Using Partners to Enhance Long-Term Weight Loss (Partner2Lose)

NCT03801174

PI: Corrine Voils, PhD
2/9/2021

USING PARTNERS TO ENHANCE LONG-TERM WEIGHT LOSS (Partner2Lose)

A phase III, single-blind, randomized controlled trial evaluating the efficacy of partner-assisted compared to patient-only intervention for long-term weight loss.

Protocol Number: 2018-1400

Principal Investigator: Corrine I. Voils

Date: 2/9/2021

Protocol Version History

Protocol Version	Date	Description of Changes
2	1/4/2019	Mediators will be measured at additional time points (Month 3, 9, 15 and 21). Dietary fat intake has been removed as an outcome from aim 2.
3	2/11/2019	Correction to the blood pressure reading at the screening visit. Added the clinicaltrials.gov number.
4	2/28/19	Revision to the exertional chest pain or dyspnea criterion.
5	4/8/19	Clarification to data analysis procedure and storage of the audio recordings.
6	5/14/19	Updated version of table 3.
7	6/11/19	Correction to table 2 and 7. New eligibility criterion added.
8	8/14/19	Clarification made regarding the maintenance text messages in section 9.2.2
9	3/11/2020	Adding that group sessions may be delivered remotely.
10	4/3/2020	Adding that self-report weight photos may be collected when classes are delivered remotely.
11	4/6/2020	Adding the option to mail participants scales if in-person interactions aren't feasible.
12	5/13/2020	Adding a new inclusion eligibility criterion, the option to do the screening visit remotely and obtain oral consent, a COVID-19 survey, and OnceHub as an online scheduling platform. Removing eligibility criterion.
13	6/17/2020	Editorial changes.
14	2/9/2021	Adding that the COVID-19 survey will be collected at month 24.

Contents

Statement of Compliance

The signature below constitutes that the research will be conducted in accordance with the approved protocol, applicable regulations, laws and institutional policies.

I agree to ensure that all staff members involved in the conduct of this study are informed about their obligations in meeting the above commitment.

PRINTED OR TYPED NAME	SIGNATURE	DATE
Corrine I. Voils		
Principal Investigator(s)		

1. List of Abbreviations

AE	Adverse event
ASA24	Automated Self-Administered 24-Hour Dietary Assessment Tool
BMI	Body mass index
CFR	Code of Federal regulations
CouPLES	Couples Partnering to Enhance Lipid-lowering Strategies
CRF	Case Report Form
DHHS	Department of Health and Human Services
DOS	Department of Surgery
DMC	Data Monitoring Committee
eCRF	Electronic Case Report Forms
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICH E6	International Conference on Harmonisation Guidance for Industry, Good Clinical Practice: Consolidated Guidance
ICTR	Institute for Clinical and Translational Research
IRB	Institutional Review Board
LDL	Low-density lipoprotein cholesterol
MAINTAIN	Maintenance After Initiation of Nutrition Training
MOP	Manual of Procedures
MNAR	Missing Not At Random
MSDS	Material Safety Data Sheet
OHRP	Office for Human Research Protections
PHI	Protected Health Information
PI	Principal Investigator
REDCap	Research Electronic Data Capture
SAE	Serious Adverse Event
SMPH	School of Medicine and Public Health
WREN	Wisconsin Research & Education Network

2. Study Summary

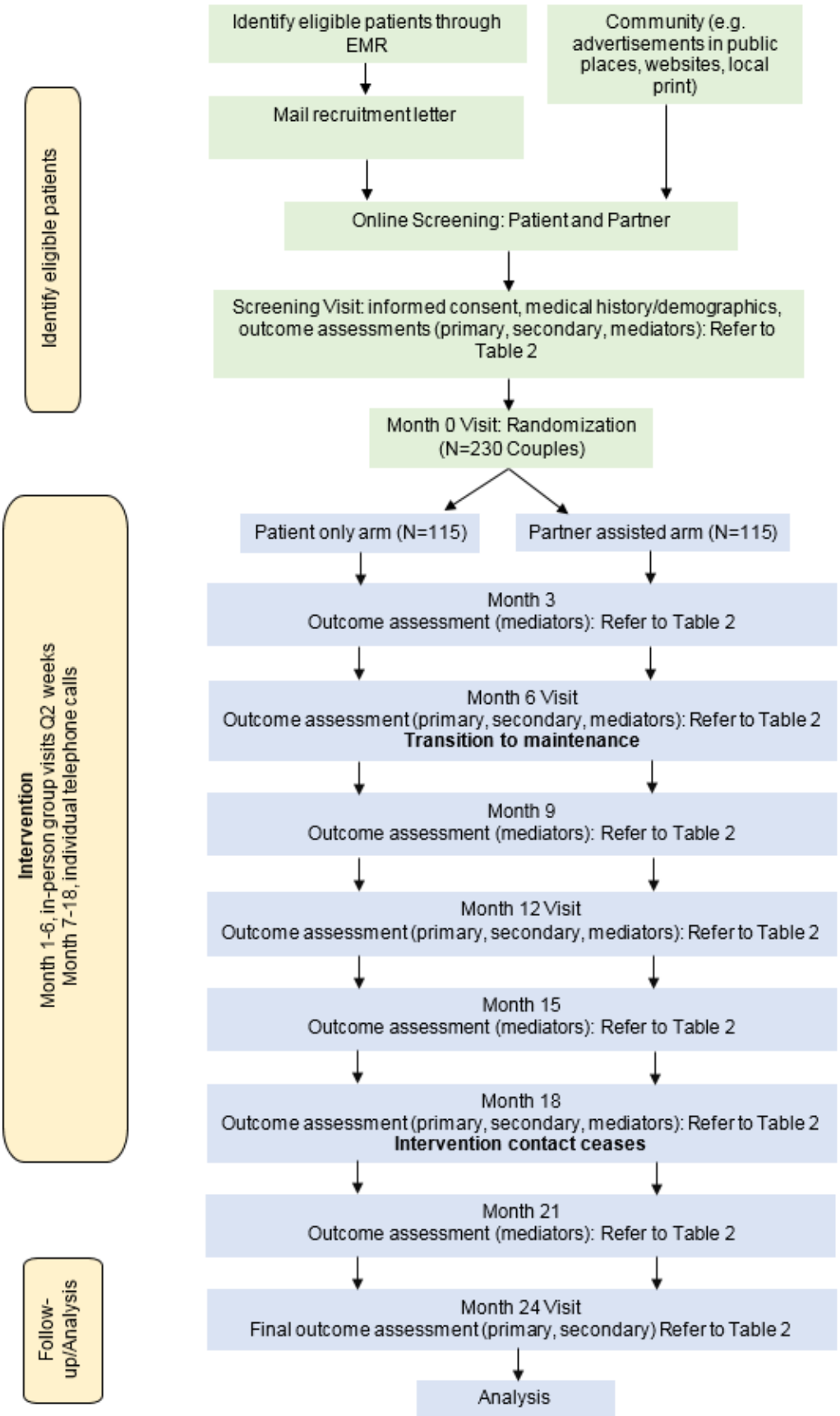
Title	Using Partners to Enhance Long-term Weight Loss (Partner2Lose)
Short Title and Precis	Partner2Lose
Protocol Number	2018-1400
ClinicalTrials.gov number	NCT03801174
Phase	Phase III equivalent
Methodology	Randomized controlled trial
Study Duration	5 years
Study Center(s)	University of Wisconsin (Madison, WI) Duke University School of Nursing and School of Medicine (Durham, NC) Research Triangle Institute (Seattle, WA)
Objectives	Aim 1: Test the hypothesis that estimated patient weight is at least 2.5 kg lower at 24 months in the partner-assisted arm than the patient-only arm. Aim 2: Test the hypotheses that estimated daily caloric intake are significantly lower and frequency of moderate intensity physical activity is greater at 24 months in the partner-assisted arm than the patient-only arm. Aim 3: Evaluate whether weight loss is mediated by increases in transformation of motivation, outcome efficacy, couple efficacy, communal coping, and social support for diet and physical activity.
Number of Participants	N=230 couples (460 total)
Diagnosis	Obese/overweight

Inclusion Criteria	<u>Patient</u> • aged 18-74 years • BMI 27-29.9 kg/m^2 plus presence of at least one obesity-related comorbidity (e.g., type 2 diabetes, blood pressure >130/80, dyslipidemia, obstructive sleep apnea, gastroesophageal reflux disease, or coronary artery disease) or BMI ≥ 30 kg/m^2 • cohabitating and at least daily contact with a spouse/domestic partner (same or opposite sex) • desire to lose weight • agrees to attend visits per protocol • access to reliable transportation • score of at least 4 out of 6 on a validated cognitive screener • able to stand for weight measurements without assistance • speak and read English • individual smart phone with data and texting plan • individual e-mail address • able to complete online screener without assistance • able to use a smartphone, tablet or computer with a video camera or webcam and microphone to download apps and to connect to a video conference call without assistance <u>Partner</u> • aged 18 or older • willing to participate • access to reliable transportation • score of at least 4 out of 6 on a validated cognitive screener • speak and read English • smart phone with data and texting plan (not shared with index patient) • e-mail address (not shared with index patient) • able to complete online screener without assistance

Exclusion Criteria	Patient
	• weight loss of at least 5 lbs in the month prior to screening
	• currently enrolled or enrollment in previous 3 months in a clinical or research program focusing on lifestyle change that could affect weight
	• current use of weight loss medications (prescription or over-the-counter)
	• history of bariatric surgery or planning to have bariatric surgery in the study timeframe
	• residing in a nursing home or receiving home health care
	• impaired hearing
	• significant dementia, drug or alcohol abuse, or unstable psychiatric illness (e.g., schizophrenia or psychosis)
	• current treatment for cancer or being treated for cancer (beside skin cancer) in the last 6 months
	• use of Insulin, Sulfonylureas, or Meglitinides for diabetes due to increased risk for hypoglycemia
	• pregnant, breastfeeding or planning to become pregnant within the study timeframe
	• diuretic medication doses higher than hydrochlorothiazide 25 mg daily, furosemide 40 mg daily, Torsemide 20 mg daily, Bumetanide 1 mg daily or any use of Metolazone). Use of potassium-sparing diuretics is acceptable.
	• chronic or unstable illness that would limit ability to participate (e.g., recent hospitalization; unstable heart disease in the 6 months prior to screening)
	  ○ having acute coronary syndrome (ACS) including STEMI (ST-elevation myocardial infarction), NSTEMI (non-ST elevation myocardial infarction) and unstable angina (UA)
	  ○ recent or impending coronary revascularization [recent coronary bypass grafting (CABG) or percutaneous coronary intervention (PCI)
	  ○ unstable arrhythmia (e.g., hospitalized for unstable atrial fibrillation, supraventricular tachycardia, ventricular tachycardia, ventricular fibrillation and/or firing of implantable cardiac defibrillator [ICD])
	  ○ recent acute congestive heart failure exacerbation [requiring increased doses of oral or intravenous (IV) diuretics or hospitalization]
	  ○ patient may be rescreened after sixth months
	  ○ chronic kidney disease at stage 4 or higher
	• exertional chest pain, dizziness or lightheadedness
	• pain or other condition that prohibits mild-moderate exercise
	• history of ascites requiring paracentesis
	• planning to relocate in the next 2.5 years
	
	Partner
	• underweight BMI (i.e., BMI < 18.5 kg/ m^2)
	• residing in a nursing home or receiving home health care
	• impaired hearing
	• any severe health issue that would impair the partner's ability to provide support, including
	  ○ significant dementia, drug or alcohol abuse, or unstable psychiatric illness (e.g., schizophrenia or psychosis)
	  ○ current treatment for cancer or being treated for cancer (beside skin cancer) in the last 6 months
	  ○ In the last 6 months prior to screening:

	▪ acute coronary syndrome (ACS) including STEMI (ST-elevation myocardial infarction), NSTEMI (non-ST elevation myocardial infarction) and unstable angina (UA) ▪ recent or impending coronary revascularization [recent coronary bypass grafting (CABG) or percutaneous coronary intervention (PCI) ▪ unstable arrhythmia (e.g., hospitalized for unstable atrial fibrillation, supraventricular tachycardia, ventricular tachycardia, ventricular fibrillation and/or firing of implantable cardiac defibrillator [ICD]) ▪ recent acute congestive heart failure exacerbation [requiring increased doses of oral or intravenous (IV) diuretics or hospitalization]
Study Product, Dose, Route, Regimen	Partner-assisted weight management counseling delivered in group visits every two weeks (months 1-6); individual telephone calls (months 7-18); and no further contact with the interventionist (months 19-24)
Duration of administration	6-month weight loss initiation intervention, 12-month maintenance intervention and 6-month no intervention contact period (24-month total follow-up)
Reference therapy	Patient-only weight management counseling
Statistical Methodology	Linear mixed models will be used to evaluate weight, dietary intake, and physical activity along with mediation analysis to evaluate the role of interdependence theory constructs

3. Schematic of Study Design



4. Key Roles

Principal Investigator:

Corrine I. Voils, PhD
University of Wisconsin-Madison
University of Wisconsin Department of Surgery
600 Highland Ave
K6/100 Clinical Science Center
Madison, WI 53792-1690
Office: 608-262-9636
voils@surgery.wisc.edu

Participating Sites:

Duke University School of Nursing
307 Trent Drive
Durham, NC 27710

Research Triangle Institute
119 South Main Street
Union Trust Building, Suite 220
Seattle, WA 98104

Sub-Investigator(s):

Heather M. Johnson, MD, MS, Cardiologist
University of Wisconsin-Madison
University of Wisconsin (UW) School of Medicine & Public Health
Division of Cardiovascular Medicine
H4/512 Clinical Science Center, MC 3248
600 Highland Avenue
Madison, WI 53792
Office: 608-263-0891
hm2@medicine.wisc.edu

Ryan Shaw, PhD, RN, Associate Professor
Duke University School of Nursing
4145 Pearson Building
307 Trent Drive
Durham, NC 27710
Office: (919) 684-9434
ryan.shaw@duke.edu

Laura Porter, PhD, Clinical Psychologist
Duke University School of Medicine
2200 West Main St, Suite 340
Durham, NC 27705
Office: (919) 416-3436
laura.porter@duke.edu

Megan Lewis, PhD, Social Psychologist
Research Triangle Institute
119 South Main Street
Union Trust Building, Suite 220
Seattle, WA 98104
Office: 206-268-3613 (3-3613)
melewis@rti.org

Data Monitoring Committee Contact:	Amy Siedschlag, MS, Protocol Review Manager UW Institute for Clinical and Translational Research (ICTR) Data Monitoring Committee (DMC) University of Wisconsin School of Medicine and Public Health 2112 Health Sciences Learning Center 750 Highland Avenue Madison, WI 53705 (608) 263-3804
Funding Sponsor:	National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) 9000 Rockville Pike Bethesda, MD 20892 1-800-860-8747 healthinfo@niddk.nih.gov
NIH Point of Contact:	Robert Kuczmarski, Program Director NIDDK, Division of Digestive Diseases and Nutrition 9000 Rockville Pike Bethesda, MD 20892 301-451-8354 kuczmarskir@mail.nih.gov
Biostatistician:	Lu Mao, PhD, Assistant Professor University of Wisconsin-Madison Department of Biostatistics and Medical Informatics 600 Highland Ave, K6/428 Clinical Science Center Madison, WI 53792 (608) 263-5674 lmao@biostat.wisc.edu

5. Background and Introduction

This document is a protocol for a human research study. This study is to be conducted according to US and international standards of Good Clinical Practice (FDA Title 21 part 312/812 and International Conference on Harmonization guidelines), applicable government regulations and Institutional research policies and procedures.

5.1 Background and Rationale

Obesity negatively affects health and is costly. Compared with normal weight peers, individuals with obesity are at increased risk for type 2 diabetes mellitus, gallbladder disease, hypertension, congestive heart failure, and coronary heart disease.(1, 2) Obesity is also associated with reduced health-related quality of life.(3, 4) People who are overweight with at least one obesity-related comorbidity are also at risk for adverse outcomes and thus targeted for treatment by the current obesity guideline.(5) The medical-care cost burden of obesity is high, with annual expenditures attributable to obesity estimated at $190 billion.(6) Among nationally representative cohorts, the average annual incremental healthcare cost associated with obesity compared to being normal weight is ~$1,308 per person.(7, 8) Effective strategies are needed to address the individual and societal impact of the obesity epidemic.

Weight loss improves health outcomes and reduces healthcare costs. Weight loss improves arthritis and functional status(9, 10) and decreases blood pressure(11) and type 2 diabetes incidence.(12) A systematic review of the impact of weight loss on health and economic outcomes concluded that several weight loss interventions are cost-effective, and some interventions may even be cost-saving in targeted populations.(13) To decrease the burden of obesity/overweight, interventions are needed that promote long-term weight loss.

Behavioral interventions that involve dietary modification and physical activity, combined with cognitive and behavioral strategies, are efficacious for short-term weight loss but less so for long-term weight loss. Several randomized trials indicate that various dietary approaches (e.g., low-carbohydrate diet, low-fat/low-calorie diet) are efficacious for inducing short-term weight loss.(14, 15) A systematic review indicated that supplementing dietary modification with physical activity improves 12-month outcomes above diet alone.(16) Incorporating behavioral strategies such as self-monitoring, stimulus control, action planning, and problem-solving helps promote adherence to these lifestyle behaviors.(14, 17) Following significant weight loss, most people tend to regain 1-2 kg per year, with the majority of people returning to baseline weight by 5 years.(17) Various strategies have been evaluated to reduce weight regain, including sequential dieting, meal replacements, medications, and behavioral approaches.(18) These strategies have not reduced the overall pattern of regain for most people.(17) Furthermore, research indicates that the best predictor of long-term weight loss is greater initial weight loss.(19) This research suggests that long-term weight loss will be enhanced by 1) identifying efficacious strategies to enhance maintenance and 2) increasing the amount of initial weight loss.

One way to improve long-term weight loss is to increase the effectiveness of social support. Decades of observational research indicates that people with greater social support—often measured by marital status as a proxy--live longer and have better health.(20) Because domestic partners share eating habits, physical activity patterns, and other health behaviors, there are frequent opportunities for partners to provide each other with informational, emotional, and instrumental support.(21) Furthermore, domestic partners are the preferred source of support for most people.(22, 23) Despite the positive effects noted in observational research, trials of weight loss interventions involving spouses/partners have not yielded uniformly positive effects.(24)

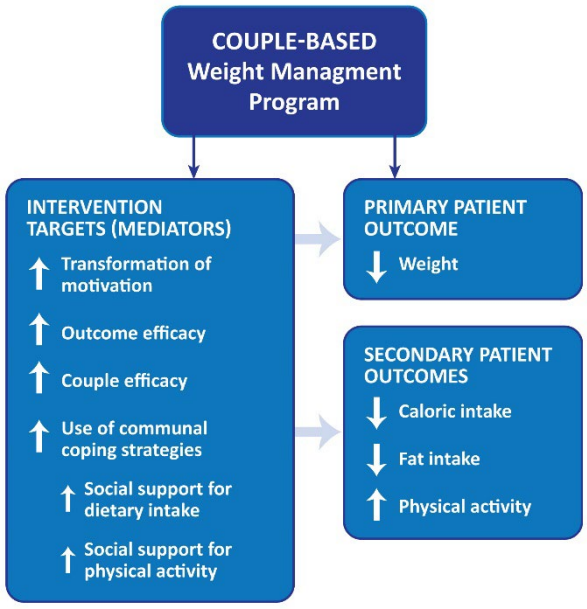
Scientifically rigorous research is needed to evaluate the efficacy of, and mechanisms underlying, partner-assisted weight management interventions. Meta-analyses comparing couples-oriented to patient-only interventions for weight loss, most of which were conducted in the 1970s-80s, indicated superiority of partner-assisted interventions immediately following treatment but not thereafter.(25, 26) These trials had significant methodological limitations. Most of those trials had small samples (mostly N<100, randomized to two or more arms); failed to specify a primary outcome, time point, or effect size; and did not include a power analysis.(27-32) Given that sample sizes were drastically smaller than today's weight loss trials, which typically involve >200 participants in order to detect clinically significant differences in weight, these studies likely were underpowered. Some trials had suboptimal retention rates.(27, 28) Several trials required a monetary deposit from the index patient or the couple,(28, 30-33) which may have mitigated or interacted with partner support. Additionally, most trials included interventions lasting 9-16 weeks that focused on initial weight loss, with no emphasis on maintenance of weight loss.(28, 30, 31) In addition to issues

with trial design and conduct, previous interventions were not grounded in theory or empirical evidence regarding the provision of effective social support. Research on mechanisms of social support did not emerge until the late 1990s; the conceptual model upon which we base our intervention was described in 2006. Furthermore, studies on the efficacy of cognitive-behavioral therapy for relationship distress and prevention in health contexts, which can be applied to weight loss, did not emerge until the 1990s. Perhaps because early trials of partner-assisted weight loss interventions were not uniformly positive, few trials have been conducted in the past 20 years. More recent investigations of the possible benefits of partner support have been limited to secondary analyses of the subset of married patients in trials that did not compare patient-only to partner-assisted weight loss interventions and did not train partners in skills for providing effective support.(34-36)

Taken together, previous research indicates a possible benefit to including partners in weight loss efforts but underscores the need for rigorous research on efficacy that builds on modern theoretical frameworks. Trials are needed that (1) are rigorous in design and implementation; (2) address weight loss initiation and maintenance; (3) systematically train couples to communicate about health and train partners in strategies for providing effective support for health behavior change; (4) isolate the partner intervention to provide a stringent test; and (5) evaluate theoretically specified mediators. This study accomplishes each of these.

Framing a health problem as “our” problem can initiate communal coping responses to promote health behavior change. The domestic partnership can be leveraged to help initiate and maintain behavior change. According to Lewis’ interdependence model of communal coping and behavior change,(37) couples who approach behavior change as a problem to be tackled together versus independently (referred to as ‘transformation of motivation’) are more likely to utilize effective communal coping processes, including higher levels of (1) outcome efficacy (i.e., a couple’s beliefs about the utility of communal coping for improving health), (2) couple efficacy (i.e., a couple’s confidence that they can engage in communal coping efforts), and (3) use of communal coping strategies (i.e., communicating about and coordinating actions relevant to the health problem, such as joint decision making and planning regarding health behavior and identifying and practicing methods of providing informational, emotional, and instrumental support). Our intervention is designed to affect these interdependence constructs to improve long-term weight loss and associated health behaviors (Figure 1). We will measure these constructs so that we can empirically assess the extent to which they mediate the effect of our partner-assisted intervention on long-term weight loss.

Figure 1. Conceptual Model Based on Interdependence Theory



5.2 Hypothesis

H1: Average patient weight is at least 2.5 kg lower in the partner-assisted arm than the patient-only arm at 24 months.

H2: Average daily caloric intake are significantly lower, and frequency of moderate intensity physical activity is significantly greater, in the partner-assisted arm than the patient-only arm at 24 months.

H3: Interdependence constructs (transformation of motivation, couple efficacy, outcome efficacy, use of communal coping) mediate the effect of the partner-assisted weight management intervention on weight loss.

5.3 Summary of Clinical Data

Previous research has shown evidence of the efficacy of patient weight loss initiation and maintenance interventions. The MAINTAIN trial involved randomization of patients who lost at least 4 kg in a 16-week program to usual care or a weight loss maintenance program.(38) To participants in the latter arm, maintenance-specific skills were delivered in 3 group meetings and 8 individual telephone calls, which decreased in frequency from every 2 weeks to every 2 months. Over 56 weeks, the maintenance group regained only 0.75 kg, whereas the usual care group regained 2.36 kg ($p < .04$). Retention was 80%.(39) This study shows that an intervention can be used to induce clinically significant weight loss and reduce subsequent weight regain among patients. The weight loss initiation and maintenance interventions implemented in MAINTAIN will be delivered to patients in both arms of this trial.

The results of the CouPLES trial showed evidence for the efficacy of training partners by telephone to provide support for the initiation of dietary change and physical activity. This trial compared usual care to a partner-assisted intervention to reduce patient LDL. This intervention comprised 9 monthly telephone calls to patients and their spouses. Patients generated behavioral goals and action plans, and spouses were taught support principles and created plans to support patient goal achievement.(40) At 11 months, there was no difference in the primary outcome of patient LDL, perhaps due to a facility-level co-intervention that increased statin prescribing and reduced LDL(41) (statins are more potent than lifestyle change for reducing LDL). Compared to usual care patients, intervention patients had lower 11-month caloric, total fat, and saturated fat intake and 20% greater frequency of moderate intensity physical activity.(42) Furthermore, social support for physical activity and dietary change increased in the intervention but not in the control group.(43) Retention was 88%. The CouPLES study demonstrates the ability to recruit and retain couples in a telephone-delivered, partner-assisted lifestyle intervention and to increase and measure social support for physical activity and eating. The partner-assisted arm of the proposed study will utilize the protocol for sharing patients' action plans with their partners and having partners develop a support plan. In CouPLES, we did not focus on maintenance, nor did we teach couples communication skills. In this study, the aim is to increase the efficacy of the CouPLES approach by addressing maintenance and incorporating communication skills training from Dr. Porter's research.

There is evidence of the efficacy of partner-assisted interventions to enhance communication and support and change behavior. Dr. Porter has developed and tested multiple interventions to enhance communication and support among dyads coping with cancer. These interventions systematically train patients and partners in communication skills to provide each other with effective informational, emotional, and instrumental support, which are central components of the partner-assisted intervention in the proposed study. Dr. Porter's studies have also included joint training in behavioral skills for pain and symptom management(44) and increasing physical activity,(45) including joint goal setting and monitoring of these behaviors. Findings indicate that these interventions led to significant improvements in couples' relationship quality and communication;(46-48) in patient outcomes regarding pain, psychological distress, quality of life, and self-efficacy;(46) and in partner outcomes of psychological distress and self-efficacy.(46) Findings have not differed by sex. Findings from a recent pilot study of a couple-based intervention for physical activity among cancer survivors (which included components similar to those in the proposed study) suggested that the intervention led to increases in physical activity among both patients and partners, as well as increases in partner support for physical activity (Porter et al under review). In a recent trial involving 14 telephone-based intervention sessions delivered at a tapered frequency (biweekly to monthly to bimonthly) to lung cancer patients and their family caregivers, retention rates were >80% despite the fact that patients were suffering from an illness associated with high rates of morbidity and mortality.(44, 49) These studies demonstrate expertise in designing effective partner support protocols and in retaining couples, which will be applied in this study.

The investigator and collaborators of this trial have expertise in collecting data from wireless devices. Drs. Voils and Shaw were PIs on an R34 that involved transmission of patient weight from cellular scales and dietary intake from MyFitnessPal to the study team to enable provision of financial incentives for weekly weight loss and dietary self-monitoring. Data were transmitted to Prompt, a web-based software application that obtains data from remote devices and sensors and can "push" multiple types of data—in this case, text messages. This study demonstrates the experience of using the Prompt system to collect data from cellular scales and mobile telephone apps and to send automated text messages to participants, which will be done in the current study.

5.4 Potential Risk and Benefits to Participants

5.4.1 Known Potential Risks

- **Physical activity**: There are small risks of injury or heart problems due to increased participation in physical activity. The risks associated with physical activity will be minimized by screening for contraindications to physical activity participation. The study physician will be available to answer patients' questions during their participation. Participants will also be instructed to consult with their physician/health care team if they have any new health problems or symptoms.

- **Low blood pressure:** In patients taking blood pressure medications, dietary changes and/or weight loss can result in low blood pressure.

- **Disclosure of data:** There is a small risk of inadvertent disclosure of participant data. As our standing operating procedure, we have policies and procedures in place to protect the confidentiality and security of participant data, see below in "Protection Against Risks".

- **Questionnaires, interactions with interventionist:** Sensitive questions about personal issues (e.g., quality of marital relationship, positive and negative interactions) may make participants uncomfortable. Participants do not have to answer any question that they do not wish to answer, as will be explained during the consent process and during subsequent visits. Participants could become psychologically distressed during group visits or telephone calls. If necessary, any individual or couple experiencing notable psychological distress will be discussed with Dr. Porter (psychologist at Duke).

- **Reproductive risks:** No reproductive risks are expected from this trial. This study does not start, change, or alter medications in any way. Patients are excluded if pregnant and if planning to become pregnant.

5.4.2 Alternative to Study Participation

The alternative to study participation for all participants is not to participate in the study. Participants may also choose to discontinue their participation in the study at any time.

Rationale for the necessity of exposing human participants to such risks: It is expected that this study will pose minimal risks to participants.

Why the value of the information to be gained outweighs the risks involved: Obesity has become increasingly prevalent in the US and is associated with myriad health problems that are alleviated by weight loss. Many of these problems (e.g., elevated cholesterol, blood pressure, and blood glucose) are major risk factors for coronary heart disease and increase in prevalence as age increases. Despite the known risk of obesity, many Americans have difficulty losing weight and even more difficulty maintaining their new weight after losing. There is a dire need for effective weight loss and maintenance interventions that can be incorporated into primary care where clinician supervision is available. Therefore, the value of the information gained from this study far outweighs the risks involved.

5.4.3 Protection Against Risks

Sensitive questions about personal issues may make participants uncomfortable. Participants do not have to answer any question that they do not wish to answer, as will be explained during the consent process and during subsequent visits. Regarding partner interactions, our team includes a clinical psychologist and cardiologist, who will be able to recommend appropriate intervention as necessary.

There are small risks of injury or heart problems due to increased participation in physical activity. We will minimize the risks associated with physical activity by screening for contraindications to physical activity participation (e.g., unstable heart disease in the past 6 months), by providing proper instruction regarding methods for engaging in physical activity safely during the group sessions, by providing handouts regarding physical activity, and by educating patients to recognize symptoms consistent with overexertion. Several aspects of our active intervention will help reduce risks associated with physical activity: 1) All patient materials promoting physical activity endorse moderate intensity physical activity during initiation phases of physical activity; 2)

Patients are encouraged to establish goals and action plans they feel capable of performing in partnership with the interventionist who will assess the feasibility of such goals and expectations; 3) Our interventionists assess barriers, which include health problems that may preclude safe physical activity, using American College for Sports Medicine (ACSM) guidelines; 4) Our written materials emphasize the need to monitor for symptoms of overexertion and other acute health problems (e.g., chest pain, excessive shortness of breath) and recommend that patients contact their physician or emergency care (for heart attack or stroke symptoms) if they experience any difficulties; and 5) The study physician will be available to answer patients' questions, and the staff exercise physiologist will be available to answer questions as well. Current guidelines from the ACSM and the Department of Health and Human Services (DHHS) do not require physician approval for initiation of moderate physical activity. In accordance with these guidelines, we will not require participants to check with their personal physician upon enrollment in our study. However, as described above, participants will be instructed about when they should consult with their physician, in accordance with ACSM and DHHS guidelines, about new health problems or symptoms that require a review of physical activity.

In patients taking blood pressure medications, dietary changes and/or weight loss can result in low blood pressure. Participants will be counseled on how to recognize and respond to symptoms of low blood pressure. Study personnel will also be trained how to respond when participants report symptoms of low blood pressure. The study physician will provide recommendations to the interventionists regarding any issues that arise with specific participants and will be available to answer patients' questions. Participants may also be referred to his/her own primary care provider for additional work up.

There is a small risk of inadvertent disclosure of participant data. Research personnel will use only those parts of the medical record necessary to determine eligibility and follow the research protocol, and measures will be taken to maintain privacy during in-person sessions. We will establish ground rules at the group sessions, advising participants that they should only communicate information they feel comfortable communicating in public and that any information learned about other participants should be kept confidential. The procedures that will be followed in order to prevent the exposure of personal identifying information or protection health information are listed in detail in section 11, Data Collection, Handling and Record Keeping of this protocol.

Some participants could become distressed during group visits or telephone calls. The risk that some participants could become distressed during the telephone calls is quite unlikely given the previous research literature and our experience in our prior studies. Dr. Porter is a licensed clinical psychologist with expertise in working with both couples and individuals. Any couples or individuals who experience notable psychological distress from the intervention will be discussed with Dr. Porter (psychologist at Duke)who will make a recommendation about intervention that cannot be addressed within the context of the ongoing intervention (e.g., recommend follow up with primary care provider, provide contact information for social work service).Study personnel may consult the study physician and the study team will attempt to determine whether the study is exacerbating a distressing condition; if so, the participant may be withdrawn from the study for his/her safety.

A Certificate of Confidentiality will automatically be granted by the NIH that will protect participants' sensitive information.

5.4.4 Potential Benefits to the Participants

All participants will receive some level of intervention, as participants in both arms will receive weight loss initiation and maintenance instruction; thus, we expect all to derive some benefit from participation. This instruction exceeds the available standard of outpatient care that is available to people in the community and involves no direct cost to participants. Patients in both arms may learn skills that help them reduce weight by adhering to dietary recommendations and participating in regular physical activity.

Participants may experience a positive change in their domestic partnership as a result of participating in the study. Although the participants themselves might not derive direct benefit, knowledge gained from the study will assist in the treatment of others with weight problems.

5.4.5 Risk Minimization:

No procedures, situations, or materials are expected to be hazardous.

6. Study Objectives and Purpose

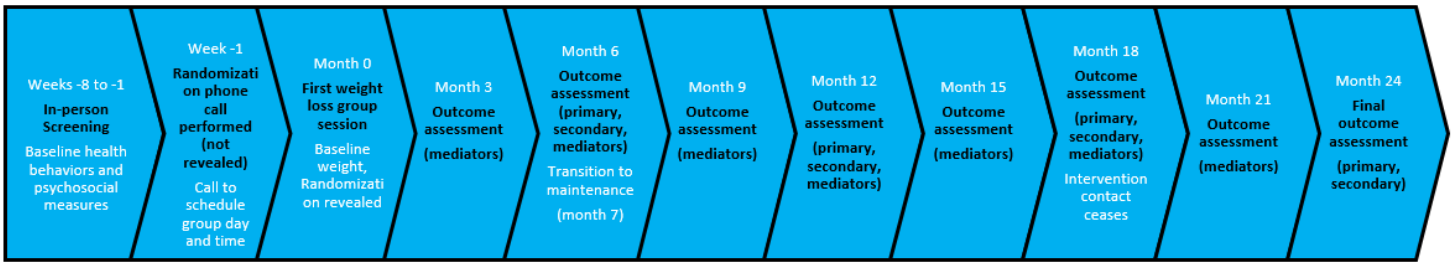
- Primary objective: To assess 24-month long-term weight loss in a patient-only vs. partner-assisted intervention.
- Secondary objective: To assess 24-month long-term self-reported patient caloric intake and physical activity in a patient-only vs. partner-assisted intervention.
- Exploratory objective: The role of theoretically hypothesized mediators of intervention effects will be examined, including transformation of motivation, couple efficacy, outcome efficacy, use of communal coping, and social support for physical activity and dietary intake at 24 months.

7. Study Design and Endpoints

7.1 General Design

In this two-arm RCT, 230 couples (460 total) will be randomized to patient-only or partner-assisted intervention. In both arms, intervention will be delivered for 18 months followed by 6 months of no intervention contact in order to evaluate sustainability of effects. The primary endpoint is weight measured at 24 months (Figure 2).

Figure 2. Study Flow



This design addresses long-term weight loss, which results from both initial weight loss and weight loss maintenance. Because social support is important for initiation and maintenance, incorporating partners in both phases is likely to have greater impact on long-term weight loss than incorporating partners in either phase alone. The patient intervention is identical between arms. The partner-assisted arm involves additional content, which increases the amount of each intervention contact. This is by design, as the partner-assisted intervention involves teaching couples to communicate about health and engage in cooperative action. Equalizing dose in both arms would require removing portions of the efficacious patient intervention in the partner-assisted arm or adding unrelated content to the patient-only arm, neither of which would provide a stringent test of the partner intervention.

7.1.1 Primary Study Endpoints

The primary outcome is long-term weight loss, defined as patient weight at 24 months.

7.1.2 Secondary Study Endpoints

Secondary outcomes include self-reported patient caloric intake and physical activity at 24 months.

8. Study Participants

Our target sample size is n=230 patients (115 per arm), randomized to receive the partner-assisted or patient-only intervention, to detect a 2.5 kg difference in mean 24-month net weight loss between arms. The sample size estimate is based on the primary hypothesis that estimated patient weight will be at least 2.5 kg lower at 24 months in the partner-

assisted than patient-only arm. This effect size was chosen because smaller differences are unlikely to be considered meaningful to researchers, providers, or patients. The sample size was determined by multiplying the number of participants required for a t-test of post scores by 2(1-ρ) and adding one extra participant per arm. Based on our previous MAINTAIN trial, we anticipate a common standard deviation of 19.9 kg and a correlation (ρ) between the *month0* and *month24* time points of 0.96. Thus, we need 160 participants total (80 in each arm) to detect a 2.5 kg difference with 80% power and a type-I error rate of 5%. We further inflate the sample size to 1) incorporate the intra-class correlation (ICC) of small group members into consideration and 2) compensate for attrition using procedures for group-randomized designs. Let m=15 (conservative upper limit) be the number of patients in each of the small groups, and let ICC=0.01 represent the intra-class correlation between patients in the same group. The updated sample size is n = 160* [1 + (m-1)ICC], or 180. We then conservatively inflate the sample size for an attrition rate of 20% through month24. To achieve the target sample, we estimate that we will screen up to 500 patients as some couples may provide consent and screen as eligible but never show for the first intervention session and thus provide a baseline weight (not counted in ITT analyses).

Eligibility will be determined via online screening. Patients who screen as eligible will provide their partner's information (name and email) so that their partner can complete a separate online screening. Couples passing the online screening will be scheduled for an in-person (or remote) screening/enrollment visit. The in-person (or remote) screening/enrollment visit will be divided up into two parts. The first part of the in-person screening visit will determine the patient's final eligibility by collecting the following measurements: weight, cognitive screen, and reconfirmation that they are not pregnant (females). For the partners, height, weight and cognitive screening measurements will be completed to determine their final eligibility. Once the patient and partner meet the final eligibility measurements, they will be asked to provide written consent (or oral consent if the screening/enrollment visit is done remotely) and complete the rest of the baseline measurements.

8.1 Participant Population

The age range of participants is 18-74 years. A key inclusion criterion is that participants need to be cohabiting with a significant other and have daily contact. As most children aged 17 or under are not emancipated, few children would be eligible for this study. The upper age range is 74 as weight loss is often contraindicated in adults aged 75 and older and more extensive health screening, in addition to consultation with their primary care physician, may be needed.

No participant will be excluded on the basis of race ethnic origins. The planned distribution of patient and partner participants by racial/ethnic group and sex is shown in the Inclusion Enrollment Report. The race and ethnicity distributions are based on the 2015 estimated Dane County Census accessed on-line at https://www.census.gov/quickfacts: ethnicity is approximately 94% non-Hispanic/Latino, 6% Hispanic/Latino; the racial make-up is 86% White, 6% Black, 6% Asian, and <1% American Indian or Alaska Native, and <1% Hawaiian/Pacific islander.

8.2 Inclusion Criteria

Patient

- aged 18-74 years
- BMI 27-29.9 kg/m^2 plus presence of at least one obesity-related comorbidity (e.g., type 2 diabetes, blood pressure >130/80, dyslipidemia, obstructive sleep apnea, gastroesophageal reflux disease, or coronary artery disease) or BMI ≥ 30 kg/m^2
- cohabitating and at least daily contact with a spouse/domestic partner (same or opposite sex)
- desire to lose weight
- agrees to attend visits per protocol
- access to reliable transportation
- score of at least 4 out of 6 on a validated cognitive screener
- able to stand for weight measurements without assistance
- speak and read English
- individual smart phone with data and texting plan
- individual e-mail address
- able to complete online screener without assistance

Partner

- aged 18 or older

- willing to participate
- access to reliable transportation
- score of at least 4 out of 6 on a validated cognitive screener
- speak and read English
- smart phone with data and texting plan (not shared with index patient)
- e-mail address (not shared with index patient)
- able to complete online screener without assistance
- able to use a smartphone, tablet or computer with a video camera or webcam and microphone to download apps and to connect to a video conference call without assistance

8.3 Exclusion Criteria

Patient

- weight loss of at least 5 lbs in the month prior to screening
- currently enrolled or enrollment in previous 3 months in a clinical or research program focusing on lifestyle change that could affect weight
- current use of weight loss medications (prescription or over-the-counter)
- history of bariatric surgery or planning to have bariatric surgery in the study timeframe
- residing in a nursing home or receiving home health care
- impaired hearing
- significant dementia, drug or alcohol abuse, or unstable psychiatric illness (e.g., schizophrenia or psychosis)
- current treatment for cancer or being treated for cancer (beside skin cancer) in the last 6 months
- use of Insulin, Sulfonylureas, or Meglitinides for diabetes due to increased risk for hypoglycemia
- pregnant, breastfeeding or planning to become pregnant within the study timeframe
- diuretic medication doses higher than hydrochlorothiazide 25 mg daily, furosemide 40 mg daily, Torsemide 20 mg daily, Bumetanide 1 mg daily or any use of Metolazone). Use of potassium-sparing diuretics is acceptable.
- chronic or unstable illness that would limit ability to participate (e.g., recent hospitalization; unstable heart disease in the 6 months prior to screening)
    - having acute coronary syndrome (ACS) including STEMI (ST-elevation myocardial infarction), NSTEMI (non-ST elevation myocardial infarction) and unstable angina (UA)
    - recent or impending coronary revascularization [recent coronary bypass grafting (CABG) or percutaneous coronary intervention (PCI)
    - unstable arrhythmia (e.g., hospitalized for unstable atrial fibrillation, supraventricular tachycardia, ventricular tachycardia, ventricular fibrillation and/or firing of implantable cardiac defibrillator [ICD])
    - recent acute congestive heart failure exacerbation [requiring increased doses of oral or intravenous (IV) diuretics or hospitalization]
    - patient may be rescreened after sixth months
    - chronic kidney disease at stage 4 or higher
- exertional chest pain, dizziness or lightheadedness
- pain or other condition that prohibits mild-moderate exercise
- history of ascites requiring paracentesis
- planning to relocate in the next 2.5 years

Partner

- underweight BMI (i.e., BMI < 18.5 kg/ m^2)
- residing in a nursing home or receiving home health care
- impaired hearing
- any severe health issue that would impair the partner's ability to provide support, including
    - significant dementia, drug or alcohol abuse, or unstable psychiatric illness (e.g., schizophrenia or psychosis)
    - current treatment for cancer or being treated for cancer (beside skin cancer) in the last 6 months
    - In the last 6 months prior to screening:
        - acute coronary syndrome (ACS) including STEMI (ST-elevation myocardial infarction), NSTEMI (non-ST elevation myocardial infarction) and unstable angina (UA)
        - recent or impending coronary revascularization [recent coronary bypass grafting (CABG) or percutaneous coronary intervention (PCI)

- unstable arrhythmia (e.g., hospitalized for unstable atrial fibrillation, supraventricular tachycardia, ventricular tachycardia, ventricular fibrillation and/or firing of implantable cardiac defibrillator [ICD])
- recent acute congestive heart failure exacerbation [requiring increased doses of oral or intravenous (IV) diuretics or hospitalization]

Given population rates of overweight/obesity and the fact that weight and health behaviors are highly correlated within couples, it is possible that both members of a couple will be eligible to be index patients. If both partners in a household desire and are eligible for the patient intervention, then we will ask them to decide which one will be the index patient. Partners may choose to make similar behavior changes as patients; however, partner behavior change is not the focus, and partners in the patient-only arm will receive no intervention. Because partner outcomes are of potential interest to society and to payers, and because previous studies targeting patients have observed "ripple" effects,(36) we will analyze partner outcomes.

8.4 Participant Screening for Recruitment

8.5 Participant Identification

We will take a two-pronged approach to recruitment. First, we will coordinate with WREN, a voluntary network of primary care clinical practices across the state of WI that participate in practice-based research, to access electronic medical records of UW Health patients from the Department of Family Medicine and Community Health and General Internal Medicine clinics. Second, we will recruit from the community. To recruit from the community, we may place advertisements in public meeting places (e.g., churches, community centers, grocery stores), websites (e.g., UW, Facebook), and local print publications (e.g., Isthmus).

8.5.1 Recruitment and Retention Strategies

Patients identified through the electronic medical record will receive a recruitment letter in the mail that will contain a url address link to an online screening website if they are interested in participating and a different url address link to a website where they can opt-out of the study. After sufficient time has elapsed allowing people to opt-out (≥1 week), the study team may begin calling people who have received recruitment letters to ascertain interest in the study. To meet our study recruitment goals, we will consent up to 500 potential index patients and partners.

For both recruitment paths (i.e., electronic medical record review and posted advertisements), eligibility will be determined via online screening. Patients who screen as eligible will provide their partner's information so that their partner can complete a separate online screening. Couples passing the online screening will be scheduled for in-person (or remote) screening/enrollment visit. The in-person (or remote) screening/enrollment visit will be divided up into two parts. The first part of the visit will determine the patient's final eligibility by collecting the following measurements: weight, height, cognitive screen, and reconfirmation that they are not pregnant (females). For the partners, height, weight and cognitive screen measurements will be completed to determine their final eligibility. If the visit is done remotely, then height and weight will not be collected. Once the patient and partner meet the final eligibility measurements, they will be asked to provide consent and complete the rest of the screening visit measurements. This study will be conducted in 5 cohorts of ~46 couples each. Each new cohort will begin as the previous cohort transitions to maintenance (in month 7 of 24). As in our previous studies, we will recruit each cohort over 4-6 weeks and will not begin group sessions until we have achieved our recruitment target for that cohort.

To enhance recruitment, we will do the following: discuss the study directly with partners to address any questions/concerns; frame weight loss as a couples' issue in recruitment materials; emphasize potential benefits of the intervention and outcome assessments to partners; offer sessions at different times of day; and offer two sessions that address communication to couples in the patient-only arm following the 24-month assessment. If partners no longer wish to receive intervention, then we will retain patients in the intervention (intent-to-treat analyses). If patients no longer wish to receive the intervention, then partners will no longer receive the intervention either. In such cases, we will ask patients (and partners) to return for outcome assessments, as we have done in our previous trials. Other efforts to maximize retention for outcome assessments include: administer the ASA24 online; e-mail/text reminders one week prior to the beginning of each window; place telephone calls and mail letters if participants are non-responsive to electronic reminders; compensate patients and partners $40 each for completed interim assessments; and increase payments for the final assessment ($60 each), as we did in the

MAINTAIN trial. In the MAINTAIN trial, 85% of patients returned for final assessments; in the CouPLES trial, 88% of patients and 70% of spouses did.(42, 50)

No participant will be excluded on the basis of race or sex. There have been mixed findings regarding the moderating role of sex in couples-based weight loss interventions. Failure to balance arms with respect to sex could, therefore, affect outcomes. Sex is explicitly accounted for in the study design in that it is a stratification variable. This variable, along with the other stratification variables of patient BMI and partner BMI, will be included in the statistical models for the primary outcome of weight, secondary outcomes of diet and physical activity, and mediation analyses.

The study is being conducted in Dane County, Wisconsin. Although the Dane County female population is 50%, there is selection bias into weight loss intervention studies, such that, typically, ~70% of patient participants are female. McLean's (2003) systematic review of previous social support interventions for weight loss indicated a similar proportion of females as index patients. Therefore, we estimate that 70% of index patients will be female. Given a sample size of 230 and 70% female index patients, we may be able to detect a large moderation effect but unable to detect a small effect. Any sex differences are likely to reflect societal *gender* roles because many support behaviors for weight management reflect cultural gender norms, such as having primary responsibility for the household's food shopping and cooking. We will therefore measure differences according to gender and sex, but with such a small sample, we are unlikely to be able to capture or make meaningful distinctions between sex as a biological variable and the distinct variable of gender.

Both same-sex and heterosexual couples are eligible for the study. We require that couples be cohabitating so as not to discriminate based on legal marital status. We expect that 5-10% of couples will be same-sex.

The planned distribution of patient and partner participants by racial/ethnic group and sex is shown in the Inclusion Enrollment Report. The race and ethnicity distributions are based on the 2015 estimated Dane County Census accessed on-line at https://www.census.gov/quickfacts: ethnicity is approximately 94% non-Hispanic/Latino, 6% Hispanic/Latino; the racial make-up is 86% White, 6% Black, 6% Asian, and <1% American Indian or Alaska Native, and <1% Hawaiian/Pacific islander.

8.6 Vulnerable Populations

TABLE 1: Vulnerable populations included and excluded from this study:

Include	Exclude	Vulnerable Population Type
	x	Adults unable to consent
	x	Individuals who are not yet adults (e.g. infants, children, teenagers)
	x	Wards of the State (e.g. foster children)
	x	Pregnant women
	x	Prisoners

No vulnerable populations will be enrolled. A key inclusion criterion is that participants need to be cohabiting with a significant other and have daily contact. As most children aged 17 or under are not emancipated, few children would be eligible for this study. Pregnant women will be excluded since the primary outcome of this study is long-term weight loss, and weight loss is contraindicated during pregnancy. Prisoners will be excluded as per the OHRP guidelines. Prisoners would not have daily contact with their study partner or the flexibility in dietary and exercise choices comparted to the general population.

8.6.1 Participant Capacity

All participants will have the capacity to give informed consent.

8.6.2 Participant/Representative Comprehension

To ensure comprehension, after hearing and reading about the study, the participant will be asked to summarize the study and the requested activities for participation in the study. The investigator or research staff will then ask the participant if anything could be clarified before consent is obtained.

Decisionally impaired adults are excluded from this study.

8.7 Informed Consent

The PI will be responsible for ensuring that valid consent is obtained in person and documented for all participants.

The activities involved to review the EMR for potentially eligible participants are considered "preparatory to research" and will be conducted by the Clinical Research Data Service or the Department of Surgery Data Analysis & Reporting Team. The Department of Surgery Data Analysis & Reporting Team will pull the data once they have the necessary approvals. Individuals will be directed to go to an online screening website or they might be contacted directly by phone by the study team if individuals do not opt-in or opt-out on their own.

Individuals and their partners who are interested in participating will be instructed to go to an online screening website which will determine their initial eligibility. For those who are potentially eligible, an in-person (or remote) screening/enrollment visit will be scheduled. The screening/enrollment visit will be divided up into two parts. The first part of the visit will determine the patient's final eligibility by collecting the following measurements: height, weight, cognitive screen, and reconfirmation that they are not pregnant (females). For the partners, height, weight and cognitive screening measurements will be completed to determine their final eligibility. If the visit is done remotely, height and weight will not be collected. Once the patient and partner meet the final eligibility measurements, they will be asked to provide written consent (or oral consent if the screening/enrollment visit is done remotely) and complete the rest of the baseline measurements. The consent process will consist of a detailed verbal description of the study including its risks, potential benefits, and requirements. Potentially eligible participants and their partner will be given an IRB-approved/stamped informed consent form with all required elements and factual correctness to read, then ample time to read and reflect on participating. If the individual and/or partner requests, they will be given additional time to consider participation, including re-scheduling the screening visit. Before obtaining consent, each individual and their partner will be allowed to ask questions until a decision can be made by either party. When ready, participants and their partner will be required to sign the consent form (or oral consent will be obtained if the screening/enrollment visit is done remotely). Study audits by the PI will include review of consent documents for signatures and use of the IRB date-stamped form to ensure compliance.

8.7.1 Process of Consent

Members of the WREN staff will be responsible for obtaining consent. The written/signed consent (original copy) will be stored in a locked file cabinet, in a locked office with the research team.

The process of informed consent will be structured to be conducive to rational and thoughtful decision making by the patient and their partner – including time for discussion, questions, and the ability to reschedule if additional time for consideration is needed. Legally authorized representatives will not be allowed to sign the consent; patients who require legally authorized representatives are excluded from the study.

Auditors, witnesses, and translators will not be part of the consent process. Non-English speakers are excluded from the study. Additionally, patients who are unable to read or write in English (*i.e.*, illiterate) are excluded.

8.7.2 Consent to Participate in Research and Authorization to Use Protected Health Information for Research Form

See Attachment for Consent to Participate in Research and Authorization to Use Protected Health Information for Research Form

Signed consent and HIPAA authorization (or oral consent if the screening/enrollment visit is done remotely) will be obtained from the patients and their partners arriving for the screening visit once their final eligibility requirements have been met. Patients and partners will be given adequate time to review the document and ask any questions they have. A copy will be given to the patient and their partner that signed the form, on the same day they each sign the form.

Information about study participants will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). PHI that will be collected from participants includes name, address, telephone numbers, Medical Record Number, e-mail, date of birth, web addresses and internet protocol addresses.

8.7.3 Revoking Consent

In the event that a participant revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of participant authorization. For participants that have revoked authorization to collect or use PHI, attempts will be made to obtain permission to collect at least vital status (i.e. that the participant is alive) at the end of their scheduled study period.

8.7.4 Costs to the Participant

Participants will not have to pay for any study procedures or materials including the Fitbit™ watch that will be used. The patient will not be billed by their healthcare system or their health insurance company for any costs related to a study procedure.

Participants will be responsible for any costs if they require any follow-up procedures with their primary care physician, including all out-of-pocket costs.

8.7.5 Payment for Participation

Payments to patients and partners will be provided as the study progresses; participants do not have to complete the entire study to receive a payment.

All patients and their partners can receive a remuneration up to $180/each ($360 for the couple) for completing all outcome assessments. For each of the Month 6, 12 and 18 month completed assessments, patients and their partners will receive $40/each ($80 for the couple). The payment will increase to $60 for completion of the final assessment ($120 for the couple) due to the importance of collecting the primary outcome data at this visit.

Month 6: $40 each/$80 per couple
Month 12: $40 each/$80 per couple
Month 18: $40 each/$80 per couple
Month 24: $60 each/$120 per couple

The remuneration will acknowledge their time and study participation, not behavior change. Additional payment will not be available to participants for travel or other costs (example: childcare) that are incurred.

8.8 Early Withdrawal of Participants

8.8.1 Premature termination of study

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to all site investigators, funding agency, DSMB (i.e., ICTR DMC), and IRB. If the study is prematurely terminated or suspended, the PI will promptly inform the IRB and will provide the reason(s) for the termination or suspension.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable

Study may resume once concerns about safety, protocol compliance, data quality are addressed and satisfy the funder, IRB and/or DMC. All participant data that were collected prior to study termination will be analyzed and continue to be handled/stored per this protocol.

8.8.2 When and How to Withdraw Participants

Participants will be educated on the consent form that they are able to withdraw at any time without adverse effects. Participants may withdraw by alerting study staff in person, by telephone, or by email. If participants withdraw from the study, then their status will be updated in the tracking database, and no further contact will be made. Participants may be withdrawn at the discretion of the PI for safety reasons (e.g., self-report of pregnancy) or because they cannot participate meaningfully in the intervention (e.g., cannot communicate well by telephone). These individuals will be informed by study staff in person or by telephone that their participation has ended and the reason for ending their study participation. Their status will then be updated in the tracking database, and no further contact will be made.

8.8.3 Data Collection and Follow-up for Withdrawn Participants

If partners no longer wish to receive intervention, then we will retain patients in the intervention. If patients no longer wish to receive the intervention, then partners will no longer receive the intervention either. Regardless of whether partners or patients request not to receive further intervention, we will ask patients and partners to return for outcome assessments. Patients who attend the first group session (i.e., provide a baseline weight) will be considered randomized and will be analyzed according to intent-to-treat principles, regardless of further intervention adherence; these individuals will not be replaced if they drop out subsequent to the first session. Consented participants who do not attend the first session (i.e., do not provide a baseline weight measurement) will not be considered randomized and thus will be replaced.

9. Study Procedures

9.1 Established Standard of Care:

Current standards of care include consultation by primary care physician or specialist; referral to dietician; and commercial weight loss programs.

9.2 Study Visits

Table 2. Patient Measurement Schedule									
Baseline medical history, demographics*	**Screening Visit – Month 0 – (0-8 weeks)**								
	Month								
Measure	**0**	**3**	**6**	**9**	**12**	**15**	**18**	**21**	**24**
Baseline weight	X								
Primary outcome: Weight*	X		X		X		X		X
Secondary outcomes									
Caloric intake*	X		X		X		X		X
Physical activity	X		X		X		X		X
Mediators									
Transformation of motivation*	X	X	X	X	X	X	X	X	
Couples' efficacy*	X	X	X	X	X	X	X	X	
Outcome efficacy*	X	X	X	X	X	X	X	X	
Use of communal coping*	X	X	X	X	X	X	X	X	
Social support for diet*	X	X	X	X	X	X	X	X	
Social support for physical activity*	X	X	X	X	X	X	X	X	
Brief pain inventory-short form *	X		X		X		X		
Weight loss methods*			X		X		X		X
COVID-19*	X	X	X	X	X	X	X	X	X
*Assessed from partners as well									

9.2.1 Screening visit:

The screening visit will occur up to 8 weeks prior to the first group intervention visit. The following measurements will be obtained at screening by the WREN Research Coordinators:

- **Medical history and demographics:** age, race, ethnicity, gender and birth sex, insurance status, financial stress, education, smoking status, alcohol use, illicit drug use, employment status, previous weight loss attempts, history of heart disease, diabetes, cancer, liver disease, and hypertension.

- **Body weight** will be obtained using a calibrated digital scale in light clothing, with shoes removed.

- **Height** will be determined without shoes using a portable or wall-mounted stadiometer.

- **BMI.** The weight and height measures will be used to calculate BMI (weight in kilograms divided by height in meter squared; kg/m^2).

- **Dietary intake** will be assessed using the Automated Self-Administered 24-hour dietary recall (ASA24).(51, 52) Patients will receive training to use the website during the screening visit and may call study staff to ask for assistance. Electronic messages via text and/or e-mail will be sent to notify participants on one randomly determined weekend day and one weekday during the measurement window to complete an unscheduled 24-hour recall. Patients who do not comply within 24 hours will be sent notifications to complete recalls on other dates within the window.

- **Physical activity** will be assessed with Fitbit™ watches. Patients will be given their Fitbit™ and download the Fitbit™ application at their screening visit, along with instructions on how to use and wear it. They will be sent a text and/or e-mail reminder about when to start wearing it continuously for 7 days. Patients will be instructed to return the Fitbit™ to the study team if they do not attend the first group session.

- **Transformation of motivation** will be assessed with both Aron's Inclusion of Other in Self (IOS) scale(56) and the Unidimensional Relationship Closeness Scale (URCS).(57) The IOS comprises 7 Venn-like diagrams representing different degrees of overlap between the partner and self. IOS scores range from 1 (completely separate, non-overlapping circles) to 7 (completely overlapping circles). The IOS has produced test-retest correlations >.80 and has been associated with relationship longevity. The theoretical basis supports the transformation of motivation concept in that self-expansion occurs when the interests and experiences of one's partner are integrated into one's self definition. The 12-item URCS has produced highly reliable scores (>.90) across different relationship types, demonstrates measurement invariance across relationship types, and is associated with relational satisfaction.

- **Couple efficacy, outcome efficacy, and use of communal coping measures** have been be adapted from previous studies. As with self-efficacy, there is no standardized measure of couple efficacy or outcome efficacy that applies across behaviors; instead, a measurement approach must be tailored to each health behavior. Dr. Lewis and others have developed items to measure these constructs in the context of smoking cessation,(58) HIV,(59, 60) vasculitis,(61) and colon cancer prevention.(62) We have adapted these items for the current study. Following Dr. Lewis' previous research, we will assess communal coping in three domains (use, confidence, and effectiveness) related to dietary and physical activity changes for both patient and partner. We focus on these three domains because of evidence showing: a) the interdependence of coping behaviors in chronic illness within couples (use)(63); b) the importance of efficacy perceptions in predicting a wide range of health outcomes (confidence); and c) the relevance of behavioral expectations (effectiveness).(64) Use of communal coping for diet and physical activity will be measured with 10 items (e.g., "How often do you and your spouse talk about ways to eat less fat?" 1 never to 5 very often). Confidence in communal coping for diet and physical activity will be measured with 10 items (e.g., "How confident are you that, as a couple, you can talk about ways to eat less fat?" 0 = not at all confident to 10 = extremely confident). Effectiveness of communal coping for diet and physical activity will be measured with 10 items (e.g., "How effective would it be to talk as a couple about ways to eat less fat in getting you to eat less fat?" 0 = not at all effective to 10 = extremely effective). Reliabilities for the all measures have been >.75.

- **Social support for diet and physical activity** will be measured by two additional measures of communal coping, using Ball and Crawford's Social Support and Eating Habits Survey and Social Support for Exercise

Habits Survey, respectively (65). These surveys will be modified to address partners. The measures have produced reliable scores and demonstrated validity in women with overweight/obesity.(66)

- **Brief pain inventory-short form** will ask participants' questions about their pain intensity and its interference in their lives in the last 24 hours.

- **COVID-19** will asks participants' questions about COVID-19 and possible effects of COVID-19 their own life and their family's lives.

When possible, the partner screening visit will occur at the same time as the patient's screening visit; when impossible, we will allow partners to schedule their screening visit any time before the first patient group session. From the partner, we will obtain medical history/demographics, weight, dietary intake, transformation of motivation, couples' efficacy, outcome efficacy, use of communal coping, social support for diet and physical activity, brief pain inventory-short form, and COVID-19 using the previously described methods.

At the end of the screening visit, once both members of a couple have been deemed eligible, they will be randomized. Patients will be informed of which group date and time they need to attend (which corresponds to their randomization assignment), but they will not be told whether they have been assigned to the partner-assisted vs. patient-only intervention until the first group session. *Only* patients will attend the first group session, where they will learn of their randomization assignment and be instructed about whether to bring their partner to the next session (depending on arm assignment). Couples will be considered randomized only when their randomization assignment has been disclosed in the first group session. We have done this in previous studies so that patients who do not attend the first group session, where the month 0 "baseline" weight is obtained, do not take a slot in the randomization scheme. To address possible dissatisfaction with randomization in the patient-alone arm, we will emphasize the importance of the patient-only comparator arm during consent and the first group session; emphasize that partners in both arms will be able to participate in assessments; and offer two group sessions to couples in the patient-only arm after final assessments. We have not observed differential dropout in prior studies.

Patients and their partners will return for outcome assessment visits at month 6, 12, 18 and 24 (Table 2). These outcome assessment visits may occur remotely via a video conference if necessary due to public health safety measures. For the patients, at months 6, 12 and 18: weight, dietary intake, physical activity, transformation of motivation, couples' efficacy, outcome efficacy, use of communal coping, social support for diet and physical activity, brief pain inventory-short form and COVID-19 will be measured by using the previously described methods. Additionally, at months 6, 12, 18 and 24, patients will complete a weight loss methods survey to see if there are any other ways they attempted to lose weight other than being in the study. For the transformation of motivation, couples' efficacy, outcome efficacy, use of communal coping, social support for diet and physical activity, brief pain inventory-short form, weight loss methods, and COVID-19 surveys, these will be sent ahead of their visits as a REDCap link via text and/or e-mail. The surveys will be completed at the outcome assessment visit if patients and partners do not complete them ahead of time, on their own. At month 24: weight, surveys (weight loss methods and COVID-19), dietary intake and physical activity assessments will be obtained. For the partners, all of the same measurements will be obtained at the same time-points except for physical activity. All outcome assessment visits will be completed by the WREN Research Coordinators. If patients or partners are unable to attend an in-person outcome assessment visit due to illness or public health safety measures, then we will collect their self-reported weight photos via a DOS REDCap link.

At months 3, 9, 15 and 21, transformation of motivation, couples' efficacy, outcome efficacy, use of communal coping, social support for diet and physical activity, and COVID-19 will be measured for both patients and partners. Patients and partner will be sent the surveys as a REDCap link via text and/or e-mail.

9.2.2 Intervention

Patient intervention overview (both arms)

We will use a low-calorie approach from our previous studies.(39, 67) The diet will consist mainly of whole-grain, complex starches, vegetables, fruits, lean meats, and low-fat dairy products.(68, 69) The goal for total caloric intake, which will be personalized for each patient, will be calculated by subtracting 500-1000 kcal from the maintenance energy requirement determined by a sex and overweight/obesity-specific outpatient formula.(70) The range is

provided to encourage participants to stay under the 500 kcal deficit level in order to lose weight at an adequate rate but above the 1000 kcal deficit level, which may require closer medical monitoring. If a participant experiences a prolonged plateau after a previous downward weight trajectory, then energy intake may be reduced further by 300-500 kcal per day. If a participant achieves goal weight before the end of the 6-month initiation period, then energy intake will be adjusted to maintenance-level calories. At the end of the initiation period, all patients will be provided with a personalized maintenance-level calorie budget.

Patients will be guided to achieve the current recommendations for physical activity The 2018 current Guideline recommends at least 150 minutes per week of moderate-intensity aerobic physical activity such as brisk walking.(71) We acknowledge that some individuals will not meet recommended guidelines. Consistent with national recommendations, they will be encouraged to do as much as they can since bouts of moderate to vigorous exercise of any duration have been found to beneficial. (71) Additionally, in accordance with the American College of Sports Medicine guidelines, we will recommend 2-3 days per week of muscle strengthening activities and stretching. (72) We will emphasize that between 150-250 minutes per week of moderate intensity exercise is recommended for weight loss, with greater weight loss achieved with more minutes of exercise and >250 minutes needed to maintain weight loss and prevent regain.(73) One group session (in month 5) will be devoted entirely to physical activity. Additionally, 15 minutes of each of the other sessions will be devoted to educating, demonstrating, and performing exercises, such as a walk, a muscle strengthening routine that can be done in the home without equipment (e.g., chair stands), and a stretching routine. The content of physical activity education, which can occur during didactic session or during the 15-minute exercise demonstrations, will encourage increased self-efficacy, awareness of health benefits, reduction of barriers, increased enjoyment, identification of strategies to overcome relapse, and development of personally meaningful incentives and reinforcements for successful physical activity engagement. Collectively, these are associated with initiation and maintenance of physical activity.(74) An overview of patient weight loss initiation and maintenance interventions is provided in Table 3.

Table 3

		Patient	Patient + Partner
Weight Loss Initiation			
Month	**Mode**	**Content**	**Additional Content**
1	G, IP	Randomization Disclosure Introduction to Low-Calorie Diet	
1	G, IP	Interpreting the Food Label SMART Goals	Orientation to Diet Role of Partner Shared Decision Making
2	G, IP	Importance of Tracking Diet & Activity Setting a Goal Weight	Sharing Thoughts and Feelings
2	G, IP	Grocery Shopping and Grocery Store Tour	
3	G, IP	Meal Planning: Setting Up for Success	Role plays Couple conversations focused on support for dining out
3	G, IP	Healthy Cooking & Modifying Recipes	
4	G, IP	Dining Out	Role plays Couple conversations focused on support for dining out
4	G, IP	Dining Out: Advanced	
5	G, IP	Physical Activity	Role plays Couple conversations focused on support for physical activity
5	G, IP	Eating More Fruits and Veggies	
6	G, IP	Mindful Eating	Role plays Couple conversations focused on support for mindful eating
6	G, IP	Emotional Eating	
6	G, IP	Weight Loss Review and Potluck	
Weight Loss Maintenance			
7	G, IP	Maintaining Weight Loss	Role plays Couple conversations focused on support for weight loss maintenance
7	I, T	Behavioral Maintenance Intervention	Support plan, problem-solving
8	G, IP	Habits of successful losers	Role plays Couple conversations focused on support for healthy habits
8	I, T	Behavioral Maintenance Intervention	Support plan, problem-solving
9	G, IP	Relapse Prevention	Role plays Couple conversations focused on support for high-risk social situations and relapse prevention Review of couple communication skills
9, 10, 11, 12, 14, 16,18	I, T	Behavioral Maintenance Intervention	Support plan, problem-solving (only in months 9, 12, 18)

G, IP=group, in-person I,T=Individual, telephone

Patient weight loss initiation intervention (months 1-6, both arms)

Groups of ~11-12 patients will meet every 2 weeks and will be led by an interventionist. Meetings will begin with weigh-ins by research staff (self-report weight photos may be collected via a DOS REDCap link if group classes are delivered remotely and participants will be mailed a scale in this situation) and will involve dietary education, physical activity demonstration, and goal setting. Partners in the partner-assisted arm will attend a subset of these sessions, whereas partners in the patient-only arm will not be permitted to attend group sessions. The group sessions may be delivered via a video call if necessary due to public health measures that would prevent classes from happening in-person. Patients will download the MyFitnessPal application to their mobile phones, to promote

self-monitoring of diet. Although patients will be recruited in Madison, WI, where the PI is located, data from the Fitbit™ will be transmitted to Prompt, a mobile health platform developed by the Duke Digital Health Institute. Using Prompt will save time and money that would be needed to develop a similar resource at UW. Study staff will assist patients during the first group meeting with installing the apps and will be available for ongoing support throughout the trial.

We have reported the theoretical orientation of the initiation and maintenance interventions.(75) The constructs and way they are operationalized are summarize in Table 4. Although the didactic content varies across contacts, the same initiation behavioral strategies are taught and practiced in each group session in months 1-6, and the same maintenance strategies are taught and practiced in each contact in months 7-18. Our model addresses social support during initiation and maintenance.(75) During initiation, patients in a group-based weight loss intervention may receive support from two sources: (1) the intervention setting (interventionist, group members) and (2) their existing social network (friends, family, coworkers). Regarding (1), patients in both arms may derive support from the intervention setting. Regarding (2), in the patient-only arm, patients will not receive instruction on how to solicit social support and partners will not receive intervention. In the partner-assisted arm, couples will receive training in how to engage in communal coping. All the in-person group sessions will be audio recorded.

Table 4

Initiation	**Maintenance**
Goal setting/action planning to enhance action self-efficacy • Set 6-month weight loss goal (1-2 lb/week) • SMART goal setting led by RD at each group session	Relapse prevention planning to enhance maintenance and recovery self-efficacy • Identify high-risk situations for lapse • Generate relapse prevention plan • Review and update plan
Monitoring by self and interventionist Self • Weight: scale • Diet: MyFitnessPal • Physical activity: Fitbit™ Interventionist • Weight: weigh-in at group sessions • Diet and physical activity: Interventionist will do informal check-ins	Monitoring by self • Weight: scale o Specify day frequency, day of week, time of day for self-weighing o Set threshold that indicate relapse (+3 pounds) • Diet and physical activity: re-initiate via MyFitnessPal and Fitbit™ if relapse occurs
Favorable expectations about future outcomes of the behavior change • Write letter to self, describing struggles with weight, anticipated outcomes	Satisfaction with outcomes of the behavior change • Review before and after pictures, letter to self • Reflect on satisfaction in several domains (e.g., fit of clothes, mobility)
Social support derived from social network, interventionist, and similar others • Participation in group conversations • Verbal reinforcement from study team	Social support derived from social network • Designate primary support person (partner, sibling, adult children, friend, coworker) • Review how that person provides support

Patient weight loss maintenance intervention (months 7-18, both arms)

Patients will transition to the behavioral maintenance intervention in month 7 regardless of whether they achieved their 6-month weight loss goal for 3 reasons: 1) It is not feasible for some patients to continue the group-based initial protocol while others transition to the individual maintenance protocol; 2) Based on previous studies, most patients achieve maximum weight loss at 6 months; 3) Our maintenance protocol allows for patients to continue pursuing weight loss during the maintenance phase if desired. The protocol also stipulates that patients who relapse (gain > 3lb.) should revert to creating dietary and physical activity goals and monitoring these behaviors, thus re-focusing on weight loss. In months 19-24, patients will not receive intervention but will be encouraged to continue self-monitoring using the provided devices. This transition mimics real-world practice in which patients would be expected to apply the maintenance skills they have learned once intervention contacts cease. The 6-month period without intervention contact will allow examination of the sustainability of intervention effects.

The maintenance intervention was designed to help patients transition from the intensity that characterizes most weigh loss interventions to the real world in which patients rarely have further intervention-related contact. This intervention involves a shift from diet initiation content to maintenance-oriented skills training, then switches mode from in-person to telephone, and finally decreases contact frequency. The interventionist will place all telephone calls using a semi-structured script programmed into a custom intervention program that records participant responses for reference in subsequent calls. There will be a 2-week window around the target call date. If the educator is unable to contact a patient in the call window, then that telephone call will be skipped. Continuity will be maintained because each call involves a review of data from the previous call and a review of the same behavioral skills. All maintenance telephone calls will be audio recorded. Dr. Voils will meet with Dr. Porter and the interventionists weekly to review a random subset of recorded calls and provide feedback using a checklist.

Partner intervention overview (partner-assisted arm)

The theoretical basis for the partner intervention is Lewis' interdependence model (Table 5), along with principles of cognitive-behavioral couples therapy.(76) Cognitive-behavioral couple therapy (CBCT) is an empirically supported, efficacious intervention for both preventing and treating relationship distress. A central feature of CBCT is communication skills training, which focuses on teaching couples skills for effectively sharing their thoughts and feelings, listening supportively to each other, and making decisions together. Our intervention incorporates treatment components of evidence-based, couples interventions for medical problems specified by Baucom, Porter, et al.(46) to target key processes in the interdependence model (Table 5). We will train couples in communication and support skills and help them apply these to 1) increase their perception of weight loss as "our problem" (transformation of motivation") and 2) enhance partners' efficacy and abilities to engage in communal coping and support patients' weight loss efforts in a way that is mutually acceptable and satisfying (communal coping processes).

Table 5

Interdependence Construct	Operationalization
Transformation of motivation	• Psychoeducation and discussion about (1) health effects of obesity and (2) interdependence of patient and partner diet and physcial activity behaviors • Patients and partners sharing their thoughts and feelings about how obesity affects their relationship • Communication skills training
Communal coping process • Outcome efficacy • Couple efficacy • Use of communal coping (including provision of social support for diet and physical activity)	• Joint action planning • Joint relapse prevention planning • Identifying and practicing methods of providing informational, emotional, and instrumental support (e.g., complimenting on changing habits, exercising together)

Partner involvement in weight loss initiation intervention (months 1-6)

The partner intervention will be delivered by the interventionist and, as explained in C.9, will be supplemented with text messages to reinforce support principles and support commitment. There is no literature to suggest the optimal dose of a partner intervention. We are using our experience in dyadic interventions to strike the balance between efficacy and burden, which will be achieved by a combination of partners participating in a subset of group and telephone patient intervention contacts and receiving supplemental text messages. Partners are not requested to attend all 12 biweekly patient sessions, as burden may lead to attrition. Instead, they will attend 6 monthly meetings. Monthly contacts led to meaningful patient behavior change in our previous trials. The month 1 partner meeting will be conducted at the same time as the patient meeting with the goals of orienting partners to the intervention, introducing social support principles, and providing example behaviors that are likely to be perceived as bilateral and supportive versus unilateral and unsupportive. For example, partners will be taught to provide empathy and avoid making comments that can be perceived as critical; comment on positive rather than negative patient behaviors; make the same lifestyle changes when possible; offer praise; and help patients reward themselves for goal achievement.

In months 2-6, partners will attend monthly sessions along with the patients; they will receive the same dietary and physical activity education as patients, which can provide the basis for instrumental support and may benefit partners who are attempting weight loss themselves. These sessions will also include continued training in communication skills and social support principles with a focus on applying skills to the educational topic presented that month. Sessions will involve group discussion and role-plays around common challenges. Participants will be encouraged to share successes and challenges if they are comfortable doing so. There will also be breakout sessions so that couples can engage in guided exercises to identify individual challenges and preferred supportive behaviors and practice providing support (partner) and reinforcing this support (patients). During these meetings, couples will work together to generate a partner support plan to enhance support commitment. The interventionist and attending co-investigator will assist couples in this task.

Partner involvement in weight loss maintenance intervention (months 7-18)

Month 7 will involve partner attendance at the three patient group sessions led by the interventionist, which includes an overview of the patient maintenance program and a discussion of the partner's role in weight maintenance. Partners will co-participate in the three monthly calls in months 7-9 because it is important for partners to learn to work together effectively to promote patient behaviors that maintain weight loss and to receive coaching from the interventionist if challenges are encountered. Partners will also participate in calls in months 12 and 18. During all joint telephone calls, partners and patients will co-develop patient relapse plans and partner support plans. They will be encouraged to communicate regularly about the identified plans, assess progress, and work together to overcome barriers. Calls to couples will be ~10 minutes longer than patient-only calls. In the CouPLES trial, patients and spouses participated on >75% of calls together even though the protocol did not require it; thus, we expect high compliance in this study.

The content from the group sessions and maintenance telephone calls will be revised iteratively until the team feels that patients understand and can engage with the content. Changes may be made to enhance comprehension of intervention material or the ability to engage in the recommended behavioral skills.

Text messages to reinforce intervention principles and reduce burden (months 1-18)

Timing, frequency and development of message content are consistent with Dr. Shaw's previous successful research that is now being translated into clinical practice.(77) To recapture intervention principles, we will use text messages that we have developed and are currently implementing in our ongoing R34 (to patients in both arms) and support principles that were included in handouts from the CouPLES study (to partners in partner-assisted arm). These will be supplemented with patients' personalized goals and relapse prevention plans (to patients both arms) and partners' support plans (to partners in partner-assisted arm). In the maintenance period, the partner text messages with be the same as the patient text messages. Research staff will schedule the messages to be delivered over 18 months by Prompt. Table 6 shows the schedule and content by arm.

Table 6

Month	Frequency	Content	Sent To
1-6	3x/week	Initiation principles	Patients (both arms)
7-9	2x/week	Maintenance principles	
10-12	1x/week		
13-18	Every 2 weeks		
1-6	3x/week	Support principles, patients' dietary and activity goals, individual support plan	Partners (partner-assisted arm only)
7-9	2x/week	Support principles, patients' relapse prevention plans, individual support plan	Partners (partner-assisted arm only)
10-12	1x/week		
13-18	Every 2 weeks		

Couples' communication sessions (patient-only arm)

Following the 24-month outcome assessment, we will offer sessions 1 and 2 from the partner-assisted intervention to couples in the patient-only arm.

9.2.3 Follow up:

Table 7. Acceptable Window for Study Visits (including weekends)

Visit	Window	Activities
Screening visit	Up to 8 weeks prior to first group session	Informed consent, medical history/demographics, weight, dietary intake, physical activity, transformation of motivation, couples' efficacy, outcome efficacy, use of communal coping, social support for diet and physical activity, brief pain inventory-short form, COVID-19
Month 0	1st group session (0-8 weeks post screening visit)	Baseline weight is recorded, randomization status is revealed to participant.
Month 3	+/- 14 days from target assessment date	Transformation of motivation, couples' efficacy, outcome efficacy, use of communal coping, social support for diet and physical activity, COVID-19
Month 6	+/- 14 days from target assessment date	Weight, dietary intake, physical activity, transformation of motivation, couples' efficacy, outcome efficacy, use of communal coping, social support for diet and physical activity, brief pain inventory-short form, weight loss methods, COVID-19
Month 9	+/- 14 days from target assessment date	Transformation of motivation, couples' efficacy, outcome efficacy, use of communal coping, social support for diet and physical activity, COVID-19
Month 12	+/- 14 days from target assessment date	Weight, dietary intake, physical activity, transformation of motivation, couples' efficacy, outcome efficacy, use of communal coping, social support for diet and physical, activity brief pain inventory-short form, weight loss methods, COVID-19

Month 15	+/- 14 days from target assessment date	Transformation of motivation, couples' efficacy, outcome efficacy, use of communal coping, social support for diet and physical activity, COVID-19
Month 18	+/- 14 days from target assessment date	Weight, dietary intake, physical activity, transformation of motivation, couples' efficacy, outcome efficacy, use of communal coping, social support for diet and physical activity, brief pain inventory-short form, weight loss methods, COVID-19
Month 21	+/- 14 days from target assessment date	Transformation of motivation, couples' efficacy, outcome efficacy, use of communal coping, social support for diet and physical activity, COVID-19
Month 24	+/- 14 days from target assessment date	Weight, dietary intake and physical activity, weight loss methods

9.2.4 Unscheduled:

- Unscheduled visits will not be included in this study.
- No concomitant therapies will be advised or suggested in this study.

9.2.5 Final Study Visit

The final study visit will occur 24 months after enrollment. At the 24 month visit, the patient's weight, dietary intake and physical activity will be assessed via the methods described previously. We will have a two-week window on either side of the target assessment date.

No additional follow-up for AEs/SAEs will occur after the final outcome measurement visit due to minimal risk. Newsletters will be sent to all participants with study results summarized across participants. Patients will be aware of their weight measurements that occur at study visits, so individual disclosure of data is not necessary.

10. Study Analysis

10.1 Sample Size Determination

The sample size estimate is based on the primary hypothesis that estimated patient weight will be at least 2.5 kg lower at 24 months in the partner-assisted than patient-only arm. This effect size was chosen because smaller differences are unlikely to be considered meaningful to researchers, providers, or patients.(78) The sample size was determined by multiplying the number of participants required for a t-test of post scores by 2(1-ρ) and adding one extra participant per arm.(79) Based on MAINTAIN, we anticipate a common standard deviation of 19.9 kg and a correlation (ρ) between the *month0* and *month24* time points of 0.96. Thus, we need 160 participants total (80 in each arm) to detect a 2.5 kg difference with 80% power and a type-I error rate of 5%. We further inflate the sample size to 1) incorporate the intra-class correlation (ICC) of small group members into consideration and 2) compensate for attrition using procedures for group-randomized designs.(66) Let m=15 (conservative upper limit) be the number of patients in each of the small groups, and let ICC=0.01 represent the intra-class correlation between patients in the same group. The updated sample size is n = 160* [1 + (m-1)ICC], or 180. We then conservatively inflate the sample size for an attrition rate of 20% through month24. Therefore, we will enroll n=230 patients (115 per arm), randomized to receive the partner-assisted or patient-only intervention, to detect a 2.5 kg difference in mean 24-month net weight loss between arms.

10.2 Statistical Methods

Descriptive statistics, including graphical displays, will be used to summarize all study variables. Distributional assumptions of the continuous outcome variables will be carefully examined and transformations made, if necessary. We will construct individual and mean trajectory plots of the longitudinal outcome variables to understand their general trends over the study period. In addition, we will explore the variability and correlation structure of the longitudinal outcome variables.

Aim 1: Test the hypothesis that average patient weight is at least 2.5 kg lower in the partner-assisted arm than the patient-only arm at 24 months. The unit of time will be months relative to randomization. The outcome is weight measured at each in-person study visit. Therefore, *month0* represents the weight at the point of randomization (i.e., the first group visit), and *month24* represents the primary study endpoint. The between-arm comparison in net weight loss from *month0* to *month24* will be examined with a multilevel longitudinal model(80) of the general form: $Y_{ijt} = X_{ijt}\beta + c_j + Z_{ij}b_{ij} + \varepsilon_{ijt}$, where Y_{ijt} is weight in kg for patient *i* in small group *j* at *t=month0*, *6, 12, 18, 24*. The predictors in the model will (X_{ijt}) include a time main effect, the intervention main effect, and the intervention arm by time interaction, and Z_{ijt} will include an intercept and a time effect. We will use a flexible polynomial model for the main effect of time and keep the treatment by time interaction linear in time. We will first explore cubic time effects. If it is inadequate for the complexity in the temporal trend, higher order polynomials will be explored. We will formally check for the adequacy of a particular form for time effects using Wald or likelihood ratio tests for higher-order terms. The effect c_j is an additional random intercept for small group *j*, capturing common effects at the small group level. The predictor vector X_{ijt} will also include indicator variables for each of the eight strata defined by the cross-classification of the stratification variables of patient sex, patient BMI, and partner BMI. As a first step, the correlation of patients' repeated measures over time will be modeled and accounted for via the patient-level random intercept and time slope, $b_{ij.}$ However, as is advised by good modeling practice,(80) various covariance structures for time will be explored, including unstructured and differential correlation structures by arm, via graphics such as the variogram and estimation with ReML,(81) all while being blinded to treatment effects. The AIC and BIC fit indices will be used to choose the best correlation structure. We will estimate the parameters in the model using the SAS procedure MIXED (Cary, NC). To test the null hypothesis that the average weight is equal in the two intervention arms, we will test if the coefficient for the time by treatment interaction is zero. Specifically, if $X_{ijt}\beta$ takes the following form$\beta_0 + \beta_1 trt + \beta_2 time + \beta_3 trt * t + \beta_4 covariates,$

where trt is the treatment indicator and t is linear time, then the null hypothesis is H_0: $\beta_3 = 0$. In addition, we will tabulate the analysis results for the (fixed) effects of the baseline covariates such as patient sex, patient BMI, and partner BMI.

Aim 2: Test the hypotheses that average daily caloric intake is significantly lower, and frequency of moderate intensity physical activity is significantly greater, in the partner-assisted arm than the patient-only arm at 24 months. Dietary adherence will be operationalized as daily intake of calories at months 0, 6, 12, 18, and 24. For each of these same assessment times, physical activity will be summarized as the total and mean minutes of moderate levels per week. Changes in dietary adherence and physical activity will be analyzed using the same methods and models as presented for the Aim 1 analyses of weight loss. Previous experience with these outcomes has shown they are often non-normally distributed; therefore, outcomes may be analyzed as generalized linear mixed models, estimated with adaptive Gaussian quadrature, as needed. As exploratory analyses, we will use the models described for Aims 1 and 2 to examine "spillover" effects(34) of the partner-assisted intervention on partner weight and dietary adherence.(50)

Aim 3: Assess the extent to which interdependence constructs (transformation of motivation, couple efficacy, outcome efficacy, use of communal coping) mediate the effect of the partner-assisted weight management intervention on weight loss. We will estimate the extent to which the effect of the partner intervention, $\mathrm{T_i}$ on participants' weight at 6 months, $\mathrm{Y_i}$, is jointly mediated by a vector of five mediating constructs, $\mathrm{M_i} = (\mathrm{M_{i1}},\ldots,\mathrm{M_{i5}})$ measured at 3 months: transformation of motivation, couples' efficacy, outcome efficacy, use of communal coping, and social support. Each mediating construct is measured by the summary scale of associated items. We will assess mediation twice: separately for the diet and physical activity domains of the mediators.

Mediation analysis requires additional assumptions beyond treatment randomization, most importantly: (i) no unobserved mediator-outcome confounders; and (ii) no observed mediator-outcome confounder is affected by the intervention. In order to render assumption (i) more plausible, we will make statistical control for a vector of baseline values, $\mathrm{B_i}$ of the blocking variables, weight, and the mediating constructs, and we will assume that the block of mediators referring to diet and the block referring to physical activity do not affect each other (we do, however, permit that the elements of each $\mathrm{M_i}$ affect each other).

We will follow VanderWeele and Vansteelandt's[9] approach to estimate the natural direct effect (NDE) and the natural indirect effect (NIE) of the intervention relative to a set of mediators, M, by estimating a set of regression equations.
$\mathrm{E[Y_i|\,T, M, B]} = \mathrm{a_0} + \mathrm{a_1 T_i} + \mathrm{a_{21} M_{i1}} + \cdots + \mathrm{a_{25} M_{i5}} + \mathrm{a_3 B_i}$

$\mathrm{E[M_{ik}|\,T, B]} = \mathrm{b_{0k}} + \mathrm{b_{1k} T_i} + \mathrm{b_{2k} B_i}$ for $\mathrm{k} = 1, \ldots, 5$.

We write $Y_i(t, M_i(t'))$ for the potential outcome of i if i received intervention t and the value the mediators if i received intervention t'. Under assumptions (i), (ii), successful randomization of the intervention (all condition on B), and correct functional form, we will then estimate the average natural direct effect of the intervention (versus not) on weight at 6 months as
$E[Y_i(1, M_i(0)) - Y_i(0, M_i(0)|B) = a_1$

and the natural indirect (mediation) effect as

$E[Y_i(0, M_i(0)) - Y_i(0, M_i(1)|B) = b_{11}a_{21} + \cdots + b_{15}a_{25}.$

We will bootstrap the standard errors for the direct and indirect effects.

10.3 Participant Population(s) for Analysis

All participants' data will be analyzed, using an intent-to-treat approach. The sample size justification appears in Section 8 Study Participants.

10.4 Planned Interim Analysis:

There is no interim analysis planned. However, we are prepared, if requested by the Data Monitoring Committee at any point, to calculate interim statistical power for its review. Projections of interim power can be made under several scenarios for future data, including assumptions that current trends continue or that the future data reflect the relative effects used in the design of the trial. Safety reports will tally adverse events by intervention assignment and postulated relationship to the trial interventions; event rates will be reported per person year of follow-up. Should excessive risk to study participants be determined during the DMC review, the study will be stopped and all participants notified in a manner appropriate to the nature of the risk as defined by the IRB and DMC.

11. Data Collection, Handling and Record Keeping

11.1 Data Confidentiality

Every effort will be made to protect participant confidentiality. Research personnel will use only those parts of the medical record necessary to determine eligibility and follow the research protocol, and measures will be taken to maintain privacy during in-person sessions. We will establish ground rules at the group sessions, advising participants that they should only communicate information they feel comfortable communicating in public and that any information learned about other participants should be kept confidential.

Data from the mobile device (Fitbit™) will be automatically transferred to the Fitbit™ smartphone app. The data are then automatically transferred to the Fitbit™ company servers. These data are not identifiable since we are providing participants with a Fitbit™ login ID that is created by the study team. Data will be maintained on the Fitbit™ servers indefinitely. Data from the Fitbit™ servers will be automatically transmitted to Dr. Shaw's team's mobile health platform (Prompt) at Duke University. The platform compiles and analyzes biological, environmental and behavioral data from mobile devices and sensors. Using these data, algorithms are developed to perform analytics and, in a feedback loop, intervene with patients or their social network, or transmit their data to providers. This software is currently used in NIH-funded trials, including another with Drs. Voils' and Shaw, and approved by the Duke IRB and security office for clinical trial use.

In this study, participants will sign a consent and HIPAA Authorization (or oral consent will be obtained if the screening/enrollment visit is done remotely) to allow data from the mobile devices to be transmitted to the platform, where it will be aggregated. Interventionists will have access to a dashboard in the software system, where they can view physical activity data from study participants. This will allow the interventionists to provide tailored feedback. All data from the platform will be transferred (with identifiers: phone number and study ID) using IRB-approved methods to the University of Wisconsin-Madison during the data analysis phase of the grant. The data can be used for ancillary analyses to examine patterns of self-monitoring and engagement with the intervention.

In order to prevent the exposure of personal identifying information or PHI, we will use the following procedures:

1. During the screening process, each potential patient and partner will be assigned a study participant number for tracking purposes.
2. Participant identifying information that is recorded on paper will be kept in a locked file cabinet in the research offices at UW-Madison of the PI or WREN.
3. Potential participants who decline participation or are ruled ineligible during the screening process will have all their identifying information destroyed.
4. Case report forms will be identified by study participant number only.
5. No results will be reported in a personally identifiable manner.
6. The recruitment tracking system will be firewalled behind the SMPH firewall, only accessible from SMPH workstations, not the internet in general. SSL (secure socket layer) encryption will be employed to access the site, guaranteeing end to end security. The server physically resides on Surgery's Virtual Infrastructure located in the data center in MFCB behind a locked, keycarded, and PIN required door. The same security measures will be in place for the online screening website except that the website will be accessible from the general internet.
7. All tracking system data will be password-protected with several levels of protection.
    a. The first password will allow access to the operating system of the computer.
    b. The second password will allow access to the basic menus of the integrated system. Administrative functions are restricted to only certain ID's. Our prior research employing similar precautions has demonstrated that these techniques are very successful in assuring the protection of participants.
8. Data from the mobile device (Fitbit™) will be aggregated using a software engine designed by Duke software engineers, called Prompt. Prompt is used in many NIH-funded studies at Duke University and has received approval to be used by the Duke IRB. Prompt uses Twilio and Amazon S3. Prompt will receive physical activity data from Fitbit™. We will not collect names in this database, only phone number and study ID of each participant, as well as data from Fitbit™ (physical activity). Study staff will login to a password-protected database to view study ID and see if participants are using the devices. We will use Amazon S3 to store data; data will be encrypted when it is stored. These are companies outside of Duke that will have access to participants' personal information (phone number and data from the devices). If these data are further disclosed by them or their business partners, it may no longer be covered under the privacy protections. Stefan Wahe, UW-Madison HIPAA Security Officer, has vetted and approved these Duke platforms.
    a. The mobile health platform, Prompt, is password-protected and only the necessary investigators (with Duke IRB approval) will have access to the software and participant data. All data that are exported from the platform will be coded with only the participant study ID linked (not their phone number).
    b. Data exported from the mobile health platform will sit on a firewall-protected Duke School of Nursing Server in a secure electronic folder (S:\SED\Partner2Lose). Only necessary investigators will have access to this folder.
    c. This data will be transferred approximately every 6 months to the University of Wisconsin-Madison via a Duke managed Box folder. Once the data are uploaded, the UW will download and store the data to the Department of Surgery (DOS) Instance of REDCap. DOS REDCap will only accessible by members of the UW research team. Each user in DOS REDCap has their own ID and can only see their projects or projects that have been shared with them. The UW Department of Surgery and School of Medicine and Public Health scan for vulnerabilities on a regular basis.
9. We will register all participants with the mobile devices using their coded study ID and a coded e-mail address. For example, for participant 'P1234' we will create a Gmail account 'P1234@gmail.com'. This coded e-mail address will be used as the registration for the Fitbit™ and will only be linked to the participant using the secured study key. The participant 'name' in the Fitbit App and at Duke will be the Study ID.
10. We will ensure that all sharing options with third party services such as online social networks or other fitness apps are disabled. Participants will be encouraged not to share information with third party services such as online social networks or other fitness apps. However, some participants may opt to do this. Thus, all participants will be encouraged to read the privacy statement for the mobile devices and to decide for themselves what information they would like to share.
11. The group sessions and maintenance telephone calls will be audio recorded. The recordings will be stored and shared with Dr. Porter via a secure Duke box folder. Only members of the research team will have access to these recordings. The audio recordings will not contain identifiers and the study team will discourage the use of identifiers at the beginning of each group session (e.g. ask the participants not to use full names). The recordings will be stored for up to 7 years after the study is completed.
12. DOS REDCap, an approved electronic database that is only accessible by members of the research team, will be used for randomization, enrollment, and questionnaire/survey completion. Each user in DOS REDCap has

their own ID and can only see their projects or projects that have been shared with them. The Department of Surgery and School of Medicine and Public Health scan for vulnerabilities on a regular basis. Particpants will be assigned a unique identifier number in this database once they are scheduled for their in-person screening visit. At that time, some of their identifiable information will be entered and stored in DOS REDCap. This unique identifier will be linked to a separately maintained master list that contains participant identifiers, which will be located in the tracking system. This linkage will allow research staff to track the enrollment process. Any additional identifiable information will be coded prior to entry into the final dataset. Consequently, the final dataset that will be retained will not include any participant identifiers.

13. We will use Duke's instance of REDCap to send text messages to participants to encourage them to self-monitor and use the devices. This software interfaces with Twilio to send text messages. We will store participant phone numbers and study IDs in Duke's REDCap, no other information is needed.
    a. Text messaging does not provide a completely secure and confidential means of communication. No PHI will be sent via text message. All of this information is included in the consent form.
    b. Duke's REDCap, is password-protected and only the necessary investigators will have access to the software and participant data. All data in Duke's REDCap will be coded with only the participant ID.
    c. Duke's REDCap will only store phone numbers and study ID codes while the UW-Madison DOS REDCap will store all other study data.
14. For data analysis and safety monitoring, the data will be downloaded from DOS REDCap to the UW secure Biostatistic servers. Data analysis will occur on the secure Biostatistic servers.
15. Access to study data will be removed for all study personnel when they are no longer part of the research team.
16. If it's necessary to have the group classes via a Webex video call, participants will be provided a link to join the call via their desktop or cell phone. Webex is approved for use by UW HIPAA.
17. The OnceHub online scheduling program is a secure and HIPAA compliant website. Participants will only use their name and email to schedule their 6, 12, 18 and 24 month in-person measurements. Only members of the study team will be able to view participant information. Participants cannot see any other participants' information.

11.1.1 Confidentiality of Participant Records

By signing the protocol, the Investigator agrees that the NIH or IRB representative may consult and/or copy study documents in order to verify CRF data. By signing the consent form (or providing oral consent if the screening/enrollment visit is done remotely), the participant agrees to this process. If study documents will be photocopied during the process of verifying CRF information, the participant will be identified by unique code only and full names and similar identifying information (such as medical record number) will be masked.

The Clinical Site Investigators will ensure that the identity of participants will be protected. All study records will be maintained in a secure fashion with access limited to essential study personnel only. All study documents submitted to the Coordinating Center will have identifiers removed other than dates of birth and service and participants will be identified with a site-specific identification number only. The Clinical Site Investigators will maintain, in a secure location, an enrollment log that includes participant identifying information and links participants to their study-specific identification number.

11.2 Data Capture

11.2.1 Source Documents

All source data will be kept and merged and/or entered into the electronic clinical trial software (DOS REDCap). Source data is all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents. Examples of these original documents and data records include: surveys recorded on hard copy or in DOS REDCap; ASA24 data; participant files.

Data will be collected during the screening visit, Month 0 (first group session: weight only), Month 6 visit, Month 12 visit, Month 18 visit, Month 24 visit. Data will also be collected during the in-person group visits and telephone calls for the intervention portion of the study.

Data will also be pulled from the mobile device Fitbit™ using our mobile health platform, known as Prompt. The data will be used for research purposes only.

11.2.2 Case Report Forms

The study case report form (CRF) is a data-reporting instrument for the study. All data requested on the CRF must be recorded. All missing data must be explained.

- All entries should be printed legibly in black ink.
- If any entry error has been made, to correct such an error, draw a single straight line through the incorrect entry and enter the correct data above it.
- All such changes must be initialed and dated.

NOTE:

- If a space on the CRF is left blank because the procedure was not done or the question was not asked, write "N/D".
- If the item is not applicable to the individual case, write "N/A".
- DO NOT ERASE OR WHITE OUT ERRORS.
- For clarification of illegible or uncertain entries, print the clarification above the item, then initial and date it.

11.2.2.1 Missing Data

Our plans for preventing and dealing with missing data follow the guidelines set forth by the National Research Council's Panel on Handling Missing Data in Clinical Trials. First, we will employ numerous strategies to achieve < 20% patient attrition. Second, as recommended by the panel, we will conduct two general types of sensitivity analyses for our primary analysis. Because we are using full likelihood methods, the primary analysis model above (as well as the exploratory aim analysis model discussed below) is valid under the MAR (missing at random) framework, where missing values may depend on treatment arm, any observed weight measurement, patient sex, and patient and partner *month0* weight. If missing values are related to other measured factors, such as physical activity measurements, then multiple imputation provides a framework for incorporating information from these auxiliary variables while still preserving a parsimonious main treatment effect model.(86) As a first sensitivity analysis, a general, multivariate imputation model will be constructed using all observed weights, treatment arm, and any covariates predictive of missingness. The primary model, specified above, will then be fit to the multiply imputed data, and the estimates and standard errors will be combined using appropriate combining rules. We acknowledge the possibility that data may be MNAR and propose as a second sensitivity analysis to explore MNAR methods, including pattern-mixture models and the toolkit of methods presented in O'Kelly & Ratitch.(87)

11.2.3 Data Collection Tools

This study will use the Department of Surgery instance of REDCap, which provides data management functionality by allowing the development of eCRFs and surveys to support data capture. DOS REDCap is a secure, web-based, flexible system with an intuitive interface to enter data and has real time validation rules with automated data type and range checks at the time of data entry.

11.3 Data Management

UW-Madison will serve as the data coordinating center, overseeing timely and accurate data collection. The data coordinating center agrees to be responsible for implementing and maintaining quality control and quality assurance systems with written standard operation procedures (SOPs) to ensure that trial is conducted and data are generated, documented, and reported in compliance with the protocol, accepted standards of Good Clinical Practice (International Conference on Harmonization E6), and all applicable federal, state, provincial, and local laws, rules, and regulations relating to the conduct of the clinical trial in an ongoing and auditable manner. The DOS instance of REDCap, a web application for managing surveys will be used for data collection of survey instruments and to randomize participants.

11.4 Data Monitoring

DOS REDCap reports will be used to provide up-to-the-minute access to all entered data. This will allow verification of completeness, timeliness, reliability, and accuracy of collection and coding of data. Consistency checks and range checks have been built into the DOS REDCap System.

In preparation for and during ICTR DMC reviews, the DMC staff will notify the study team if any questions regarding data arise. This may include, but is not limited to, missing data elements, outliers, and/or conflicting data points.

11.5 Records Retention

For this non-FDA regulated study, all study data will be retained for at least 5 years after the last manuscript published under this clinical trials protocol number. If the analysis data will be retained beyond this window (example: for another study), a separate protocol and IRB approval will be obtained.

12. Assessment of Safety

This is a minimal risk study. The PI will be notified of any AEs/SAEs and ensure that all notifications (IRB, DSMB, etc.) occur according to protocol.

12.1 Specifications of Safety Parameters

12.1.1 Definition of Adverse Events (AE)

Adverse event means any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related (21 CFR 312.32 (a)).

12.1.2 Definition of Serious Adverse Events (SAE)

An AE or suspected adverse reaction is considered "serious" if, in the view of either the investigator or sponsor, it results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

12.1.3 Definition of Unanticipated Problems (UP)

OHRP considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research (“possibly related” means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

This study will use the OHRP definition of UP.

Corrective actions or changes that will be considered in response to an UP will include:

- Modification of inclusion or exclusion criteria to mitigate the newly identified risks
- Implementation of additional safety monitoring procedures
- Suspension of enrollment of new participants or halting of study procedures for enrolled participants
- Modification of informed consent documents to include a description of newly recognized risks
- Provision of additional information about newly recognized risks to previously enrolled participants.

12.2 Classification of an Adverse Event

12.2.1 Severity of Event

The following guideline will be used to describe severity:

Mild – Events require minimal or no treatment and do not interfere with the participant's daily activities.
Moderate – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
Severe – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating.

12.2.2 Relationship to Study Intervention

For all collected AEs, the clinician who examines and evaluates the participant will determine the AE's causality based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.

Definitely Related – There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out. The clinical event occurs in a plausible time relationship to intervention and cannot be explained by other factors.
Probably Related – There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. The clinical event occurs within a reasonable time after administration of the intervention and is unlikely to be attributed to other factors.
Possibly Related – There is some evidence to suggest a causal relationship (e.g., the event occurred within a reasonable time after administration of the intervention). However, other factors may have contributed to the event (e.g., the participant's clinical condition, other concomitant events). Although an AE may rate only as "possibly related" soon after discovery, it can be flagged as requiring more information and later be upgraded to "probably related" or "definitely related," as appropriate.
Unlikely to be related – A clinical event whose temporal relationship to drug administration makes a causal relationship improbable (e.g., the event did not occur within a reasonable time after administration of the trial medication) and in which other behaviors or underlying disease provides plausible explanations (e.g., the participant's clinical condition, other concomitant treatments).
Not Related – The AE is completely independent of intervention and/or evidence exists that the event is definitely related to another etiology. There must be an alternative, definitive etiology documented by the clinician.

12.2.3 Expectedness

The study clinician will be responsible for determining whether an AE is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the intervention.

12.3 Time period and frequency for event assessment and follow-up

The occurrence of an AE or SAE may come to the attention of study personnel during study visits and interviews of a study participant presenting for medical care. All AEs, including local and systemic reactions not meeting the criteria for SAEs, will be captured on the appropriate CRF. Information to be collected includes event description, time of onset, clinician's assessment of severity, relationship to study intervention, and time of

resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE. UPs will be recorded in the data collection system throughout the study.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

12.4 Reporting procedures

This study will follow the HS-IRB reporting and submission timeframes:
https://kb.wisc.edu/images/group78/18324/ReportingTimeframesJanuary2013.pdf

Reporting time frames are in the Attachment.

This document will take priority for timeframes. The PI is responsible for reporting to the IRB, DMC, and NIH.

12.4.1 Adverse Event Reporting

Adverse events must be reported once the participant undergoes any study procedures and adverse events must be reported during the entire active study period. The IRB, DMC, and NIH will receive notifications about AEs.

12.4.2 Serious adverse event reporting

Any SAE (including death, irrespective of the cause) occurring during the study will be immediately reviewed by the PI/study physician(s). Only SAEs meeting the Health Sciences IRB's reporting requirements will be submitted for IRB review. These SAEs will be submitted within the timeframe that is required by the HS-IRB and will also be reported to the DMC within the same timeframe.

The DMC will review all SAEs, regardless of reporting requirements to the IRB, every 12 months or ad hoc depending on the clinical case at the discretion of the PI/study physician(s). Each SAE will be followed until it is resolved or can be explained satisfactorily.

12.4.3 Unanticipated problem reporting

The site investigator will be responsible for creating and completing a UP report form. Incidents that meet the OHRP criteria for UPs will be reported promptly per the HS IRB timeline (See Attachment).

- All UPs should be reported to appropriate institutional officials as required by the HS-IRB, the NIH, DSMB, and OHRP upon receipt of the report of the problem from the investigator per the HS IRB policy: https://kb.wisc.edu/images/group78/18324/ReportingTimeframesJanuary2013.pdf

The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number;
- A detailed description of the event, incident, experience, or outcome;
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP;
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

12.4.4 Reporting of pregnancy

Participants will also be immediately withdrawn from the study if they report being pregnant or planning to become pregnant. Study data acquired up to the withdrawal date will be analyzed. No additional routine pregnancy reporting is indicated for this study.

12.5 Study Halting Rules

12.5.1 Participant Stopping Rules

Participants will be informed that they have the right to withdraw from the study at any time for any reason, without prejudice to their medical care. The investigator also has the right to withdraw participants from the study for any of the following reasons:

- If study intervention is discontinued due to AE
- Protocol violation
- Study terminated

Participants may be withdrawn at the discretion of the PI for safety reasons. Women that are currently pregnant or plan to become pregnant during enrollment screening will be excluded from study participation. If a participant becomes pregnant during the study, she will be excluded immediately from further participation in all study activities. Pregnancy testing is not part of the study protocol. Once enrolled in the study, individuals in either the usual care or intervention group who become ineligible during the study (e.g., self-report of pregnancy) will be informed that their participation has ended and will be provided the reason for ending their study participation.

12.5.2 Study Stopping Rules

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to investigator, funding agency and the regulatory authorities. If the study is prematurely terminated or suspended, the PI will promptly inform the IRB and DMC and will provide the reason(s) for the termination or suspension.

Circumstances that may warrant termination or suspension include, but are not limited to the following:

- Determination of unexpected, significant, or unacceptable risk to participants
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable

12.6 Safety Oversight

Independent safety oversight will be provided by The UW ICTR Data Monitoring Committee (DMC). The UW ICTR DMC is comprised of experienced members (core plus ad hoc) with expertise required to oversee this study. The DMC members will review protocol-specific reports created by statisticians using data pulled from DOS REDCap data management tool. These standard reports will include an overview of study objectives, a review of actual and projected accrual rates, an evaluation of patient demographics for balance of randomization, and a summary of the number and seriousness of adverse events. Source documents may be reviewed to allow the DMC to independently judge whether the overall integrity and conduct of the protocol remain acceptable based on data provided and reported by the PI. The DMC will make recommendations to the PI that could include actions of continuation, modification, suspension, or termination.

12.7 Unblinding Procedure

Blinding of participants is not possible in behavioral interventions. Only WREN outcome assessors will be blinded.

13. Study Monitoring, Auditing, and Inspecting

13.1 Medical Monitoring

13.1.1 Study Monitoring Plan

No independent study monitoring will be conducted.

13.2 Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol, GCP, or MOP requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

The site PI/staff will be responsible for continuous vigilance to identify and report deviations to the protocol. These will be reported per the HS IRB requirements (see attachment). All deviations must be addressed in study source documents, reported to NIH Program Official, DMC, and IRB. Protocol deviations will be sent to the local IRB per their guidelines. The site PI/study staff is responsible for knowing and adhering to their IRB requirements.

13.2.1 Internal Data and Safety Monitoring Board

We plan to utilize the UW ICTR Data Monitoring Committee (DMC) to oversee the study. The UW ICTR DMC is comprised of experienced members with expertise required to oversee this study. The DMC members will review protocol-specific reports created by statisticians using data pulled from the DOS REDCap data management tool. These standard reports will include an overview of study objectives, a review of actual and projected accrual rates, an evaluation of patient demographics for balance of randomization, and a summary of the number and seriousness of adverse events. An interim analysis of study results may be performed and source documents may be reviewed to allow the DMC to independently judge whether the overall integrity and conduct of the protocol remain acceptable based on data provided and reported by the Principal Investigator. The DMC will make recommendations to the Principal Investigator that could include actions of continuation, modification, suspension, or termination.

In providing oversight for the conduct of this study, the ICTR DMC will meet annually during the 5-year study to review all adverse events. Additional meetings may be scheduled as determined by the DMC or as requested by the PI. Additional information about the ICTR DMC can be found in the ICTR DMC Charter and Composition, located in the Attachment section of this protocol.

13.3 Auditing and Inspecting

The investigator will permit study-related monitoring, audits, and inspections by the EC/IRB (or their representatives), the sponsor, government regulatory bodies, of all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g. pharmacy, diagnostic laboratory, etc.).

13.4 Participant Compliance Monitoring

Adherence to the behavioral interventions will be tracked by the study team. At each group visit, an attendance sheet will be kept. All missed group visits and telephone calls will be recorded in the tracking database. No

participant will be excluded from the study or analyses for noncompliance. Compliance with study treatment may be used in secondary analyses (e.g., dose-response relationship).

14. Ethical Considerations

This study is to be conducted according to US and international standards of Good Clinical Practice (FDA Title 21 part 312 and International Conference on Harmonization guidelines), applicable government regulations, applicable local and state laws, and Institutional research policies and procedures.

This protocol and any amendments will be submitted to a properly constituted independent Ethics Committee (EC) or Institutional Review Board (IRB), in agreement with local legal prescriptions, for formal approval of the study conduct. The decision of the EC/IRB concerning the conduct of the study will be made in writing to the investigator and a copy of this decision will be provided to the sponsor before commencement of this study. The investigator should provide a list of EC/IRB members and their affiliate to the sponsor.

All participants for this study will be provided a consent form describing this study and providing sufficient information for participants to make an informed decision about their participation in this study. See Attachment for a copy of the Participant Informed Consent Form. This consent form will be submitted with the protocol for review and approval by the EC/IRB for the study. The formal consent of a participant, using the EC/IRB-approved consent form, must be obtained before that participant undergoes any study procedure. The consent form must be signed by the participant, and the investigator-designated research professional obtaining the consent. If it's necessary to do the screening/enrollment visit remotely, participant's oral consent will be obtained by the investigator-designated research professional.

15. Study Finances

15.1 Funding Source

This study is funded by a grant from the National Institute of Diabetes and Digestive and Kidney Diseases.

15.2 Conflict of Interest

Any investigator who has a conflict of interest with this study (patent ownership, royalties, or financial gain greater than the minimum allowable by their institution, etc.) must have the conflict reviewed by a properly constituted Conflict of Interest Committee with a Committee-sanctioned conflict management plan that has been reviewed and approved by the study sponsor prior to participation in this study. All UW investigators will follow the UW conflict of interest policy.

15.3 Participant Stipends or Payments

All participants and their partners can receive a remuneration up to $180 each/$360 per couple for study completion. For each of the Months 6, 12 and 18 month in-person assessments, patients and their partners will receive $40 each/$80 per couple. The payment will increase to $60 each/$120 per couple for completion of the final assessment. Payments will be made by check to the participant at each visit.

Month 6: $40 each/$80 per couple
Month 12: $40 each/$80 per couple
Month 18: $40 each/$80 per couple
Month 24: $60 each/$120 per couple

16. Publication Plan

Neither the complete nor any part of the results of the study carried out under this protocol will be published or passed on to any third party without the consent of the PI. The PI has primary responsibility for publication. All publications resulting from the study will be uploaded to PubMed per NIH policy.

17. References

1. Serdula MK, Mokdad AH, Williamson DF, Galuska DA, Mendlein JM, Heath GW. Prevalence of attempting weight loss and strategies for controlling weight. Journal of the American Medical Association. 1999;282(14):1353-8.
2. Kenchaiah S, Evans JC, Levy D, Wilson PW, Benjamin EJ, Larson MG, et al. Obesity and the risk of heart failure. New England Journal of Medicine. 2002;347(5):305-13.
3. Wilson PW, D'Agostino RB, Sullivan L, Parise H, Kannel WB. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. Archives of Internal Medicine. 2002;162(16):1867-72.
4. Fontaine KR, Barofsky I. Obesity and health-related quality of life. Obes Res. 2001;2(3):173-82.
5. Jensen MD, Ryan DH, Apovian CM, Ard JD, Comuzzie AG, Donato KA, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. J Am Coll Cardiol. 2014;63(25 Pt B):2985-3023.
6. Cawley K, Meyerhoefer C. The medical care costs of obesity: An instrumental variables approach. Journal of Health Economics. 2012;31(1):219-30.
7. Tsai AG, Williamson DF, Glick HA. A Quantitative Assessment of Cost of Obesity Studies. Working Paper2006.
8. Finkelstein EA, Trogdon JG, Cohen JW, Dietz W. Annual medical spending attributable to obesity: payer-and service-specific estimates. Health Affairs. 2009;28(5):w822-31.
9. Bales CW, Buhr G. Is obesity bad for older persons? A systematic review of the pros and cons of weight reduction in later life. Journal of the American Medical Directors Association. 2008;9:302-12.
10. Felson DT, Zhang Y, Anthony JM, Naimark A, Anderson JJ. Weight loss reduces the risk for symptomatic knee osteoarthritis in women: The Framingham Study. Annals of Internal Medicine. 1992;116(7):535-9.
11. Neter JE, Stam BE, Kok FJ, Grobbee DE, Geleijnse JM. Influence of weight reduction on blood pressure: A meta-analysis of randomized controlled trials. Hypertension. 2003;42(5):878-84.
12. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. New England Journal of Medicine. 2002;346(6):393-403.
13. Avenell A, Broom J, Brown TJ, Poobalan A, Aucott L, Stearns SC, et al. Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement. Health Technology Assessment. 2004;8(21):iii-iv, 1-182.
14. Foster GD, Wyatt HR, Hill JO, Makris AP, Rosenbaum DL, Brill C, et al. Weight and metabolic outcomes after 2 years on a low-carbohydrate versus low-fat diet: A randomized trial. Annals of Internal Medicine. 2010;153(3):147-57.

15. Wadden TA, Berkowitz RI, Womble LG, Sarwer DB, Phelan S, Cato RK, et al. Randomized trial of lifestyle modification and pharmacotherapy for obesity. New England Journal of Medicine. 2005;353(20):2111-20.
16. Johns DJ, Hartmann-Boyce J, Jebb SA, Aveyard P. Diet or exercise interventions vs combined behavioral weight management programs: a systematic review and meta-analysis of direct comparisons. Journal of the Academy of Nutrition and Dietetics. 2014;114(10):1557-68.
17. MacLean PS, Wing RR, Davidson T, Epstein L, Goodpaster B, Hall KD, et al. NIH working group report: Innovative research to improve maintenance of weight loss. Obesity. 2015;23(1):7-15.
18. Dombrowski S, Knittle K, Avenell A, Araujo-Soares V, Sniehotta F. Long term maintenance of weight loss with non-surgical interventions in obese adults: Systematic review and meta-analyses of randomised controlled trials. British Medical Journal. 2014;348:g2446.
19. Wing RR, Phelan S. Long-term weight loss maintenance. American Journal of Clinical Nutrition. 2005;82(1 Suppl):222s-5s.
20. Reblin M, Uchino BN. Social and emotional support and its implication for health. Current Opinion in Psychiatry. 2008;21(2):201-5.
21. Meyler D, Stimpson JP, Peek MK. Health concordance within couples: A systematic review. Social Science & Medicine. 2007;64(11):2297-310.
22. Keicolt-Glaser J, Newton T. Marriage and health: His and hers. Psychol Bull. 2001;127:472-503.
23. Umberson D. Gender, marital status and the social control of health behavior. Social Science & Medicine. 1992;34(8):907-17.
24. Martire LM, Schulz R, Helgeson VS, Small BJ, Saghafi EM. Review and meta-analysis of couple-oriented interventions for chronic illness. Annals of Behavioral Medicine. 2010;40(3):325-42.
25. Black DR, Gleser LJ, Kooyers KJ. A meta-analytic evaluation of couples weight-loss programs. Health Psychology. 1990;9(3):330-47.
26. McLean N, Griffin S, Toney K, Hardeman W. Family involvement in weight control, weight maintenance and weight-loss interventions: A systematic review of randomised trials. International Journal of Obesity and Related Metabolic Disorders. 2003;27(9):987-1005.
27. Murphy J, DA W, Buxton A, Moody S, Absher N, Warner M. The long-term effects of spouse involvement upon weight loss and maintenance. Behavior Therapy. 1982;13:681-93.
28. Black D, Lantz C. Spouse involvement and a possible long-term follow-up trap in weight loss. Behavioral Research Therapy. 1984;22(5):557-62.
29. Pearce JW, LeBow MD, Orchard J. Role of spouse involvement in the behavioral treatment of overweight women. Journal of Consulting and Clinical Psychology. 1981;49(2):236-44.
30. Wing RR, Marcus MD, Epstein LH, Jawad A. A "family-based" approach to the treatment of obese type II diabetic patients. Journal of Consulting and Clinical Psychology. 1991;59(1):156-62.
31. Rosenthal B, Allen GJ, Winter C. Husband involvement in the behavioral treatment of overweight women: initial effects and long-term follow-up. Int J Obes. 1980;4(2):165-73.
32. Saccone AJ, Israel AC. Effects of experimenter versus significant other-controlled reinforcement and choice of target behavior on weight loss. Behavior Therapy. 1978;9:271-8.
33. Brownell KD, Stunkard AJ. Couples training, pharmacotherapy, and behavior therapy in the treatment of obesity. Archives of General Psychiatry. 1981;38(11):1224-9.
34. Schierberl Scherr AE, McClure Brenchley KJ, Gorin AA. Examining a ripple effect: Do spouses' behavior changes predict each other's weight loss? Journal of obesity. 2013;2013:297268.
35. Golan R, Schwarzfucks D, Stampfer MJ, Shai I. Halo effect of a weight-loss trial on spouses: the DIRECT-Spouse study. Public Health & Nutrition. 2010;13(4):544-9.
36. Gorin AA, Wing RR, Fava JL, Jakicic JM, Jeffery R, West DS, et al. Weight loss treatment influences untreated spouses and the home environment: evidence of a ripple effect. International Journal of Obesity. 2008;32(11):1678-84.
37. Lewis MA, McBride CM, Pollak KI, Puleo E, Butterfield RM, Emmons KM. Understanding health behavior change among couples: an interdependence and communal coping approach. Social Science & Medicine. 2006;62(6):1369-80.
38. Voils CI, Gierisch JM, Olsen MK, Maciejewski ML, Grubber J, McVay MA, et al. Study design and protocol for a theory-based behavioral intervention focusing on maintenance of weight loss: the Maintenance After Initiation of Nutrition TrAINing (MAINTAIN) study. Contemp Clin Trials. 2014;39(1):95-105.
39. Voils CI, Olsen MK, Gierisch JM, McVay MA, Grubber JM, Gaillard L, et al. Maintenance of Weight Loss After Initiation of Nutrition Training: A Randomized Trial. Annals of internal medicine. 2017;166(7):463-71.
40. Voils CI, Yancy WS, Jr., Kovac S, Coffman CJ, Weinberger M, Oddone EZ, et al. Study protocol: Couples Partnering for Lipid Enhancing Strategies (CouPLES) - A randomized, controlled trial. Trials. 2009;10:10.
41. Goldberg KC, Melnyk SD, Simel DL. Overcoming inertia: Improvement in achieving target low-density lipoprotein cholesterol. American Journal of Managed Care. 2007;13(9):530-4.

42. Voils CI, Coffman CJ, Yancy Jr WS, Weinberger M, Jeffreys AS, Datta S, et al. A randomized controlled trial to evaluate the effectiveness of CouPLES: A spouse-assisted lifestyle change intervention to improve low-density lipoprotein cholesterol. Prev Med. 2013;56(1):46-52.
43. McVay MA, King HA, Jeffreys AS, Coffman CJ, Voils CI. Mechanisms of patient health behavior change in a randomized controlled trial of a spouse-assisted intervention. Psychology, Health, & Medicine. 2015;e-pub ahead of print March 16.
44. Porter LS, Keefe FJ, Garst J, Baucom DH, McBride CM, McKee DC, et al. Caregiver-assisted coping skills training for lung cancer: Results of a randomized clinical trial. J Pain Symptom Manage. 2011;41(1):1-13.
45. Porter L, Xiaomei G, Lyna P, Kraus B, Patterson E, Puleo B, et al. Brief report: Couple-based physical activity for cancer survivors. under review.
46. Baucom DH, Porter LS, Kirby JS, Gremore TM, Wiesenthal N, Aldridge W, et al. A couple-based intervention for female breast cancer. Psycho-Oncology. 2009;18(3):276-83.
47. Porter L, Keefe F, Baucom D, Olsen MK, Zafar S, Uronis H. A randomized pilot trial of a videoconference couples communication intervention for advanced GI cancer. Psycho-oncology. in press.
48. Porter LS, Keefe FJ, Baucom DH, Hurwitz H, Moser B, Patterson E, et al. Partner-assisted emotional disclosure for patients with GI cancer: 8-week follow-up and processes associated with change. Support Care Cancer. 2012;20(8):1755-62.
49. Porter LS, Keefe FJ, Garst J, Baucom D, McBride C, McKee D, et al. Caregiver-assisted coping skills training for early stage lung cancer: Results of a randomized clinical trial. Journal of Pain & Symptom Management. 2011;41:1-13.
50. King HA, Jeffreys AS, McVay MA, Coffman CJ, Voils CI. Spouse health behavior outcomes from a randomized controlled trial of a spouse-assisted lifestyle change intervention to improve patient low-density lipoprotein cholesterol. Journal of behavioral medicine. 2014.
51. Subar AF, Thompson FE, Potischman N, Forsyth BH, Buday R, Richards D, et al. Formative research of a quick list for an automated self-administered 24-hour dietary recall. J Am Diet Assoc. 2007;107(6):1002-7.
52. Blanton C, Moshfegh A, Baer D, Kretsch M. The USDA Automated Multiple-Pass Method accurately estimates group total energy and nutrition intake. Journal of Nutrition. 2006;136:2594-9.
56. Aron A, Aron E, Smollan D. Inclusion of Other in the Self Scale and the structure of interpersonal closeness. J Pers Soc Psychol. 1992;63(596-612).
57. Dibble JL, Levine TR, Park HS. The Unidimensional Relationship Closeness Scale (URCS): reliability and validity evidence for a new measure of relationship closeness. Psychol Assess. 2012;24(3):565-72.
58. Grinberg A, Rohrbach M, Lewis M, Ranby K, Toll B, Lipkus I, editors. Measurement of communal coping in dual-smoker couples. American Psychological Association; 2012; Chicago, IL.
59. Salazar LF, Stephenson RB, Sullivan PS, Tarver R. Development and validation of HIV-related dyadic measures for men who have sex with men. J Sex Res. 2013;50(2):164-77.
60. Lewis MA, Gladstone E, Schmal S, Darbes LA. Health-related social control and relationship interdependence among gay couples. Health Educ Res. 2006;21(4):488-500.
61. Lewis M, Kalinowski C, Sterba K, Barrett T, DeVellis R. Interpersonal processes and vasculitis management. Arthritis Care and Research. 2006;55:670-5.
62. Lewis M, McBride C, Pollak K, Puleo E, Fish L, Butterfield R, et al., editors. Couples' preferences for beahvior change following polypectomy. American Society of Preventive Oncology; 2003.
63. Cutrona C. Social support in couples. Thousand Oaks: Sage Publications; 1996.
64. Bandura A. Self-efficacy: The exercise of control. New York: Freeman; 1997.
65. Ball K, Crawford D. An investigation of psychological, social, and environmental correlates of obesity and weight gain in young women. International Journal of Obesity. 2006;30:1240-9.
66. Donner A, Klar, N. Design and Analysis of Cluster Randomization Trials in Health Research. New York: Oxford University Press; 2000.
67. Yancy WS, Jr., Mayer SB, Coffman CJ, Smith VA, Kolotkin RL, Geiselman PJ, et al. Effect of allowing choice of diet on weight loss: A randomized trial. Annals of Internal Medicine. 2015;162(12):805-14.
68. Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Circulation. 2007;116(9):1081-93.
69. Hu FB, Willett WC. Optimal diets for prevention of coronary heart disease. Journal of the American Medical Association. 2002;288(20):2569-78.
70. Institute of Medicine. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. Washington, DC: The National Academies Press; 2002.
71. 2018 Physical Activity Guidelines Advisory Committee. 2018 Physical Activity Guidelines Advisory Committee Scientific Report. Washington, DC: U.S. Department of Health and Human Services, 2018.

72. American College of Sports Medicine. ACSM's Guidelines for Exercise Testing and Prescription. Philadelphia: Wolters Kluwer, 2018: 289.
73. Donnelly JE, Blair SN, Jakicic JM, Manore MM, Rankin JW, Smith BK. American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. Med Sci Sports Exerc. 2009;41(2):459-71.
74. Martinson BC, Sherwood NE, Crain AL, Hayes MG, King AC, Pronk NP, et al. Maintaining physical activity among older adults: 24-month outcomes of the Keep Active Minnesota randomized controlled trial. Preventive medicine. 2010;51(1):37-44.
75. Voils CI, Gierisch JM, Yancy Jr WS, Sandelowski M, Smith R, Bolton J, et al. Differentiating behavior initiation and maintenance: Theoretical framework and proof of concept. Health Education & Behavior. 2014;41(3):325-36.
76. Epstein N, Baucom D. Enhanced cognitive-behavioral therapy for couples: A contextual approach. Washington, DC: American Psychological Association; 2002.
77. Shaw RJ, Bosworth HB, Silva SS, Lipkus IM, Davis LL, Sha RS, et al. Mobile health messages help sustain recent weight loss. American Journal of Medicine. 2013;126(11):1002-9.
78. Ludwig D, Ebbeling C. Weight-loss maintenance-Mind over matter? New England Journal of Medicine. 2011;363(22):2159-61.
79. Borm G, Fransen J, Lemmens W. A simple sample size formula for analysis of covariance in randomized clinical trials. J Clin Epidemiol. 2007;60(12):1234-8.
80. Fitzmaurice G, Laird N, Ware J. Applied Longitudinal Analysis. Hoboken, NJ: Wiley; 2004.
81. Diggle PJ, Heagerty P, Liang K, Zeger SL. Analysis of longitudinal data. New York: Oxford University Press; 2002.
82. Fritz M, MacKinnon D. Required sample size to meet the mediated effect. Psychological Science. 2007;18:233-9.
83. Fritz M, Taylor A, MacKinnon D. Explanation of two anomalous results in statistical mediation analysis. Multivariate Behavioral Research. 2012;47:61-87.
84. Hochberg Y. A sharper Bonferroni procedure for multiple tests of significance. Biometrika. 1988;75(4):800-2.
85. Hayes A, Scharkow M. The relative trustworthiness of inferential tests of the indirect effect in statistical mediation analysis: Does method really matter? . Psychological Science. 2013;24(1918-1927).
86. Collins L, Schafer J, Kam C. A comparison of inclusive and restrictive strategies in modern missing data procedures. Psychological Methods. 2001;6(4):330-51.
87. O'Kelly M, Ratitich B. Clinical trials with missing data: A guide for practitioners. West Sussex, United Kingdom: John Wiley & Sons; 2014.

18. Attachments

- Consent to Participate in Research and Authorization to Use Protected Health Information for Research Form
- ICTR DMC Charter and Composition
- H-S IRB Reporting Time Frames
- Inclusion Enrollment Report
- Self-report surveys
- Statistical Analysis Plan