

**PROmoting Successful Weight Loss in Primary CarE in Louisiana
(PROPEL) Trial**

PROTOCOL

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1. Abbreviations

AAHRPP	Association for the Accreditation of Human Research Protection Programs
ACC	American College of Cardiology
ACP	American College of Physicians
AE	Adverse Event
AHA	American Heart Association
AHEAD	Action for Health in Diabetes
BEV-Q	Beverage Intake Questionnaire
BMI	Body Mass Index
BV	Baseline Visit
CAHPS	Consumer Assessment of Healthcare Providers and Systems
CALERIE	Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy
CC	Coordinating Center
CMS	Centers for Medicare and Medicaid Services
CTS	Computer Tracking System
DPP	Diabetes Prevention Program
DSMB	Data and Safety Monitoring Board
DSMP	Data and Safety Monitoring Plan
HDL-C	High-Density Lipoprotein Cholesterol
HIPAA	Health Insurance Portability and Accountability Act
HTE	Heterogeneity of Effects
ID	Identification
IRB	Institutional Review Board
IPAQ-SF	International Physical Activity Questionnaire - Short Form
IWQOL	Impact of Weight on Quality of Life

LA	Louisiana
LA CaTS	Louisiana Clinical & Translational Science Center
LDL-C	Low-Density Lipoprotein Cholesterol
LEAP	Lifestyle Eating and Activity Program
LOSS	Louisiana Obese Subjects Study
MET	Metabolic Equivalent
MM	Medical Monitor
MMT	Medical Monitoring Team (MM, NP and CC)
MOP	Manual of Procedures
NCI	National Cancer Institute
NHANES	National Health and Nutrition Examination Survey
NIH	National Institutes of Health
NP	Nurse Practitioner
PCORI	Patient Centered Outcomes Research Institute
PCP	Primary Care Provider
PI	Principal Investigator
POWER	Practice-based Opportunities for Weight Reduction
PROACTIVE	Prevention and Reduction of Obesity through Active Living
PROMIS®	Patient Reported Outcomes Measurement Information System
PROPEL	<u>PRO</u> moting Successful Weight Loss in <u>PR</u> imary Car <u>E</u> in <u>L</u> ouisiana
RD	Registered Dietician
REALM	Rapid Estimate of Adult Literacy in Medicine
RE-POWER	Rural Engagement in Primary Care for Optimizing Weight Reduction
REDCap	Research Electronic Data Capture
SAE	Serious Adverse Event
SF	Short Form

SOP	Standard Operating Procedures
SV	Screening Visit
TOS	The Obesity Society
US	United States
VA	Veterans Affairs
YMCA	Young Men's Christian Association

2. Technical Abstract

Background

Obesity is a highly prevalent and serious medical and social condition in the United States, with Louisiana (LA) currently among the states with the highest rates of obesity. Obesity accounts for \$2.4 billion in yearly health care expenditures in this state, 42.5% of which are financed by Medicaid/Medicare.¹ Obesity and its health outcomes disproportionately affect underserved populations, and LA is characterized by high levels of poverty, low health literacy, and food insecurity, all of which may contribute to the high obesity levels in the state.

Primary care physicians are the cornerstone of medical care in the United States. The US Preventive Services Task Force has recommended that physicians should offer intensive multi-component behavioral interventions to obese individuals², and the Centers for Medicare and Medicaid Services (CMS) covers intensive behavioral therapy for obesity by a qualified primary care practitioner (PCP). However, the sole reliance on physicians, nurse practitioners, or physician assistants to deliver intensive behavioral therapy for obesity has limitations, in part due to the limited time available during a typical primary care visit, and lack of training among PCPs in the delivery of behavior therapy protocols. Further research is required to develop evidence-based models of delivery of obesity treatment within primary care. There is a critical need to test models that incorporate the recently released *2013 AHA/ACC/TOS Guidelines for the Management of Overweight and Obesity in Adults*³, which are adaptable to real-life settings and which provide effective and cost conscious delivery methods for obesity treatment in the primary care setting.

Objectives

The primary aim of this trial is to develop and test the effectiveness of a 24 month, patient-centered, pragmatic and scalable obesity treatment program delivered within primary care in an underserved population. We hypothesize that:

- 1) Relative to patients who receive usual care, patients who receive a high-intensity, health literacy-appropriate and culturally adapted lifestyle intervention targeting increased physical activity and reduced dietary intake delivered by trained health coaches embedded in a primary care setting and supervised by providers trained in obesity science will have greater percent reductions in body weight; and
- 2) Relative to patients in usual care, patients who receive the intervention will have significant improvements in quality of life, functional capacity, satisfaction with medical care, and improve obesity co-morbidities (hypertension, dyslipidemia, insulin resistance, urinary incontinence and respiratory problems such as sleep apnea).

There are three secondary aims. Secondary Aim 1 is to evaluate relationships between adherence to intervention components (physical activity, diet, sessions, etc.) and corresponding changes in body weight and secondary outcomes (post-hoc analyses). Secondary Aim 2 is to examine the effects of the intervention on system-level practices and patient satisfaction with care. Secondary Aim 3 is to test the heterogeneity of effects across clinics and across subgroups of patients (men versus women, white versus African American, older versus younger adults).

Methods

Study Design. This study is a cluster-randomized, two-arm controlled trial in a primary care setting. Study Population. A total of 18 primary care clinics inclusive of low income populations

with a high percentage of African Americans from urban and rural areas of Louisiana will be randomized to either 1) intervention or 2) usual care. The sample will include up to 850 patients (18 clinics, 47 patients/clinic). Justification of Sample Size. The sample size calculations were based on the Louisiana Obese Subjects Study (LOSS), a pragmatic clinical trial conducted by Pennington Biomedical comparing intensive medical intervention for obesity versus usual care.⁴ According to the 2013 Obesity Guidelines, as little as 3-5% weight loss is likely to result in clinically meaningful health outcomes.³ Thus, the sample size calculations assume that the study is powered to detect a mean weight loss in the intervention arm of 3.5% at 2 y, relative to usual care, in race- and sex-specific subgroups. We are targeting a mean weight loss of >5% which we anticipate to be 3.5% more than usual care. Both the total and relative weight loss meet accepted levels of clinical significance. Power calculations used a nominal 0.05 significance level with a two-tailed test with minimal power of 80%. Based on LOSS, the standard deviation for weight change for patients nested within clinics was 8.4%. For the subgroup analysis, a net sample size of 92 patients/arm is sufficient for detecting a 3.5% weight loss with 80% power with patient-level randomization. After accounting for the design effect, at least 134 patients per arm are required to realize 80% power in a trial randomized at the clinic level. Allowing for 30% attrition, at least 192 patients per arm are needed with a total enrollment of 384 patients per subgroup. Inclusion/Exclusion Criteria. Given that this is a pragmatic trial, the inclusion criteria are broad and include having a BMI 30 to 50 kg/m², and an age 20 to 75 years. Women will be required to be non-pregnant and agree to avoid pregnancy during the study. Exclusion criteria include a history of major depression, suicidal behavior or eating disorder, hospitalization for mental disorder or substance abuse in the previous year, active cancer, cardiovascular or cerebrovascular disease event in the past year, heart failure, and current use of weight loss medications or recent weight loss. Outcomes. The primary outcome is percent change in body weight from baseline. Secondary outcomes include change in quality of life, functional capacity, satisfaction with medical care, and obesity co-morbidities (hypertension, dyslipidemia, insulin resistance, urinary incontinence and respiratory problems such as sleep apnea). The secondary outcomes were selected based on the prior experience of the investigators working with obese patients, and they should be considered preliminary, as they could change based on our planned patient focus groups. Analytic Methods. Analyses will be performed on an intent-to-treat basis. For continuous outcomes, a linear mixed model for repeated measures over time will be used, including the fixed effects of intervention, time, and their 2-factor interactions, with age, sex and clinic as covariates. For dichotomous outcomes, a generalized linear mixed model with a logit link will be applied using the same modeling approach. Estimated within-group changes between baseline and 6 to 24 months will be estimated and compared using contrasts within the mixed models. Baseline outcomes will further be included in the models as covariates to determine the change in outcome from baseline. The study design will also allow for analysis of clinic-level characteristics that are associated with better outcomes. Anticipated Effect Size. Weight loss in the lifestyle intervention arm of Look Ahead was 6.4% at 2 y, compared to 1.1% in the education arm.⁵ The original Diabetes Prevention Program (DPP) intensive lifestyle intervention produced a weight loss of 5.8% at 2 y⁶, and this effect has been replicated in a DPP adaptation for deployment through the YMCA, with an initial weight loss of 6% in the intervention versus 2% in control group at 6 months⁷; a reduction which was maintained in the intervention arm at 2 y.⁸ Further, the 2 y results from LOSS showed between 4.9% (baseline carried forward analysis) to 9.6% (completers only) weight loss in the intensive medical intervention arm, compared to 0.4% for usual care.⁴ Thus, based on these prior studies, and the delivery of the proposed intervention in a primary care setting, we anticipate achieving at least a 3.5% weight loss differential between intervention and usual care. Treatment Arms. Trained coaches under provider supervision will deliver the active intervention - a comprehensive, "high-intensity" program, as recommended

first-line therapy by the 2013 Obesity Guidelines, and based on the Look Ahead intensive lifestyle intervention.⁹ This intervention will include 15 in-person sessions in the first six months, followed by at least monthly sessions for the remaining 18 months. The intervention will include evidence-based components and several behavioral strategies. Innovative aspects of the intervention include the addition of a trained “health coach” to the primary care team, a provider education program about energy balance and medical aspects of obesity, and a tailored treatment approach using a computer tracking system and novel toolbox strategies and algorithms.¹⁰ In addition, the intervention materials will be adapted to be health-literacy and culturally appropriate, which is both novel and important for the target population. The usual care arm will receive the obesity treatment currently approved by CMS. A baseline webinar will be conducted with the primary care providers randomized to usual care, describing the current CMS approach to reimbursing for obesity treatment, and background on obesity interventions; a reminder informational brochure will be sent to the providers at 1 y.

Patient Outcomes

The patient outcomes include reductions in body weight, improvements in quality of life, functional capacity, satisfaction with medical care, and resolution of obesity co-morbidities (hypertension, dyslipidemia, insulin resistance, urinary incontinence and respiratory problems such as sleep apnea). From our experience, “weight loss” *per se* is an important patient outcome and is the primary outcome of this trial. Further, in one of the few studies that have addressed patient-centered outcomes related to obesity surgery, the most important outcomes were weight loss and “*a desire for changing medical co-morbidities*”.¹¹

Anticipated Outcomes

This study will have a direct impact on “improving healthcare delivery and outcomes”, which are key components of the PCORI mission. Given the low uptake of the current CMS reimbursement for obesity in primary care, it is anticipated that the results will impact the way that CMS funds obesity treatment in the future. This is a five-year carefully designed and implemented research project; however, the intervention is designed to be economical and scalable to large patient populations, with all of the economies of scale that that entails.

3. Public Abstract

Obesity is a very common and serious medical and social condition, with Louisiana currently ranked among the states with the highest levels of obesity. Obesity is a condition that increases the risk of type 2 diabetes, heart disease, stroke, gallbladder disease, respiratory problems, quality of life, and several cancers. Obesity and its health problems greatly affect underserved populations, and Louisiana is characterized by high levels of poverty, low health literacy, and food insecurity, all of which may contribute to the high obesity levels in the State. While the high rates of obesity are of great concern, a greater concern is that our health care system has failed to deliver medical interventions capable of producing even modest weight loss.

Recently, the American Heart Association, American College of Cardiology, and the Obesity Society released a set of treatment guidelines for obese patients which are adaptable to real-life settings and which could add effective methods for obesity treatment in the primary care setting. Based on this, we know that modest weight loss is achievable in some settings; however, there has been no successful translation of this achievement to primary care practices.

Primary care physicians remain the cornerstone of medical care in the United States. Thus, the primary aim of this study is to test the effectiveness of a 24 month, patient-centered, pragmatic and scalable obesity treatment program delivered within primary care in an underserved population. We will randomly assign 18 primary care clinics serving low income populations with a high percentage of African Americans throughout Louisiana to either a comprehensive obesity treatment program or to a usual care group that receives the current obesity treatment under Medicaid/Medicare.

Patients and stakeholders will be engaged at all phases of the project. We will initiate and maintain the process of building trust among the community, investigators and the primary care clinics by expanding existing and fostering new trusted relationships. The partnerships will seek the well-being of its people through research, education and service. The four key aspects of community engagement and outreach rooted in the Community-Based Participatory Research principles will be: 1) create community and patient awareness; 2) inform the community of the study's benefits; 3) involve patients and stakeholders as collaborators through active participation in the study, and 4) provide mechanisms to convey healthy weight information back to the community.

This intervention is designed to be economical and scalable to large patient populations. Given the low uptake of the current Medicaid/Medicare reimbursement for obesity, it is anticipated that the results will impact the way that obesity treatment options are funded in the future. This study will have a direct impact on improving healthcare delivery and outcomes, which are key components of the PCORI mission.

4. Specific Aims

The **primary aim** of this trial is to develop and test the effectiveness of a 24 month, patient-centered, pragmatic and scalable obesity treatment program delivered within primary care in an underserved population. We hypothesize that:

- 1) Relative to patients who receive usual care, patients who receive a high-intensity, health literacy-appropriate and culturally adapted lifestyle intervention targeting increased physical activity and reduced dietary intake delivered by trained health coaches embedded in a primary care setting and supervised by providers trained in obesity science will have greater percent reductions in body weight; and
- 2) Relative to patients in usual care, patients who receive the intervention will have significant improvements in quality of life, functional capacity, satisfaction with medical care, and improve obesity co-morbidities (hypertension, dyslipidemia, insulin resistance, urinary incontinence and respiratory problems such as sleep apnea).

There are three secondary aims:

Secondary Aim 1 is to evaluate relationships between adherence to intervention components (physical activity, diet, sessions, etc.) and corresponding changes in body weight and secondary outcomes (post-hoc analyses).

Secondary Aim 2 is to examine the effects of the intervention on system-level practices and patient satisfaction with care.

Secondary Aim 3 is to test the heterogeneity of effects across clinics and across subgroups of patients (men versus women, white versus African American, older versus younger adults).

5. Background and Significance

Background

Obesity is a highly prevalent and serious medical condition in the United States, with Louisiana (LA) currently ranked among the states with the highest levels of adult obesity.¹² Obesity is a condition that increases the risk of type 2 diabetes, heart disease, stroke, gallbladder disease, respiratory problems, poor quality of life, and several cancers.¹³ Further, obese adults have an elevated risk of dying prematurely¹⁴, resulting in lower estimates of life expectancy at the population level.¹⁵

We are intimately familiar with the health burden that obesity imposes, since our region sits firmly in the “*Chronic Disease Belt*”, characterized by high prevalence of cancer¹⁶, cardiovascular disease^{17,18}, diabetes¹⁹, and obesity.²⁰ Furthermore, we are familiar with and have engaged in programs to address health management in minority populations (32% of LA population is African American)²¹, for those living in poverty (19% of residents live in poverty)²¹, and for those with low health literacy (LA is ranked 49th among the states for low levels of health literacy).²² Obesity accounts for \$2.4 billion in yearly health care expenditures in LA, 42.5% of which are financed by Medicaid/Medicare.¹

While the high rates of overweight and obesity are of great concern, a greater concern is that our health care system has failed to deliver medical interventions capable of producing even modest weight loss.²³ Modest weight loss can dramatically reduce the rates of conversion to type 2 diabetes among patients with pre-diabetes.²⁴⁻²⁶ With 15-30% of the 79 million Americans with pre-diabetes projected to progress to type 2 diabetes in the next 5 years without lifestyle intervention and weight loss^{27,28}, the failure of current medical practice to address this issue effectively mandates action. Modest weight loss can improve levels of blood pressure, HDL cholesterol, triglycerides, C reactive protein, symptoms of sleep apnea, urinary incontinence, and sexual dysfunction and prevent loss of mobility.²⁹ While we know that modest weight loss is achievable in some settings, such as in >2500 participants from 16 academic sites of the Look AHEAD trial³⁰, there has been no successful translation of this achievement to primary care practices.

Primary care physicians are the cornerstone of medical care in the United States. The U.S. Preventive Services Task Force recommends that physicians offer intensive multi-component behavioral interventions to obese individuals², and the Centers for Medicare and Medicaid Services (CMS) covers intensive behavioral therapy for obesity by a qualified PCP.³¹ However, the sole reliance on physicians, nurse practitioners, or physician assistants to deliver intensive behavioral therapy for obesity has limitations, in part due to the limited time available during a typical primary care visit, and lack of training among PCPs in delivery of behavior therapy.^{23,32}

A recent review of obesity management in primary care indicated that obesity treatment options delivered in primary care have resulted in limited success, demonstrating only 1-3 kg (about 1-3% of baseline weight on average) weight loss over 6-24 months of intervention.²³ The authors concluded that this low weight loss is likely due to the low intensity of the interventions, as most studies typically only employed monthly or quarterly visits of 10-15 min duration.²³ Thus, further research is required to develop sustainable, evidence-based models of obesity treatment in primary care.

The recently released *2013 American Heart Association (AHA)/American College of Cardiology (ACC)/The Obesity Society (TOS) Guidelines for the Management of Overweight and Obesity in Adults*^{3,29} are emphatic that comprehensive lifestyle intervention delivered *intensively* is the centerpiece of weight loss for health benefit. These guidelines, based on an exhaustive systematic review³³, emphasizes that the gold standard is on-site, high intensity (>14 sessions in 6 months) comprehensive intervention delivered in group or individual sessions by a

trained interventionist and persisting for a year or more. However, to date there is no evidence of effectiveness of using these guidelines in primary care. Treatment models based on the *AHA/ACC/TOS Guidelines* which are adaptable to real-life settings and which add effective and cost conscious delivery methods for obesity treatment in the primary care setting are needed.

Significance

This study is a comparative effectiveness trial of a sustainable, pragmatic obesity intervention set within primary care. This primary aim is directly related to the significance of the proposed research. As described above, obesity is a prevalent, serious medical condition, and effective weight management is not being adequately addressed in primary care practices. Thus, there is an urgent need to develop and test pragmatic treatment strategies in the primary care setting, especially those recommended in the *2013 AHA/ACC/TOS Guidelines for the Management of Overweight and Obesity in Adults*.^{3,29} There is a gap between current guidelines and what is currently implemented in clinical practice; the goal of modest weight loss is not being achieved; thus, comparative effectiveness studies are required to change the way that primary care practitioners approach the problem of obesity, and engage and assist patients with obesity. This study directly addresses this gap by testing the effectiveness of intensive behavioral treatment for obesity relative to usual care.

This study will have a direct impact on “improving healthcare delivery and outcomes”, which are key components of the PCORI mission. Given the low uptake of the current CMS reimbursement for obesity in primary care, it is anticipated that the results will impact the way that CMS funds obesity treatment in the future. As described above, effective obesity treatment programs currently exist; however a “translation-gap” also exists where the current science has not been implemented in primary care in any scalable format. The adaptation of an intensive lifestyle intervention³⁴ for deployment in primary care settings has the potential to significantly address this gap. PROPEL is a five-year, carefully designed and implemented research project; however, the intervention is designed to be economical and scalable to large patient populations that can impact obese patients throughout the United States.

By design, this is a patient-centered intervention with a strong focus on tailoring weight loss efforts to the individual patient. First, we are involving patients at every stage of the study, from the identification of patient-centered outcomes, to providing input on feasible intervention approaches, to the final dissemination of results and the potential for sustainability of the intervention in primary care. Second, the patient-centered intervention itself is personalized and individually adaptable. The focus of the intervention is on developing personalized, *patient-centered* obesity treatment plans, through the close interaction between the patient, a health coach, and the primary care team. As described below, a range of “toolbox” options are available to aid in maintaining weight loss, all of which are tailored to patient preferences.

6. Overview of Research Design

This study is a cluster-randomized, two-arm controlled trial in primary care settings. A total of 18 primary care clinics inclusive of low income populations with a high percentage of African Americans from urban and rural areas across Louisiana will be randomized to either 1) intervention or 2) usual care. The sample will include up to 850 obese (BMI 30-50 kg/m²) patients (18 clinics, 47 patients / clinic).

The primary aim of this trial is to develop and test the effectiveness of a 24 month, patient-centered, pragmatic and scalable obesity treatment program delivered within primary care, inclusive of an underserved population. Patients in the intervention arm will attend weekly (15 in-person) sessions in the first six months, followed by monthly sessions for the remaining 18 months. The behavioral intervention will be delivered by a trained health coach embedded in the primary care clinic. PCPs in the intervention arm will receive a series of webinars on obesity science to help them manage and treat obese patients. Patients assigned to the usual care arm will continue to interact with their PCP according to their usual schedule, and will be provided newsletters and/or invited to attend group sessions where a listing of health promotion events offered in the community is combined with information on topics of interest, including importance of sleep for health, household money management, family coping skills, smoking cessation, etc. PCPs in the usual care arm will receive a webinar describing the current CMS approach to reimbursing for obesity treatment, and a reminder informational brochure will be sent to the PCPs each year. Patients in both arms will be assessed on primary and secondary outcome measures at baseline, and at 6, 12, 18 and 24 months of intervention. **Figure 1** presents a schematic representation of patient flow through the trial.

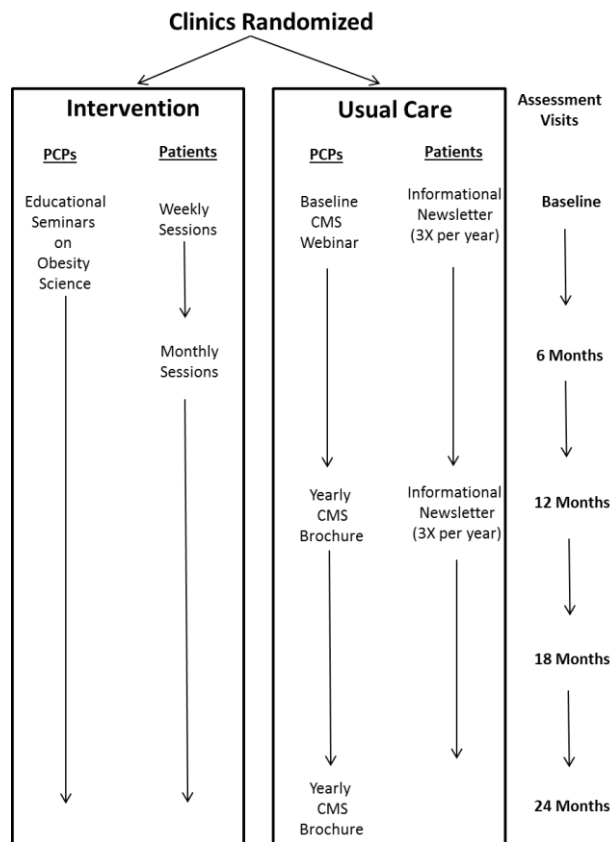


Figure 1. Overview of PROPEL intervention

7. Inclusion/Exclusion Criteria

PROPEL is a pragmatic trial to be conducted in primary care clinics. Thus, the inclusion criteria are broad and designed to capture a large cross-section of the target population, including patients with controlled diabetes, hypertension and dyslipidemia. The specific inclusion and exclusion criteria are provided in **Table 1**.

Table 1. Eligibility Criteria for the PROPEL trial.

Inclusion Criteria

- Age 20.0 – 75.0 years
- BMI 30.0 – 50.0 kg/m²
- Able to provide written informed consent
- Willing to change diet, physical activity and weight
- Patient of a participating clinic
- Able to participate in scheduled sessions

Exclusion Criteria

- Currently participating in a weight loss program
 - Current use of weight loss medication or recent weight loss (>10 lbs in last six months)
 - Plans to move from the area within 2 years
 - Given birth within the past year, is currently pregnant or plans to become pregnant within 2 years
 - Past bariatric surgery or plans for bariatric surgery within 2 years
 - Current major depression
 - History of suicidal behavior or diagnosed eating disorder (bulimia, anorexia)
 - Hospitalization for mental disorder or substance abuse in the previous year
 - Active cancer (except prostate, skin and thyroid if approved by physician)
 - Serious arrhythmias or cardiomyopathy
 - Severe congestive heart failure
 - Stroke or heart attack in previous six months
 - Chronic Inflammatory conditions, including but not limited to severe arthritis, lupus, or inflammatory bowel disease(i.e. Crohn's disease or ulcerative colitis)
 - Disease that is life threatening or that can interfere with or be aggravated by exercise or weight loss
 - Discretion of primary care physician or principal investigator
-

8. Recruitment and Retention of Patients

Patients will be recruited in the clinics through the primary care practitioners, who will identify patients who meet the inclusion criteria and provide them with a brochure about the study. A trained recruiter will follow up with the patient to assess their interest in participating and screen them for eligibility during a screening visit (SV) in which they will have their height, weight and blood pressure measured, and they will answer several questionnaires (see Section 11) to determine their eligibility. Importantly, the recruiter will administer a *Study Feasibility Interview* (see Appendix A) to identify and exclude from enrollment patients who will not be capable of completing the trial. For example, patients who intend to move out of the area or women who plan to become pregnant will be excluded. The interview does not evaluate the likelihood of the patient being able to adhere to the intervention (usual care or active intervention). The potential participant will provide written informed consent prior to participating in measurements during the SV. Following the SV, if the patient is deemed eligible, he/she will be formally enrolled in the study at the baseline visit. Patients who participate in the SV activities will not be considered enrolled in the study until they have received permission from their primary care physician to participate in the trial, and they return for their baseline visit.

A variety of approaches will be used to retain patients. Based on our experience, we understand the importance of creating a pleasant clinic environment and friendly and welcoming staff presence. We are also very clear from the initial screening session onward about what we expect from patients and what they can expect from us, as keeping patients well informed enhances adherence to the intervention and test schedules. Further, we will provide small gifts to patients including hats, umbrellas, coffee cups, etc., with the study logo, which has improved retention in our previous studies. Finally, a total of \$375/patient is budgeted for incentives related to the provision of outcome measures. All patients will be paid at the completion of each assessment visit (\$75 at each of baseline, 6, 12, 18 and 24 months).

9. Randomization and Blinding

Randomization

This is a cluster-randomized trial, and enrolled patients at a given clinic will receive the intervention assigned to their clinic. A pool of 18 clinics will be randomized to either 1) usual care or 2) intervention, after stratification by health system. Stratification by health system is necessary to ensure adequate local staffing of clinics assigned to the intervention arm, representation from all regions of the state and types of health systems in both arms of the trial.

Blinding

Given that this trial is randomized at the clinic level and the interventions are very distinct, PROPEL patients will know their group assignment, as will clinic staff and health educators that are involved in delivering the intervention. However, every effort will be made to blind staff involved in data collection to the clinic randomization, and all intervention staff will be blinded to the patients' official study measurements.

10. Intervention Methods

Overview of Intervention Arms

The overall study design of the PROPEL trial is a two-arm, cluster-randomized trial with clinics randomized to 1) intervention or 2) usual care. Trained health coaches will deliver the active intervention - a comprehensive, “high-intensity” program, as recommended first-line therapy by the 2013 AHA/ACC/TOS Obesity Guidelines²⁹, and based on the Look AHEAD intensive lifestyle intervention.³⁴ The Look AHEAD intervention was an adaptation of the Diabetes Prevention Program (DPP) which demonstrated that a lifestyle intervention decreased the risk of developing type 2 diabetes among overweight and obese individuals with impaired glucose tolerance.²⁵ Following closely upon DPP, the Look AHEAD multi-center trial was designed to determine whether weight loss reduces cardiovascular morbidity and mortality in overweight individuals with type 2 diabetes.³⁵ The Look AHEAD trial was stopped early on the basis of futility analysis on the primary cardiovascular outcome after 9.6 years; however, weight loss was significantly greater in the intervention group compared to control throughout the study.³⁰ Patients in the usual care condition will receive the obesity treatment guided by what is currently approved by CMS.³¹

Intervention Arm

The active intervention arm of the PROPEL trial is an adaptation of the Look AHEAD intensive lifestyle intervention, and will include 15 in-person sessions in the first six months, followed by monthly sessions for the remaining 18 months. The intervention will include evidence-based components such as the use of portion control and behavioral strategies. The intervention components have been adapted through input of patient focus groups and patient advisory boards. Innovative aspects of the intervention include the addition of a trained “health coach” to the primary care team, a PCP education program about energy balance and medical aspects of obesity, a tailored, *patient-centered* treatment approach using a computer tracking system (CTS) with novel toolbox strategies¹⁰, and a special emphasis on health literacy. The health coaches will have an educational background in nutrition and/or physical activity/kinesiology and will be formally trained at baseline by experienced interventionists from Pennington Biomedical and health literacy experts at LSUHSC-Shreveport and will attend refresher courses each year. Ideally, the health coaches will have a Bachelors or Masters degree, and/or a professional degree such as an R.D. Health coaches will be recruited from communities in close proximity to where the intervention will be delivered. In addition, the intervention materials will be adapted to be health-literacy and culturally appropriate, which is both novel and important for the target population. The key components of the intervention are described below, as well as novel adaptations for integrating the original Look AHEAD intervention into the primary care setting.

Behavioral Therapy

Patients in the intervention arm will attend weekly (15 in-person) sessions in the first six months, followed by monthly sessions for the remaining 18 months (see **Figure 2**). The behavioral intervention will be delivered by a trained health coach embedded in the primary care clinic. The health coaches will be trained by experienced interventionists from Pennington Biomedical with experience from DPP and Look AHEAD, similar to the training deployed in the LOSS trial.⁴ Training will include: 1) study protocol review, 2) peer-tutored review of earlier lessons, 3) small group exercises to practice therapeutic skills, and 4) trainees’ observation of senior interventionists conducting individual and small-group sessions. Topics will include the use of

meal replacements, physical activity, calorie balance, self-monitoring, structured diets, health literacy and toolbox approaches (see description below under “*Toolbox Strategies*” heading). Health literacy training will include use of plain language, summarization and “teach back” to confirm understanding as well as strategies to help patients set personal health goals and action plans for how they will meet these. Certification will ensure that the health coaches have a clear understanding of the study protocol, manual of procedures, lifestyle manuals and health literacy approaches. To ensure ongoing fidelity of the intervention, Pennington Biomedical staff will conduct monthly monitoring of each site via conference call or site visits and monthly CTS reports.

Results from Look AHEAD demonstrated that the greater the initial weight loss (at year 1), the greater the weight loss at year 4.³⁶ Further, individuals who accumulated greater incremental weight losses and/or whose weight loss was more sustained during the first year had better maintenance of weight loss at year 4,³⁷ and our group has found that fostering weight loss in the first weeks greatly improves patient engagement and motivation. Thus, a strong focus of the intervention will be on maximizing the initial (three month) weight loss in this group. Look AHEAD relied heavily on large group sessions to deliver the intervention, whereas DPP used mainly individual sessions. Large group sessions are not very feasible in the primary care setting due to a lack of adequate space, and lack of access during non-clinic hours when sessions are typically scheduled (evenings, weekends, etc.). Therefore, our intervention will rely

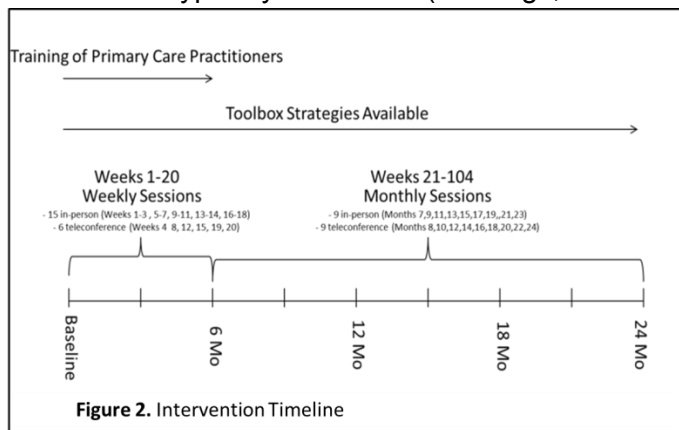


Figure 2. Intervention Timeline

more on individual and small group sessions in the clinic (3-5 patients, based on scheduling availability) during the initial 6-month phase, similar to DPP, followed by individual and small group in-person and telephone contact (alternating months) in the final 18 months (see **Figure 2**). A comparative effectiveness trial³⁸ provided evidence that remote contact (telephone, web, email) was as effective as in-person contact in obesity interventions in clinical practice, suggesting that a shift from in-

person to telephone contact in the final 18 months of the intervention will be effective at sustaining initial weight loss.

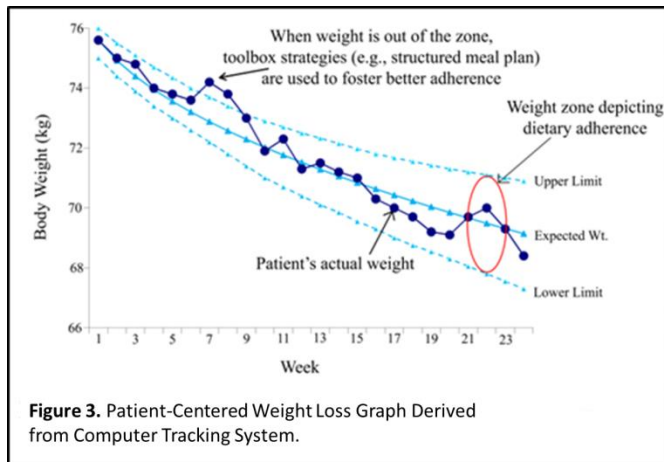
An important component of the behavioral intervention is shared short-term goal setting between the health coach and the patient in order to reach the broader study goals, as described below. Two important goals in this trial are related to weight loss and physical activity. The weight loss goal for each of the study centers in Look AHEAD was 7% of initial weight by year 1.³⁴ However, the participants in that trial were given a higher personal weight loss goal of 10% in order to increase the likelihood that the study would achieve a mean weight loss of 7%.³⁴ Indeed, participants in the Look AHEAD intervention arm had a mean weight loss of 8.6% at year 1 versus 0.7% in the education arm.³⁰ This difference was reduced, but remained significant at year 2, with a maintained loss of 6.4% in the intervention arm versus 1.1% in the education arm.³⁶ Given the successful weight loss achieved in Look AHEAD, we will retain the personal goal of 10% weight loss for patients in the intervention arm of this trial. Patients will then be coached to set their own goals and develop eating and physical activity action plans to meet that goal.

The results from both DPP and Look AHEAD indicate that an important goal is related to physical activity, as increases in physical activity were significantly related to weight loss success.^{36,39} The *2008 Physical Activity Guidelines for Americans* call for ≥150 minutes of

moderate-to-vigorous physical activity per week.⁴⁰ This was also the goal for DPP; however, Look AHEAD selected a more ambitious goal of ≥ 175 minutes/week, given evidence that prescribing higher levels of physical activity may improve outcomes.⁴¹ Further, the American College of Sports Medicine also recommends higher levels of physical activity for weight loss maintenance.⁴² Given the importance of physical activity for successful weight loss and weight loss maintenance, the goal for this trial is for patients to achieve at least 175 minutes per week of moderate-to-vigorous physical activity.

Computer Tracking System (CTS)

A novel adaptation of the Look AHEAD intervention for the purpose of this study is the addition of a CTS into the intervention, which will allow for tailoring of the intervention to the individual patient. Patients will be encouraged to weigh themselves daily using an electronic scale (provided) that directly uploads data via a cellular signal to a website. We developed computer code that automatically retrieves the data from this website and plots it onto their personal weight graph (**Figure 3**). This weight graph will be available to the patient, his/her health coach, and primary care provider via the CTS over the internet. We have used this approach in other trials, including CALERIE, an intensive 2 y intervention.¹⁰ The CTS will be



used by the health coaches to identify patients who are struggling to meet their weight loss goals, triggering the algorithm to deploy strategies from the “toolbox” (described below). Information from the CTS is also used by the intervention team to observe adherence on a study-wide basis, for each of the clinics, and for each patient. Reports generated from the CTS on session attendance, self-monitoring, dietary adherence, and weight loss serve as indices of adherence to the intervention and are used by the team to evaluate compliance.

We will use a weight loss calculator to:

- 1) calculate personalized daily energy targets for each patient that, if met, will result in 10% weight loss, and 2) create a weight graph that displays each patient’s weight loss over time (see **Figure 3**). This weight graph determines if they are meeting their energy intake target and losing weight at the rate expected. The weight loss calculator was developed by members of this research team and colleagues. The calculator accurately predicts weight loss and accurately estimates the amount of energy intake needed to achieve specific weight loss goals (a version of the calculator can be found at www.pbrc.edu/research-and-faculty/calculators/weight-loss-predictor/).⁴³⁻⁴⁶

We have experience using the weight graph to track dietary adherence in the delivery of the personalized meal plan that, if followed, will result in the rate of weight loss depicted in the graph. We stress that this approach is very patient-centered as each patient’s graph is unique and the rate of weight loss is personalized to their age, weight, height, and sex. Further, the meal plans consider dietary preferences and dislikes, eating patterns, work schedules, etc. Indeed, the intervention is a collaborative. Patients are active in intervention delivery and receive on-going training to learn how to interpret weight graphs and modify their meal plans.

Dietary Component

The restriction of calories from dietary sources is the cornerstone of weight loss efforts.²⁹ The diet in this trial is based on Look AHEAD and DPP^{34,47}, though we made modifications to improve scalability, sustainability, and the ability to disseminate the approach through primary care clinics. The diet plans will be further refined from feedback obtained in the patient focus groups. Once the energy intake target is identified, the patient will develop a structured calorie restricted meal plan in collaboration with the health coach that considers their food preferences, dislikes, etc. The meal plan for weeks 1-4 will include portion-controlled foods, which include items that are easily available and affordable, such as fruits (bananas, apples) and granola bars. Additionally, pre-packaged portion-controlled foods will be available as part of our tool-box approach for patients who are interested in using them (see below). After week 5, portion-controlled foods will be utilized as needed, though the meal plan will become less structured over time as the patient learns to purchase, prepare, and package foods to manage portion size and energy intake. The meal plans will be consistent with dietary guidelines, i.e., ~55% carbohydrate, ~15% protein, and ~30% fat,⁴⁸ will include nutrient-dense foods (e.g., whole grains, fruits, lean protein), and will be formatted for easy creation and dissemination through physician offices.

Physical Activity Component

The first month, the health coach will work with the patient to derive personal goals and specific action plans to meet the goals the patient sets. The patient will be challenged to aim for a goal of 50 minutes/week, in bouts of at least 10 minutes. The study physical activity goal will be to increase to 125 minutes/week by week 16 and to 175 minutes/week by week 24.³⁴ The health coach will review the health benefits of physical activity and help patients to develop achievable, patient-preferred strategies to increase physical activity. In addition, the health coach will give patients easy to use pedometers (step counters) and show them how to use them. Patients will also be told of the benefits of using pedometers as an effective way to increase physical activity.^{49,50} A major focus of the physical activity intervention is on increasing lifestyle activities, such as taking the stairs instead of the elevator, parking further away, actively commuting (walking or riding bicycle), and replacing sedentary activities with more active options. The health coach will be trained to teach patients how to walk at a “moderate-to-vigorous” pace and use the “teach-back/show back” technique to ensure proper understanding. They will also provide tips and feedback to patients on how to increase their daily steps to levels approximating their goals. For example, recent data from NHANES and our work in Louisiana suggest that 8000-9000 steps/day are good targets for achieving at least 30 min/day of moderate-to-vigorous physical activity.^{51,52}

Toolbox Strategies for Behavioral Therapy

A novel aspect of the proposed intervention is the expansion of the “toolbox” weight loss approach to the primary care setting. The toolbox has been successfully deployed in previous clinical trials and shown to lead to improvements in intervention efficacy.^{10,34,47} By systematically following pre-specified decision rules, it is possible to intervene quickly in order to overcome obstacles to success and improve adherence to the intervention. This approach also fosters treatment fidelity among health coaches and across sites. Additionally, the toolbox enables health coaches to tailor treatment to address patient preferences and lifestyles, as well as regional, cultural and ethnic differences among patients. The intervention will be tailored to the needs of the patient, with specific nutritional, physical activity and behavioral strategies selected

from the toolbox. Examples include increasing dietary fiber, modifying recipes to decrease energy density, adding novel foods to relieve boredom, strategies to avoid impulse eating, limiting calories in restaurants, parties or at work, adding variety to physical activity routines, and so on. Additional toolbox options include recipe modifications and low calorie substitutions, mindful eating, portion size training, increased meal planning and preparation, meal repetition, increase frequency of contact with health coach, Remote Food Photography Method (RFPM) or other method of daily recording of food intake (paper food record or online app), and cabinet clean-outs. The tool box will also include the provision of portion controlled foods, such as nutrition shakes, bars, and pre-packaged entrees. We intend to rely on two types of portion-controlled foods during PROPEL, Health One shakes and pre-packaged entrees and snacks from Nutrisystem. Additionally, participants will be encouraged to purchase other portion-controlled foods as part of their meal plan, and these foods consist of, among other foods, bananas, granola bars, small boxes of raisins, 100 calorie snack packs, small bags of baby carrots, frozen entrees such as Lean Cuisines, etc. Finally, as participants' nutrition knowledge improves, they will be encouraged to prepare healthy food items and weigh and package individual portions that meet the requirements of their meal plan. Selections from the toolbox will depend on the patient's success in achieving adherence, and on overcoming problems that arise. This approach is highly individualized and the health coach will work with the patient to develop acceptable strategies, including how long they will be deployed, and how to evaluate their effectiveness. Thus, this approach is very patient-centered and provides for continuous communication between patients and health coaches. A centrally maintained tracking system, containing data needed for decisions about selecting and modifying toolbox selections for each patient (e.g., data on adherence, attendance at group meetings) will be used in implementing the algorithm. The toolbox will be open continuously until a patient completes the intervention.

Health Literacy Adaptation of Intervention Materials

Health literacy refers to the ability to obtain, understand and act on health information and services needed to make appropriate health care decisions.⁵³ As described above, Louisiana is ranked 49th nationally with respect to health literacy.²² Further, given that the target population for this trial includes an underserved population, the problem of health literacy is compounded. Thus, it is important to adapt intervention approaches and materials to be health-literacy appropriate. Drs. Davis and Arnold (Co-investigators) have a lengthy record of seminal health literacy research among vulnerable populations. As the Co-directors of the Health Literacy Core of LA CaTS, they have considerable experience in adapting intervention materials and informed consent documents to be health-literacy appropriate for the target population. Look AHEAD intervention materials will be adapted, and health coaches will be trained in principles of health literacy and motivational interviewing techniques to enhance patient communication and education and encourage patient activation.^{54,55} Patients will be engaged in the development of study materials through consultation with the Patient Advisory Boards, and by focus group input on feasible and understandable intervention components.

In addition to adapting all intervention materials to be appropriate for the level of health literacy, the patient toolbox will also contain options that are specially developed for patients with low health literacy. For example, with funding from the American College of Physicians (ACP), Drs. Davis and Arnold along with a team of national health literacy experts, developed and evaluated literacy-appropriate diabetes and weight loss self-management guides and brief counseling procedures for coaching patients to set personal health goals and create easily achievable action plans aimed at improving health behaviors such as eating and physical activity.⁵⁶⁻⁵⁹ These guides and accompanying counseling framework, which have been

distributed by ACP to over 5 million people nationally, will be important options in the patient toolbox.

Training of Primary Care Practitioners

An important, novel component of our adaption of Look AHEAD to the primary care setting is the incorporation of obesity science education for the primary care practitioners. There is a knowledge gap between the current state of weight loss science and primary care practice. Thus, we will develop and deliver continuing education on the science of obesity and weight loss to the primary care practitioners in the intervention arm. This education (designed for later dissemination and translation) will also include information on the management of complex obesity and co-management of morbidities such as type 2 diabetes and hypertension. Education will be delivered to accommodate the schedules of the practitioners, and will involve a series of webinars and face-to-face brown-bag seminars conducted in the clinics by experienced obesity, patient engagement and health literacy experts.

Usual Care Arm

Patients in the usual care condition will receive the obesity treatment guided by what is currently approved by CMS.³¹ A baseline webinar will be conducted with the PCPs randomized to usual care, describing the current CMS approach to reimbursing for obesity treatment; a reminder informational brochure will be sent to the primary care providers each year. If updates to CMS policies occur, we will schedule another webinar to inform the physicians. Patients in the usual care arm will receive their normal, usual care from their primary care team, and they will participate in the measurement of the outcomes at 6, 12, 18 and 24 months.

Because the study's success depends on comparable retention of patients in *both* arms, we are providing a special program for patients in usual care. The aims of the program are to maintain contact and build loyalty to the study. Patients participate in the design of this program which consists of 3 yearly newsletters and/or group sessions where a listing of health promotion events offered in the community is combined with an informational program. Topics that may be covered in this program include the importance of sleep for health, household money management, family coping skills, smoking cessation, etc.

11. Data Collection

Data will be collected at a screening visit (SV), a baseline visit (BV), and at 6, 12, 18 and 24 month visits. The physical measurements that that will be made as well as the questionnaires to be used are described below. All physical measurements will be recorded on the Physical Measurements Form (see Appendix A).

Physical Measurements

Weight

Weight is the primary outcome for this study and will be measured with the patient in light indoor clothes without shoes to the nearest 0.1 kg using a digital scale at each assessment visit. Patients will be instructed to stand still in the middle of the scale with head erect and eyes looking straight ahead. After the weight is recorded, the patient will step off of the scale and the research assistant will set the scale to zero, then repeat and record the second weight measurement. If the two readings differ by more than 0.5 kg, a third measurement will be obtained. The closest two measurements will be averaged for analysis. The accuracy of the scales will be checked at scheduled monitoring visits using standard weights. Weight will be measured at the screening visit, the baseline visit, and at the 6, 12, 18 and 24 month assessment visits.

Height

Height will be measured at the screening visit and the baseline visit using a portable stadiometer. The patient will be asked to remove their shoes and have their heels, buttocks and upper part of the back remain in contact with the stadiometer with their arms hanging naturally at their side. The patient is asked to inhale and hold their breath, while the technician lightly applies traction to the patient's head in order to maintain alignment with the Frankfort Plane. The slide is lowered until it reaches the vertex of the skull and the reading from the indicator is recorded to the nearest 0.1 centimeter. This process will be repeated, and if the two readings differ by more than 0.5 cm, a third measurement will be obtained. The closest two measurements will be averaged for analysis. Calibration of the portable stadiometer is not required, however the accuracy of the stadiometer will be checked at scheduled monitoring visits against a standard meter stick. It is not necessary for the stadiometer to be calibrated once all Baseline Visits are completed as height is not measured at follow-up measurement visits.

Waist Circumference

Waist circumference will be measured at all assessment visits using a non-elastic anthropometric tape. The measurement is made midway between the lower rib margin and the iliac crest, at the end of gentle expiration. The patient will be asked to expose the areas to be measured by pulling undergarments down and to stand in an upright position with their feet together and arms slightly forward (at a 45° angle). The midpoint will be marked on the right side of the patient using a washable marker or pen. The tape will be aligned with the markings and positioned in the horizontal plane at the correct height. Measures are made at the end of normal expiration with special attention paid to ensure the tape lays perpendicular to the long axis of the body and parallel to the floor. This process will be repeated, and if the two readings

differ by more than 0.5 cm, a third measurement will be obtained. The closest two measurements will be averaged for analysis.

Blood Pressure and Pulse

Resting systolic and diastolic blood pressures and resting pulse will be measured using a validated automated Omron device, after the patient has been sitting comfortable for at least 5 minutes prior to the first blood pressure and pulse measurement.^{60,61} Two sitting measurements will be made. A third measurement will be obtained if the first two systolic measurements are greater than 20 mmHg apart, or the first two diastolic measurements are greater than 10 mmHg apart. A cuff of appropriate size will be identified at the baseline visit and used thereafter at all subsequent visits.

Fasting Finger-stick Blood Sample

Finger-stick blood samples will be used to measure fasting levels of lipids (total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides) and glucose using a validated Cholestech LDX point-of-care device^{62,63} at baseline, month 12 and month 24 visits. The patients will be asked to arrive at the clinic after fasting from 10 pm on the prior evening. The LDX is a small, portable analyzer that requires only a single drop of blood from a finger stick and eliminates the anxiety of a venipuncture. The research assistant will clean the patient's fingertip with an alcohol wipe and obtain a drop of blood using a lancet. The blood is collected via capillary tube and transferred to the LDX cassette. The results will available in less than five minutes, and LDX printout will be transferred to the PROPEL Physical Measurement Form (see Appendix A) and data-entered by the research staff. The LDX will print a second results label which will be attached to the Cholestech Patient Results Label Log.

Questionnaires

All questionnaires will be completed in paper form by patients, and subsequently data-entered by research staff. Patients with low health literacy, as established by the REALM SF (described below) will complete the questionnaires using a semi-structured interview format with the help of research staff.

Baseline Demographic and Health History Questionnaire

A self-report demographic and health history questionnaire (see Appendix A) asks the patients about their age, sex, race/ethnicity, use of tobacco and alcohol, health insurance status, post-menopausal status, income and employment, education level, and history of chronic diseases. Further, the questionnaire collects information on their physical home address and nearest cross-street for the purpose of built-environment analyses. This questionnaire will be administered at SV.

Change in Health History Questionnaire

A self-report questionnaire captures changes in health outcomes that have occurred across the 2 years of the intervention (see Appendix A). This questionnaire is administered at the 6, 12, 18 and 24 month assessment visits.

REALM-SF

The REALM short form (SF) is a nine-item health literacy assessment (see Appendix A) that will be administered at SV.⁶⁴ The patient will first read two unscored test words (“flu” and “pill”) followed by a standardized series of seven words provided on a laminated sheet, and the research assistant will record the number of words pronounced correctly on an un-laminated copy that is attached to a clipboard. The score (0-7) provides an assessment of how well the patient will be able to understand health information. Patients who are unable to correctly read one or both of the practice words will be deemed ineligible for PROPEL. Patients scoring 0-3 on the REALM SF at the screening visit will be provided assistance in completing the other questionnaires using a semi-structured interview. Patients scoring 4-7 on the REALM SF will be allowed to complete the other questionnaires on their own, but we will offer assistance as required.

Food Security

Household food security is measured at baseline and at the 12 and 24 month assessment visits using a 6-item subscale of the 12-month Food Security Scale Questionnaire (see Appendix A).⁶⁵

PROMIS-29

PROMIS® stands for the Patient Reported Outcomes Measurement Information System (www.nihpromis.org), which is a system of highly reliable, precise measures of patient-reported health status for physical, mental, and social well-being (see Appendix A).⁶⁶ The PROMIS-29 is a 29-item health-related quality of life questionnaire that includes questions covering health-related domains of physical function, anxiety, depression, fatigue, sleep disturbance, ability to participate in social roles and activities, pain interference and pain intensity. The PROMIS items were developed using a rigorous methodology funded by the National Institutes of Health (NIH) with a goal to develop valid, reliable, and standardized questionnaires or tools to measure patient-reported outcomes.⁶⁷ A previous study has shown that among people with disabilities, health-related quality of life was significantly lower among the obese as measured by the PROMIS scales as compared to the non-obese.⁶⁸ The PROMIS 29 will be administered at the baseline visit, and at the 6, 12, and 24 month visits.

Impact of Weight on Quality of Life – Lite (IWQOL-Lite)

The IWQOL-Lite is a 31-item measure (see Appendix A) designed to measure obesity-specific aspects of quality of life, which produces a total score and separate scores for physical function, self-esteem, sexual life, public distress, and work or daily activities.^{69,70} The IWQOL-Lite is administered at baseline and at the 6, 12 and 24 month assessment visits.

International Physical Activity Questionnaire – Short Form (IPAQ-SF)

Physical activity levels are measured at baseline and at the 6, 12 and 24 month assessment visits using the IPAQ-SF (see Appendix A)⁷¹ which asks questions related to physical activity performed over the previous 7 days. The IPAQ-SF has acceptable reliability⁷¹ and has been shown to be sensitive to change within the context of a weight loss intervention.⁷² The results are reported as a continuous measure in median metabolic equivalent of task (MET)-minutes per week of physical activity.

Dietary Intake Questionnaire

A questionnaire that assesses dietary fat, fruit, vegetable and alcohol intake is administered at baseline and at the 6, 12 and 24 month assessment visits (see Appendix A). The questionnaire contains scales derived from several sources. The National Cancer Institute (NCI) fat screener estimates the percentage of energy from fat by asking patients to report the frequency of consuming specific foods over the past 12 months.⁷³ A standard 7-item fruit and vegetable screener developed by the NCI and National 5 a Day Program grantees asks how often fruit and vegetables were consumed in the past month.^{74,75} Three questions related to the frequency of alcohol intake (beer, wine, hard liquor) were adapted from the Brief Questionnaire to Assess Habitual Beverage Intake (BEVQ-15).⁷⁶

Eating Inventory

The Three-Factor Eating Inventory is designed to measure different dimensions of eating behavior. Three factor-analyzed subscales (Cognitive Restraint, Disinhibition, and Hunger) are derived from the questionnaire.⁷⁷ For the purpose of the PROPEL trial, only the Cognitive Restraint and Disinhibition sub-scales will be administered to patients. This questionnaire will be administered at baseline and at the 6, 12 and 24 month assessment visits.

Patient-Provider Survey

A patient-provider survey is completed by each patient at the baseline visit and at the 24 month assessment visit (see Appendix A). This is an 11-item instrument that was adapted from the POWER trial.⁷⁸ The POWER investigators compiled the patient-provider survey from several sources, including six questions adapted from the validated *Consumer Assessment of Healthcare Providers and Systems (CAHPS) 2.0 Adult Core Survey*, which asks patients how often their providers explained things clearly, listened carefully, showed respect, provided easy to understand instructions, knew their medical history and spent enough time with them.⁷⁹ A CAHPS global rating of the provider (rating from 0–10) is also included. Finally, a question addresses patient-centeredness or the perception of “being known as a person” has been identified as an important domain in the patient–provider relationship.⁸⁰ The framing of all questions in the survey was adapted by asking patients about their care over the past 2 years given that the both the POWER and PROPEL trials were 2 years in duration. A summary patient–provider relationship score is computed by adding up the total responses from the 8 questions (and reversing the 2 opposite scales). This summary score has a minimum of 14 and a maximum of 32.

Intervention Satisfaction Survey

A self-report questionnaire that asks about the patients experience with the intervention and satisfaction with care is administered to patients enrolled in the active intervention arm of the trial at the 6 month and 24 month assessment visits (see Appendix A). This questionnaire was developed by the RE-POWER study and includes questions obtained from the VA DPP, Rural LEAP and Hopkins POWER trial.

Provider Survey

The Provider Survey is completed by each patient’s primary care provider (not the patient) prior to the trial beginning and at the trial’s end (see Appendix A). The Provider Survey was

developed for the POWER trial⁷⁸ and has been adapted for PROPEL. The questionnaire assesses the primary care provider’s demographic information (age, race, training, specialty, years in practice, weight, and height), and knowledge about weight management practices (calculation of BMI, weight loss counseling and referral, etc.). The survey will be programmed into the REDCap system, which will also send each participating provider an email requesting that they complete the web-based survey. If a provider has not completed the survey within 2 days, the REDCap system will send 2 additional reminder emails 2 days apart. All contact information and survey responses will be kept private.

Concomitant Medications Form

Patients will be asked to bring their medications to the screening visit and all subsequent assessment visits. A concomitant medications form (see Appendix A), adapted from prior trials, will be completed by a member of the research team at each visit to track changes in the patient’s medications throughout the trial.

Adverse Events

A surveillance form, adapted from prior trials, will be used to screen for adverse events and serious adverse events (SAEs) at each assessment visit (see Appendix A). The following events will not be recorded as they are viewed as expected or unrelated to the study (unless the event meets the definition of an SAE): constipation, joint/muscle pain, and fall-related injuries (other than those related to a secondary condition such as vertigo). All SAEs will be recorded and reported. Serious, unexpected AEs that are related or are possibly related to the study will be reported to the IRB in accordance with requirements.

Table 2. Data measurement and collection schedule for patient data.

Measurement	SV	BV	V6	V12	V18	V24
Anthropometry						
Weight	X	X	X	X	X	X
Height	X	X				
Waist Circumference		X	X	X	X	X
Risk Factors						
Blood Pressure and Pulse		X	X	X	X	X
Fasting Finger-stick Blood Sample		X		X		X
Questionnaires						
Baseline Demographics and Health History	X					
Change in Health History			X	X	X	X
REALM-SF	X					
Food Security		X		X		X
Eating Inventory		X	X	X		X
PROMIS-29		X	X	X		X
Impact of Weight on Quality of Life – Lite		X	X	X		X
IPAQ-SF		X	X	X		X
Dietary Intake Questionnaire		X	X	X		X
Concomitant Medications		X	X	X	X	X
Adverse Event Form			X	X	X	X
Patient-Provider Survey		X				X

Intervention Satisfaction Survey*			X			X
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*completed by patients in the active intervention arm only

Parallel Medical Record Data Collection

In addition to the “gold standard” data collection of outcome measurements by the research staff, a parallel data collection effort will be done in PROPEL by utilizing the medical records at the participating clinics. For each of the participating patients in both arms, a retrospective chart review covering the period of the intervention will be done to abstract data on changes in weight and other clinical variables of interest over the course of the intervention. The electronic medical records of the patients will be obtained, or in cases where electronic records are not available, paper medical records will be abstracted by hand and data-entered by research staff.

12. Quality Assurance and Control

Quality assurance and quality control is of utmost importance in a randomized clinical trial. Standardized protocols for all measurements have been developed, and adherence to the written protocols is of paramount importance. All data collection personnel will be certified as competent to make the required measurements by trained experts. The following provides an outline of the quality assurance and control program developed for PROPEL:

- Training and certification of all data collection personnel by experts
- Development of detailed manual of operations
- Retraining and recertification of all data collection personnel twice-yearly
- Maintenance of logs of certified personnel
- Routine calibration of all equipment following manufacturers guidelines
- Maintenance of logs of calibrated equipment
- Performance of routine clinic site-visits and source document verification
- Setting realistic limits on data entry fields in REDCap
- Remote monitoring of data entry, missing data and lag times through REDCap
- Creating both real-time and subsequent executable data quality checks in REDCap
- Querying appropriate personnel regarding missing data
- Preparing quality control reports for personnel, investigators and Data and Safety Monitoring Board

There are logistical issues that limit the research staff's ability to perform site visits and monitor data collection readily at 18 remote clinics (budgetary restrictions, time constraints, limited staff, etc.). Therefore, consent will be obtained from participants who are willing to have their intervention sessions audio and video recorded; consent status will be data entered and tracked in REDCap. These recordings will be used as a means of monitoring to ensure treatment fidelity. All components of the intervention sessions will be recorded and reviewed, including but not limited to, weight status, diet and exercise logs, barriers to weight loss, goal-setting, etc. Participants who sign the consent will be informed before each visit begins when the visit is being recorded. Due to the intimate nature of the intervention sessions, this consent will also include consent to have sessions monitored in-person by research staff.

13. Data Management

Assessment (REDCap)

All data collected by the assessment team at SV, BV, and at month 6, 12, 18 and 24 assessment visits will be transferred from paper form to the Research Electronic Data Capture (REDCap) system⁸¹ through data entry by study personnel. REDCap is a secure, HIPAA-compliant, web-based application that can be utilized for electronic collection and management of research and clinical trial data. Study data and electronic data capture tools are housed in a secure data center at Pennington Biomedical, and all web-based information transmission is encrypted. The server is backed up nightly and is protected by an enterprise network security firewall. REDCap will be accessed through the Pennington Biomedical secure website, <https://redcap.pbrc.edu>, where research personnel are required to enter user ids and passwords previously approved and set up by the Pennington Biomedical REDCap Administrator.

The level of user access and privilege will be determined on an individual basis and will rely upon each user's role in the study and clinics they are associated with. Only select project management personnel will be able to edit participant record IDs or export data; the data collection staff will only be able to view and edit (not export) the participant data and run quality checks for the clinics with which they are associated, and investigators will only be able to view data collected at their site. All data entered will be run through multiple checks for internal consistency and biologic plausibility; these will be conducted in REDCap with either real-time error messages and data stoppage rules or user-initiated query reports, as well as with study-specific SAS programs designed by the data manager. Missing or questionable data will be assessed and corrected by research staff at the clinics or project management staff at Pennington Biomedical. All users will be thoroughly trained in the use of the PROPEL REDCap data entry and validation system. Once it is determined that data collection, entry and verification is complete, the REDCap project will be locked so that users will no longer be able to edit the data, but investigators may still export and preserve it.

Intervention – Computer Tracking System (CTS)

The internet-based Computer Tracking System (CTS) will facilitate intervention delivery, treatment fidelity, scheduling of intervention visits with patients, and tracking of process measures for intervention delivery, such as attendance. The CTS will allow for tailoring the intervention to individual patients, and it will be used by the intervention team to quantify process measures related to intervention delivery. Specifically, it will be used to review participant attendance, adherence to the diet based on the weight graph, weight loss, exercise levels, and the frequency with which weight and exercise data are collected from participants. These process data will be provided in reports generated by the CTS and these data can be viewed at the study, clinic, counselor, and patient level. The CTS will be housed on a HIPAA compliant server.

14. Safety and Data Monitoring

This Human Subjects Research meets the definition of a clinical trial.

Potential Risks to Subjects

Human Subjects Involvement, Characteristics, and Design

This study is a two-year, cluster-randomized, two-arm controlled trial in a primary care setting. A total of 18 primary care clinics inclusive of low income populations with a high percentage of African Americans from urban and rural areas of Louisiana will be randomized to either 1) intervention or 2) usual care. The sample will include up to 850 patients (18 clinics, 47 patients per clinic). Given that this is a pragmatic trial, the inclusion criteria are broad.

Inclusion criteria include:

- Age 20.0 – 75.0 years
- BMI 30.0 – 50.0 kg/m²
- Able to provide written informed consent
- Willing to change diet, physical activity and weight
- Patient of a participating clinic
- Able to participate in scheduled sessions

Exclusion criteria include:

- Currently participating in a weight loss program
- Current use of weight loss medication or recent weight loss (>10 lbs in last six months)
- Plans to move from the area within 2 years
- Given birth within the past year, are currently pregnant or plans to become pregnant within 2 years
- Has had or plans to have bariatric surgery within 2 years
- Current major depression
- History of suicidal behavior or diagnosed eating disorder (bulimia, anorexia)
- Hospitalization for mental disorder or substance abuse in the previous year
- Active cancer (except prostate, skin and thyroid if approved by physician)
- Serious arrhythmias or cardiomyopathy
- Severe congestive heart failure
- Stroke or heart attack in previous six months
- Chronic Inflammatory conditions, including but not limited to severe arthritis, lupus, or inflammatory bowel disease(i.e. Crohn's disease or ulcerative colitis)
- Disease that is life threatening or that can interfere with or be aggravated by exercise or weight loss
- Discretion of primary care physician or principal investigator

The intervention arm will receive a comprehensive, "high-intensity" program, as recommended first-line therapy by the *2013 AHA/ACC/TOS Obesity Guidelines*, and based on the Look AHEAD intensive lifestyle intervention, delivered by trained health coaches. The intervention will include 15 in-person sessions in the first six months, followed by monthly sessions for the remaining 18 months, and will include evidence-based components such as the use of portion control and several behavioral strategies.

The usual care arm will receive the obesity treatment currently approved by CMS. A baseline webinar will be conducted with the primary care providers randomized to usual care, describing the current CMS approach to reimbursing for obesity treatment and background on obesity interventions; a reminder informational brochure will be sent to the primary care providers at 1 y. Patients in the usual care arm will receive their normal, usual care from their primary care team, and they will participate in the measurement of the outcomes at 6, 12, 18 and 24 months.

Sources of Materials

Materials will be collected from human subjects in the form of outcome data at a screening visit, at baseline, and at 6, 12, 18 and 24 month assessment visits and will include questionnaire data, anthropometric measurements, blood pressure measurements (not performed at SV), and finger-stick blood samples (baseline, month 12 and month 24 only). We will conduct parallel data collection using the electronic medical records from the participating clinics in addition to data collection by our trained assessment team. We will rely on the primary care staff to track changes in body weight over the course of the intervention. Our study informatics staff will extract data on clinical variables (blood pressure, glucose, cholesterol, etc.) from the electronic medical records in the clinics.

All outcomes will be assessed using validated scales and tests where they exist. For example, height, weight, and waist circumference will be measured using standard procedures. Blood pressure will be measured in all clinics using a validated Omron automated device, and finger-stick blood samples will be used to measure fasting levels of cholesterol, triglycerides and glucose using a validated Cholestech LDX point-of-care device. In addition to direct health measures, several patient-reported outcomes will be measured by questionnaire, including quality of life, functional capacity, and satisfaction with care.

The assessment team, health coach, and data management staff will have access to personally identifiable private information about human subjects. All volunteers are assured of their confidentiality both verbally and in the informed consent form. The facilities are strictly limited to the staff of the research institution, clinics and to research volunteers. All medical records are locked in a secure area. Access to these areas is limited to the clinical support staff and the study investigators. Medical records are filed according to identification (ID) numbers. All forms in the chart, with the exception of the consent form and participant contact form, display only the ID number. Electronic data storage is similarly restricted with only the data management staff having access to the databases containing confidential records, i.e. those containing names or identifying information.

Potential Risks

This study does not involve major risks to participants. Efforts to minimize the potential risks of the assessment methods and outcome variables include frequent monitoring by the investigators to assure that no volunteer suffers any adverse effects from participating in the research. Our staff have performed similar testing procedures in many studies. Participants with known serious disease will be excluded from the study.

Potential risks associated with the study procedures include:

- a) Body height, weight and waist circumference. There is minimal risk to participants from these measurements.

- b) Blood pressure testing. Participants may experience temporary discomfort during blood pressure recordings due to the pressure of the cuff inflating on their arm.
- c) Finger stick blood sample. There is the possibility of pain and bruising on the finger where the finger prick is made. Aseptic (sterile) technique and trained personnel minimize these risks.
- d) Diet. Patients in the intervention arm will undergo a calorie-reduced diet that is safe for humans and has been tested repeatedly in numerous clinical trials.
- e) Increased physical activity. Patients in the intervention arm will be counseled to increase physical activity to levels that are consistent with the recommendations for US adults (30 minutes of moderate intensity activity per day). There is the possibility of adverse events such as minor musculoskeletal problems, but risk is minimized by excluding potential participants with contraindications to exercise. Considering these types of events are expected in this trial they will not be recorded or reported unless they meet the definition of a Serious Adverse Event. Patients with diabetes or prior CVD must have physician approval to begin exercise.
- f) Hypoglycemia during weight loss for patients on insulin and insulin secretagogues. To minimize hypoglycemia with weight loss in persons with type 2 diabetes, we will ask patients to monitor their blood sugar at least twice a day, once in the morning before breakfast and once in the evening before dinner.
- g) Gall bladder disease with weight loss. All physicians will be educated on the health risks associated with weight loss. With the slow weight loss we anticipate, we do not expect gall bladder disease exacerbation and will not give patient prophylaxis with ursodiol or fat bolus; for patients with symptoms of gall bladder disease, we will advise appropriate evaluation and treatment.

Adequacy of Protection against Risks

Recruitment and Informed Consent

The patients are volunteers that will be recruited through the primary care clinics. Potential subjects will then be screened in person to determine that they meet the initial recruitment criteria (such as age and BMI) and have no obvious contraindications to participating in the study. Screening of study participants will be conducted by a trained recruiter following a written manual of procedures. In a one-on-one or group consenting session, the potential participant(s) will be informed of the nature and requirements of the study, either via face-to-face interview or informed consent presentation. All patients will be given time to read the consent form and ask questions one-on-one with PROPEL staff. To continue, the participant must read and sign an informed consent to participate in further assessment and treatment.

Protection against Risks

This study will be required to have approval from the PBRC Institutional Review Board as well as IRBs at partner institutions. PBRC has full accreditation by the Association for the Accreditation of Human Research Protection Programs (AAHRPP). Efforts to minimize the potential risk of the assessment methods include frequent monitoring by the investigators to assure that no participant suffers any adverse effects.

All volunteers are assured of their confidentiality both verbally and in the informed consent form. The clinical facilities are strictly limited to the staff of the research institution, clinics and to research volunteers. This is accomplished by a variety of stringent security measures. All medical records are locked in a secure area. Access to these areas is limited to the clinical support staff, director of clinical facilities, and the investigators. Volunteers' medical records are filed according to ID numbers. All forms in the chart, with the exception of the consent form, display only the ID number. Electronic data storage is similarly restricted with only data management staff having access to the databases containing confidential clinical records, i.e. those containing names or other identifying information.

Potential Benefits of the Proposed Research to the Subjects and Others

We cannot ensure direct benefits for patients in this study. However, it is likely that patients in the intervention arm will experience health benefits associated with a healthier diet, increased physical activity and weight loss. The results of the study will provide important information about the effectiveness of an innovative intervention delivered through primary care that can be replicated in other regions of the United States.

Importance of the Knowledge to be Gained

This study proposes a comparative effectiveness trial of a pragmatic obesity intervention set within primary care. Obesity is a prevalent, serious medical condition that disproportionately affects underserved populations. Thus, there is an urgent need to develop and test pragmatic treatment strategies in the primary care setting, especially those recommended in the *2013 AHA/ACC/TOS Guidelines for the Management of Overweight and Obesity in Adults*. There is a gap between current guidelines and what is currently implemented in clinical practice; thus, comparative effectiveness studies are required to change the way that primary care practitioners approach the problem of obesity. This study directly addresses this gap by testing the effectiveness of intensive behavioral intervention for obesity relative to usual care.

Pregnancy and Other Exclusions

If a participant experiences a pregnancy lasting beyond the first trimester, her data will be censured from the time of estimated conception and she will be excluded from further participation. In the case of a miscarriage or pregnancy termination within the first trimester, or if a participant develops another exclusionary condition, such as cancer, unstable angina, or another condition for which weight loss or exercise might be contraindicated, further participation will be determined by the medical monitoring team.

Data and Safety Monitoring Plan

I. Study Identification Information

- A. PCORI Study Number – OB-1402-10977
- B. Study Title - PROMoting Successful Weight Loss in Primary CarE in Louisiana (PROPEL) Trial (Funded under the PCORI proposal “The Louisiana Trial for Obesity Reduction in Primary Care”)
- C. Name of Principal Investigator(s) - Peter T. Katzmarzyk, PhD
Medical Monitor - Tina Thethi, MD, MPH

II. Study Overview

A. Brief Description of the Purpose of the Study – The primary aim is to test the effectiveness of a 24 month, patient-centered, pragmatic and scalable obesity treatment program delivered within primary care in an underserved population. We will randomize 18 primary care clinics serving low income populations with a high percentage of African Americans to a comprehensive obesity treatment program or usual care. The study procedures pose little to no risk for human subjects. However, a Data and Safety Monitoring Board (DSMB) will review the protocol and monitor conduct of this study.

B. Adherence Statement - The Data Safety Monitoring Plan (DSMP) outlined below will adhere to the protocol approved by the PBRC IRB.

III. Confidentiality

A. Protection of Subject Privacy – All volunteers are assured of their confidentiality both verbally and in the informed consent forms. The facilities are strictly limited to the staff of the research institution, clinics and to research volunteers. This is accomplished by a variety of stringent security measures. All medical records are stored in locked areas. Access to these areas is limited to the clinical support staff and the PI of the study. Volunteers' medical records are filed according to ID numbers. All forms on the chart, with the exception of consent form, display only the ID number.

B. Database Protection – Electronic data storage is similarly restricted with only the data management staff having access to databases containing confidential clinical records, i.e. those containing name or other identifying information.

C. Confidentiality during AE Reporting – Adverse events will be reported to the study PI, Project Manager, Medical Monitor, DSMB and Chair of the IRB throughout the trial. Adverse event data will be analyzed quarterly, but serious or life-threatening adverse events require immediate reporting and follow-up. AE reports and quarterly summaries will not include subject-identifiable material. Each will include the identification code only.

IV. Adverse Event Information

A. Definition - An adverse event (AE) is any untoward medical occurrence in a subject temporally associated with participation in the clinical study. An adverse finding can include a sign, symptom, abnormal assessment (laboratory test value, vital signs, electrocardiogram finding, etc.) or any combination of these. A Serious Adverse Event (SAE) is any adverse event that results in one or more of the following outcomes: death; a life-threatening event; inpatient hospitalization or prolongation of existing hospitalization; a persistent or significant disability/incapacity; a congenital anomaly or birth defect; important medical event based upon appropriate medical judgment.

B. Classification of AE Severity – AEs will be labeled according to severity which is based on their impact on the patient. An AE will be termed 'mild' if it does not have a major impact on the patient, 'moderate' if it causes the patient some minor inconvenience and 'severe' if it causes a substantial disruption to the patient's wellbeing. The Site Staff for this trial will be responsible for determining the 'severity' of AEs. Site Staff will also make an initial evaluation of the 'seriousness' of the AE in order to determine if the AE needs to be elevated to the MMT

immediately upon discovery. The MM and/or NP make the final and official determination of the 'seriousness' of an AE. We anticipate most adverse events will be "mild" and the participant will be able to resume daily activities within a day or two of reporting the event.

C. AE Attribution Scale – AEs will be categorized according to the likelihood that they are related to the study intervention. Specifically, they will be labeled as either related or unrelated to the study intervention, and this relationship will be confirmed by the Medical Monitoring Team (MMT) for this trial.

D. Expected Risks – This study does not involve major risk to screeners and trial participants. Efforts to minimize the potential risks of the assessment methods and outcome variables include frequent monitoring by the investigators to assure that no volunteer suffers any adverse effects from participating in the research. The expectedness of an AE will be determined by the Medical Monitoring Team (MMT).

The study procedures include:

- a) Body height, weight and waist circumference. There is minimal risk to participants from these measurements.
- b) Blood pressure testing. Participants may experience temporary discomfort during blood pressure recordings due to the pressure of the cuff inflating on their arm.
- c) Finger stick blood sample. There is the possibility of pain and bruising on the finger where the finger prick is made. Aseptic (sterile) technique and trained personnel minimize these risks.
- d) Diet. Patients in the intervention arm will undergo a calorie-reduced diet that is safe for humans and has been tested repeatedly in numerous clinical trials.
- e) Increased physical activity. Patients in the intervention arm will be counseled to increase physical activity levels which are consistent with the recommendations for US adults (30 minutes of moderate intensity activity per day). There is the possibility of adverse events such as minor musculoskeletal problems, but risk is minimized by excluding potential participants with contraindications to exercise. Considering these types of events are expected in this trial they will not be recorded or reported unless they meet the definition of a Serious Adverse Event. Patients with diabetes or prior CVD must have physician approval to begin exercise.
- f) Hypoglycemia during weight loss for patients on insulin and insulin secretagogues. To minimize hypoglycemia with weight loss in persons with type 2 diabetes, we will ask patients to monitor their blood sugar at least twice a day, once in the morning before breakfast and once in the evening before dinner.
- g) Gall bladder disease with weight loss. All physicians will be educated on the health risks associated with weight loss. With the slow weight loss we anticipate, we do not expect gall bladder disease exacerbation and will not give patients prophylaxis with ursodiol or fat bolus; for patients with symptoms of gall bladder disease, we will advise appropriate evaluation and treatment.

E. SAE Reporting - SAEs that are unanticipated, serious, and possibly related to the study intervention will be reported to the PBRC Medical Committee, Medical Monitoring Team, the DSMB, and the PBRC IRB in accordance with requirements. Anticipated SAEs or those

unrelated to the study intervention will be reported to the same individuals/entities in accordance with requirements. Clinics will be required to report to the Medical Monitoring Team adverse events that are serious or in doubt about being serious within 24 hours of discovery. Other adverse events that are not serious but are unexpected and are associated with the study procedures will be reported within 10 days.

V. Data Quality and Safety Review Plan and Monitoring

A. Data Quality and Management – A Data and Safety Monitoring Board (DSMB) will be convened and will meet regularly throughout the study period. The DSMB will meet twice per year throughout the trial, and will be convened for a first meeting prior to recruitment of patients. A minimum of 1 meeting each year will be conducted in person, and the second meeting may be conducted via conference call. Prior to the start of recruitment the DSMB will give formal approval of the study protocol and informed consent.

Size and Composition of DSMB: The DSMB will consist of 4 members both internal and external to the Pennington Biomedical Research Center. The planned composition is as follows: biostatistician (1), exercise physiologist or dietician (1), clinician (1) and layperson (1).

Major Responsibilities of DSMB Members:

1. Sign and abide by a statement of confidentiality
2. Disclose any actual or potential conflicts of interest
3. Create a charter to define its function, signed by all members
4. Be familiar with the research protocol and plans for safety monitoring
5. Oversee safety of participants, which will include review of interim/cumulative data for evidence of study-related adverse events (including serious adverse events)
6. Review data quality, completeness, and timeliness (including recruitment)
7. Review adherence to the protocol
8. Review factors that might affect the study outcome or compromise the confidentiality of the trial data (such as protocol violations, unmasking, etc.)
9. Review reports of related studies, as appropriate
10. Review major proposed protocol modifications

Reports: Following each meeting, the DSMB will provide written documentation regarding findings for the study as a whole and any relevant recommendations related to continuing, changing, or terminating the study. All DSMB recommendations will be submitted to the Principal Investigator and/or his designee, with a copy provided to the Pennington Biomedical Research Center IRB and PCORI Project Officer or designee.

The DSMB will monitor and review recruitment, adverse events, data quality, outcome data, and overall awardee performance. The PI and Project Manager will regularly review all data collection forms and source documents on an ongoing basis for data completeness, accuracy, and compliance with the protocol and Standard Operating Procedures (SOPs) of PBRC. A statement reflecting the results of the review and describing any protocol deviations will be sent to the PBRC IRB in an annual report (non-competing continuation).

B. Subject Accrual and Compliance - Review of subject accrual, adherence to inclusion / exclusion criteria, and rates of study completion will occur quarterly. These data will be reviewed by the study PI and Medical Monitoring Team and presented to the DSMB.

C. Out of Range Data – Laboratory and physical measurement reports will be reviewed weekly by the Medical Monitoring Team for the study. Out-of-range values for clinical chemistry and blood pressure will be reported to the patient as soon as possible so that they can follow up with their PCP. See Table 3 for Alert and Emergency values and actions.

Table 3. Alert and Emergency Values and Actions

Measure	Alert Value	Notify Participant	Notify PCP
Blood Pressure	Systolic ≥ 150 mmHg <u>or</u> Diastolic ≥ 100 mmHg	Within 1 week or sooner as indicated by exact value and judgment of Medical Monitor	Instruct the participant to notify their PCP within 1 week or sooner as indicated by exact value and judgment of Medical Monitor
Blood Glucose	≥ 200 mg/dl or ≤ 400 mg/dl	Within 1 week or sooner as indicated by exact value and judgment of Medical Monitor	Instruct the participant to notify their PCP within 1 week or sooner as indicated by exact value and judgment of Medical Monitor
Triglycerides	>650 mg/dl	Within 1 week or sooner as indicated by exact value and judgment of Medical Monitor	Instruct the participant to notify their PCP within 1 week or sooner as indicated by exact value and judgment of Medical Monitor

Measure	Emergency Value	Notify Participant
Blood Pressure	Systolic ≥ 170 mmHg <u>or</u> Diastolic ≥ 110 mmHg	Instruct the participant to take their medications if they have not already and immediately walk with them to find clinic personnel who can evaluate them for possible additional treatment.
Blood Glucose	<50 mg/dl or >400 mg/dl	Immediately walk with the participant to find clinic personnel who can evaluate them for possible additional treatment.

D. Stopping Rules - This study will be stopped prior to its completion if: (1) adverse effects that significantly impact the risk-benefit ratio have been observed; (2) study recruitment or retention becomes futile; (3) any new information becomes available during the trial that necessitates stopping the trial; and (5) other situations occur that might warrant stopping the trial. Because one of the most likely reasons for stopping the trial is the inability to recruit the study sample, the PI will include an assessment of recruitment futility in the annual progress report to PCORI and will consult with a biostatistician if necessary to assess the impact of significant data loss due to problems in recruitment, retention or data collection.

E. Justification of Sample Size - The sample size calculations for PROPEL were based on LOSS, a pragmatic clinical trial conducted by Pennington Biomedical in eight primary care clinics across the state of Louisiana comparing intensive medical intervention for obesity versus usual care.⁴ According to the *2013 AHA/ACC/TOS Obesity Guidelines*, as little as 3-5% weight loss is likely to result in clinically meaningful health outcomes.²⁹ The calculations assume that

the study will be powered to detect a mean weight loss in the intervention arm of 3.5% at 2 y, relative to usual care, in race- and sex-specific subgroups. We are targeting a mean weight loss of >5% which we anticipate to be 3.5% more than usual care. Both the total and relative weight loss meet currently accepted levels of clinical significance.

Power calculations used a nominal 0.05 significance level with a two-tailed test with minimal power of 80%. Based on the LOSS study, the standard deviation for weight change for patients nested within clinics was 8.4%. For the subgroup analysis, a net sample size of 252 patients (126/arm) is sufficient for detecting a 3.5% weight loss with 90% power when randomization is performed at the patient level. After accounting for the design effect, at least 134 patients per arm are required to realize 80% power in a trial randomized at the clinic level. A previous study in primary care (PROACTIVE) had 20% attrition over 24 months. However, given the challenges of working with a clinic population across an entire state, we have allowed for a conservative estimate of 30% attrition for this trial. Thus, allowing for 30% attrition, at least 192 patients per arm are needed with a total (2 arms) enrollment of at least 384 patients per subgroup analyses. Based on data from the patient population served by Louisiana safety net hospitals⁸² and Federally Qualified Health Centers in Louisiana which is approximately 50% African American and 50% female, this translates into a total sample size of at least 768 patients, which will provide at least 97% power to detect a mean weight loss in the intervention arm of 3.5% at 2 y, relative to usual care in the total sample. To account for the increased rate of attrition in Federally Qualified Health Centers, up to 850 (425 patients per arm / 47 patients per clinic / 18 clinics) participants will be enrolled. Although Hispanics will be included in the trial, the low Hispanic population in LA (4%)²¹ precludes sub-group analysis.

F. Designation of Medical Monitoring Team - The Medical Monitor will be the leader of the Medical Monitoring Team and will be a medical doctor appointed by the PI. He/she will have an understanding of the types and severity of adverse events commonly experienced as a result of the testing protocols for this study. The Medical Monitoring Team will consist of the Coordinating Center Staff, a Nurse Practitioner and the Medical Monitor. The Medical Monitoring Team reviews all safety reports and determines whether there is any corrective action, trigger an ad hoc review, or a stopping rule violation that should be communicated to the PI, the PBRC IRB, and PCORI. In addition, the Medical Monitoring Team may comment on whether the PI needs to report any specific out of range laboratory data to the patient and/or his/her physician.

G. Safety Review Plan - The PI will monitor the progress of the study weekly, including reasons for attrition and whether all participants met entry criteria. Further, progress and safety will be reviewed quarterly. These progress reports will include information on recruitment, retention/attrition, and AEs and will be provided to the Medical Monitor quarterly. The Medical Monitor will also receive a yearly report that details data relevant to the possible early termination of the study. We will establish a DSMB and we will provide reports to the DSMB prior to each meeting on adverse events and recruitment.

VI. Informed Consent

Patients are volunteers that will be recruited through primary care clinics. The PBRC's Institutional Review Board (IRB) as well as the IRBs of the partner institutions will approve the study protocol and all consent forms. Trained recruiters will obtain informed consent from all participants as well as HIPAA authorization. All questions and concerns are clarified before any forms are signed.

Inclusion of Women and Minorities

I. Inclusion of Women - Women will be included in this intervention with equal probability as men as the inclusion criteria include both men and women.

II. Inclusion of Minorities - We have selected clinics with a high proportion of patients with low socio-economic status and African Americans; however, our inclusion criteria do not specify any specific ethnicity. Thus, we anticipate that the socio-demographic distribution of patients will follow closely the patient population in selected clinics.

Inclusion of Children

The focus of the PCORI Funding Announcement under which this study was funded is on obesity reduction in adults therefore the patients in this study are mainly adults (20 - 75 y of age). The treatment of childhood obesity is beyond the scope of this intervention.

15. Power and Sample Size

The sample size calculations for PROPEL were based on LOSS, a pragmatic clinical trial conducted by Pennington Biomedical in eight primary care clinics across the state of Louisiana comparing intensive medical intervention for obesity versus usual care.⁴ According to the 2013 *AHA/ACC/TOS Obesity Guidelines*, as little as 3-5% weight loss is likely to result in clinically meaningful health outcomes.²⁹ The calculations assume that the study will be powered to detect a mean weight loss in the intervention arm of 3.5% at 2 y, relative to usual care, in race- and sex-specific subgroups. We are targeting a mean weight loss of >5% which we anticipate to be 3.5% more than usual care. Both the total and relative weight loss meet currently accepted levels of clinical significance.

Power calculations used a nominal 0.05 significance level with a two-tailed test with minimal power of 80%. Based on the LOSS study, the standard deviation for weight change for patients nested within clinics was 8.4%. For the subgroup analysis, a net sample size of 184 patients (92/arm) is sufficient for detecting a 3.5% weight loss with 80% power when randomization is performed at the patient level. After accounting for the design effect, at least 134 patients per arm are required to realize 80% power in a trial randomized at the clinic level. A previous study in primary care (PROACTIVE) had 20% attrition over 24 months. However, given the challenges of working with a clinic population across an entire state, we have allowed for a conservative estimate of 30% attrition for this trial. Thus, allowing for 30% attrition, at least 192 patients per arm are needed with a total (2 arms) enrollment of at least 384 patients per subgroup analyses.

Based on data from the patient population served by Louisiana safety net hospitals⁸² and Federally Qualified Health Centers in Louisiana which is approximately 50% African American and 50% female, this translates into a total sample size of at least 768 patients, which will provide at least 97% power to detect a mean weight loss in the intervention arm of 3.5% at 2 y, relative to usual care in the total sample. To account for the increased rate of attrition in Federally Qualified Health Centers, up to 850 participants (425 patients per arm / 47 patients per clinic / 18 clinics) will be enrolled. Although Hispanics will be included in the trial, the low Hispanic population in LA (4%)²¹ precludes sub-group analysis.

16. Data Analysis Plan

To address the primary aim, weight loss will be analyzed as mean percent of baseline weight loss at months 6, 12, 18 and 24 in the context of linear mixed (fixed and random) effects multi-level models. In addition to intervention group, clinics and assessment time, and their interaction terms, the model may include and patient-level (weight, age, sex, race) and clinic-level (clinic size, %African American, % Medicaid/Medicare, etc.) variables as explanatory covariates.

Preliminary analytical findings will be used to choose the most plausible and efficient repeated measures covariance structure (e.g., compound symmetric, autoregressive, unstructured) to use. Although substantial effort will be employed to minimize missing data, it is inevitable that some missing data will occur. An intention-to-treat analysis that includes all randomized patients, regardless of the number of assessments obtained, will be conducted. The primary analysis will use the mixed effects model mentioned above and employ restricted maximum likelihood using all available data. The analytical plans are flexible and will be adapted as scientific perspectives are advanced.

Additional analyses to test the secondary aims are described below:

Secondary Aim 1. Evaluate relationships between adherence to intervention components (physical activity, diet, sessions, etc.) and corresponding changes in body weight and secondary outcomes (post-hoc analyses).

The first secondary aim will be accomplished by conducting analyses of adherence data and changes in the outcomes, and by conducting sub-analyses in different compliant groups (attended at $\geq 80\%$ of sessions, etc.).

Secondary Aim 2. Examine the effects of the intervention on system-level practices and patient satisfaction with care.

The second secondary aim will be accomplished using a similar strategy as the primary aim.

Secondary Aim 3. Test the heterogeneity of effects (HTE) across clinics and across subgroups of patients (men versus women, white versus African American, older versus younger adults).

Analyses of HTE is an important aspect of this study, as the identification of systematic differences in response to the intervention will be important for broad dissemination of our model, and for further tailoring the intervention to specific sub-groups. We currently have three confirmatory HTE analyses planned: 1) white versus African American, 2) men versus women, and 3) younger (20-44 y) versus middle-aged (45-64 y) versus older (65+ y) adults. Further, we have one planned exploratory HTE analysis, which is to explore clinic-level differences in response within the intervention and usual care groups and identify factors that explain the clinic-level heterogeneity.

Confirmatory HTE Analyses. Based on one-year results in patients in the Look AHEAD intervention, men lost more weight than women, older adults (65+ y) lost significantly more weight than younger adults, and white participants lost more weight than African Americans.⁸³ Thus, we hypothesize that men, white patients, and older patients will lose significantly more weight in the primary care setting than women, African Americans and younger patients, respectively.

Exploratory HTE Analysis. There is potential for heterogeneity in response across the clinics in this study. We plan to explore clinic-level variability in response and identify factors

associated with clinic-level variability. Potential factors that will be considered include clinic size, number of physicians, number of residents, percentage Medicaid/Medicare, percentage minority, and geo-spatial characteristics of the clinic location (population density, crime, etc.).

Heterogeneity of treatment effect will be investigated in several subgroup analyses: men vs women, whites vs African Americans, ages 20-44 y vs 45-64 y vs ≥ 65 y. The intervention effect on weight loss will be investigated using a subgroup variable in mixed effects multilevel models analogous to the primary analysis with a focus on intervention-by-subgroup interactions coupled with illustrative graphics. Subsequent analyses will focus on elucidating underlying reasons for the subgroup differences and how these differences influence guidelines that may translate to the general population. Exploratory analyses using fixed and random effects models will determine treatment differences among clinics and estimate the variability associated with these differences.

Significant subgroup heterogeneity in outcome response (e.g., significant sex differences in effectiveness), supported by significance of the test for intervention-by-sex interaction, would lead to further investigation in search of the underlying reasons for the differential response. Previous studies provide evidence that responses to weight loss interventions vary by age, race and sex.⁸³ It is anticipated that these will be confirmed in this trial. Less is known about the influence of clinic-level variables on treatment response; thus, these analyses are considered exploratory.

Handling of Missing Data

Missing data are expected due to drop outs and missed visits. Weight loss is a subject-level variable and missing assessments would influence tests relative to treatment-by-time interactions. The primary analysis described above will employ restricted maximum likelihood using all data. No patients will be deleted from the analysis because of partial data. To assess the sensitivity of results, weight loss will be analyzed using: 1) all patients irrespective of missing data to perform analysis of variance using mixed effects multi-level models with repeated measures; 2) only patients who have completed all assessment visits and have no missing data, to perform analysis of variance employing mixed effects multi-level models with repeated measures; 3) all patients, irrespective of missing data, to conduct analyses using mixed effects multi-level time trend models with random coefficients to capture individual time trends (does not require complete data across time); and 4) multiple imputation.

Multiple imputation will be employed to perform statistical inferences that properly account for statistical uncertainty due to missingness. Rubin's multiple imputation procedure replaces each missing value with a set of plausible values that represent the uncertainty about the appropriate value to impute.⁸⁴ Missing values are imputed by drawing random samples, and the process is replicated to provide K data sets with pseudo-complete data. Estimates and corresponding confidence intervals will be plotted against K to determine the optimal K to use in subsequent sensitivity analyses. Mean weight loss is estimated for each data set, and the multiple imputation estimator is the average of the individual estimates. The variance of the estimator is estimated from between- and within-imputation variability.⁸⁵ The SAS® procedure PROC MI provides four relevant options for imputation models and will be used in quantifying uncertainty due to missing data.

Statistical summaries will be compiled on the number of patients overall and by arm and who completed study per protocol, did not complete study per protocol, and reasons for not completing. Patient characteristics (age, sex, race, BMI) will be summarized similarly. Multi-level logistic regression will be used to investigate the significance of correlates of failure to complete the study per protocol.

17. Trial Organization

The Principal Investigator will oversee and monitor progress to reach the milestones with decisions concerning short-term goals and the evaluation of longer-term progress being discussed with the research staff via weekly meetings. Broader management of the project will be undertaken by the Project Management Committee, as described below. The research team will be organized into sub-teams of investigators and staff. The overall organizational structure will be reviewed and amended as required.

Project Management Committee

The Project Management Committee will be comprised of the Principal Investigator, selected co-investigators (i.e. Intervention Director, Assessment Director, and Community Engagement Co-Directors), Project Manager and two patient partners. The Project Management Committee will be responsible for overseeing the day-to-day management of the trial, and the Principal Investigator will make adjustments to the approach used by the team to achieve the milestones.

Intervention Team

The Intervention Director will lead the intervention team, which will consist of health psychology, health literacy, nutrition and physical activity experts who will develop the intervention materials, and the interventionists (health coaches) who will deliver the behavioral lifestyle intervention in primary care clinics.

Assessment Team

The Assessment Director will lead the assessment team, which will consist of data collection technicians trained by the assessment director and experts in anthropometry, questionnaire administration and health literacy. The assessment team will be responsible for collecting data on the outcome measures at screening, baseline, and at the 6, 12, 18 and 24 month visits.

Education Team

The Education Director and his/her team will be responsible for developing an educational program on obesity science and obesity management for PCPs in the intervention arm of the trial, and for developing a webinar and brochure for PCPs in the usual care arm on the current CMS reimbursement for obesity treatment.

18. Timeline

The PROPEL trial is designed as a two-year intervention for patients. However, the trial itself is embedded within a broader timeline of research, consisting of two stages. Stage 1 involves establishing Patient Advisory Boards (quarterly meetings), a Community Monitoring Board (yearly meetings), conducting focus groups, adapting intervention materials from Look AHEAD, development of a Manual of Procedures (MOP), and training of the health coaches and assessment team. Stage 2 involves the recruitment of patients and the execution of the trial itself. A detailed timeline for both stages of the research project is presented in Table 4 below.

Table 4. Timeline of activities (by Quarter) for the PROPEL trial

Stage/Activities	2015				2016				2017				2018				2019			
	Q 1	Q 2	Q 3	Q 4	Q 1	Q 2	Q 3	Q 4	Q 1	Q 2	Q 3	Q 4	Q 1	Q 2	Q 3	Q 4	Q 1	Q 2	Q 3	Q 4
Stage 1																				
Patient Advisory Board Meetings (quarterly)																				
Community Monitoring Board (yearly)																				
Execution of Subcontractor Agreements																				
IRB Submission/Approval for Focus Groups																				
Focus Groups																				
Adaptation of Look AHEAD Materials																				
Development of Manual of Procedures																				
IRB Submission/Approval for Intervention																				
Training of Health Coaches																				
Training of Outcomes Assessment Team																				
Trial Registered at www.Clinicaltrials.gov																				
Stage 2																				
Recruitment																				
Intervention																				
Data Analysis/Evaluation of the Intervention																				
Refinement of Intervention for Sustainability																				
Publication of Results																				

19. Literature Cited

1. Trogdon JG, Finkelstein EA, Feagan CW, Cohen JW. State- and payer-specific estimates of annual medical expenditures attributable to obesity. *Obesity* 2012;**20**:214-220.
2. U.S. Preventive Services Task Force. Screening for and management of obesity in adults: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2012;**157**:373-378.
3. Jensen MD, Ryan DH. New obesity guidelines: Promise and potential. *JAMA* 2014;**311**:23-24.
4. Ryan DH, Johnson WD, Myers VH, Prather TL, McGlone MM, Rood J, et al. Nonsurgical weight loss for extreme obesity in primary care settings: Results of the Louisiana Obese Subjects Study. *Arch Intern Med* 2010;**170**:146-154.
5. Wadden TA, Neiberg RH, Wing RR, Clark JM, Delahanty LM, Hill JO, et al. Four-year weight losses in the Look AHEAD study: factors associated with long-term success. *Obesity* 2011;**19**:1987-1998.
6. Hamman RF, Wing RR, Edelstein SL, Lachin JM, Bray GA, Delahanty L, et al. Effect of weight loss with lifestyle intervention on risk of diabetes. *Diab Care* 2006;**29**:2102-2107.
7. Ackermann RT, Finch EA, Brizendine E, Zhou H, Marrero DG. Translating the Diabetes Prevention Program into the community. The DEPLOY Pilot Study. *Am J Prev Med* 2008;**35**:357-363.
8. Ackermann RT, Finch EA, Caffrey HM, Lipscomb ER, Hays LM, Saha C. Long-term effects of a community-based lifestyle intervention to prevent type 2 diabetes: the DEPLOY extension pilot study. *Chronic Illn* 2011;**7**:279-290.
9. Wadden TA, West DS, Delahanty L, Jakicic J, Rejeski J, Williamson D, et al. The Look AHEAD study: a description of the lifestyle intervention and the evidence supporting it. *Obesity* 2006;**14**:737-752.
10. Rickman AD, Williamson DA, Martin CK, Gilhooly CH, Stein RI, Bales CW, et al. The CALERIE Study: Design and methods of an innovative 25% caloric restriction intervention. *Contemp Clin Trials* 2011;**32**:874-881.
11. Karmali S, Kadikoy H, Brandt ML, Sherman V. What s my goal? Expected weight loss and comorbidity outcomes among bariatric surgery patients. *Obes Surg* 2011;**21**:595-603.
12. Centers for Disease Control and Prevention. Behavioral Risk Factor Surveillance System. Available on-line at: www.cdc.gov/brfss/. 2013.
13. Eyre H, Kahn R, Robertson RM, Clark NG, Doyle C, Hong Y, et al. Preventing cancer, cardiovascular disease, and diabetes: a common agenda for the American Cancer Society, the American Diabetes Association, and the American Heart Association. *Stroke* 2004;**35**:1999-2010.
14. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW, Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. *N Engl J Med* 1999;**341**:1097-1105.
15. Olshansky SJ, Passaro DJ, Hershov RC, Layden J, Carnes BA, Brody J, et al. A potential decline in life expectancy in the United States in the 21st century. *N Engl J Med* 2005;**352**:1138-1145.
16. U.S. Cancer Statistics Working Group. *United States Cancer Statistics: 1999–2010 Incidence and Mortality Web-based Report*. Available at: <http://www.cdc.gov/uscs>. . Atlanta, GA: Department of Health and Human Services, Centers for Disease Control and Prevention, and National Cancer Institute; 2013.
17. Brown JR, O'Connor GT. Coronary heart disease and prevention in the United States. *N Engl J Med* 2010;**362**:2150-2153.

18. Mensah GA, Mokdad AH, Ford ES, Greenlund KJ, Croft JB. State of disparities in cardiovascular health in the United States. *Circulation* 2005;**111**:1233-1241.
19. Mokdad AH, Bowman BA, Ford ES, Vinicor F, Marks JS, Koplan JP. The continuing epidemics of obesity and diabetes in the United States. *JAMA* 2001;**286**:1195-1200.
20. Sherry B, Blanck HM, Galuska DA, Pan L, Dietz WH, Balluz L. Vital Signs: State-specific obesity prevalence among adults- United States, 2009. *Morb Mortal Wkly Rep* 2010;**59**:1-5.
21. US Census Bureau. 2010 Demographic Profile: Louisiana 2010: <https://www.census.gov/popfinder/>. 2014.
22. National Institute for Literacy. *State of Literacy in America: Estimates at the Local, State and National levels* Washington, DC: U.S Government Printing Office; 1998.
23. Carvajal R, Wadden TA, Tsai AG, Peck K, Moran CH. Managing obesity in primary care practice: A narrative review *Ann NY Acad Sci* 2013;**1281**:191-206.
24. Pan XR, Li GW, Hu YH, Wang JX, An ZX, Hu ZX, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diab Care* 1997;**20**:537-544.
25. The Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002;**346**:393-403.
26. Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001;**344**:1343-1350.
27. Centers for Disease Control and Prevention. National diabetes fact sheet: National estimates and general information on diabetes and prediabetes in the United States, 2011. Available at: http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf. 2011.
28. Centers for Disease Control and Prevention. Prediabetes Facts. Available at: <http://www.cdc.gov/diabetes/prevention/factsheet.htm>. 2014.
29. 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. *Circulation* 2013.
30. The Look AHEAD Research Group. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. *N Engl J Med* 2013;**369**:145-154.
31. Decision memo for intensive behavioral therapy for obesity. Accessed at: <http://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?&NcaName=Intensive%20Behavioral%20Therapy%20for%20Obesity&bc=ACAAAAAAIAAA&NCAId=253&>. 2011.
32. Pagoto SL, Pbert L, Emmons K, Farber D, Society of Behavioral Medicine Public Policy Leadership Group. Policy Brief: The Society for Behavioral Medicine position statement on the CMS decision memo on intensive behavioral therapy for obesity. *Transl Behav Med* 2012;**2**:381-383.
33. National Heart Lung and Blood Institute. *Managing Overweight and Obesity in Adults: Systematic Evidence Review from the Obesity Expert Panel, 2013*. Available at www.nhlbi.nih.gov/guidelines: US Department of Health and Human Services; 2013.
34. The Look AHEAD Research Group. The Look AHEAD Study: A description of the lifestyle intervention and the evidence supporting it. *Obesity* 2006;**14**.
35. Ryan DH, Espeland MA, Foster GD, Haffner SM, Hubbard VS, Johnson KC, et al. Look AHEAD (Action for Health in Diabetes): design and methods for a clinical trial of weight loss for the prevention of cardiovascular disease in type 2 diabetes. *Control Clin Trials* 2003;**24**:610-628.

36. Wadden TA, Neiberg RH, Wing RR, Clark JM, Delahanty LM, Hill JO, et al. Four-year weight losses in the Look AHEAD Study: Factors associated with long-term success. *Obesity* 2011;**19**:1987-1998.
37. Neiberg RH, Wing RR, Bray GA, Reboussin DM, Rickman AD, Johnson KC, et al. Patterns of weight change associated with long-term weight change and cardiovascular disease risk factors in the Look AHEAD study. *Obesity* 2012;**20**:2048-2056.
38. Appel LJ, Clark JM, Yeh HC, Wang NY, Coughlin JW, Daumit G, et al. Comparative effectiveness of weight-loss interventions in clinical practice. *N Engl J Med* 2011;**365**:1959-1968.
39. Hamman RF, Wing RR, Edelstein SL, Lachin JM, Bray GA, Delahanty L, et al. Effect of weight loss with lifestyle intervention on risk of diabetes. *Diab Care* 2006;**29**:2102-2107.
40. US Department of Health and Human Services. *2008 Physical Activity Guidelines for Americans*: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2008.
41. Jeffery RW, Wing RR, Sherwood NE, Tate DF. Physical activity and weight loss: does prescribing higher physical activity goals improve outcome? *Am J Clin Nutr* 2003;**78**:684-689.
42. 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**:459-471.
43. Thomas DM, Ciesla A, Levine JA, Stevens JG, Martin CK. A mathematical model of weight change with adaptation. *Math Biosci Eng* 2009;**6**:873-887.
44. Thomas DM, Das SK, Levine JA, Martin CK, McDougall A, Strauss BJ, et al. New fat free mass - fat mass model for use in physiological energy balance equations. *Nutr Metab* 2010;**7**:39.
45. Thomas DM, Martin CK, Heymsfield S, Redman LM, Schoeller DA, Levine JA. A simple model predicting individual weight change in humans. *J Biol Dyn* 2011;**5**:579-599.
46. Thomas DM, Schoeller DA, Redman LA, Martin CK, Levine JA, Heymsfield SB. A computational model to determine energy intake during weight loss. *Am J Clin Nutr* 2010;**92**:1326-1331.
47. The Diabetes Prevention Program Research Group. The Diabetes Prevention Program (DPP): Description of lifestyle intervention *Diab care* 2002;**25**:2165-2171.
48. U.S. Department of Agriculture, U.S. Department of Health and Human Services. *Dietary Guidelines for Americans 2010, 7th Edition*. Washington, DC: U.S. Government Printing Office; 2010.
49. Bravata DM, Smith-Spangler C, Sundaram V, Gienger AL, Lin N, Lewis R, et al. Using pedometers to increase physical activity and improve health: a systematic review. *JAMA* 2007;**298**:2296-2304.
50. Kang M, Marshall SJ, Barreira TV, Lee JO. Effect of pedometer-based physical activity interventions: a meta-analysis. *Res Q Exerc Sport* 2009;**80**:648-655.
51. Harrington DM, Tudor-Locke C, Champagne CM, Broyles ST, Harsha D, Kennedy BM, et al. Step-based translation of physical activity guidelines in the Lower Mississippi Delta. *Appl Physiol Nutr Metab* 2011;**36**:583-585.
52. Tudor-Locke C, Leonardi C, Johnson WD, Katzmarzyk PT, Church TS. Accelerometer steps/day translation of moderate-to-vigorous activity. *Prev Med* 2011;**53**:31-33.
53. Ratzan SC, Parker RM. National Library of Medicine Current Bibliographies in Medicine.NLM pub no. CBM 2000-1. In: Selden CR, Zorn M, Ratzan SC, Parker RM, eds. *Health Literacy* Bethesda, MD: National Institutes of Health; 2000.

54. Weiss B, Schwartzberg J, Davis T, Parker R, Sokol P, Williams M. *Health literacy and patient safety: Help patients understand: Manual for clinicians*: AMA Foundation; 2007.
55. US Department of Health and Human Services, Office of Disease Prevention and Health Promotion. *National Action Plan to Improve Health Literacy*. Washington, DC: U.S. Department of Health and Human Services; 2010.
56. Wolf MS, Seligman H, Davis TC, Fleming DA, Curtis LM, Pandit AU, et al. Clinic-based v. outsourced implementation of a diabetes health literacy intervention. *J Gen Intern Med* 2013;**E Pub**.
57. Davis TC, Seligman H, Dewalt D, Bass P, Platt D, Reynolds C, et al. Diabetes implementation of a self-management program in resource poor and rural community clinics. *J Prim Care Comm Health* 2012;**3**:239-242.
58. Wallace AS, Seligman HK, Davis TC, Schillinger D, Arnold CL, Bryant-Shilliday B, et al. Literacy appropriate educational materials and brief counseling improves diabetes self-management. *Patient Educ Couns* 2009;**75**:328-333.
59. DeWalt DA, Davis TC, Wallace AS, Seligman HK, Bryant-Shilliday B, Arnold CL, et al. Goal setting in diabetes self-management: taking the baby steps to success. *Patient Educ Couns* 2009;**77**:218-223.
60. Ostchega Y, Nwankwo T, Sorlie PD, Wolz M, Zipf G. Assessing the validity of the Omron HEM-907XL oscillometric blood pressure measurement device in a National Survey environment. *J Clin Hypertens* 2010;**12**:22-28.
61. Wan Y, Heneghan C, Stevens R, McManus RJ, Ward A, Perera R, et al. Determining which automatic digital blood pressure device performs adequately: a systematic review. *Journal of human hypertension* 2010;**24**:431-438.
62. Dale RA, Jensen LH, Krantz MJ. Comparison of two point-of-care lipid analyzers for use in global cardiovascular risk assessments. *Ann Pharmacother* 2008;**42**:633-639.
63. Carey M, Markham C, Gaffney P, Boran C, Maher V. Validation of a point of care lipid analyser using a hospital based reference laboratory. *Ir J Med Sci* 2006;**175**:30-35.
64. Arozullah AM, Yarnold PR, Bennett CL, Soltysik RC, Wolf MS, Ferreira RM, et al. Development and validation of a short-form, rapid estimate of adult literacy in medicine. *Med Care* 2007;**45**:1026-1033.
65. Bickel G, Nord M, Price C, Hamilton W, Cook J. *Guide to Measuring Household Food Security, Revised 2000*. Alexandria, VA: U.S. Department of Agriculture, Food and Nutrition Service; 2000.
66. Cella D, Yount S, Rothrock N, Gershon R, Cook K, Reeve B, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH Roadmap cooperative group during its first two years. *Med Care* 2007;**45**:S3-S11.
67. Cella D, Riley W, Stone A, Rothrock N, Reeve B, Yount S, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. *J Clin Epidemiol* 2010;**63**:1179-1194.
68. Salem R, Bamer AM, Alschuler KN, Johnson KL, Amtmann D. Obesity and symptoms and quality of life indicators of individuals with disabilities. *Disabil Health J* 2014;**7**:124-130.
69. Kolotkin RL, Crosby RD. Psychometric evaluation of the impact of weight on quality of life-lite questionnaire (IWQOL-lite) in a community sample. *Qual Life Res* 2002;**11**:157-171.
70. Kolotkin RL, Crosby RD, Kosloski KD, Williams GR. Development of a brief measure to assess quality of life in obesity. *Obes Res* 2001;**9**:102-111.

71. Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* 2003;**35**:1381-1395.
72. Fuller NR, Williams K, Shrestha R, Ahern AL, Holzapfel C, Hauner H, et al. Changes in physical activity during a weight loss intervention and follow-up: A reandomized controlled trial *Clinical Obesity* 2014;**4**:127-135.
73. Thompson FE, Midthune D, Subar AF, Kipnis V, Kahle LL, Schatzkin A. Development and evaluation of a short instrument to estimate usual dietary intake of percentage energy from fat. *J Am Diet Assoc* 2007;**107**:760-767.
74. Havas S, Heimendinger J, Damron D, Nicklas TA, Cowan A, Beresford SA, et al. 5 A Day for better health--nine community research projects to increase fruit and vegetable consumption. *Public Health Rep* 1995;**110**:68-79.
75. Thompson FE, Kipnis V, Subar AF, Krebs-Smith SM, Kahle LL, Midthune D, et al. Evaluation of 2 brief instruments and a food-frequency questionnaire to estimate daily number of servings of fruit and vegetables. *Am J Clin Nutr* 2000;**71**:1503-1510.
76. Hedrick VE, Savla J, Comber DL, Flack KD, Estabrooks PA, Nsiah-Kumi PA, et al. Development of a brief questionnaire to assess habitual beverage intake (BEVQ-15): sugar-sweetened beverages and total beverage energy intake. *J Acad Nutr Diet* 2012;**112**:840-849.
77. Stunkard AJ, Messick S. *Eating Inventory Manual*. San Antonio, TX: The Psychological Corporation; 1988.
78. Bennett WL, Wang NY, Gudzone KA, Dalcin AT, Bleich SN, Appel LJ, et al. Satisfaction with primary care provider involvement is associated with greater weight loss: Results from the practice-based POWER trial. *Patient Educ Couns* 2015.
79. Hargraves JL, Hays RD, Cleary PD. Psychometric properties of the Consumer Assessment of Health Plans Study (CAHPS) 2.0 adult core survey. *Health Serv Res* 2003;**38**:1509-1527.
80. Beach MC, Keruly J, Moore RD. Is the quality of the patient-provider relationship associated with better adherence and health outcomes for patients with HIV? *J Gen Intern Med* 2006;**21**:661-665.
81. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap) - A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;**42**:377-381.
82. Li W, Wang Y, Chen L, Horswell R, Xiao K, Besse J, et al. Increasing prevalence of diabetes in middle and low income residents in Louisiana from 2000 to 2009. *Diab Res Clin Pract* 2011;**2011**:262-268.
83. Wadden TA, West DS, Neiberg RH, Wing RR, Ryan DH, Johnson KC, et al. One-year weight losses in the Look AHEAD study: factors associated with success. *Obesity (Silver Spring)* 2009;**17**:713-722.
84. Rubin DB. *Multiple imputation for nonresponse in surveys*. New York: John Wiley and Sons, Inc.; 1987.
85. Huang X, Jiao L, Wei L, Quan H, Teoh L, Koch GG. Missing radiographic data handling in randomized clinical trials in rheumatoid arthritis. *J Biopharm Stat* 2014;**23**:1435-1452.

20. Appendices

Appendix A: PROPEL Forms and Questionnaires

Appendix B: Lifestyle Intervention

Appendix C: PROPEL Recruitment Materials