DVD Lifestyle Intervention (DELITE)

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Summary of Edits:

Version 1.1, September 27, 2017:

Minor typographical corrections and rewording for clarity throughout

List of Abbreviations: Updated

D-ELITE change to DELITE throughout

Section 5.2.5: Research Invitation:
- Clarification about posting blank participant packets on the HSR&D public website.

Section 5.3.1: Telephone screen, consent, and baseline assessment:
- Clarified who the research team will contact for enrollment.
- Updated time by which baseline assessments must be received after index weight.

Section 5.3.3: Randomization:
- Added time by which randomization must occur after index weight.
- Updated materials provided to participants.

Section 5.3.5.2: Intervention format, structure, and content:
- Clarified contents of GLB curriculum.

Section 5.5.3: Secondary outcomes:
- Updated secondary outcomes.

Section 5.5:
- Updated Table 5 per changes in secondary outcomes.

Version 1.2, January 8, 2018:

Cover Page:
- Added RIDS and Grant Number

Section 5.5:
- Updated methods of contact for delinquent surveys

Version 1.3, July 27, 2018

Section 5.2.5
- Added informing participants who have opted-in but are not yet randomized that enrollment is closed, once randomization target met.

Section 5.5
- Added mailing retention letter around 4, 8, 16, and 20 months

Section 6.3
- Replaced Dr. Alexis Beatty with Dr. Ashok Reddy on the Data Monitoring Committee

Version 1.4, January 10, 2019

Section 1.0
- Updated study staff

Section 5.5
- Added mailing retention letter around 4, 8, 16, and 20 months

Section 6.3
- Replaced Dr. Alexis Beatty with Dr. Ashok Reddy on the Data Monitoring Committee

Version 1.5, February 25, 2019
Section 5.5.2
- Clarified when Drs. Au or Hoerster may enter weights into CPRS.

Version 1.6, June 6, 2019
Section 1.0
- Updated study staff

Version 1.7, August 12, 2019
Section 1.0
- Updated study staff

Version 1.8, December 9, 2019
- Title Page Updated PI

Section 1.0 Study Personnel
- Change Hoerster to PI and Au to Co-PI
- Addition of Lucas Donovan as co-investigator
- Edit list of names to follow same format First Name Last Name, degree

Section 5.5.2.1 Weight
- Added clarification "starting with 12 months prior to index weight" for time line of CDW pulls for primary care weight

Section 5.5.3 Secondary outcomes
- Added clarification "starting with 12 months prior to index weight through 27 months" for time line of blood pressure data pulls
- Added blood sugar levels to secondary outcomes
- Clarified Table 5 to include data pulls 12 months prior to index weight

Section 5.5.4 Participant Payment
- Clarified payment timeline
- Added new procedure of potentially sending a "close out" letter after completion of 24m survey and payment sent or 90 days after reminder mailing for non-responders.

Section 5.6.3 Hypothesis testing and statistical analysis
- Added HbA1c levels to secondary outcomes analysis

Version 1.9, March 23, 2020
Section 1.0 Study Personnel
- Updated staff list to reflect changes in staffing as found on current Study Staff page

Section 5.5.2.1 Weight
- Added alternate procedure for clinic weight at 24months during times when going into the clinic for a weight is not feasible

Version 2.0, January 20, 2021
Throughout:
- Revised incorrect use of "obese" as an adjective

Abstract
- Updated to reflect revisions implemented in ClinicalTriasl.gov June 2020

Section 1.0 Study Personnel
- Updated staff

Section 5.1 Study design

- Corrected timepoint for primary outcome from 24 months to 12 months

Section 5.5.3

- Clarified the dietary quality/self-efficacy scale

Section 5.6 Analysis

- Updated analysis section to reflect decision made in preparation for submitting the Protocol manuscript to Contemporary Clinical Trials (available online May 28, 2020: https://doi.org/10.1016/j.cct.2020.106045)

Section 6.1

- Modified description of staff who will review adverse events to remove specific names

Version 2.1, March 17, 2021

Section 5.3.3 Randomization, 5.4 Inclusion/Exclusion Criteria, and 5.6.3 Hypothesis Testing and Statistical Analyses

- Added specificity to BMI randomization strata

Section 5.4 Inclusion/Exclusion Criteria

- Corrected timeframe for inclusionary weights

Section 5.5.2 Outcomes

- Clarified outcome descriptions
- Specified how we will measure “Reach”
- Updated Table 5 according to the above

Section 5.6.3 Hypothesis Testing and Statistical Analyses

- Added analysis details

Section 5.6.5 Misclassification and Missing Data

- Moved information about missing data from section 5.6.3 to this section

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Abstract

Most Veterans who receive VA healthcare have obesity (41%) or are classified as overweight (37%), putting them at higher risk for multiple serious chronic health conditions. Providing evidence-based behavioral weight management programs to Veterans with obesity is a priority for the VA National Center for Health Promotion and Disease Prevention (NCP). While the VA NCP's MOVE! program - primarily delivered with in-person group visits - helps Veterans with obesity lose weight, its reach has been limited because of various barriers to care. Some Veterans may do better with a program they can complete from home at their own pace. In this trial, study investigators are examining the effectiveness among Veterans of a previously proven self-directed lifestyle intervention (called DVD Lifestyle Intervention (D-ELITE)) that targets modest, clinically meaningful weight loss over the course of a year using recorded video lessons (DVD or online streaming), written self-study aids, and optional lifestyle coaching. The study will compare participants randomly assigned to receive D-ELITE to those continuing in usual care on weight and self-reported general physical health status, one year after enrollment. Secondary outcomes include weight and general physical health status two years after enrollment; and obesity-related biometric measures (blood pressure and HbA1c) and self-report psychological and behavioral factors such as physical activity and sleep quality, at one- and two-years following enrollment.

Veterans with obesity living in the western US were identified using the VA Corporate Data Warehouse (CDW), recruited to participate via mail and telephone, and randomly assigned to receive the study intervention or usual care alone. The study uses CDW to assess weight change and biometric outcomes. To assess self-report outcomes, participants completed questionnaires, by mail or telephone, at baseline and 12 months after randomization, and are currently completing 24-month follow-up questionnaires. The D-ELITE intervention focuses on gradual lifestyle behavior change aimed at improving eating habits and increasing physical activity. It encourages participants to gradually achieve and maintain a 5-10% loss of baseline body weight and at least 150 minutes of moderate-intensity physical activity, such as brisk walking, each week. The D-ELITE intervention program consists of watching one video, completing corresponding written self-guided learning materials, and tracking food intake and physical activity each week for the first 12 weeks, then working through 10 additional written handouts and continued food and activity tracking for the next nine months. Intervention participants have access to a lifestyle coach, as desired, for the full 12-month intervention period. In addition to patient outcomes, this study will examine the cost of delivering the intervention, information relevant to decision-makers and potential future dissemination. Evidence-based programs like this, which can be delivered remotely and with likely minimal resources required from the VA healthcare system, are greatly needed, especially now as the SARS-CoV-2 pandemic has required VA to rapidly transition to providing more remotely-delivered care.

Impact: The DELITE trial has potential to provide the evidence needed for deciding whether a low-cost, low-technology, self-directed program can be used to expand the treatment of obesity to a population-based level by improving access to obesity treatment regardless of Veteran place of residence.

List of Abbreviations

- Adverse event (AE)
- American Heart Association (AHA)
- Body mass index (BMI)
- Cardiovascular disease (CVD)
- Centers for Disease Control and Prevention (CDC)
- Centers for Medicare and Medicaid Services (CMS)
- Chronic obstructive Pulmonary Disease (COPD)
- Community based outpatient clinic (CBOC)
- Compensation & Pension Record Interchange (CAPRI)
- Computerized Patient Record System (CPRS)
- Confidence interval (CI)
- Corporate Data Warehouse (CDW)
- Data Monitoring Committee (DMC)
- Department of Defense (DoD)
- DVD Lifestyle Intervention (DELITE)
- Diabetes Prevention Program (DPP)
- Diabetes Prevention Support Center (DPSC)
- Digital video disc (DVD)
- Evaluation of Lifestyle Interventions to Treat Elevated Cardiometabolic Risk in Primary Care (E-LITE)
- Health Economics Resource Center (HERC),
- Health-related quality of life (HRQoL)
- Health Services Research & Development (HSR&D)
- Institute for Healthcare Improvement (IHI)
- International Physical Activity Questionnaire (IPAQ)
- Intra-class correlation (ICC)
- Institutional Review Board (IRB)
- Information Security Officer (ISO)
- Intention to treat analysis (ITT)
- Group lifestyle Balance (GLB)
- Health Economic Resource System (HERC)
- Managerial Cost Account (MCA)
- Medical Outcomes 12-item short form (SF-12)
- MOVE! Weight Management Program for Veterans (MOVE!)
- MyFitnessPal (MFP)
- National Archives and Records Administration (NARA)
- National Center for Health Promotion and Disease Prevention (NCP)
- National Institute of Health (NIH)
- Office of Information & Technology (OI&T)
- Patient-Reported Outcomes Measurement Information System (PROMIS
- Pragmatic clinical trial (PCT)
- Primary care provider (PCP)
- Protected health information (PHI)
- Principal Investigator (PI)
- Randomized controlled trial (RCT)
- Record control schedule (RCS)
- Serious adverse event (SAE)
- United States Preventive Services Task Force (USPSTF)
- University of Pittsburgh (UP)
- Usual care (UC)
- VA Informatics and Computing Infrastructure (VINCI)

- VA integrated service network (VISN)
- VA Puget Sound Health Care System (VAPSHCS)
- Veterans Affairs (VA)
- Veterans Health Administration (VHA)
- VHA Support Services Center (VSSC)
- Veterans Health Information Systems and Technology Architecture web (VistAWeb)

1.0 Study Personnel

Name/ Contact	Role/ Affiliation	Access PHI	Recruit-ment	Surveys/ Interviews	Data Analysis
David H. **Au**, MD, MS david.au@va.gov	Co-Investigator (key) VA Puget Sound	Y	N	N	Y
Anna **Baron** Anna.baron@cuanschutz.edu	Biostatistical consultant VA Eastern Colorado Health Care System	N	N	N	N
Margaret **Collins**, PhD margaret.collins@va.gov	Project Manager VA Puget Sound	Y	Y	Y	Y
Lucas **Donovan**, MD Lucas.Donovan@va.gov	Co-Investigator VA Puget Sound	Y	N	N	Y
Eric **Epler**, BS eric.epler@va.gov	Coordinator VA Puget Sound	Y	Y	Y	Y
Emily **Gleason**, BS Emily.gleason@va.gov	Coordinator VA Puget Sound	Y	Y	Y	Y
Katherine **Hoerster**, PhD, MPH katherine.Hoerster@va.gov	Principal Investigator (key) VA Puget Sound	Y	Y	Y	Y
Rachel **Hunter-Merrill** Rachel.Hunter-merrill@va.gov	Analyst VA Puget Sound	Y	N	N	Y
Jun **Ma**, MD, PhD maj2015@uic.edu	Co-Investigator for Implementation oversight University of Pittsburgh: IPA	N	N	N	N
Elizabeth **Mattox**, AARNP Elizabeth.mattox@va.gov	Co-Investigator VA Puget Sound	Y	N	N	N
Jennifer **McDowell**, MS jennifer.mcdowell@va.gov	Coordinator VA Puget Sound	Y	Y	Y	Y
Brianna **Moss**, BS Brianna.moss@va.gov	Coordinator VA Puget Sound	Y	Y	Y	Y
Tanya **Nguyen** Tanya.Nguyen@va.gov	Coordinator VA Puget Sound	Y	N	Y	Y
Robert **Plumley** robert.plumley@va.gov	Programmer SIBCR: VA WOC	Y	N	N	Y
Peter **Rise**, MS peter.rise@va.gov	Biostatistician VA Puget Sound	Y	N	N	Y
Mary **Schooler** Mary.Schooler@va.gov	Coordinator VA Puget Sound	Y	N	N	Y
Linnaea **Schuttner**, MD Linnaea.Schuttner@va.gov	Co-Investigator VA Puget Sound	Y	N	N	Y
Edwin **Wong**, PhD Edwin.wong@va.go	Co-Investigator VA Puget Sound	Y	N	N	Y

2.0 Introduction

2.1 Background

More than a third of Veterans in primary care are obese,[1] which was cited in 2004 by the undersecretary as the single greatest modifiable "health risk...even surpassing the adverse effects of smoking."[2] Losing even modest amounts of weight reduces the risk of multiple chronic conditions.[3] In 2006, National Center for Health Promotion and Disease Prevention (NCP) developed and disseminated MOVE! Weight Management Program for Veterans (MOVE!), which is primarily an in-person group lifestyle intervention that combines evidence-based diet and physical activity counseling with behavior change strategies.[4,5] Despite being in place for nearly a decade, the reach of MOVE! has been low, with <5% of Veterans who are eligible for the program participating in one or more sessions, and with only modest weight loss on the order of 1.3 and 0.9 pounds more than nonparticipants after six and 12 months, respectively.[6] As described below, NCP is exploring alternative ways of delivering MOVE! and other weight loss interventions in order to improve its reach and adoption for population-based weight management among Veterans with obesity. NCP's overall goal is to develop a suite of programs that meet the diverse needs and preferences to optimize reach and adoption

among different segments of Veteran populations, as “one size does not fit all.” With input and support from the NCP, we propose this PCT that tests whether a low-tech, low-resource, self-directed lifestyle intervention is more effective at improving weight and physical function than the standard of care for Veterans with obesity, providing an evidence base for adoption by VA if proven successful.

VA’s existing weight loss program is unable to meet the diverse needs of Veterans with obesity:[5] The current iteration of MOVE! is the result of a decade of implementation, evaluation, and refining. The program structure is complex, relatively resource intensive and concentrated within larger medical facilities and selected CBOCs. Enrollment relies on provider referral and patient self-referral. Participants meet with their primary care provider and/or a MOVE! health team member to set a few specific, short-term, self-directed goals. Veterans are encouraged to participate in the 16 in-person weekly group-based sessions that provide education and support for goal setting and monitoring. The intensity and dissemination of the intervention limits the number of participants at any given time. NCP acknowledges that given the magnitude of the obesity problem among Veterans, providing Veterans with choices about how to engage in a suite of obesity treatment approaches, including those outside medical facilities, is likely to expand the reach of obesity treatment and possibly increase availability of in-person visits for those who may require that format.

Heterogeneity in MOVE! facility level adoption: The initial program was pilot tested at 17 VHA facilities starting in 2002. A revised program was launched VA-wide in 2006. By 2010, MOVE! had been implemented at every VHA hospital facility and more than 50% of CBOCs, and about 95% of Veterans were screened for obesity.[7] Facility-level MOVE! utilization rates ranged from 0.05% to 16%.[6,8] Leadership engagement, program staffing, space and equipment, engagement of champions, and communications with multi-disciplinary teams were identified as key elements in a facility’s ability to implement and maintain a MOVE! program.[7,9] Beyond being able to improve access to weight loss interventions, providing Veterans effective weight loss programs that are inexpensive and can be managed outside a medical facility has a number of potential benefits to Veterans and the healthcare system. Having a program that is independent of facility personnel hiring, administered at a VISN, regional or central level, and does not require intensive personnel support may in fact decrease demand on local resources, leading to improved wait-times and access for in-person participation. Moreover, being able to provide these resources using a low-cost, low technology requiring program may enhance eventual implementation at a national-level.

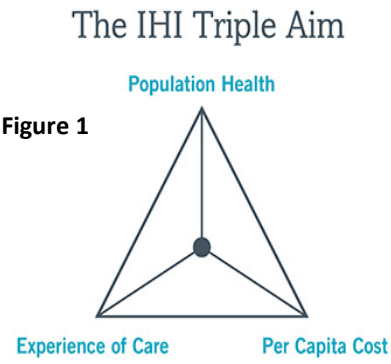
Heterogeneity in participation and patient outcomes associated with MOVE! Using data collected from clinical record measurement, Dahn et al.[10] and Romanova et al.[11] found that MOVE! participants lost on average 1.6-2.2 kg up to one year after enrolling, compared to an average gain of 1.4-2.0 kg per year pre-enrollment.[10,11] The slope for weight change differed significantly during the pre- and post-enrollment periods among MOVE! participants, suggesting a beneficial treatment effect. Others have found that more intensive engagement in the program resulted in more weight loss.[6,7] Using weight measurements obtained from VHA databases for the years 2006-2010, Kahwati et al. found that 18.6% of Veterans who attended two or more MOVE! visits lost at least 5% (clinically meaningful) of their body weight after 6 months, compared to 31.6% of those who had more intense, sustained involvement, compared to12.5% of those not involved in MOVE!. However, even as late as 2012, within VISN 20, less than 5% of all patients who were overweight and obese participated in MOVE!.[6] Greater distance to facility and lower number of primary care visits was associated with lower enrollment in MOVE!. Because of the geographic distances encountered in the Pacific Northwest, the authors attributed the limited reach of the program, in part, to the in-person group component. In addition, patients who have a higher body mass index (BMI) or who already experienced obesity-related comorbidities such as diabetes and hypertension had higher MOVE! utilization, suggesting that the program may not be used as much for primary prevention. As a result, the overall public health impact of MOVE! has been constrained though could potentially be expanded by having a diverse suite of interventions available to address facility and patient level barriers.

NCP is seeking new methods to reach and engage Veterans, including low-tech approaches. NCP has begun to pilot a number of alternative delivery modalities to address barriers to MOVE!’s implementation including MOVE! Coach, which provides an iPhone/iPad app that guides Veterans through self-management tools over 19 weeks; home telephone messaging; interactive voice response for coaching messages via phone; and MOVE! Telephone LifeStyle Coaching, which involves regular coach telephone contact. Specialty consultation is available for Veterans with more specialized needs. An ongoing pilot comparing a VA-adapted Diabetes Prevention Program (DPP) to MOVE!, both delivered in in-person groups, among Veterans with diabetes

suggested promising results for the VA-DPP over MOVE!,[12] possibly in part because the VA-DPP group sessions were of fixed-length, closed-group, and used a single lifestyle coach. NCP is also piloting the VA-DPP program for online delivery. However, considering the relatively low uptake of the use of My Health-E Vet, relying on smart phone technology and online engagement is likely to engage those who are younger, more technology savvy and have higher incomes.[13] Given the wide variety of Veterans' situations and needs, some may achieve weight loss with in-person group visits or by internet and mobile technology-intensive programs, while the 41% of Veterans who use VA health care who do not have access to internet[14] may be better served with a self-directed program that uses minimal technology. NCP has identified low-technology, self-directed approaches as an important gap in its portfolio of weight loss programs under evaluation. The current study is a self-directed, low technology DVD Lifestyle Intervention (DELITE). It modifies the self-directed arm of the E-LITE intervention that was effective in a community-based, non-VA primary care practice.[15]

Framework: The DPP-based and the E-LITE interventions were grounded in social cognitive theory and have been demonstrated to be effective among patients at high risk of developing type 2 diabetes and in primary care clinics of largely privately insured populations. Based on strong evidence from the E-LITE trial, we designed the current pragmatic study using the Institute for Healthcare Improvement (IHI) Triple Aim to guide our application. The Triple Aim provides a system-level framework to optimize health system performance by simultaneously addressing three interdependent dimensions targeting the: (1) patient experience of care; (2) population health; and (3) per capita cost of health care (**Figure 1**). The VA adopted this model and it is required reading for all VA healthcare leaders; how DELITE aligns with the three dimensions follows. *Experience of Care.* From the patient experience, the self-directed, remotely delivered approach provides the opportunity to bring a potentially effective weight loss program into the homes of Veterans. DELITE increases opportunity for participation because its remote delivery eliminates travel distance and time or inconvenience such as having to take time off from work. In addition, as described above and further in Sections 2.3.1 and 5.1, Veterans participating in DELITE will have patient-centered flexible options to access and engage with intervention components. *Population Health*. Patient eligibility targets all Veterans who are obese, and patient participation is not dependent on the Veteran being seen in the clinical context. DELITE is designed to be practical and scalable. The approach lends itself to central implementation approach common for a number of telehealth initiatives, and exploits the VA data infrastructure for identification and recruitment of patients. DELITE reaches Veterans without access to or self-efficacy with internet use. For those who prefer, DELITE DVDs are available online. *Per Capita Cost*. The DVD is ~$10/person. With a single FTE lifestyle coach to manage these patients across multiple states/regions, this will be a low-resource intervention per capita. This model will also shift burden away from local behavioral therapists by expanding their availability to others who would benefit from in-person programs.

Figure 1



2.2 Significance

According to the 2014 VA/DOD Clinical Practice Guideline update on management of overweight and obesity, 61-83% of Department of Defense (DoD) beneficiaries and 78% of Veterans were overweight or obese, resulting in an estimated excess cost of $370 per patient per year in additional medical and non-medical costs.[16] Translated to the VA primary care population of approximately 5 million Veterans equates to an annualized excess cost of nearly $2 billion. In 2013, of the 4,869,451 Veterans who had a height and weight available, slightly more than 4 in 10 Veterans were obese. In addition to the commonly associated conditions including diabetes, hypertension, and cardiovascular disease (CVD), obesity is likely the primary risk factor for non-alcoholic fatty liver disease, estimated to be as high as 40% of the US general population and which has surpassed alcohol, and is likely to surpass hepatitis C, as the leading cause of liver transplantation in the next decade.[17-20] Finally, Dr. Au, the Principal Investigator (PI) and colleagues, have shown that obesity commonly leads to dyspnea and misdiagnoses of chronic obstructive pulmonary disease (COPD) leading to unnecessary care, such as inhaled corticosteroids that increase risk of pneumonia and yet provide no benefit.[21-26]
As noted in the VA/DOD clinical practice guideline update, "comprehensive lifestyle intervention is the foundation of treatment for overweight and obesity" as a part of personalized proactive Veteran-driven care.

The best practice strategies recommended in this document include the combination of dietary, physical activity, and behavioral components that lead to gradual and consistent energy deficits of 500-1000 kcal/day for effective weight loss, which are embedded in DELITE. In addition, the guideline acknowledges that although effective in primary care settings, clinicians often do not aggressively address excess weight with their patients, hypothesizing that the etiology is often complex and due to "limited availability of the multi-component resources needed for treatment."

The express purpose of this pragmatic study is to provide the evidence needed for deciding whether a low-cost, low-technology, self-directed program can be used effectively to expand the treatment of obesity to a population-based level, improving access to obesity treatment regardless of Veteran place of residence and access to or familiarity with information technology. This study seeks to inform whether expending VA resources toward implementation is warranted by assessing the program's overall potential reach and effectiveness. By comparing DELITE to usual care, we address the question "how does the intervention compare to what we are doing now?" The usual care in VA includes the MOVE! program although the uptake has been relatively low. A head-to-head comparison of DELITE and MOVE! does not address our research question and would be of limited utility for the ultimate decision-making about program adoption because these interventions are likely suitable for different segments of the population. Even modest expansion of the reach of obesity treatments to Veterans through an alternative delivery model, as in DELITE, would have the potential to reduce the incidence of diabetes and reduce need for hypertensive or other medications. Moreover, our project seeks to address this epidemic using a low cost, low-technology approach that would greatly facilitate the ability to expand this intervention if found to be effective. Finally, as we noted previously, if effective, this product could be one additional intervention that is incorporated into a suite of interventions offered as part of the MOVE! program. These various interventions could be offered based on Veterans' preferences, level of comfort with technology, economic abilities or distance to VA.

2.3 Preliminary Studies/Gaps in Knowledge

Table 1. Evolution of weight loss intervention programs that have resulted in D-ELITE	
Study/Program	**Brief Description**
DPP Trial	Multicenter efficacy trial that demonstrated the superiority of the DPP lifestyle intervention to metformin and to placebo.
GLB program	Direct adaptation of the DPP lifestyle intervention which is recognized by the CDC National DPP initiative and being disseminated through the UP Diabetes Prevention Support Center (DPSC).
E-LITE trial	Randomized clinical trial in primary care integrating the GLB core curriculum with Heart360.org. Compared delivery in-person or by take-home DVD to usual care. Results: The two GLB delivery modes showed comparable efficacy vs. usual care among privately insured patients.
D-ELITE trial	Pragmatic trial building on E-LITE DVD-based intervention, evaluating effectiveness among Veterans.

2.3.1 Predecessor to DELITE:

DELITE was adapted from Dr. Ma's E-LITE self-directed intervention that translated the original DPP lifestyle intervention for obesity management in a non-VA primary care setting.

Table 1 demonstrates the progression and adaptations from DPP to the current trial. The landmark DPP trial established the gold standard in diabetes prevention by demonstrating that an intensive lifestyle intervention targeting modest weight loss and increased physical activity markedly lowered type 2 diabetes incidence (by a mean of 58% net of control) among high risk adults across all age, sex, and race/ethnicity subgroups,[27] and the benefit persisted for at least 10 years.[28] Weight loss was the dominant predictor of reduced diabetes risk where every kilogram of weight loss resulted in a 16% reduction in risk.[29] Despite the enormous benefit of DPP on diabetes risk, the lifestyle intervention was highly intensive and did not readily lend itself to implementation in clinical practice. To promote dissemination and implementation, DPP investigators at the University of Pittsburgh (UP) adapted the resource intensive, primarily one-on-one lifestyle intervention to a group program with fewer sessions called Group Lifestyle Balance (GLB),[30-33] which is a Centers for Disease Control and Prevention (CDC)-recognized national DPP translation program.[34] The program has shown effectiveness for weight and cardiometabolic risk reduction in a number of uncontrolled and controlled translation studies implemented using existing staff (e.g., dietitians, lay health educators) in varied community settings (e.g.,

primary care practices, urban medically under-served, rural, senior centers, Hispanic Women Infant and Children clinics, and African American churches).[30,31,35-41] One of these studies, a randomized controlled trial (RCT) in 8 rural communities, found that the GLB program led to comparable weight loss and cardiovascular risk factor control regardless of the delivery modality (face-to-face, DVD, internet, or self-selection of any of the 3 modalities).[38] Another study showed an intervention combining the GLB-DVD and telephonic lifestyle coaching was effective in a primary care practice.[31] The GLB-DVD is available in English with Spanish subtitles.

Briefly, **E-LITE** was a 3-arm RCT (n=241) that sought to compare the efficacy of a **highly portable and inexpensive** self-directed lifestyle intervention to a more intensive coach-led group intervention and to usual care for clinically significant weight loss among adults who were overweight or obese with prediabetes and/or metabolic syndrome. The E-LITE study protocol[42] and the primary[15] and 5 additional publications[43-47] detail the design, methods, and outcomes. The **E-LITE** self-directed intervention adapted the DPP to have three core components: following a single group orientation, participants received a set of **take-home DVDs** and corresponding handouts containing 12 weekly sessions (~25 min ea. **Table 2**). The content focused on healthy eating, physical activity, and behavior change,[48] plus online **self-monitoring** of weight and physical activity and online **access to a trained lifestyle coach**. The American Heart Association (AHA) Heart360.org online platform provided a free, secure patient portal for self-tracking (e.g. physical activity and weight), messaging between participant and coach, and text messaging for automated reminders. Dr. Ma and others have successfully used this platform in research-based interventions.[49,50] Ten additional handouts used with the original DPP program also were provided as an additional resource as desired.

Table 2. DVD session topics

1.	Getting Started Losing Weight
2.	Be an Excess-Calorie Detective
3.	Healthy Eating
4.	Move Those Muscles
5.	Tip the Calorie Balance
6.	Take Charge
7.	Problem Solving
8.	Four Keys to Healthy Eating Out
9.	Slippery Slope of Lifestyle Change
10.	Jump Start Your Activity Plan
11.	Make Social Cues Work for You
12.	Ways to Stay Motivated

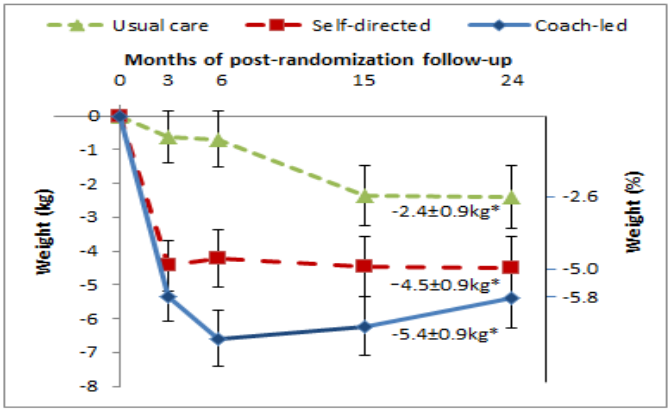


Figure 2. Estimated mean ± SE weight change over a 24-month period, in kilograms (left y-axis) and as percentages (right y-axis), in the intention-to-treat population.

In comparison to usual care, both self-directed lifestyle intervention and intensive coach-led group intervention produced comparable clinically significant weight loss over 2 years among adults who were overweight or obese with prediabetes and/or metabolic syndrome (**Figure 2**). This finding has important implications because weight regain is common in weight loss interventions, whereas weight loss maintenance for at least 2 years is a strong predictor of continued maintenance success.[51,52] The self-directed intervention also led to significantly lower waist circumference and fasting plasma glucose, compared with usual care.[15] A post-hoc analysis of E-LITE data found that mean (SD) change in the SF-12 physical component scores improved by 1.6 (4.7) in the self-directed intervention versus a decline of 0.4 (6.5) in the usual care control group (p = .01) and an increase of 0.7 (8.5) in the coach-led intervention (p = 0.51). In addition, increasing physical component scores were significantly correlated with weight loss in both interventions (**Figure 3**). The difference in physical component score change between the self-directed intervention and usual care (2.0; 95% CI, -0.1 to 4.0) was 4% of baseline (baseline *M* [SD], 50.5 [7.5]); 3% was the minimally important difference used in the DPP.[53] The SF-12 mental health scores changed slightly in both intervention

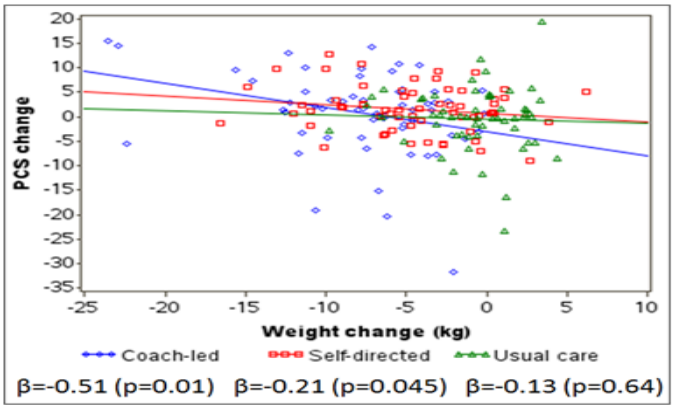


Figure 3. Correlation between changes in weight and SF-12 physical composite score (PCS) from baseline to 15 months.

groups and did not differ significantly from usual care. These findings are consistent with the DPP and other behavioral weight-loss intervention studies.[53-55] They further demonstrate the favorable outcomes of the E-LITE self-directed intervention. As the first RCT that successfully translated the DPP-GLB lifestyle intervention into primary care in the U.S., E-LITE was cited as key evidence in the 2014 USPSTF behavioral counseling recommendations for CVD prevention in primary care.[56]

In sum, compared with usual care, the E-LITE self-directed intervention led to significant reductions in body weight and cardiovascular risk factors that were sustained through 2 years, and a clinically meaningful, albeit statistically nonsignificant, increase in physical health status despite a normal baseline. Dr. Ma continues to extend her work examining the effects of integrating the E-LITE self-directed intervention for adults in primary care (R01 HL119453), comorbidities (depression, coronary disease and asthma), populations (Latinos, R01 HS022702), and diverse care delivery systems (multispecialty group practice, HMO and safety net).

To improve the E-LITE self-directed intervention for ease of participation among Veterans, **DELITE** will replace the single group-orientation session with a telephone-based visit, and will offer participants options for how to engage with the intervention subsequently: DVD or online access to the same 12-session videos, self-monitoring using paper booklets or MyFitnessPal (MFP), and coach access via MFP secure messaging or by phone. For weight loss, research has shown the method of self-tracking is less important than the actual process of self-tracking behavior itself.[57] Telephone-based lifestyle coaching is recommended in the latest obesity treatment guideline.[3] Adding these options improves flexibility of delivery and, potentially, participant engagement and outcomes, including for Veterans who do not readily engage in technology. **Table 3** summarizes the key modifications incorporated into the proposed DELITE intervention. Building on their strong collaborations including a recently funded NIH clinical trial (U01HL128868) examining weight loss for patients who were overweight or obese with COPD, Drs. Au and Ma seek to examine in a PCT the broad-scale effectiveness of the self-directed approach among Veterans with obesity in the proposed intervention, DELITE.

Table 3. Original E-LITE self-directed and D-ELITE intervention components summary

E-LITE self-directed	**D-ELITE**
Patients with prediabetes/Metabolic syndrome	Veterans with obesity
One-time initial **group based in-person** orientation	One time **telephone** orientation
Take-home DVDs with participant handouts for 12 weekly sessions (~25 min ea.) (cost: $10 a set)	**Mailed** DVD with participant handouts for 12 weekly sessions (~25 min ea.) (cost: $10 a set)
Recommended daily self-monitoring of weight and physical activity via **Heart360**; participants entered weights and minutes of physical activity and pedometer steps, if available (cost: free)	Recommended daily self-monitoring of weight and physical activity via **MyFitnessPal or paper tracker**; participants enter weights and minutes of physical activity (cost: free)
Access to a trained lifestyle coach for questions and counseling, at participant request, via **online secure messaging** (cost: minimal coach time-average 2 messages/month/participant)	Access to a trained lifestyle coach for questions and counseling, at participant request, via **secure messaging or telephone** (cost: minimal coach time- average 2 messages/month/participant)

There is a national call for the provision and coverage of multicomponent lifestyle interventions for obesity in primary care settings.[58,59] The challenge historically with such interventions is that they are often too intensive to implement in the real world. The Centers for Medicare and Medicaid Services reimbursement policy promotes brief (15 minutes), lower-intensity (compared with efficacy studies), face-to-face behavioral counseling within a limited timeframe (i.e., 6-12 months).[59] The DELITE intervention (see **Tables 2** and **3** above) fits this general pragmatic framework with likely better efficiency due to use of a self-directed approach with remote delivery and low staffing requirements. The current study will contribute to the evidence base needed to inform and guide policy change, in the context of growing interest and evidence in effective and pragmatic interventions.

2.3.2 Experience with using Clinical vs Research Measured Weights:

Using a similar approach to what we propose in DELITE, E-LITE compared the differences in slope between clinically and research measured weights to examine whether clinically obtained weights would lead to a different conclusion.[15,42] **Table 4** shows both intervention arms had significant weight loss whereas the usual care arm did not. Moreover, **slopes obtained from in-clinic and research measured weights were not statistically different.** This finding was replicated in a separate weight loss intervention study, BE WELL,[60,61] which involved a different health system and patient population than E-LITE. Collectively, these results demonstrate that there would have been no difference in interpretation of these two interventions using either clinic or research weights.

Table 4. Difference in slope between clinic and research measured weights from two separate clinical trials of weight loss

	Number	Clinic (slope)	Research (slope)	Slope difference (95% CI)	p-value
E-LITE					
Self-directed	81	-0.05	-0.11	0.06 (-0.03, 0.15)	0.17
Coach-led	79	-0.11	-0.12	0.01 (-0.07, 0.08)	0.85
Control	81	0.0	0.01	-0.01 (-0.09, 0.06)	0.74
BE WELL					
Coach-led	165	-0.02	-0.04	0.02 (-0.01, 0.06)	0.21
Control	165	0.0	-0.02	0.02 (-0.02, 0.06)	0.43

3.0 Objectives

The overall goal of this trial is to produce evidence on the effectiveness of a proven, pragmatic lifestyle intervention targeted at modest, clinically meaningful weight loss and increased physical activity among Veterans with obesity. In this simple, pragmatic clinical trial (PCT), and with input from the National Center for Health Promotion and Disease Prevention (NCP), we focus on the intervention's reach and its effectiveness on weight loss and generic health-related quality of life (HRQoL). We will examine secondary aims that include physical activity, sedentary behavior, dietary intake, blood pressure, sleep quality and self-efficacy. With success framed in reach and effectiveness, this VA-based PCT tests a low-cost, low-resource, behavioral weight loss intervention previously shown to be effective in non-VA primary care settings.

3.1 Scope of Problem to be Addressed

- Obesity is common; ~1/3 of Veterans in VA integrated service network (VISN) 20 and beyond are obese.
- As a preventable health risk, obesity and sedentary lifestyle surpass the prevalence and adverse effects of tobacco smoking.
- The MOVE! Weight Management Program for Veterans (MOVE!), developed by NCP, produces modest weight loss among those who participate. However, participation is currently limited to <5% of eligible Veterans. NCP is seeking approaches that improve the reach of obesity programs to more Veterans.
- The Blueprint for Excellence prioritizes the need to improve timely and efficient access to proven effective therapies for all Veterans by overcoming diverse geographic and technology-based barriers to care.
- The medical facility-focused care delivery model that requires in-person visits to VA facilities (both medical centers and outpatient clinics) limits reach and access to care based on distance and staffing availability.
- Multiple medical conditions compete with obesity for recognition and treatment in primary care.

3.2 Challenge

- Improve access to lifestyle interventions using a patient-centered and population-based approach.
- Provide obesity services to a diverse Veteran population through a broad selection of modalities.
- Overcome barriers to MOVE!'s population health impact for Veterans highlighted by VISN 20 evaluation:1.
- Low reach: <5% of Veterans eligible for MOVE! have used the program. Reach was likely limited by a number of factors, including: Distance with ~50% of Veterans living >30 miles from a local VA medical center or community based outpatient clinic (CBOC); Provider or patient self-referral enrollment system leading to differential participation based on the frequency of exposure to healthcare providers; Selection biases of patients who already experienced complications of obesity

were more likely to participate in MOVE!, which limits its potential for population health management.
- Heterogeneous adoption: A 14-fold variation in program use between VA medical centers among MOVE! eligible patients due to limitations of available resources and competing demands.
- Modest effectiveness among users: In-person MOVE! sessions at a VA facility constrains program effectiveness. Among Veterans who used MOVE!, ~50% had only one program encounter resulting in small amounts of weight loss of 1.3 lb (95% CI,−2.6 to −0.02 lb) and 0.9 lb (95% CI, −2.0 to 0.1 lb) at 6 and 12 months, respectively. Participating in six or more sessions resulted in greater weight loss at 12 months (−3.7 lb; 95% CI, −5.1 to −2.3 lb). Additionally, 15% of MOVE! enrollees lost 5% or more body weight, while 11% gained more than 5% of body weight.[2]

3.3 Opportunity

- The Evaluation of Lifestyle Interventions to Treat Elevated Cardiometabolic Risk in Primary Care (E-LITE) compared two active interventions with each other and usual care.[42] Adapted from the Diabetes Prevention Program (DPP) lifestyle intervention,[27] the two E-LITE interventions were designed for primary care delivery through coach-led, in-person groups or self-directed-video with the option of remote coach support.
- The self-directed intervention[46,62] was effective, simple, pragmatic and comparable to the group-based intervention and superior to usual care (at 2 years: Mean [s.e.], –4.5 [0.9] kg; 44% with >5% weight loss). These results informed and were incorporated into the 2014 United States Preventive Services Task Force (USPSTF) guidelines for behavioral counseling for CVD prevention in primary care.[56]
- We will implement the E-LITE self-directed intervention (now called DELITE) in a patient-level randomized PCT of 500 Veterans with obesity. Our specific aims are to test whether, compared with usual care (UC) controls, intervention participants have better outcomes, including:

  1. **Primary measures:** Greater weight loss and improved physical function through 12 months.
  2. **Secondary measures:** Improvements in sustained weight loss, physical function and activity, sedentary behavior, diet quality, blood pressure, sleep quality, self-efficacy, and reach of the program to participants with obesity through 24 months. Budget impact analyses to aide NCP in decision making about potential dissemination.

3.4 Impact

Effective, pragmatic obesity treatment will address the most common preventable cause of disease in VA, having high clinical and public health importance.

4.0 Resources and Personnel

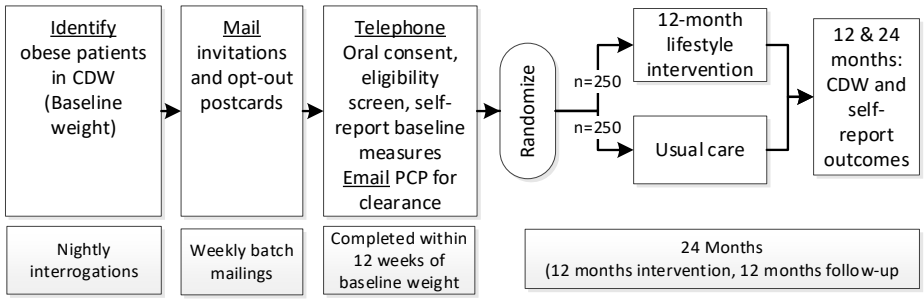
All study personnel are listed in section 1.0, including their contact information. Also detailed in that section: affiliation, role in study, who will have access to protected health information, who will be recruiting, consenting, administering surveys and who will perform data analysis.

5.0 Study Procedures

5.1 Study Design

DELITE is a simple, two-arm PCT in which 500 Veterans with obesity will be randomized to usual care (UC) or UC plus the DELITE self-directed lifestyle intervention for 12 months. We will assess weight change from baseline via CDW over a 24-month period and self-report assessment at 12 and 24 months. We hypothesize that intervention participants will have more weight loss and greater improvements in self-reported physical function at 12 months relative to UC controls. The design is depicted in **Figure 5** and described below.

Figure 5. Overall study flow



5.2 Recruitment Methods

5.2.1 Enroll Veterans within the Pacific and Mountain Time zones:
This broad area includes urban, rural and very rural areas, while allowing the lifestyle coach to retain normal working hours.

5.2.2 Identify Eligible Participants through CDW:
Before we begin recruitment, we will refine our algorithms that we will apply to CDW data to identify potentially eligible participants within the past year and verify with chart review.

5.2.3 Screening for Index Weight/BMI:
Using CDW, we will identify Veterans who had a primary care visit with an eligible BMI (index weight), a weight measurement in the previous 12 months indicating obesity (to minimize spurious inclusion), and who are likely free of exclusionary conditions searchable in CDW. We will retain pertinent socio-economic, demographic, and healthcare utilization data on all individuals identified to inform our organizational partners about the potential reach of the program.

5.2.4 Oversampling:
We will oversample:

- Women – our goal is to enroll approximately 30% of the cohort being women;
- Minorities, if necessary, to have a balanced proportion of the cohort;
- At VA Puget Sound HCS/CBOC's for study staff to obtain in-person weights for approximately 50 participants should the study team determine it is necessary to validate clinic weight measurements.

5.2.5 Research Invitation:
Using patients identified through CDW, we will mail invitations to enough Veterans to enroll 500 Veterans with obesity. The invitation packet will contain:

- Invitation Letter;
- Information Sheet;
- Opt in/out Post Card;
- Copies of Baseline Surveys with optional postage-paid return envelope.

We will pursue the option of posting the packet on the HSR&D public website for easy access in the future.

Once we meet our randomization goal, we will inform participants who have opted-in but are not yet randomized that enrollment is closed.

5.3 Informed Consent and Randomization

5.3.1 Telephone Screen, Consent, and Baseline Assessment:

For those potential participants who do not return an opt-out postcard within 2 weeks (or who return the opt/in card), a research coordinator may telephone to:

- Describe study and answer questions.
- Assess eligibility, including potential exclusions for safety. (Section 5.4)
- Obtain consent under a waiver of documentation of written informed consent.
- Administer baseline surveys; or participant may complete paper copies and return via postage-paid mail.
- Baseline assessment must occur no more than twelve weeks after the date of the index weight.

5.3.2 Medical Clearance:

For individuals who consent at the telephone screen and have fulfilled safety requirements, study staff will send a secure email to the patient's primary care provider to inform them of their patient's participation and to alert us if there is any reason that their patient should not participate. If the primary care provider does not respond after four days, we will send a second email. If no response to the second email, we will send a third email informing the PCP that we will enroll the individual in three business day unless they contact us otherwise. We will inform interested participants if their provider responded that this intervention is not appropriate.

5.3.3 Randomization:

DELITE staff will perform stratified randomization into the usual care or intervention group at a ratio of 1:1 within strata defined by age (<65 vs. ≥65), BMI (three categories: ≥30 and <35 vs. ≥35.0 and <40 vs. ≥40.0 and <45), and population density (Rural vs. Urban). Randomization mush occur no more than twelve weeks after the date of the index weight. We will notify participants of their randomization group via mail. The mailing will include a weight scale, water bottle with a DELITE logo for all participant and the intervention materials (DVDs, binder containing introduction/instructions and the GLB curriculum, scale, CalorieKing Fat & Carbohydrate Counter, and paper tracking booklets) for intervention participants.

5.3.4 Continuation of Usual Care:

All participants will continue to receive standard medical care from their usual providers. The study will not interfere with ongoing patient care, including provider or patient referral to MOVE! or other available weight loss interventions. To account for changes in medical practice and secular trends and to protect external validity, no participant will be restricted from seeking or instructed not to seek weight loss treatment once enrolled and will be included in the intent-to-treat analyses.

5.3.5 Intervention:

5.3.5.1 Evidence-based intervention goals:

Weight: The intervention is designed to achieve and maintain a weight loss of 5-10% of baseline body weight in a gradual stepwise fashion. This amount of weight loss is safe, feasible and associated with clinically significant reductions in the risk of diabetes and cardiovascular disease such as hypertension.[27,63-65] To help achieve and maintain the weight goal, participants are advised to reduce their calorie intake by 500-1000 kcal/day, as recommended in adult obesity guidelines, including the recent VA DOD clinical practice guideline.[66] Participants will gradually achieve the calorie goals through portion control, choices of low-energy and nutrient-dense meals and snacks (e.g., whole fruit, vegetables, whole grains, and low-fat, non-sweetened dairy products), reduced consumption of refined and/or added carbohydrates/sugars, healthy food preparation techniques, and careful selection of restaurant items.

Physical Activity: The physical activity goal is to achieve and maintain a minimum of 150 minutes per week of moderate-intensity physical activity (such as brisk walking). This goal is consistent with the 2008 Physical Activity Guidelines for Americans,[67] and is deemed safe and attainable for most adults, including those with chronic health conditions. Participants will gradually and steadily increase daily walking with a goal of achieving 150 minutes of brisk walking per week by the end of the 12-week video program **(Table 2)**. Participants may also choose to adopt regular activities of moderate intensity other than brisk walking.[68,69] After attaining the

minimum goal of 150 minutes per week, participants may choose to be more active; or if participants reach the 150-minute goal but are not achieving the weight goal, they will be encouraged to further gradually increase to 60 minutes/day of moderate physical activity[61,68,70] while continuing to work on dietary changes.

5.3.5.2 Intervention format, structure, and content.

Within two weeks of randomizing a participant to the intervention group, a DELITE lifestyle coach will call to confirm receipt of the intervention package, review the materials and instructions, confirm understanding, and address any questions.

The DELITE core curriculum consists of watching one ~25-minute GLB video session (see Table 2 for list of topics) each week for 12 weeks, and using a corresponding GLB handout. The GLB also includes additional "Physical Activity Resource" videos with a corresponding handout. Participants may watch the sessions on DVD or online through the University of Pittsburg GLB training center. The lifestyle coach will instruct participants about how to use the MFP website or paper-tracking booklets, depending on preference, for self-monitoring which may include weight, food intake, physical activity, GLB materials used, and how to contact the lifestyle coaching via MFP secure messaging or phone if they have questions or would like guidance with the lifestyle program. A lifestyle coach will send standardized reminders through MFP secure messaging or via mail for participants who choose to use paper trackers. As recommended by guidelines, the main objective of the core curriculum is to facilitate gradual weight loss through successive and progressive changes in diet and physical activity and behavioral skills training.

Months 4-12 focus on continued self-directed/monitored gradual weight loss and maintenance, and use of additional GLB handouts. Participants will have access to a lifestyle coach via MFP secure messaging or telephone as desired for the 12 months of the intervention. The choice to engage with a lifestyle coach is strictly up to the participant and will occur as seldom or often as the participant chooses. Self-monitoring is key to success in behavioral weight-loss interventions.[71] The lifestyle coach will continue to send standardized reminders throughout the 12 months of the interventions.

5.3.5.3 Intervention adherence.

Other than sending the standardized reminders (Section 5.3.5.2), DELITE will not use special strategies to maintain or improve participant adherence to the intervention.

5.4 Inclusion/Exclusion Criteria

DELITE uses inclusion and exclusion criteria (Table 4) aimed at ensuring each participant's safety and maximizing internal validity, including minimizing error associated with the primary outcomes, and preventing possible missing data.

Table 4. Eligibility criteria

Inclusion

- Primary care measured BMI ≥30 and <45 kg/m^2 and BMI measured in prior week indicating obesity;
- Able to participate fully in all study protocol/procedures including informed consent;
- Access to DVD player or internet.

Exclusion

- Inability to speak, read, or understand English;
- Participating in active weight loss intervention including use of prescription weight-loss medications in the past 3 months, current participation in group or individual weight loss programs provided by trained personnel, had/have plans for bariatric surgery during the study period;
- Expected weight loss because of alternate explanations, such as from illness;
- High variability in weight due to fluctuations in volume status (ascites – liver disease, chronic heart failure);
- Safety and/or adherence concerns due to severe physical or mental health issues or life expectancy <24 months;

- Pregnant, lactating, or planning to become pregnant during the study period;
- Participation in other intervention studies.

5.5 Study Evaluations

Table 5 shows the study measures and data collection schedule. We will send self-administered questionnaires to participants via mail with the option to complete and return by postage-paid mail. If the participant does not return the questionnaires by mail within two weeks, we may send a reminder letter or a study coordinator may attempt to administer them by telephone. To improve retention and the likelihood that participants will complete the follow-up evaluations, we will send a letter reminding them of their participation in the study at around the 4th, 8th , 16th , and 20th month after randomization.

5.5.1 Baseline Variables and Co-variates:

We will collect baseline variables and co-variates from CDW to the extent possible, and supplement with participant self-report surveys, MFP logs, and/or paper trackers.

5.5.2 Outcomes:

- Weight:
    - For all participants, we will extract all outpatient-based weight measurements from CDW starting with 12 months prior index date through 27 months of follow up. For participants without a CDW weight:
        - We may include a reminder with the outcomes surveys to visit their primary care clinic to be weighed if a clinic visit is safe and feasible.
        - During times when a clinic visit is not feasible (i.e., currently, during SARS-CoV-2 pandemic), we will include a self-weight form with the outcomes surveys for those without a CDW weight to weigh themselves at home. The self-weight survey and instructions for self-weighing will be in lieu of a reminder to visit their clinic to avoid encouraging participants seeking medical care unnecessarily, given public health guidance to avoid healthcare settings for anything other than urgent care requiring in-person contact. All participants without a 24-month CDW outcome will be asked to self-weigh using a letter asking the participant to weigh themselves using the scales provided by DELITE at baseline. The mailing will include instructions about how to make the measurement (e.g., light indoor clothing, no shoes or other heavy items), a form to record the weight, and a postage-paid return envelope. If we do not receive a mailed response from participants within 2-weeks, a study coordinator may call the participant and ask them to weigh themselves and report the weight over the telephone.
        - A participant's primary outcome weight will be the one measured closest to 12 months AND between nine and 15 months, in a primary care-based clinic, and extracted from CDW. We will consider other weights as secondary outcomes.
    - To validate clinic weights, we asked some VA Puget Sound HCS/CBOC participants to visit the Seattle or American Lake campus for an in-person weight collected by study staff. We coordinated those visits with an existing clinic visit to have a clinic-based weight for comparison. If the scheduled visit is in a non-primary care clinic, we may ask the participant if we may accompany them to primary care for a weight check. If primary care does not enter the weight into CPRS, Drs. Au or Hoerster may do so. We have completed this process as of early 2020 and won't add it again, given the pandemic.

- Generic health status: Assessed using the SF-12[55] at 12 months as a primary outcome and at 24 months as a secondary outcome. The SF-12 has been extensively tested and shown to be valid, reliable and responsive to change.
- Reach: We selected the most relevant measure for the present trial from the well-established RE-AIM framework[72]: "reach," defined as the "number, proportion, and representativeness of individuals willing to participate in a given intervention." First, we will estimate the proportion of those eligible who agreed to participate, with total recruitment letters sent, and total eligibility screenings conducted as denominators.

Second, we will capture "representativeness" by comparing participants' demographic characteristics to the VA patient population and to those who were eligible for the study.

- Physical activity: 7-item International Physical Activity Questionnaire (short IPAQ) which evaluates weekly walking, vigorous and moderate-intensity activity.[73]
- Dietary quality/self-efficacy: Starting the Conversation[74] questionnaire with items pertaining to fat, fruit and vegetable intake, and sugar intake, as well as diet self-efficacy measures.[75]
- Sleep-Related Disturbance and Impairment: 4-item sleep disturbance and 8-item sleep-related impairment scales from the NIH PROMIS measures.[76]
- Blood pressure: diastolic and systolic values from 12 months prior index date to 27 months follow-up will be obtained from the CDW.
- Blood sugar levels: HbA1c levels from 12 months prior index date to 27 months follow-up will be obtained from CDW
- Other weight loss interventions: We will monitor through CDW data extraction for participation in MOVE! and by patient report for participation in programs outside VA, and we will control for such use in secondary analysis.
- Engagement of participants to the intervention will be assessed by: Through MFP and/or mailed survey:
    - Number of GLB sessions viewed, modality used (DVD vs. online), and use of handouts;
    - Number and topic of contacts with lifestyle coaches.
- Cost: We will conduct a budget impact analysis and determine implementation costs using VA Managerial Cost Account (MCA) System.

Table 5. Measures and timing of data collection.

Variable	Potential source of data	12 months prior	Baseline	3 months	12 months	24 months
Program reach, baseline characteristics, and covariates						
Height	CDW		x			
Comorbidities	CDW/self-report	x	x		x	x
Medications	CDW	x	x		x	x
Healthcare utilization	CDW	x	x		x	x
Distance from primary care clinic	CDW		x			
Demographics	CDW; Self-report		x			
Weight loss programs	CDW/self-report				x	x
Self-monitoring	Self-report				x	x
Outcome assessments						
Primary						
Weight	CDW (primary care-based measurement through 15 mos)		x		x	
SF-12	Self-report		x		x	x
Secondary						
Weight	CDW (all outpatient measurements* through 27 mos) or participant measured*	x	x		*x	x
Physical activity	Self-report		x		x	x
Dietary quality/self-efficacy	Self-report		x		x	x
Sleep disturbance / impairment	Self-report		x		x	x
Blood pressure	CDW	x	x		x	x
HbA1c	CDW	x	x		x	x
Other weight loss interventions	CDW/self-report	x	x		x	x
Engagement	Self-report			x	x	
Percent accepting invitation	Invitation response		x			
Cost**	MCA					x
Reach	CDW/self-report/study tracking		x			
Adverse Event Surveillance						
Event form	CDW/Self-report				x	x

**other potential sources are Health Economics Resource Center (HERC), Non-VA Medical Care Files, VA/CMS Data for Research, and VHA Support Services Center (VSSC) via the following tools: Compensation & Pension Record Interchange (CAPRI), the Computerized Patient Record System (CPRS), VistAWeb, VINCI.

5.5.3 Participant Payment:

After the 24-month time point, we will compensate participants $20 for completing the 12- or 24-month survey packets. We will pay participants an additional $10 if they complete both packets, for a total possible of $30.

Following payment submission, we may mail a letter notifying participants that participation is complete and payment has been submitted.

5.6 Data Analysis

5.6.1 Power/Sample Size:

This study is powered on weight and SF-12 PCS outcomes, using ANCOVA for 12-month follow-up weight adjusted for baseline weight, and applying a t-test for the 12-month SF-12 [77]. See Table 6 for a summary. A two-sided type I error rate of α = 0.025 was chosen based on a multiple comparisons Bonferroni adjustment. In order to ensure adequate power for this pragmatic trial, we are enrolling 500 Veterans.

We based expected outcomes in D-ELITE on clinically meaningful outcomes. Regarding weight loss, we based it on the weight lost in E-LITE's self-directed arm among male participants (since we anticipate the majority of our Veteran participants will be male): 11 ± 2 lbs [62]. This is an amount of weight loss likely to be clinically meaningful [3]. We expect weight loss in the control condition to be similar to that achieved in the standard MOVE! program: 3.3 pounds [78]. Thus, we expect to be able to detect a 7.7-pound absolute difference in 12-month mean weight between treatment arms, which requires 78 patients per treatment arm (156 patients in total), assuming a 12-month weight standard deviation of 50 lbs [79], correlation of 0.97 between baseline and 12-month weight, 90% power, two-sided Type I error rate α = 0.025, and 20% attrition at 12 months [62]. This scenario has a Cohen's d effect size of 0.154 [80]. A more conservative set of assumptions with a 6.7-pound difference (25% reduction in Cohen's d effect size) and a weaker correlation of 0.95 between baseline and 12-month weight measures requires 225 patients per treatment arm (450 patients in total) with all other assumptions unchanged.

For SF-12 PCS at 12 months, we assume a Minimal Clinically Important Difference (MCID) of a 5.00-point absolute mean difference for the SF-12 PCS [81] between treatment arms, with a standard deviation of 8.88 points based on unpublished E-LITE data, which corresponds to a Cohen's d effect size of 0.563 [80]. Also assuming 90% power, two-sided Type I error rate α = 0.025, and 20% attrition at 12 months, this would require 100 patients per treatment arm (200 patients in total). A more conservative scenario that assumes a 4.33-point absolute mean difference (25%-reduced effect size) requires 176 patients per treatment arm (352 patients in total) with all other assumptions unchanged.

Table 6. Sample size requirements for 12-month weight, SF-12 PCS.

12-Month Outcome (Testing Method)	Significance Level	Power	Scenario Type	Mean Diff. (SD) Cohen's *d*	Sample Size (w/ 20% Attrition)	
					Per-Group	Total
Weight (ANOVA, with adjustment for baseline weight)	0.025	0.90	Mean Diff. = 7.7 SD = 50.0 Corr. b/w Baseline, 12-Mo. Measures = 0.97	7.7 (50.0) *d* = 0.154	78	156
			Conservative (25% Cohen's *d* reduction, Corr. = 0.95)	6.7 (57.7) *d* = 0.116	225	450
SF-12 PCS (t-test)	0.025	0.90	MCID = 5.00 SD = 8.88	5.00 (8.88) *d* = 0.563	100	200
			Conservative (25% Cohen's *d* reduction)	4.33 (10.25) *d* = 0.422	176	352

5.6.2 Retention:

As in other studies, we will carefully train and regularly review with staff best practices for retaining participants, including fully informed roles and responsibilities of staff and participants, and conveying an appreciation of participation and study identification. We will train staff to conduct effective informed consent to assure that participants fully understand the demands and nature of the study before they enroll. Coordinators will carefully review study requirements with participants, explain the concept of random assignment and what each treatment involves, and stress the importance of follow-up assessment even if they are not adhering to their assigned

treatment. We will use a database to systematically track participant activities, prompt the study team when action is required, and regularly produce quality control reports, all proven elements for participant retention.

5.6.3 Hypothesis Testing and Statistical Analyses:

We will use intention to treat (ITT) for all primary and secondary analyses. We will evaluate the dropout and missing data patterns for informative missingness[82]. To test for non-zero intervention effects on weight and SF-12 PCS, we will compare mean outcome between intervention and control groups at 12 month follow-up using the repeated-measures mixed-effects linear model:[83-85]

$$y_{ij} = \beta_0 + \beta_1(j) + \beta_2\left(\mathrm{InterventionFollowUp_{ij}}\right) + \beta_3(\mathrm{Age65Plus}_i) + \beta_4(\mathrm{BMICat1}_i) + \beta_5(\mathrm{BMICat2}_i) + \beta_6(\mathrm{Urban}_i) + \alpha_i + e_{ij}$$

y_{ij} is the outcome (weight or SF-12 PCS) for patient *i* at baseline (*j* = 0) or 12-month follow-up (*j* = 1). $\mathrm{InterventionFollowUp}_{ij}$ is an indicator variable equal to 1 if patient *i* was randomized to the intervention arm and y_{ij} corresponds to a 12-month follow-up outcome (*j* = 1), and it is equal to 0 otherwise. $\mathrm{Age65Plus}_i$ is an indicator variable for whether the patient's age was at least 65 years at initial CDW pull. $\mathrm{BMICat1}_i$ is an indicator variable for whether the patient's BMI at initial CDW pull was ≥35 and <40, and $\mathrm{BMICat2}_i$ is an indicator variable for whether the patient's BMI at initial CDW pull was ≥40.0 and <45. Urban_i is an indicator variable for whether the patient's population density at initial CDW pull is urban. The adjustment for $\mathrm{Age65Plus}_i$, $\mathrm{BMICat1}_i$, $\mathrm{BMICat2}_i$, and Urban_i is based on the use of these variables in our stratified randomization procedure.[86] The α_i are patient-level random effects, independently distributed Normal(0, σ_α^2). The e_{ij} are measurement-level errors, independently distributed Normal(0, σ^2). Our primary weight and SF-12 PCS models do not adjust for the main effect of the intervention, and the coefficient estimates for $\mathrm{InterventionFollowUp_{ij}}$ will serve as our treatment effect estimates. Our randomization is expected to promote equality across treatment arm with respect to our baseline outcomes and patient characteristics. Under this assumption, the coefficient for the main effect of treatment is expected to be zero, and our power is increased by excluding its estimation from our models.[87]

We will adjust the co-primary outcome analyses for multiple testing using a Bonferroni adjustment,[88] which will allow for individualized assessment of our two primary outcomes at significance level 0.025 while maintaining a familywise error rate equal to 0.05. If exactly one hypothesis test leads to a null hypothesis rejection, we will infer that the intervention had a significant effect on that primary outcome but not the other. Two null hypothesis rejections and two failures to reject are also possibilities, in which case we will infer that the intervention had a significant effect on both or neither of our primary outcomes, respectively.

Exploratory analyses of Aim 2's biometric, psychological, and behavioral outcomes will be examined using tests of mean difference between groups after adjusting for baseline measures and randomization covariates in linear or logistic models, drawing on models used for primary analyses. We also will examine effects among women, and have estimated—with the assumptions of 80% power, ICC of 0.9, and 150 women participants—that we will have power to detect a similarly-sized effect among women as in the prior E-LITE trial.[62] Given these outcomes are exploratory and are not focused on hypothesis testing, adjustment for multiple comparisons will not be performed.[89] Rather, these analyses will report effect sizes and 95% confidence intervals, along with p-values, to aid with interpretation of clinical significance.

5.6.4 Budget Impact Analysis:

To assess the economic impact of the intervention, we will focus on budget impact analyses to establish a business case for future implementation if the intervention is successful. We will perform a budget impact analysis from the VA perspective using a 12-month intervention period. First, we will compare costs of care potentially associated with weight loss therapies between the intervention and control groups: VA nutrition and behavioral weight management healthcare visits and weight loss medication from the VA Managerial Cost Account (MCA) System and Health Economic Resource System (HERC).[90,91]. Second, we will estimate potential future D-ELITE implementation costs, combining estimated potential patients based on trial reach

findings with costs of identifying and recruiting patients; training lifestyle coaches; and activities performed by the lifestyle coach using detailed project logs, incorporating data on staff salaries.[92]

5.6.5 Misclassification and Missing Data:
We anticipate that any misclassification of outcome measurement will be non-differential with respect to randomization and effectively biasing our results toward the null. We will attempt to minimize misclassification by using approaches to decrease measurement error within the CDW data as well as by collecting patient-measured data when necessary. We will use data collected from primary care clinics preferentially. We will not collect weight data that was part of hospital admissions because of potential of changes in weight due to management. We will ask participants to use the scales provided only when not available in the CDW. If we find no evidence of informative missingness we will be able to rely on our use of well-specified mixed models to test effects of the intervention as these are known to lead to valid conclusions even when data are missing at random (MAR).[87,93] If we detect informative missing data patterns, we will apply sensitivity analyses using pattern mixture models.[82] Complete case analysis will only be performed as a sensitivity analysis, to provide useful inference if the data are mostly complete and the bias introduced by dropping the small proportion of incomplete cases is negligible.

5.6.6 Interim Analyses:
We plan no formal interim analysis of efficacy or futility. We will provide interim safety reports semi-annually to the Data Monitoring Committee (DMC).

5.7 Withdrawal of Subjects
We do not anticipate a need to withdraw a participant from the research entirely. If a participant becomes pregnant, we become aware of a serious physical or mental health issue, or the participant's primary care provider notifies us that the individual should not continue the intervention, the participant will cease participation in the intervention activities of the research; however we will continue to follow the individual through completion of the study via CDW and self-report.

If a participant chooses to withdraw him/herself from the research, we will confirm with the individual that we may continue to follow him/her in CDW. If the individual declines, we will respect his/her choice and not collect additional data from CDW; however we will use any data collected up to the date of withdrawal.

6.0 Reporting

6.1 Safety Assessment
Physical, psychological, social, legal or other risk will be low in association with participation in the proposed research. We base this assertion on the original diabetes prevention program where serious adverse event rates were similar in the intervention and placebo groups (NEJM, 2002,346:393-403). Moreover, Dr. Ma's ELITE trial showed no study-related serious adverse events in the self-directed DVD group upon which the DELITE intervention is based.

To ensure unbiased determination across treatment arms, at each follow-up contact we will ask participants to complete a survey about potential adverse events (AE), serious adverse events (SAE) and unanticipated problems (UP) employing a body system-based assessment. A study investigator with appropriate clinical training and will assess (using participant self-report and chart review) each AE for duration (start and stop dates and times), expectedness in the study population, severity, outcome, treatment and relation to study activity.

The following are expected adverse events in the DELITE population of participants who have a high BMI, and adopt healthy eating and physical activity program:
- Gastrointestinal symptoms related to change in diet;
- Musculoskeletal symptoms or injury resulting from increased physical activity, including increasing symptoms such as chest discomfort, shortness of breath, and leg cramping;

- Development of weight associated disorders including diabetes, hypertension, liver disease, cardiovascular disease, asthma, COPD, clotting problems, and other lung related conditions;
- Development of other conditions associated with unhealthy health behaviors, such as from tobacco and alcohol disorders (e.g. cancer);
- Age related illnesses, such as pneumonia, urinary tract and skin infections.

6.2 Quality Monitoring

The investigators will closely monitor and prepare semiannual summary reports on:

- Patient accrual and follow-up completion/retention in relation to goals and timeline;
- Randomization process and group comparability on the balancing variables;
- Key baseline characteristics of the sample, by blinded group, on the primary and secondary outcome variables;
- Intervention adherence;
- Protocol violations.

6.3 Data Monitoring Committee (DMC)

This is a single-site study with minimal risks; therefore, we will form a Data Monitoring Committee (DMC) consisting of Charles Maynard, PhD, and Ashok Reddy, MD. The committee will convene at least semiannually.

Upon discovering an unexpected and related SAE, study staff will provide the IRB and DMC with a report describing the duration (start and stop dates and times), severity, outcome, treatment, and relation to study activity, according to the required timelines. The DMC may request additional information if it deems additional deliberation is warranted.

For all other events, staff will summarize and report to the DMC on a semi-annual basis the numbers and types of all AEs by unidentified treatment arms. At their discretion, the DMC may request unblinded results in order to determine the nature and extent of effect of the intervention. Should the DMC make this request, we will maintain blinding of the investigators and the staff involved in follow-up data collection and analysis. If, at any time, the investigators believe they are seeing an unexpected increase in SAEs that is a cause of concern, they will bring this to the attention of the DMC.

For semiannual reporting, staff also will provide the quality monitoring report to the DMC.

At the semiannual meeting, the DMC will review AE/SAEs and the quality of data, as well as review study progress and provide objective recommendations, as appropriate, with respect to:

- Determination of any actions to be taken in response to SAEs;
- Reports related to study operations and the quality of the data;
- Consideration of early termination of the study because of treatment safety concerns or inadequate performance;
- Modifications in the study protocol concerning recruitment, participant retention, data quality, outcome assessment, statistical analysis, or general trial operations.

7.0 Privacy and Confidentiality

This study will use PHI. We will not disclose the PHI outside the the VA.

To ensure the data are secure, the study team will code study data with a unique study code. We will maintain the master list separately from the study data. The researchers will maintain data on the VA HSR&D network in password protected and permission specific directories and databases. Our network has multiple levels of protections and access is restricted to IRB-approved staff. If a staff member leaves the study, we will remove his/her permissions to access the data. We will follow all VA HSR&D data security policies.

Paper copies will be stored in a secure office suite in locked files accessible by approved study staff only. The ISO and Privacy Officer will be notified within one hour of the improper use or disclosure, as well as any other local policies.

All study information is accessible only by IRB approved study staff on a need-to-know basis.

To report study results, we will use only aggregate data.

The study team considers all participant information confidential. We will share information with participants' physicians only as needed to protect participants' safety. We inform the participant of this practice as part of the informed consent process.

We will offer participants the option of tracking their diet and exercise through MFP, which is a publicly available web-based platform. The loss of privacy with MFP is no greater than the risk of ordinary use of numerous similar publicly available online programs. As part of informed consent decision-making, we will describe this risk, as well as the potential benefits of participating in an intervention with demonstrated effectiveness and safety in other populations. With that in mind, participants can choose if they wish to use MFP or a paper tracker.

8.0 Communication Plan

This is a single-site study. To ensure all elements of the study protocol are followed and that study goals are met, the project manager will conduct regular meetings with project staff to review study procedures and status, barriers encountered, and develop responses to any identified issues.

9.0 Information Security and Data Storage/Movement

DELITE staff will store paper-recorded data in secure, locked file cabinets within HSR&D secure office suite, and electronic data in password protected files on secure VA network servers or VA Office of Information and/or Technology (OI&T) managed archived back-up media, according to VA data security policy. Our network has multiple levels of protections and access is restricted to IRB-approved staff. Limited analytic datasets are shared between authorized study personnel via secure transmission and/or via a secure virtual private network employing industry-standard password protection and data encryption. Study information is not disclosed to any third party except as required by law.

Once the study is closed, we will retain these research data for the minimum period required for records retention in accordance with the National Archives and Records Administration (NARA) VHA Record Control Schedule (RCS). The VAPSHCS Research and Development Office will be responsible for overseeing the storage of the data during the RCS required records retention period and for the eventual destruction of the data as authorized by the RCS. When the minimum data retention period has ended, all research data records in the possession of VAPSHCS will be destroyed. At this same time, we will also work with VINCI staff to destroy these records from any VINCI server(s) and archived tape backups/media. For electronic data, the Office of Information and Technology (OI&T) is responsible for maintaining the security of the electronic records during the records retention period. The data will be destroyed by a method to be determined by the VAPSHCS Information Security Officer (ISO) in a manner that is compliant with VA Handbook 6500.1 and National Institute of Standards and Technology NIST SP 800-88.

Study staff will enter all study data into SQL databases housed within HSR&D. All of the data entry systems will employ automatic, real-time range, logic, and missing value checks. We will employ double data entry and logic controls to minimize data entry error. We will maintain one official copy of all the study data and a master data dictionary.

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