Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Protocol Number: H-55723
Status: Approved
Initial Submit Date: 6/17/2024
Approval Period: 10/9/2024 - 7/2/2029

Section Aa: Title & PI

A1. Main Title

FEASIBILITY OF THE "PASO A PASO" WEIGHT LOSS PROGRAM FOR MEXICAN & CENTRAL AMERICAN PATIENTS WITH METABOLIC-DYSFUNCTION ASSOCIATED STEATOTIC LIVER DISEASE (MASLD).

A2. Principal Investigator

Name:	MAYA BALAKRISHNAN	Phone:	7138733503
Id:	187420	Fax:	713 8733505
Department:	MEDICINE: GASTROENTEROLOGY	Email:	mbalakri@bcm.edu
Center:		Mail Stn:	BCM285

A3. Administrative Contact

None

A3a. Financial Conflict of Interest

Does any member of study personnel (Investigator (including investigator's spouse and/or dependent children)) that are involved in the design, conduct, or reporting of the research have a Significant Financial Interest (SFI) that would reasonably appear to be affected by the research for which funding is sought and/or associated with an entity/business that would reasonably appear to be affected by the research?

No

Section Ab: General Information

A4. Co-Investigators

Name:	ANEES FATIMA	Phone:	
Id:	234914	Fax:	
Department:	FAMILY & COMMUNITY MEDICINE	Email:	u234914@bcm.edu
Center:		Mail Stn:	
Name:	XIMENA VARGAS	Phone:	
Id:	240553	Fax:	
Department:	MEDICINE: GASTROENTEROLOGY	Email:	u240553@bcm.edu
Center:		Mail Stn:	
Name:	SHERLYN FUENTES	Phone:	
Id:	254847	Fax:	
Department:	MEDICINE: GASTROENTEROLOGY	Email:	u254847@bcm.edu
Center:		Mail Stn:	
Name:	IVONNE ARGUELLES	Phone:	
Id:	256749	Fax:	
Department:	MEDICINE: GASTROENTEROLOGY	Email:	u256749@bcm.edu
Center:		Mail Stn:	

Name:	PAOLA MARTINEZ	Phone:	
Id:	256767	Fax:	
Department:	MEDICINE: GASTROENTEROLOGY	Email:	u256767@bcm.edu
Center:		Mail Stn:	

Name:	JENNIFER GUTIERREZ	Phone:	
Id:	258533	Fax:	
Department:	MEDICINE: GASTROENTEROLOGY	Email:	u258533@bcm.edu
Center:		Mail Stn:	

A5. Funding Source:

Organization: NATIONAL INSTITUTE ON MINORITY HEALTH AND HEALTH DISPARITIES

A5a. Associated ESP2 funding proposal linked to this protocol:

A6a. Institution(s) where work will be performed:

BCM: Baylor College of Medicine
Community Center or Church
HCHD: Harris County Hospital District
HCHD: Harris County Hospital District Ben Taub
HCHD: Harris County Hospital District Community Health Clinics
Harris Health System- Smith Clinic
Harris Health System: Casa de Amigos

A6b. Research conducted outside of the United States:

Country:
Facility/Institution:
Contact/Investigator:
Phone Number:

If documentation of assurances has not been sent to the Office of Research, please explain:

A7. Research Category:

A8. Therapeutic Intent

Does this trial have therapeutic intent?
No

A9. ClinicalTrials.gov Registration

Does this protocol/trial require registration on ClinicalTrials.gov due to it: meeting the definition of an Applicable Clinical Trial, being required under the terms and conditions of an award, or being proposed to be published in ICMJE journals?
Yes

Who will be responsible for registering and maintaining the registration of this Applicable Clinical Trial?
The BCM PI will register the trial because either:

- the trial is BCM PI-initiated,
- BCM is the lead site of this multicenter trial, or,
- the industry sponsor has instructed the BCM PI to register the trial, or,
- registration of this trail is required as a term and condition of the reward by the funding agency.

ClinicalTrials.gov Identifier:
NCT

Section B: Exempt Request

B. Exempt From IRB Review

Not Applicable

Section C: Background Information

Metabolic dysfunction associated steatotic liver disease (MASLD) is the leading cause of chronic liver disease in the U.S. MASLD is characterized by an accumulation of liver fat consequent to excessive body fat and the metabolic syndrome. People of Mexican and Central American heritage (M/CA), bear the highest burden of disease compared to NHW, Blacks, and other Hispanic subgroups1-4.

MASLD can progress from quiescent liver fat to necroinflammatory fat (steatohepatitis) with progressive fibrosis to cirrhosis. Patients with severe fibrosis (stage F2-4 on liver biopsy) have the highest risk of liver related complications and mortality. Age, sex, specific genetic variants, type 2 diabetes, adiposity, and specific health behaviors (unhealthy diets, physical inactivity) are risk factors for severe fibrosis in MASLD. Of these, health behaviors are the only modifiable factors associated with MASLD improvement.

Behavioral change is the cornerstone of MASLD treatment. The American Association for the Study of Liver Disease, American College of Gastroenterology, and American Gastroenterology Association recommend weight loss via behavioral change as the first line treatment for MASLD. Weight loss of 5-10% through sustained lifestyle modifications improves hepatic fat, steatohepatitis, and fibrosis8,9. Dietary change (reductions in total calories and simple sugar intake) and increased aerobic physical activity are also associated with improvements in liver fat and insulin resistance, independent of weight loss10,11.

The data show that patients with MASLD do not lose weight under standard Hepatology care. In a systematic review of 24 papers worldwide, we found that patients with MASLD and engaged in routine hepatology care, gain an average of 1% weight (rather than lose weight) over 1 year12. Locally, in a single center study of 322 patients with MASLD (90% M/CA) followed over 16 months, we found that 84% did not lose weight despite receiving the current standard of care (“usual care”), which is to promote weight loss behaviors through brief clinician and dietitian led discussions13. These data highlight the need for interventions that lead to sustainable weight loss in MASLD.

In qualitative research, I have found that M/CA patients struggle with several barriers to making weight loss behavioral changes14. Many of the behavioral change barriers are longstanding, predating their MASLD diagnosis. Patients express feeling alone, unsupported, and confused in their weight loss journey. They articulate a need for more structured behavioral support from medical providers (BRAIN IRB protocol #H-49779, unpublished data).

For all these reasons, there is a clear need for structured behavioral weight loss interventions for M/CA patients with MASLD. To address this need, my team has adapted an existing evidence-based weight loss intervention called the “Look AHEAD Lifestyle Program” for the clinical, social, and cultural needs of M/CA patients with MASLD. We have done this via principles of intervention mapping and use of focus group discussions with expert stakeholders (ie dietitians, physical therapists, physicians) and patients (BRAIN IRB protocol # H-51086). The adapted intervention's title is "Paso a Paso: Rumbo a Un Higado Sano" (Step by Step: Journey to a Healthy Liver." The intervention consists of a series of 16 one-hour long weekly to biweekly group counseling sessions delivered over 6 months. This protocol outlines a single arm study to test the feasibility of the intervention among 50 M/CA patients with MASLD.

References 1. Rich NE, Oji S, Mufti AR, Browning JD, Parikh ND, Odewole M, et al. Racial and Ethnic Disparities in Nonalcoholic Fatty Liver Disease Prevalence, Severity, and Outcomes in the United States: A Systematic Review and Meta-analysis. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2018;16(2):198-210.e2. 2. Kallwitz ER, Daviglus ML, Allison MA, Emory KT, Zhao L, Kuniholm MH, et al. Prevalence of suspected nonalcoholic fatty liver disease in Hispanic/Latino individuals differs by heritage. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2015;13(3):569-76. 3. Zhang X, Heredia NI, Balakrishnan M, Thrift AP. Prevalence and factors associated with NAFLD detected by vibration controlled transient elastography among US adults: Results from NHANES 2017-2018. PloS one. 2021;16(6):e0252164. 4. Shaheen M, Pan D, Schrode KM, Kermah D, Puri V, Zarrinpar A, et al. Reassessment of the Hispanic Disparity: Hepatic Steatosis Is More Prevalent in Mexican Americans Than Other Hispanics. Hepatology communications. 2021. 5. Friedman SL, Neuschwander-Tetri BA, Rinella M, Sanyal AJ. Mechanisms of NAFLD development and therapeutic strategies. Nature medicine. 2018;24(7):908-22. 6. Hagstrom H, Nasr P, Ekstedt M, Hammar U, Stal P, Hultcrantz R, et al. Fibrosis stage but not NASH predicts mortality and time to development of severe liver disease in biopsy-proven NAFLD. Journal of hepatology. 2017. 7. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. Hepatology (Baltimore, Md). 2017. 8. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2020:154455. 9. Vilar-Gomez E, Martinez-Perez Y, Calzadilla-Bertot L, Torres-Gonzalez A, Gra-Oramas B, Gonzalez-Fabian L, et al. Weight Loss Through Lifestyle Modification Significantly Reduces Features of Nonalcoholic Steatohepatitis. Gastroenterology. 2015;149(2):367-78.e5; quiz e14-5. 10. Marchesini G, Petta S, Dalle Grave R. Diet, weight loss, and liver health in nonalcoholic fatty liver disease: Pathophysiology, evidence,

and practice. Hepatology (Baltimore, Md). 2016;63(6):2032-43. 11. Keating SE, George J, Johnson NA. The benefits of exercise for patients with non-alcoholic fatty liver disease. Expert Rev Gastroenterol Hepatol. 2015;9(10):1247-50. 12. Balakrishnan M, Liu K, Schmitt S, Heredia NI, Sisson A, Montealegre JR, et al. Behavioral weight-loss interventions for patients with NAFLD: A systematic scoping review. Hepatol Commun. 2023;7(8) 13. Heredia NI, Gaba R, Liu Y, Jain S, Rungta M, Rungta M, et al. Perceptions of weight status and energy balance behaviors among patients with non-alcoholic fatty liver disease. Sci Rep. 2022;12(1):5695. 14. Heredia NI, Thrift AP, Balakrishnan M. Perceived Barriers to Weight Loss among Hispanic Patients with Non-alcoholic Fatty Liver Disease. Hisp Health Care Int. 2022;20(3):171-8.

Section D: Purpose and Objectives

The purpose of this study is to assess the feasibility and preliminary effects of an adapted behavioral weight loss intervention on weight, clinical, and behavioral outcomes over 6 months among M/CA patients with MASLD.

The primary objective is to evaluate the intervention’s feasibility, defined as session attendance.

The key secondary objective is to compare average percent change in weight at the end of 6months among M/CA enrolled in the intervention (as part of this study) with a parallel observation cohort of M/CA patients who received routine Hepatology care (derived from BRAIN IRB protocol # H-36814).

The additional secondary objectives among intervention recipients are to assess changes in the following over 6 months: - Total body weight, muscle mass, Fat mass (measured by bioelectrical impedance analysis) - Waist and hip circumference - Muscle strength (hand grip dynomometry) - Hepatic steatosis, steatohepatitis, and liver stiffness, ALT and AST - Metabolic syndrome features (triglycerides, HDL, hemoglobin a1c, HOMA-IR) - Dietary pattern - Average daily calorie intake - Average time spent doing moderate to vigorous physical activity every week - Quality of life - Behavioral determinants (perceived disease severity, treatment expectations, etc)

This proposal also has exploratory objectives, which are to assess changes in the following over 6 months among family members of intervention recipients: - Awareness and perceived severity of MASLD in the patient - Perceived treatment expectations of weight loss in the patient - Social support of weight loss changes in the patient

Embedded in to this study is a qualitative assessment of intervention feasibility and acceptability that will be conducted among a smaller subset of patients who decline study participation, drop out of the study, complete the study but attend 8 or fewer intervention sessions, and complete the study with attendance of more than 8 intervention sessions.

Section E: Protocol Risks/Subjects

E1. Risk Category

Category 1: Research not involving greater than minimum risk.

E2. Subjects

Gender:
Both

Age:
Adult (18-64 yrs), Geriatric (65+ yrs)

Ethnicity:
Hispanic Or Latino

Primary Language:
English, Spanish

Groups to be recruited will include:
Healthy, non-patient, normals; Patients

Which if any of the following vulnerable populations will be recruited as subjects?

Vulnerable populations require special protections. How will you obtain informed consent, protect subject confidentiality, and prevent undue coercion?

E3. Pregnant woman/fetus

Will pregnant women and/or fetuses (as described in 45 CFR 46 Subpart B) be enrolled in the research?

No

E4. Neonates

Will neonates of uncertain viability or nonviable neonates (as described in 45 CFR 46 Subpart B) be enrolled in the research?

No

E5. Children

Will children be enrolled in the research?

No

Section F: Design/Procedure

F1. Design

Select one category that most adequately describes your research:

c) Pilot

Discuss the research design including but not limited to such issues as: probability of group assignment, potential for subject to be randomized to placebo group, use of control subjects, etc.

This study uses as a single arm (quasi-experimental) study design. All participants will receive the behavioral weight loss intervention. The study's primary study population are Mexican and Central American patients with MASLD. This study includes an optional sub-study among patients' family/household members.

Inclusion Criteria:

MAIN STUDY PARTICIPANTS: The target population are adult patients (between 18 and 65 years of age) who self-report Mexican or Central-American ethnicity, have a documented diagnosis of MASLD, and body mass index ≥25kg/m2. Inclusion criteria: - Willing to participate in the study, the 6-month long intervention, and provide written informed consent. - Male and female adults 18 to 65 years of age. - Diagnosis of MASLD, based on standard clinical criteria. - Self identify as Mexican or Central American - Speak English or Spanish - Body mass index ≥25kg/m2

FAMILY/HOUSEHOLD SUB-STUDY PARTICIPANTS: To address exploratory objectives of this study, we plan to recruit one family member/household member or friend that patients identify as potentially influential on their eating and exercise habits: - Identified household/family member or friend of patient - Age>18 years - Able to speak English or Spanish - Willing to participate in study assessments and provide written informed consent.

EMBEDDED QUALITATIVE SUB-STUDY 1) Substudy among Main study decliners: This substudy includes patients who qualify for the main study (ie fulfill main study's inclusion criteria and do not have exclusion criteria) but decline the study. No exclusions. 2) Substudy among study dropouts: This includes main study participants (ie they qualified for, consented, and enrolled into the main study) but dropped out. No exclusions. 3) Substudy among study completers who but attend fewer than 8 intervention sessions: This includes main study participants (ie they qualified for, consented, and enrolled into the main study) and completed the study, but attended less than 8 intervention sessions. No exclusions. 4) Substudy among study completers who attended8 or more intervention sessions: This will include main study participants who attended 8 or more intervention sessions. No exclusions.

Exclusion Criteria:

MAIN STUDY PARTICIPANTS: Patients who meet any of the following exclusion criteria will not be eligible to participate in the study. 1. Competing etiologies of liver disease: a. Active HCV infection or untreated HBV b. Autoimmune hepatitis c. Primary biliary cholangitis d. Wilson disease e. Primary sclerosing cholangitis f. Acute hepatic injury 2. Ongoing heavy alcohol use defined as >320 grams/week. 3. Advanced liver disease: platelet count < 150,000, presence of esophageal varices, any history of decompensations history of liver transplant 4. History of hepatocellular carcinoma 5. Current pregnancy/nursing or immediate plans for pregnancy. Current pregnancy/nursing and immediate plans for pregnancy will be assessed based on self-report by patient. 6. Conditions that limit the ability to reduce dietary intake or increase physical activity 7. Poorly controlled diabetes, with hemoglobin A1C>8.5% 8. Active cancer 9. Unstable cardiac disease 10. Intestinal resection or malabsorption disorders 11. Life expectancy<2 years 12. Competing serious medical or psychiatric comorbidity 13. History of any organ transplant 14. HIV infection 15. ≥5% weight loss over the prior 3 months 16. Glucagon-like peptide 1 (GLP-1) agonist therapy for diabetes treatment (eg, exenatide, liraglutide, lixisenatide, albiglutide, dulaglutide, semaglutide, and albiglutide) must be a stable dose for at least 12 weeks prior to study initiation. GLP-1 agonists for weight loss (eg, semaglutide at doses up to 2.4 mg subcutaneous weekly) must be at stable doses for at least 6 months (including body weight change ≥5% weight loss in the 12 weeks prior to study initiation). 17. History of bariatric surgery 18. History of noncompliance with medical visits

FAMILY/HOUSEHOLD/FRIEND SUB-STUDY PARTICIPANTS: None

F2. Procedure

All patients with MASLD will have the opportunity to hear about this study during routine GI/Hepatology, Endocrinology, Primary care clinic visits.

RECRUITMENT & STUDY ENROLLMENT PROCEDURES - see section J2

INTERVENTION - All participants will receive the intervention (see Appendix A for summary). The intervention is an adapted version of the Look AHEAD Lifestyle Program, an NIH developed weight loss intervention, which we adapted using principles of intervention mapping and focus group discussions among clinicians and patients (BRAIN IRB protocol # H-51086). The adapted intervention is called "Paso-a-Paso: Rumbo a Un Higado Sano." It consists of a series of 16 one-hour-long semi-structured group counseling sessions led by a health educator every 1-2 weeks over 26 weeks. Each session has a curriculum with a counselor's guide and patient facing materials, covers specific topics (eating, physical activity, behavioral change strategies). Teaching methods include discussions, practice activities, demonstrations.

INTERVENTION SITES & DELIVERY: We will deliver the intervention in a hybrid format (in-person and via Zoom, because of patient preferences expressed during prior focus groups), in English and Spanish separately. Potential participants are spread across Harris County. To accommodate this, we will deliver the program at 5 sites, near where patients most commonly reside. We will cohort participants into groups based on their site preference, which they will remain assigned to for the entire program. Session timing will be determined by each group's majority preference. The 5 sites include 2 Harris Health Clinics and 3 Community Centers without BCM affiliation where we will only be using space to teach the program and take participant weight using a portable scale. we will not use site resources or personnel or conduct other study procedures (see letters of support)

MAIN STUDY PARTICIPANT STUDY VISITS AND PROCEDURES - (Appendix B outlines main study timeline and procedures): 1) questionnaires: these will be self-administered or research staff assisted, in-person, online, or by telephone, based on participant preference. 2) Body weight obtained via calibrated scale . 3) Muscle strength: this is measured using hand-grip dynamometer. 4) Transient Elastography of the liver (fibroscan) - this is a liver ultrasound that measures continued attenuation parameter of the liver and liver stiffness. 5) Clinical data abstracted from electronic medical record review: current medications, past medical history, routine clinical lab parameters relevant to MASLD (liver enzymes, CBC, hemoglobin a1c, fasting glucose, fasting insulin, lipids, blood pressure). 6) Diet and pedometer data abstracted from 7-day food log and pedometer recordings participants maintain as part of their intervention participation. 7) Physical activity assessment by accelometer 8) Optional research blood samples to assess inflammatory and fibrosis biomarkers 9) Optional qualitative sub-study, involving semi-structured interviews among a sub-sample of participants (see "Qualitative Sub-Study").

TIMELINE OF PROCEDURES There 4 study time points:

1. BASELINE STUDY ASSESSMENT - These assessments will be completed at start of intervention (they will be completed over a time frame of 3 months prior to intervention to 1 week after session 1. They will not be done during a single research visit). Anticipate 90 minutes to complete: 1)questionnaire (see attached REDCAP and DHQ III surveys), 2) body weight, 3) muscle strength, 4) transient elastography of the liver, 5) abstracted clinical data, 6) abstracted diet and pedometer data from session 2, 7) actigraph assessment. Additional time for 8) optional research blood sample (2 min)

2. MID-INTERVENTION ASSESSMENT - These assessment will be completed after 3 months of the intervention (around session 12). Anticipate 10 minutes to complete: 1)questionnaire (see attached REDCAP survey), 2) body weight, 3) muscle strength, 4) abstracted diet and pedometer data from session.

3. END-OF-INTERVENTION ASSESSMENT - These assessments will be completed after intervention completion. The assessments do not have to be done during a single research visit. Anticipate 60 minutes to complete: 1)questionnaire (see attached REDCAP and DHQ III surveys), 2) body weight, 3) muscle strength, 4) transient elastography of the liver, 5) abstracted clinical data, 6) abstracted diet and pedometer data from session 7) actigraph. 8) Additional time for optional blood sample (2 min)

4. POST-INTERVENTION ASSESSMENT - These assessments will be completed 6 months after intervention completion. The assessments do not have to be done during a single research visit. Anticipate 30 minutes to complete: 1)questionnaire (see attached REDCAP survey), 2) body weight, 3) muscle strength, 4) transient elastography of the liver, 5) abstracted clinical data.

EARLY STUDY TERMINATION VISIT - Among participants who elect to terminate the study early, we will request to complete the end-of-intervention study procedures.

MAIN STUDY - SPECIFIC STUDY ASSESSMENTS FOR PATIENTS The following are the specific study procedures. See Appendix B for schedule of assessments

SURVEYS can occur in person, online, or by phone. All questionnaires will be administered using BCM REDCAP (see REDCAP survey) with the exception of the Diet History Questionnaire (DHQ III, see section below). - demographic questionnaire - Stages of Change Questionnaire in Weight Management - 3-Item health literacy screen - Hunger Vital Sign - AUDIT-C - Tobacco use questionnaire - PHQ-9 - Perceived stress - Binge eating with BEDS-7 - IPAQ - Schwarzer & Renner Nutrition and Physical activity self-efficacy scales - Modified brief illness perception and perceived treatment efficacy questionnaires - PROMIS Global Health short form - DHQ III (Diet History Questionnaire III): trained RCs will assist participants in-person to complete the DHQ III, which is exclusively hosted by the National Cancer Institute's online

survey platform (https://epi.grants.cancer.gov/dhq3/ffq-administration.html; see DHQ 3 survey for questions). RCs will first create an anonymous DHQ III user ID for each participant and download system-generated login credentials that will be used to access DHQ III. Then, using the DHQ 3 portion size booklet, the RCs will administer the questionnaire and enter online responses.

These procedures will be conducted as study procedures - Muscle strength via hand grip dynometer (baseline, end-of intervention, 6 month follow up) - Body weight obtained via calibrated scale.(baseline, end-of-intervention, 6 month follow up) - Waist and hip measurement (baseline, end-of-intervention) -Actigraph assessment (baseline, end-of-intervention) by ActiGraph wGT3X+ device: An accelerometer measures movement/acceleration and captures PA by converting movement into electrical signals named counts which can be transformed to metabolic equivalent of task values. Participants will wear the actigraph at the waist using an elastic band for 7 days while awake and maintain a log documenting periods >5 minutes when they remove the accelerometer for any reason. Afterward, they will return the actigraph by mail (using prepaid envelope) or in-person (see “Actigraph Participant Instructions”) - Fibroscan - (baseline, End of Intervention, 6-month follow-up) - Research blood sample collection (baseline, end-of-intervention)

These data will be abstracted from weekly session records maintained by participants - 7 day food and exercise log - 7 day pedometer data

These data will be abstracted from medical records - Routine clinical lab testing (liver enzymes, blood sugar, lipids) (baseline, End of Intervention, 6-month follow up) - History of alcohol and drug use. For each, we will record duration, ongoing use, quantity, substance misuse/dependence, treatment history.

In the case of participants who have diabetes: We will notify their diabetes providers (standard of care teams) of their participation in the weight loss program, in case diabetes medication changes are required. Also, as part of the weight loss program, participants are advised to monitor their blood sugars and report episodes of low blood sugar measurements or episodes of symptomatic hypoglycemia to the study team. When reported, the study team will communicate the hypoglycemia to participants' diabetes providers (standard of care teams), so that the diabetes providers can advise appropriate changes to diabetes medications as needed.

EMBEDDED QUALITATIVE SUB-STUDY PROCEDURES This sub-study involves a single procedure, a semi-structured interview among 5-10 people who fall into the following categories: 1) study decliners: a single interview is planned at the time that they decline the main study. (patients who decline study participation; sample size=5 to 10; see appendix D for interview guide; 5-10 minutes to complete) 2) study drop-outs: a single interview planned at time of early study termination (main study participants who drop-out of the study; sample size=5 to 10; see appendix D for interview guide, 10 minutes to complete) 3) Main study completers who attend fewer than 8 intervention sessions: a single interview planned at end-of-intervention (sample size=5 to 10; see appendix D for interview guide (15-20 minutes) 4) Main study completers who attend 8 or more intervention sessions: a single interview at end-of-intervention. (sample size=5 to 10; see appendix D for interview guide (15-20 minutes) We will obtain written consent to complete these interviews at the time of main study consent. (see section J2). Interviews are anticipated to take 10-20 minutes.

FAMILY/HOUSEHOLD MEMBER SUB-STUDY PROCEDURES Sample study = 50. We will give family/household substudy participants an electronic copy of Paso program materials and meal plan. No other intervention or contact is planned. Study procedures will include a survey at 2 time points (Baseline, end-of-intervention). Participants can optionally complete a phone interview, which we will conduct among a 5-10 family/household participants. 1. Baseline study assessment-will be obtained within 12 week prior to intervention Day 1. All family member participants will be asked to complete the questionnaire, which will require 10 minutes to complete. An optional the qualitative interview will be conducted among a group of 5-10 family participants, and will require an additional 10 minutes. 2. End-of-intervention study assessment-will be obtained between 1 week prior to and 1 month following the last intervention session. All family member participants will be asked to complete the questionnaire, which will require 10 minutes to complete. An optional qualitative interview will be conducted among a group of 5-10 family participants, and will require an additional 20 minutes.

QUALITATIVE INTERVIEWS We plan to conduct all interviews (as part of Embedded qualitative sub-study and family sub-study) either by telephone or in-person, according to the participants' preference. The interviews will be audio-recorded (if participant declines this, then notes taken), and transcribed and translated (either by 3rd party or internally be research staff based on participant preference). The interview data will be coded (with a non-identifiable study ID) and stored on the BCM server.

INTERVENTION FIDELITY Intervention fidelity will be assessed through completion of a checklist during each study intervention session. A research coordinator, who will observe the sessions, will complete the checklist. The session counselor and PI will both be blinded to the checklist finding until after the session is completed.

Section G: Sample Size/Data Analysis

G1. Sample Size

How many subjects (or specimens, or charts) will be used in this study?

Local: 110 Worldwide: 110

Please indicate why you chose the sample size proposed:

MAIN STUDY - We propose enrolling a total of 50 patient participants into the main study (all of whom will receive the intervention). The primary objective of this study is to assess the intervention's feasibility, defined as an average of >8 group counseling sessions attended among the participants over the course of the intervention. A one-sample one-sided t-test at a 5% significance level will provide >80% power to detect that the average number of classes attended will be greater than 8 with 50 participants. This assumes that the SD of classes attended will be 2.8 or less. The rationale for the feasibility outcome is as follows: Studies of Diabetes Prevention Program (DPP) and Look AHEAD Intervention show that higher session attendance is associated with greater degrees of weight loss 1. We define the primary outcome as average number of classes attended >8 because CDC DPP recognition criteria2 includes attendance of ≥9 sessions in months 1-6 as part of its definition of a program "completer." An evaluation of the DPP over 2015-2018 found that compared with participants who attended <9 sessions, those who attended ≥9 sessions in the first 6 months were 1.8 to 2.2 times more likely to achieve ≥ 5% weight loss from baseline3. 1. Wadden T, one-year weight losses in Look AHEAD Study, Obesity 2009. 2. https://www.cdc.gov/diabetes/prevention/requirements-recognition.htm; 3. Clennin MN. Weight Loss Disparities Among Hispanic and Underserved Participants, Colorado, 2015–2018. Prev Chronic Dis 2020.

QUALITATIVE SUB-STUDY For the qualitative sub-study we propose enrolling a sample of approximately 5-10 people from among 4 groups, outlined below. The rationale for the stated sample size is based on thematic saturation, which is the standard method for determining sample size in qualitative research. Thematic analysis is the point at which new themes no longer emerge with progressive interviews. Thematic analysis typically occurs with a sample size of 5-10. Pls note that groups #2-#4 will be main study participants. Only group #1 represents a group of patients who are not already enrolled in the main study and, thus, add another 10 potential participants to the overall sample size. 1) patients who decline study participation, (estimated sample size=5 to 10) 2) study participants drop out of the study early (estimated sample size=5 to 10, recruited from participants in the main study) 3) study participants who complete the study but attend fewer than 8 intervention sessions (estimated sample size=5 to 10, recruited from participants in the main study) 4) complete the study with attendance of 8 or more intervention sessions" to specify the subsample size for each of these categories (estimated sample size=5 to 10, recruited from participants in the main study)

FAMILY SUBSTUDY - for the family substudy, we propose to enroll 50 family members of study participants.

G2. Data Analysis

Provide a description of your plan for data analysis. State the types of comparisons you plan (e.g. comparison of means, comparison of proportions, regressions, analysis of variance). Which is the PRIMARY comparison/analysis? How will the analyses proposed relate to the primary purposes of your study?

MAIN STUDY- We will summarize baseline demographic and clinical characteristics using means with standard deviations, medians with minimum and maximum values, or frequencies with percentages. Comparisons between intervention recipients and those in the observational control group will be done using the independent t-test, Wilcoxon rank-sum, Fisher's exact or Chi-square test. To address this study's primary objective (feasibility), a one-sample t-test will be used to test whether intervention recipients attended more than an average of 8 classes. Logistic regression will be used to determine whether there are any differences in retention in the intervention group based on sociodemographic factors (ex acculturation, nativity, baseline health literacy), and odds ratios (OR) with 95% CI for retention will be reported.

To address this study's key secondary objective, we plan to compare average weight loss among this study's participants (all of whom receive the weight loss program) with 50 participants of a parallel observational cohort study (derived from H36814) who do not receive this weight loss program (and receive routine Hepatology care). After approval of this intervention feasibility study protocol, we plan to submit an amendment to the H36814 protocol to request data to be used to make this weight loss comparison. If approved, then comparisons between intervention recipients and those in the observational cohort group (derived from H36814) will be done using the independent t-test, Wilcoxon rank-sum, Fisher's exact or Chi-square test. The percent change in weight from baseline to 6 months will be calculated for patients in both the intervention and the observational group. Since the observational control group patients may not have their weight recorded at 6 months, their available weights will be used to calculate the rate of weight change up to 1 year, and this will be used to estimate percent weight change over 6 months. Linear regression will be used to see if the percent change in weight differs between group while adjusting for BMI, age, and any other factors found to be significantly different between the groups or associated with the change in weight.

To address this study's additional exploratory objectives, a general linear mixed model (GLMM) will be used to test the null hypothesis that there is no change in each of the following among intervention patients: liver fat, sugar intake, physical activity, self-efficacy, outcome expectations, motivation, and self-regulation. A separate model will be used for each outcome, and each GLMM will include a fixed effect for time. Residual analysis will assess model fit, and data transformation will be used to address any departures from model assumptions. $P<0.05$ will be considered significant.

QUALITATIVE SUB-STUDY Interviews conducted as part of the qualitative sub-study will provide additional insight into feasibility of the intervention. We will analyze the transcripts for content using Atlas.ti 8 software. We will use framework analysis to address 2 main domains across all 4 planned study groups: feasibility/acceptability of intervention participation and feasibility/acceptability of study participation. Among participants who complete the study, we will additionally conduct framework analysis to address domain of social support for weight loss.

Two members of the research team will independently review each transcript line by line to identify and sort segments of

data with similar concepts into distinct categories. We will code data as they amass. After each round of independent coding, the 2 reviewers will convene for review, negotiation, and consensus to resolve discrepancies in coding. We will revise the interview guide to investigate emerging themes. With successive transcripts, we will expand, refine, and apply the coding system to previously coded data. The process of coding and participant recruitment will stop once we have reached thematic saturation in all 3 domains. Dominant themes and sub-themes from the final coding scheme will be presented as study findings. We will choose illustrative quotations to justify the definition and basis of themes. Disagreements about coding decisions will be resolved through group consensus, using a third independent reviewer as a tiebreaker.

FAMILY SUB-STUDY We will conduct an exploratory analysis to assess for changes in family members' knowledge of disease and outcome expectations. A general linear mixed model (GLMM) will be used to test the null hypothesis that there is no change in each of the specified domains. In addition, we will carry out thematic analysis to explore the effect of the intervention on family members' knowledge of disease, outcome expectations, and social support for behavior change.

Section H: Potential Risks/Discomforts

H1. Potential Risks/Discomforts

Describe and assess any potential risks/discomforts; (physical, psychological, social, legal, or other) and assess the likelihood and seriousness of such risks:

It is completely up to the participants to agree to this study. Refusal of participation will not impact their healthcare in the office.

The risks expected as part of participation in this trial are minimal and outlined here. INTERVENTION-The intervention is a weight loss program that consists of group sessions during which participants are given counseling for dietary modification and increased physical activity. These are the potential risks: 1) Participants who have type 2 diabetes are at risk for hypoglycemia during the intervention due to reductions in caloric intake and if they lose weight. To mitigate this risk, the health educator (overseen by the PI) will discuss risk, signs, and management of hypoglycemia with each diabetic participant. With the PI, the health educator will review diabetic participants' blood sugars prior to intervention start and weekly through the intervention. The PI will advise patients of necessary diabetes medications changes accordingly. She will do this in conjunction with participants' primary diabetes providers. 2) With initiation of or increases in physical activity, there is the risk of injury. To mitigate this risk, the program teaches participants safety measures to follow and warning signs to monitor as they increase their physical activity levels. 3) With dietary modifications, there's the risk of discomfort (feeling hungry, increased abdominal bloating). As part of the program, participants are counseled to anticipate this discomfort and how to manage it.

STUDY PROCEDURES-The study procedures involve questionnaires, muscle strength and body weight measurement, and transient elastography of the liver. It also involves the optional procedures of one-on-one interview and a research blood sample. These are the potential risks: 1) Questoinnaire and interview are associated with potential loss of time, inconvenience, emotional distress. 2) Transient elastography is a form of ultrasound obtained using a probe placed on the abdomen. Aside from mild pressure that is applied on the abdomen to obtain measurements of the liver, it is not associated with any specific risks 3) Optional study blood sample: This involves venipuncture and the main risks are related discomfort and transient bruising.

Confidentiality: Despite the precautions we are taking to ensure participant privacy (outlined in Sections J and K), there is small risk of loss of confidentiality. We are mitigating loss of privacy through the measures outlined in section K.

H2. Data and safety monitoring plan

Do the study activities impart greater than minimal risk to subjects?

No

H3. Coordination of information among sites for multi-site research

Is the BCM Principal Investigator acting as the SPONSOR-INVESTIGATOR for this multi-site research?

No or Not Applicable

Is BCM the COORDINATING CENTER for this multi-site research?

No or Not Applicable

Section I: Potential Benefits

Describe potential benefit(s) to be gained by the individual subject as a result of participating in the planned work.

Patients who participate in this study may directly benefit by losing weight, which is associated with improvement in MASLD. They may also gain greater knowledge about their liver disease and healthy eating and physical activity habits

Family members who participate in this study may directly benefit by learning more about participants' liver disease and weight loss.

Describe potential benefit(s) to society of the planned work.

This project will help to improve MASLD among Mexican and Central American patients by investigating the feasibility of a useful weight loss intervention and generating evidence to guide interventions among this population.

Do anticipated benefits outweigh potential risks? Discuss the risk-to-benefit ratio.

The potential benefits for individual participants, family members, and society are much greater than any risk. For individual participants, the potential benefit is weight loss. Weight loss can reverse MASLD related liver injury and slow down progression to cirrhosis. Changes in diet and physical activity (which are promoted by this trial's weight loss program) and weight loss can also improve the metabolic comorbidities (diabetes, hypertension, dyslipidemia) that accompany MASLD. Thus, the benefits of participating in this study outweigh the risks of potential hypoglycemia (risk of which will be mitigated through measures described and monitored closely), mild discomfort associated with study procedures. For society, the potential benefit is greater information about how to intervene for weight loss among the target population, which is high risk for progressing to MASLD cirrhosis.

Section J: Consent Procedures

J1. Waiver of Consent

Will any portion of this research require a waiver of consent and authorization?

No

J1a. Waiver of requirement for written documentation of Consent

Will this research require a waiver of the requirement for written documentation of informed consent?

Yes

Explain how the research involves no more than minimal risk to the participants, and the specifics demonstrating that the research does not involve procedures for which written consent is normally required outside of the research context.

We are requesting a waiver for written documentation of consent for two aspects of this study 1) the Family/Household Member Sub-study and Participants and 2) embedded qualitative substudy among main study decliners

Family/Household Member Substudy - We will obtain verbal consent from family/household members who participate in this study. There is no medical or physical risk to any participant in this substudy. All study procedures can be conducted over the phone and involves no more than minimal risk. We are opting for verbal consent to mitigate the inconvenience associated with coming into the clinic only to provide written study consent. Taking time off simply to provide written consent may adversely impact participants' employment, pay, and/or other responsibilities. We will obtain verbal consent using the verbal consent form attached. After obtaining consent we will send a copy of the form to the participant.

Embedded qualitative substudy - To learn how to improve the feasibility and acceptability of weight loss programs and studies, we would like to carry out 5-10 in-depth qualitative interviews among patients who decline the main study (ie study decliners). This information will be useful for understanding how to improve feasibility, acceptability, and other aspects of the project to augment participation. There is no medical or physical risk to participating in the interview and involves no more than minimal risk. Among the study decliners alone, we would like to obtain verbal consent using the telephone script and verbal consent form attached.

J2. Consent Procedures

Who will recruit subjects for this study?

PI
PI's staff

Describe how research population will be identified, recruitment procedures, any waiting period between informing the prospective participant and obtaining consent, steps taken to minimize the possibility of coercion or undue influence and consent procedures in detail.

All patients with MASLD who come into clinic for their Gastroenterology, Hepatology, Endocrinology or Primary care clinic visit will have the opportunity to hear about the study.

RECRUITMENT 1. Identify Potential Participants We will identify potentially eligible patients in the following ways: 1) pre-clinic review of clinic schedules 2) The research team will inform clinicians in gastroenterology, hepatology, endocrinology, and primary care clinics about this study, its intervention, and inclusion criteria. We will ask providers to let us know of potentially eligible patients that we can contact.

2. Introduce study to potential participants We will share information about the study with potentially eligible patients in the following ways: 1) with permission from the patients' medical providers, research staff will approach patients to let them know about the study and its intervention. 2) we will also publicize this study among physicians and midlevel providers who will be encouraged to inform their patients about the study/intervention if felt to be relevant. If the patient expresses interest to hear more about the study, then study staff will discuss the study and also give patients a copy of the consent form to read about the study and its intervention so that they can review on their own.

3. Following up with potentially interested participants Among patients who have expressed an interest in the study, staff will assess eligibility and proceed with screening (which means reviewing patient charts to assess for inclusion/exclusion criteria). If patient is still potentially eligible, then staff will follow up with telephone calls. If the patient qualifies for the study based on inclusion/exclusion criteria, then research staff will move forward with the consent.

4. Patients who decline the study MRNs of patient who decline will be recorded, so that research staff do not inadvertently re-approach these patients about the study. We are requesting waiver of written consent to allow for verbal consent to interview approximately 5 – 10 people who decline study participation to learn their reasons for doing so (see qualitative sub-study below, see verbal consent form).

STUDY ENROLLMENT MAIN STUDY-Research staff will discuss the study, intervention, and informed consent in-person, remotely, or video visit, according to patient preference. Staff will obtain informed consent via paper consent form administered either in-person or via mail. Afterward, staff will work with the enrolled patient to schedule the baseline study assessments.

QUALITATIVE SUBSTUDY-This consists of a single interview among a sub-sample of 5-10 participants who fall into the following 4 categories: study decliners, study drop-outs, study completers with low program attendance, and study completers with high attendance. Among study decliners, we will obtain verbal consent (see verbal consent form.). Among study participants, we will get written consent as part of the main study consent form. Subsequently, we will contact those participants who agreed to the interviews (see Telephone scripts). At the beginning of each interview, we will ask participants for permission to audiorecord and only take notes if they decline. (see Appendix F).

FAMILY/HOUSEHOLD MEMBER SUBSTUDY - Staff will ask enrolled patients whether they have a family member who may be interested in the substudy. Staff will then contact the family member, discuss the substudy and review the verbal consent form (see attached verbal consent form). If interested in participating, we will document verbal consent and mail a copy .

SPANISH SPEAKING SUBJECTS-Will be consented to the protocol by a research team member fluent in Spanish or with translator support. We will implement separate Spanish and English program sessions, led by a bilingual health educator. All materials will be translated to Spanish and submitted for IRB approval prior to use.

Are foreign language consent forms required for this protocol?

Yes

Which of the following ways will you document informed consent in languages other than English?

A full-length informed consent document

J3. Privacy and Intrusiveness

Will the research involve observation or intrusion in situations where the subjects would normally have an expectation of privacy?

No

J4. Children

Will children be enrolled in the research?

No

J5. Neonates

Will non-viable neonates or neonates of uncertain viability be involved in research?

No

J6. Consent Capacity - Adults who lack capacity

Will Adult subjects who lack the capacity to give informed consent be enrolled in the research?

No

J7. Prisoners

Will Prisoners be enrolled in the research?

No

Section K: Research Related Health Information and Confidentiality

Will research data include identifiable subject information?
Yes

Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
Yes

Specific information concerning alcohol abuse:
Yes

Specific information concerning drug abuse:
Yes

Specific information concerning sickle cell anemia:
No

Specific information concerning HIV:
No

Specific information concerning psychiatry notes:
No

Demographic information (name, D.O.B., age, gender, race, etc.):
Yes

Full Social Security #:
Yes

Partial Social Security # (Last four digits):
No

Billing or financial records:
No

Photographs, videotapes, and/or audiotapes of you:
Yes

Identifiable biospecimens
Yes

Will identifiable biospecimens be stored for future research?
Yes

If yes, is the storage of biospecimens optional for subjects?
Yes

Will identifiable private information be stored for future research?
NA

If yes, is the storage of information optional for subjects?
NA

Questionnaire, Survey, and/or subject diary
Yes

Other:
No

At what institution will the physical research data be kept?
Patient files and study forms will be stored in a locked cabinet in the PI's locked office. The office is located at the following address: Ben Taub Hospital, 5th floor, #5 PI 71-006 & 5-SP70 006; 1504 Taub Loop; Houston, TX 77030.

How will such physical research data be secured?
All physical data (patient study forms, files, binders) will be kept in a locked cabinet in the PI's locked office. The office belongs only to the PI. Only the PI and research staff assigned to this study key access to the cabinet and office.

At what institution will the electronic research data be kept?

We will maintain an electronic copy of a master identifier log. This log will be kept in a password protected file stored on the BCM server. This log will match patient and patient household/family member (name, medical record number, contact information) to their anonymous study ID (i.e. study code).

This study ID will also be linked to 1) interviews conducted among the subsample of participants who participate in the qualitative sub-study 2) research blood samples and 3) the DHQ III user ID.

The DHQ III survey is hosted exclusively online by the national cancer institute (NCI); responses are uploaded into the NCI's DHQ 3 server. Here is a description of how researchers access the online survey (https://epi.grants.cancer.gov/dhq3/dhq3-respondent-privacy-statement.html): Researchers do not provide the National Cancer Institute (NCI) or the DHQ III system with any personally identifiable information (PII) associated with study respondents. Rather, researchers specify a user ID for each respondent and download system-generated login credentials (username and password) that are used to to access DHQ III. Since we plan to administer this questionnaire in a RC assisted manner (rather than participant self-administered), we will give participants the option of logging in themselves or having the RC do this for them. In either case, we will use secured BCM electronic platforms to access the online survey. The DHQ III system also does not capture any personally identifiable data from Respondents. Respondent data are protected using industry standard security controls. The communication between the DHQ III server and the computer used for data collection and all data entered into the DHQ III system database are encrypted. DHQ III data can then be downloaded to the BCM server. The DHQ III data will be saved separately from the master identifier log.

Such electronic research data will be secured via BCM IT Services- provided secured network storage of electronic research data (Non-Portable devices only):

Yes

Such electronic research data will be secured via Other:

No

Will there be anyone besides the PI, the study staff, the IRB and the sponsor, who will have access to identifiable research data?

No

Please describe the methods of transmission of any research data (including PHI, sensitive, and non-sensitive data) to sponsors and/or collaborators.

1. Research blood samples (labeled with study IDs) will be transported by an RA to the BCM Population Sciences Biorepository (PSB) lab where they will be stored. The PSB, in turn, re-labels each research sample aliquot with its own lab specific ID (PSB lab ID) which can not be directly linked to identifiers (pls see section N for additional details). The PSB lab ID-labeled samples will be sent to outside labs for specialized testing of inflammatory and fibrosis biomarkers. 2. Interview audio-recordings (labeled with study IDs) may be sent to 3rd party transcription service if the participant agrees. The audiorecording will be reviewed, stripped of any identifiers, and then uploaded into the secured transcription service portal. The transcription service sends completed transcriptions via the same portal. 3. Internal transfer of data between study members will be done as coded data sets via encrypted email or file sharing services managed by BCM (for example, one drive). 4. At this time, no external transfers of data are planned. If this changes in the future, then a separate amendment and Data Use Agreement or Materials Transfer Agreement will be requested as appropriate.

Will you obtain a Certificate of Confidentiality (COC) for this study?

Yes

Please further discuss any potential confidentiality issues related to this study.

We are taking several measures to protect participant confidentiality.

1. Clinical information from the medical record, alcohol and drug use information that is collected will be stored in a password protected spreadsheet saved on the BCM server and linked to the participant only through study ID.

2. Audiorecordings and transcripts of interviews obtained as part of the qualitative substudy and family substudy will be handled in the following manner. During the interview, we will avoid using any personal identifiers. Post -interview, the audiorecording will be reviewed and, if any personal identifiers are inadvertantly shared by a participant, they will be redacted. The deidendified audiorecording will then be sent for transcription. the original audiorecording and transcripts will be linked only to participants' anonymized codes.

3. Study blood samples will be linked only to participants' anonymized codes.

4. The intervention consists of group sessions of 8 to 12 patients who are MExican and Central American and have MASLD. During the group sessions, personal topics may emerge in response to discussions (for example experiences related to weight, difficult personal experiences, emotions). Thus, patients will know that everyone in the class with them has MASLD, may learn about each others' identities and personal details, and details about their identities and personal details will be know to others. The nature of a group intervention classes is such that confidentiality can not be completely guaranteed. The research team will discuss this with participants so that they are aware; we will further explain to

participants that they should not repeat any personal information that may be shared during intervention sessions with others outside of the group. In addition, during Intervention session 1, the counselor set ground rules with the group which includes a verbal agreement not to share personal information divulged during the classes.

Will information about the subject's participation be included in subject's medical records?

Yes

Please further discuss any potential confidentiality issues related to this study.

Harris Health System (the site of this study intervention and procedures) requires that patients' electronic charts in EPIC flags whether patients are participating in research and details about the research study. This is for safety reasons, specifically to make sure that patients' medical team are aware of their participation in research, as it may have implications for their care. However, this information will be seen by anyone who has EPIC access to the patient's chart.

Blood samples for inflammatory and fibrosis markers will be labelled with an assigned research ID and blood will drawn by PSB lab research coordinator. The samples will be processed in the PSB lab is located on the 5th floor, room R531E of the Alkek Building for Biomedical Research (ABBR) at Main Baylor. The samples will be banked in LN2 vapor freezer in the PSB lab. The LN2 freezer is consistently maintained at -191°C.

Section L: Cost/Payment

Delineate clinical procedures from research procedures. Will subject's insurance (or subject) be responsible for research related costs? If so state for which items subject's insurance (or subject) will be responsible (surgery, device, drugs, etc). If appropriate, discuss the availability of financial counseling.

Subjects/subjects' insurance will not be responsible for any other costs of procedures carried out as part of this study.

If subjects will be paid (money, gift certificates, coupons, etc.) to participate in this research project, please note the total dollar amount (or dollar value amount) and distribution plan (one payment, pro-rated payment, paid upon completion, etc) of the payment.

Dollar Amount:

140

Distribution Plan:

MAIN STUDY PARTICIPANT COMPENSATION - patients who participate in the main study will be compensated if all study procedures are completed at each of the 4 time points. Baseline assessment - $50; Mid-intervention assessment - $20; End-of-intervention assessments - $50; Post-intervention/6month follow up assessments - $20; Total amount for all assessments required by main study: $140; If the participant completes the optional interview, then additional $20 will be given.

QUALITATIVE SUB-STUDY - Main study participants who complete an interview will be compensated $20 as described above; Main study decliners will not be compensated for interviews.

FAMILY SUB-STUDY PARTICIPANTS: Family sub-study participants will be compensated $10 for baseline interview completions and another $10 for end-of-intervention interview completion. Total potential compensation: $20. We will compensate participants using ClinCard and at completion of study

Section M: Genetics

How would you classify your genetic study?

Discuss the potential for psychological, social, and/or physical harm subsequent to participation in this research. Please discuss, considering the following areas: risks to privacy, confidentiality, insurability, employability, immigration status, paternity status, educational opportunities, or social stigma.

Will subjects be offered any type of genetic education or counseling, and if so, who will provide the education or counseling and under what conditions will it be provided? If there is the possibility that a family's pedigree will be presented or published, please describe how you will protect family member's confidentiality?

Section N: Sample Collection

SAMPLE: Blood

What is the purpose of the sample collection?

The blood drawn specifically for this study will be used to measure inflammatory (cytokines, adipokines), apoptosis (CK-18), fibrosis, and metabolite (aminoacids, free fatty acid) markers.

For blood draws, specify the amount drawn, in teaspoons, at each visit and across the course of the subjects entire participation time.

Blood will be collected from among all participants who sign main consent form and agree to the optional research blood samples. Blood will be collected from each participant at 2 time points: baseline and at end-of-intervention. Each time, about 10 to 20cc (2 to 4 tsp) of blood will be obtained.

Is there the possibility that cell lines will be developed with this sample?No

Sample will be obtained from:

Clinical Labs, Research Labs, Other: PI or RAs with phlebotomy certification

Will the sample be stripped of identifiers?

No

If sample will be released outside the hospital:

Will sample be released to anyone not listed as an investigator on the protocol? Will the information be identifiable, coded or de-identified?

Coded blood samples will be stored in PSB and sent to outside labs for specialized testing.

Will sample material be sold or transferred to any third parties? Will the information be de-identified?

Blood samples with study codes will be transported to the the Population Sciences Biorepository (PSB) located at the Feigin Center. The PSB will process and store all collected samples. The PSB creates a separate specimen specific code for each sample. The PSB maintains a link between aliquots' specific PSB sample codes and this study's codes; the PSB sample codes can not be immediately linked to study identifiers. Samples may be sent to outside labs for specialized testing. The samples will not be released to other investigators for topics unrelated to this protocol.

If sample will be banked for future use:

Where will the sample be banked and for how long?

The coded samples will be biobanked in the secure and restricted PSB for an indefinite amount of time.

Does the banking institution have an approved policy for the distribution of samples?

Yes, BCM has an approved policy for distribution of samples.

If the entire sample will NOT be used during the course of this research study:

Will the remaining tissue be discarded? If not what will be done with the remaining sample after study completion and how long will the sample be kept?

The entire sample from each patient may not be used up in this study. Any remaining sample will be bio-banked as coded samples for an indefinite amount of time. The biobanking is for purposes of continued research on these samples by the study team on this protocol as it pertains to the conditions studied on this protocol. The biosamples would not be released to other investigators for topics unrelated to this protocol.

Will samples be made available to the research subject (or his/her medical doctor) for other testing?

No

If a subject withdraws from the study:

Will subject have the option to get the remaining portion of their sample back?

No

Will samples be destroyed? If not, will they be kept anonymously? What will happen to the sample if the subject revokes authorization?

If a subject withdraws from the study, his/her sample will be retained and analyzed per protocol. If the subject specifically revokes authorization for use of the sample, then the sample will be destroyed.

Will data obtained from their sample be deleted? What will happen to the sample if the subject revokes authorization?

If a subject revokes authorization to use the blood sample, data previously obtained from their sample will not be deleted if the subject revokes authorization. However, any further testing of the blood sample will cease and the blood sample will be destroyed.

Will study data or test results be recorded in the subject's medical records?

No

Will results of specific tests and/or results of the overall study be revealed to the research subject and or his/her doctor?

All the results will be made available to the subjects if requested or if clinically deemed necessary.

Please identify all third parties, including the subject's physician, to receive the test results.

None. The subjects' treating physicians will have the results of tests relevant to the clinical management of patient available in the medical records.

Section O: Drug Studies

Does the research involve the use of ANY drug* or biologic? (*A drug is defined as any substance that is used to elicit a pharmacologic or physiologic response whether it is for treatment or diagnostic purposes)

No

Does the research involve the use of ANY gene transfer agent for human gene transfer research?

No

O1. Current Drugs

Is this study placebo-controlled?

No

Will the research involve a radioactive drug?

No

Section P: Device Studies

Does this research study involve the use of ANY device?

No

Section Q: Consent Form(s)

Feasibility of Paso a Paso

Section R: Advertisements

None