Protocol

Jump Starting Shared Medical Appointments for Diabetes with Weight Management

Funding Agency
HSR&D

Principal Investigator
William S Yancy, Jr, MD, MHSc

MIRB # **01794**

Submission
Version 1: September 18, 2013
Version 2: December 18, 2013
Version 3: May 7, 2014
Version 4: September 19, 2014
Version 5: January 23, 2015
Version 6: March 19, 2015
Version 7: October 8, 2015
Version 8: March 3, 2016
Version 9: June 14, 2016
Version 10: August 25, 2016
Version 11, September 22, 2016
Version 12, January 20, 2017

Purpose

Shared medical appointments (SMAs), a subtype of group medical visits, are a health care system redesign that show promise for providing efficient, high-quality health care. SMAs involve groups of patients who share a common chronic condition and meet over time to receive education, self-management enhancement, and medication management to improve clinical outcomes. Veterans Affairs (VA) Quality Enhancement Research Initiative's (QUERI) Evidence-based Synthesis Program (ESP) recently reviewed the extant literature regarding SMAs for chronic medical conditions and found moderate strength of evidence of effectiveness for modestly improving glycemic control (hemoglobin A_{1c} mean difference = -0.55, 95% CI -0.99 to -0.11) and blood pressure (systolic BP mean difference = -5.2, 95% CI -7.4 to -3.1) in patients with diabetes.[1] Based on results from these prior trials, several of which were performed in VA healthcare settings, Veterans Health Administration (VHA) is implementing SMAs for multiple risk factor control in patients with type 2 diabetes at selected sites.

SMAs are advantageous because they provide education and teach patients self-management skills such as self-monitoring of blood glucose and foot care. However, SMAs have some disadvantages. For one, the primary method through which they have improved hemoglobin A_{1c} is via medication intensification, which can have undesirable side effects such as weight gain and hypoglycemia that may attenuate the macrovascular benefits of glycemic control, as noted in several large clinical trials.[2-4] Another disadvantage of SMAs is that they inadequately address weight loss or weight control strategies. Weight management is critical in patients with type 2 diabetes because it is a potent predictor of improved glycemia[5-8] and has been associated with lower risk for certain complications of diabetes, independent of glycemic control.[9, 10] Because dietary changes, physical activity and resulting weight loss can improve glycemic control while reducing antiglycemic medication needs, subsequent risk for hypoglycemia may be lower.[7, 11, 12]

These findings converge to suggest that SMAs may be more beneficial in affecting a range of diabetes outcomes if supplemented with a weight management component. In addition to improving diabetes outcomes and lowering weight, such a combined intervention could ultimately result in lower antiglycemic medication needs, leading to fewer hypoglycemic events and other side effects. This intervention strategy may be ideal for patients with uncontrolled diabetes because weight loss can be more difficult than in non-diabetic patients, and because their diabetes care needs, including medication management, require additional attention that many weight loss programs are unable to provide.

In this 2-arm randomized controlled trial (RCT), 308 overweight patients with type 2 diabetes from VA outpatient clinics will participate in traditional SMAs focused primarily on medication management and self-management skills (SMA) or in SMAs that additionally include a weight management component (WM/SMA). The weight management component is based on a group-based intervention we have developed that effectively induces weight loss and improves glycemic control and blood pressure to a similar degree as SMAs but while reducing medications.[13] Based on this knowledge, we hypothesize that WM/SMA will be non-inferior for glycemic control but more effective at reducing hypoglycemic events, antiglycemic medications, weight and costs compared to SMA alone. Outcomes will be assessed at baseline and at 16, 32, and 48 weeks. We will test the following hypotheses from baseline to 48 weeks of follow-up:

(H_1) Mean hemoglobin A_{1c} at 48 weeks in the WM/SMA group will be less than 0.5% higher (non-inferiority limit) than in the SMA group.
(H_2) Hypoglycemic events will occur less in the WM/SMA group than in the SMA group.
(H_3) Antiglycemic medication use will be less in the WM/SMA group than in the SMA group.
(H_4) Weight loss will be greater in the WM/SMA group than in the SMA group.
(H_5) The WM/SMA intervention will be cost-effective compared with the SMA intervention.

The goal of this program of research is to identify effective and cost-effective weight management programs that can improve diabetes outcomes, decrease medication burden and reduce complications. Positive results from this study could expand the options available for management of diabetes and potentially lead to the re-emphasis of the lower glycemic targets that appear to reduce diabetes complications.

Background

Uncontrolled type 2 Diabetes is Debilitating and Costly. Diabetes is a debilitating, deadly, and costly disease.[14, 15] In the United States, diabetes is a leading cause of blindness, kidney failure, and non-traumatic lower-limb amputations.[14] Patients with diabetes have a 2-4 times increase in risk for death from heart disease or stroke compared with non-diabetic patients. In 2012, the cost of care for diabetes totaled $245 billion, including $176 billion in direct medical costs, which is 2.3 times higher than costs in people without diabetes.[15]

Compared with type 1 diabetes, type 2 diabetes is by far more prevalent (90-95% of cases) and is closely associated with obesity; 80-90% of patients with type 2 diabetes are overweight or obese.[14] The prevalence of obesity has increased dramatically over the past 25 years with over 69% of adult Americans currently classified as overweight or obese.[16] This obesity epidemic is the major cause for the parallel rise in prevalence of type 2 diabetes, currently estimated at 8.3% in the US.[17] The rates of both overweight/obesity (75% in a Veteran population sample) and diabetes (24% of VHA users), and their complications, are as high or higher in US Veterans than they are in the general population.[18-20]

Observational studies have convincingly demonstrated that lower versus higher glycemia is related to reductions in both microvascular and macrovascular complications of diabetes. An observational analysis of the United Kingdom Prospective Diabetes Study (UKPDS) found that each 1% reduction in updated mean hemoglobin A_{1c} was associated with reductions in risk of 37% for microvascular complications, 21% for deaths related to diabetes and 14% for all-cause mortality.[21] A meta-analysis of prospective cohort studies demonstrated that a 1-percentage point decrease in hemoglobin A_{1c} translated into an 18% risk reduction for incident cardiovascular disease or stroke.[22] As a result, improved glycemic control has been a focus of diabetes management, not only for prevention of acute complications such as infection, ketoacidosis, and hyperosmolar coma but also for the long-term complications.

Despite this knowledge, glycemic control has persistently been suboptimal in a substantial percentage of the population. For example, the percentage of Americans with diabetes whose hemoglobin A_{1c} was above 7% in 2003-4 was 43%.[23] *In recent estimates for the VA, 16% of patients with diabetes have hemoglobin A_{1c} above 9%, a level of hyperglycemia that puts patients at risk for short-term and long-term complications of diabetes.*[19]

Glycemic Management Improves Health Outcomes in Patients with Type 2 Diabetes. The importance of glycemic management in patients with type 2 diabetes was demonstrated in the United Kingdom Prospective Diabetes Study (UKPDS).[2] In UKPDS, antiglycemic agents such as sulfonylureas and insulin were used to lower hemoglobin A_{1c} to a mean of 7.0% (compared with 7.9% for control), resulting in lower rates of diabetes-related microvascular complications (e.g., retinopathy, nephropathy) but not the macrovascular complications that more commonly lead to mortality. More recent trials have shown that striving for even lower hemoglobin A_{1c} targets (below 6.0-6.5%) still does not result in improved macrovascular outcomes.[3, 4] Diabetes medication intensification strategies lead to weight gain and hypoglycemia, both of which may increase risk for mortality and therefore offset benefits that might accrue from glycemic control.[2, 4] As a result, a more moderate goal of hemoglobin A_{1c} <7% remains the recommendation of VA/Department of Defense and American Diabetes Association (ADA), and will be the goal for the proposed study.[5, 8]

What has been less emphasized during debates about appropriate glycemic targets are the long-term results from UKPDS and results from a smaller trial within UKPDS which tested metformin.[24, 25] After 10 years of follow-up in the main UKPDS trial, and despite dissipation of any hemoglobin A_{1c} difference between the two groups one year after the end of the original trial, the group treated with intensive therapy during the study had lower risk for any diabetes outcome, myocardial infarction, and all-cause mortality. More importantly, a subset of overweight patients recruited into the original UKPDS was randomized to intensive therapy with metformin (instead of sulfonylurea or insulin) versus control (no medication). In this study, glycemic control with metformin did not lead to weight gain, led to lower rates of hypoglycemic events relative to other intensive therapies, and led to lower rates for microvascular *and* macrovascular events. In the 10 year follow-up study, these benefits persisted. *In other words, minimizing weight gain and hypoglycemic events while improving glycemic control maximizes the desired outcome of reducing microvascular and macrovascular events.*

Glycemic and Blood Pressure Control Can Be Achieved Via Shared Medical Appointments (SMAs).

SMAs involve groups of patients who share a common chronic condition and meet over time to receive education, self-management enhancement, and medication management to improve clinical outcomes. The strategy is efficient because education that is appropriate for all patients with a certain condition can be delivered to a group of patients rather than one at a time. Break-out sessions are used to provide individualized counseling such as medication adjustment. During the break-out sessions, patients remaining in the group can exchange self-management strategies and provide each other social support.

Investigators from our Center who are part of the VA Quality Enhancement Research Initiative (QUERI) Evidence-based Synthesis Program (ESP) recently reviewed the literature regarding SMAs for chronic conditions and found 16 studies (comprising 13 trials) that evaluated SMA interventions in patients with diabetes. SMAs were generally led by teams of 1 to 3 clinicians, usually including a physician and/or a registered nurse, and typically targeted patients with poor glycemic control. Sessions typically involved fixed patient panels with individual breakouts for medication management with a visit frequency ranging from every 3 weeks to every 3 months and follow-up from 4 to 48 months. Group size was typically 6 to 10 members but included up to 25 members. In all studies, SMAs were compared to usual care or mildly enhanced usual care.

The review found moderate strength of evidence of effectiveness for modest improvement of glycemic control (hemoglobin A_{1c} mean difference = -0.55, 95% CI -0.99 to -0.11) and blood pressure (systolic BP mean difference = -5.2, 95% CI -7.4 to -3.1) in patients with diabetes. 'Moderate' strength of evidence refers to variability in the effect and means that further research is likely to have an impact on our confidence in the estimate of effect and may change the estimate. Five studies reported large improvements (albeit low strength of evidence) in health-related quality of life (standardized mean difference = -0.84; CI, -1.64 to -0.03), with greater effects noted in studies using a disease-specific measure. In five studies examining hospital or emergency room admissions, rates tended to be lower with SMAs but were statistically significant in only a few instances and a meta-analysis was not performed.

Although the SMA programs almost universally included education regarding diet and physical activity, medication intensification was the primary strategy. In fact, weight was reported in only 5 of the 13 trials, changed minimally (+0.2 to -1.4 kg) and was significantly lower than in the control condition in only 1 trial. *SMAs have effectively lowered glycemia and improved other important diabetes outcomes but have not been combined with first line therapy for diabetes: intensive diet and weight management.*

Weight Management Improves Health Outcomes.

Based on the health benefits, weight loss via a high-intensity educational and behavioral intervention (defined as at least 2 individual or group face-to-face sessions per month for at least the first 3 months) is recommended by the U.S. Preventive Services Task Force (USPSTF), and even more intensive counseling (up to 21 sessions over 1 year) is now covered by Centers for Medicare & Medicaid Services (CMS).[26] The health benefits are numerous. A meta-analysis of 25 randomized, controlled weight loss intervention studies demonstrated that a 5.1 kg weight loss decreases systolic blood pressure by an average of 4.4 mm Hg and diastolic blood pressure by 3.6 mm Hg.[27] Weight loss also improves arthritis and functional status; overweight women who lost approximately 5 kg reduced their odds for developing knee osteoarthritis by over 50% over 10 years of follow-up.[28, 29] A systematic review of the impact of weight loss on health and economic outcomes concluded that several weight loss interventions are cost-effective, and some interventions may even be cost-saving, in targeted populations.[30] *Salient to this proposal was that weight loss interventions were found to be cost-effective even though the analyses focused on cost savings related to diabetes only.*

Supplementing SMAs with Weight Management Could Improve Health Outcomes Further.

One of the best indicators of the powerful effect of weight loss on diabetes comes from Diabetes Prevention Program (DPP) study, in which a mean weight loss of 5.5 kg in patients at risk for diabetes resulted in a 58% reduction in the incidence of diabetes over approximately 3 years.[31] In the DPP, lifestyle modification was more effective than metformin for preventing diabetes incidence, and of the three main lifestyle intervention recommendations (reduce fat intake, increase physical activity, and lose weight), weight loss was primarily responsible for this effect.[32] Another strong indicator of the effect of weight loss on diabetes is the evidence that weight loss medications, which effectively work by reducing calorie intake, lead to improved glycemia compared with placebo.[12]

Another important example of the weight loss effect on diabetes outcomes is the LookAHEAD trial, which focused on patients with diabetes. LookAHEAD showed that a mean difference of -7.9% weight loss (intensive lifestyle intervention compared to usual care) at 1 year resulted in significantly greater improvements in hemoglobin A_{1c} (-0.5%), blood pressure (-4.0 and -1.2 mm Hg for systolic and diastolic, respectively), HDL cholesterol, triglycerides, and albumin:creatinine ratio.[33] These benefits remained at 4 years despite mild weight regain in the intensive lifestyle intervention group.[34] Although the study was recently stopped early because the primary outcome (major cardiovascular disease [CVD] event rates) was unlikely to become different between arms, pursuing weight management in patients with type 2 diabetes remains important for several reasons. First, CVD event rates in LookAHEAD were much lower than expected, limiting its ability to detect benefits from weight loss.[35] Second, LookAHEAD noted improvements in other pertinent outcomes (e.g., sleep apnea, depression, urinary incontinence, health-related quality of life).[36-39] Lastly, LookAHEAD used a high carbohydrate diet, but diets that lower carbohydrate intake appear more effective for improving glycemia and, in particular, reducing antiglycemic medication. Nevertheless, LookAHEAD demonstrates that *weight management in patients with type 2 diabetes improves glycemic control and several other health-related and patient-oriented outcomes.*

Lowering Dietary Carbohydrate Intake Reduces Weight and Glycemia. Randomized, controlled trial (RCT) data provide evidence of the effectiveness and safety of low carbohydrate diets (LCDs) for up to 2 years duration.[40, 41] Meta-analyses[42, 43] of trials totaling over 2500 primarily healthy participants indicate that the LCD is effective for weight loss, beneficial for serum lipids and blood pressure, and has not resulted in a disproportionate amount of serious adverse events. In these studies, the LCD typically led to greater weight loss than comparison diets for durations up to 6 months, and sometimes greater weight loss in studies of longer durations.

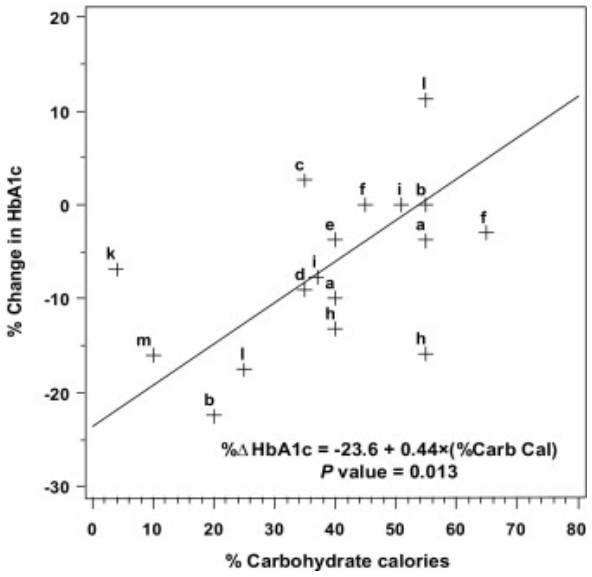

Figure 1. Correlation between % Change in HbA1c and % Daily Calories from Carbohydrate. Source: Kirk JK et al. *J Am Diet Assoc*, 2008.

There are physiologic reasons for lowering carbohydrate intake in patients with diabetes. Feeding studies show that lowering carbohydrate content in a meal can dramatically lower the glycemic response.[44] Clinical trials have shown beneficial effects of the LCD on glycemia over longer durations. A meta-analysis showed that greater decreases in carbohydrate intake were associated with greater decreases in hemoglobin A_{1c} (**Figure 1**).[11] An updated review by the ADA found additional evidence for improvement in glycemic parameters from LCDs in patients with diabetes.[45] Further, the review noted that antiglycemic medications were more frequently lowered with an LCD versus comparison diets. *In our experience (see Section B.9.1.4.), weight loss via reduction of dietary carbohydrate intake has resulted in improved glycemic and blood pressure control and decreased medications for these health parameters.*

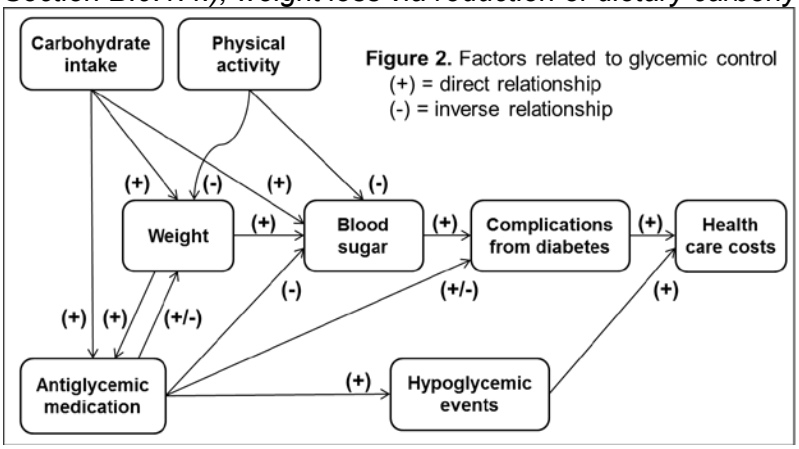

Figure 2. Factors related to glycemic control
(+) = direct relationship
(-) = inverse relationship

Conceptual Model for Improved Diabetes Outcomes

The conceptual model (**Figure 2**) describing how diabetes outcomes might improve with the WM/SMA intervention is based on clinical and physiologic concepts described previously in this proposal. The primary factors that impact glycemia (blood sugar), that is, carbohydrate intake, physical activity, weight, and antiglycemic medication, will be the focus of intensive counseling in the WM/SMA arm. In contrast, the SMA alone arm will receive intensive counseling

regarding antiglycemic medication but the other factors will be covered more generally and less intensively. The model demonstrates how reducing blood sugar could lead to fewer complications from diabetes and therefore, lower health care costs. Alternatively, antiglycemic medications may reduce some complications from diabetes (e.g., retinopathy) but not others (e.g., cardiovascular disease), and may increase weight and the frequency of hypoglycemic events, leading to higher health care costs.

Chronic Care and Cooperative Health Care Clinics (CHCC) Models as a Framework.
SMAs are based in the core concepts of the Chronic Care Model (CCM), which has been successfully used for improving management of complex chronic diseases like diabetes.[46] The CCM provides a framework of 6 interrelated structural components used to enhanced disease management and care delivery: community resources and policies, organization of health care, delivery system design, decision support, clinical information systems, and self-management support. Addressing any of these components can improve interactions among the patient and the health care team leading to better health care delivery, disease management, and outcomes; the proposed SMA intervention, included in both arms of the study, takes advantage of several of these components, with delivery system design and self-management support being the components of primary focus..

SMAs are a *delivery system design* that offers several advantages over traditional one-on-one provider-patient appointments. Because key topics are comprehensively covered in a group setting, SMAs can more efficiently and completely deliver evidence-based, proactive counseling messages and clinical case management strategies common to a particular health problem like diabetes or overweight. Additionally, SMAs can effectively allow multi-disciplinary staff (provider, nurse, assistant) to work within defined roles to help the patient focus on one problem (diabetes or overweight) and minimize distractions of competing individual problems while enhancing the opportunity to overcome barriers to health improvement via knowledge and experience from topic experts and peer patients. *Self-management support* is another key component of SMAs for diabetes with discussion topics covering home blood glucose and weight monitoring, medication adjustment, and foot care. The SMA delivery system design also allows unique opportunities for problem-solving, professional and peer support, and frequent follow-up, enhancing behavior change and monitoring of progress toward goals. *Clinical information systems* will be used to develop a registry of eligible patients for recruitment purposes; we have identified a large subsample of overweight patients with diabetes (see **Section D.3.5.** and **Table 1**) at Durham VAMC who will be invited to participate. *Decision support* is incorporated into the intervention in the form of diabetes management guidelines that will be discussed and acted upon during meetings, and medication management algorithms that will be used to guide therapy. *Community resources* will be enhanced primarily by enhancing awareness and social support via counseling regarding healthy food shopping, provision of lists of locally available exercise facilities/venues, further input from peer patients and by allowing spouses or significant others to attend the meetings.

The proposed intervention is specifically derived from the Cooperative Health Care Clinics (CHCC) model which combines the self-management benefits gained from traditional support groups and group education sessions with a health care delivery redesign that provides access to a multispecialty team that makes clinical care decisions during the visit.[47] This model is ideal for the planned combined weight and diabetes management intervention because group face-to-face interventions are frequently superior to other modes of weight management intervention delivery, resulting from the social and educational support derived from other members in the group. Additionally, clinical care decisions can be made efficiently in patients with diabetes who need more frequent monitoring and medication adjustment during weight loss.

Preliminary Research
Clinical Trials of the LCD Performed by the Research Team (Yancy). We have accomplished several projects examining the LCD and low fat, reduced-calorie diet (LFD) as treatments for obesity, diabetes, hyperlipidemia, and other metabolic disorders, and their effects on health-related quality of life.[48-52]

Single-Arm Trial of the LCD. Our first trial of the LCD was a single-arm pilot study in 51 healthy, overweight volunteers (mean age 44 years, mean BMI 31 kg/m^2).[48] Participants were instructed to restrict carbohydrate intake to <20 g initially, and methodically add carbohydrates back into their diet as goal body weight was approached; energy intake was not restricted. In the 41 participants who completed the 6-month study, the

mean weight loss was 9.0 ± 5.3 kg (-10.3% ± 5.9% of initial body weight, p<0.001). Beneficial effects were seen on serum fasting lipid profiles: high-density lipoprotein cholesterol (HDL-C) increased 19% (p<0.001), LDL-C decreased 7% (p=0.01), and triglyceride decreased 43% (p<0.001). No serious adverse events occurred, although participants reported symptomatic side effects such as constipation and headache. *The LCD was effective for weight loss and improved serum lipids but was associated with minor side effects that may require clinical attention in order to improve diet adherence.*

LCD versus an LFD in Participants with Hyperlipidemia. In a randomized trial, we compared the LCD with an LFD in healthy, hyperlipidemic individuals over 6 months.[50] The mean age of the 119 participants was 45 years and mean BMI was 34 kg/m^2; 75% were women and 77% were White. The mean weight loss was substantial for both diet groups, but greater in the LCD group (LCD –12.0% vs. LFD –6.5%, p<0.001). In addition, fasting serum triglycerides and HDL-C improved more in the LCD than in the LFD. *This study demonstrated substantial weight loss and beneficial metabolic effects from the LCD in relatively healthy participants over 6 months. Questions remained regarding the LCD's longer term effects in patients who might benefit the most from weight loss, those with diabetes, CHD, and other illnesses common to VA patients.*

LCD in Participants with Type 2 Diabetes. In a pilot study, we followed 28 Durham VAMC overweight outpatients with type 2 diabetes for 4 months.[49] To prevent hypoglycemic episodes, antiglycemic medications were reduced at diet initiation. Twenty-one participants (75%) completed the study. From week 0 to week 16, the primary outcome, hemoglobin A_{1c}, decreased significantly from 7.5 ± 1.4% to 6.3 ± 1.0% (p<0.001). This occurred while medications for diabetes were eliminated in 7 participants, reduced in 10, and unchanged in 4.

Next, we performed a randomized, parallel-design trial comparing the LCD to a low-glycemic index diet (LGID) over 6 months. Eighty-four community volunteers with obesity-related type 2 diabetes were randomized to either the LCD or a low-glycemic, reduced-calorie diet (500-1000 kcal/day deficit; approximately 55% of daily caloric intake from carbohydrate). Blood glucose and blood pressure medications were managed by a physician according to a pre-specified algorithm; in contrast with medication management in SMAs, however, the primary goal was to reduce medication to aid weight loss. Mean age was 52 years; 79% were women and over 40% were of minority race. The LCD led to greater reduction in weight, antiglycemic medication and hemoglobin A_{1c} compared with the LGID. *These studies gave the PI experience managing patients with diabetes as they received focused dietary interventions for weight loss. While glycemic control improved, it was not the primary aim of these studies. Moreover, not all of the participants were out of control at baseline nor were they all taking antiglycemic medication.*

LCD versus LFD+Orlistat. In a VA-funded study (VA CLIN-5-03F, PI-Yancy), we compared the LCD to the LFD plus orlistat for weight loss and metabolic changes over 1 year in 146 medical outpatients from the Durham VAMC.[13] Enrollment for this study was reached within our targeted timeframe of 1 year. We assessed 525 individuals for eligibility; 280 were screened in the clinic, 160 were randomized, and 146 attended the first group intervention session. Of this enrolled sample, mean age was 52 years and mean BMI was 39.3 kg/m^2; 41 (28%) were women, 81 (55%) were Black, and 46 (32%) had type 2 diabetes. Fifty-seven (79%) LCD and 65 (88%) LFD+O participants completed 48 weeks, a high completion rate for a weight loss study even though we offered no monetary compensation for research participation. Weight loss was substantial but similar in the two groups (LCD: -9.5%, LFD+O: -8.5%; p=0.6), and blood pressure improved more in the LCD than the LFD+O group (systolic: -5.9 vs. 1.5 mm Hg; diastolic -4.5 vs. 0.4 mm Hg; p<0.001 for both comparisons).

In a subgroup analysis of patients with type 2 diabetes, weight loss was less than in the overall sample (LCD: -6.7%, LFD+O: -7.3%). Nevertheless, hemoglobin A_{1c} improved in the LCD group, and to a greater degree than in the LFD+O group (-0.7% vs. +0.2%, difference -0.8%, 95% CI -1.6, -0.02). Moreover, an antiglycemic medication summary score, based on medication potency and total daily dose, decreased by over 50% in a greater proportion of LCD than LFD+O participants (71% vs 30%, p=0.01). *This study highlights the weight loss struggles that patients with diabetes experience, and the medical supervision they require during weight loss. The proposed WM/SMA intervention is modeled closely after this study in regard to personnel, facilities, recruitment methods, outcome assessment, and dietary approach.*

Shared Medical Appointments in Patients with Diabetes (Edelman).
Dr. Edelman led a randomized controlled trial at two VAMCs of SMAs on which the SMA intervention in this proposal is based.[53] In this trial, 239 VA outpatients with uncontrolled diabetes received the SMA intervention or usual care. The SMA intervention was based on the Cooperative Health Care Clinics (CHCC) model (see **Section B.8.**). SMAs occurred every 2 months for 12 months and consisted of discussion topics pertinent to diabetes management, review of clinical data, and medication management. The SMA intervention improved systolic blood pressure 7 mmHg and LDL-cholesterol by 9 mg/dl compared to usual care, and there was a modest, not statistically significant between-groups improvement in hemoglobin A_{1c} (mean difference -0.3%; 95% CI -0.8, 0.1; p=0.16). The economic analysis showed statistically significant reduction in per patient cost and fewer hospitalizations in the second year after the end of the intervention when compared to usual care. For the proposed study, we have enhanced the SMA intervention in two ways based on the most successful SMA interventions included in the VA QUERI ESP systematic review (see **Section B.3.**): 1) we increased the number of sessions from 7 to 9 visits over 1 year, increasing the frequency to every 4 weeks in the first 16 weeks when increased monitoring and feedback may be most important and 2) we will allow the participant to invite his/her spouse or another family member, a strategy that has been successful in our prior research and prior SMA studies. *This study demonstrated feasibility, acceptability, and effectiveness of the SMA intervention at Durham VAMC and is the basis for the SMA intervention.*

DESIGN
This study is a randomized, two-arm trial of 308 participants followed over a 48-week period (**Figure 3**). The WM/SMA group will receive dietary and weight management counseling every 2 weeks for 16 weeks followed by diabetes counseling and medication management every 8 weeks for the remaining 32 weeks; weight management will be addressed briefly at these latter meetings to enhance maintenance of initial weight loss. The SMA group will receive diabetes counseling and medication management every 4 weeks for 16 weeks with continuation of this counseling every 8 weeks for the remaining 32 weeks.

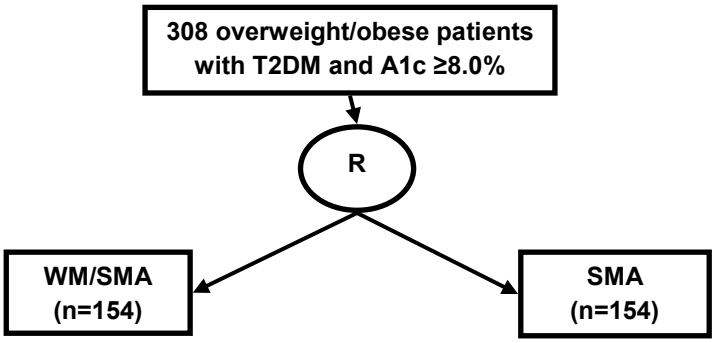

Figure 3. Study Design

Justification of Key Design Features.
Justification of Using SMA as the Comparator Intervention. Usual care controls are appropriate for establishing the efficacy of novel interventions. This study assesses the comparative effectiveness of two interventions known to be effective for glycemic control. Therefore, implementing a usual care arm would not be an ethical control. Our goal in comparing two efficacious interventions is to assess the comparative effectiveness of two viable strategies for diabetes management while examining possible advantages of the WM/SMA intervention over the SMA alone intervention such as fewer adverse effects (i.e., hypoglycemic events), reduced need for diabetes medication, lower costs, and improved health-related quality of life. The WM/SMA intervention may ultimately demonstrate greater improvement in glycemic control over SMA alone; however, even if the study shows similarity between the two arms in this primary outcome, we believe that improvements in the secondary outcomes will deem this a more desirable intervention than SMA alone for patients, providers, and the healthcare system.

Although the SMA intervention did not significantly improve glycemic control over usual care in our previous study, we have chosen it as the comparator for the following reasons. SMAs for diabetes care are being implemented and increasingly emphasized with VA's Patient-Aligned Care Teams (PACT) initiatives and therefore may become standard of care.[46] Because the combined intervention requires more frequent visits than typical SMAs, adoption of the combined intervention will require demonstration that it is superior to an SMA intervention as opposed to usual care. Finally, we have enhanced the SMA intervention in two ways based on other successful SMA interventions found in the VA QUERI EPC review: 1) we increased the number of sessions as described above and 2) we will allow the participant to invite his/her spouse or another family member, a strategy that has been used successfully in our prior weight loss studies and prior SMA studies.

Justification of Intervention Meeting Frequencies. The WM/SMA intervention meeting frequency is based on current evidence, guideline recommendations and contemporary health care coverage. The U.S. Preventative Services Task Force (USPSTF) evidence report that was performed for the obesity screening guideline indicated that weight loss interventions of low or moderate intensity are variably effective;[26] therefore, the guideline recommends only high-intensity counseling interventions, defined as at least 2 individual or group face-to-face sessions per month for at least the first 3 months.[54] Meeting frequency in our prior studies has been every 2 weeks for the first 3-6 months.[13, 50] Thus, the WM/SMA intervention fits with current standards and our prior research. The intervening meetings that exist in the WM/SMA arm but not in the SMA arm will focus on weight management only; the timing of monitoring non-weight outcomes (e.g., blood pressure) and delivering medication management will happen in parallel with the SMA intervention meetings.

The SMA intervention meeting frequency is based on our previous trial but with increased frequency in the beginning of the intervention--every 4 weeks in the first 16 weeks followed by every 8 weeks (instead of every 8 weeks throughout). The reasons for a higher visit frequency at the beginning were twofold. The first reason is to enhance effectiveness for lowering glycemia and is based on the observation that many of the successful SMA interventions in the systematic review met monthly in the first 6 months. We felt that increased monitoring and feedback is most important at the beginning of the intervention. The second reason is that it allows a parallel decrease in meeting frequency at the 16 week time point in both arms.

RISK/BENEFIT ASSESSMENT

Potential Risks.

The benefits of the intervention strategy outweigh the risks. Subjects enrolling in the study with a diagnosis of diabetes are already at increased risk for many complications of diabetes (e.g., hypoglycemia, infections, foot ulcers), and increased risk of blindness, kidney failure, and non-traumatic lower-limb amputations. Patients with diabetes have a 2-4 times increase in risk for death from heart disease or stroke compared with non-diabetic patients. Weight management is already considered first line therapy for overweight patients with diabetes, and antiglycemic adjustment with and without attention to weight loss is another mainstay of glycemic management, which reduces the acute and chronic complications from diabetes. However, there are still potential risks associated with the low carbohydrate diet (LCD) and medication management.

Much of the potential risk associated with the LCD results from its macronutrient composition. In epidemiological research, diets that are high in saturated fat and cholesterol have been shown to elevate LDL-C, a risk factor for CHD. While few individual trials have shown the LCD to result in LDL-C elevations, a meta-analysis of several RCTs noted a mild increase. Therefore, we will monitor serum fasting lipid profiles every 4 months. In addition, serum sodium, potassium, chloride, bicarbonate, urea nitrogen, creatinine, glucose, and calcium will be performed at week 2 and at the other time points to monitor for electrolyte abnormalities and dehydration. Results will be reported in the electronic medical record (CPRS) for both the research personnel and clinical providers to view.

Progression of chronic kidney disease may be hastened by a high-protein diet, however, an observational study did not show that a high-protein diet adversely affected kidney function in participants with normal kidney function at baseline.[55] Because the potential for an adverse effect remains, kidney function must be normal at baseline (serum creatinine <1.5 mg/dL in men, <1.3 mg/dL in women) and will be monitored by serum tests every 4 months.

Other potential risks include hypoglycemia and hypotension. Participants in the WM/SMA group who are taking hypoglycemic or anti-hypertensive agents may require dosage adjustments at diet

initiation to avoid hypoglycemia or hypotension. Participants in both groups may require dosage adjustments during the study to avoid these complications. Participants will be counseled on how to recognize and respond to these symptoms. In addition, the study physician will be on call at all times to assist with any symptoms that occur. Patients in both groups will meet with the study physician and study staff to review their blood sugar logs and blood pressure readings and will be instructed to record their blood glucose measured by glucometer at least twice a day (AM fasting and 2 hours post prandial to the largest meal) to monitor for hypoglycemia that may result from weight loss, calorie reduction, and potentially increased activity level.

Other potential adverse effects of the LCD include nephrolithiasis and increased bone turnover. The potential for these side effects is derived from pathophysiologic theory, from studies of the LCD using intermediate endpoints, and from extrapolation from similar diet approaches such as the ketogenic diet for epilepsy. Because kidney stones and bone fractures have not been reported as an actual adverse effect of the LCD in the literature, we cannot estimate their frequency. We will be recording all adverse events that occur during the study and thus will know if rates of kidney stones or bone fractures are different between the intervention groups, but we will not be performing highly-sensitive testing (e.g. computerized tomography, markers of bone turnover, DXA) for these potential adverse effects due to their substantial cost. Finally, several minor adverse effects may occur including orthostatic hypotension, constipation, headache, halitosis, muscle cramps, diarrhea, general weakness, and rash. Most of these occur at diet initiation, are short-lived, and are generally alleviated by adequate fluid intake and other minor diet modifications, which will be emphasized during the weight management intervention.

Adequacy of Protection from Risks

Protection Against Risk. In addition to the planned procedures for minimizing risk to participants above, estimates of the quantity of risk are given when data is available and the likely effectiveness of procedures to minimize risk is discussed when appropriate. In the event of an adverse effect necessitating medical or professional intervention, referral to the participant's primary care provider or an appropriate specialist will occur. In emergency situations when a participant contacts one of the research personnel first, the particular research staff member will either make contact with emergency personnel or advise the participant to do so immediately and follow-up with the emergency personnel to ensure communication of the study interventions and their associated risks.

Additionally, a Data Monitoring Committee (DMC) consisting of the study statistician and two additional members (at least one will be a physician with experience in diabetes care and at least one will have research experience) who are independent of the study team, will review the clinical data routinely with safety as its primary objective. A study physician will be on call at all times. Hypoglycemic events and other clinical adverse effects will be recorded at each visit using standardized, self-administered forms. In addition, patients will monitor hypoglycemic episodes by testing twice daily at home. All adverse events will be reported to the IRB according to local IRB requirements. There are a wide variety of cardiac and endocrine events that are anticipated due to the study population. The DMC will also review adverse events, screening, enrollment, and data collection reports at each study meeting to maximize the efficiency of recruitment and the validity of the data. Meeting frequency will be determined by the members of the DMC but will occur at least yearly.

In regard to participant confidentiality, research personnel will use only those parts of the medical record necessary to determine eligibility and follow the research protocol. Measures will be taken to ensure confidentiality during group sessions, including a patient group visit contract agreeing to treat all information discussed in the group confidential from participants and non-participants (e.g., spouses, significant others).

Potential Benefit of the Proposed Research to the Subject and Others

Weight loss can result in improvements in quality of life, pain, blood pressure, glycemia, and hyperlipidemia. By reducing body weight, patients may reduce the incidence and complications of diabetes as well as the medications used to treat diabetes and prevalent associated illnesses (e.g., hypertension, arthritis). Patients in both groups are expected to benefit from frequent visits for

education and medication management for diabetes and group support during shared medical appointments.

Importance of the Knowledge to be Gained

Knowledge gained from the study could change current practices in diabetes care. Most VA hospitals do not yet offer weight management strategies targeting patients with diabetes, yet this patient population is arguably most in need of weight loss and has the highest requirement for medical supervision during weight loss. As a testament to the unique needs of patients with diabetes, and that these needs lend themselves well to the efficiency and social support advantages of group interventions, shared medical appointments for chronic disease have most commonly been attempted, and successful, in patients with diabetes. As a result, VHA is implementing shared medical appointments at selected sites. Another testament to their unique needs is that patients with diabetes, or patients with more severe diabetes, are frequently excluded from weight loss studies. A combined weight and medication management intervention has the potential for substantially improving disease parameters more than either approach alone. Such an intervention also has potential for reducing the many complications of diabetes (e.g., hypoglycemia, infections, foot ulcers) and therefore emergency room visits and hospitalizations. Finally, this combined intervention could dramatically improve health-related quality of life as glycemia and blood pressure become better controlled in the setting of weight loss and medication management that does not universally add to the regimen and escalate doses.

SELECTION OF SUBJECTS

We will screen and consent individuals until we meet the desired sample of 308 subjects. Women and men are eligible for participation; however, because the majority of Veterans are male, we expect the majority of participants to be male. This will preclude sex-specific analyses. Minorities are also eligible. The general patient population at the Durham VAMC is approximately 60% White and 40% non-white, primarily Black. In our previous study, we recruited 53% non-white participants using similar procedures as those proposed in the current study. Thus, we expect to recruit a significant number of minorities. Children are not eligible for participation per VA guidelines.

We will monitor subject recruitment and enrollment on a weekly basis to ensure that we are on track to meet our target goals. Recruitment will take place in 5 waves resulting in 5 cohorts of approximately 62 participants with start dates separated by 4 months. If we enroll 25% of eligible subjects annually, we will reach our enrollment target of 308 Veterans within 16 months, well within our project timeline. In our previous study, the overall enrollment rate was 60% of patients screened by telephone, thus we anticipate no problems with recruitment.

Inclusion Criteria:

1. Diagnosis of type 2 diabetes,
2. Hemoglobin A_{1c} ≥8.0%, or ≥7.5% in patients younger than 50,
3. BMI ≥27 kg/m^2,
4. Interest in losing weight,
5. Agrees to attend regular visits per study protocol,
6. Has access to a telephone and reliable transportation,
7. Has a VAMC provider.

Exclusion Criteria:

1. Age ≥75 years old,
2. Hemoglobinopathy that interferes with measurement of hemoglobin A_{1c},
3. Certain chronic or unstable diseases that may put the participant at increased risk. These include the following:
    a. Kidney disease (serum creatinine >1.5 mg/dL in men, >1.3 mg/dL in women),
    b. Type 1 diabetes,

Unstable CHD (an ongoing workup or treatment for a cardiac symptom such as unstable angina, coronary ischemia).),

c. Blood pressure ≥160/100 mm Hg,
d. Triglycerides ≥600 mg/dL,
e. Serum LDL-C ≥190 mg/dL,

4. Pregnancy, breastfeeding, or lack of birth control if premenopausal,
5. Dementia, psychiatric illness, or substance abuse that may interfere with adherence (e.g. illness that is currently unstable or resistant to first-line therapy; substance abuse in the past year),
6. Enrollment in another research study that might affect the main outcomes of this study.

Those individuals who were excluded because of blood test or blood pressure levels may be rescreened for eligibility.

SUBJECT RECRUITMENT

Participants will be recruited from the Durham VAMC outpatient clinics using strategies similar to those successfully used in our previous studies (VA CLIN-5-03F, PI-Yancy; VA IIR 09-381, PI-Yancy). Patients will also be recruited from the Greenville Health care Center, and Greenbrier Creek location, other sites under the Durham VAMC. The primary strategy will be via mailed introductory letters to potentially eligible patients. We will review electronic medical records (EMR) to identify patients meeting the inclusion/exclusion criteria and send them a recruitment letter. Patients may indicate their interest (or disinterest) in the study by calling a toll-free number included in the letter; otherwise they will be contacted by research staff after 5 days to invite participation. Supplemental recruitment strategies include advertisements to patients via flyers and VA TargetVision, which transmits messages to VA patients via television monitors located in Durham VAMC. In addition, health care personnel may refer potential participants for enrollment via the Research Consult option in the EMR. A provider may also request a list of their patients that meet study inclusion/exclusion criteria and review the list for referral.

When potential participants are self-referred or referred by health care providers, research personnel will review the electronic medical records for eligibility criteria. The potential participant will be contacted by phone to address eligibility and schedule a screening appointment to confirm eligibility.

CONSENT PROCESS

We are requesting a waiver of consent to conduct recruitment activities including identification of potential participants via ICD-9 codes, mailing letters to participants, and conducting a brief telephone eligibility screener.

Written informed consent will be obtained at the beginning of the screening appointment by a one-on-one discussion of the informed consent document between the potential participant and study personnel in a private space. The Informed Consent will include the following information: Understand that participation in this study is strictly voluntary. Subjects may choose not to participate. If they agree to participate in the study, they may refuse to answer any question or group of questions. A subject may also withdraw from the study at any time. After completing the session, if a subject decides to withdraw their responses from the study, they will be instructed to contact and inform the research coordinator at a provided phone number. A subject's decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which they are entitled, and will not affect access to health care at VA. The signed informed consent document will then be photocopied with one copy provided to the participant and one kept in the participant's research file. In addition, a note will be entered into the participant's electronic medical record (EMR) documenting that informed consent was obtained and a flag will be entered to notify EMR readers that the patient is enrolled in the study.

All study personnel will maintain certification of completed training in research ethics and confidentiality, data privacy and security. The study PIs will meet with research staff before the study begins to review eligibility and study procedures including obtaining informed consent and documentation of informed consent and authorization. This procedure will require the research assistant to enter the research consent note into CPRS within 24 hours of the subject signing the consent and attach the scanned informed consent and HIPAA authorization as soon as possible but no later than 14 days from the signed consent.

After informed consent has been obtained, the potential participant will complete a screening medical history and study questionnaires, height and weight will be measured to determine BMI.

Participants will also complete blood tests. If it is more convenient for the patient to have the blood tests prior to the consent visit, we will obtain verbal consent over the phone for the purposes of the blood draw using a script. Fasting will not be required for the screening visit labs. Final eligibility will be determined by the results of the baseline laboratory tests as listed in the inclusion/exclusion criteria. Individuals who are ineligible will be informed of other weight loss and diabetes programs, including Durham VAMC's MOVE! and diabetes education classes. Once the potential participant is determined eligible, s/he will be randomized to one of the study arms. The initial group visit will be scheduled as soon as possible, however, intervention assignment will not be revealed to the participant until the initial group visit.

The study will be conducted according to Good Clinical Practice guidelines, the U.S. Code of Federal Regulations (CFR) Title 21 CFR (Part 50 – Protection of Human Subjects and Part 56 – Institutional Review Boards) and the Declaration of Helsinki.

STUDY INTERVENTIONS

Randomization. 308 participants will be randomized to the WM/SMA versus SMA arms using a computerized random number generator in blocks (size <10; all study personnel except the statisticians are blinded to block size) within strata defined by baseline hemoglobin A_{1c} (7.5-8.9% or ≥9%) and use of a complex vs. simple insulin regimen (i.e., multiple types vs. one type only or no insulin). The aim of stratification is to achieve approximate balance across the two primary treatment groups with respect to these two important variables thought to be strongly correlated with post-treatment outcomes.

After a patient's screening information has been reviewed and found to meet eligibility criteria, the study coordinator will access a computer program in which to enter the values of the stratification variables; in turn, the computer program will provide the participant's randomly assigned study arm: WM/SMA or SMA. The study coordinator may access the computerized randomization program only once per participant. The computer program tracks and saves usage history and final intervention assignment. These data are available only to the study statistician. After a participant is assigned to one of the two interventions, the participant will be called to schedule the initial small group visit but is not made aware of intervention assignment during the phone call. This phone call will be made by a staff member who is blind to intervention assignment. Intervention assignment will be revealed to the participant at the initial group visit. The goal of this strategy is to avoid participants starting behavior changes prior to the onset of the intervention (they will be given these instructions during the phone call) and to maximize attendance at the first group visit. Participants are considered randomized when they learn of their assignment to either the WM/SMA or SMA arms at the first group visit. Participants who drop out before the first visit and do not learn of their randomization assignment will not be included in data analysis.

Study Procedures (See Appendix A JUMP START Study Flow)

Overview. Participants will be assigned to small groups (goal of 10-20 participants per group) based on their randomly-determined assignment (WM/SMA or SMA). The group sessions for WM/SMA arm will occur independently of the SMA arm (**Table 2**). Participants in the WM/SMA groups will meet every 2 weeks for 16 weeks to receive diet and weight management counseling followed by meetings every 8 weeks for 32 weeks for continued weight management counseling plus diabetes counseling and medication management. Participants in the SMA groups will meet every 4 weeks for 16 weeks, then every 8 weeks for diabetes counseling and medication management. Sessions for both the WM/SMA and SMA arms will last approximately 2 hours. Content for these meetings will be adjusted to ensure balance between arms regarding duration of the meetings; therefore, in the latter part of the WM/SMA intervention when participants receive both diet and diabetes counseling, the content of each will be abbreviated to keep meetings of comparable duration to the diabetes counseling in the SMA arm. All of the intervention groups and outcome assessments will occur at the Durham VAMC (and associated CBOCs), the Duke Stedman Center (located at the Center for Living on Erwin Road), or the Greenville Health Care Center location.

Table 2. Comparison of WM/SMA and SMA Arms

	WM/SMA	SMA
Week 0	• Measure weight, waist, BP, labs, all questionnaires • **WM** counseling • Medication adjustment	• Measure weight, waist, BP, labs, all questionnaires • **Diabetes** counseling • Medication adjustment
Weeks 2, 6, 10, 14	• Measure weight • View SMBG and hypoglycemia logs • **WM** counseling	• No visit
Weeks 4, 8, 12	• Measure weight and BP • Collect SMBG and hypoglycemia logs • **WM** counseling • Medication adjustment	• Measure weight and BP • Collect SMBG and hypoglycemia logs • **Diabetes** counseling • Medication adjustment
Week 16	• Measure weight, waist, BP, labs, all questionnaires • Collect SMBG and hypoglycemia logs • **Diabetes and WM** counseling • Medication adjustment	• Measure weight, waist, BP, labs, all questionnaires • Collect SMBG and hypoglycemia logs • **Diabetes** counseling • Medication adjustment
Weeks 24, 32, 40, 48	• Measure weight and BP • Measure waist, labs, all questionnaires at Weeks 32 and 48 only • Collect SMBG and hypoglycemia logs • **Diabetes and WM** counseling • Medication adjustment	• Measure weight and BP • Measure waist, labs, all questionnaires at Weeks 32 and 48 only • Collect SMBG and hypoglycemia logs • **Diabetes** counseling • Medication adjustment

Key: WM=weight management; SMA=shared medical appointment; BP=blood pressure; SMBG=self-monitored blood glucose.

WM Intervention.

We will use the following low-carbohydrate diet, physical activity and weight management counseling protocol in the WM/SMA arm only. The WM counseling will comprise the meeting content in the first 16 weeks of the WM/SMA arm, and comprise half of each meeting content for the latter 32 weeks (the other half of each meeting will be the SMA diabetes counseling, **Section D.5.3.**). Medication management will be aimed at reducing antiglycemic medication with the goal of preventing hypoglycemia and minimizing medications that can interfere with weight loss. In our previous and current studies using this protocol (VA CLIN-5-03F, PI-Yancy; VA IIR 09-381, PI-Yancy), participants were able to understand the instructions, achieve weight loss, and maintain a >80% retention rate for the one-year intervention.

Using a low-carbohydrate diet book[56] and handouts developed for previous studies (see **Appendix 2**), the first group meeting will provide education about the theoretical underpinnings of carbohydrate restriction as well as specific details on the induction phase of the low-carbohydrate diet. This instruction will include a review of foods that are emphasized and foods that are avoided. Initially, carbohydrate intake will be restricted to approximately 20-30 grams per day. Caloric intake will not be specified, as ad libitum instruction in an LCD typically leads to spontaneous calorie reduction.[48, 50] The diet will begin with unlimited amounts of animal foods (meat, chicken, turkey, other fowl, fish, shellfish), unlimited eggs, limited amounts of hard cheese, salad vegetables, and other low-carbohydrate vegetables. Other allowed foods are listed in **Appendix 2**. Artificial

sweeteners can be used whereas caffeine and alcohol are avoided. Early in the study, participants will set their weight loss goal for the 16-week period with the help of study personnel.

As a participant's weight loss approaches half of his/her goal, the participant will be instructed to add approximately 5 grams to the daily carbohydrate intake each week as long as weight loss continues. If the participant maintains weight or adds weight, then he/she will return to the daily carbohydrate intake of the previous week. Similarly, as the participant approaches goal weight, he/she will add approximately 5 more grams to the daily carbohydrate intake each week until weight regain occurs. At that point, the participant will return to the daily carbohydrate intake from the previous week. This will become the maintenance level of carbohydrate intake for the individual. Added carbohydrates can be extra servings of salad vegetables, low-carbohydrate vegetables, avocado, or cheese, or the addition of servings of nuts or soft cheese (e.g. cottage). In addition, participants can begin to try low-carbohydrate products such as snack bars and shakes to satisfy cravings for sweet foods. In our previous studies, good adherence to these instructions has resulted in approximately 10% of daily calorie intake coming from carbohydrate.[13, 48, 50]

Due to the diuresis that occurs at diet initiation, low-dose diuretics (hydrochlorothiazide 25 mg daily or less, furosemide 20 mg daily or less, or equivalent doses of other medications) will be discontinued if the participant has low blood pressure (e.g., systolic blood pressure <100). Higher doses of diuretics will be reduced in that situation. These participants will be monitored for hypertension and edema at the group visits. Medications will be restarted during the study if blood pressure or peripheral edema warrants; the concern for dehydration lessens after 2-4 weeks. To avoid hypoglycemia, diabetes medications other than metformin will be decreased or discontinued at diet initiation, depending on the baseline hemoglobin A_{1c} level. These decisions will be made by a study physician using an algorithm used in our previous research (see **Appendix 3**), and communicated to the primary care practitioner (PCP). In our experience, such medication adjustments are needed predominantly in the first 4 months of the diet. Participants will be given contact information for the study physician, who will be on call 24 hours a day. We have used this monitoring strategy successfully in our previous and current studies (CLIN-5-03F, PI- Yancy; VA IIR 09-381, PI-Yancy).

Group meetings will be led by a healthcare professional (such as Registered Dietitian, Registered Nurse, and/or Certified Diabetes Educator) trained in the low carbohydrate diet. Interventionist for the Greenville cohort will be trained by the original study team in Durham. Meetings will start with data collection by the trained research staff. After measurements are completed, participants will receive dietary, behavioral and supportive counseling from the diet specialist. Topics for these meetings include low carbohydrate diet-specific instructions in regard to food choices, grocery shopping, restaurant eating, dealing with social situations, recipe makeovers, and mindfulness eating, among others (see **Appendix 2**), and frequently incorporate behavioral techniques to aid adherence. Participants will also be advised of the current recommendations to strive for 30 minutes of moderate-intensity aerobic physical activity 5 days per week.[57] Selected group session topics will be dedicated to overcoming barriers to physical activity and to demonstrating exercises that can be performed easily at home (or work), regardless of the presence of physical disabilities. Physical activity will be emphasized more frequently in the latter sessions, given that 1) physical activity typically becomes more feasible after weight loss and 2) physical activity plays a fundamental role in the maintenance of weight loss. Other strategies for maintenance of weight loss (e.g., self-monitoring, eating breakfast) will also be emphasized in latter sessions. Because the spouse may be the predominant food shopper and/or preparer for the study participant, spouses (or partners) will be invited to attend group counseling sessions.

SMA Intervention

The SMA intervention will be used in both arms. In the WM/SMA arm, the SMA intervention will not begin until week 16 and will be abbreviated in that fewer SMA topics will be covered and each topic will be condensed to allow time for weight monitoring and management during the other half of the 2 hour session. The SMA intervention is based upon our prior study, but with modifications to increase its potency (derived from the VA QUERI ESP systematic review; see **Section B.3.**), including: (1) higher frequency of visits to enhance understanding, adherence, and safety when important, complex concepts (e.g., self-monitoring, medication

characteristics) are covered and the most dramatic changes to the medication regimen are anticipated; (2) fostering social support at home by allowing spouses (or significant others) to attend meetings with patients.

Protocol for each group visit meeting.

Overview. The goal of each group visit is to improve medical management for each patient's blood glucose and blood pressure until these parameters are optimally controlled. Efficiency is derived from the focus of the care team on the specific management issues (as opposed to individual patient issues) and from communicating common messages to the group, saving more tailored counseling to the individual during brief break-out sessions.

Group Visit Protocol. Prior to each group visit, a record review will be performed by the nurse/Certified Diabetes Educator (CDE) and physician for each patient including medications, lab tests, and clinical notes to discern possible regimen changes and barriers to glycemic or blood pressure control.
Each group visit session will last approximately 2 hours. The patients and staff will all have specific activities planned for each of three blocks of time during the session (**Table 3**). For ease of presentation, the example uses a 9:00 AM start time. The group sessions proceed in three distinct phases: information gathering, information processing and synthesis, and clinical management. The table shows the protocol for each group visit session.

Table 3. Activities for each group visit participant, by time block.

	Patients	RN/CDE assisted by RA	Diet specialist	Physician
900-930 *"Information gathering"*	Complete questionnaires; turn in logs; have BP and weight measured	RN/CDE orRA: Assess logs and questionnaires; measure BP and weight		
930-1015 *"Information processing and synthesis"*	Participate in education session (directed by healthcare professional)	RA: Enter data into database; alert MD of urgent problems RN/CDE: Deliver education	Deliver education	Review of new BP and BG values, making a plan for BG, BP, and blood lipids for each patient
1015-1100 *"Clinical management"*	Receive/discuss plans in ~5 minute visit with RN/CDE or MD	RN/CDE: Deliver straightforward medication plans to patients; make contacts with PCP as needed		Deliver and negotiate plans in ~5 minute sessions, handle any urgent problems; assist RN/CDE with communication to PCP

RN=registered nurse, CDE Certified Diabetes Educator, MD=physician, RA=research assistant, BG=blood glucose, BP=blood pressure, PCP=primary care practitioner

Information Gathering: This phase will be coordinated by the nurse/CDE (assisted by the research assistant [RA]) during the first 30 minutes and will include:

- Collect and review patients' logs of home blood glucose and blood pressure. To facilitate collection and organization of the blood glucose data, we will use CoPilot software, which allows us to upload data from the participant's glucometer via our laptop or desktop computer into our research database. It also displays the data graphically so that we can make medication adjustment decisions at the point of care. CoPilot software is on the Technical Reference Model (TRM) list and approved for VA use.
- Collect completed hypoglycemic event logs and questionnaires from the patients
- Assess blood pressure and weight
- Assess urgent medical needs. Urgent medical needs fall into three categories:
    - Emergent—requires removal from group and referral to emergency care for immediate medical attention. These include active or escalating chest pain, dyspnea, significant blood pressure or heart rate abnormalities, new severe weakness, and altered mental status.

- Urgent, related to diabetes—requires attention from the group physician at the time of visit, e.g., diabetic foot ulcer, home blood sugar over 400 mg/dl in the last 48 hours.
- Urgent, unrelated to diabetes. These will be noted, and patients will be urged to contact their PCP. If the patient desires, the group nurse/CDE will initiate PCP contact.

Information Processing and Synthesis: During the next 45 minutes, patients will eat a healthy snack provided by the group personnel and/or socialize with other group members. During this period, the healthcare professional will deliver a talk focusing on a specific aspect of diabetes care. The first group meeting for each group will include a brief group discussion designed to elicit the predisposing, enabling, and reinforcing factors common to the members of each individual group. Subsequent sessions will be tailored to the factors discovered in the initial session. Predisposing factors that we have found tend to be common among patients with diabetes include fear of hypoglycemia, lack of knowledge of causes of complications of diabetes, and lack of knowledge of appropriate foot care. We will be prepared to offer sessions on those topics, and will craft sessions for other topics that groups identify are of interest to them (see **Appendix 2** for a booklet[58] and handouts used in our previous study). In the WM/SMA group, the topic will be covered more briefly to allow time for additional WM counseling. In the SMA alone group, some of the topics may include nutrition, physical activity or weight management but these topics will not be covered repeatedly or in the structured fashion as with the WM/SMA group. Talks will last ~45 minutes and will be interactive, with questions permitted at any time during the session. Meanwhile, the physician will plan how to address medication management issues, maximizing medication doses or adding medications as needed in attempt to achieve disease parameter goals.

Clinical Management: During the final 45 minutes, patients have clinical contact with the team. The nurse/CDE will assist by preparing the patients for their brief visits with the physician and by communicating any straightforward medication plans to patients. The nurse/CDE or physician will also communicate all management changes and urgent non-diabetic needs to each participant's PCP in the manner that each PCP has chosen (see Section Embedding of group visits within primary care). The physician will communicate to the patient any changes in the medication management of blood glucose, blood pressure, or serum cholesterol proposed for the time period until the next meeting, and address any possible adherence or medication procurement issues. The physician will also attend to any urgent, diabetes-related concerns expressed by patients and assist the nurse/CDE with communication to the PCPs.

Procedures Common to WM/SMA and SMA Arms.

Counseling and Materials Provided to Both Arms. All participants will receive a pocket calorie, fat, and carbohydrate counting guide to aid with dietary changes.[59] Participants will be strongly encouraged to drink at least 6 glasses of water and take a standard multivitamin daily, which can be ordered via VA pharmacy if desired. Participants will also be advised of the current recommendations to strive for 30 minutes of moderate-intensity aerobic physical activity 5 days per week.[57] A list of community resources such as healthy food markets and physical activity venues in those communities represented by participants will be provided.

Embedding of Group Visits within Primary Care. All medical decisions made at the meetings will be communicated to the patient's PCP. Each PCP will be asked prior to the study how he/she would like to receive communications about these decisions. Physicians may choose to approve decisions in real time, in which case at the end of the assessment and planning meeting the PCP will be paged to provide input regarding the decision. Alternatively, the PCP may choose to allow the group team to make management decisions and be notified afterward. In that case, the PCP will be made a cosigner of the clinic note detailing all management decisions and their rationale. A new note will be used each time to document changes to ensure PCP's receive up to date information.

Strategies to Enhance Attendance

Selection of Convenient Times. Enrolled patients will be asked to choose from a menu of 2-3 available half-days (e.g., Monday morning) for their group session. Based on our previous experience, we will have 8-15 patients per group. As soon as 8-15 patients randomized to one arm are willing to attend on a given half-day, a group will be formed and patients will be called and notified about the time and place. Once set, this group will meet on the same half-day for the duration of the study. If necessary, subjects may attend another group time if they cannot attend their regularly scheduled group session.

Continuity of Patients and Providers. Each group of patients will remain together throughout the study. To enhance continuity and deliver a homogeneous intervention, the same nurse/CDE, diet specialist, and physician will attend all visits for a particular group.

Attendance Contracts. Above and beyond the usual encouragement to attend group sessions, we will attempt to increase attendance by having patients sign attendance contracts. Behavioral contracts have been shown in randomized, controlled trials to improve attendance to group sessions in patients undergoing substance abuse treatment. In one study that offered no additional incentives, signing contracts was associated with substantially higher rates of attendance over 7 monthly sessions (23% in the control group versus 51% in the intervention group). Patients will sign the attendance contract immediately after randomization and prior to scheduling the first group session, when they choose their preferred half-days.

Outcome Measures. All study measurements will be performed or collected by trained research personnel. All measures are done at parallel time points in the two arms except weight and hypoglycemic events, which are additionally assessed (but not used as outcomes) at the intervening visits during the first 16 weeks in the WM/SMA arm. Participants who wish to discontinue the study will be asked to return at the 16-, 32- and 48-week time points during which all specified measurements will be made. Participants will be compensated $25 for completing measurements at each time point and an additional $25 for the 48-week time point to improve the retention rate for the final assessment.

Laboratory Measurements. The primary outcome, hemoglobin A_{1c}, will be performed by the Durham VAMC Central Laboratory or Greenville Health care Center (Moye Boulevard, Greenville, NC) at baseline and every 16 weeks. The Central Laboratory assesses hemoglobin A_{1c} via high performance liquid chromatography on a TOSOH G-7 (San Francisco, CA), certified by the National Glycohemoglobin Standardization Program (NGSP) and standardized to the Diabetes Control and Complications Trial (DCCT) assay. Blood will be collected with the participant fasting and the following additional tests will be performed using standard methods: sodium, potassium, chloride, bicarbonate, urea nitrogen, creatinine, glucose, calcium, magnesium, total cholesterol, triglycerides, HDL-C, LDL-C. Serum sodium, potassium, chloride, bicarbonate, urea nitrogen, creatinine, glucose, calcium, and magnesium will be performed additionally at week 2 in the WM/SMA group to monitor for electrolyte abnormalities and dehydration. Results will be reported in the electronic medical record (CPRS) for the research personnel and clinical providers to view.

Baseline Characteristics. Demographic information and medical history, including weight-related history such as number of previous weight loss attempts and strategies used, will be recorded on self-administered standardized forms.

Anthropometric and Vital Sign Measurements.

Body Weight. Trained research personnel will measure body weight at every visit on a standardized digital scale, with participants wearing light clothing and shoes removed. The scale will be calibrated annually. Weight measurements at weeks 2, 6, 10, and 14 in the WM/SMA group will be for patient feedback only.

Waist Circumference. Trained personnel will measure waist circumference every 16 weeks using a non-elastic tape measure placed on the skin in a horizontal plane around the abdomen at the level of the iliac crest.[60] An average of two measurements will be used for analyses.

Vital Signs. Trained personnel will measure blood pressure and pulse rate every 4 weeks using an automatic sphygmomanometer with appropriately-sized cuff on the right arm (left arm if the right arm is missing or unsuitable) after the participant has been seated quietly for 5 minutes. Participants will be asked to refrain from eating, smoking, or drinking caffeine for at least 30 minutes prior to blood pressure measurements. The measure will be performed twice, with a third measurement if the first 2 measurements (systolic or diastolic) deviate more than 10%. An average of the two latter measurements will be used for analyses.

Measures of Adherence and Health and Psychological Effects.

Medication Changes. At each visit, participants will record any medication changes since the previous visit on a printout of their medications, which is updated after every visit. Research personnel will confirm with the participant any changes to medications for hypertension or diabetes. If there is concern for hypo- or hyperglycemia or hypo- or hypertension based on home or clinic readings, appropriate medications will be

reduced by a study physician using an algorithm developed by study investigators with expertise in this area (see Appendix 3), and the participant's PCP will be notified.

Antiglycemic Medication Use. Antiglycemic medications, dosages, and schedules will be assessed carefully with the participant and updated at each visit. For analysis, we will first calculate the total daily dose for each medication for each subject. Next, we will compute the proportions of subjects per group in each of the following categories compared with baseline: 1) diabetes medication increased, 2) diabetes medication unchanged, 3) diabetes medication decreased, and 4) diabetes medication eliminated. For participants with increases in some medications and decreases in others, the summary medication effect score (MES) described below will facilitate placing participants into one of the 4 categories. The MES will also be used to determine the overall antiglycemic medication use for each participant, one of the key secondary outcomes.

The MES, based on the potencies and dosages of the medications in a patient's regimen, was devised to reflect the overall intensity of antiglycemic medication, allowing comparison across different regimens. For the MES, the percentage of maximum daily dose for each medication (obtained from the package insert or Physicians' Desk Reference) will be computed. For insulin, the maximum daily dose will be 1 unit per kilogram of baseline body weight, which is considered a delineation of insulin resistance.[61] For subjects who use more than one type of insulin, all of the types will be summed together. Subjects who use a sliding scale will be asked to estimate their average total daily dose over the preceding 2 weeks. The percentage of maximum daily dose will not exceed 100% for subjects who take more than the maximum. The percentage of maximum daily dose for each medication will then be multiplied by an adjustment factor, and these products will be summed for the final MES. The adjustment factors applied are based on the reported median absolute decrease in hemoglobin A_{1c} for each medication, as delineated in the ADA and EASD consensus algorithm.[62] For the most commonly used non-insulin antiglycemic agents, metformin and the sulfonylureas, the adjustment factor was 1.5; for other less potent antiglycemic agents, the adjustment factor was lower: for α-glucosidase inhibitors it was 0.65, thiazolidinediones 0.95, meglitinides 1.0, exenatide 0.75, and pramlintide 0.75. For insulin, the adjustment factor was 2.5.

As an example, a subject taking pioglitazone 4 mg once a day (50% of maximum dose of 8 mg daily), metformin 850 mg three times a day (100% of maximum dose of 2550 mg daily), insulin regular 8 units three times a day with meals, and insulin glargine 20 units once a day (44 units total of insulin is 44% of maximum dose of 100 units daily) would have the following summary score: Summary score = 50%*1.0 + 100%*1.5 + 44%*2.5 = 310.

Dietary Adherence. Dietary adherence will be assessed at baseline and every 16 weeks with a 3-day food record. Participants will be instructed to document all food and drink consumed over 3 consecutive days including 1 weekend day. They will be taught the types of details to document and how to estimate quantities accurately. From these diaries, a registered dietician will use Food Processor software (Version 10, ESHA Research, Salem, OR) or comparable software to estimate calorie intake and the percentage of dietary intake from each of the macronutrients (i.e. protein, carbohydrate, and fat). If a participant does not complete a 3-day food record, a study staff member will perform a 24-hour dietary recall with the participant, contacting the participant by phone if needed.

Physical Activity. Daily physical activity will be assessed at baseline and every 16 weeks with the International Physical Activity Questionnaire (IPAQ), which was developed and validated by an international team (12 countries) of physical activity experts and is indicated for use in young and middle-aged adults (15-69 years).[63] We will use the long version, which assesses activity over the past 7 days in six domains (as compared to the short version, which only includes two domains): occupational, transport, yard/garden, household, leisure, and sitting. The IPAQ provides estimates of metabolic equivalent tasks (MET) energy expenditure, which can be reported for each activity or as a total score. We selected this measure because it has been validated against a more objective method (i.e., accelerometer), yet it has the advantage of being convenient and cost effective as a self-report method.

Medication Nonadherence. Medication nonadherence will be assessed at baseline and every 16 weeks using a questionnaire developed and validated by Drs. Voils, Maciejewski and Yancy. The questionnaire contains 3 items that assess the extent to which participants have missed doses of their medications over the past 7 days. Participants will be instructed to consider nonadherence specifically to their antiglycemic medications. The instrument demonstrated good reliability (α=0.84, 95% CI 0.80–0.87), and convergent, discriminant, and predictive validity.[64]

Health-related Quality of Life (HRQOL). We will assess HRQOL at baseline and every 16 weeks using the Problem Areas in Diabetes Scale (PAID), a disease-specific HRQOL scale, and the EQ-5D-5L, a global measure. The PAID is a well-validated measure used in randomized trials regarding diabetes, and is a sensitive and responsive measure of HRQOL in patients with diabetes.[65, 66] The PAID has 20 items that assess emotional adjustment to life with diabetes and has demonstrated high internal reliability, sound concurrent validity with a number of theoretically related measures (e.g., hypoglycemia fear), and evidence of predictive validity for adherence to treatment and blood glucose control.[67]. Patients rate the degree to which each item is currently problematic on a 6-point scale, from 0 (not a problem) to 4 (serious problem). . The global measure, EQ-5D-5L, is a highly sensitive 5-item health status measure with good performance in VA outpatients that assesses five domains of health (Mobility, Self-Care, Usual Activities, Pain/Discomfort, and Anxiety/Depression).[68] The sensitivity of the EQ-5D-5L improves upon the prior EQ-5D by increasing the response scale for each of the five domains from 3 response options to 5 response options. In validation work, the EQ-5D-5L was shown to be more sensitive to change and less subject to ceiling effects than the prior EQ-5D. The EQ-5D-5L yields a single score from 1-100 and can be used to derive utilities for use in constructing quality-adjusted life years (QALYs) for the cost-effectiveness analysis (Aim 5).

Group Cohesion Scale-Revised (GCS-R). The GCS-R is designed to assess group cohesion in terms of interaction and communication among group members (including domination and subordination), member retention, decision-making, vulnerability among group members, and consistency between group and individual goals.[69] A total score is formed by averaging across all items. Group cohesion will not be assessed at baseline because participants will be meeting for the first time but will then be measured every 16 weeks.

Additional questionnaires*.* We will also assess depressive symptoms, sleep, and pain interference at baseline and every 16 weeks. Depressive symptoms will be assessed by the Patient Health Questionnaire-2 (PHQ-2), which is currently used by the VA to screen for depression. It consists of 2 items about depressed mood and anhedonia assessed over the past 2 weeks on a scale of 0 (not at all) to 3 (nearly every day).[70] Sleep will be assessed by Medical Outcomes Study (MOS) 6-Item Sleep Scale Standard – Revised 2010 which consists of 6 items assessed over the past 4 weeks on a scale of 1 (All of the time) to 5 (None of the time).[71] The pain interference scale comes from the Patient Reported Outcomes Measurement Information System (PROMIS), funded by the National Institutes of Health (NIH), which has developed reliable, valid, responsive, and efficient assessment tools to measure patient–reported health status. The scale is the Pain Interference 8a, which consists of 8 items that assess pain interference in daily activities over the past 7 days using a 5-point scale (Not at all to Very much).[72]

Cost Measurement. To address Aim 5, we will assess intervention-related costs of interventionists and study participants and VA health care costs to create a complete picture of the costs associated with this intervention. Intervention-related costs include labor and capital costs. Labor will include interventionist time for the initial weight loss intervention and subsequent weight loss maintenance interventions, assessed using VA Human Resources data for salaries and study data on time spent per task. Capital costs include costs to develop and implement the interventions, overhead costs, office space, supply costs, and telephone services costs. Capital cost data will come from the Durham VA accounting department.

VA health care costs include expenditures that VA incurs for hospital admissions, outpatient visits, laboratory tests, pharmacy fills, radiology tests, surgical procedures, nursing care, and all other care provided by a VAMC. The VA cost data will be obtained from the patient treatment file (PTF) data, Outpatient Care file (OPC), and VA Health Economic Research Center (HERC) average unit cost estimates. We will examine whether outpatient visit, outpatient medication and inpatient expenditures differ between study arms because prior studies have shown that intensive lifestyle modification can reduce medication utilization and expenditures.[73]

Timing of Outcome Measures

Table 4. Timing of Outcome Measures

Outcome	Method (# items)	Baseline	Weeks 4, 8, 12	Week 16	Week 24	Week 32	Week 40	Week 48
Primary Outcome								
Glycemia	Hemoglobin A_{1c}	*		*		*		*
Secondary Outcomes								

Hypoglycemic events	Event log/ questionnaire	*	*†	*	*	*	*	*
Antiglycemic medication use	Antiglycemic medication effect score (MES)	*	*	*	*	*	*	*
Weight	Calibrated digital scale	*	*†	*	*	*	*	*
Waist circumference	Non-elastic measuring tape	*		*		*		*
Blood pressure	Automatic digital sphygmomanometer	*	*	*	*	*	*	*
Diabetes-specific HRQOL	PAID (20)[67]	*		*		*		*
Dietary adherence	3-day food record	*		*		*		*
Physical activity	IPAQ (27)[63]	*		*		*		*
Medication nonadherence	Voils MNQ (3)[64]	*		*		*		*
Group cohesion	GCS-R (25)[69]			*		*		*
Health utility	EQ-5D-5L (5)[68]	*		*		*		*

†Hypoglycemic events and weight will be measured every 2 weeks in the first 16 weeks of the WM/SMA arm but only the data from baseline and weeks 4,8,12, and 16 will be used for outcomes.

ADVERSE EVENTS

Hypoglycemic Events. Hypoglycemic events will be assessed at every visit but data collected at weeks 2, 6, 10, and 14 in the WM/SMA group will be for medication adjustment only and not used for outcomes. Events will be assessed using several redundant methods. Following a procedure described in Zammitt et al., participants will log all hypoglycemic events and return logs at specified visits.[74] All participants will be provided education and a handout that lists mild and severe hypoglycemic symptoms, and distinguishes between unassisted (self-aborted) and assisted (requiring help from another individual) events. All episodes of hypoglycemia will be recorded by participants on provided standard log forms, noting the date, time, duration, symptoms, treatment received (including need for assistance from bystanders or medical attention), and concurrent blood glucose. Subjects will be asked to record all episodes (symptomatic or non-symptomatic) associated with a blood glucose <70 mg/dL or any episodes associated with symptoms typical of hypoglycemia, as described by ADA Workgroup on Hypoglycemia.[75] Subjects will be encouraged to measure blood glucose at the time and prior to treatment when possible but episodes will be counted as valid if typical hypoglycemic symptoms resolved with carbohydrate, even if no blood glucose measurement was available. Episodes associated with glucose levels >70 mg/dL will not be considered valid. Subjects will return forms with recorded hypoglycemic episodes every 4 weeks for the first 16 weeks followed by every 8 weeks thereafter. If a participant misses a visit or forgets to bring the form, research staff will follow-up with the patient by telephone to obtain the information. In order to improve collection of data regarding serious events, participants will additionally be asked if they received medical attention for hypoglycemia, and the details if so, since the last assessment. This strategy will allow collection of data regarding serious hypoglycemic events that are treated outside the VA. During the cost analysis, VA clinic or emergency room visits, or hospitalizations, with diagnostic codes for hypoglycemia will be sought to verify the self-report of hypoglycemic events treated at VA. To avoid double-counting one episode of hypoglycemia, and because the intensity of hypoglycemic symptoms can be diminished following an episode, only one episode will be counted per 24 hours.[76] Serious episodes, defined as <50 mg/dL or 50-69 mg/dL and requiring assistance, will supersede minor episodes in this case.

Other Adverse Effects. Serious adverse effects (i.e., life-threatening, hospitalization, persistent disability) will be assessed at 4- and 8-week visits using standardized forms. Anticipated adverse events and side effects for weight-reducing diets and/or medication intensification may include hypoglycemia, hypotension, gallbladder disease, headache, weakness, muscle cramps, constipation, diarrhea, and dehydration. Many of these effects related to dietary change are transient or easily treated, and can be prevented with adequate hydration, which will be emphasized in the dietary counseling. A study physician will be on call at all times to manage any adverse events felt to be related to the study. Patients with adverse events that are not related to the study will be referred to appropriate health care sources. All adverse events will be reported to the IRB

according to local IRB requirements and reviewed by a Data Monitoring Committee (DMC) consisting of the study statistician and two additional members (at least one will be a physician with experience in diabetes care and at least one will have research experience) who are independent of the study team.

COSTS AND/OR PAYMENTS TO SUBJECTS

Subjects will be paid a total of $125 for travel expenses and time spent at key measurement visits: $40 at week 0, $20 at weeks 16 and 32, and $45 at week 48. In addition, participants can receive small token gifts with the study logo of approximately $2 value (e.g., water bottle, drawstring tote bags/backpacks) for session attendance milestones. To make these awards equitable in the 2 arms with different visit frequency, participants in the WM/SMA arm can receive a token after attending 5 cumulative sessions up to 2 tokens (10/13 sessions=77% attendance) and participants in the SMA arm can receive a token after attending 4 cumulative sessions and again after attending 3 cumulative sessions (7/9 sessions=78% attendance). Every Veteran on medication for diabetes is eligible for a glucometer through the Durham VAMC so this will not be provided through the study. Diet instruction books and Precision Xtra glucometer strips will be provided, and all lab costs will be covered by the study.

DATA AND SAFETY MONITORING

All research material obtained from participants will be gathered prospectively and will include anthropometric and vital sign measurements, serum samples, and participants' responses to questionnaires and food records. Serious (i.e., life-threatening, hospitalization, persistent disability) and unanticipated adverse events will be assessed at every visit using standardized questions in Illume. Anticipated adverse events and side effects for weight-reducing diets and/or medication intensification will also be collected at every visit. These may include hypoglycemia, hypotension, gallbladder disease, headache, weakness, muscle cramps, constipation, diarrhea, and dehydration. Many of these effects related to dietary change are transient or easily treated, and can be prevented with adequate hydration, which will be emphasized in the dietary counseling. A study physician will be on call at all times to manage any adverse events felt to be related to the study. Patients with adverse events that are not related to the study will be referred to appropriate health care sources. All adverse events will be reported to the IRB according to local IRB requirements and reviewed regularly by the study DMC.

PRIVACY AND CONFIDENTIALITY

All study personnel will maintain certification of completed training in research ethics and confidentiality, data privacy and security.

In regard to participant confidentiality, research personnel will use only those parts of the medical record necessary to determine eligibility and follow the research protocol. Measures will be taken to ensure confidentiality during the consent visit, meeting in a private space that allows the patient to ask questions. Confidentiality will be addressed in group sessions, including a patient group visit contract agreeing to treat all information discussed in the group confidential from participants and non-participants (e.g., spouses, significant others).

To prevent the exposure of personal identifying or protected health information, we will use the following procedures. During the screening process, each potential participant will be assigned a study participant number for tracking purposes. Identifying information will be recorded only at the time of screening and will be kept secure in research offices of the principal investigator. All other case report forms will be identified by study participant number only. Potential participants who decline participation or are ruled ineligible will have their identifying information destroyed. Data from case report forms (study questionnaires, medication change forms) will be entered into password-protected databases. Only Dr. Yancy and his research staff will have access to participant records and computer databases.

INFORMATION SECURITY

All study data will be kept in accordance with VA Records Control Schedule (RCS) 10-1.
Identifiable information will be collected. Demographic information including first and last name, address, phone number, date of birth, and full social security number, and medical and weight related history will be collected at screening. Medical history will include information necessary to determine eligibility, including

recent lab values for hemoglobin A1c, serum creatinine, LDL-C, and triglycerides, weight, and medical conditions including type I diabetes, kidney disease, unstable coronary heart disease, dementia, psychiatric illness, substance abuse in the past year, and a flag indicating enrollment in another research study. A waiver of HIPAA and informed consent for recruitment purposes will be requested. In addition to the measures above, marital and socioeconomic status, education and employment will be collected from the patient at baseline.

All data will be collected by trained VA research staff either by paper and pencil surveys, onto a VA approved FIPS 140-2 validated encrypted laptop or directly into a secure VA server. We will minimize the use of paper data collection by entering as much information as possible from the group visits, baseline and follow-up assessments, and intervention tracking directly into the computer database using only the subject's study ID number. When transporting paper records from VA site to VA site and Duke to VA, paper records will be carried in a locked carrying case with directions on the outside that say "if found, return to (research assistant information)" and "property of Durham VAMC, Dr. William Yancy" Serum samples (previously described) will be collected at key time points during the study and will not be stored. Samples will be analyzed by the VA lab, posted in the medical record, and destroyed according to standard protocol. No mobile devices will be used. All paper questionnaires are identified with the subject's study ID number only. All data will be stored electronically behind the VA firewall at p:\\vhadurhsrdfile1\$projects\Jump Start.

The Durham HSR&D Center of Excellence (CoE) adheres to VA policy and Durham VAMC IRB requirements, but has also developed additional Standard Operating Procedures for data security which have been designed to ensure continued confidentiality, integrity, and availability of research data. All patient information collected in the context of this research study, and even the fact that an individual is participating in the study, will be considered confidential. This confidentiality will be assured through several mechanisms. These procedures, which protect both paper and computer based records, have been used successfully in many studies, and will be followed for the proposed study.

With respect to all data, these procedures mandate the following to ensure confidentiality and safe handling of all data:

1. Study data will only be accessible to key personnel whose job functions require access to these data. Only individuals officially assigned to the study team will have access to individually identifiable information about human subjects. Study team members will be included on a staff listing and removed should they end participation on the study. Access to research data will be removed for personnel that are no longer part of the research team.
2. Participants will not be identified by name in any reports or publications, nor will data be presented in such a way that the identity of individual participants can be inferred.
3. Each participant will be assigned an anonymous study ID which will be used on all study forms. Data will be coded with the study ID and direct identifiers removed; however, data will remain identifiable using a password-protected codebook stored in a protected file on a secure server that is available only to the study team.
4. All study personnel will maintain certification with the Durham VAMC IRB that they have completed training in research ethics and confidentiality, data privacy and security.
5. Research data will not be removed from the VA protected environment.

With respect to paper based records, these procedures mandate the following:

1. All study records that contain participant information will be kept in secured, locked areas when not in use. Paper records for this study will be kept in a locked cabinet in the office of the research coordinator located in Legacy Tower, HSR&D suite 600. Greenville participant records will be kept by Greenville staff member Carrie May in a locked cabinet in her office at Greenville Health Center for the duration of the study. She may periodically (every few months) transport paper records, in particular the dietary recalls, to the Durham Legacy building by personally transporting paper files using the method described under information security.
2. In addition, such materials, when in use, will be kept safe from public scrutiny.
3. Materials that need to be discarded will be destroyed.

With respect to computer based records, the following practices are followed:

1. All research data are stored on VA-administered servers which are physically secured in a Durham VAMC server room.
2. Individual computer accounts, password protected, are issued to staff members.
3. Access to computer data is granted by OI&T personnel after confirming appropriate documentation through the IRB, per CoE policies.
4. Personnel are granted access to only those elements of the data management system to which they are authorized.
5. Data will not be stored on the hard drive of a PC. Should a laptop be necessary for data collection (e.g. visits at the Duke Stedman Center), only a VA approved FIPS 140-2 validated encrypted laptop will be used. In this case, any data collected will be via Illume within the VA firewall.

Utilization data, in particular, will be downloaded directly from national files to the Durham HSR&D CoE servers. Of study personnel, only the Statisticians and Economist will have access to these data, which will not be moved from this secured environment. Dr. Coffman, the lead statistician, will work closely with the programmer and the Masters–level statistician to develop and maintain the relational database for the study. Data from study participants is collected using both a commercial product, "Illume", and locally developed intervention software with quality measures such as mandatory fields and range checks. Study and participant management is accomplished through MS-SQL databases, which are accessed with MS-Access or .Net-based applications, and SQL Reporting Services, all supported by a software development group. All study data will be stored on certified and accredited VA Servers that are located in the Durham VA Medical Center IRM Server Room and backed up on a regular schedule. Technicians will constantly monitor server hardware, operating system, and database service performance. The HSR&D IT group contingency plan documents processes for insuring continuity of IT services in the event of equipment failure or network interruption.

Should loss of information occur, it will be reported immediately upon discovery to the PI, and the Durham ISO, privacy and security officers. The patient's permission for use of Personal Health Information will expire at the end of the study.

Study data will be maintained on secure servers for the duration of the study and for a period of time after the completion of the study that will be compliant with all VA guidelines and regulations in place at the time of study closure.

DATA ANALYSIS AND STATISTICAL CONSIDERATIONS

General Considerations. We hypothesize for the primary aim of this study that hemoglobin A_{1c} in the WM/SMA group will be less than 0.5% higher (non-inferiority limit) than in the SMA group at the end of study. The threshold of 0.5% for hemoglobin A_{1c} is reasonable and on the border of what would be considered a clinically important effect. Our primary analysis and sample size calculations are based on a test of noninferiority.[77-79] The null hypothesis in the noninferiority framework is that WM/SMA is inferior to SMA in management of glycemia based on some specified threshold amount, in our case 0.5%. The threshold of 0.5% implies that in order to determine noninferiority of the WM/SMA intervention to SMA, mean hemoglobin A_{1c} needs to be less than 0.5% higher (non-inferiority limit) in the WM/SMA group than the SMA group. If we find that the upper limit of the 95% CI of mean hemoglobin A_{1c} is 0.5% or higher in the WM/SMA group compared to SMA, we could not reject the null hypothesis and could not conclude that WM/SMA is noninferior to SMA for management of glycemia. However, if we reject the null hypothesis and therefore conclude that WM/SMA is noninferior to SMA, we can then conduct a superiority test to determine if WM/SMA is superior to SMA with no correction for multiple testing required.[80]

Data Summary. Descriptive statistics, including graphical displays (i.e., frequency distributions and box plots), will be used to summarize all study variables. We will construct individual and mean trajectory plots of the longitudinal outcome variables to understand their general trends over the study period. In addition, we will

explore the variability and correlation structure of the longitudinal outcome variables. Statistical analyses will be performed using SAS for Windows (Version 9.2: SAS Institute, Cary, NC) and R (http://www.R-project.org/).

Primary Analyses.

(H_1) Mean hemoglobin A_{1c} at 48 weeks in the WM/SMA group will be less than 0.5% higher (non-inferiority limit) than in the SMA group.

The outcome for the main study hypothesis is hemoglobin A1c, a continuous, longitudinal value measured every 16 weeks for 48 weeks, so participants will contribute up to 4 measurements (including the baseline measure). We plan to use a linear mixed model (LMM) that will account for the correlation between a participant's repeated outcome measurements over time; and the correlation between participants who are in the same small meeting group. Because of the small number of time points (4), we will apply an unstructured covariance matrix to take into account the within-patient correlation between repeated measures over time. A random effect will be included in the model to account for clustering of patients within small groups. The predictors in the model will include a dummy coded treatment and time effect. The fixed-effect portion of the model will have the form:

$$Y_{ijk} = \beta_0 + \beta_1*(time16) + \beta_2*(time32) + \beta_3*(time48) + \beta_4*(WM/SMA*time16) + \beta_5*(WM/SMA*time32) + \beta_6*(WM/SMA*time48)$$

for small group *i*, patient *j,* at time *k*.

The model specified above is participant-specific, so each participant may have an unequal number of observations at unequally-spaced time intervals. Under this model all participants' data are used in the analysis. As indicated above, if plots of the observed data suggest there is additional structure in the participant profiles that needs to be included in the model, we will modify the random and/or fixed effects as appropriate. We will test the noninferiority hypothesis, by examining the estimate of the difference in hemoglobin A_{1c} between WM/SMA and SMA at 48 weeks (β_6 parameter). Specifically, we will examine the 95% CI of the estimated β_6 parameter, and if the upper limit of the interval is less than the threshold value of 0.5%, we can conclude noninferiority of WM/SMA to SMA.[80] If we conclude noninferiority, we test for superiority of WMA/SMA to SMA at 48 weeks by examining the 95% CI of β_6 for inclusion of 0 and the p-value for the test of $\beta_6=0$. We plan to estimate the parameters in the model with a full-likelihood method using the SAS procedure MIXED (SAS Version 9, Cary, NC). Our model will also include randomization stratification variables baseline hemoglobin A_{1c} (8.0-8.9% or ≥9%) and use of a complex (i.e., multiple types) insulin regimen or not.

Secondary Analyses.

(H_2) Hypoglycemic events will occur less in the WM/SMA group than in the SMA group.

(H_3) Antiglycemic medication use will be less in the WM/SMA group than in the SMA group.

(H_4) Weight loss will be greater in the WM/SMA group than in the SMA group.

For secondary aims 2, 3 and 4, the outcomes are hypoglycemic events, antiglycemic medication use and weight, respectively. Hypoglycemic events will be calculated as the number of events per person-year in the 48 weeks following enrollment in the study. As this will be a count type variable, we will apply mixed-effects Poisson or Negative Binomial regression models[81] adjusted for the clustering of patients within small groups. We will test the hypothesis that subjects in the WM/SMA group will have fewer hypoglycemic events than those in the SMA alone arm. Antiglycemic medication use (MES score) and weight (kg) are continuous outcomes that will be measured every 4 weeks the first 16 weeks of the study and then every 8 weeks until the end of the study. We will fit a linear mixed model similar to what is described for the primary analyses except because we have more time point assessments, time will be a continuous variable and will not be dummy coded. We will fit random intercepts and slopes (random coefficients model) for time and a random intercept for the clustering effect of the small groups. Using this model we will set up contrasts of model parameters to test the hypothesis that the MES score (or weight) will be lower in the WM/SMA group compared to the SMA alone group.

The secondary outcomes blood pressure, waist circumference, diabetes specific HRQOL, dietary adherence, physical activity, medication non-adherence and health utility are all continuous, longitudinal outcomes; thus, similar models as described for the analyses of hemoglobin A_{1c}, MES and weight, depending

on the number of measurement occasions, will be fit. Tests for the secondary outcomes will be superiority tests.

Missing Data. As in any longitudinal study, values in the clinical outcomes may be missing due to dropout, inability to reach the patient for follow-up, or item non-response. To deal with missing data adequately, a thorough investigation of the mechanisms for missing data will be conducted. This includes a description of missingness by intervention groups, the identification of missing data patterns, and importantly, understanding which observed (baseline and time-varying) covariates predict missingness. Thus, we will work to understand the missing data mechanism to the extent that we can, using all of the observed data gathered in this study. Because the main predictors of interest for the primary analysis are collected at baseline, we do not anticipate much missing data in these variables. Our primary analytic method handles dropout in a principled manner; this method includes all available data on all subjects. This main analysis technique, LMM, implicitly accommodates missingness when the response is Missing At Random (MAR)[82]; that is, when missingness is due either to treatment, to prior outcome, or to other baseline covariates included in the LMM.
LMM's implicit accommodation of missingness avoids the explicit imputation of missing values of the outcome variable, yet provides a valid analysis within the context of MAR. Depending on the type and scope of missing data, we will also explore multiple imputation (MI), as a sensitivity analysis to use in conjunction with our primary analytic tools.[83] This strategy is particularly useful when covariates have missing data, when there exist time-varying covariates (including surrogates for the primary outcome measurements) that are predictive of future missingness, or when there is no scientific interest in conditioning on baseline covariates that are found to be predictive of missingness in the final LMM.

Intention-to-Treat Principle. In superiority trials, conducting primary and secondary analyses on an intent-to-treat basis where patients are analyzed in the arm to which they were randomized regardless of intervention adherence is standard practice and this is generally a conservative approach. For a noninferiority trial, the intention-to-treat (ITT) analysis would not be the conservative approach, therefore, it is recommended to perform analysis on both an intent-to-treat and per-protocol basis.[79, 80] Our secondary analyses are based on superiority tests and will be conducted on an intent-to-treat basis regardless of intervention adherence, using all data up to the 48 week follow-up or last available measurement prior to exclusion or dropout.

Sample Size Estimation. The sample size estimate of n=154 patients per arm (total n=308) is based on the primary noninferiority hypothesis that mean hemoglobin A_{1c} at 48 weeks in the WM/SMA group will be less than 0.5% higher (non-inferiority limit) than in the SMA group. In our proposed analysis, this involves testing the *WM/SMA*time48* interaction in our model. Sample size calculations are based on these comparisons and use methods appropriate for ANCOVA analyses, which are equivalent in terms of efficiency to our linear model as noted above, in randomized trials.[84] For the noninferiority test this method is based on performing a one-sided two-sample t-test sample size calculation at the alpha=0.025 level for the between group difference at the 48-week time point, multiplied by a factor 1-(rho)^2, where rho represents the Pearson correlation between baseline and follow-up time point outcome measures.[85] This sample size is then adjusted to reflect the clustering of patients within small groups (using the method of Donner & Klar)[86] and subsequent to that, inflated to compensate for potential missing observations due to attrition. The ICC is generally difficult to know in advance, particularly in studies in which interventions are delivered in groups. However, most clinical studies with cluster design experience an ICC of approximately 0.002 – 0.02.[87] For our calculations we use an ICC=0.01. Based on previous data, we assume a correlation of 0.5 between hemoglobin A_{1c} at baseline and at 48 weeks and an SD for hemoglobin A_{1c} of 1.5%. With 80% power, alpha=0.025, ICC=0.01, SD=1.5%, rho=0.50, and a 20% attrition rate by 48 weeks, 154 patients per group, for a total n of 308, need to be enrolled at baseline to identify less than a 0.5% difference in hemoglobin A_{1c} between the two treatment groups. If noninferiority is determined in our test of hypothesis 1, with 154 patients per arm we will have greater than 80% power to detect 0.7% improvement in mean hemoglobin A_{1c} in the WM/SMA group compared to SMA.

Health Economic Analyses.

(H_5) *The WM/SMA intervention will be cost-effective compared with the SMA intervention.*

To assess the cost-effectiveness of the WM/SMA intervention compared to the SMA intervention, we will examine variation in health care and intervention costs between the two arms, and variation in effectiveness between both arms. We will then calculate an incremental cost-effectiveness ratio (ICER) that summarizes the relative costs and benefits of WM/SMA over SMA alone. Health care costs will be obtained from the HERC Average Cost datasets to be comparable to Medicare-based pricing systems, and intervention costs will also be captured. The measure of effectiveness in this study is a continuous amount of glycemic control, so we will estimate the ICER as the difference in the average cost per participant between study arms divided by the difference in the average level of glycemic control between the two groups. We will also assess effectiveness on the basis of QALYs, derived from the EQ-5D-5L, which provides a global assessment of the two study interventions on quality of life. We will apply a "limited" social perspective in this cost-effectiveness analysis, which implies capturing a subset of costs under the full social perspective (including e.g., participant time, productivity and out-of-pocket costs) but excluding other costs (e.g., caregiver costs) that are expected to be a small proportion of total costs in this intervention. This approach has been used in several published cost-effectiveness analyses of self-management interventions implemented in the Durham COE.[88]

To conduct the cost-effectiveness analysis, an enumeration of the staff time and resources necessary to provide the intervention will be conducted. These intervention resources will include: 1) time of investigators to train the interventionist, 2) research assistant time spent recruiting study participants, 3) weight loss curriculum development and modification, 4) communication between interventionist and providers regarding changes in participants' care management, 5) communication between interventionist and participants, and 6) supplies needed by intervention staff (e.g., computers, office equipment). To track interventionist time spent communicating with participants during the in-person and telephone-based intervention, we will provide the interventionist with a spreadsheet to log these communications by participant and date. Interventionist time spent conducting research activities will be explicitly tracked as well so that these costs can be excluded from intervention costs. Other intervention costs (e.g., software modification, interventionist training) will be based on the specific personnel's annual salary plus benefits. Costs for intervention supplies (computers, telephones) will be based on their acquisition price from the manufacturer and office space will be calculated based on standard VA rates and will be allocated over their expected 'lifetime' of use.

To capture indirect costs associated with individual loss of productivity, study participants will be asked to fill out survey questions about number of days in the past three months that a person was unable to do usual activities (e.g., work, school, housework) due to illness. The costs associated with intervention participation and lost productivity will be based on employment and annual salary/hourly wage questions in the baseline participant survey. To capture participant costs associated with travel to each outpatient visit and out-of-pocket payments for medication and outpatient visit copays, we will ask questions in each participant survey about costs incurred for these items. Participant-level data will be available to estimate costs and effectiveness, so stochastic methods can be used to evaluate variability associated with the cost-effectiveness ratio. If the difference in weight loss is significantly higher in the intervention relative to the usual care arm, the 95% confidence interval for the base-case cost-effectiveness ratio will be computed with nonparametric bootstrapping using the bias-corrected percentile method.[89] Discount and inflation rates of 3% will be applied to out-year costs, and sensitivity analyses will be conducted allowing these rates to range from 2% to 5%. We will conduct a number of sensitivity analyses to assess the robustness of our base-case ICER results.

Blinding. It is not possible to blind patients to their intervention assignment because of the nature of the interventions. We considered options for blinding the outcomes assessors and the physicians making medication adjustments but ultimately decided to forego blinding for several reasons. First, the risk of outcomes assessors becoming unblinded is high given that most participants in one arm will be losing weight to a noticeable degree and decreasing medications early in the study when participants in the other arm will be increasing medications. Second, some of the measures (e.g., hypoglycemic event logs, blood pressure measurement) are needed for decision-making and counseling purposes. Third, the logistical difficulty of having additional blinded research staff and physicians meeting with participants separately from the SMA clinical team made this unwieldy and likely burdensome to the participant and to research staff.

In order to minimize bias, outcome measurements will be collected as objectively as possible. The primary outcome, hemoglobin A_{1c} will be performed by the central laboratory. Weight and blood pressure will be measured with automatic digital devices with strict protocols to minimize variability with the blood pressure

measurement. Other measures will be patient self-report; participants will be advised to respond to the best of their ability and as completely as possible. Research staff will be instructed not to influence responses. Medication adjustment recommendations by physicians will be directed by an explicit algorithm.

Fidelity. Fidelity to the intervention will be assessed at all group meetings in the following manner. Checklists for each meeting will be made a priori and list the key components to be performed. An observer will complete the checklist in real time during the group session. Any missed or altered components will be discussed at a debriefing after the session and rectified at the following participant group session. In addition, such issues will be discussed at study staff meetings to prevent recurrence. Medication adjustments will also be reviewed by the collective study physicians to ensure fidelity to the algorithm by the individual physicians.

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Appendix A: JUMP START Study Flow

1. **Data Pull:** We will review the electronic medical record to identify patients meeting inclusion/exclusion criteria.
   Inclusion Criteria:
   - Diagnosis of type 2 diabetes,
   - Hemoglobin A1c ≥8.0%, ≥ 7.5 in patients under age 50
   - BMI ≥27 kg/m2,
   - Has a VAMC provider

2. **Recruitment Letter**: Selected patients are mailed a recruitment letter with study contact information.

3. **Medical Record Review**: Research staff review the medical records of interested participants to confirm eligibility criteria. This information is entered directly into Illume.
   Exclusion Criteria:
   - Age ≥75 years old,
   - Hemoglobinopathy that interferes with measurement of hemoglobin A1c,
   - Certain chronic or unstable diseases that may put the participant at increased risk, including:
     a. Kidney disease (serum creatinine >1.5 mg/dL in men, >1.3 mg/dL in women),
     b. Type 1 diabetes,
     c. Unstable CHD (unstable angina, coronary ischemia workup in past 30 days),
     d. Blood pressure ≥160/100 mm Hg,
     e. Triglycerides ≥600 mg/dL,
     f. Serum LDL-C ≥190 mg/dL,
   - Dementia, psychiatric illness, or substance abuse that may interfere with adherence (e.g. illness that is currently unstable or resistant to first-line therapy; substance abuse in the past year),
   - Enrollment in another research study that might affect the main outcomes of this study.

4. **Brief Telephone Screening**: to confirm eligibility and schedule a consent/enrollment visit. This information follows a script and is entered directly into Illume. In addition to information above:
   - Not pregnant, breastfeeding, or lack of birth control if premenopausal
   - Confirm patient is not enrolled in another research study

5. **Visit 1**: RA obtains informed consent
   - Study questionnaires and medical history collected on self-administered standardized forms
     a. Demographics
     b. weight-related history such as number of previous weight loss attempts and strategies
   - Blood tests collected: Hemoglobin A1c, Chem 7 and lipid profile.
   - Height and weight measured to compute BMI, blood pressure

   Confirm eligibility: Final eligibility is determined once the results of the blood tests are received.

   If ineligible, subject is referred to other weight loss and/or diabetes programs.
   If determined eligible, subject is randomized by study coordinator via a computer program

6. **Randomization**: Into one of 2 groups: Weight Management/Shared Medical Appointments (WM/SMA) or Shared Medical Appointments (SMA).

Schedule first group session: RA calls to inform subject of first group session. RA is blind to group assignment. Subject is not informed of group assignment until the first group visit.

7. **Begin group visits (Week 0)**
   - Prior to each group visit in both arms, a record review will be performed by the nurse/CDE and physician for each patient including medications, lab tests, and clinical notes to discern possible regimen changes and barriers to glycemic or blood pressure control.
   - Subjects are given a healthy snack following the measurements in each session.

	WM/SMA	SMA
Week 0 – intervention assignment revealed	• RA: Measures weight, waist, BP, collects labs, all questionnaires • Diet specialist: **WM** counseling • Study MD/RN: Medication adjustment	• RA: Measures weight, waist, BP, collects labs, all questionnaires • MD/RN **Diabetes** counseling and Medication adjustment
Weeks 2, 6, 10, 14 – weight management group only	• RA: Measure weight • RN/RA: View SMBG and hypoglycemia logs • Dietitian: **WM** counseling	• No visit
Weeks 4, 8, 12 - collect outcome measures in both groups	• RA: Measure weight and BP • RN/RA: Collect SMBG and hypoglycemia logs • Diet specialist: **WM** counseling • Study MD/RN: Medication adjustment	• RA: Measure weight and BP • RN/RA: Collect SMBG and hypoglycemia logs • MD/RN **Diabetes** counseling and Medication adjustment
Week 16 - begin SMA intervention	• RA: Measure weight, waist, BP, collect labs, all questionnaires • RN/RA: Collect SMBG and hypoglycemia logs • Diet specialist: **WM** counseling **and** • MD/RN **Diabetes** counseling and Medication adjustment	• RA: Measure weight, waist, BP, collect labs, all questionnaires • RN/RA: Collect SMBG and hypoglycemia logs • MD/RN **Diabetes** counseling and Medication adjustment
Weeks 24, 32, 40, 48 – outcome measures	• RA: Measure weight and BP • RA: Measure waist, collect labs, all questionnaires at Weeks 32 and 48 only • RN/RA: Collect SMBG and hypoglycemia logs • Diet specialist: **WM** counseling **and** • MD/RN **Diabetes** counseling and Medication adjustment	• RA: Measure weight and BP • RA: Measure waist, labs, all questionnaires at Weeks 32 and 48 only • RN/RA: Collect SMBG and hypoglycemia logs • MD/RN **Diabetes** counseling and Medication adjustment