutations identified.		

					Caucasians		European ancestry			
	Other options discussed	X					X			
	Diagnostic testing	X			Genetic testing preferred-Liver biopsy detects but unsafe	Genetic testing then liver biopsy		Genetic testing, FTT and Liver biopsy dangerous	No FTT	
	Differential Diagnoses	X				X				
	Confusion with FM	X				X				
	Patients are diagnosed later in life.		X	X	X					X
Intervention	Early diagnosis and diet	X	X	X	X	X				X
	Time to see positive change	Days				“rapidly”				
	Clinical changes post-intervention	X (138)								
	Tx for hypoglycemia	Glucose			Glucose or milk iv/PO	glucose				
Dangers	Deaths during			X	X	X				X

	hospitalization									
	Increase Sugar in food				X					X
	Caretakers not understanding				X					

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Appendix C

Evidence Table for PICO Question

EBP Question: Will introducing a teaching tool of best practices for Hereditary Fructose Intolerance lead to increased awareness among health care providers?

Article abbreviated title	Author & Year	Evidence Type	Sample, Sample Size, Setting	Findings that help answer clinical questions/ Notes	Limitations	Factors Discussed S/SX; DX; treatment; follow up recommendations for follow-up	Evidence Rating† Level/Quality	
Non-alcoholic fatty liver in hereditary fructose intolerance	Aldámiz-Echecarria et al., 2018	Cross-sectional, observational	16 genetically diagnosed patients between 3 and 48 on an HFI diet for at least two years	Assessing the prevalence of nonalcoholic fatty liver in HFI patients Great description of the importance of Aldolase B. Looks at the correlation between specific mutations and the likelihood to have NAFLD (7 of 9 with Ala150, 3 of those had hepatomegaly compared to 2 of 6 with c.360_363delCAAA-0 had hepatomegaly	Inclusion criteria include dietary compliance- what diet are they following, what maximum daily amount of harmful sugars? How do they measure this? Nutritional status based only on BMI Patients had different genetic mutations. Vague dietary recommendations	Begin with an introduction to foods Sxs: FTT, vomiting and pain, jaundice, liver failure. Metabolism alterations-hypoglycemia, metabolic acidosis, hypophosphatemia, hyperuricemia, hypermagnesemia, hyperalaninemia, elevated serum carbohydrate-deficient transferrin Late dx without dietary intervention-renal and hepatic seizures, coma, or death	III	B/C
Diverse mutations in the	Ali & Cox, 1995	Letter to the editor	Department of Medicin	The frequency of HFI is not precise, and recognition is vital	The article's focus is to increase genetic screening		V	A

Article abbreviated title	Author & Year	Evidence Type	Sample, Sample Size, Setting	Findings that help answer clinical questions/ Notes	Limitations	Factors Discussed S/SX; DX; treatment; follow up recommendations for follow-up	Evidence Rating† Level/Quality	
aldolase B gene underlie the prevalence of hereditary fructose intolerance.			e. U. of Cambridge. Addenbrooke's Hospital	since it responds well to the dietary exclusion of fructose, sucrose, and sorbitol. Evidence that there are more mutant alleles of aldolase B than initially thought because Nonconsanguineous parents have had more kids with HFI After making it through infancy, more people may identify with having HFI Administration of fructose-based solutions has resulted in at least 16 deaths of patients who unknowingly had HFI Some reports of a large amount of HFI within extended, nonconsanguineous families suggest the disease alleles are prevalent in the USA in European populations. Emphasis on the dangers of IV sugars during things such as minor procedures and the severity (risk of death)	to determine the actual frequency of HFI.			
Hereditary fructose intolerance	Ali, Rellos et al., 1998	Opinion of nationally recognized experts	Department of Medicine. U. of Cambridge. Addenb	The function of aldolase B "catalyzes the specific and reversible cleavage of the glycolytic hexose substrates, fructose 1-phosphate, into 3-carbon sugars,	Article from 1998		V	A

Article abbreviated title	Author & Year	Evidence Type	Sample, Sample Size, Setting	Findings that help answer clinical questions/ Notes	Limitations	Factors Discussed S/SX; DX; treatment; follow up recommendations for follow-up	Evidence Rating† Level/Quality	
			rooke's Hospital	dihydroxyacetone phosphate, D-glyceraldehyde 3-phosphate, and D-glyceraldehyde. Aldolase B is found in the liver, kidneys, and small intestine. Aldolase B is under dietary control and is inactive under resting conditions. Infants are most vulnerable when weaning from breastmilk- sxs when given formula/fruit/vegetables Vomiting Nausea Hypoglycemia Metabolic acidosis Lg quantities- more severe reactions, lethargy, seizures, and coma Persistent intake- syndrome of chronic toxicity, irreversible damage to liver and kidney, cirrhosis, and death The mother/caretaker plays a critical role in nutrition and keeping the patient safe. Must be cautious of interference from other family members (grandparents giving honey) Self-protective aversion to food that causes distress is refined through trial and error.				

Article abbreviated title	Author & Year	Evidence Type	Sample, Sample Size, Setting	Findings that help answer clinical questions/ Notes	Limitations	Factors Discussed S/SX; DX; treatment; follow up recommendations for follow-up	Evidence Rating† Level/Quality	
				Hazard uses fructose infusions for parenteral feedings (20+ fatal cases)- fructose IVs are no longer used- glucose is better for people with diabetes (who fructose was thought to be better for). It is destructive for HFI and toxic for everyone else. Treatment- strict exclusion diet with an experienced dietician- normal health and development return quickly if tissue damage is not too severe. Caution using meds and syrup (sucrose and sorbitol are used often) Pts should take supplements of water-soluble vitamins, folic acid, and vitamin c. Medic alert bracelet with prohibited sugars and appropriate treatment for hypoglycemia (glucose and milk for parenteral and oral use. In HFI, incorporation of fructose to glycogen was less than 6%- suggests that the fructose is primarily catalyzed by Aldolase B and that alternative pathways for direct conversion of fructose 1-phosphate to fructose-1,6				

Article abbreviated title	Author & Year	Evidence Type	Sample, Sample Size, Setting	Findings that help answer clinical questions/ Notes	Limitations	Factors Discussed S/SX; DX; treatment; follow up recommendations for follow-up	Evidence Rating† Level/Quality	
				biphosphate in human liver tissue are limited.				
Null alleles of the aldolase B gene in patients with hereditary fructose intolerance	Ali, Tuncman, et al., 1994	Case Report	Four symptomatic patients in Southern Turkey	Rare mutant alleles of aldolase B can be overlooked and fail to diagnose the condition by this means.		1 in 20,000 Sxs: hypoglycemia, hypophosphatasemia, and acidosis. Continued exposure leads to growth retardation, hepatic injury, and eventually death. DX: intravenous fructose tolerance test but this procedure, and others based on enzymatic assay of tissue biopsy samples (liver biopsy) or 31P magnetic resonance spectroscopy, five are too cumbersome or invasive for general use in the population. Recommends genetic testing	V	A

Article abbreviated title	Author & Year	Evidence Type	Sample, Sample Size, Setting	Findings that help answer clinical questions/ Notes	Limitations	Factors Discussed S/SX; DX; treatment; follow up recommendations for follow-up	Evidence Rating† Level/Quality	
Association of the Widespread A149P hereditary fructose intolerance mutation with newly identified sequence polymorphisms in the aldolase B gene	Brooks & Tolan, 1993	Assessing DNA for new mutations	DNA sequencing on 32 blood samples			Sxs- severe pain, vomiting, hypoglycemia Chronic intake- kidney damage, growth retardation, coma, death IV fructose loading and measuring Aldolase B activity with liver biopsy are dangerous for pt.	V	B
An independent diagnosis	Cox, 1990	Opinion of the nationally recognized expert					V	
Fructose intolerance: diet and inheritance	Cox, 1991	Opinion of nationally recognized experts					V	
Hereditary fructose intolerance	Cox, 1990	Opinion of nationally recognized experts					V	A
Iatrogenic deaths in hereditary fructose intolerance	Cox, 1993	Opinion of nationally recogniz		Fatal cases continue to occur. Sucrose and fructose in infant formula Before diagnosis, adults with HFI only		Sxs: vomiting, symptomatic hypoglycemia, FTT during	V	B

Article abbreviated title	Author & Year	Evidence Type	Sample, Sample Size, Setting	Findings that help answer clinical questions/ Notes	Limitations	Factors Discussed S/SX; DX; treatment; follow up recommendations for follow-up	Evidence Rating† Level/Quality	
		ed experts		ingest a few grams of fructose or sucrose a day (a fraction of what normal adults do), and cavities are rare, but they still have abdominal Sxs and intermittent hypoglycemia (due to accidental dietary ingestions) In the absence of fructose – pts have no Sxs. Ut exposure to small amounts of sugar induces functional impairment (i.e., renal tubular acidosis and eventually structural injury in the tissue sites for metabolism. Intracellular sequestration of fructose-1-phosphate depletes the intracellular pool of free inorganic phosphate (seen in P magnetic resonance spectroscopy in vivo), which inhibits glycogenolysis and gluconeogenesis, leading to refractory hypoglycemia. Feedback inhibition of ketohexokindase reduces further metabolism of fructose so that when the renal threshold is exceeded, this reducing sugar is in the urine. Parenteral administration of		weaning or transfer from breast milk to fruit juice or artificially sweetened foods- infant has episodes of disturbed consciousness, hypoglycemia seizures. Chronic ingestion- jaundice, liver enlargement, renal tubular dysfunction, hemorrhagic tendency, hepatic failure, possible death. Growth retardation accompanied by biochemical abnormalities occur unless dietary fructose is reduced to less than 40 mg/kg/day. DX- IV FTT and Liver biopsy used to be done. Now PCR based		

Article abbreviated title	Author & Year	Evidence Type	Sample, Sample Size, Setting	Findings that help answer clinical questions/ Notes	Limitations	Factors Discussed S/SX; DX; treatment; follow up recommendations for follow-up	Evidence Rating† Level/Quality	
				fructose and invert sugar or sorbitol is rapidly converted to fructose by sorbitol dehydrogenase in the liver leading to acute liver cell necrosis and profound metabolic acidosis 15 cases resulted in irreversible hepatorenal failure-use of these fluids has decreased but still done in German-speaking countries when an article published Phenylketonuria occurs with similar frequency and responds entirely to appropriate dietary treatment. Population screening before weaning may be justified as the most common mutations can be easily detected with PCR methods. Pilot studies have been successful using Guthrie blood stops.		methods of DNA analysis are well established.		
Hereditary Fructose Intolerance	Gaughan et al., 2015	Clinical Practice Guidelines	N/A	Reviews clinical characteristics, diagnostics, and testing, management, suggestive findings, differential diagnoses, treatment of acute episodes No formal guidelines regarding surveillance Discussed the use of sweet ease in neonates Avoid Hydrogen breath tests and	Management recommendations are very vague. Inaccurate dietary guidelines	Medic alert bracelets Has dietary guidelines (not accurate) Caution with formula, medication, nutritional drinks, enemas, etc., parenteral medications	IV	B

Article abbreviated title	Author & Year	Evidence Type	Sample, Sample Size, Setting	Findings that help answer clinical questions/ Notes	Limitations	Factors Discussed S/SX; DX; treatment; follow up recommendations for follow-up	Evidence Rating† Level/Quality	
				fructose tolerance testing. Very little evidence about HFI in pregnancy. Consider banking the DNA of affected individuals for future research		should be cleared by the pharmacist and team on a case by case basis. Use of vitamins- which ones? Use medic alert- what info is the MD going to find?		
Neonatal screening for hereditary fructose intolerance: frequency of the most common mutant aldolase B allele (A149P) in the British population	James et al., 1996	Systematic review	A random cohort of 2050 subjects born in 1994 and 1995	PCR was used to amplify the AdolB gene in Guthrie card blood spots. 1.32 +/1 0.49% (95% confidence interval) of samples were heterozygous for HFI. The estimated prevalence of 1 in 23,000 Findings have implications for inclusion in newborn screening	Prevalence is different in different countries, as are mutations.		I	A
An empirical estimate of carrier frequencies for 400+ causal Mendelian variants: results from an ethnically diverse clinical sample of 23,453 individuals	Lazarin et al., 2013	Nonexperimental study	Twenty-three thousand four hundred fifty-three individuals-results from genetic testing. Ethnically diverse	Looks at the prevalence of carriers of AldoB mutation associated with HFI in a large population and the genetic majority of HFI compared to genetic prevalence in the literature. Caucasians, 1 in 90.1 in the study but 1 in 81.1 in literature. *African Americans 1 in 226, but no literature to compare to*	75% female. Research to compare findings is not done. Most Americans in the study and genetic mutations are different in different countries.		III	A

Article abbreviated title	Author & Year	Evidence Type	Sample, Sample Size, Setting	Findings that help answer clinical questions/ Notes	Limitations	Factors Discussed S/SX; DX; treatment; follow up recommendations for follow-up	Evidence Rating† Level/Quality	
				Middle Eastern 1 in 97, but no literature to compare to				
Chronic Fructose Intoxication After Infancy in Children with Hereditary Fructose Intolerance: A Cause of Growth Retardation	Mock, Perman, Thaler & Morris, 1983			Decreasing dietary fructose increased the growth rate in children. Patients' diet was already low enough to prevent symptoms, but they instituted more stringent guidelines (appx 40 mg/kg/day)				
Newborn Screening for inherited metabolic disorders; news and views	Pourfarzam, & Zadhoush, 2013	Guidelines on newborn screening	n/a	Newborn screening is used to identify genetic metabolic disorders in apparently healthy infants. These are usually corrected by diet or medications. Newborn screening allows for the early detection of many disorders. Each disorder is individually rare, but their cumulative incidence is relatively high, around 1 in 1500 to 1 in 5000 live births. WHO Wilson–Jungner criteria, a disease that has the following properties should be screened: (1) a vital health problem; (2) the natural history of the condition should be adequately understood; (3) it	No specific HFI information		IV	A

Article abbreviated title	Author & Year	Evidence Type	Sample, Sample Size, Setting	Findings that help answer clinical questions/ Notes	Limitations	Factors Discussed	Evidence Rating†	
						S/SX; DX; treatment; follow up recommendations for follow-up	Level/Quality	
				should be recognizable in the early stages; (4) there should be a suitable test or examination; (5) the test should be acceptable to the population; (6) intervals for repeating the test should be determined; (7) there should be an accepted treatment for patients; (8) facilities for diagnosis and treatment should be available; (9) there should be an agreed policy concerning whom to treat as patients; and (10) the costs of case finding should be economically balanced against the benefits				

†Use John Hopkins Evidence Level and Quality Guide

Appendix D

Evidence Synthesis Table

Article Number	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Level 1: Systematic review or meta-analysis														
Level II: Randomized Control Trial														
Level III: Controlled Trial without Randomization							X							
Level IV: Case-control or cohort study	X					X							X	
Level V: Systematic Review of quality and descriptive studies														
Level VI: Qualitative or descriptive study, CPG, Lit Review, QI, or EBP project			X					X						X
Level VII: Expert opinion		X		X	X				X	X	X	X		

Article Number	15	16	17	18	19	20	21	22	23	24	25	TOTAL
Level 1: Systematic review or meta-analysis												0
Level II: Randomized Control Trial												0
Level III: Controlled Trial without Randomization												1
Level IV: Case-control or cohort study	X				X	X						6

Level V: Systematic Review of quality and descriptive studies												**0**
Level VI: Qualitative or descriptive study, CPG, Lit Review, QI, or EBP project		**X**	**X**	**X**					**X**	**X**	**X**	**9**
Level VII: Expert opinion							**X**	**X**				**9**

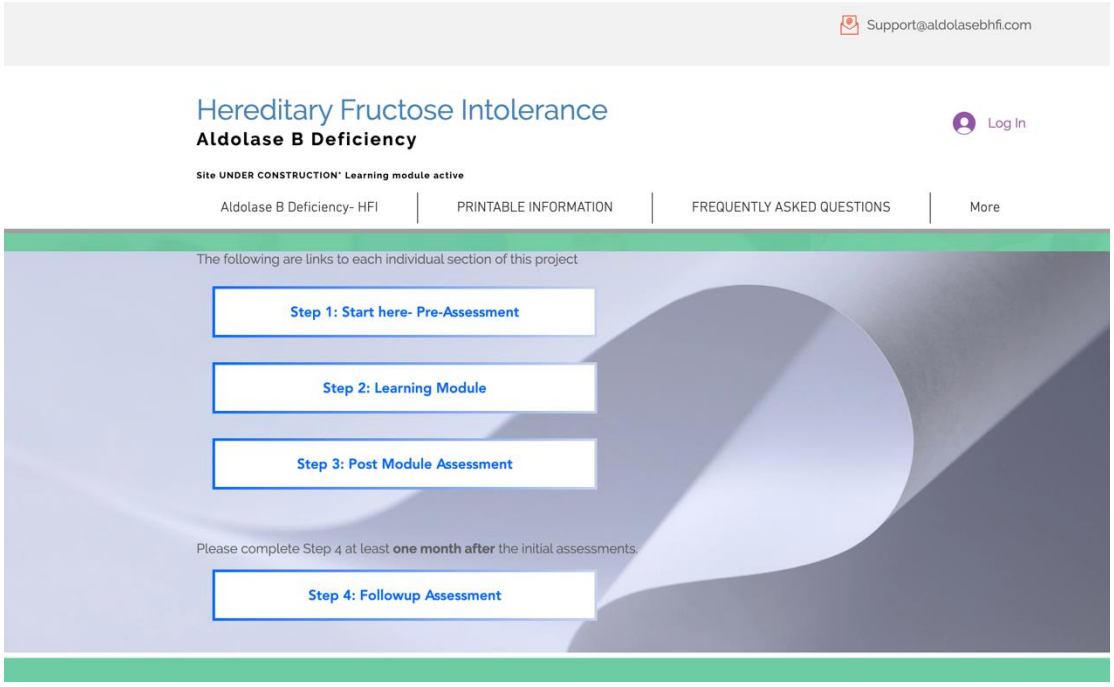
Appendix E

Rationale for Answer Options

	Patient Presentation				Diagnostic Test			
	N/V	PP Hypo	Distaste for Sweet Tastes	FTT	Genetic Testing	Liver Biopsy	IV FC	HBT/ Avoid dietary sugar
Akram, & Hamid, (2013)	X	X			ND	ND	ND	X
Aldámiz-Echevarría et al., (2019)	X	X		X	X			X
Ali, & Cox, (1995)	X	X	X	X	-		X	X
Ali, Rellos, & Cox, (1998)	X	X	X	X	X	X	X	X
Ali, Rosien & Cox, (1992)	X	X	X	X	X	X	X	X
Ali, Tuncman, et al.,1994	X	X	X	X	X	X	X	X
Brooks & Tolan, 1993	X	X	X	X	X	X	X	X
Cox, 1991	X	X	X	X	X			X
Cox, 1990a	X	X	X	X	X		O	X
Cox, 1990b	X	X	X	X	X	X	O	X
Cox, 1993	X	X	X	X	X	X	X	X
Cross & Cox, 1990	X	X	X				O	X
Gaughan et al., 2015	X	X	X	X	X	X	X	X
James et al., 1996	X	X	X	X	X	X	X	X
Kim et al., 2020	X	X	X	X	X			X
Kim et al., 2021	X	X	X	X	X	X	X	X
Li et al., 2018	X	X	X	X	X			X
Mock et al., 1983	X	X	X	X			O	X
Steinmann & van den Berghe, 2006	X	X	X	X	X	X	X	X

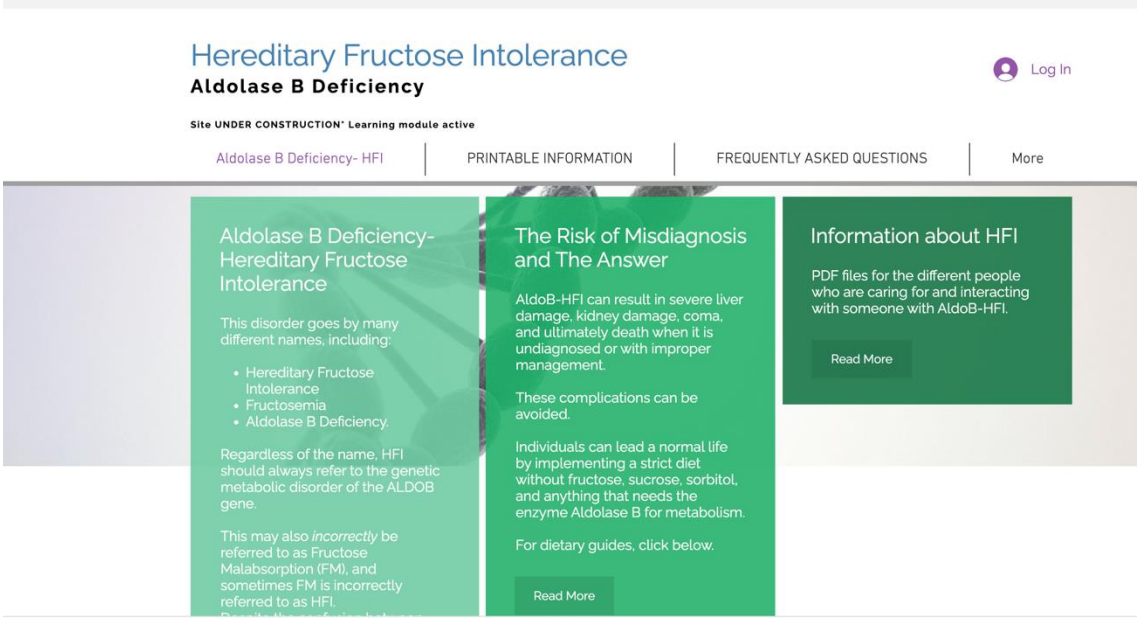
Appendix F

Screenshot of Homepage



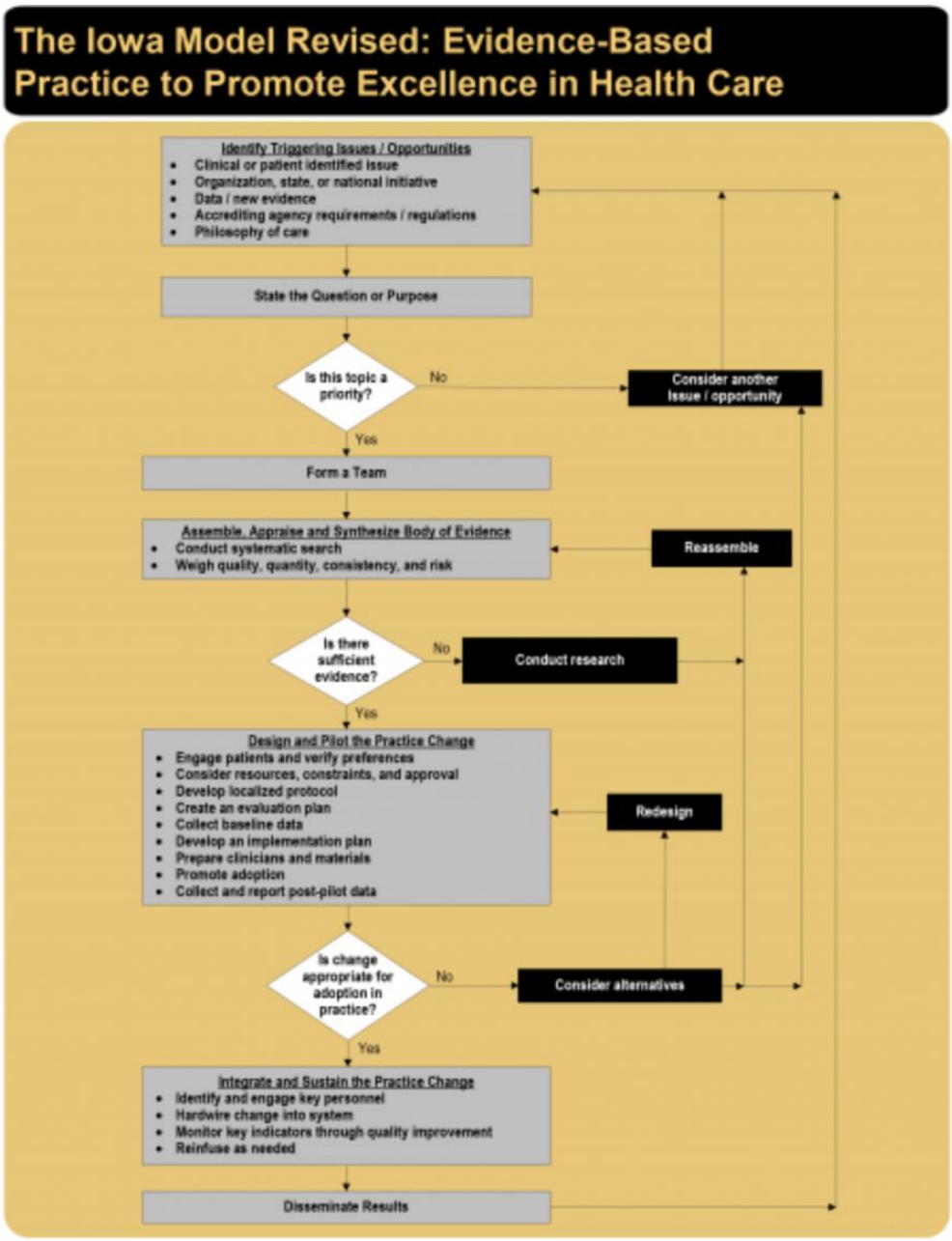
Appendix G

Contents of Website



Appendix H

Iowa Model for Evidence-Based Practice



(uihc.org, 2020)

Appendix I

Introductory Letter for Providers

DR. SUSAN L. DAVIS, R.N., & RICHARD J. HENLEY COLLEGE OF NURSING
Sacred Heart University

Dear Dr., APRN, or PA,

My name is Jacqueline Bridge. I am a Doctorate of Nursing Practice (DNP), Family Nurse Practitioner (FNP) student at Sacred Heart University, College of Nursing. I am currently recruiting primary care medical providers in Connecticut who specifically care for pediatric patients to participate in an evidence-based learning module for my DNP doctoral project.

My project focuses on **Hereditary Fructose Intolerance (HFI),** an autosomal recessive metabolic disorder, which is not readily included in pediatric medicine or nursing educational programs and often missed on diagnosis: which delays treatment and, in some cases, can be fatal. My personal experience with HFI includes being misdiagnosed as a child resulting in severe liver and organ compromise. I was diagnosed with failure to thrive after being weaned from breastmilk and introduced to fruit. After more than three years of searching for help, I was eventually diagnosed. However, other patients are often not so lucky.

The aim of this project is to increase awareness of HFI as an often-misdiagnosed metabolic disorder and highlight the clinical symptoms in which patients may present. The global aim is to create awareness in practicing pediatric clinical care providers in order to avoid unnecessary illness and suffering of patients and their families, where diagnosis is often delayed or missed altogether.

This activity includes a provider pre-survey, a brief learning module estimated to take 20 minutes, and then a post-survey. I will reach out to you in three months after the initial learning module for follow-up questions. This learning module is available 100% online.

I will be launching this project in August-September of 2020. The purpose of this email is to identify clinics and primary care providers willing to participate in this project. If you are willing to participate, can you please respond in this email and include how many providers at your practice are willing to participate?

If you have any questions or concerns, please feel free to reach me at Mahonyj@mail.sacredheart.edu or on my cell phone at 203-331-6004.

Thank you for your time and consideration,

Jacqueline Mahony Bridge

Jacqueline Mahony Bridge, RN
Anna Goddard, PhD, APRN *(Faculty Advisor)*

5151 Park Avenue, Fairfield, Connecticut 06825-1000 | www.sacredheart.edu

Appendix J

Introductory Letter for Sacred Heart Department Directors

DR. SUSAN L. DAVIS, R.N.,
& RICHARD J. HENLEY
COLLEGE OF NURSING
Sacred Heart University

May 13, 2020

Dear Dr. DeNisco, DNP, APRN, FNP- BC, FAANP

My name is Jacqueline Bridge. I am a Doctorate of Nursing Practice (DNP), Family Nurse Practitioner (FNP) student at Sacred Heart University, College of Nursing. My DNP doctoral project includes an evidence-based learning module aimed at increasing knowledge of an inborn metabolic disorder known as **Hereditary Fructose Intolerance (HFI).**

Hereditary Fructose Intolerance (HFI), an autosomal recessive metabolic disorder, is not readily included in pediatric medicine or nursing educational programs. In clinical practice, HFI is often missed on diagnosis which delays treatment and, in some cases, can be fatal. One aim of this project includes increasing awareness in advanced practice provider students (PA and APRN graduate students) on HFI as an often-misdiagnosed metabolic disorder and highlight the clinical symptoms in which patients may present. This activity includes a pre-survey, a brief learning module estimated to take 20 minutes, and then a post-survey. I will reach out to all participants in three months after the initial learning module for follow-up questions. This learning module is available 100% online and can be done asynchronously. I will be launching this project in August-September of 2020.

I am writing to inquire whether you would be willing to share this project with your students either through 1) a broad email to your graduate APRN students or; 2) to include this topic as a learning module one week in a fall 2020 course to students. Can you please let me know at your earliest convenience if you would be willing to do either of those options?

If you have any questions or concerns, please feel free to reach me at Mahonyj@mail.sacredheart.edu or on my cell phone at 203-331-6004.

Thank you for your time and consideration,

Jacqueline Mahony Bridge

Jacqueline Mahony Bridge, RN
Sacred Heart University, Davis & Henley College of Nursing
Hybrid - FNP/DNP Program
Anna Goddard, PhD, APRN *(Faculty Advisor)*

5151 Park Avenue, Fairfield, Connecticut 06825-1000 | www.sacredheart.edu

Appendix K

Preassessment

HFI Pre-assessment

Your email address will only be used to contact you to complete a reassessment.

Thank you for your time and cooperation.

If you have any questions please contact Mahonyj@mail.sacredheart.edu

* Required

1. What is your email address? *

2. What is your current discipline? *

Mark only one oval.

- ◯ Medical Doctor
- ◯ Doctor of Osteopathic Medicine
- ◯ Practicing Physician Assistant
- ◯ Practicing Advance Practice Registered Nurse/ Nurse Practitioner
- ◯ Physician Assistant Student
- ◯ Advance Practice Registered Nurse/ Nurse Practitioner Student
- ◯ Other: _____

3. Number of years experience in advanced clinical practice (not including time in school). *

Mark only one oval.

- ◯ Current student
- ◯ Less than 1 year
- ◯ 1-5 years
- ◯ 6-10 years
- ◯ Greater than 10 years

4. Do you have prior healthcare experience in any of the following prior to practice as physician or in other advance practice role? Select all that apply. *

Check all that apply.

- ☐ No other healthcare experience
- ☐ Certified Nurse Assistant
- ☐ Medical Assistant
- ☐ Licensed Practical Nurse
- ☐ Emergency Responder (Emergency Medical Technician/ Paramedic)
- ☐ Registered Nurse

Other: ☐ _____

5. If you had prior healthcare based experience, how many years of experience do you have? *

Mark only one oval.

- ◯ Current student/ no other healthcare experience
- ◯ Less than 1 year
- ◯ 1-5 years
- ◯ 6-10 years
- ◯ More than 10 years

6. What was the your specialty/focus in your past healthcare experience (i.e. emergency medicine, pediatrics, long term care etc.)

7. *Sacred Heart Students Only* Please select your program

Mark only one oval.

- ◯ Physician Assistant Program- year 1, full time
- ◯ Physician Assistant Program- year 1, part time
- ◯ Physician Assistant Program- year 2, full time
- ◯ Physician Assistant Program- year 2, part time
- ◯ APRN Program- year 1, full time
- ◯ APRN Program- year 1, part time
- ◯ APRN Program- year 2, full time
- ◯ APRN Program- year 2, part time
- ◯ APRN Program- year 3, full time
- ◯ APRN Program- year 3, part time
- ◯ Unsure, PA program
- ◯ Unsure APRN program

6. What was the your specialty/focus in your past healthcare experience (i.e. emergency medicine, pediatrics, long term care etc.)

7. *Sacred Heart Students Only* Please select your program

Mark only one oval.

- ◯ Physician Assistant Program- year 1, full time
- ◯ Physician Assistant Program- year 1, part time
- ◯ Physician Assistant Program- year 2, full time
- ◯ Physician Assistant Program- year 2, part time
- ◯ APRN Program- year 1, full time
- ◯ APRN Program- year 1, part time
- ◯ APRN Program- year 2, full time
- ◯ APRN Program- year 2, part time
- ◯ APRN Program- year 3, full time
- ◯ APRN Program- year 3, part time
- ◯ Unsure, PA program
- ◯ Unsure APRN program

11. A patient presents stating that they feel sick after eating sweet foods. They describe symptoms including nausea, fatigue, shakiness, and have been found to be hypoglycemic during these episodes. What tests would you order for this patient initially? *

Check all that apply.

- ☐ Hydrogen Breath Test
- ☐ Liver Biopsy
- ☐ Endoscopy
- ☐ Genetic Testing for Metabolic Disorder
- ☐ Intravenous Fructose Challenge
- ☐ Hemoglobin A1C

Appendix L

Post Module Assessment

Hereditary Fructose Intolerance Post-Assessment

Thank you for completing this learning module. Please feel free to contact me with any questions.

MahonyJ@mail.sacredheart.edu

Please watch your email for a reminder to complete a follow up post assessment in mid December.

* Required

1. What is your email address? *

2. Are you familiar with Hereditary Fructose Intolerance? *

Mark only one oval.

- ◯ Yes, very familiar
- ◯ Yes, somewhat familiar
- ◯ I am not sure
- ◯ No, not at all

3. Are you familiar with Fructose Malabsorption? *

Mark only one oval.

- ◯ Yes, very familiar
- ◯ Yes, somewhat familiar
- ◯ I am not sure
- ◯ No, not at all

4. What symptoms could a patient with HFI present with (Select all that apply) *

Check all that apply.

- [ ] Nausea/Vomiting
- [ ] Postprandial hypoglycemia
- [ ] Distaste for sweet flavors
- [ ] Failure to thrive

5. A patient presents stating that they feel sick after eating sweet foods. They describe symptoms including nausea, fatigue, shakiness, and have been found to be hypoglycemic during these episodes. What tests would you order for this patient initially? *

Check all that apply.

- [ ] Hydrogen Breath Test
- [ ] Liver Biopsy
- [ ] Endoscopy
- [ ] Genetic Testing for Metabolic Disorder
- [ ] Intravenous Fructose Challenge
- [ ] Hemoglobin A1C

Appendix M

Follow Up Assessment

Hereditary Fructose Intolerance Post-Assessment

Thank you so much for coming back to complete my project.

This portion of the project is to be completed one month after the initial assessment.

If you have any questions, please contact MahonyJ@mail.sacredheart.edu

* Required

1. What is your email address? *

2. Are you familiar with Hereditary Fructose Intolerance? *

Mark only one oval.

- ◯ Yes, very familiar
- ◯ Yes, somewhat familiar
- ◯ I am not sure
- ◯ No, not at all

3. Are you familiar with Fructose Malabsorption? *

Mark only one oval.

- ◯ Yes, very familiar
- ◯ Yes, somewhat familiar
- ◯ I am not sure
- ◯ No, not at all

4. What symptoms could a patient with HFI present with (Select all that apply) *

Check all that apply.

- [ ] Nausea/Vomiting
- [ ] Postprandial hypoglycemia
- [ ] Distaste for sweet flavors
- [ ] Failure to thrive

5. A patient presents stating that they feel sick after eating sweet foods. They describe symptoms including nausea, fatigue, shakiness, and have been found to be hypoglycemic during these episodes. What tests would you order for this patient initially? *

Check all that apply.

- [ ] Hydrogen Breath Test
- [ ] Liver Biopsy
- [ ] Endoscopy
- [ ] Genetic Testing for Metabolic Disorder
- [ ] Intravenous Fructose Challenge
- [ ] Hemoglobin A1C

Appendix N

Differentiating Quality Improvement and Research Activities

Differentiating Quality Improvement and Research Activities Tool

Question		Yes	No
1.	Is the project designed to bring about immediate improvement in patient care?	X	
2.	Is the purpose of the project to bring new knowledge to daily practice?	X	
3.	Is the project designed to sustain the improvement?	X	
4.	Is the purpose to measure the effect of a process change on delivery of care?	X	
5.	Are findings specific to this hospital/setting?	n/a	
6.	Are all patients who participate in the project expected to benefit?	X	
7.	Is the intervention at least as safe as routine care?	X	
8.	Will all participants receive at least usual care?	X	
9.	Do you intend to gather just enough data to learn and complete the cycle?	X	
10.	Do you intend to limit the time for data collection in order to accelerate the rate of improvement?	X	
11.	Is the project intended to test a novel hypothesis or replicate one?		X
12.	Does the project involve withholding any usual care?		X
13.	Does the project involve testing interventions/practices that are not usual or standard of care?		X
14.	Will any of the 18 identifiers according to the HIPAA Privacy Rule be included?		X

Adapted from Foster, J. (2013). Differentiating quality improvement and research activities. Clinical Nurse Specialist, 27(1), 10–3. https://doi.org/10.1097/NUR.0b013e3182776db5

An answer of yes to all of the items in l-l0 and no to all of the items in 11-I4 indicates that this project meets criteria for a Quality Improvement Project, does not qualify as human subjects' research, and does not have to go through the Institutional Review Board at Sacred Heart University.

Appendix O

Timeline for Implementation

Project Title: Increasing Awareness of Hereditary Fructose Intolerance: An Evidence-Based Practice Implementation Project

Project Mentor: Dr. Anna Goddard

Doctor of Nursing Practice Project Roadmap

Component	Definition	Date Done
Phase 1: Problem Identification and Evidence Review		
Clinical Inquiry includes the background and significance of the problem	Describe the local situation and its importance. Have data to frame local issues.	1/20
Organizational priority	Summarizing information that supports the topic/problem is an organizational priority.	1/20
Searchable Question	Write a focused, searchable question using an established method (e.g., PICO).	1/20
Evidence search	External evidence	1/20
	• Summarize search strategy (e.g., databases, keywords, filters/limits, article selection criteria, critical appraisal tools). Include practice-based evidence (e.g., evidence-based solutions that experts/other health systems have implemented to address practice problems).	
	Internal evidence	n/a
	• Summarize applicable unit/community/department/hospital/organizational level data or data required for national entities (e.g., CMS, NDNQI, AHRQ).	
	Perform needs assessment if applicable.	n/a
Evidence appraisal, summary, and recommendations	Organize evidence that answers focused clinical questions clearly and concisely (e.g., table or matrix).	
	Appraise literature for quality and applicability of evidence using an established method (e.g., Johns Hopkins Nursing EBP Research Evidence Appraisal	1/20-8/20

	Tool, Joanna Briggs Institute Critical Appraisal Tools, Fuld Institute for EBP critical appraisal tools, etc.).	
	State recommendations(s) and link to evidence strength, quality, and risk/benefits.	
Phase 2: Project Planning		
Project goals	The state intended realistic outcomes of the project using an established method (e.g., SMART criteria).	4/2-6/20
Framework	Select framework/model to guide implementation (e.g., EBP model, QI framework, Change model).	4/20-6/20
Context	Describe the project setting and participants or population, or other elements central to where the change will occur.	6/20
Key stakeholders	Identify agencies, departments, units, individuals needed to complete the project and affected by the project, and strategies to gain buy-in.	6/20
Practice change/intervention	Provided detailed description of practice change or intervention (e.g., new or revised policy).	6/20
Evaluation	Summarize the plan for evaluating the effectiveness of the practice change. Identify applicable process and outcomes data to be collected/tracked and tools. Identify the methods for analyzing/interpreting the data (e.g., control, run, or Pareto charts).	6/20
Possible barriers to implementation	Identify possible barriers and implementation strategies to mitigate these barriers.	6/20
Sustainment	Identify strategies to sustain the change.	6/20
Timeline	Create a realistic timeline for project completion.	6/20
Resources	Identify all resources (e.g., indirect and direct) needed to complete the project.	6/20
Ethical merit	Identify and obtain the required review and approval for implementation (e.g., institution, community agency, IRB).	6/20
Phase 3: Implementation		
Implement project	Carry out the project using the selected implementation framework/model.	10/2-complete by 2/20/22
	Track any deviations/changes from the project plan.	10/21-complete by 2/20/22

Phase 4: Evaluation		
Results/Interpretation	Using an established method (e.g., run or control charts), display data and interpret project outcomes.	Currently collecting data- complete by 2/20/22
	Report evaluation of the effectiveness of the practice change, including the extent to which the practice change was implemented (process outcome) and the extent to which the desired product (s) were achieved.	Pending data collection completion - complete by 2/20/22
Return on investment	Identify the final resources that were used to implement the project. Calculate and report the return on investment.	Pending data collection completion - complete by 2/20/22
Phase 5: Dissemination		
Traditional	Disseminate the project set in a manner meaningful to them (i.e., executive report, poster, presentation at a meeting, sign with QR code to access details of the project, etc.) Disseminate in the format required by the academic institution (i.e., poster, public presentation, etc.), and Prepare final project write-up using established reporting guidelines (e.g., EPQA, SQUIRE) and educational institution requirements.	3/22-5/22
Non-traditional	Develop a website to display projects and use personal or program social media (e.g., Twitter, Facebook) to share project information.	1/21- current

PICO, Population, Intervention, Comparison, Outcome; **CMS**, Center for Medicaid and Medicare Services; **NDNQI**, National Dataset of Nursing Quality Indicators; **AHRQ**, Agency for Healthcare Research and Quality; **SMART**, specific, measurable, attainable, relevant, timely; **IRB**, Institutional Review Board; **EPQA**, Evidence-Based Practice Process Quality Assessment Guidelines; **SQUIRE,** Standards for Quality Improvement Reporting Excellence

Appendix P

Expenses Related to Website Maintenance