PROTOCOL TITLE:
Clinical Effectiveness of Body Fat Distribution Imaging in Real-World Practice: The BODY-REAL Study (STUDY20201918)

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OTHER DEPARTMENTS INVOLVED IN THIS STUDY (IF APPLICABLE):
☒ N/A

VERSION NUMBER:
☐ 2

Objectives
Our **overall goal** is to determine the real-world feasibility and utility of body fat imaging using rapid MRI to enhance risk perception, induce behavioral change, and improve clinical outcomes in overweight and obese individuals. Here, we will perform a pragmatic clinical effectiveness pilot trial using a 2x2 factorial design to test the hypothesis that provision of a detailed individualized visual report of body fat distribution directly to patients will translate into changes in patient risk perception, behavior, and improved clinical outcomes. We will accomplish this objective by completing the following two **specific aims:**

Specific Aim 1: To compare the clinical effectiveness of communicating the body weight and BMI using a visual aid alone versus a detailed body fat distribution report including individualized images and values relative to normative data using a visual scale in a population of overweight and obese adults with prediabetes or type 2 diabetes and at least one additional cardiovascular disease risk factor. **Hypothesis 1**: Provision of a detailed body fat distribution report contextualized with information describing the relevance of each body fat parameter will be superior to provision of body weight/BMI information alone on risk perception, behavioral change (enhanced physical activity, dietary choices, and preventive provider practices and medication adherence), and clinical outcomes (reduction in weight and waist circumference, blood pressure, triglycerides, and glycosylated hemoglobin).

Specific Aim 2: To compare the clinical effectiveness of communicating body fat information to the medical provider (with the intent that the provider interprets the data and translates it to the patient) versus communicating the body fat information directly to the patient. **Hypothesis 2**: Provision of body fat information directly to the patient will be superior to provision of the

information to the provider on risk perception, behavioral change, and clinical outcomes (as assessed in Aim 1).

Background

SIGNIFICANCE

Scope and costs of the obesity epidemic. Nearly 40% of American adults have obesity.[1] In specific segments of the population, the prevalence is even higher; non-Hispanic black women, for example, have a prevalence of obesity of 55%. Obesity-related health expenses in the U.S. were estimated to be a staggering $190 billion a year in 2005.[2] This figure does not account for additional indirect costs, such as loss of workplace productivity. The direct costs include both the cost of obesity treatment and the cost of treating obesity-related conditions such as diabetes, which are difficult to separate. It is known that a great deal is spent on obesity treatment. Outside of the health care system alone, Americans spend roughly $72 billion annually on weight loss products and services, including commercial weight loss programs, supplements, diet foods, etc.[3] Despite this enormous expenditure, rates of obesity continue to increase.

Body fat distribution is fundamental to obesity-related disease. The marked increase in the prevalence of overweight and obesity[4] has contributed to a doubling in type 2 diabetes incidence over the past three decades.[5] This has counterbalanced reductions in other cardiovascular disease (CVD) risk factors, and is the primary factor contributing to a slowed decline in CVD event rates in the population.[6] In turn, professional societies and stakeholders have renewed efforts targeting obesity in order to reduce the diabetes burden.[7] Clinical trials aimed at lifestyle,[8] pharmacologic,[9] and surgical[10] approaches to diabetes consistently focus on reducing weight or body mass index (BMI). However, emerging data suggests that obesity, simply characterized by increased BMI, is neither necessary nor sufficient to promote diabetes and its consequences. BMI does not adequately discriminate diabetes risk among obese individuals[11] and many obese persons appear resistant to the development of metabolic disease.[12] Rather, it appears that risk for diabetes varies substantially across different fat depots,[13-15] and that an excess of visceral adipose tissue (VAT) may be central to the pathogenesis of insulin resistance and diabetes.[16, 17]

Behavioral motivation programs for weight loss are impactful and less expensive. An effective in-person 6-month program described by Krukowski et al all in 2011 reported a cost per participant, for example, of $706.[18] However, utilization of behavioral interventions for obesity, including those with high risk conditions such as diabetes, remains low.[19] Overall, there is evidence that behavioral motivation programs for treatment of obesity can have a modest but significant positive impact (e.g. significant enough to improve cardiovascular risks) upon body weight and weight-related behaviors.[20] This is especially true for visceral and ectopic fat depots where exercise/physical activity is highly impactful for reducing VAT and related risk.[21]

Physicians lack the time, training, and priority to address obesity with patients. Most physicians are inadequately equipped to address obesity with their patients.[22, 23] In a recent survey of 81 internal medicine residencies, ~50% of programs reported that obesity management education was covered to a "very little extent" or "not at all".[22] Furthermore, primary care physicians surveyed about their top priorities in delivery of preventive care did not often include diet, exercise, and weight loss although these were among the 3 preventive services most likely to improve life expectancy.[23] Access to obesity treatment remains a significant challenge. Access

is especially poor in rural areas, where the obesity rate is high and the ability of residents to take advantage of evidence-based treatment programs in hospitals and academic centers is limited.[24] Expanding the reach of obesity treatment is an important priority. In this regard, many programs have been developed to deliver obesity treatment in primary care and community-based settings.[25, 26] Rao and Kirley describe three main characteristics of successful new obesity treatment strategies, apart from their ability to help patients lose weight.[27] First, programs should be convenient and accessible to those in need; second, such programs should be cost-effective; finally, and most importantly, participation should be sustainable. Obesity is a lifelong condition, and a successful program should be patient-centered, highly informative, transparent, and provide a perspective on risk that the patient can simply understand. We strongly believe a program of providing visual imaging evidence of body fat burden/distribution directly to the patient meets these criteria and will empower individuals to make serious lifestyle changes to improve health outcomes.

High risk overweight and obese patients with prediabetes or diabetes are highly prevalent in our health system. The UH Wellness Dashboard is a comprehensive enterprise data warehouse aggregated from 10 sources encompassing all patients within the University Hospitals Health System (UHHS) with a UH medical record number attributed to the accountable care organization. As of December 24, 2020, there were 554,417 total patients accounting for 1.9 million ambulatory visits in the year 2020, of whom, 115,078 have a measurement of glycosylated hemoglobin (Hb A1c). Among this group, over 50% have a diagnosis of prediabetes or diabetes accounting for >65,000 patients in the UH network (Figure 1). Among those with diagnosed diabetes, ~6000 (or 19%) have severely uncontrolled diabetes with a mean Hb A1c of 10.9%. The UHHS serves a historically underserved and economically disadvantaged population (Figure 2), in whom behavioral interventions such as the one described in this proposal may have a significant impact. Five of the 8 counties served by UHHSHS have >10% of individuals living below poverty levels; 7/8 counties have >30% with less than a college education; 6/8 counties have patients with high levels of physical inactivity (>25% of population), and all 8/8 counties have diabetes prevalence above the US median. The significant health burden in our health system

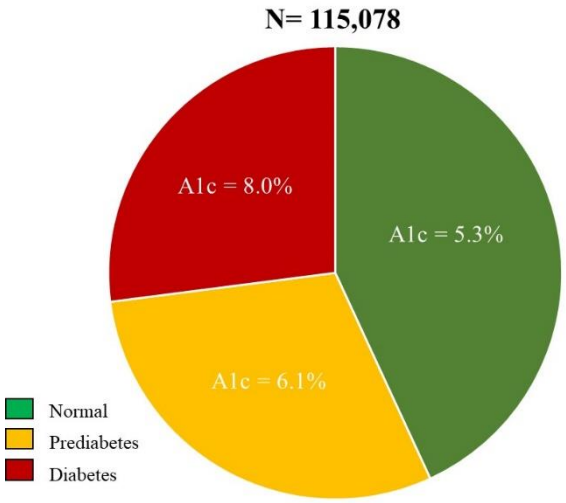

Figure 1. Proportion of patients in the UHHS Population Health Network with normal glycemia, prediabetes, and diabetes along with corresponding mean Hb A1c level.

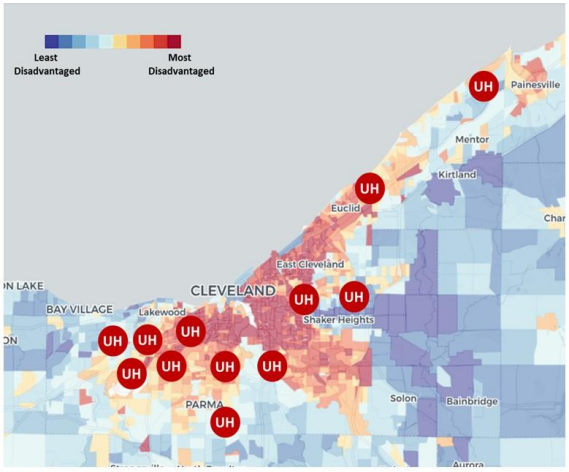

Figure 2. UHHS hospital and outpatient locations. Heat-map depicting national ranking of area deprivation index (Kind et al. NEJM 2018), with red showing most-disadvantaged neighborhoods with referral locations for imaging (UHHS red signs).

speaks to both the high prevalence of patients who would qualify for our study, as well as the potential impact the outcomes of this project would provide to our high risk Northeast Ohio population.

RATIONALE. Despite its availability for the last 30 years,[36, 37] advanced body fat imaging has been, to date, relegated to the research domain only. Many experts in the field believe that since readily available routine risk indicators, such as blood pressure, blood lipids, blood glucose, waist circumference, and body weight, could be taken from the existing patient record and used, why would quantification and distribution of body fat and lean mass through graphic imaging be a superior motivational tool for patient behavior modification? The lack of a clear answer to this question is precisely the rationale for the proposed project. Without a dedicated study evaluating the real-world utility and feasibility of an advanced body fat imaging approach, the field will never answer this question and fail to evolve despite rapidly improving technology, increased accessibility, and lower cost of advanced imaging. The evolution of coronary artery calcium (CAC) scoring is a paradigm example of how advanced imaging can inform risk assessment and preventive/therapeutic decision making. Much in the same way that CAC provides important risk information beyond traditional risk factors, it is possible that advanced body fat imaging may add to and improve current obesity-related risk algorithms, something that BMI and WC have failed to do.[38] Despite the general understanding in the lay public that obesity has long-term adverse health effects, in more recent years, due to the increase in the average weight/BMI of the population, many patients describe complacency regarding their weight and are often unprepared to take up provider advice.[39] Behavioral science has long understood the importance of visual cues to modify behavior and motivation. It is well understood that habit learning is facilitated when the new behavior is consistently preceded by specific (e.g. visual) cues.[40] A leading theory is the Health Belief Model, comprising several behavior constructs focusing on the individual's perception of societal influence, one's ability to overcome behavior barriers, and one's reaction to cues. According to health behavior models, compliance with external (e.g. visual) cues will depend on one's belief that the potential hazard actually carries a significant personal impact.[41] This is especially important for behavioral motivation to lose weight as other health issues are often felt to take precedence, and patients describe inconsistent provision of information and resources to assist them in tackling their weight problems.[39] Therefore, there is strong rationale to implement highly effective visual cues that influence the patient's understanding of the hazard of excess body fat and offer a personalized, visually interpretable representation of that hazard. It is on the basis of this rationale that this project is proposed and promises to be highly impactful and innovative, as detailed in the next section.

INNOVATION

Although the potential importance of VAT as a risk factor and therapeutic target for obesity and diabetes has been appreciated since Reaven's description of *Syndrome X* in 1988,[42] no approach to date has been effective in moving beyond the status quo of using simple anthropometric targets as surrogates for VAT.[43, 44] Contemporary guidelines emphasize the importance of including waist circumference (WC) as a risk factor to guide recommendations for weight loss among those with overweight or obesity.[19] WC is correlated with excess abdominal fat[45], and within a given BMI, the addition of WC improves prediction of intra-abdominal (visceral) fat beyond the BMI alone[46]. However, only ~40% of the variance of visceral fat is explained by WC[47-49] making precise estimation of excess abdominal fat without imaging impossible. Several

other anthropometric and/or laboratory markers for abdominal adiposity have been utilized clinically but have modest correlation with direct imaging-based assessments of body fat. Furthermore, surrogate markers do not differentiate between different body fat depots nor between fat and lean mass. Therefore, clinical implementation of more accurate and precise imaging measures of obesity, specifically fat amount and distribution, are vital to improve the diagnosis of obesity, guide decision-making for appropriate interventions, and monitor responses to treatment. The proposed research in this application is innovative, in our opinion, because it represents a new and substantive departure from the status quo, namely 1) clinical implementation of a rapid, non-contrast MRI protocol to accurately measure visceral and ectopic fat, and 2) use of a simple, pragmatic, clinical effectiveness design for the first time in humans to test the hypothesis that provision of direct imaging-based reports of body fat burden and distribution to patients will enhance risk perception, induce behavioral change, and improve clinical outcomes in overweight and obese individuals. Preliminary data (see Approach) strongly suggest that this approach will be feasible in obtaining findings that will lead to more definitive, hypothesis-driven trials to test the clinical effectiveness of our approach. As a consequence, a more profound understanding of the utility and acceptability of direct body fat imaging for obesity management will be elucidated with highly significant potential impact on future implementation science interventions and clinical effectiveness studies in cardiometabolic care to improve the lives and health of millions of people.

Preliminary Data. Important foundational work has been performed that establishes the feasibility and utility of this proposal.

Body fat distribution imaging is feasible, accurate, and reproducible in our hands. MRI allows complete separation of adipose and lean tissues into fat-only (adipose) images and water-only (lean) images using fat-sensitive imaging techniques, such as chemical-shift or Dixon imaging.[50] Intravenous contrast is not necessary for the purpose of fat segmentation. The PI and his team have cumulatively performed >400 body fat MRI scans using the same protocol over the last 6 years in three separate clinical studies on three different scanners (Philips, GE, Siemens) (Figure 3). To test intra- and inter-scanner reproducibility, eighteen healthy volunteers of varying BMI and adiposity were each scanned twice on five

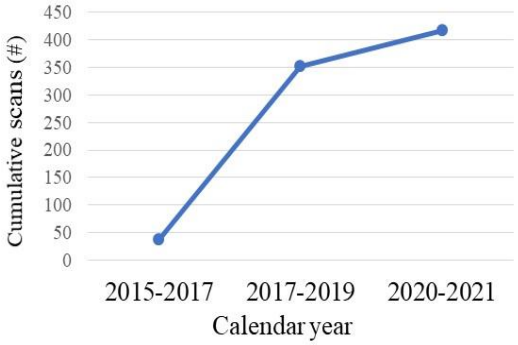

Figure 3. Body fat MRI scans performed by the PI

	Intra-scanner		Inter-scanner	
Measurement	**Within-subject SD (range)**	**Coefficient of variation (CV)**	**Within-subject SD**	**Coefficient of variation (CV)**
Visceral AT (cl)	4.55 (2.73-6.18)	2.89%	7.51	4.43%
Abdominal subcutaneous AT (cl)	8.82 (6.01-10.63)	1.81%	15.33	3.24%
Total thigh muscle volume (cl)	6.28 (4.02-9.09)	0.45%	11.22	0.87%
Left posterior thigh muscle fat infiltration (%)	0.18 (0.12-0.34)	2.94%	0.80	11.41%
Liver fat (%)	0.46 (0.21-0.70)	15.70%	0.86	28.76%

Table 1. Intra- and inter-scanner variability of fat distribution imaging for 18 participants (72% male, mean age 37 yrs, mean BMI 26 kg/m^2). AT–adipose tissue, cl–centiliter, SD–standard deviation

different 1.5T and 3T scanners from three different vendors by members of the study team. Two-point Dixon neck-to knee images and an additional liver scan were acquired with similar protocols. VAT volume, abdominal subcutaneous adipose tissue (ASAT) volume, thigh muscle volume, and muscle fat infiltration (MFI) in the thigh muscle were measured. Liver proton density fat fraction (PDFF) was assessed using a 6-point ROI method. Within-scanner test-retest repeatability and between-scanner reproducibility were calculated using analysis of variance and are presented in Table 1. Overall there was with excellent accuracy and reproducibility for body fat distribution, with very low coefficient of variation seen in VAT, ASAT, and thigh muscle volume, and more variation seen in MFI and liver fat. These results speak to the excellent rigor and reproducibility of the imaging methods to be used in this study.

University Hospitals has established behavioral motivation programs for weight loss with a successful track record. "Fitter Me" is a medical obesity treatment program established at UH in 2018. "Fitter" implies both fitness and individualization. Since inception, the program has had nearly 200 participants. The program is clinic based. Initial visits include a detailed medical evaluation, as well as identifying key habits contributing to obesity and motivations for weight loss. Participants then meet with a trained behaviorist who helps them implement behavioral goals, using a variety of techniques such as motivational interviewing. Patients are seen roughly monthly through clinic visits to monitor progress. The behaviorist is available between appointments by phone, email and text for support and problem solving. Pharmacotherapy is prescribed by a provider depending upon progress and patient interest. We have follow-up outcomes data for 85 patients. The average weight loss has been 2.96kg across a number of different time frames. Mean weight loss is 1.5kg for patients with 2-3 total visits, compared to a weight loss of 44.45kg for one patient with 15 visits. Weight loss has averaged 2.5kg for women and 5.75kg for men. Weight loss has averaged 3.63kg for white participants compared to 2.28kg for black participants.

Inclusion and Exclusion Criteria

	Inclusion Criteria
1.	Age ≥ 35 years
2.	Able to provide informed consent
3.	Overweight or Obese (BMI ≥25 kg/m^2)
4.	Prediabetes or Type 2 Diabetes: • Fasting glucose ≥100 mg/dl, or • Hb A1c ≥5.7%, or • Medical (i.e. pharmacologic) treatment for type 2 diabetes
5.	At least 1 additional cardiovascular risk factor (defined by ATP III criteria[2]) including: • Hypertension (BP>130/80 or on medical therapy for hypertension) • Low HDL-cholesterol (<40 mg/dL in men and <50 mg/dL in women) • High triglycerides (≥150 mg/dL or on treatment for hypertriglyceridemia) • Obstructive sleep apnea (clinical diagnosis) • Coronary artery disease (clinical diagnosis) • Congestive heart failure (clinical diagnosis) • Atrial fibrillation (clinical diagnosis)

	Exclusion Criteria
1.	Receipt of any anti-obesity drug or supplement within 1 month prior to screening for this trial or plan to initiate therapy during the trial.
2.	Self-reported or clinically documented history of significant fluctuations (>5% change) in weight within 1 month prior to screening for this trial.
3.	Current or history of treatment with medications that may cause significant weight gain, within 1 month prior to screening for this trial, including systemic corticosteroids (except for a short course of treatment, i.e., 7- 10 days), tri-cyclic antidepressants, atypical antipsychotic and mood stabilizers (e.g., imipramine, amitryptiline, mirtazapine, paroxetine, phenelzine, clorpromazine, thioridazine, clozapine, olanzapine, valproic acid and its derivatives, and lithium).
4.	Surgery scheduled for the trial duration period, except for minor surgical procedures, at the discretion of the Investigator.
5.	Language barrier, mental incapacity, unwillingness or inability to understand.
6.	Females of childbearing potential who are pregnant, breast-feeding or intend to become pregnant or are not using adequate contraceptive methods. These include abstinence and the following methods: diaphragm with spermacide, condom with spermacide (by male partner), intrauterine device, sponge, spermacide, Norplant®, Depo-Provera® or oral contraceptives.
7.	Unable to complete/tolerate magnetic resonance imaging (MRI) due to severe claustrophobia or metallic implants.
8.	≥2 no-shows to recruitment clinic within the 6 months prior to screening.

Number of Research Participants
Planned number of subjects to be screened: 200
Planned number of subjects to be randomized:140
Anticipated number of subjects to be analyzed: 126 (assumes 10% drop-out)
Number of trial sites: Single center

Recruitment Methods
Participants for the proposed study will be recruited primarily from two sources at UH: the Fitter Me program (described above) and The Center for Integrated and Novel Approaches in Vascular-Metabolic Disease (CINEMA) program. We founded CINEMA in order to address the significant health burden in our Northeast Ohio population. CINEMA is an integrated, patient-centered, team-based intervention for patients with type 2 diabetes at high risk for cardiovascular disease events (i.e. those with established atherosclerotic cardiovascular disease, high risk coronary calcium score >100, and/or chronic kidney disease stages 2-4). The program was launched in May 2020 by UH, a large health care network in Northeast Ohio, comprising 11 hospitals and 18 regional medical centers with the intent of impacting the care of type 2 diabetes with complex cardiovascular and renal disease. The CINEMA team (including the PI who is Co-Director of the program) consists of a program administrator; 5 cardiologists with a special interest focus on diabetes, prevention, cardiovascular imaging, and vascular medicine; a nurse coordinator; a certified diabetes care and education specialist; and a dedicated pharmacist who aim to target lifestyle and pharmacologic therapies to the cardiac, vascular, and renal manifestations of diabetes. Within the second half of 2020, despite the COVID-19 pandemic, we

have cumulatively enrolled 132 patients in CINEMA, with steady increases in monthly referrals since the start of the program. The CINEMA and Fitter Me programs will be the sources for participant enrollment for the trial proposed here.

Setting
Participants will be recruited from the CINEMA and Fitter Me clinics described above. As the directors of these clinics are members of the study team, staff will identify potential participants who attend these clinics and study coordinators will engage the patients for their interest in the study. If participants are interested in enrolling and initial inclusion/exclusion criteria are satisfied, written informed consent will be obtained and the participant will be enrolled in the study. Once enrolled, the surveys will be administered either after the clinic visit in-person or provided electronically for the participant to complete at home. Participants will then be randomized using a computer-generated code and those assigned to body fat imaging will be contacted by phone or email to set up an MRI imaging appointment. All MRI imaging will occur in the Lerner MRI (MR7) in the basement of Lerner Tower on the Cleveland Medical Center campus. All additional clinical data and outcomes will be obtained from the electronic health record (EHR).

Consent Process
All participants will undergo written, informed consent for this study. The study team will be requesting a partial HIPPA waiver in order to screen potential participants from the Fitter Me and CINEMA clinics using the EHR in order to identify potential eligibility.

Sharing of Results with Research Participants
By design of this study, the results of the MRI imaging will be shared with either the participant or the participant's physician via a detailed body composition report. Other clinical and laboratory data are readily available in the EHR and can be accessed by the physician and patient as per clinical routine.

Study Design
The study design is a pragmatic, clinical effectiveness trial using a two-by-two factorial design to test the hypothesis that provision of a detailed individualized visual report of body fat distribution directly to patients will translate into changes in patient risk perception, behavior, and improved clinical outcomes. Participants will be randomized to i) receive body weight and body mass index information using a visual aid alone or a detailed body fat distribution report including individualized images and values relative to normative data using a visual scale, and ii) the report will be provided directly to the medical provider or the report will be provided directly to the participant (patient).

Study Procedures
Aim 1 – Compare the clinical effectiveness of communicating the body weight and BMI using a visual aid alone versus a detailed and visual body fat distribution profile report

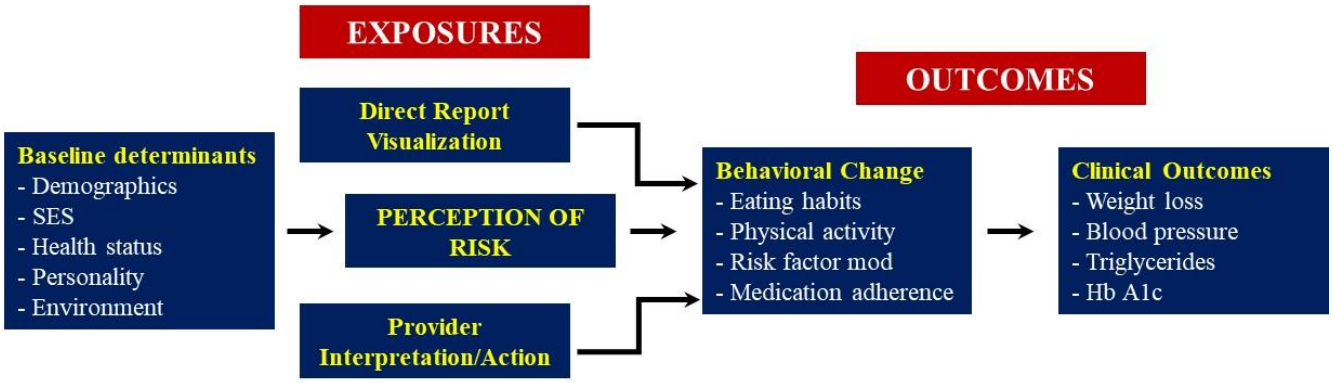

Figure 5. Conceptual model to understand how direct visualization of cardiometabolic risk may affect behavior change translating to changes in clinical outcomes

Overall design. Our trial is designed to address the hypothesis that provision of a detailed individualized visual report of body fat distribution directly to patients will translate into changes in patient risk perception, behavior, and improved clinical outcomes. It is consistent with the "health belief model" of behavior change, whereby an individual is more likely to adopt a healthy behavior if they perceive increased personal risk and believe that specific behaviors will reduce risk (Figure 5).[51, 52] In this 2-by-2 factorial design (Figure 6), we will randomly assign overweight/obese patients with high cardiovascular risk to a detailed body fat distribution report or provision of standard weight/BMI and to provision of the report directly to the patient or to the provider. Specific Aim 1 is dedicated to the randomized comparison of the body fat distribution report vs. provision of standard weight and BMI information.

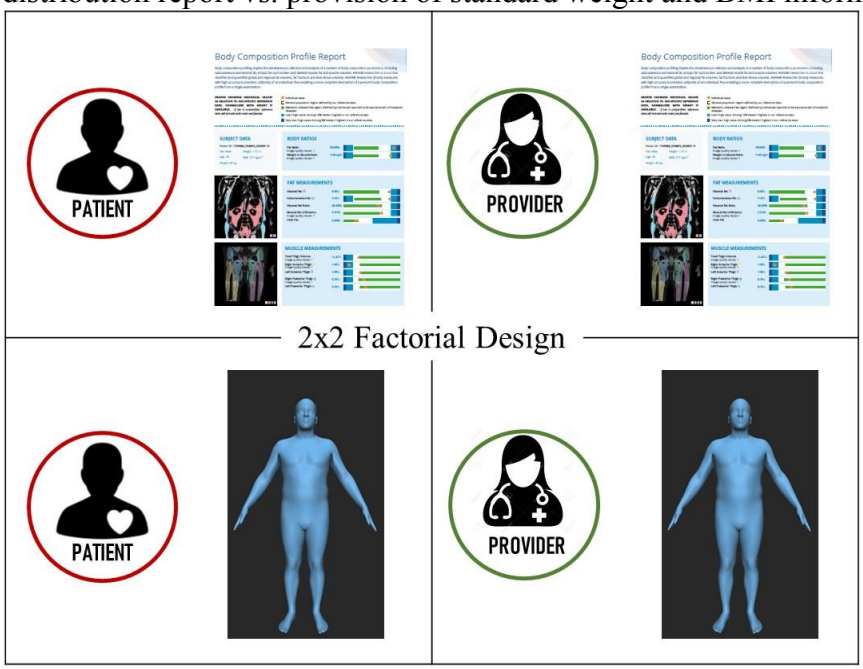

Figure 6. In this 2-by-2 factorial design, we will randomly assign overweight/obese patients with high cardiovascular risk to a detailed body fat distribution report or provision of standard weight/BMI and to provision of the report directly to the patient or to the provider.

Study population. The study population will consist of overweight and obese adults with prediabetes or type 2 diabetes and at least one additional cardiovascular disease risk factor (see Inclusion/Exclusion criteria in the Human Subjects and Clinical Trials information section of the Appendix). Participants will be recruited from clinical programs (described above) targeted to this population. Efforts will be made to recruit equally from both men and women and between race/ethnicity with a goal of 50% men/50%

women and 50% White/50% Black with at least 20% Hispanic participants. Sex- and race/ethnicity-stratified analyses (see Statistical section) will be performed to better understand the influence of sex and race/ethnicity on the intervention and outcomes.

Randomization. After screening and written informed consent, participants will be randomized to receive either the detailed body fat distribution report or standard weight/BMI information using a computerized randomization code generated by the UH Translational Science Unit. Given the pragmatic nature of the trial, neither providers nor patients will be blinded to the treatment assignment. However, outcomes adjudication (see below) will be obtained through the electronic medical record and chart abstractors will be blinded to the treatment assignment so as not to bias the collection of outcomes.

Anthropometrics and body fat distribution imaging methods. All participants will undergo standard anthropometric measurements of height and weight using a standard scale (model HBF-514C, Omron Healthcare, Lake Forest, IL). The scale will be calibrated on a weekly basis using a standard 10 kg weight to ensure accuracy and precision over the course of the study. BMI will be calculated as weight (kg)/height $(m)^2$. Waist circumference will be measured with a standard tape 1 cm above the iliac crest and hip circumference will be measured at the widest circumference of the buttocks at the area of the greater trochanters. These measurements are routinely obtained in both the Fitter Me and CINEMA programs in a standardized manner. Those randomized to body fat distribution imaging will be scanned on a 1.5T Siemens Aera MRI scanner (Siemens Healthineers, Erlangen, Germany), located in the Center for Advanced Heart and Vascular Care using a 6-minute dual-echo Dixon Vibe protocol providing a water and fat separated volumetric data set covering neck to knees, and a multiecho Dixon acquisition for proton density fat fraction assessment in the liver. Images of the liver will be acquired using a 16-channel SENSE XL Torso coil and images from the rest of the body will be acquired using the body coil. Volumetric imaging datasets of the body derived by MRI will be generated using validated and readily-available protocols with rapid scan time to perform precise measurements of total and regional body composition and fat distribution. Apart from quantifying adipose tissue depots, such as in the abdominal subcutaneous compartment (ASAT), visceral compartment (VAT), and hips and buttocks (lower body fat); we will employ more recently developed MRI techniques to measure the proton density fat fraction of the liver (i.e. hepatic steatosis) as well as the quality of lean (skeletal muscle) including muscle volume and degree of fat infiltration (Figure 7).[53] Quantification of body fat distribution parameters will be performed using AMRA Profiler Research (AMRA Medical AB, Linköping, Sweden).[50, 54-56]

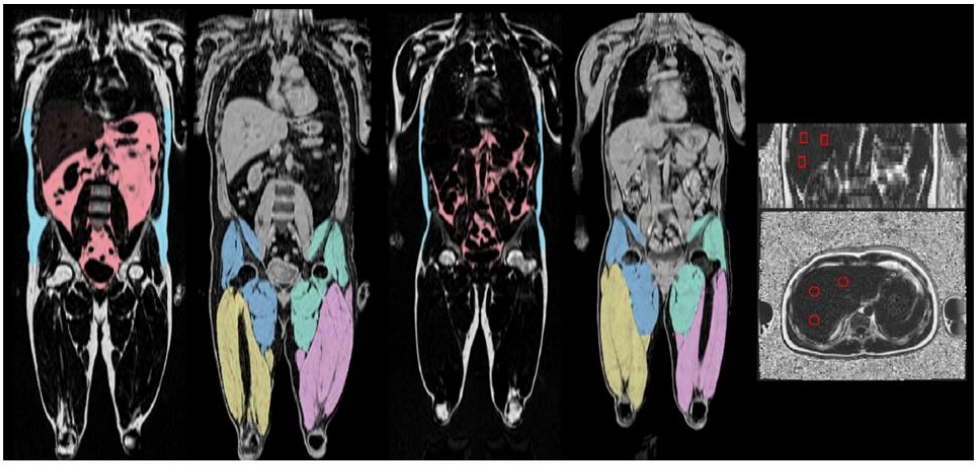

Figure 7. Examples of segmentation of visceral AT (red), subcutaneous AT (blue), and thigh muscles in and obese (left) and lean (right) participant. Example of liver fat fraction (in coronal and axial views, note: regions of interest denoted by red circles)

Briefly, the image analysis consists of (1) image calibration, (2) fusion of image stacks, (3) image segmentation, and (4) quantification of fat and muscle volumes and included manual quality control by an analysis engineer. Dr. Neeland has personally recruited >250 participants and supervised >400 MRI body fat scans utilizing this identical protocol. Drs. Linge and Dahlqvist Leinhard will supervise the measurement and interpretation of the acquired images and provide the dedicated reports.

Provision of reports. Participants randomized to weight/BMI information alone will receive a simple informational report consisting of weight, BMI, and a visual representation of their BMI (www.bmivisualizer.com, last accessed December 30, 2020). This report also categorizes their BMI into underweight, normal weight, overweight, or obese categories according to the World Health Organization categorization schema.[57] Those randomized to the body fat distribution report will receive a detailed body composition profile report that consists of the following elements: basic demographic data, percent body fat, weight to muscle ratio, visceral fat and abdominal subcutaneous fat volume, visceral fat ratio (the fraction of visceral divided by total abdominal fat), muscle fat infiltration and liver fat (%), and thigh muscle volumes (also separated into right and left, anterior and posterior compartments). Each parameter is presented on a visual scale in the context of the individual value, general population defined by reference

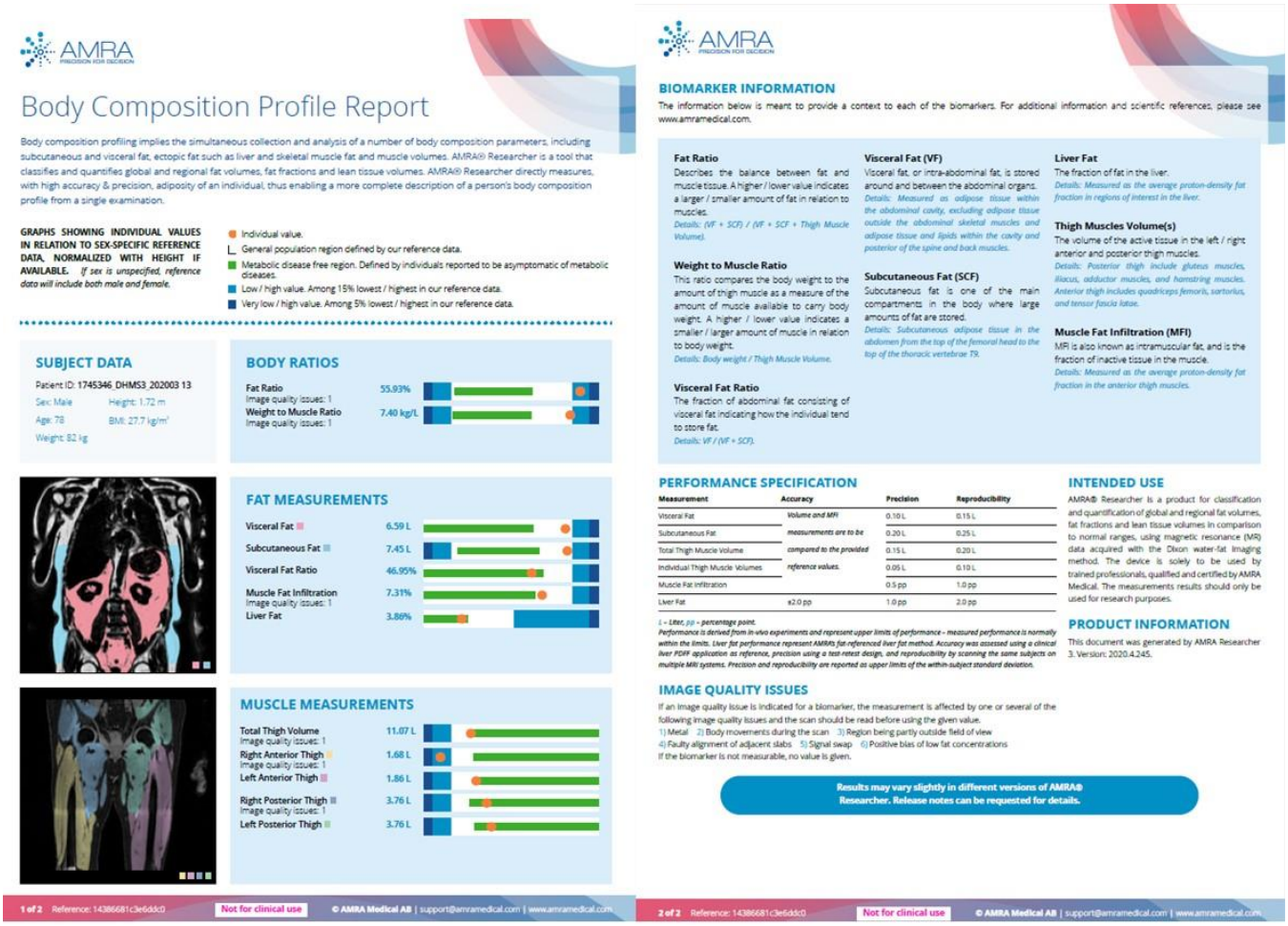

Figure 8. Sample body fat distribution report. Individualized data are provided in the context of a normative, disease-free population (from UK Biobank)

data (from UK Biobank population), a metabolic disease-free population (also from UK Biobank), low/high and very low/very high, corresponding to 15th and 5th percentiles, respectively. There are also descriptions of each biomarker and how they are derived to provide context for the recipient. A sample report is shown in Figure 8.

Outcomes. The planned outcomes for this study combine both traditional participant data acquisition (validated survey instruments) as well as pragmatic data obtained from the electronic health record (EHR) (provider practice patterns and clinical outcomes). The rationale underlying this design is that our goal is to assess "real-world" impact of the intervention, in a pragmatic, cost-effective manner to provide feasibility/pilot data for this small R01 project. Physician practice data and clinical outcome variables will be collected from the EHR linked to the translational research warehouse (CLEARPATH, described in detail below, 4.5.5) which will provide extensive, albeit "clinically-driven", data. One of the biggest strengths of the UHHS EHR system is its integration of 11 hospitals and 18 regional medical centers translating to ~2 million ambulatory visits per year. The UHHS laboratory system is extensive and highly available throughout NE Ohio and also captures laboratory data obtained at other health systems in the Cleveland metro-area, allowing broad capture of clinical laboratory data with minor anticipated missingness, especially for the common clinical variables we are collecting. Outcomes will be assessed at as close as possible to the following time points: Baseline, 2 weeks (survey data only), 3 months, and 6 months. The rationale for the spacing of time points in this manner is to assess both "immediate" impact of the information on risk perception and behavior, as well as more intermediate/long term changes in risk perception, behavior, and clinical outcomes. Given that the biggest impact of weight reducing interventions occur between 3-6 months (with plateau and regain usually seen thereafter), we are using this time interval to assess clinical outcomes.

Risk perception. Cardiovascular risk perception will be measured using the *Perception of Risk of Heart Disease Scale* which has been shown to be reliable and well-validated for use in this population.[58-63] Diabetes risk perception will be assessed using the validated *Risk Perception for Developing Diabetes Risk (RPS-DD) instrument*. The instrument consists of 4 sections with responses recorded on a Likert scale. These sections assess knowledge of diabetes risk factors, perceptions of personal control, perceptions of the benefits and barriers, and optimistic bias about developing diabetes.[64, 65] Motivation to change diabetes risk behaviors will be measured using the Treatment Self-regulation Questionnaire (TSRQ) that consists of 15 self-report Likert scale items assessing motivation across sub-domains (e.g., exercise, diet).[66] Each participant will be queried as to their perception of T2D and CVD risk at 4 time points during the study: i) after written informed consent but prior to randomized allocation of the intervention, ii) within 2 weeks (±3 days) of randomized allocation of the intervention, iii) after 3 months (±3 days) post-randomized allocation of the intervention, and iv) after 6 months (±3 days) post-randomized allocation of the intervention.

Behavioral change. Outcomes of behavioral change will be assessed generally in the following categories: i) enhanced physical activity, ii) dietary choices, and iii) preventive medication prescription/adherence.

Physical activity. Physical activity will be assed using the Global Physical Activity Questionnaire (GPAQ) available from the World Health Organization. The GPAQ uses metabolic equivalent (MET) levels to identify physical activity level. MET scores will be calculated for each domain and subdomain of the GPAQ. A categorical indicator will be created that accounts for the time spent on physical activity during a typical week, the number of days,

and the intensity of the activity. Although this is a self-report of physical activity, we believe that, in this pragmatic trial, the GPAQ, which is widely used in population-level studies, will provide a measure sufficient for our purposes.

Dietary choices. All participants will undergo a standardized, validated dietary questionnaire (Automated Self-Administered 24-Hour Dietary Assessment Tool or "ASA24", accessed online at https://epi.grants.cancer.gov/asa24/) to better understand their dietary choices. The ASA24 is a free, web-based tool that enables multiple, automatically coded, self-administered 24-hour diet recalls and/or single or multi-day food records, also known as food diaries, available from the National Cancer Institute. Since AS24 was released in 2009, >6000 studies have registered to use it and >521,000 record days have been collected as of January 2020. No dietary counseling will be mandated during the study but it is anticipated that participants will receive dietary counseling from their providers and/or outside sources during the course of the study and that the study intervention may influence seeking out dietary advice and instituting dietary changes. Each participant will complete a dietary questionnaire at 4 time points during the study: i) after written informed consent but 1 week prior to prior to randomized allocation of the intervention, ii) within 2 weeks (±3 days) of randomized allocation of the intervention, iii) after 3 months (±3 days) post-randomized allocation of the intervention, and iv) after 6 months (±3 days) post-randomized allocation of the intervention.

Table 2. Preventive Provider Practice Outcomes Extracted from EHR Data

Outcome over 12-months	Query/RxNorm/CPT Definition
Prescriptions	
New/additional prescription of lipid medication	New prescription of any agent in LIPID MODIFYING AGENTS / id: C10 / class type: ATC1-4
New prescription of aspirin	Aspirin / id: N0000006582 / class type: CHEM
New prescription of smoking cessation medication	Varenicline / id: N0000179790 / class type: CHEM Or Bupropion / id: N0000006417 / class type: CHEM AND/or Nicotine
New or additional antihypertensive	ANTIHYPERTENSIVES / id: C02 / class type: ATC1-4
New prescription of metformin	Metformin / id: N0000006631 / class type:CHEM
Counseling services	
Initial consultation with dietician/nutrition	CPT code 97802
Prevention counseling by physician	99401 or 99402
Smoking cessation counseling	99406 or 99407
Follow-up care	
Frequency of primary care visits	# per 12-month follow-up period

Medication adherence and preventive provider practices. Medication adherence will be measured using the *Medication Adherence Rating Scale (MARS)*, 4-item self-report instrument developed and tested in a wide range of populations.[67] Although the MARS is not a precise measure of adherence to the medication prescription, we believe the domains assessed (attitudes and skills associated with medication taking) are appropriate for our purpose. **Patient burden in completing all of the aforementioned measures is low in that the complete profile takes less than 30 minutes.** Preventive provider practices will be accessed through the EHR (Table 2) and data warehouse, known as Clinical and Demographic Data Retrieval: Translational Research Data Warehouse (CLEARPATH). This is a unique Cleveland-based combination of robust electronic health record clinical data and bio-specimen annotation data from several health systems in Cleveland, collected into an aggregated, de-identified limited data set available to researchers to perform queries from across the entire database. Some of its unique capabilities are: Common Data Model: Clinical data from many different sources harmonized, profiled, and mapped to a common data model to support aggregate analytic capabilities. The common data model utilizes several different mapped ontologies that enables the description of these complex data sets

across domains, information system vendors, and institutions. Person De-duplication: Utilizing a unique technology, each person in the CLEARPATH database is assigned a master person ID. This allows for constructing a single person's medical information from across multiple health care systems. This will allow information on participants undergoing care at UHHS but being admitted to another hospital in NE Ohio allowing us unprecedented access to information. Even more impressive, this is accomplished without sharing Personal Health Information (PHI) information between various institutions using a state-of-the-art, trusted privacy preservation network enabled by a hash-based matching algorithm. It is implemented in accordance with HIPAA Privacy Rules 164.514 (b) (1) and 164.514(c) which enables the source institution to re-identify patients from an identified group through approved IRB protocol. For the purposes of this study, we will use data from patients undergoing care through UHHS, but collect outcomes data from all CLEARPATH partner institutions. We acknowledge that outcomes data is likely to be missing from a significant number of patients. For example, a preventive service may be delivered to a patient from a non-CLEARPATH institution. Our primary purpose is to demonstrate a substantial relative impact of risk scoring on outcomes, rather than to measure that impact with great precision. We believe that missing data will be randomly distributed among the 4 groups of patients, and will therefore not influence our measure of relative impact. To control for changes that may occur unrelated to our pragmatic intervention of providing image based reports and how they affect physician behavior, and to possibly understand directionality of physician practices as being related to our imaging-report, we will include a non-cardiometabolic health care outcome (influenza vaccine), to determine if any change in prevention practice is specifically related to cardiometabolic care or is more general in nature. **Clinical outcomes.** Given the pragmatic nature of our trial, we will obtain clinical outcomes parameters from the electronic health record as part of routine clinical care. Sitting systolic and diastolic blood pressure, body weight, BMI, and waist circumference will be recorded routinely at clinic visits. HbA1c, lipid profile, and blood glucose will be performed by UHHS Clinical Chemistry labs using standard clinical procedures. Blood pressure is typically measured through out UHHS using automated oscillometric devices as recommended by guidelines using trained clinical staff. **A summary of all outcomes measures is provided in Table 3 below.**

Aim 2 – Compare the clinical effectiveness of communicating body fat information to the medical provider versus communicating the body fat information directly to the patient. Overall design. This aim is designed to address the hypothesis that provision of body mass/fat information directly to patients, compared with provision to the provider, will translate into changes in patient risk perception, behavior, and improved clinical outcomes. This hypothesis is consistent with the belief that many, if not most primary care providers (PCPs) or other health care providers, find it challenging to provide lay interpretations of obesity-related risk for T2D and CVD in the time available of a busy office visit for the scope of counseling needed. Most PCPs already know the risk of elevated BMI in combination with other clinical health risk indicators; the primary issues are lack of training in behavioral lifestyle counseling skills, lack of clinic time, lack of reimbursement for counseling, and lack of appropriate referral mechanisms to other allied health professionals with appropriate intensive behavioral lifestyle coaching skills which are already known to be efficacious. Moreover, patients do not always have the time or financial means to attend visits with these allied health professionals, many of whom are not covered by standard medical insurance plans. Furthermore, potentially complex explanations associated with elevated risk associated with subcutaneous vs. visceral and ectopic fat

distribution beyond body weight/BMI and other standard risk factors alone to enhance patient risk perception and induce behavioral change may not be feasible or readily accepted/understood by the patient. Therefore, it is imperative to assess whether direct provision of this information to the patient may be superior to relying on the provider to contextualize and interpret the information and relay it to the patient adequately. Given that we live in a technologically savvy and open-information world, it is possible that patients would prefer and benefit from having the direct information accessible in order to research and learn about its impact on their health risks. In this 2-by-2 factorial design (see Figure 6 above), we will randomly assign overweight/obese patients with high cardiovascular risk to provision of the report directly to the patient or to the provider. Specific Aim 2 is dedicated to the randomized comparison of the patient vs. the provider being the recipient of the body weight/fat distribution report. Given the 2x2 factorial design of this trial, the study population, randomization and allocation, data and outcomes assessments are identical to Aim 1 except for the different allocation assignment.

Study Timeline

Table 3. Study specific outcomes and timeline	**Pre-screening**	**Baseline**	**2 wk**	**3 m**	**6 m**
Estimated time requirement of visit for participant	0 hr	1 hr	1 hr	1 hr	1 hr
Chart review for eligibility (inclusion/exclusion criteria)	X				
DATA EXTRACTION FROM ELECTRONIC MEDICAL RECORDS					
Clinical Outcomes					
Clinically driven visits with assessment of weight, BMI, waist circumference and blood pressure		X		X	X
Lipid profile, HbA1c, fasting glucose		X		X	X
Physician Practices					
Medication prescriptions, referrals for weight loss counseling, and lifestyle programs		<----------> Collected throughout the study			
DATA TO BE OBTAINED DIRECTLY FROM THE PARTICIPANT					
Patient Risk Perception and Behavior					
Perception of Risk for Diabetes (RPS-DD)		X	X	X	X
Perception of Heart Disease (PRHDS)		X	X	X	X
Motivation to change behaviors (TSRQ)		X		X	
Global Physical Activity Questionnaire (GPAQ)		X	X	X	X
ASA24 Dietary instrument		X	X	X	X
Medication Adherence (MARS)		X	X	X	X

Data to be Collected for your study
(AFTER consent and HIPAA Authorization have been obtained)

See Table 3 above and description of all data to be collected in the Study Procedures section.

Data Analysis Plan

We hypothesize that provision of a detailed body fat distribution report contextualized with information describing the relevance of each body fat parameter will be superior to provision of body weight/BMI information alone on the outcomes described above. Characteristics will be compared between participants randomized to a brief vs. detailed report using chi-square tests for dichotomous variables and Wilcoxon rank-sum tests for continuous variables. All analyses will be based on the intention-to-treat principle. For continuous endpoints, an analysis of covariance model with both fixed and mixed (time-updated) effects will be used to analyze mean changes.

For categorical endpoints, logistic regression will be used with the same fixed and mixed effects and covariates as the analysis of covariance model. The models will include randomized allocation, age, sex, obesity status at baseline, T2D status at baseline, interaction between obesity and T2D status strata as fixed effects, with the baseline and subsequent values of the relevant variable as a mixed effects covariate. Effects will be reported as mean ± standard deviation or proportion in each group with between group differences reported as control group-adjusted difference with 95% confidence interval. Given the inherent nature of the study (pilot/feasibility), we also will perform separate analyses between baseline and 2 weeks, baseline and 3 months, and baseline and 6 months without adjustment for multiple testing. Although pilot/feasibility trials are, by definition, not fully powered to answer the question, we provide a basic rationale for our planned inclusion of 126 participants. This trial is powered to detect a 5% control-corrected relative reduction in body weight. The FDA considers the 5% mark for weight loss clinically significant, and uses this benchmark for development of drugs and therapeutic biologics regulated within the Center for Drug Evaluation and Research (CDER) in the Food and Drug Administration (FDA).[68] Assuming a mean 2% relative reduction in weight among control (standard weight/BMI) participants and a 7% relative reduction in weight among those provided a detailed report (with a standard deviation of 10%, based on prior data), we expect to require 126 total participants (in a 1:1 randomization scheme) to achieve 80% power to detect an 5% difference between groups at an alpha level of 0.05. Assuming an estimated 10% of participants might not attend clinical visits within the planned 6 months time frame, we expect to enroll a total of 140 participants in order to achieve at least 126 participants with outcome measures.

Study Timeline

This is a three-year study. Table 5 shows the study timeline. The research team assembly is expected to start early on in the process in the third quarter of 2021. The third quarter of 2021 will also be used to finalize study surveys/questionnaires, and establish an EHR extraction protocol with IT department. Recruitment is expected to start in the last quarter of 2021 and will continue for ~2 calendar years, through the third quarter of 2023. Clinical follow-up and follow-up questionnaire/survey administration will commence as early as recruitment of first patient and will last for 6 months after the last patient is recruited. EHR data extraction for clinical variables will also run in parallel with follow-up questionnaire administration. Data and safety monitoring (see plan below) will commence with first patient-first visit and continue through the end of study procedures, followed by an annual progress report. Analysis of data will commence in 2024, which will be followed by presentations and manuscripts.

Table 5. Study Timeline

Action Item	2021		2022				2023				2024			
	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Research Team Assembly														
Recruitment														
Follow-up														
EHR Data Extraction														
Data & Safety Monitoring														
Annual Progress Reports														

Analysis of Completed Data														
Presentations and Manuscripts														

Risks to Research Participants

Loss of Confidentiality

Although every effort will be made to keep information collected about patients confidential, there is a small risk that this information may be seen by unauthorized persons. Loss of confidentiality will be minimized by storing data in locked cabinets and electronic data will be password protected on the University Hospitals and CWRU computer network using secure research data collection software. Only de-identified and encrypted data will be sent electronically to study staff. All email with subject-identifiable information will be password protected. Only key personnel will have access to the information in the study database on an as-needed basis. Key personnel may not alter the data in the database or directly view all of it without specific cause and approval of the PI.

Risks of Magnetic Resonance Imaging (MRI)

There are no known risks from exposure to magnetic fields. Participants may experience nervousness and/or anxiety due to the loud banging made by the machine while it is taking pictures and from confinement in a tight space (claustrophobia). The study team will make all attempts to identify the potential risk for claustrophobia/anxiety prior to enrollment; however, occasionally, participants underestimate their reaction once in the scanner environment. If a participant becomes anxious, the procedure can be halted at any time. The MRI machine uses a strong magnet and radiofrequency magnetic fields to make images of the inside the body. A known risk is that the MRI scanner uses a very strong magnet that will attract some metals and affect some electronic devices. Patients with retained bullets, shrapnel, or MRI non-compatible ferromagnetic objects will be excluded from this study. Participants will be asked to remove any metal objects before entering the magnet room. University Hospitals Cleveland Medical Center standard screening guidelines for MRI safety will be followed. The participant may also feel temporary muscle stiffness and minor discomfort due to lying still during the study.

MRI may not be appropriate if the participant is pregnant. MRI may not be appropriate if the participant has permanent eyeliner or eyebrows or any pieces of metal in their body, such as the following:

- heart pacemaker, heart valve replacement, or aortic clips
- metal fragments in the eyes, skin, or elsewhere in the body
- brain clips or pieces of metal used in aneurysm surgery or intercranial bypass
- venous umbrella
- pieces of metal in the body resulting from work as a sheet-metal worker or welder
- clips placed in an internal organ
- prosthetic devices, such as middle ear, eye, joint, or penile implants
- joint replacement.
- hearing aid that cannot be removed
- neurostimulator
- insulin pump
- intrauterine device (IUD)

- shunts or stents
- metal mesh or coil implants
- metal plate, pin, screws, or wires, or any other metal implants

Reproductive risks

Being a part of this study while pregnant may expose an unborn child to serious risks. The reason for this is that the goal of the study is to lose weight. Women who are pregnant or lactating should not necessarily undergo a medical weight loss program unless it is under the supervision of their gynecologist and other treating physicians. The reason for this is that it may affect the fetus/newborn's nutritional status and growth. Therefore, pregnant and lactating women will be excluded from this study as participation in a weight loss program may pose risk to the fetus/newborn.

Psychological Stress from Survey Questions

Although only health-related information will be obtained in this study, some of the surveys relate to the potentially sensitive subject matter of patient weight/obesity. There is a small risk that some of the questions we will ask as part of this study may make the participant feel uncomfortable. The participant may refuse to answer any of the questions, take a break or stop participation in this study at any time.

Provisions to Protect the Privacy Interests of Research Participants

Loss of confidentiality will be minimized by storing data in locked cabinets and electronic data will be password protected on the University Hospitals and CWRU computer network using secure research data collection software. Only de-identified and encrypted data will be sent electronically to study staff. All email with subject-identifiable information will be password protected. Only key personnel will have access to the information in the study database on an as-needed basis. Key personnel may not alter the data in the database or directly view all of it without specific cause and approval of the PI. University Hospitals Cleveland Medical Center standard screening guidelines for MRI safety will be followed. Patients with retained bullets, shrapnel, or MRI non-compatible ferromagnetic objects will be excluded from this study. Participants will be asked to remove any metal objects before entering the magnet room. The study team will make all attempts to identify the potential risk for claustrophobia/anxiety prior to enrollment; however, occasionally, participants underestimate their reaction once in the scanner environment. If a participant becomes anxious, the procedure can be halted at any time. Pregnant and lactating women will be excluded from this study.

Potential Benefit to Research Participants

There may be direct benefit to the research participants in the form of knowledge (report) about their health status as it pertains to body weight/fatness, which may induce behavioral change to improve health. Otherwise, there is no direct benefit of the proposed research to study participants. Knowledge gained from this project will likely lead to better understanding of diabetes in the general population and across ethnic minorities and women as well as potentially lead to improved targets of therapies aimed at reducing diabetes and cardiovascular disease risk. The minimal risks outlined in this proposal are reasonable for this societal benefit as it may lead to improved care to

reduce diabetes and cardiovascular disease risk, leading causes of morbidity and mortality in the U.S.

Withdrawal of Research Participants
The study team may determine it is necessary to withdraw participants from the research without their consent if:

i. The researchers believe that participation in the research is no longer safe.
ii. The sponsor or the FDA stops the research for the safety of the participants.
iii. The sponsor cancels the research.
iv. The participant is unable to keep appointments or to follow the researcher's instructions.

Partial withdrawal from this study by the participant is highly unlikely since the intervention is a one-time provision of health information and the study endpoints are primarily survey based. However, in the event this does occur and the participant partially withdrawals from study procedures (e.g. surveys) but does not withdraw consent for inclusion in the study, the research team may still actively obtain EHR related health information for use in the study.

Alternatives to Participation
Since all treatment is part of routine clinical care and not mandated by the study, there is no specific alternative to participation other than electing not to participate in the research.

Costs to Research Participants
There will be no direct costs to research participants. All MRI acquisition, interpretation, and reporting will be funded by the study sponsor. All other study outcomes are part of routine clinical care.

Research Participant Compensation
There will be no reimbursement for study participation.

Provisions to Monitor the Data to Ensure the Safety of Research Participants
Type of Research Data or Events to be Monitored:
All research activities described in the project summary will be monitored in addition to study data accrual, protocol deviations, protocol violations, unanticipated problems, and adverse events.

Methods and Frequency of Analysis:
All research staff will have appropriate training to ensure the safety of participants, the appropriate conduct of research, and the integrity of safety and/or efficacy of data. This training includes completion of all University-required training in the policies and procedures to protect the rights and welfare of people who participate in research.

Subjects will be fully informed about the study requirements throughout the conduct of the trial by the study personnel. At the beginning of the study, it will be noted in the research record that the subject received complete information about the study requirements. Study personnel will give participants information relevant to continued participation.

The PI will perform monitoring activities. Monitoring will be performed monthly by the PI. The conclusions of the monitoring will be reported to the IRB in writing if there is any change in the risk/benefit ratio for subjects or if there is any new information which may affect a subject's willingness to continue participation. Monitoring will include consideration for (1) progress of the trial, (2) data quality, (3) timeliness of data collection, (4) recruitment, (5) accrual and retention, (6) risk vs. benefit for participants, (7) protocol violations, and (8) other factors that could affect the outcome of the study. Monitoring will be documented in the research record.

Person(s) Responsible for Data Monitoring:
The persons responsible for data monitoring in this research are Ian J. Neeland, MD and the primary study coordinator, Ann Dever. Dr. Neeland will oversee study operations. The study coordinator will be responsible for aiding in subject recruitment and retention, protocol execution, and general study coordination.

Reporting Unanticipated Problems, Adverse Events, Protocol Deviations and Protocol Violations:
The principal investigator and research coordinator will monitor subject involvement in the study on a monthly basis. An adverse event is defined as both an expected side effect that is of a serious nature, or an unexpected side effect/event regardless of severity. All events will be graded as to their attribution (unrelated to protocol, or possibly, probably, or definitely related to protocol), as well as to the severity of the event (adverse - not serious (adverse event, AE) and adverse-serious (serious adverse event, SAE)). Any event that is reported to either the PI or his designated research associates by the subject or medical staff caring for the subject and which meets the criteria will be documented as such. The PI will report all classes of unexpected adverse events and any serious adverse events within 48 hours of recognition to the Federal agencies and University and hospital offices as specified by the IRB. The PI will submit a summary of adverse events in continuing review reports to the IRB at intervals specified by the IRB. Subject identifiers will be excluded from all reports.

Stopping Rules:
Subjects will be informed of the voluntary nature of the research and their option to stop study procedures for any reason. They will also be advised that the PI may stop their participation if it is deemed to be in the subject's best interest, if new information becomes available during the research, or if a subject cannot follow study instructions or keep appointments.

Drugs or Devices
N/A

Additional Information
A partial waiver of HIPPA authorization for screening purposes will be requested. This is a waiver used only for collection of initial screening data to determine eligibility and/or recruit potential research subjects. Authorization by the subject will be obtained at the time of consent. This is justified because it is not practical to obtain a signed HIPPA Authorization form prior to review of the records of potential participants because review of records is required to screen for a participant's eligibility for study participation. This is not practical and the study could not be effectively conducted in this manner. Inclusion and exclusion criteria could not be determined

without access to the PHI. This would also not be possible with the use of de-identified information.

Community-Based Participatory Research
N/A

International information
The images obtained from the study MRI will be de-identified and sent via secure, encrypted electronic transfer to AMRA Medical, a digital health company physically located in Linköping, Sweden, for interpretation and report generation. Prior to any study procedures, a formal contract and data transfer/data use agreement will be executed between University Hospitals and AMRA Medical to ensure confidential, secure transfer of data. The PI is already working with the UH Office of Research Compliance/Legal (Lynsay Carrigan) and Research IT (Donna Gattis) to ensure all requirements are satisfied for collaboration with this international company.

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