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## I. PURPOSE BACKGROUND AND RATIONALE

### A. Aim and Hypothesis

#### A1. Introduction

Nearly 20% of the U.S. population lives in rural communities. These rural residents suffer disproportionately from obesity and obesity-related illnesses, including diabetes, heart disease, and arthritis. Primary care is an important resource for treating obesity in rural areas because of a lack of other community resources. Currently, primary care practices operate under the Centers for Medicare and Medicaid Services (CMS) fee-for-service (FFS) model, but there are wide variations in practice patterns, and only 20 to 40% of patients living with obesity receive counseling from their primary care physician (PCP). Patient centered medical home (PCMH) and disease management (DM) models of care are two viable alternatives that address provider barriers and provide enhanced patient access, yet no studies have directly compared these two approaches to the FFS model. These models include **in-clinic individual visits (FFS), in clinic group visits (PCMH), and phone group visits (DM)**. This comparison is especially relevant in the rural setting given the higher obesity prevalence, related health disparities, and limited access to evidence-based community weight loss programs.

#### A2. Aims and hypotheses

##### *Primary Aims:*

1. Test the hypothesis that **PCMH (in clinic group visits)** is more effective than **FFS (in clinic individual visits)** in reducing weight at 24 months.
2. Test the hypothesis that **DM (phone group visits)** is more effective than **FFS (in clinic individual visits)** in reducing weight at 24 months.

##### *Secondary Aims:*

3. Test the hypothesis that **DM** is more effective than **PCMH** in reducing weight at 24 months.
4. Compare the effects of the three arms on patient-centered outcomes, including blood pressure, laboratory measures (fasting glucose and lipids), quality of life, sleep, and stress.
5. Assess heterogeneity of treatment effects across participants based on race/ethnicity, education level, income level, employment status, and distance traveled to receive care.
6. Evaluate the reach and sustainability of the three arms following the RE-AIM evaluation framework.<sup>1</sup>

##### *Hypotheses:*

1. **PCMH** is more effective than **FFS** in reducing weight at 24 months.
2. **DM** is more effective than **FFS** in reducing weight at 24 months.
3. **DM** is more effective than **PCMH** in reducing weight at 24 months.
- 4a. **PCMH** is more effective than **FFS** at improving patient-centered outcomes, including blood pressure, laboratory measures (fasting glucose and lipids), quality of life, sleep, and stress.
- 4b. **DM** is more effective than **FFS** at improving patient-centered outcomes, including blood pressure, laboratory measures (fasting glucose and lipids), quality of life, sleep, and stress.
5. **DM** and **PCMH** will show larger effects over **FFS** for those with lower education, lower income, who travel longer distances to receive care, and who are employed full-time.
6. Aim 6 includes exploratory qualitative and quantitative process measures with no explicit hypotheses.

## B. Background and Significance

### B1. Study significance

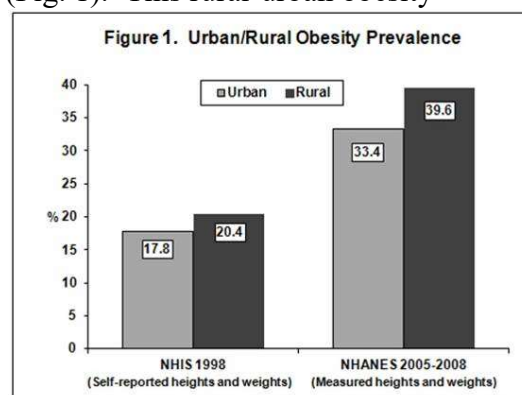
#### *Health burden of obesity*

Obesity in the U.S. has been characterized as an epidemic increasing from a prevalence of 14% in 1980<sup>2</sup> to 35% in 2010.<sup>3</sup> Far from simply a cosmetic condition, obesity is associated with serious morbidity, mortality, disability, and lost productivity.<sup>4</sup> Obesity is associated with a 7-fold increased risk of Type 2 diabetes<sup>5</sup> with the diabetes epidemic paralleling that of obesity. Obesity is also associated with an increased risk of myocardial infarction, hypertension, arthritis, sleep apnea, asthma, cancer, and disability.<sup>6</sup> The annual health care costs associated with obesity are estimated to be as high as \$200 billion per year.<sup>7</sup>

#### *The health burden of obesity in rural America*

Obesity disproportionately affects rural Americans, a growing disparity that we demonstrated with data from the 2005-2008 National Health and Nutrition Examination Survey (Fig. 1). This rural-urban obesity disparity exists for Whites and racial/ethnic minorities alike.

The higher obesity prevalence among rural Americans is accompanied by higher rates of heart disease and diabetes and a 32% higher age-adjusted death rate compared to urban residents outside of the inner cities. Moreover, rural residents constitute one of the largest medically underserved populations in the nation representing over 20% of the U.S. population and 25% of the Midwestern U.S. population.<sup>8,9</sup> Decreasing rural health disparities is a high national priority as outlined in the agendas of Health and Human Services,<sup>10</sup> the Surgeon General,<sup>11</sup> and the CDC.<sup>12</sup>



### B2. Facts, events, thought processes

This study was designed in response to a RFA from Patient Centered Outcomes Research Institute (PCORI) titled “Obesity Treatment Options Set in Primary Care for Underserved Populations: Pragmatic Clinical Trials to Evaluate Real-World Comparative Effectiveness.” The RFA required a comparative effectiveness cluster randomized trial where the current fee-for-service care delivery model (modeled after the Intensive Behavior Therapy provision from Medicare, as described below) was the comparator arm. The RFA also specified the age and BMI eligibility criteria, the primary endpoint (weight change at 2 years) and stipulated that the active arm (or one of the active arms with a 3-arm trial) include a minimum of 14 face-to-face counseling visits.

The PI was in the process of planning a rural primary care trial addressing obesity at the time the RFA was released, in response to observations made in her current trial examining delivery of a weight control intervention among rural breast cancer survivors. Observations from that trial and our prior research had confirmed what we have seen in the literature regarding a lack of resources and evidence-based programs or commercial programs in the rural setting. In addition, we heard first-hand from many participants the importance of encouragement and assistance from their PCP in maintaining their motivation for weight control behaviors, however most participants had not even spoke to their PCPs about their weight.

In preparation of the grant proposal, we convened our Patient Advisory Board (PAB) and spoke with rural PCP stakeholders to solicit input on the study design, intervention components, and measures. Our PAB expressed a uniform desire for help and encouragement from their PCPs but did not want to travel long distances and wait in the clinic to be seen for a brief PCP obesity counseling visit. They would be more

willing to travel for more intensive visits or group visits. They were particularly interested in telephone-based programs and e-mail or text message support that might allow them to avoid travel and long waiting times. PCP stakeholders were also skeptical about the feasibility of physicians themselves providing intensive counseling for obesity. Most of our providers were, however, in the process of implementing a patient-centered medical home (PCMH), and consistent with PCMH delivery models, they were intrigued about training one or more members of their staff to coordinate and deliver obesity treatment. Others were more interested in a ‘diagnosis and referral’ model such as the remote phone-based ‘disease management’ model that we describe below. All noted the importance of having the right infrastructure and training to provide obesity treatment. These insights drove our choice of study treatment conditions.

### **B3. Literature review**

#### ***Disparities in access to obesity treatment***

Rural residents report a lack of healthy lifestyle and weight control programs in their communities. Although evidence-based commercial programs offering in-person support such as Weight Watchers are available in some large rural towns, this is not the norm. With much of the rural population living in isolated areas there is a substantial distance barrier for these types of programs.<sup>13</sup> Although the majority of rural residents now have internet access,<sup>14</sup> a digital divide remains for older rural resident. In addition, the effectiveness of web-based programs has been mixed especially during extended care for weight loss maintenance. With limited availability of evidence-based programs, many rural residents who are interested in losing weight are not practicing effective strategies. Most rural residents do however, have a primary care provider<sup>15</sup> and look to their physician to guide them towards healthy lifestyles. As such, primary care in rural areas has the potential to fill a major gap in weight loss intervention.

#### ***Rural patient preferences and barriers***

When asked about their preferences for obesity treatment, patients state that they want information about their individual weight-related health risks, personalized advice delivered in an encouraging and non-judgmental manner, and referrals to programs. In contrast to what patients want, many report feeling judged or experiencing weight-related bias from their doctors.<sup>16</sup> In a survey we conducted in rural primary care practices, we found that patients were more motivated and more optimistic about losing weight than their providers thought. These differences in perceptions have implications for the quality of patient-physician interactions and ultimately patient behavior change. In our qualitative research among obese rural patients, participants stated that they want their PCPs to address weight, but they felt this rarely occurred. They looked to primary care offices as a potential community resource for lifestyle programs that were otherwise lacking in their communities. Taken together, these findings suggest that from patients’ perspectives, the PCP’s role should be to provide encouraging brief advice and referrals, which in the rural setting could include referral to programs either inside or outside of the primary care office.

#### ***Treatment of obesity in primary care not living up to its potential***

The U.S. Preventive Services Task Force recommends that clinicians screen for obesity and offer intensive multicomponent behavioral obesity treatment (12-26 sessions in the first year) either by providing the treatment themselves or by referring patients to other providers.<sup>17</sup> This is not routinely happening. Primary care providers (PCPs) across a variety of settings often fail to diagnose obesity and offer weight loss counseling to only 20-40% of obese patients. Direct observations of PCPs have shown wide variations in the provision of weight loss counseling,<sup>18</sup> with greater inconsistency and less specific recommendations compared to counseling for other behaviors such as smoking cessation.<sup>19</sup> When counseling is provided, it tends to be brief and far short of the intensity needed to drive meaningful weight change. This brief PCP counseling, even when provided at monthly visits, has produced weight losses at one year of only 0.1 to 1.0

kg.<sup>20</sup> Systematic reviews have concluded that low intensity PCP counseling is not sufficient to achieve clinically meaningful weight loss. This study will examine the viability of two alternative models of care for obesity treatment in rural settings. PCPs cite multiple barriers including limited time, inadequate counseling expertise, and limited treatment effectiveness. Providers report additional barriers in rural communities, including the patient's reluctance to go to the doctor until they are ill, increased distance patients have to travel for an appointment, lower health literacy, and lack of referral services<sup>21,22</sup>.

#### ***Fee for service obesity treatment in primary care: the current reimbursable model of care***

The existing model for healthcare reimbursement, based on fee-for-service (FFS) delivery, may be a major contributor to the poor quality of obesity treatment in America. In 2011, the Centers for Medicare and Medicaid Services (CMS) approved the provision of intensive behavioral therapy for obese patients when delivered by PCPs (physicians, nurse practitioners, or physician assistants).<sup>23</sup> The CMS provision covers 15 min weekly counseling sessions for one month, followed by bi-weekly sessions for 5 months. Those who lose  $\geq 3$  kg are eligible for an additional 6 monthly sessions. While this provision covers more intensive counseling than the brief relatively ineffective PCP-delivered approaches described above, its effectiveness remains unknown. Payment for the counseling sessions are made on a fee-for-service basis with little regard to the skills or training of the provider or the resources needed to provide effective treatment. The uptake of this CMS provision appears to be slow, e.g., none of our 36 interested practices are providing or billing for this care, and 80% were not even aware of it. Without appropriate training PCPs appear to be ill-equipped to provide intensive behavior therapy in a manner patients prefer.<sup>24</sup> Moreover, this model requires frequent in-person visits during clinic office hours, posing scheduling barriers for practices and limiting access for patients, especially those who travel long distances to receive care or who work full-time during regular business hours. This study will examine the viability of two alternative models of care for obesity treatment in rural settings.

#### ***Alternative models for obesity treatment in primary care***

The failure of the FFS system in management of chronic illness has been well described and includes failure to provide consistent preventive care services, shortcomings in diabetes care, and failure to control hypertension.<sup>25</sup> These failings have led to calls for major changes in healthcare delivery design<sup>26</sup> and stimulated proposals for population-based approaches that recognize the need to empower patients and extend treatment services outside of the confines of the practitioner's office. In the U.S. healthcare system, two alternative models have evolved to improve chronic disease management: the patient-centered medical home (PCMH)<sup>27</sup> and centralized disease management (DM).<sup>28</sup> Both the PCMH and DM approaches offer coordinated delivery of services that extend beyond the limitations of a face-to-face office visit. The major difference between the two approaches is that with the PCMH model, the coordination of services is retained within the primary care practice whereas with DM, services are coordinated by a centralized provider that may care for patients across multiple practices. Both PCMH and DM approaches allow for delivery of services by health professionals based on their expertise rather than their ability to bill for their services. This opens the door for delivery of services by professionals with more specific training in behavioral counseling and obesity management. PCMH and DM models are the two most prominent alternatives to coordinating care for chronic diseases. In this study, we will compare both PCMH and DM approaches to the FFS model.



## C. Rationale

### C1. How the literature supports the proposed hypotheses

Prior research supports the hypotheses that both PCMH and DM models will outperform the traditional FFS model.

#### ***The PCMH model for addressing obesity treatment in primary care (in clinic group visits)***

The PCMH model uses care coordinators to organize care across providers, support patients in managing their health, and provide increased accessibility for patients with improved scheduling, extended hours, and phone/email communication.<sup>29</sup> Members of the PCMH team may include registered dietitians and nurses specially trained in behavioral counseling. Patients have described the PCMH model with the tagline “Healthcare that Revolves Around You.”<sup>30</sup> The number of practices meeting the National Committee for Quality Assurance (NCQA) PCMH designation has dramatically grown from 28 practices at the end of 2008 to over 6,800 in 2014.<sup>31</sup> In rural areas, adoption of the PCMH model has been stimulated by federal funding initiatives.<sup>32</sup> Studies on the benefits of PCMHs have been largely favorable with improved quality of care and cost savings.<sup>33</sup> Preliminary evidence supports a PCMH model for treating obesity. Prior studies within primary care offices have shown greater weight loss when counseling is provided by registered dietitians or other auxiliary health professionals rather than PCPs, with weight losses ranging from 2.9 to 5.1 kg at 24 mo. Mayer-Davis et al. conducted a PCMH-like pilot weight loss study in two rural practices in South Carolina among patients with diabetes. Compared to the control arm, they found significantly greater weight loss in patients receiving the PCMH-like intervention that incorporated a disease registry, care coordination, and counseling sessions delivered by a registered dietitian in the PCP’s office.

#### ***The DM model for addressing obesity treatment in primary care (phone visits)***

The DM model involves centralized remote care coordination through phone-based assessments and counseling. Driven by some notable early successes, the DM industry has grown substantially over the past decade and is now widely used by insurers, health maintenance organizations, and employee wellness programs.<sup>34</sup> A 2013 survey of employer health benefits showed that 57% offer disease management.<sup>35</sup> Systematic reviews of disease management programs have identified common features associated with success, including patient education, feedback, and accountability—elements that we have incorporated into the design of our program. One of the primary drawbacks of disease management programs has been a lack of integration with the participant’s PCP. Participants are typically recruited through administrative databases, and health coaches often do not have any interaction with the PCP caring for the patient. Our proposed intervention will overcome this limitation by incorporating a DM model that recruits patients within the context of the PCP’s office and provides regular feedback to the PCP on the participant’s goals, barriers, and progress.

There is already a strong evidence base to support the DM model for obesity treatment. Appel et al. conducted an effectiveness trial in primary care comparing a remote phone-based program delivered by a disease management company versus an in-person program with group and individual sessions delivered from an academic medical center. Results showed that both treatment groups lost significantly more weight at 24 months compared to the control group (4.6 kg in the remote arm and 5.1 kg in the in-person arm), with no differences between the two active intervention groups. Additional trials conducted by members of our team with the intervention delivered from an academic medical center<sup>36</sup> and in the rural community setting<sup>37</sup> have shown equal effects across phone-based and in-person interventions and greater cost-effectiveness from phone-based approaches. In our prior studies in the rural community setting, our phone-based interventions have resulted in weight losses ranging from 10.0 to 12.5 kg at 6 months and 8.8 to 10.2 kg at 18 months. We

also conducted a pilot study of a DM-like intervention in three primary care practices in isolated frontier areas of western Kansas. Using the chronic care model<sup>38</sup> as a guide, we used a behavioral specialist to provide a series of 8 individual phone counseling sessions to obese patients and engage the PCP through periodic progress reports. The results were promising with 4.3 vs. 0.9 kg of weight loss in the intervention and control groups, respectively. A process analysis showed that the intervention needed a higher intensity of sessions, more incorporation of behavioral strategies, and better integration into the practice setting as we propose to do in this study.

## **C2. Advancing knowledge in the field**

Primary care is an important resource for obesity treatment in the rural setting, however, PCPs face numerous barriers for delivering intensive weight loss counseling themselves. The fee-for-service approach to obesity treatment embodied in Medicare reimbursement policy may not be consistent with patients' desires or practitioners' perceived needs. PCMH and DM models of care are two viable alternatives that could provide enhanced patient access, yet no studies have directly compared these two approaches to the fee-for-service model. Both the PCMH and DM models are consistent with the interests of patients, providers, and other stakeholders in that they provide alternatives to the traditional in-person office visit. Moreover, both of these models are being adopted throughout the country for other diseases, thereby enhancing the potential for widespread dissemination and adoption should they prove effective.

## **C3. Improving obesity treatment in rural America**

The comparison of primary care delivery models is especially relevant in the rural setting given the higher obesity prevalence, related health disparities, and limited access to evidence-based community weight loss programs. As such, primary care has the potential to fill a major gap in access to evidence-based weight control programs in rural America. Not only will our study identify which of the three approaches is most effective, but our process evaluation will provide valuable information on how these treatment models can be successfully implemented in rural primary care practices.

# **II. RESEARCH PLAN AND DESIGN**

## **A. Study Objectives**

**Research Goal:** To advance our knowledge of obesity treatment in rural primary care by directly comparing the effectiveness of two alternative models of care with the current standard of care. If the hypotheses are correct, the results may warrant a new standard of care for obesity treatment in rural primary care practices.

**Study Aims:** The primary aims of the study are to test the hypotheses that both the PCMH model (with in clinic group visits) and DM model (with group phone visits) are more effective than the currently reimbursed FFS model (with in clinic individual visits) in reducing weight at 24 months.

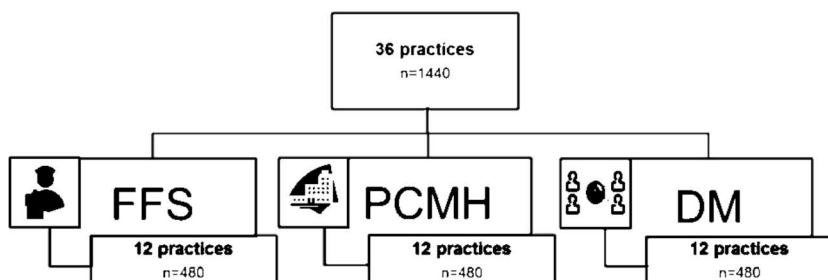
The secondary aims of the study are to 1) test the hypothesis that the DM is more effective than the PCMH model in reducing weight at 24 months, 2) to compare the effects of the three arms on patient-centered outcomes (i.e. blood pressure, fasting glucose and lipids, quality of life, sleep, and stress), 3) to assess the heterogeneity of treatment effects across demographic subgroups (i.e. race/ethnicity, education level, income level, employment status, and distance traveled/travel time to receive care), and 4) to evaluate the reach and sustainability of the three arms following the RE-AIM evaluation framework.<sup>1</sup>

**Statement of Purpose:** The purpose of this study is to test the comparative effectiveness of three viable treatment models for addressing obesity in rural primary care.

## B. Study Type and Design

The study is a cluster randomized pragmatic trial comparing **PCMH (in clinic group visits)** and **DM (phone group visits)** to **FFS (in clinic individual visits)** in 36 rural primary care practices throughout the rural Midwestern U.S (Figure 2). The FFS condition will include PCP delivered (or supervised) obesity counseling sessions following the session schedule reimbursed by the Medicare Intensive Behavioral Therapy provision.<sup>23</sup> The PCMH and DM arms will include a common group-based evidence-based comprehensive lifestyle intervention, but the delivery mechanism will differ. In the PCMH arm, the intervention will be delivered by personnel within the office practice using in-person group office visits, option to switch to group phone conference calls, plus individual phone contacts and email/text support as deemed feasible and appropriate by the practice. PCMH practices will receive intensive and on-going training to build their capacity for delivering this care. In the DM arm, the intervention will be centrally delivered by obesity treatment specialists using group visits via conference calls, and patient progress will be routinely communicated back to the PCPs. The primary outcome is weight loss at 24 months, and secondary endpoints include other patient-centered outcomes. See study flow for more details (Figure 4; page 27)

Figure 2. Study Design



## C. Sample Size, Statistical Methods, and Power Calculation

### C1. Analytic and statistical methods (including randomization)

**Randomization.** Thirty-six primary care practices from the rural Midwestern U.S. will be randomly allocated in equal proportions (1:1:1) to each of the three arms (FFS, PCMH, DM). Randomization will be stratified by institutional affiliation (KUMC, UNMC, Marshfield Clinic) within three cohorts.

**Missing data.** Based on our prior history using a similar retention plan in the rural setting, we expect to retain a minimum of 80% of participants (with a goal of 90%) at 24 months across all three treatment arms. We will document reasons for loss to follow-up. Participants who are removed from study for pregnancy, bariatric surgery, medical safety reasons, behavioral problems, or death will be excluded from analyses. All primary analyses will be conducted using intent-to-treat. We will evaluate the missing data pattern for differential loss to follow-up based upon treatment arm. All of the covariates (other than the outcomes) will be collected at baseline, and with our data quality controls we don't expect this data to be missing. In the absence of differential loss to follow-up, missing weight data will be treated as missing at random and addressed using maximum likelihood methods.

**Primary aims 1-3: weight loss at 24 months and leading up to 24 months**

Weight loss at 24 months will be compared between PCMH vs FFS and DM vs FFS, as well as DM vs PCMH. Hierarchical linear mixed models will be used to examine the group differences, accounting for the correlation between patients from the same clinic.

We will fit a hierarchical linear mixed model with longitudinal weight change at 6, 18, and 24 months study visits. This model will account for the correlation between patients in the same clinic as well as correlation of measures from the same patient. In secondary analysis, percent weight loss will also be compared across the three groups using the same approach. Clinical cutpoints of 5% and 10% will be compared across arms at 6 and 24 months using generalized linear mixed models. The analytical plans may be adapted to provide the best approach using the latest methodological advancements.

**Secondary aim 4: patient-centered outcomes**

Each patient-centered outcome at 24 months (and all relevant intermediate study visits) will be compared across all treatment arms using separate hierarchical linear mixed models.

**Secondary aim 5: assess heterogeneity of treatment effects (HTE) across participants**

We anticipate treatment effects will vary across participants based on characteristics identified by the literature and by our patient partners as important for service utilization. Specifically, we hypothesize that DM and PCMH will show larger effects over FFS for racial/ethnic minorities (compared to White non-Hispanic), those with lower education (less than Bachelors degree), and those with lower income (e.g., less than \$50K household income). This is because the more intensive treatment in DM and PCMH may be especially important for subgroups who have fewer resources and face greater life stress,<sup>39</sup> as is often the case for rural minorities in a predominantly White rural Midwestern region.<sup>40,41</sup> We also hypothesize that DM and PCMH will show larger effects over FFS for participants who travel longer distances/have longer travel time to receive care or who are employed full-time because the traditional face-to-face office visit during regular clinic hours may limit their uptake of treatment. We will also explore interactions between treatment conditions and weight loss history (particularly any history of seeking assistance for weight loss)<sup>42</sup> as participants with prior knowledge and skills for successful weight loss may benefit more from the brief counseling provided in FFS. Using separate hierarchical linear mixed models predicting weight loss over 24 months, we will examine interactions between each participant factor and treatment arms.

**Secondary aim 6: evaluate the reach and sustainability of the interventions with the RE-AIM framework (Reach, Adoption, Implementation, Maintenance)**

Adoption within KUMC-affiliated sites will be evaluated by comparing practice characteristics across participating and non-participating practices (that were contacted about the study) using two sample comparisons (chi square or t-tests). After aggregating to the practice level, patient-level factors for reach (e.g., participation rates) and implementation (e.g., session attendance, ratings of care) will be tested and compared across arms using separate analysis of variance (ANOVA) models. Maintenance of weight loss services at the practice-level will be reported as simple frequencies.

**Potential confounders:** For all statistical models, sensitivity analyses will be performed using the models above but also adjusting for potential confounders among the baseline variables identified as varying across arms based on their standardized differences.

**C2. Blinding**

Randomization happens at the practice level. Blinding practice staff or study staff is not feasible during a behavioral trial. However, throughout the study investigators and study personnel will communicate and

demonstrate equipoise (genuine uncertainty) with practice staff and patients about the relative benefit of the three arms.

### **C3. Power calculation and sample size**

A total of 36 practices with 40 participants per practice will be enrolled in the study (1440 participants total). Twelve practices (480 participants total) will be enrolled in each arm (FFS, PCMH, DM). A net treatment effect of 2.75 kg is supported by the available literature and our previous work. Treatment effects for PCP counseling alone with varying levels of intervention intensity have ranged from 0.1 to 1.7 kg at 12 to 24 months follow-up with the majority falling below 1 kg.<sup>43</sup> For this pragmatic trial conducted in underserved rural areas, we expect the FFS treatment effect to fall in the lower end of this range. Team-based care approaches with obesity counseling delivered by auxiliary staff (PCMH) have ranged from 2.9 to 5.1 kg at 24 mo. In an entirely remote disease management program, Appel et al. reported weight loss of 4.6 kg at 24 mo. Our remote group phone-based program currently being delivered outside the primary care setting has shown 10.2 kg loss at 18 mo in preliminary analyses. We expect this to be lower in a pragmatic primary care trial, however a net effect  $\geq 2.75$  kg is achievable. To determine sample size, we set the type I error at 0.025 (overall type I error rate of 0.05 for first two aims), intraclass correlation coefficient at 0.05,<sup>44</sup> and 40 patients/clinic. With 36 clinics, the trial will have 80% power to detect a net treatment effect of 2.75 kg (SD = 8).

## **D. Subject Criteria**

### **D1. Inclusion criteria**

Patients of both genders and all races will be eligible for this study if they are between the ages of 20.0 and 75.0, have a BMI between 30.0 kg/m<sup>2</sup> and 45.0 kg/m<sup>2</sup>, reside in a rural location as defined by Rural-Urban Commuting Area (RUCA) Codes, Urban Influence Codes, amount of agricultural income, and/or individual commuting patterns,<sup>45</sup> and have clearance from their primary care provider to participate in a diet and exercise weight control intervention. Participants must have access to a telephone. One individual per household will be permitted to enroll in the study. Patients who are eligible but unable to attend at least some of the counseling visits according to the type, location, and frequency specific to each arm will be documented as eligible but declined, with the reason noted.

### **D2. Exclusion criteria**

As a pragmatic trial, the exclusion criteria were kept minimal to maximize generalizability and reduce patient screening burden but include necessary exclusions to minimize safety concerns and major confounds on the primary endpoint. Individuals with a history of bariatric surgery or planned bariatric surgery within 2 years, myocardial infarction (MI) in the last 6 months, stroke in the last six months, new cancer diagnosis in the last six months (with the exception of non-melanoma skin cancer), pregnancy in the last 6 months/planned within the next 2 years or currently lactating, and serious medical conditions where weight loss is contraindicated will be excluded from the study. A history of miscarriage in the last 6 months, in and of itself, will not be considered an exclusion. Individuals with end stage renal disease, known GFR < 25, current or anticipated dialysis or transplant within the next two years will be excluded; a history of renal transplant is not an exclusion per se if patient does not meet stated renal criteria. Similarly, patients with end stage liver disease or anticipated liver transplant within the next two years will be excluded; a history of liver transplant is not an exclusion per se, if patient does not meet stated hepatic criteria. Other medical contraindications will be determined by the patient's PCP, and documented PCP clearance will be obtained. Participants who are already enrolled in, or planning to enroll in another research study where weight loss is targeted will be excluded. Participants who plan to relocate outside of their provider's service area or who

plan to leave their primary care clinic in the next two years will be excluded. Participant eligibility screening, assessments, and counseling sessions will be delivered in English; individuals who do not speak English will be unable to participate in the study.

### **D3. Withdrawal/termination criteria**

#### *Medical Removal for Safety Purposes*

Participants who experience an injury or new medical condition for which exercise or weight loss may be contraindicated will be asked to see their medical provider for treatment and evaluation. After consultation with the KUMC study physician and/or the practice study PCP, participants will be removed from the study if the onset of a medical condition contraindicates their participation. Participants will be removed for pregnancy past the first trimester and bariatric surgery while on study.

Members of the study team, the care coordinators/counselors, and the PCPs retain the right to remove a participant from the study if it is deemed that the participant is unsuitable for group or individual weight loss counseling sessions due to behavioral problems caused by mental illnesses, substance abuse, or any other reason.

### **D4. Other studies**

Participants enrolled in this study may not participate in other research studies where weight loss is targeted.

## **E. Specific Methods and Techniques Used Throughout the Study (Figure 4. Study Flow; page 26)**

### **E1. Laboratory tests**

Blood draws will occur at baseline, 6 months, and 24 months. Blood draws will be collected at the local practices by a phlebotomist or nurse. The practice staff will monitor and record self-reported fasting compliance. The collection, processing, analysis and storage of samples will differ depending on the site.

#### *KUMC and UNMC Affiliated Practices*

A phlebotomist or nurse will collect 5 ml of blood in an appropriate vacutainer-type tube specified by the analyzing laboratory. Practices with in-house analyzing labs will process the samples onsite prior to analysis according to their standard operating procedures. Practices that send samples off-site for testing will send either whole blood samples off-site or will process samples prior to shipment, again, according to their standard operating procedures. Study samples will be analyzed for fasting glucose and a lipid panel, to include LDL, HDL, triglycerides, and total cholesterol. Laboratory results will be sent to the patient's PCP per their normal standard operating procedures. Practice staff, in turn, will provide the laboratory results to KUMC study personnel.

#### *Marshfield Clinic Health Practices*

The ten Marshfield Clinic Health Practices participating in the study will use Marshfield Laboratories as their clinical laboratory testing facility. Marshfield Clinic Research Institute's (MCRI) Integrated Research and Development Laboratory (IRDL) will be used as the bio-storage facility for the study. All freezers, refrigerators, centrifuges, and analytical instruments used for the study are monitored at least annually for safety and performance; daily temperature monitoring of refrigerators and freezers is conducted.

Practices will be provided study lab kits for efficient specimen collection and processing. Kits will be assembled by study staff members or IRDL staff, and will include the following: a biohazard bag, absorbent material, specimen collection containers to include one lithium-heparin green top plasma tubes (GTPT) (5

ml) and two lavender top tubes (LTT), a sample transfer tube, a clinical lab requisition (for Marshfield Lab use) and a processing lab slip (for IRDL use). Staff will use the kits to obtain samples from the subjects at their scheduled data collection visits. A total of 15 mls of blood will be collected from each patient at each visit when labs are required.

Staff at practices remote to the main Marshfield Lab will process the GTPT samples on site in accordance with laboratory protocols. The processed GTPT samples and LTT tubes will then be sent to Marshfield Lab via the Marshfield Lab courier system. The courier service provides regular daily stops at the practices (M-F). Samples collected at practices located on the Marshfield Main campus will not be processed at the practices, but rather transported to the main lab for processing and analysis via the laboratory's automated transport system.

All samples will be received by the Marshfield Labs specimen processing staff. The GTPT aliquoted plasma will be used to assay the fasting glucose and lipid panel (total cholesterol, triglycerides, HDL, LDL). Test results will be imported into each patient's MCHS electronic health record. Study staff will enter the laboratory data into REDCap, the study database. Primary care providers will be automatically notified per normal procedures when results are flagged for review.

LTT samples and the IRDL lab slip will be retrieved from the Marshfield Lab by IRDL staff. Samples will be processed in accordance with instructions on the lab slip. The resulting plasma and buffy coat layer will be stored separately in multiple aliquots. Each processed sample will retain Study ID and visit number identification and will be stored in a -80°C freezer. Samples from patients who do not give consent for future storage and use will be destroyed at specific time points during the study period.

## **E2. Study Procedures**

### **E2a. Intervention overview**

An overview of the three intervention arms is provided in Table 1. Below we describe the basic training we offer to all participating PCPs, the FFS (comparator) arm, the PCMH intervention, and the DM intervention. Both the PCMH and DM conditions offer a common, evidence-based, group-based comprehensive lifestyle intervention. The recommendations for caloric intake and physical activity will be consistent across all three arms. The intervention manual and session frequency are the same across PCMH and DM but the delivery model differs. Table 2 summarizes practice personnel roles.

**Table 1. Clinic Roles, Training, and Office Support by Condition**

	<b>Fee-for-Service</b>	<b>PCMH</b>	<b>Disease Management</b>
Obesity counselor	PCP or clinic-employed auxiliary health professional under PCP supervision	Care Coordinator/counselor (clinic-employed nurse, registered dietitian, or behavioral counselor)	Remote obesity treatment specialist
Session Type and Frequency	Individual in-person, 15 min <ul style="list-style-type: none"> <li>• Weekly for mo 1</li> <li>• Every other week for mo 2-6</li> <li>• Monthly for mo 7-24</li> </ul>	Group visits in-person, 60 min <ul style="list-style-type: none"> <li>• Weekly for mo 1-3</li> <li>• Every other week for mo 4</li> </ul> Group visits by phone or in-person, 60 min <ul style="list-style-type: none"> <li>• Every other week for mo 5-6</li> <li>• Monthly for mo 7-24</li> </ul> Email and text support as needed and feasible	Group visits by phone, 60 min <ul style="list-style-type: none"> <li>• Weekly for mo 1-3</li> <li>• Every other week for mo 4-6</li> <li>• Monthly for mo 7-24</li> </ul> Email and text support as needed
PCP Role	Provide sessions or supervise and be immediately available during the counseling visits	Follow-up and provide encouragement in routine medical visits	Follow-up and provide encouragement in routine medical visits
Patient Care Coordination	Centered on face-to-face visit only	<ul style="list-style-type: none"> <li>• Group visits to enhance peer social support</li> <li>• Care Coordinator/counselor encouraged to summarize and share patient's progress with PCP</li> </ul>	<ul style="list-style-type: none"> <li>• Group phone visits to enhance peer social support</li> <li>• Text/email support in between visits</li> <li>• PCP receives individual patient reports from remote provider</li> </ul>
PCP and Counselor Training	<ul style="list-style-type: none"> <li>• Half-day training on assessing and treating obesity</li> <li>• IBT toolkit including session guide and patient hand-outs modeled after 5 A's approach, instructions for dietary assessment and feedback, and web-based resources</li> </ul>	<ul style="list-style-type: none"> <li>• Half-day training on assessing and treating obesity</li> <li>• For care coordinators/counselors: <ul style="list-style-type: none"> <li>○ Full-day workshop on group visits</li> <li>○ Bi-weekly to monthly telementoring</li> <li>○ Standardized session-by-session treatment manual</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Half-day training on assessing and treating obesity</li> <li>• For obesity treatment specialists: <ul style="list-style-type: none"> <li>○ Relevant graduate degree and experience with weight loss counseling</li> <li>○ Weekly training/quality control</li> <li>○ Fidelity monitoring of audio-recorded sessions</li> </ul> </li> <li>• Standardized session-by-session treatment manual</li> </ul>
Office Support/ Practice Facilitation	Assistance with: <ul style="list-style-type: none"> <li>• developing patient registry</li> <li>• identifying appropriate practice staff to deliver counseling sessions</li> </ul>	Assistance with: <ul style="list-style-type: none"> <li>• developing patient list</li> <li>• design and conduct of group visits</li> <li>• identifying appropriate practice staff to deliver counseling sessions</li> <li>• developing systems to track group visits and email/text contacts</li> </ul>	Assistance with: <ul style="list-style-type: none"> <li>• developing patient list</li> <li>• integrating progress reports from remote provider into electronic medical record</li> </ul>



**Table 2. Practice Personnel Roles**

Personnel	Role
<b>Primary Care Provider</b> (MD, DO, PA, or NP)	<ul style="list-style-type: none"> <li>• Study Champion</li> <li>• Provides counseling in the FFS arm or supervises health professional</li> <li>• Provides feedback and encouragement in PCMH and DM arms</li> </ul>
<b>Practice Liaison</b> (office manager, nurse, etc)	<ul style="list-style-type: none"> <li>• Point of contact at practice</li> <li>• Communicates regularly with study team at KUMC</li> <li>• Schedules participants, ensures forms are completed, and protocols are being adhered to</li> </ul>
<b>Care Coordinator/Counselor</b> (nurse, dietitian, or behavioral counselor)	<ul style="list-style-type: none"> <li>• Provides counseling in the PCMH arm</li> <li>• Oversees and organizes enrolled participants' care</li> <li>• <i>Can be same person as Practice Liaison</i></li> </ul>

**E2b. Provider training**

**Obesity 101.** Participating PCPs in all treatment arms will complete basic training on obesity, weight management and communication techniques. This training will be sufficient to enable PCPs (or other clinicians under PCP supervision) to implement the FFS counseling or provide support to patients during routine medical visits in any of the arms. The training will be the same across all three treatment arms and will address the core elements required for Medicare reimbursement for Intensive Behavioral Therapy, including implementation of dietary assessments and counseling based on the 5 A's model (Assess, Advise, Agree, Assist, Arrange).<sup>46</sup> The training will take place in-person at our central training and via televideo and on-line resources for practice staff who cannot attend the central training. The training will be provided to PCPs along with any staff who will be involved in delivering the intervention in all three arms. The training will cover effective communication and motivational interviewing strategies for encouraging patients to lose weight. We will specifically address potential issues of weight bias and educate providers on how they can show empathy for patients struggling with weight loss. The training will include tools that can be incorporated into practice, including instructions for dietary assessment and feedback, evidence-based guidelines for diet and physical activity recommendations, and patient hand-outs.

**Practice facilitation.** To assist practices with implementing study-related activities, a Practice Coordinator (central study personnel) will provide practice facilitation to clinics in all arms, working directly with a Practice Liaison (primary contact) at each clinic. Practice facilitation is an effective strategy for improving care delivery through the creation of an on-going, trusting relationship with an external facilitator who works with the practice on workflow redesign and quality improvement.<sup>47</sup> The workflow issues that require practice facilitation will vary across arms as well as from one practice to the next. Practice Coordinators will work closely with clinics in all arms prior to study implementation to assist with developing a registry of patients with a BMI > 30 kg/m<sup>2</sup>, assure that office personnel have received appropriate training that workflows are in place, and that intervention tools and tracking tools are ready for participant visits. Practice Coordinators will conduct additional in-person follow-up visits to each clinic approximately once each year; additional visits will be conducted as needed to ensure adequate training and study progress.

**E2c. Intervention delivery models (comparator arms)*****Fee-For-Service arm (FFS), In Clinic Individual Visits***

We designed the FFS comparison condition to reflect the current Medicare reimbursement model. PCPs will provide behavioral obesity treatment with traditional face-to-face 15-minute patient office visits following the session schedule reimbursed by the Medicare Intensive Behavioral Therapy provision (weekly for one month, followed by every other week for 5 months then monthly thereafter). Practices in this arm may

choose a variety of different scheduling approaches to deliver this care, including having auxiliary health professionals employed by the practice deliver the sessions with the PCP immediately available for consultation, in accordance with the Medicare ‘incident-to’ billing provision.<sup>23</sup> Practice Coordinators (central study personnel) will assist practices in identifying who within the practice will provide the counseling sessions and help facilitate workflow modification for scheduling these new visits. Providers will complete the ‘obesity 101’ training described above.<sup>48</sup> The training provided to practice staff delivering the counseling sessions in FFS is less intensive compared to PCMH, but it focuses on the standard of care that this is consistent with current Medicare reimbursement policy. The training will include evidence-based guidelines for diet and physical activity recommendations for weight control targeting 10% weight loss. Patient handouts will provide instructions for following a reduced calorie diet, increasing physical activity, and self-monitoring. Dietary recommendations are based on the USDA Dietary Guidelines for Americans, 2010<sup>49</sup> and corresponding My Plate guidelines. Specifically, patients will be encouraged to fill half their plate with fruits and vegetables, make at least half their grains whole, go lean with protein and eat calcium rich foods.<sup>50</sup> Patients will be encouraged to gradually increase their physical activity up to 225min/wk (45min/day, 5 days per week) of moderate intensity physical activity, according to physical activity guidelines for weight loss maintenance.<sup>51</sup> Practice personnel conducting FFS counseling visits will complete visit notes in REDCap documenting patient goals, progress, and topics covered.

### ***Patient Centered Medical Home arm (PCMH), In Clinic Group Visits***

This arm uses a PCMH model to deliver the comprehensive lifestyle intervention. Practices assigned to the PCMH arm may have previously adopted the PCMH model to varying degrees. Consistent with patient preferences as informed by our Patient Advisory Board, the PCMH intervention allows delivery by a non-PCP, offers opportunities for interactions with other patients struggling with obesity, and takes advantage of group visits and the option for telephone visits. Counseling sessions will be delivered by a designated counselor who may be nurse, registered dietitian, or behavioral counselor. Patients will receive 12 weekly in-person group visits in the first 3 months, followed by every other week in-person group visits through month 4, every other week group visits through month 6, and monthly group visits after that. After 14 in-person group visits, counselors may decide to offer the group sessions in-person or by phone depending on patient group preferences. Group in-person and phone visits will last 60 minutes. Patients will remain in the same groups when transitioning from group in-person meetings to group phone meetings to maintain the rapport established during the first 4 months. Counselors will provide email and text support to patients as needed and to the extent it is feasible for individual practice workflow. The session type and frequency are centered on what patients want and what is associated with success. Group visits provide peer support and interpersonal learning. Subsequent group phone visits enhance ease of access while maintaining accountability over the long-term. The counselor will document session attendance and patient-level notes in a group REDCap form and will be encouraged to document progress in the medical record and flag to the attention of the patient’s PCP according to workflow processes unique to that practice. Practice Coordinators (central study personnel) will assist practices in identifying who within the practice will serve as the counselor (may be the same person as the Practice Liaison) and provide the counseling sessions and what space for small practices may be used for in-person group visits. They will also facilitate workflow modification for incorporating new group visits and facilitate methods for enhancing care coordination and communication within the practice regarding patient progress.

***Additional Training for PCMH (In Clinic Group Visit) Counselors.*** In addition to completing the ‘Obesity 101’ training, counselors will receive intensive training on the delivery of the comprehensive lifestyle intervention program.<sup>52</sup> Our research team has experience in training a broad spectrum of providers on this intervention, including training of cooperative extension staff from rural communities. Training will follow a hybrid model that includes an initial intensive full day workshop delivered in-person (and by

podcast or tele-video if needed) followed by every other week to monthly telementoring. The workshop will be interactive and will focus primarily on group facilitation skills, counseling skills that are informed by motivational interviewing principles,<sup>53</sup> and health behavior change principles and strategies. Counselors will receive a detailed standardized treatment manual that includes session-by-session instructions and patient hand-outs, modeled after the Look AHEAD Lifestyle Intervention Counselor's Manual.<sup>54</sup> Prior to completion of the core training, all participants will demonstrate competency in the basic elements of the intervention. A full day training was chosen because it likely represents a best-case scenario for the amount of initial training that a practice might provide for a chronic disease coach/counselor. Following the workshop, counselors will receive just-in-time information through the session-by-session detailed instruction manual and bi-weekly group telementoring training sessions held with all the practices assigned to the PCMH arm. This approach will link the practices with our central intervention experts on an every other week basis. Brief didactic presentations during these calls will reinforce core issues or address solutions to problems encountered. Counselors from PCMH sites will present de-identified cases to the expert team and to one another. This model of training has been applied in real-world conditions to build capacity for PCPs in rural and underserved areas to effectively treat a number of chronic conditions. We will use it in a new and unique way to build capacity for delivering a comprehensive lifestyle intervention, providing ongoing training and quality control. The experts providing content for the sessions will include Dr. Befort and Danny Kurz, MPH. Telementoring will go from a bi-weekly to a monthly basis once all intervention groups per cohort are in the maintenance phase of the intervention. In addition, to further monitor fidelity and augment training, a Practice Coordinator will observe program delivery at least once in each clinic.

#### ***Disease Management Arm (DM), Phone Group Visits***

As with the PCMH arm, the DM model will deliver a group-based comprehensive lifestyle intervention. Sessions in the DM condition will be delivered in groups via conference call by obesity treatment specialists, employed at KUMC, with Masters' degrees in nutrition, exercise science, public health or psychology. Our preliminary research has shown that group phone counseling is more effective compared to individual phone counseling<sup>55</sup> (also R18 HL122720). We have found this delivery approach to be especially ideal for rural residents, because it eliminates travel burden, and also because it provides social support while preserving a level of anonymity. In the DM delivery model, groups will be formed across multiple practices and regions of the Midwest. Calls will occur approximately at 6:30am, 12:00pm, 5:30 pm, or 7:00pm on Monday, Tuesday, Thursday or Friday which has been the most universally available time and avoids conflicts related to Wednesday evening church activities common in our rural communities. Group norms are established early on regarding active participation, no multi-tasking, maintaining a supportive tone, and attendance and punctuality. All group members participate up to their comfort level, providing support and strategies for one another. Counselors encourage group cohesiveness and facilitate participants interacting directly with one another. Participants are encouraged to submit personal bio-sheets with a picture for sharing with the group. Counselors set expectations for participants to treat sessions as a standing appointment. Counselors will document session attendance and patient notes in REDCap.

***Integration with primary care.*** Obesity treatment specialists will send periodic progress reports to the patients' PCP at the practice. Timing of the reports will be based on group start dates and subsequent study milestones. The first report will be sent after 3-months of counseling participation; the remainder of the reports will be sent on or around the time of the follow-up data collection visits and survey completion—specifically at 6, 12, 18 and 24 months.

In addition, ad hoc reports will be sent to the PCP if critical information occurs during the course of treatment (e.g. a participant experiencing hypoglycemia or worsening depression). To maximize the chance that PCPs will act on these reports, they will be kept brief and will follow a structured format that includes

concise recommendations for PCP action (e.g. ‘Please provide patient with positive feedback on weight loss to date’). Reports will also include information on specific program recommendations, patient’s self-reported progress to date for weight loss, diet, and physical activity, and reported barriers and personal motivators for weight loss. This format for provider engagement has been well received in previous disease management studies conducted by this team.

***Counselor training and quality control.*** One of the major theoretical advantages of the DM model is the ability to implement much tighter quality control on the training of the providers and conduct of the sessions. Accordingly, counselors in the DM arm will participate in a year-long training program that included didactics, reading evidence-based literature, listening to recordings of treatment sessions, motivational interviewing training, and shadowing an experienced counselor. Ongoing training and quality monitoring during the conduct of this study will include weekly staff meetings where recorded sessions are listened to, upcoming lessons are discussed, and problems regarding participant adherence and group facilitation are addressed. In addition, counselors will follow a standardized checklist of the content to be covered for each session. Fidelity to the intervention is reviewed for at least 10% of recorded sessions. If a counselor falls below a threshold of fidelity, additional review and training will be provided.

## **E2d. Comprehensive lifestyle intervention components**

The lifestyle intervention incorporates strategies from the Look AHEAD Lifestyle Intervention and is guided by a social-cognitive framework emphasizing factors Bandura identified as influencing self-efficacy, specifically social modeling and social persuasion.<sup>56</sup> The primary objective is to decrease caloric intake and increase physical activity to produce gradual weight loss with an individual goal of 10% weight loss at 6 months (Weight Loss Phase I) followed by maintenance of diet and physical activity to sustain a 5 to 10% weight reduction through 24 months (Weight Loss Maintenance Phase II). The intervention has been targeted to the rural setting (Table 3).

Table 3. Tailored intervention components

- Simplified educational materials and self-monitoring forms to address lower education levels
- Recipes of low-fat, high FV versions of traditional “country” or “potluck” dishes
- Problem-solving re: barriers to accessing PA facilities and healthy foods in grocery stores and restaurants
- Alternative home-based activities when walking is not feasible due to weather/environmental constraints
- Linking behavior change to cultural values related to hard work and family priorities

Values and culture in rural communities are influenced by access difficulties, lack of privacy, isolation, greater poverty, and older populations.<sup>57</sup> These aspects of rural life influence rural values which include conservatism, self-reliance, and orientation toward work, family, and religion.<sup>58</sup> However, traditions and customs vary from town to town and from farm to town. Thus, the intervention highlights the shared identity among rural residents while at the same time attending to differences in values that may exist. **Behavioral strategies** are taught and reinforced throughout the program. Participants in both group-based arms will receive a treatment handbook with session-by-session content and general study information (session schedule, conference call information, self-monitoring instructions). Intervention components across all arms are summarized in Table 4.

**Diet.** During weight loss, participants receive instructions to follow a reduced-calorie diet that includes a calorie goal and  $\geq 5$  fruit and vegetable (FV) servings per day. Emphasis is placed on portion control and

Table 4. Lifestyle intervention goals and self-monitoring strategies for PCMH and DM arms		
	<b>Weight loss phase</b>	<b>Weight loss maintenance phase</b>
Weight loss goal	10% weight loss	Maintain within 2%
Diet goals	1200 – 1500 kcal/day if $< 250$ lbs 1500 – 1800 kcal/day if $\geq 250$ lbs	Calorie goal personalized
	Portion control, recommended up to 2 prepackaged meals and 2 shakes/day (optional)	Portion control, recommended up to 2 prepackaged meals/shakes (optional) and at least 1 home prepared healthy meals/day
	$\geq 5$ 1-cup fresh or frozen fruit and vegetable servings/day	Same
	Reduced sodium	Same
	High fiber	Same
Physical activity goals	Work up to 225 min/wk of moderate intensity activity in bouts $\geq 10$ min	Maintain 225 min/week; increase up to 300 min/week if achieve 225 min/wk
	10,000 steps/day	10,000 steps/day
Frequency of self-weighing	At least weekly	At least weekly, daily recommended
Self-monitoring diet Frequency and content	Daily food log and counting calories and FV servings	Same
Method	Paper/calorie counter book or commercial app/	Same
Self-monitoring physical activity Frequency and content	Daily minutes and steps	Same
Method	Activity tracker	Same

consuming low calorie, high volume foods (Volumetrics) with high amounts of FVs, fiber, and water. To facilitate adherence, pre-portioned meals and shakes are recommended (but are not provided and are optional) consistent with the DPP and Look AHEAD dietary interventions. Pre-portioned meals may include frozen entrees ( $< 350$  kcal each) that are widely available even in small grocery stores, canned soup, or other shelf stable portion-controlled meals. Pre-portioned meals are affordable and have consistently shown greater weight loss, long-term weight loss maintenance up to four years, and greater increases in FVs and fiber compared to relying completely on individuals preparing all their own meals. We have successfully used this dietary approach with rural residents, respecting participant's autonomy to make healthy food choices and encouraging modifications as needed based on family values and cooking practices (e.g. preparing foods for large farm crews during harvest). Participants living in more isolated areas typically stock up on foods including a variety of frozen FVs when they make their regular shopping trips to larger towns. During weight loss maintenance, participants are given a new personalized calorie goal calculated from the Harris-Benedict equation to sustain their reduced body weight.<sup>59</sup> Throughout the intervention, participants keep weekly food logs and counselors provide feedback. All participants receive a calorie

counter book or web-based calorie counters and sample meal plans for their calorie profile. For participants in the DM arm and PCMH arm who have smartphones or are regular internet users, we will pay for their use of a web-based app for self-monitoring diet (i.e. Lose It). Group leaders will have access to participants' LoseIt data and will send feedback to participants directly through the Lose It app. Those without internet access and those who do not wish to use LoseIt may text, email, or leave a voicemail with their weight and physical activity minutes and use paper self-monitoring forms provided in the treatment handbook.

**Physical activity.** Physical activity (PA) will be increased through a guided home-based program. Home-based programs have been shown to produce greater long-term adherence compared to on-site programs and are preferred among many rural residents. Participants will be guided to gradually increase their PA over the first 12 weeks to 225 min/wk of moderate intensity activity, consistent with national guidelines for weight loss maintenance. The PA progression begins with 15 min/day, 3 days/wk and progresses up to the goal by week 12. Using this program, our previous participants have reported an increase to 190 min/wk at 6 mos. The intervention addresses problem-solving regarding barriers to physical activity in the rural Midwest (e.g., no solid surfaces for walking on isolated farms, extreme temperatures with high winds).

**Weight loss maintenance intervention.** Continued support, accountability, and help with addressing routine problems are the key elements during the maintenance period. The maintenance intervention incorporates a social cognitive approach to relapse prevention<sup>60</sup> using the successful 5-step problem-solving model developed by our co-investigator Dr. Perri.<sup>61-63</sup> Counseling strategies are used following principles of motivational interviewing<sup>53</sup> to help participants resolve ambivalence about continuing to exercise and eat healthy once weight loss plateaus or regain is experienced. Individuals are often ill-equipped to cope with life circumstances that result in lapses in new behaviors. These lapses can erode self-efficacy and motivation such that eventually the entire self-management effort is abandoned.<sup>64</sup> Thus, the maintenance intervention represents a change from the more didactic approach of initial treatment and focuses on support and problem-solving for enhancing motivation and long-term coping skills.

## **E2e. Outcome measures**

Outcome measures have been selected with input from our Patient Advisory Board and are supported by the literature. See Table 5 for the list of measures and estimated time to complete. The goal will be to complete the assessment visits within a -7 days/+21 day window of the target date. We will allow for a 3 month window for 6 and 18 month visits if an assessment visit appointment needs to be rescheduled and a 4 month window for the 24 month visit if an assessment visit appointment needs to be rescheduled. Chart review may be used to capture medications and number of clinic visits as well as missing weight data.

**Anthropomorphic measures.** Weight, and blood pressure will be directly measured and recorded at baseline, 6, 18, and 24 months during in-clinic assessment visits. Height will be measured at baseline only. These measures will be collected by clinic staff. Participants will be weighed in light clothing (shorts and t-shirt) in a fasting state using a calibrated digital scale accurate to 0.1 kg. Height will be measured with a stadiometer to calculate BMI. Blood pressure will be measured by clinic staff after the patient rests in a seated position for 5 minutes. Two measurements will be taken and recorded. If either the systolic or diastolic measurements are greater than 5mm Hg apart, a third measurement will be taken after a one-minute break. Estimated time for in-person assessment visit procedures is 15-20 minutes. If a patient is unable to come to the clinic for the data collection visit, an in-home visit or a visit at another location convenient for the patient, may be conducted.

**Fasting glucose and lipids.** A clinic phlebotomist or nurse will collect blood samples required for analysis of fasting glucose and lipids, to include LDL, HDL, triglycerides, and total cholesterol. Laboratory results

will be sent to the PCP per the laboratory and practice's standard operating procedures. The practice will in turn provide the results to KUMC study personnel (see section E1 for specifics).

**Questionnaires.** Self-report questionnaires will be administered via on-line REDCap surveys sent by email or by hard copy surveys sent via regular mail, depending on patient preference. Patients will be asked to complete questionnaires at all five time points (baseline, 6, 12, 18, and 24 month visits). Patients must complete the baseline questionnaires prior to enrolling in the trial (see section C1).

**Demographic information.** Information will be collected at baseline on date of birth, race, ethnicity, income, marital status, level of education, employment status, time off work for study counseling visits, physical address, insurance status and type, and years living in rural area. Updates will occur at 12 and 24 months.

**Medical history.** Self-reported medical history, including smoking and weight loss history<sup>65</sup> will be collected at baseline. At each follow-up questionnaire, patients will be asked to report hospitalizations/serious adverse events, exercise-related injuries/illnesses, and changes to smoking status. Any serious adverse events reported by patients via the self-reported medical history will be followed up on by KUMC study personnel (see Section I6).

**Medication Information.** Baseline medications will be collected through a phone interview after the patient has signed the baseline survey consent (see Section IIIC1). Changes in medications will be self-reported at 6mo, 12mo, 18mo, and 24mo.

**SF-12** (general quality of life) is a 12-item survey that measures physical and mental health-related quality of life.<sup>66</sup> The SF-12 is a shortened version of the original SF-36, which has been established as a reliable and valid measure of quality of life and has been widely used, however has been insensitive to quality of life based on BMI and weight change over time.<sup>67</sup> The SF-12 has been shown to detect differences in quality of life among overweight and obese individuals when compared to normal weight controls.<sup>68</sup>

**Impact of Weight on Quality of Life-Lite (IWQOL-L)**<sup>69</sup> is a 31-item self-report measure specifically designed to measure the effects of weight on quality of life that is an abbreviated version of an original 74-item IWQOL measure.<sup>70</sup> The IWQOL-L assesses five domains of functioning: physical function, self-esteem, sexual life, public distress, and work and responses are measured on a 5 point Likert scale from "never true" to "always true." The measure yields a total score and five subscale scores. For overweight/obese samples, the IWQOL-L has demonstrated reliability and internal consistency, construct validity, and discriminant validity when compared to other quality of life measures, detects quality of life changes in response to weight loss during an intervention, and distinguishes differences in quality of life based on BMI.

**Pittsburg Sleep Quality Index (PSQI)** is a 10-item measures that assesses sleep timing and disturbances over the past month and is reliable and valid in a variety of populations.<sup>71</sup> The PSQI distinguishes between sleep quality in individuals with obesity/metabolic syndrome and those who are of normal weight and predicts magnitude of weight loss during an intervention.<sup>72</sup>

***Perceived Stress Scale (PSS)*** is a 10-item survey that is widely used measure to assess perception of stress.<sup>73</sup> The PSS has established internal consistency reliability, factorial validity, and construct validity in a variety of samples, including obese adults.

***Patient Reported Outcomes Measurement Information System-29 (PROMIS-29)*** is a health-related quality of life questionnaire developed to address patient-reported outcomes.<sup>74</sup> The current study will use the 4-item anxiety and the 4-item depression symptom scales.<sup>75</sup> PROMIS anxiety and depression scales have been shown to have good internal reliability and strong convergent validity with well-established measures of anxiety and depression, including the generalized anxiety disorder (GAD)-7 and the PHQ-9<sup>76</sup> in a sample of primary care patients with chronic pain.

***Patient Health Questionnaire-9 (PHQ-9)*** is a 9-item, reliable, valid criteria-based measure of depression severity.<sup>77</sup>

***Modifiable Activity Questionnaire (MAQ)*** is a questionnaire measuring participation in 38 leisure time physical activities that asks participants to report the duration and frequency of each activity in the last 7 days. The MAQ has evidence of reliability and validity when compared to accelerometer measurements of activity.<sup>78</sup>

***NCI's Energy Screener*** is a 17-item survey designed to estimate an individual's percentage calorie intake from fat in the past 12 months. This measure has demonstrated validity when compared to the Food Frequency Questionnaire and 24-hour dietary recall<sup>79</sup> and has been shown to have similar validity among obese and normal weight individuals.<sup>79</sup>

***Frequency of fast food and sugar sweetened beverage consumption*** will be assessed with three items from the Behavioral Risk Factors Surveillance System (BRFSS).<sup>80</sup> A fourth item will also assess frequency of eating out at non- fast food restaurants.

***Fruit and Vegetable Screener*** is a brief 2 item questionnaire assessing the number of cups of fruits and vegetables eaten each day.

***AUDIT C (Alcohol consumption):*** The Alcohol Use Disorders Identification Test- Consumption (AUDIT-C) is a well-established 3-item screener of typical alcohol consumption and identifies individuals with a pattern of hazardous alcohol use. An additional item assesses heavy drinking as the largest number of drinks consumed during a single drinking episode in the past 6 months.<sup>81</sup>

***Program Satisfaction and Experience of Care.*** Satisfaction with program components and experiences of care will be assessed from surveys developed for this trial, in addition to process interviews described below.



Table 5. Measures						
	MONTH					EST. TIME
In-Clinic Measures**						
	0	6	12	18	24	
Weight	X	X	*	X	X	1 minute
Height	X					1 minute
Blood draw	X	X			X	5-10 minutes
Blood pressure	X	X		X	X	5 minutes
Questionnaires (phone, on-line or mail surveys)						
Demographic info and updates	X		X		X	5 minutes
Medical history, smoking and weight loss history <sup>42,82/</sup> updates	X	X	X	X	X	5-10 minutes
Medication information and updates	X	X	X	X	X	2-5 minutes
SF-12 (general quality of life)	X	X			X	2-5 minutes
Impact of Weight on Quality of Life –Lite (IWQOL-L)	X	X			X	5minutes
Pittsburgh Sleep Quality Index (PSQI)	X	X			X	2-5 minutes
Perceived Stress Scale (PSS)	X	X		X	X	1-2 minutes
Patient Health Questionnaire-9 (PHQ-9)	X					1-2 minutes
Patient Reported Outcomes Measurement Information System-29 (PROMIS-29)	X	X		X	X	2-3 minutes
Modifiable Activity Questionnaire (MAQ)	X	X	X	***	X	2-5 minutes
NCI’s Energy Screener <sup>83</sup> fruit and vegetable screener, Frequency of Fast Food and Sugar Sweetened Beverage Consumption <sup>80</sup> , and alcohol consumption <sup>84</sup>	X	X	X		X	5 minutes
Program Satisfaction and Experience of Care		X			X	2-5minutes

\*12-month weight is self-report, no in-person visit.

\*\*An in-home visit or a visit at another location convenient for the patient may be conducted, if a patient is unable to come to the clinic for the visit.

\*\*\*MAQ added at 18-months after initiating 18-month visits, based on patient feedback that measures were too focused on mood-related outcomes only; 18-month MAQ measure will not be included in the primary analysis of PA outcomes.

## **E2f. Process measures**

We will use the RE-AIM framework to evaluate Reach (at the patient level), Adoption (at the practice level), Implementation (at patient and practice level), and Maintenance (at the practice level). Table 6 describes quantitative RE-AIM measures. To inform and augment our quantitative RE-AIM implementation measures, we will also conduct a qualitative process evaluation.

<b>Table 6. RE-AIM Measures</b>
<b>Reach (representativeness of participants)</b> <ul style="list-style-type: none"> <li>• % of patients in registries who respond to recruitment mailings</li> <li>• % of patients in clinic registries who enroll</li> <li>• Comparison of demographics and co-morbidities between enrolled participants at the ten Marshfield clinic sites and all patients on the original study registries at the Marshfield clinic sites, given their ability to query their common EMR.</li> <li>• Comparison of demographics between enrolled patients and patients on mailing lists who do not enroll (all sites)</li> </ul>
<b>Effectiveness (impact at participant level)</b> <ul style="list-style-type: none"> <li>• measured with patient-centered outcomes (Aims 1-5)</li> </ul>
<b>Adoption (representativeness of practices)</b> Comparison between participating and non-participating practices within KUMC network on characteristics such as the following: <ul style="list-style-type: none"> <li>• practice type (e.g., FQHC, hospital-owned, stand-alone)</li> <li>• practices and systems to address counseling for diet, physical activity, and weight management (for participating sites only).</li> <li>• presence of registered dietitians or behavioral counselors</li> <li>• degree of rurality as this corresponds to access to other community resources</li> <li>• distance to a large hospital as this is associated with scope of practice in the rural setting<sup>22</sup></li> </ul>
<b>Implementation (process by which interventions are delivered)</b> <ul style="list-style-type: none"> <li>• Counseling session attendance</li> <li>• Provider completion of trainings</li> <li>• Provider self-assessed competencies</li> <li>• Provider-reported barriers to implementation (survey measure, qualitative interviews)</li> <li>• Patient satisfaction and experience of care (survey measure, qualitative interviews)</li> </ul>
<b>Maintenance (translation at the practice level)</b> <ul style="list-style-type: none"> <li>• % of participating practices who begin billing Medicare</li> <li>• % of participating practices who continue to offer weight loss services</li> </ul>

**Qualitative process evaluation.** Qualitative interviews provide in-depth information during the course of a study to understand facilitators and barriers to the intervention, and it can illuminate why it did (or did not) work as designed. In addition, the qualitative process evaluation will provide valuable ‘how to’ information for practices that might want to implement one of these interventions in the future. Consequently, we anticipate that our process evaluation, with corresponding stories about lessons learned, will be an integral piece of the results that we share with our Patient Advisory Board and stakeholders during dissemination planning meetings.

We will conduct structured interviews with participating providers, practice staff, and study participants. Structured interviews will last about 30 minutes, and responses will be documented in detail for later analysis of content and themes. Interviews with providers and practice staff will occur at baseline, mid-study, and post-study for all practices affiliated with KUMC and will focus on the inner practice setting and barriers/facilitators to implementing the intervention according to the Consolidated Framework for Implementation Research.<sup>85</sup> At mid-study and post-study timepoints, the interview questions will be sent to respondents in survey format before the interview to encourage consideration of questions prior to the

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interviews and to foster discussions. The surveys will also be sent to practice staff at non-KU affiliated sites. Interviews with study participants will occur after they have completed the final follow-up visit, with 1-2 participants randomly selected from each practice. We will attempt to sample participants by level of participation (session attendance high vs low), level of weight loss (< 5%, 5-10%, >10%), and sex. Participant interviews will focus on facilitators and barriers to uptake and adherence. We will ask about satisfaction with intervention components, including session type, location, and time, helpfulness of counselors and PCPs, and usefulness of intervention components. We will pay particular attention to barriers related to sociocultural and environmental constraints from living in a rural community.

## **E2g. Patient and stakeholder engagement**

From the point of preparing the grant application for this study, we have solicited input on the study design and outcome measures from our Patient Advisory Board (PAB) and provider stakeholders. The study activities include on-going engagement with the PAB and provider stakeholders, whose roles are like that of consultants or advisors. They are paid \$250 consultation remuneration quarterly. To launch our study engagement and enhance working relationships across our PAB, provider stakeholders, and investigators, we held a day-long kick off meeting in Kansas City on Feb 6<sup>th</sup> 2015. 9 PAB members, 6 provider stakeholders, 9 investigators, and 11 project staff were in attendance, with 23 traveling to attend the meeting. We facilitated panel discussions on patients' experiences with weight control in their rural communities and on primary care physicians' experiences with attempting to address obesity in their practices. We presented details of what would be required of practices and patients, and we shared the recruitment and retention plans. Small, facilitated breakout discussions addressed various topics such as barriers and solutions to practice and patient participation, recruitment plans, and retention plans. Plans for on-going engagement with the PAB and provider stakeholders are described below.

***Patient Advisory Board.*** The PAB includes 10 men and women living with obesity in rural communities throughout Kansas, Nebraska, Wisconsin, and Iowa. We have included long-standing patient partners who have advised our work for the past five years as well as new members invited specifically for this study. Some of our PAB members have successfully lost weight and kept it off whereas others are currently considering making a weight loss attempt. Thus we have input from patients at varying stages of change. We will continue to meet with the PAB approximately monthly via conference calls to solicit their input on a variety of study related materials and strategies, including training materials, recruitment materials, recruitment and retention strategies, content of the process evaluation, interpretation of findings, and dissemination plans. The PAB will have direct input into the nature and timing of our meetings, which may include additional in-person meetings at a central location as well as communication through email and social media. Participation in the PAB is voluntary, and the members may likely change over the course of the 5 year study.

***Provider Stakeholders.*** Provider stakeholders include 5 rural primary care physicians with a vested interest in improving treatment of obesity in their practices as well as in quality improvement and research participation. We will meet with the provider stakeholders by video calls, conference calls, and email as needed to solicit on-going input on strategies for recruiting providers and practices to participate, helping practices implement the study procedures, and disseminating awareness about the study and the findings.

## **E3. Research Purposes/Standard Care**

The four in-clinic assessment visits and the accompanying lab work will not be billable to patients or their insurance companies. In the fee-for-service arm, the practice may elect to bill Medicare for the counseling sessions for patients with Medicare coverage. There is no patient co-pay for this provision. In addition,

participants will likely be visiting their PCP more frequently than usual for study-related visits. As a result, the PCP may request to see their patients more regularly to deliver standard medical care for other co-morbid conditions (i.e. hypertension or diabetes). All standard medical care will be billed to the participant's insurance in the usual way. The participant will be responsible for any co-pays or deductibles according to their insurance coverage.

#### E4. Marshfield Clinic Sample Storage

Samples from Marshfield Clinic practices will be stored at the Marshfield Clinical Laboratories Core repository facility. Samples will be labeled with participant initials, study ID number, and assessment time point. Specimens will be inventoried by a secure password protected database. The unique identifiers for the patients and specimen locations within the freezers assigned by the laboratory technicians are verified by the data entry team via data management measures. All protected health information is removed from the biospecimen. Biospecimens are assigned a unique study code, which is the only source of identification visible on the biospecimens and any accompanying paperwork (e.g., demographic data, family history data, medical history data, clinical history data, pathology reports, etc.). Additionally, the central laboratory adheres to rigorous standard operating procedures to ensure the highest quality specimen processing.

These de-identified samples will be stored at the MCLC repository indefinitely or until KUMC requests transfer to their storage facilities. Samples will be made available for the use of other researchers using an honest broker system. Researchers wishing to use these samples will be required to submit a formal proposal along with a completed application for use and documentation of HSC approval/HSC determination of not human subjects research. The broker will provide only non-identifiable information to the requestor after the application is approved. These samples may be used for future research involving biomarkers of obesity, weight loss, or other chronic health conditions.

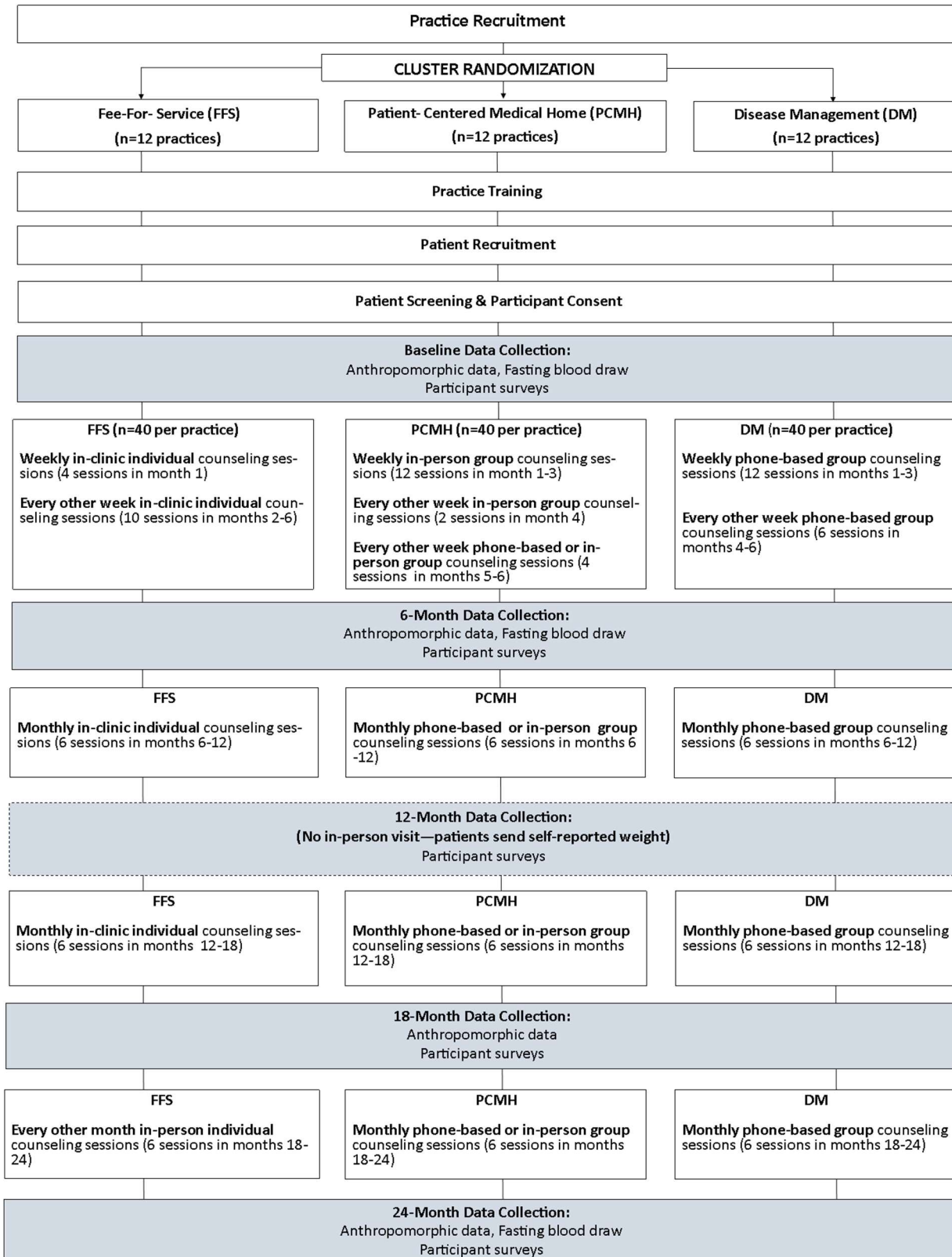
#### E5. Timeline (Figure 3)

The original funding period for this study was 5 years, January 1, 2015 to December 31, 2019. A global contract modification fully executed in February 2018 extended the period of performance through April 30, 2020. The final timeline is included in Figure 3. All project milestones, as required by PCORI, will be completed within this time frame. The study will be implemented in three cohorts, with 12 primary care practices in each cohort (4 in each of the 3 arms). Patient recruitment will begin in January 2016 for cohort 1, June 2016 for cohort 2 and September 2016 for cohort 3. Practices in the PCMH and DM arms will enroll 40 patients over a 6 month time period. The FFS arm will enroll 40 patients over a 9 month period (indicated in the timeline below with dotted lines). Each patient in all arms will be followed for 2 years. Analysis and dissemination of the primary outcomes will happen in the final 6 months of the project period.

Figure 3. Study Timeline

	Year 1 - 2015				Year 2 - 2016				Year 3 - 2017				Year 4 - 2018				Year 5 - 2019				Year 6 - 2020	
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2
Cohort 1	Study Preparation IRB Approval Practice Recruitment DSMB Charter Obesity Trainings		Practice Training		Recruitment		Phase 1		Phase 2												Analysis and Dissemination	
Cohort 2					Practice Training		Recruitment		Phase 1		Phase 2											
Cohort 3					Practice Training		Recruitment		Phase 1		Phase 2											

Figure 4. Study Flow



## F. Risk Benefit Assessment

### F1. Physical risks to participants

**Exercise.** Risks in this study are primarily related to exercise, an intervention component in all three study arms. Moderate intensity physical activity has few serious risks especially for those with clearance from a medical provider. Physical activity may cause temporary discomfort associated with exertion, muscle soreness, or musculoskeletal injuries. Accidents with physical activity, such as falls or sprained ankles, are also possible. In the DPP study, the occurrence of musculoskeletal injuries was 3% higher in the lifestyle intervention compared to the placebo control arm.<sup>86</sup> Some risk for cardiovascular complications exist for participants with cardiovascular risk factors (e.g., history of MI, hypertension, diabetes). Maximum risk estimates of major cardiovascular events during strenuous exercise are 0.6 to 6.0 events per 10,000 person-hours for women and 0.3 to 2.7 events per 10,000 person-hours for men.<sup>87</sup> However, exercise of all levels is beneficial for reducing cardiac events overall (both at rest and during exercise).

**Diet.** The dietary recommendation for all three study arms is  $\geq 1,200$  kcal/day and therefore avoids the risks associated with very low calorie diets. Although not common in this type of program or this level of caloric intake, calorie restriction can lead to inadequate nutrition or rapid weight loss. Rapid weight loss (>3 lbs per week for several weeks) typically associated with very low calorie diets, unlike the one used in this intervention, may lead to gallstones. Some patients with diabetes may be susceptible to hypoglycemia. Weight loss also has the potential to increase risk of hypotension for patients who are using medications that lower blood pressure.

**Protection against risk.** We have appropriate inclusion/exclusion criteria, and most importantly, physician clearance to participate and physician monitoring to protect patients against risk. We will implement plans to protect against risk of moderate intensity physical activity, caloric restriction is  $\geq 1,200$  kcal/day, and weight loss for each participant. In the FFS arm, all counseling, physical activity recommendations, and dietary recommendations will be provided or supervised by the PCP with appropriate medical oversight. In the PCMH arm, the intervention will be delivered by the primary care clinic staff and coordinated with the PCP with medical oversight. In the DM arm, the intervention will be delivered remotely by KUMC research personnel. PCPs, clinic staff providing counseling sessions, and KUMC remote counselors will receive training in the measures taken as described below to protect against risk.

The diet and physical activity recommendations are evidence-based and generally considered to be safe. The physical activity progression is slow, beginning at 15 min/day, 3 days/week, and progressing up to the goal of 225 min/week over a 3 month period. Participants will be instructed in appropriate warm-up, monitoring intensity, and avoiding injuries and falls during exercise. They will be instructed to keep their physical activity in the moderate range (50-70% max HR) and to monitor intensity through heart rate or ratings of perceived exertion. They will be educated about the symptoms of hypoglycemia, hypertension, and hyperglycemia, and instructed to contact their physician if they experience any such symptoms. In the DM arm, participants who self-report to their counselor increasing their physical activity too quickly in regards to duration or intensity will be counseled again regarding safety precautions. When a DM counselor or other central study staff member learns that a cardiovascular event has occurred, the physical activity component of the intervention will be suspended and may be resumed with possible modifications after approval from the treating PCP. For exercise-related injuries, the treating PCP will be consulted according to the symptoms reported. If appropriate, the participant's exercise goals or type will be modified. If the symptoms or injury do not resolve after an appropriate period of time, the participant will be asked to schedule a visit with his or her PCP for further evaluation. Participants who self-report to their counselor consuming nutritionally inappropriate diets with regard to quantity or quality of intake will receive additional counseling. Participants

will be advised that marked and sustained calorie restriction can have serious health risks such as gallstones and/or cholecystitis as well as other risks such as hair loss. In the DM arm, if a participant is unresponsive to advice from the remote counselor, and nutritional deficiency continues to be suspected, the intervention will be suspended and the participant will be asked to schedule a visit with his or her PCP.

Participants will be educated about symptoms of hypotension and hypoglycemia and urged to contact their PCP if they have these symptoms. Overall management of diabetes, hypertension, and cardiovascular disease will remain under the control of the participant's PCP. All laboratory results obtained as part of study visits will be sent directly to the PCP. The analyzing laboratory and PCP will follow their standard operating procedures for notification and management of critical and panic laboratory values. The practice will provide the laboratory results to KUMC upon receipt. If participants indicate any injury or illness on their medical follow-up form (6, 12, 18, 24 months) that may indicate a safety risk for participation, the study team will follow-up with the participant and the treating PCP as needed.

## **F2. Psychological risks to participants**

In all study arms there is a risk of potential discomfort in talking about weight-related behaviors.

**Protection against risk.** Participants will be informed that sharing of all information is voluntary both during data collection and counseling sessions. They will be encouraged to share concerns with weight-related issues during the sessions only to the extent that they feel comfortable. Participants who have suspected mental health diagnoses that may interfere with ability to adhere to program recommendations will be referred to the treating PCP. PCPs will also be alerted if participants score  $\geq 20$  on the PHQ-9 and/or endorse the suicide ideation question. In addition, patients will be advised to follow-up with their PCP or mental health provider if they score  $\geq 15$ , and if they also endorse the suicide ideation question, the PI (clinical psychologist) or a clinical psychologist in training under supervision of the PI, will call the patient within 2 business days, with up to 2 contact attempts, to rule out suicide plan. This timeframe for response is seen as appropriate given 1) the extremely low likelihood that a person with an imminent suicide plan would be completing a baseline survey packet to enroll in a 2-year lifestyle intervention, and 2) the high false positive rate between the PHQ-9 suicide ideation question and an actual suicide plan.<sup>88</sup> Alert values and actions for the PHQ-9 are listed in Table 7.

**Table 7. Alert Values and Actions**

Measure	Alert Value	Notify Participant	Notify PCP
PHQ-9 (Depression Questionnaire)	Total Score $\geq 15$ and $< 20$	Advise to follow up with PCP or mental health care provider	None
	Total Score $\geq 20$ but no endorsement of suicidal ideation	Advise to follow up with PCP or mental health care provider	Within 1 week
	Endorsement of suicidal ideation (regardless of total score)	Call within 2 business days to assess for suicide plan. Advise to follow up with PCP or mental health care provider.	Within 1 week

### **F3. Social risks to participants**

Personal information will be collected during the study. Group visits in the PCMH and DM arms will involve sharing personal information with other patients. A breach in data security would present a privacy risk to participants.

**Protection against risk.** Respect for confidentiality will be established as a group norm in the first session and reinforced by the group leader throughout the program. To protect confidentiality of study information and data, each participant will be assigned a unique number which will be used on all data collection forms. All electronic data capture will be stored in REDCap. Hard copy forms (e.g. original consent forms, hard copy data collection forms used by the practice), will be collected from the practice at regular intervals (via mail and in-person visits). Documents will be stored in locked secure file cabinets at KUMC. Hard copy survey forms mailed to KUMC by participants will also be stored in locked secure file cabinets.

### **F4. Economic risks to participants**

In all three arms, participants may suffer lost income or leave time from work when they attend the four in-person assessment visits, which will likely occur during regular work hours. In the FFS and PCMH arms, participants may suffer lost income or leave time as a result of in-person counseling sessions, which in the FFS arm will likely occur during regular work hours, and in the PCMH arm may occur during regular work hours or evening hours. Although we compensate for mileage to and from assessment visits, participants in the FFS and PCMH arms will be responsible for mileage costs associated with in-person counseling visits. Participants will likely be visiting their PCP more frequently than usual for study-related visits. As a result, the PCP may request to see their patients more regularly to deliver standard medical care for other co-morbid conditions (i.e. hypertension or diabetes). All standard medical care will be billed to the participant's insurance in the usual way. The participant will be responsible for any co-pays or deductibles according to their insurance coverage. In the PCMH and DM arms, participants may be billed by their cellphone companies for time spent on the phone during phone-based counseling sessions. Participants and their health insurance companies will not be charged for any visits or blood sample analysis done for this study. All information regarding economic risks are detailed in the consent form.

### **F5. Potential benefits of participation**

**F5a. Benefits to the individual.** The benefits to participants are the known benefits that weight loss and physical activity have on risk for diabetes, cardiovascular disease, arthritis, cancer, and other morbidities. Participants may also benefit from an increased ability and self-control to regulate diet and physical activity behaviors, as well as improved mental functioning, quality of life, and well-being. They will receive an evidence-based behavioral weight loss intervention, mileage reimbursement for assessment visits (not counseling visits), and debit ClinCard deposits (\$25 for survey completion at five time points, \$30 for assessment visit attendance at baseline, 6 month, and 18 month visits and \$50 at the 24 month visit).

**F5b. Benefits to the population.** Other obese adults within participants' family, social networks, and rural communities may vicariously benefit to the extent that participants share what they learn in the intervention. Participating rural practices will gain increased knowledge and effectiveness in addressing weight loss with patients, and the opportunity to collaborate with other rural practices – all of which may result in improved and expanded services available in the rural communities.

**F5c. Benefits to science and society.** The benefits to science and society include increased knowledge of the most effective model for addressing obesity in rural primary care. With 4 out of 10 rural residents currently living with obesity and a major gap in availability of obesity treatment programs, there are numerous



potential benefits for reducing chronic disease morbidity and mortality and improving quality of life in this underserved population.

### **G. Location Where the Study Will Be Performed**

This is multi-site study that will be completed in collaboration with three academic medical institutions, KUMC, the University of Nebraska Medical Center (UNMC) and the Marshfield Clinic in Wisconsin. KUMC, UNMC, and Marshfield Clinic will be responsible for coordinating study activities in practices affiliated with their institution (see Section I). Across all arms, personnel at the primary care practices will collect informed consent and conduct assessment visits. Across all arms, self-reported questionnaires will be collected outside of the in-person assessment visits, via online forms in REDCap or by mail for those patients without internet access. The location of counseling sessions will vary by arm: **FFS** participants will receive counseling sessions at their primary care practice. **PCMH** participants will receive counseling sessions from primary care clinic personnel, in-person at the primary care practice for the first four months and subsequently via group conference call. **DM** participants will receive counseling sessions via group conference calls conducted by KUMC personnel. ***Participant electronic research records*** will be stored on the secure REDCap database, developed and overseen by KUMC Medical Informatics. Hard copy forms will be stored long-term in a secure locked file cabinet at KUMC.

### **H. Collaboration**

KUMC will serve as the IRB of record for UNMC and Marshfield Clinic (see Section I).

### **I. Single IRB Review for a Multi-Site Study**

#### **I1. IRB of record**

All primary care practices, with the exception of 3 or 4 possible clinics from the VA Nebraska Western Iowa Health Care System (overseen by UNMC site PI), will be approved under the KUMC IRB. UNMC and Marshfield Clinic have an IRB reciprocity agreement established through the Clinical Data Research Network (PI Waitman). The VA Nebraska Western Iowa Health Care System IRB application will be overseen by UNMC site PI, Dr. Cyrus Desouza.

#### **I2. Study activities**

Centralized mail and phone-based patient recruitment and screening will occur at KUMC (see Section III). Provider trainings will be delivered both centrally and locally within the practices with collaboration and uniformity across all three institutions. Tracking of provider training completion will be managed by KUMC study personnel. Patient consent, in-person assessment visits, and FFS and PCMH counseling visits will occur within the primary care practices; these procedures will be the same across practices affiliated with KUMC, UNMC, and Marshfield Clinic. Some data collection visits may be conducted at a patient's home, or another location convenient for the patient, if they are unable to come to the primary care practice for the visit. Counseling visits for the DM arm will be conducted by KUMC study personnel for all 12 practices randomized to this arm. KUMC study personnel will also handle (for all 36 practices and 1440 patients) centralized distribution of self-report questionnaires (on-line and by mail) and related data entry, tracking of patient recruitment and retention rates, retention phone calls to patients who miss assessment visits and have not been reached by the practice, and reporting requirements for KUMC IRB and PCORI.

#### **I3. Site evaluation**

Capacity at the *institutional level* has been vetted during the grant application and review process. KUMC, UNMC, and Marshfield Clinic have ample rural primary care practice affiliations. The site investigators are

experienced in conducting clinical trials in the area of obesity and diabetes control, particularly in the rural setting, and have achieved 85-90% patient retention rates. Capacity at the *local primary care practice level* will be ascertained through multiple phone calls and in-person visits made by a group of study personnel consisting of a study physician, PI or other non-physician investigator, and a Practice Coordinator staff member. Numerous conversations with PCPs and practice staff are anticipated regarding the study requirements and activities. All practices will be required to identify a PCP champion and Practice Liaison (primary point of contact) and must be able to develop a patient registry of approximately 300-400 patients with a BMI  $\geq 30$  kg/m<sup>2</sup>. Based on obesity prevalence rates in rural Midwest, even the smallest practices (~2000 patients) are expected to have sufficient patient numbers. Capacity will depend largely upon ability to integrate assessment visits and counseling visits into staff workloads and practice workflow. After fully vetting capacity and interest, the PCP champion and Practice Liaison will be required to commit by signing an KUMC Research Institute approved RE-POWER Practice Agreement form detailing the requirements and expectations for study participation.

#### **14. IRB-approved protocols**

All sites will use the same recruitment materials and IRB-approved protocol and consent form (consent form varying by arm). All practice staff who serve as research personnel will complete HSC training and training in protocols for collecting patient consent, conducting assessment visits, and conducting counseling visits (FFS and PCMH only). As a pragmatic trial, we will not strictly monitor adherence to counseling session guidelines but rather will offer training and support for the FFS and PCMH arms that is consistent with real-world models of care. As such, by design we are retaining the inherent differences in quality control and training in behavioral obesity treatment across the three arms, with the greatest level of training and quality control in the DM arm. In contrast, adherence to protocols for consenting patients and collecting data will be closely monitored. Initial training in study protocols will occur in-person during a central training at the start (see I5 below). Consenting protocols and assessment protocols will be demonstrated and practiced. On-going training will occur in-person during routine visits made by the Practice Coordinator, as well as through use webinars, and a written Standard Operating Procedures manual provided to each practice. The Practice Liaison at each practice will be trained to help ensure that only HSC-approved study materials are used and that the HSC protocol is followed. Practice Coordinators will oversee adherence to the protocols at the clinics by working closely with the Practice Liaisons. The Practice Coordinator will meet regularly with the Practice Liaison by phone and email and will visit the practice in-person at a minimum twice per year with more visits as needed.

#### **15. Communication**

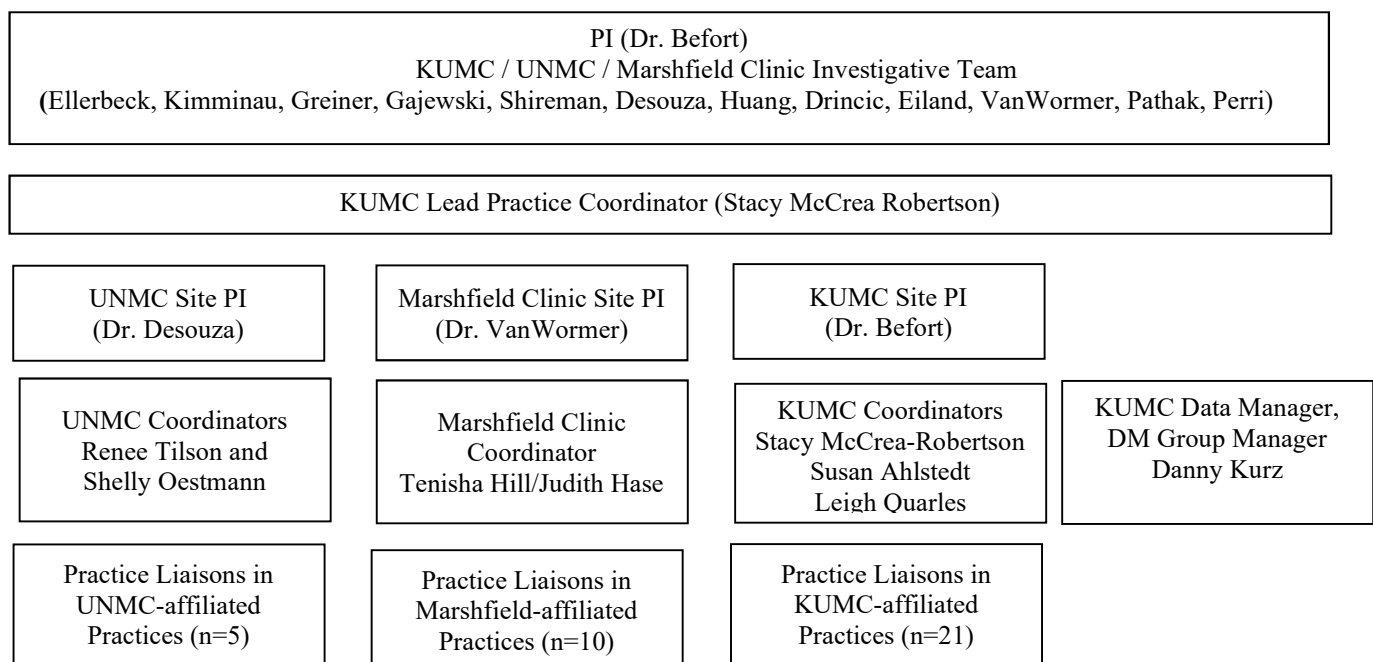
The study team includes investigators and staff from the three institutions (KUMC, UNMC, and Marshfield Clinic) and personnel from the 36 local primary care practices (20 practices through KUMC, 6 through UNMC, and 10 through Marshfield Clinic); See Organizational Chart. The PI will meet with her research staff at least weekly to oversee all aspects of the study. The PI will meet with all co-investigators at KUMC, UNMC, and Marshfield Clinic at least monthly via conference call or Skype to discuss project updates, questions and concerns, and progress with recruitment and retention for each clinic to ensure consistency in study implementation across the three institutions.

Communication between primary care clinics and the affiliated institution will occur primarily between the Practice Coordinator (central study personnel) and Practice Liaison (clinic study personnel). The KUMC study team includes a full-time Lead Practice Coordinator responsible for coordinating implementation of the study protocols across the primary care clinics. In addition to working closely with the other Practice Coordinators (staff from KUMC and one each at UNMC and Marshfield Clinic), she will serve as the primary contact for approximately 12 clinics affiliated with KUMC. The Lead Practice

Coordinator will manage delivery of all provider trainings and regulatory compliance across all 36 clinics and facilitate communication with practices related to the study activities they oversee.

Prior to launching each cohort, we will hold a central day-long training for practices enrolling patients for that cohort. The PCP and Practice Liaison will be asked to attend, as well as any other clinic staff who may conduct visits or counseling sessions. It is expected that not all clinic staff involved in the study will attend the central training, especially given the likelihood of staff turn-over during the course of the study. Therefore, all training material covered during the central trainings will also be made available through podcasts, and on-line materials. The central training will serve to enhance working relationships, build enthusiasm for the larger scope and mission of the project, and facilitate effective communication at the start that will be maintained throughout the study period. The central training will cover human subjects protection (delivered by study personnel with prior approval from IRB), use of REDCap, study protocols, and obesity treatment guidelines and counseling skills.

## Organizational Chart



## 16. Protocol compliance & Serious Adverse Events

The Practice Liaison or other practice staff will be responsible for completing the Serious Adverse Event Record Form in REDCap to the extent possible for all serious events that become known to the practice. The Practice Coordinators, overseen by site PIs, will work closely with each site to routinely assess protocol compliance and reporting of SAEs in a timely fashion. Central study personnel will initiate the Serious Adverse Event Record Form for events that become known outside of patients presenting at the practice; the practice will be asked to final the form with the more complete information available to them at the site. The PI will oversee compliance to SAE reporting timeframes with close monitoring of automated reports of Serious Adverse Event Record Forms in REDCap.

**I7. KUMC points of contact:**

Christie Befort: PI

Stacy McCrea-Robertson: Lead Practice Coordinator

**J. Personnel Who Will Conduct the Study****J1. Titles of those who will be present during study procedures**

- a. Informed Consent: Practice Liaison, Care Coordinator (i.e. nurse, RD, or behavioral counselor) or another clinic-employed health professional under PCP supervision
- b. Assessment Visits: Practice Liaison, Care Coordinator or another clinic-employed health professional under PCP supervision
- c. Counseling Visits:
  - FFS** arm: PCP, Care Coordinator, or another clinic-employed health professional under PCP supervision
  - PCMH** arm: Care Coordinator (nurse, RD, or behavioral counselor)
  - DM** arm: KUMC obesity treatment specialists (RD, psychologist, or other trained obesity treatment specialist)

**J2. Primary responsibility for study activities**

- a. Determining eligibility: KUMC Recruitment Coordinator, PI, and primary care clinic study personnel
- b. Obtaining informed consent: Practice Liaison, Care Coordinator or another clinic-employed health professional
- c. Providing on-going information to the study sponsor and the IRB: Lead Practice Coordinator and PI
- d. Maintaining participants' research records: Practice Liaison, Care Coordinator, and KUMC research team
- e. Taking anthropomorphic measures: Care Coordinator or another clinic-employed health professional
- f. Collecting laboratory specimens: Nurse or phlebotomist at or serving primary care practice.
- g. Performing counseling interventions: PCP, Care Coordinator or another clinic-employed health professional under PCP supervision; KUMC study personnel (obesity treatment specialists).
- h. Completing patient-report questionnaires: participants will complete questionnaires via email or mail distributed by KUMC study personnel
- i. Entering study data into REDCap: Practice Liaison, Care Coordinator or other clinic-employed health professional; KUMC research team
- j. Managing study database: the study database will be managed by the KUMC Medical Informatics, the KUMC Department of Biostatistics (Biostatistician: Byron Gajewski; Data Analyst: Lexie Brown), and study personnel under the PI.

## K. Assessment of Subject Safety and Development of a Data and Safety Monitoring Plan

### K1. Data and safety monitoring plan

- a. **Persons/groups who will review the data:** The PI, investigative team, and the DSMB will monitor data regarding recruitment, retention, and safety. The DSMB will consist of three individuals, not otherwise affiliated with the trial, who have the relevant expertise to monitor the study progress and participant safety. This includes individuals with expertise in nutrition and dietary intervention for weight loss, general medicine in rural settings, and exercise physiology and physical activity. The members and qualifications of the DSMB are as follows:

Debra K. Sullivan, PhD is Professor and Chair of the Department of Dietetics and Nutrition at KUMC and Director of the nutrition core for the Clinical and Translational Science Unit. She has extensive experience in conducting diet and behavior modification interventions as well as measuring dietary intake of diverse populations. Dr. Sullivan has led the nutrition components of numerous NIH R01-funded obesity intervention trials over the past 16 years, including overseeing all nutrition safety issues.

Joseph LeMaster, MD is an Associate Professor in the Department of Family Medicine at KUMC and a physician-scientist with clinical and research responsibilities. He has developed and evaluated cross-cultural communication interventions for healthcare providers who serve underserved populations. His prior research includes an intervention study in 5 rural clinics in mid-Missouri to promote better self-management of diabetes, during which time he learned first-hand how to solve recruitment and retention challenges.

Craig Harms, PhD is Professor and Chair of the Department of Kinesiology at Kansas State University. He is an exercise physiologist with a research program investigating cardiopulmonary limitations to exercise and the environment. He is NIH funded, Associate Editor-in-Chief for Medicine and Science in Sport and Exercise, and a Fellow of the American College of Sports Medicine.

- b. **Data/events that will be reviewed:**

Participant accrual. The DSMB will review study enrollment to help assure recruitment goals are met.

Participant attrition. Attrition will be reviewed at least monthly by the investigative team, and bi-annually by the DSMB. If the DSMB has concerns about whether attrition has reached a level that may inhibit the primary aim, they may initiate a conference call with investigators to discuss methods for improving retention.

Serious adverse events. The number and nature of all SAEs, unmasked to treatment condition, will be reviewed.

- c. **Frequency of review:** The DSMB will meet twice per year until active intervention with study participants is completed. The PI, designated staff, and study statistician (as needed) will prepare and present data reports to the DSMB. The DSMB will review all related serious adverse events both during scheduled meetings and during interim contacts for fatal or life threatening serious adverse events.

**d. Types of analyses to be performed:** Enrollment and attrition numbers will be presented as a percentage of the overall goal and broken down by institution and by primary care site. Number of SAEs will be tabulated, and the Serious Adverse Event Record Form will be included for each serious, related event. The DSMB will identify any needed modifications to data parameters and format as the study progresses.

**e. Safety-related triggers that would cause the PI to stop or alter the study:**

Stopping rules regarding recruitment and retention. Given the low risk nature of this diet and exercise trial, the most likely scenario for stopping the trial would be failure to recruit or retain participants. We have strategies in place to continually assess and improve recruitment and retention. The DSMB will review retention and initiate a meeting if needed with the investigative team to devise additional strategies to improve recruitment and retention if needed. If enrollment is 50% or less of goal by 3 years, or if attrition exceeds 30%, the DSMB will determine if the study should continue.

Stopping rules regarding exercise-related SAEs. Risk estimates of major cardiovascular events during strenuous exercise range from 0.3 to 2.7 events per 10,000 person-hours for men and 0.6 to 6.0 events per 10,000 person-hours for women.<sup>87</sup> The DSMB will review serious cardiovascular events related to study participation, evaluate the expected likelihood based on the current enrollment numbers and estimates of exercise person-hours, and determine if the study should continue. Other unanticipated situations may warrant stopping the trial; accordingly, the DSMB will review all serious adverse events.

## **K2. Serious Adverse Event reporting**

Surveillance for serious adverse events (SAEs) will occur at 6, 12, 18, and 24 months using a participant self-reported medical history update survey form. In addition, participants may report SAEs to practice or central study staff at other time points, e.g., during assessment visits, counseling sessions, retention contacts, and routine clinical care. All serious adverse events will be documented via a SAE Record Form. The form will capture information to include the date of onset, the date no longer serious, who first learned of the event and how, a description of the event, a classification of the seriousness, the outcome, and evaluation of the potential relationship to the intervention, and if at least possibly related, an evaluation of the expectedness.

Practice or central study staff, to include KUMC staff, who first become aware of the SAE will be responsible for initiating the SAE Record Form in REDCap. Central study staff and practice personnel have been asked to make a good faith effort to initiate the SAE Record Form within 2 business days of learning of the event. In some instances, however, meeting this two business day time frame may be difficult. Information obtained via online or hard copy surveys (patient self-report of hospitalizations) needs to be corroborated with the practice and/or patient before the report is initiated, to ensure the event was a true SAE (e.g., overnight hospitalization). Information provided by patients communicating with study counselors or practice staff may need to be corroborated via medical record review prior to reporting; this may take additional time especially if the hospitalization occurred at a facility not directly affiliated with the study practice; i.e., additional time may be needed to obtain hospital admit and discharge summaries prior to initiating the report. Given the noted circumstances, a delay in the reporting time period may be understandable in some instances. Given the minimal risk posed by the study intervention, a delay in initiating the report can be accepted if all parties act in good faith and attempt to maintain reporting timelines to the extent feasible.

Once the SAE Record Form is initiated, the KUMC Lead Coordinator will work with central study staff and practice personnel to collect any missing information on each event and complete each SAE report as soon as possible. This will include, confirming, in consultation with the site PCP and PI, and the KUMC study physician as needed, the evaluation of potential relationship to the intervention. Site physicians will make the final determination of study relatedness. The PI and Lead Practice Coordinator will help ensure adequate information is included in the description of the event for the DSMB to review the evaluation of study relatedness. Upon completion of an SAE Report, KUMC will report to the DSMB according to the timeframe described below and to the KUMC IRB in accordance with IRB guidelines. Non-serious adverse events will not be tracked or reported as part of safety monitoring activities.

Type of Data	Report to DSMB after SAE form completed	Timeline of DSMB Review	Data Reviewed By
All serious adverse events, enrollment, and retention; total and by site	Bi-annually	Bi-annually	Entire DSMB
Life-threatening or fatal SAEs—-independent of relatedness, unexpectedness	Within 1 working day	Within 1 week of SAE report	DSMB Chair or entire DSMB at discretion of Chair
Related and unexpected SAEs	Within 1 working day	Within 1 week of SAE report	DSMB Chair or entire DSMB at discretion of Chair
Related and expected SAEs	Within 5 working days	Within 2 weeks of SAE report	DSMB Chair or entire DSMB at discretion of Chair

### K3. Patient safety

If central study personnel become aware of new or worsening medical symptoms through information reported by patients during retention phone calls or during counseling sessions in the DM arm, they will refer the patient back to their PCP. Study laboratory results will be sent directly to the PCP per their standard operating procedures. Panic or critical value laboratory results will be managed per their standard operating procedures as well. All providers will be trained in SAE reporting during the central training and in ongoing discussions with the practice throughout the course of the study. Overall management of diabetes, hypertension, cardiovascular disease, and other medical conditions remains under the control of the treating PCP. The treating PCP, in communication with the KUMC PI and study physician, will determine if it is unsafe for the participant to remain in the study based on a change in medical status.

***Exercise-related AEs.*** If a cardiovascular event occurs during prescribed exercise, the physical activity component of the intervention may be suspended and/or later resumed with possible modifications after approval from the treating PCP. For exercise-related events and injuries for patients in the DM arm, the study clinician and/or the treating PCP will be consulted according to the symptoms reported. If appropriate, the participant's exercise goals or type will be modified. If the symptoms or injury do not resolve after an appropriate period of time, the participant will be referred to his or her PCP for further evaluation and may

be removed from the study. In the FFS and PCMH arms, management of any non-serious exercise-related AEs remains under the control of the PCP.

**Diet-related AEs.** If participants suffer negative health consequences from consuming nutritionally inappropriate diets (such as rapid weight loss, gallstones) and counseling to change nutritional intake have been ineffective, the treating PCP (in consultation with the central counselors for the DM arm) may decide to suspend the intervention. This scenario is uncommon but may occur.

### **III. SUBJECT PARTICIPATION**

#### **A. Recruitment**

##### **A1-2. Recruitment location and personnel**

The primary method of recruitment will be through mailings of a study invitation and brochure from the PCP. This method is necessary to reach patients who otherwise would not visit the practice during the recruitment window, i.e., if we relied solely on recruitment during routine visits to the clinic we would risk a bias toward selecting patients with greater medical co-morbidities. This recruitment method also allows us to track and evaluate the enrollment rate and representativeness of participants.

Each practice will develop a registry of patients with a BMI in the target range. Providers may review the registry to identify and exclude patients who may be inappropriate (e.g. terminal cancer, communication disorders, other medical contraindications). The mailing will include an invitation letter on practice letterhead, signed by the provider, a study brochure (which will include the study phone number and the web address for our study website), and a pre-stamped, opt-in post card for those who prefer to receive a phone call. The letter will ask interested patients to contact the study line or return the post card. Patients will also have the option of contacting the study team via a contact link on our study website. In our current R01 trial in the rural setting, the opt-in postcard had a higher response rate and higher enrollment rate compared to relying on patients to make the initial call.<sup>89</sup> The mailing will be assembled by central study team with an approved HIPPA waiver. Practices may elect to assemble the mailing themselves, however our experience indicates it will not be feasible for busy practices.

Recruitment will also occur through in-clinic approaches. Study brochures will be distributed at various places in the clinics (passive approach), and providers will be able to directly refer patients during routine medical visits (active approach). Study brochures will contain a link to our RE-POWER website containing basic study information. The website will be contained within the KUMC system and is being developed with the help of KUMC Information Technology personnel. Clinic staff will instruct interested patients to contact the central recruitment and screening line. If practices have difficulty attaining their stated goal of 40 patients, additional recruitment efforts may be utilized to identify patients. Examples of these additional avenues include the use of press releases/news briefs in local newspapers, on practice websites and Facebook pages; placement of referral posters in the local community, and/or welcoming existing study participants to refer their acquaintances who go to the same clinic by sharing the study line.

##### **A3. Copy of recruitment brochures**

See Attachments

##### **A4. Copy of participant recruitment letter and opt-in postcard**

See Attachments



## **B. Screening Interview**

KUMC study personnel will screen potential participants who call the study line or return the opt-in postcard. These personnel are trained in human subjects research and are experienced in clinical trial recruitment and screening. They will inform patients about the study, obtain verbal assent for eligibility assessment, and then screen for eligibility by phone. See attachment for the screening questionnaire.

## **C. Informed Consent Process and Timing of Obtaining Consent**

### **C1. Obtaining consent**

If deemed eligible for the study following the telephone screening, the patient will have the option of receiving an email with a link to the baseline survey consent form or a hard-copy consent/survey via mail. The baseline survey consent will include information about the purpose of the baseline survey. The consent will indicate agreement to complete the survey is separate from giving full consent for the trial. Participants must complete the baseline survey in order to be enrolled in the study.

After a patient completes the baseline survey, medical clearance will be obtained from their primary care provider or lead physician at the practice. Practice personnel will then schedule for the patient for the consent/baseline visit at the practice. Patients must complete the consent/baseline visit within 60 days of the phone screening.

At the consent/baseline visit, informed consent for the full trial will be administered. Practice staff will give detailed and comprehensive information about the 2-year trial and answer all patient questions.

Practices will be encouraged to verify BMI prior to consenting patients. BMI verification may, however, occur before or after consent depending on practice workflow. If a patient is ineligible based on measured BMI, but is within 0.5 BMI points (3-5 lbs), the patient may elect to return for BMI verification after a minimum of one week. If a patient is ultimately ineligible based on BMI verification, the patient will be considered a screen-fail. The ineligible BMI status will be documented in the study database, and the patient will not be enrolled in the study. Signed consent forms for both eligible and ineligible subjects will be retained.

### **C2. Consent process**

Consent will occur in-person at the participating practice with trained practice personnel. A brief video will be available to help standardize the consent process, and practice personnel will be present to answer questions. The consent process will include explicit indications (verbal and written) that participation is always voluntary, and that patients are free to leave the study at any time with no consequences for their routine medical care at the local practice or affiliated institutions (KUMC, UNMC, Marshfield Clinic). All participants will receive a signed copy of their signed trial consent form. A copy of the signed consent will be placed in the patient's medical record at the practice. Practices will fax or secure email copies of the consent to KUMC within approximately two business days, or upload a copy of the consent into the secure study database, REDCap. Original consent forms will be retrieved from the practices by central study staff or mailed to KUMC in pre-addressed envelopes provided to them, or to UNMC or Marshfield Clinic study personnel who will then forward to KUMC. All original hard copy consents will ultimately be maintained at KUMC in a secure locked file cabinet.

### **C3. Ability to give informed consent**

Participants' ability to give informed consent will be assessed 1) by KUMC staff conducting eligibility screenings and baseline surveys, 2) the primary care physician or lead physician at the practice prior to the consent visit, and 3) by the clinic staff administering the consent during the baseline/consent visit. Those with compromised ability to consent will not be enrolled.

#### **C4. Patient retention protocol**

**As a pragmatic trial, we will not implement stringent retention protocols to improve retention to counseling visits, and we expect differential attendance across arms. However, we will implement retention contacts to ensure adequate retention to assessment visits.**

The REDCap scheduling forms will specify date ranges for assessment visits. Designated practice staff will use the REDCap scheduling form as a guide to schedule study visits into the practice's preferred scheduling software (e.g. their EMR, practice management tool and/or REDCap). Practices will utilize their own appointment reminder system as available. Practices may opt to send automated text messages and/or emails to patients to remind them of upcoming visits. If participants do not have access to email, practice staff will be prompted by REDCap report to call patients to remind them of their upcoming assessment visits. KUMC study staff will work with the practices to define the most efficient and productive manner of conducting appointment reminders with the means available through the practice and REDCap capabilities.

Practice Coordinators will work closely with the Practice Liaisons to follow-up with participants who miss an assessment visit. After failed contact attempts by the practice, KUMC study personnel will take over attempt to contact and reschedule the patient. Retention will be monitored and discussed in a weekly project management meeting among KUMC staff. Practice Liaisons will be contacted as needed to trouble shoot retention strategies at the practice level. For patients who miss an assessment visit, attempt will be made to capture missing weight data from chart review.

#### **D. Alternatives to Participation**

Participants may choose not to participate in this research study. Some of the other options instead of participating include joining a commercially available weight loss program (e.g. Weight Watchers on-line or in-person where available) self-help groups (TOPS), using online resources (e.g., [www.ediets.com](http://www.ediets.com), [mypyramid.com](http://mypyramid.com)), and/or following self-help diet books.

#### **E. Costs to Participants**

Participants will likely be visiting their PCP more frequently than usual for study-related visits. As a result, the PCP may request to see their patients more regularly to deliver standard medical care for other co-morbid conditions (i.e. hypertension or diabetes). All standard medical care will be billed to the participant's insurance in the usual way. The participant will be responsible for any co-pays or deductibles according to their insurance coverage.

Participants will be responsible for the cost of their food including any pre-portioned meals, nutritional shakes, and other groceries purchased during the study. They will also be responsible for phone costs associated with the weight-management counseling calls in PCMH and DM, and cell phone data or internet costs incurred during the study if they choose to use a smartphone application or web-based program to track weight, activity, and meals.

#### **F. How New Information Will Be Conveyed to Study Participants and Documented**

New information will be communicated to participants by mail, in addition to communication that may occur during counseling visits or assessment visits. Communication of new information will be documented in the secure REDCap database.

## **G. Payments**

Participants will receive payment for each of four completed in-clinic assessment visits (baseline, 6-month, 18-month, and 24-month) and mileage to these visits. Participants will receive \$30 for the first three in-person data collection visits (baseline, 6 month, 18 month) and \$50 for the 24 month visit. Following each in-person assessment visit payment + mileage will be transferred to the participant's designated ClinCard. Following each patient questionnaire completion (baseline, 6-mo, 12-mo, 18-mo, and 24-mo), \$25 will be transferred to the participant's designated ClinCard. If the patient completes some but not all of the surveys, they will receive half of the survey payment (\$12.50). Participant will receive up to a total of \$265 + mileage by the end of the study. Mileage costs will be calculated at the current government approved rate.

## **H. Payment for a Research-Related Injury**

The research team does not take financial responsibility for any injury incurred as a result of participating in the study. Treatment claims will be submitted to the participant's health insurance policy, their government program, or another third party, but the participant will be billed for the costs that are not covered by their insurance.

# **IV. DATA COLLECTION AND PROTECTION**

## **A. Data Management and Security**

### **A1. Persons with access**

Designated study staff from KUMC, UNMC, and Marshfield Clinic will have access to the study data including the PI, co-investigators, , data manager, practice coordinators, other study staff members, and designated staff from KUMC Biostatistics and Medical Informatics. Study personnel from the primary care practices will have access to the data for their patients only.

### **A2. Data security**

All electronic files will be stored within the REDCap database, which is password protected and available only to designated study personnel. Study data gathered during in-clinic assessment visits and counseling sessions will be entered directly into REDCap, captured into the practice EMR, or recorded on hardcopy study forms depending on workflow unique to each practice. Existing data management procedures and staffing levels at each practice will drive the data collection method chosen at the practice. Central study staff will work with the practices to define the most efficient manner for collecting study data.

Data collected originally on hardcopy forms will ultimately be entered into REDCap by practice or central study staff. Any hard copy forms containing study data will be maintained at the practice in a secure location, in a designated RE-POWER box. Forms will be held on-site until they are retrieved during site visits or until practice staff are instructed by central study staff to send to KUMC. QA/QC of data entry will be performed on an ongoing basis.

Self-report surveys will be completed on-line (entered directly into REDCap) for the majority of participants. For participants who do not have access to email, they will be mailed hardcopies of the surveys labeled with their study ID. Participants will return the completed forms to KUMC in pre-addressed envelopes. KUMC study personnel will enter the survey responses into REDCap and check for data entry accuracy. All hard copy forms will be kept in secure locked file cabinets for 6 years following the submission of the final report and close-out procedures for the research project.

Participants in the DM arm and PCMH arm will be given the option of setting up a Lose It! account to aid in dietary tracking. Account set up requires an email address, however, should participants prefer not to use their personal email they will have the option of logging on using a de-identified email account

created by the group leader. Lose It! Terms and Conditions of Use allow for the storage and use of all information indefinitely. However, in the case our study participants, this information need not be connected to PHI. This is outlined in the consent form.

Participants in the DM arm and PCMH arm who do not have a smartphone or internet access will have the option of texting their weight and physical activity minutes to a REDCap survey. The texting option is a part of REDap's telephony feature (sending and receiving SMS text messages as a part of survey functionality) and utilizes Twilio – an external third-party company. No data will be stored on the 3<sup>rd</sup> party Twilio servers and logged transaction will be removed by REDcap instantaneously. The survey is initiated by the participant texting a predefined code to the Twilio phone number assigned to our project. Once the code is sent, the participant is prompted to enter their weight (numeric only), total physical activity minutes over the past seven days (numeric only), and their primary phone number (numeric only). The survey results are stored in our REDCap database, which is password protected and only accessible to approved study personnel.

Arkadin will store conference call recordings for 30 days and phone numbers of participants who join the calls. The call information and participant phone numbers are stored on secure and encrypted servers and are only visible to administrators of Arkadin accounts. All administrators have signed confidentiality waivers protecting the PHI information of their customers. This will be outlined in the consent form. Conference call recordings will be kept by KUMC on secure and encrypted servers for a minimum of six years after the completion of the study.

Some blood samples collected during assessment visits at Marshfield Clinic sites are designated for long term storage. These samples will be de-identified and stored in the Marshfield Clinical Laboratories Core. Samples will be inventoried in a secure password protected database maintained solely by the MCLC. These de-identified samples will be stored in the central laboratory indefinitely or until KUMC requests transfer to their storage facilities.

### **A3. Identification of human subjects**

The secure database REDCap will be used to store names, addresses and social security numbers, and will link this identifiable information to the participants' unique study ID.

### **A4. Coding**

Study IDs will be used on all biospecimens in lieu of patient names or other identifiers.

### **A5. Data links**

Study IDs will be linked to patient information in the REDCap database.

### **A6. Data storage and protection**

Data management will be overseen by the KUMC Department of Biostatistics following standard procedures for data security and access. Data will be stored on the secure REDCap database and on the KUMC- supported network drive as password protected files. Networked file servers provide constant hardware backups of stored data through mirrored storage systems, and daily tape backups are also performed. Weekly tape backups are stored off-site for additional protection of research data.

### **A7. Mobile devices**

Participants may choose to respond to REDCap surveys using personal mobile devices such as smartphones, tablets, or laptop computers.

## **A8. Security measures**

See section A2.

## **B. Sample / Specimen Collection**

Blood samples will be collected by authorized health care providers at baseline, 6 months, and 24 months. Please see section IIE4.

## **C. Tissue Banking Considerations**

Plasma and buffy coat samples collected at Marshfield Clinic sites will be banked for future use at MCLC. Samples will be used for future analysis of biomarkers indicated in pathways between obesity, weight loss and other chronic medical conditions. In addition, there is a potential to analyze for markers that have not yet been identified including genetic markers. See section IIE4 for more details. At any time, participants can request that their blood samples be destroyed. The storage of samples in the repository is voluntary; participants will have the option of opting-out of sample storage at the time of consent and will be able to change their minds at any time.

## **D. Procedures to Protect Participant Confidentiality**

Identifiable information will be required on the physician clearance form, hardcopy consent forms, which, and hardcopy data collection forms at some sites that are not entering directly into REDCap, will be collected by practice staff and held in a secure location until they are mailed/faxed to, or picked up by KUMC research staff. After the KUMC study team receives the physician clearance forms, consent forms, and all source documents they will be kept in a locked file cabinet.

Attendance sheets may be printed and used for note taking during group meetings in the PCMH and DM arms. Attendance sheets will include the each participant's study ID, first name, session attendance, and notes. After each meeting, the group leader will enter all attendance info and notes into REDCap and will store hardcopies in a locked file cabinet.

Participants in the PCMH and DM arms will be given the option to complete a biosheet including a family or individual photo, name, and questions about their hometown, family, and hobbies. Group members will submit their biosheet to their group leader via mail or email after the first week of the intervention. Group leaders will compile and send biosheets to all group members. Once biosheets are sent to the group members, the group leader will keep a password protected PDF in the KUMC server and will store all hardcopies in a locked file cabinet. The biosheet activity is voluntary for all participants.

Participants will be informed that sharing of all information is voluntary both during assessment visits and counseling sessions. They will be encouraged to share concerns regarding weight-related issues with the clinic and study staff only to the extent that they feel comfortable. Respect for confidentiality during group visits will be highlighted as a group norm at the outset and reinforced throughout the intervention period.

Participants in the DM and PCMH arms have the option to create Lose It! accounts. Participants will enter an email address and user name when they set up their account. Counselors in the PCMH and DM arms will have access to group member's Lose It! data for the purposes of giving dietary feedback. Lose It! account set up and use will be voluntary and confidential information will be discussed in the consent form. The texting option will also be voluntary and will be discussed in the consent form.

Group phone meetings will be recorded through Arkadin and written notes for each counseling session may be taken by the counselor. The audio recordings will be downloaded by the counselor and saved on the KUMC secure network. Recordings will be labeled with the date of the recording and a de-identified group number. There will be no identifying participant information included in the recording labels. Information concerning these recordings will be discussed in the consent form.

## **E. Quality Assurance / Monitoring**

### **E1. Basic Approach**

Our basic approach to quality assurance will be as follows:

- Pilot test all REDCap forms
- Prepare a well-documented Standard Operating Procedure for each arm
- Train and certify all practice staff (See Section IIE2b)
- Maintain an up-to-date list in REDCap of trained and certified practice personnel
- Annually observe practice staff to ensure study protocols are being followed

### **E2. Data accuracy**

Whenever possible, data collected at clinic visits will be entered directly into REDCap. The REDCap database will be designed to alert users when forms are incomplete and when the reported data is suspect (i.e. when data is outside the expected range). All hardcopy study forms generated at the practices will be entered into REDCap preferably by practice staff, otherwise it will be sent to KUMC study staff for data entry.

All hardcopy forms (whether generated at the practice, by participants (i.e. surveys), or by KUMC or other central study staff), will be double checked for completeness and accuracy by a KUMC study staff member. All hard copy forms will be subsequently stored at KUMC in a locked file cabinet. Accurate data entry of patient survey forms into REDCap will be verified through double data entry and reconciliation with source documents when necessary.

Designated KUMC biostatistical personnel will monitor data quality and accuracy throughout the data collection process. Dr. Byron Gajewski will provide statistical oversight for data management. Ms. Lexie Brown, Senior Research Analyst, will perform edit, logic, and range checks on the finalized study database and send on-going queries for resolution to the clinical team. Data logic checks for the primary endpoint (weight) will be conducted on a weekly basis during data collection. Once all database queries have been resolved by the clinical team, she will be responsible for creating data sets for analysis. Ms. Brown will perform initial database restructuring in preparation for analysis by Dr. Gajewski. In addition, she will conduct the initial analyses under the direction of Dr. Gajewski. Dr. Gajewski will perform the final statistical analyses for the study aims listed in the protocol.

### **E3. Third party monitoring**

There are no plans for third party data monitoring.

## **V. DATA ANALYSIS AND REPORTING**

### **A. Statistical and Data Analysis**

See section IIC for detailed information on statistical procedures and data analysis. Interim analyses will not occur. +

### **B. Outcome**

In this comparative effectiveness pragmatic trial, we expect participants in the PCMH and DM arms to have better outcomes compared to participants in the FFS arm. We also expect participants in the DM arm to have better outcomes compared to participants in the PCMH arm. In order to have adequate power for the analyses of clinically significant weight loss differences across the three arms, a successful trial will randomize the targeted number of practices ( $n = 36$ ), enroll an average of 40 patients per practice (total patient  $n = 1440$ ) and achieve  $\geq 80\%$  complete data for the primary endpoint (weight at 24 months).

### **C. Study Results to Participants**

We will not conduct interim analyses and will maintain equipoise throughout the intervention implementation period. After all data have been collected, we will engage our Patient Advisory Board and other stakeholders in dissemination planning to help ensure the findings are disseminated to patients and providers through non-academic and local channels.

### **D. Publication Plan**

A Dissemination Planning meeting will take place in year 5 of the study. This will be an in-person meeting of the Patient Advisory Board (PAB), provider and health system stakeholders, and investigators. The purpose of the meeting is to review findings together, identify key highlights of participants' experiences, share lessons learned, and identify the appropriate messages and vehicles for disseminating study findings. Both quantitative and qualitative findings from the study will be presented. Selected study participants, PCPs, and staff from participating practices will be invited to this meeting so that they can directly ask and address questions. Patient advisors and stakeholders will review findings to assure that messages are easily understandable by both lay and professional audiences. We expect our PAB and stakeholders to contribute new ideas for venues for dissemination. Venues like Kansas Connections magazine, Rural Roads magazine, Harvest Public Radio, and local newspapers may be some of the trusted news sources for reporting results within the region. Our PAB and provider stakeholders will also participate in the scientific process of disseminating the study findings wherever we can empower them to meet criteria for authorship, and present or co-present at public health/obesity/primary care conferences.

We will present the findings at a variety of national meetings such as the Obesity Society, the Society of General Internal Medicine, North American Primary Care Research Group, the AHRQ-sponsored PBRN Conference, and the Society of Behavioral Medicine. We will also aim to publish the findings in top-tier journals.

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