STATISTICAL ANALYSIS PLAN (SAP)

Randomized Explanatory Trial of a Mediterranean Dietary Pattern Weight Loss Intervention for Primary Care Practices

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STATISTICAL ANALYSIS PLAN: DELISH

PROTOCOL: Randomized Explanatory Trial of a Mediterranean Dietary Pattern Weight Loss Intervention for Primary Care Practices (DELISH)

SAP VERSION 4.0

SAP DATE: Final protocol approved before blinded outcome analysis undertaken on 10/28/24. Last edited 6/9/25.

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SPONSOR: Center for Health Promotion and Disease Prevention (a CDC funded Prevention Research Center) at the University of North Carolina at Chapel Hill.

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1 List of Abbreviations

DELISH	Delicious Eating for Life in Southern Homes
Med	Mediterranean
HPDP	UNC Center for Health Promotion and Disease Prevention
WW	Weight Watchers

2 Date of current draft.

The draft was prepared on 9/10/24, after all participants were randomized but before analysis of outcomes.

3 Introduction

The DELISH (Delicious Eating for Life in Southern Homes) Study will test if a weight loss intervention emphasizing a healthful eating pattern (Med-style) can yield long-term weight loss and improved CVD risk profiles.

Patients were recruited from 7 primary care practices located in the Chapel Hill area of central NC. Study participants were randomized to the Med-Style Weight Loss Intervention (hereafter called Med-South Intervention) or Augmented Usual Care (Weight Watchers™ and also called WW™ during the time frame of this study) in 1:1 ratio. The interventions are given free of charge. Study measurement visits are at baseline and 4-, 12-, and 24-month follow-up.

4 Objectives

a) The primary objective of the DELISH Study is to determine if mean weight loss in the intervention group will exceed that in augmented usual care by ≥ 4% of initial body weight (e.g., ≥ 5% intervention, ~1% control).

Secondary objectives include:

b) assessing difference between study groups in proportion losing ≥ 5% body weight and differences in mean weight loss and proportion losing ≥ 5% across 3 pre-specified subgroups: 1) with vs. without diabetes; 2) females vs. males; and 3) Whites vs. African Americans,

c) assessing change in blood pressure, A1c, markers of inflammation, skin carotenoids, and self-reported dietary patterns by study group,

d) assessing process variables (attendance, fidelity, and acceptability of the Med-style dietary intervention), and key behavioral and psychosocial variables, including self-regulation/monitoring skills, self-efficacy, motivation, and quality of life, and

e) assessing implementation cost, and incremental cost-effectiveness of the intervention relative to control in terms of cost per percentage reduction in weight (i.e., kg lost) and cost per quality adjusted life years (QALYs) gained.

5 Study Design

5.1 Randomization and Blinding

This is a single-site (per NIH definition) open-label randomized controlled trial enrolling 360 participants for 7 local practices desiring weight loss and followed over 24 months. Participants were enrolled in 3 sequential waves as described below. Participants were randomized in 1:1 ratio. Statistician will be blinded for the primary analyses.

Group 1: Med-South Weight Loss Program (the intervention)
Group 2: Weight Watchers (WW™) (augmented usual care)

Randomized assignment were done by a computer program stratifying on Wave and diabetes status and using randomly permuted blocks of random sizes (4 and 6) to achieve balance in the participants' allocation.

5.2 Planned Enrollment

The overall sample size is 360. The study plan was to conduct contemporaneous enrollment of sub-groups to ensure that at least 40% of participants will be African American, diagnosed with diabetes, and male. At the initial study practice, the UNC General Internal Medicine practice, the contemporaneous enrollment protocol was followed for the enrollment of approximately ½ the sample, after which there were not sufficient potential participants in sub-groups of interest to continue this protocol. Instead, complete sampling was done of specific of subgroups of interest (e.g. African American men).

Enrollment was conducted in 3 sequential waves. Wave 1 included the large UNC General Internal Medicine practice located in Chapel Hill, NC. Wave 2 included two internal medicine practices in Chapel Hill, NC (Chapel Hill Internal Medicine and UNC Internal Medicine at Weaver Crossing) and one family medicine practice in Hillsborough, NC (Orange Family Medicine Group). Wave 3 included two family medicine practices in Durham, NC (UNC Family Medicine Center at Durham and UNC Family Medicine at Southpoint) and one internal medicine and pediatrics practice located near Chapel Hill, NC (North Chatham Pediatrics & Internal Medicine). Study enrollment and measurement visits were conducted at the Center for Health Promotion and Disease Prevention, located at 1700 Martin Luther King, Jr. BLVD, Chapel Hill, NC. For the Med-South intervention group, the first counseling session was conducted in person with the large majority of follow-up visits conducted by phone. For the WW group, the intervention was primarily given via web-based app for use on personal computers, tablets, or smart phones. WW participants had the option to attend group sessions once these were offered by WW after closure due to the Covid 19 pandemic.

5.3 Study Medication

None.

5.4 Assessments

Our enrollment dataset will include participants' screening ID, diabetes status, sex, and race. All these variables were obtained from the UNC electronic health record. In addition, we will ask participants to report race on our demographic form and this will be the official race variable).

Participants will be assessed according to the schedule described below.

Study data will be collected at measurement visited conducted at baseline, 4, 12, and 24 months. Process data for the intervention group (Med-South Weight Loss Program) will be collected as part of the intervention via the web-based platform and via REDCap questionnaires completed by counselors immediately after counseling sessions. Process data for the WW group will be assessed via a Data Use Agreement with WW™ and by REDCap questionnaire completed by study participants just prior to or at the follow-up measurement visits. As recommended by NIH, our measures include ADOPT[137-139] core constructs (in blue) and specific instruments (in blue underlined) as noted in Table 1 below, with more detail provided in Appendix A.

Original study windows for follow-up measures as outlined below:

- 4 months: 3-8 months.
- 12 months: 11-18 months.
- 24 months: 23-30 months.

After data review, but before analysis of outcomes, these allowable windows were revised because for a variety of reasons (covid-10 issues, behind in counseling visit sequence, etc.) participants returned later than expected. Following up windows were expanded at 4 and 12 months to include the number of months after anticipated visit above to number of months after observed median follow-up date. 24 month interval was not changed as all participants were instructed to return within 30 months of randomization.

- 4 months: 3-8 months, change to median follow-up days (154), plus 4 months (4 x 30.4 [days in month) to yield 276 for end of interval. Operational interval is 90-276 days
- 12 months: 11-18 months, change to median follow-up dates (414), plus 6 months (6 x 30.4 [days in month) to yield 596 for end of interval. Operational interval is 335-596 days
- 24 months: 23-30 months, change to median follow-up dates (772), plus 6 months (6 x 30.4 [days in month) to yield 954 for end of interval. Operational interval is 700-954 days

Table 1: Outcomes/ Measures
Weight (primary outcome), by electronic scale measured in pounds as the average of two measures (three measures if difference between the first two is > 1 pound), and height (baseline only, measured to the nearest 1/8 inch). SECA 874dr scales will be used.
Secondary Outcomes
Biomarkers
--Blood pressure by noninvasive automated monitor (Omron HEM-907XL, Vernon Hills, IL) with a first measure after seated for 5 minutes and two repeat measures at 1-minute intervals. The average of the 3 measurements will be used.
--For blood work fasting status is requested for 9 hours and fasting status at phlebotomy is assessed. Blood tests performed at LabCorp includes: total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, A1c, ALT, and CRP. Inflammatory markers, to be assess on frozen specimens after all are collected will include: interleukin (IL)-6, tumor necrosis factor (TNF)-alpha, insulin, and leptin.
--*Skin carotenoids, Reflection Spectroscopy Device ("Veggie Meter"™)*[1-3]
Questionnaires:
--Demographics, literacy screener[4] and medical history (baseline only)
--Diet assessment: brief assessment of diet quality,[5] adapted PREDIMED checklist[6,7]
--Detailed assessment of diet quality: Willett Food Frequency Questionnaire, 2007 booklet administered as REDCap survey[8]
--Physical activity and sedentary behaviors: *GPAQ for physical activity and sedentary behavior*,[9] participant report of monitored steps
--Quality of life (EQ5D[10])
--Food insecurity[11]
--Predictors of behavioral change
-- weight loss self-efficacy,[12] self-regulation,[13] eating behaviors,[14] and *self-weighing behaviors*[15]
--Medications for high BP, high blood lipids, diabetes, and weight loss (self-report with EHR review)
--Adverse outcomes, CVD events, ER visits, and hospitalizations (follow-up only)
--Acceptability (follow-up only)
Diet and PA goals and success achieving goals (collected by web-based intervention platform)
Other
--EHR to assess/confirm adverse health outcomes

6 Analysis Populations

Potential participants who were screened but not randomized will not be included in any efficacy or safety analyses of study data.

6.1 Intent-to-Treat Population (ITT)

The Intent-to-Treat population will consist of all subjects who are randomized. No protocol violations will lead to exclusion from the intent-to-treat population. Subjects in the intent-to-treat population will be grouped according to the treatment assigned by the randomization procedure. This population will form the basis for the primary and

secondary efficacy analyses of study data as well as for safety analyses. In this analysis, the mixed model with account for missing as missing at random.

Analysis for the primary outcome will be conducted with a dummy variable for randomization group. After the biostatistical team and MPIs are confident with analysis, the actual randomization status will be revealed.

6.2 Intent-to-Treat Population (ITT) using Missing Weights from the Medical Record

For missing weights, we will review the electronic health record and use weights as follows:

Weights will be used if they fall within the time frame allowed for follow-up measurement visits (see above Sect 5.4) and if consistent with prior weights (to avoid the occasional situation where pounds are mistakenly entered as kilograms). If more than one weight is available within the specified time window, the weight closest to the median for the window will be used. After the additional of weights so identified from the electronic medical record, we anticipate less than 5 % of follow-up weights will be missing.

6.3 Intent-to-Treat Population (ITT) censoring data for those with greater than 5% weight loss attributed to medical condition

For participants with > 5% weight loss at any follow-up time point, an electronic health record chart review will be conducted. If weight loss is attributed to a new medical condition typically associated with weight loss (for example, pancreatic cancer), participant outcome data will be censored from the time of diagnosis onward.

6.4 Intent-to-Treat Population (ITT) censoring data for those using weight loss medication

Note: at baseline, potential participants with diabetes on GLP-1 agonists and/or other medications used for diabetes that may be associated with weight loss were allowed to participate. For those without diabetes, current use of weight loss medication was an exclusion criterion. For participants who initiated use of GLP-1 agonists during the course of the study, weight change data will be censored at the time point where use of these medications is documented. We will not censure data for use of other medications that may impact weight loss when impact on weight change is typically minimal to modest (< 3%).

Added 10/28/24. Medications listed as weight loss

Amendment added 4/19/25: as only 2 pts had medical illness and 1 had bariatric surgery, we will combine 6.3 and 6.4

6.5 Per Protocol Population

The Per Protocol Population for assessment of weight change at 24 months will be a subset of the ITT population and will exclude participants who did not adequately adhere to the protocol as defined below for their assigned treatment arm, for whatever reason, and did not attend the final measurement visit.

Specifications to be included in per protocol analysis.

Both study groups.

- Measurement visits: attends the final measurement visit

Group 1: Med-South (Phase 1 = 4 months; Phase 2 = 8 months; Phase 3 = 12 months. There were 30 planned visits over 24 months; 75% would be 22 visits total; 75% of each = approximately 3, 10, 9, respectively.)

- **Phase 1** -- 4 major counseling sessions: attended at least 3 visits
- **Phase 2** -- 14 sessions planned (8 weekly → 6 monthly; optional brief follow-up): attended at least 10 visits.
- **Phase 3** -- 12 sessions planned (monthly; optional brief follow-up): attended at least 9 visits.

Group 2 WW

- As of 9/10/24, we have not received data from WW, though we are expected to receive these data. When available we will operationalize definition akin to 75% engagement of group 1.

We will also assess per protocol outcomes at 4 and 12 months for those meeting definitions as above and will follow-up data at these time points respectively.

6.6 Sensitivity Analysis and missing data

As outlined above, we will obtain weights from the electronic health record for study participants who did not return for measurement visits. These weights are collected on high quality electronic scales. The weight protocol in the clinic does not include removing shoes, though we expect some variability of shoe removal. We will not adjust weights obtained from the medical record for shoe removal.

After adding weights within range from the electronic health record, we anticipate that > 90% of study participants will have weights within the specified measurement windows. After including these weights, we anticipate missing weights will be less than 5%. If less than 5% of weights are missing at 24 months, the data will be analyzed by linear mixed models. If 5% or more of the weights at 24 months are missing, we will proceed as follows.

We made every effort to prevent missing data and to minimize attrition, however some dropouts occurred. We know the reasons for some dropouts but not all cases. We also know that some dropouts may be related to the underlying weight outcome so the missingness is not random. To address the missing data, we will first compare respondents and non-respondents for differences on values of selected baseline variables to assess for missing at random. We will also conduct a series of sensitivity analyses to evaluate the robustness of conclusions drawn from the primary model to departures from missing at random (MAR) assumption by comparing the magnitude of the primary treatment contrast.[16,17] The linear mixed model with maximum likelihood estimation is capable of dealing with data that are MAR. In case data are not missing at random, we will use 1) multiple imputation to include auxiliary information about the missingness; 2) shared-parameter models where one variable is the efficacy outcome and the second variable is time to dropout, linked by a set of latent variables that are assumed to influence both the outcome and the time to dropout; (3) patterning-mixture model, with models for each pattern of missingness (e.g., by study phase); and (4) worst-case imputation, with baseline carried forward for intervention participants and best observation carried forward for control participants.[16,17]

7 Outcome Definitions

7.1 Primary Study Endpoint

The primary outcome for this study is the percent change in body weight defined as (Follow-up weight – baseline weight)/baseline weight x 100%.

We will also assess proportions of participants losing ≥ 5% baseline body weight at each follow-up visit.

7.2 Key Secondary Outcomes

Key secondary outcomes include changes in the following outcomes from baseline to 24 months.

- blood pressure
- A1c

- markers of inflammation
- skin carotenoids
- self-reported dietary patterns

7.3 Additional Secondary Outcomes

We will also assess process variables including attendance, fidelity, and acceptability of the Med-style dietary intervention), and key behavioral and psychosocial variables, including self-regulation/monitoring skills, self-efficacy, motivation, and quality of life. If there is a material treatment effect (> 2.5% difference in weights per primary outcome), we will also undertake an Economic analysis as outline in Objective D.

7.4 Additional Outcomes not Specified in Study Research Strategy

We will also undertake analysis of a variety of other secondary study outcomes including stool microbiome conducted on a subset of study participants.

8 Other Data and Definitions

8.1 Demographics and Participant Characteristics

8.1.1 Race

All screened subjects will select as many races as applicable. For the analysis, race with be defined as non-Hispanic black, white, or other and analysis by race will compare NHB to other.

Table 2, Race Categories
White
Black or African-American
Asian
American Indian or Alaska Native
Native Hawaiian or Other Pacific Islander
Some other race

8.1.2 Ethnicity

All screened subjects will be given the option to report Hispanic or non-Hispanic ethnicity.

8.1.3 Gender

All screened subjects will be given the option to report gender. For the analysis based on gender, we will include those identified as male and female (note 1 participant identified as trans and 1 non-binary)

Table 3, Gender
male
female
transgender
additional category
non-binary

8.1.4 Diabetes

A participant will be classified as having diabetes if either 1) a doctor ever told him/her that he/she have diabetes, 2) A1c ≥ 6.5, or 3) are currently using any diabetes medication (Insulin, metformin, sulfonylurea, GLP-1 receptor agonists, SGLT2 inhibitors, thiazolidinediones, and/or DPP-4 inhibitor).

9 Statistical Analysis

9.1 General Considerations

9.2 Data Handling

The primary data collection and management program with be REDCap as administered by the NC TraCS. The data manager and Dr. Keyserling will be responsible for making corrections. A log of all corrections/edits will be maintained.

Table 4, Data Handling

Type/Use of Data	Data Source	Data Storage	Ident.	Data Review/Other Comments
Data from the electronic medical record	NC TraCS data warehouse	• NC TraCS server • HPDP server	yes	These data, extracted from the data warehouse utilized by NC TraCS, will be provided in an Excel format for each primary care clinician at participating study sites. Output will be carefully inspected by research staff for completeness before it is sent to providers who must recommend participation of their patients in this study.
Data for providers to review regarding participation of their patients	Primary care clinicians	HPDP server	yes	Providers will either be sent a link to a password protected Excel file with a listing of their patients who meet basic study inclusion criteria or these data will be provided on a password protected thumbdrive (a flash drive or USB stick). They will be asked to review and note the patients who they refer to the study to receive an intensive multimodal weight loss program.
Eligibility data	From participants, collected by phone by research staff	REDCap server	yes	Reviewed by staff before randomization.
Consent forms	Participants	• For consent completed on-line, REDCap server	yes	Research staff insure that consent documents are signed after all questions are answered.
Participant study data collected using REDCap forms and surveys—	Participants	REDCap server	yes	Surveys and forms will have study ID. Data will be collected via phone for those who do not want to complete online.

electronic questionnaires				
Willett Food Frequency Questionnaire	Participants	• Data collected using REDcap version • At Harvard School of Public Health	no	Data sent to Harvard is de-identified.
Anthropometrics, blood pressure, skin carotenoids	Participants	REDCap server	yes	Data entered by research field staff from instruments used for these assessments. Note special protocol for primary outcome variable, body weight. • For assessment at data collection time points, weight is assessed 2 times. If difference between weights is 1 pound or greater a third assessment is performed. For analysis, weights are averaged, using the 2 weights that differ by less than a pound. • For follow-up assessments, a photo of the weights will be taken and the data entered by study staff blinded to the randomization assignment of participant.
"Clinical" blood work	Participants	• At LabCorp per storage of routine lab work. • REDCap	yes	These clinical lab results will be scanned in the electronic health record and except for CRP, results will be reported to participants.
Blood markers of inflammation and diabetes markers (leptin and insulin)	Participants	• At Hursting lab • HPDP	yes	Samples will be stored at Hursting Lab until all are collected. Results will be entered into Excel spreadsheet and sent to HPDP.
DNA analysis	Participants	--	yes	Blood for DNA analysis will be stored as part of this study for possible future analysis. Samples will be stored at Hursting Lab.
Process data collected use Web-based counseling program.	Participants	• Sheps server • HPDP	yes	Data collected by web-based counseling program. These data will reside on the Sheps Center server until downloaded into a Excel file and sent to HPDP.
Data sets for analysis	Participants	• REDCap • HPDP	yes and no	Analysis datasets created from REDCap datasets. Will be stored on Study's Microsoft Teams account and on the HPDP O drive . These datasets will have identifiers in REDCap. Data exported from REDCap to be used for analysis is de-identified.

9.3 Interim Reports for the Data and Safety Monitoring Board

These are prepared by study staff in advance of each meeting.

9.4 Efficacy Analyses

Efficacy analyses will be based on comparisons between the Med-South dietary pattern intervention to WW with respect to efficacy endpoints.

9.4.1 Primary Efficacy Analyses

The primary analyses will be conducted using the ITT Population (i.e., all randomized participants) and will be repeated secondarily using the Per Protocol Population. We will compare the longitudinal mean % change in body weight between groups using analysis of covariance (ANCOVA), conducted using a linear mixed model. A mixed model will allow for the inclusion of all observed follow-up data for all participants. The model will include fixed effects for group, follow-up visit (4, 12, or 24 months), group-by-visit interactions, site (see operational definition as below), baseline weight, race/ethnicity, gender, and diabetes status. (When reviewing the analysis in May, 2025, we realize we inadvertently did not include age in the model. Our final models included age.) There is no plan to include other baseline variables (including those different) in the model. To account for within-participant correlation, the model will allow for correlated error terms using an unstructured covariance matrix. For the primary comparison, we will use a linear contrast (i.e., group -1 1 group*follow-up visit 0 0 -1 0 0 1) of the model parameters to test for a treatment effect at 24-months at the 5% significance level. Secondarily, we will compare the groups at other time points and will estimate effect sizes along with 95% confidence intervals for each comparison. Additionally, we will expand the model by including appropriate interaction terms, one at a time, to examine the potential heterogeneity of intervention effect in sub-groups, including diagnosis (diabetes vs. no diabetes), race/ethnicity, sex (for gender, 2 participants not binary, so will for these will use sex as captured in the electronic health record), and by degree of baseline obesity (BMI ≥ median vs. less). Interaction terms will be tested at the 5% significance level.

Next, we will use a longitudinal mixed effects logistic regression model to compare the groups for proportions losing ≥ 5% baseline body weight at each follow-up visit. Estimates of odds ratios and 95% confidence intervals will be provided. This model will control for the same covariates specified for the primary model and test the same interaction terms.

Study sites: Wave 3: Durham family medicine: 17, Durham family medicine at Southpoint 9: total 26. North Chatham internal medicine and pediatrics 27. Will combine the 2 Durham family medicine sites as they are physically located close to one another and are our 2 Durham practices.

9.4.2 Interim Analysis for Efficacy

Not planned.

9.4.3 Interim Analysis for Futility

Not planned.

9.4.4 Secondary Analyses

The ITT Population will be used in the primary analyses of all secondary outcomes. Similar ANCOVA methods to those described in the primary outcome analyses will be used to compare groups on each of the secondary outcomes. For any outcome measured at baseline, the corresponding ANCOVA will control for baseline value in addition to the covariates noted above. Because they are of secondary interest, tests on secondary outcomes will each be conducted at the two-sided 5% significance level without adjustments for multiple comparisons. All estimates of effect size will be accompanied by 95% confidence intervals. Data from all secondary outcomes will be presented regardless of extent of "significance".

Descriptive summaries of process data (attendance at intervention contacts, fidelity to intervention delivery, and acceptability of the Med-South dietary pattern) will be provided for participants randomized to the Med-South dietary pattern intervention group in the ITT Population. No inferential statistics (p-values or confidence intervals) will be presented.

9.5 Safety and Tolerability Analyses

Prior to analysis, any data-captured adverse events will be coded by the principal investigators. Each type of event (by seriousness, severity, relationship to study) will be descriptively summarized in frequency tables by group (including only a single occurrence of any distinct type of event for any participant). The number of CVD events, ER visits, and hospitalizations will also be descriptively summarized by group. No inferential statistics (p-values or confidence intervals) are planned for comparing safety data between groups.

9.5.1 Exposure to Study Medication and Compliance

NA.

9.5.2 Interim Analysis for Safety

NA.

9.5.3 Adverse Events

This protocol uses the definition of adverse event from 21 CFR 312.32 (a): any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related.

For this study a serious adverse event includes, as outlined at: https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html:

1. results in death;

2. is life-threatening (places the subject at immediate risk of death from the event as it occurred);

3. results in inpatient hospitalization or prolongation of existing hospitalization;

4. results in a persistent or significant disability/incapacity;

5. results in a congenital anomaly/birth defect; or

6. based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse)

9.6 Sample Size Justification

For our primary outcome, percent change in weight at 24 months, we have calculated sample size based on a two-sided test of significance with α=0.05 and the standard deviation (SD) of percent change in weight of 7.3% as observed in the Heart Health Lenoir Project.[18,19] Table 5 illustrates sample size calculations (allowing for 20% attrition) for various differences in mean changes between study groups based on a 1:1 randomization allocation ratio. This table also provides power calculations to detect differences in weight change compared to augmented usual care separately for pre-specified subgroups (those with vs. without diabetes, female vs. male, and white vs. African American assuming no sub-group is less than 40% of the overall sample). We expect the intervention to reduce weight by at least 5% and that average weight loss in the intervention group will exceed that in augmented usual care by at least 4% (we estimate weight loss in usual care of ≤ 1%). Our plan to enroll 360 participants provides excellent power for our primary outcome

(>99%) and reasonable power (82%) within each of our pre-specified sub-groups. For a difference between groups as small as 3%, we still have robust power for our primary outcome. Although we do not anticipate major differences in weight loss between those in our pre-specified subgroups, we will test the potential for large differential effects between subgroups using interaction terms. However, under the assumptions described above, our power to detect realistic difference in effects of 2-3% between these subgroups will be limited (about 20-40%). Also, for a difference in proportions of those losing ≥ 5% body weight as small as 15% (e.g., 15% control vs. 30% intervention), allowing for attrition, the proposed sample size provides 85% power. For several secondary outcomes, we present in Table 5 minimally detectable differences corresponding to effect size of 0.33 for the sample size of 360 with 20% attrition, 80% power, and α =0.05.

Note, the table below assume sample size of 350. After funding, the investigative team elected to increase sample size to 360 with a goal of 120 participants per wave.

Table 5. Power Estimates for % Change in Weight at 24 Month Follow-up

Assumed Mean % Change Difference Between Groups	Total Sample Size	Overall Power to Detect Difference	Minimum Power within Each Subpopulation (Diabetes status, sex, and race) to Detect Specified Difference
3%	300	0.89	0.51
	350	0.93	0.58
	400	0.96	0.64
4%	300	0.99	0.76
	350	0.99	0.82
	400	0.99	0.87

10 Software and Statistical Programming

Tabulations and statistical analyses will be performed using SAS Version 9.4 (SAS Institute Inc., Cary, NC). All programming will be done by the statistician, Dr. Qiang Wu in the Department of Public Health at East Carolina University. The research staff will submit a written statistical computing request to the statistician and the request will be assigned a version number. After the statistician undertakes the request, the research staff will review the programs and output. If necessary, changes will be requested in writing and new version numbers will be assigned. After the programming has been completed to the satisfaction of the research staff, all materials will be archived, which will include the original computing request, any subsequent changes, the SAS programs and any output, including log and list files and datasets created in the requests will be archived.

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Appendix A: Summary of Assessments

Table 3: Outcomes/ Measures	Collection Time (min)	Data collected times (months)				Comment
		0	4	12	24	
Weight (primary outcome), by electronic scale as the average of two measures, and height (baseline only). SECA 874 dr scales will be used and assessed monthly for accuracy with standardized weights..	5	x	x	x	x	At study outset, seven standardized 50 lb. weights certified for accuracy by NC state standards lab.*
Secondary Outcomes						
Objective measures						
--Blood pressure by noninvasive automated monitor (Omron HEM-907XL, Vernon Hills, IL) with a first measure after seated for 5 minutes and 2 repeat measures at 1-minute intervals	10	x	x	x	x	
--Blood work: Non-fasting total & HDL cholesterol, A1c, interleukin (IL)-6, tumor necrosis factor (TNF)-alpha, and C-reactive protein (C-RP)	10	x	x	x	x	Creatinine collected at baseline for those without measure in preceding 2 years.
--*skin carotenoids, Reflection Spectroscopy Device ("Veggie Meter"™)*[1-3]	5	x	x	x	x	
Questionnaires:						These data collected before the actual visit, on-line via REDCap or by phone. Window before baseline visit is 4 weeks. Window before follow-up at 4 months is 2 weeks. Window before follow-up visits at 12 and 24 months is 4 weeks.
--Demographics, literacy screener[4] and medical history (baseline only)	15	x				
--Diet assessment: diet quality,[5] fat quality,[20] adapted PREDIMED checklist[6,7]	10	x	x	x	x	
--Detailed assessment of diet quality: Willett Food Frequency Questionnaire[8]	20-30	x	x	x	x	
--Physical activity and sedentary behaviors: *GPAQ for physical activity and sedentary behavior,*[9] participant	5	x	x	x	x	

report of monitored steps						
--Quality of life (EQ5D[10])	5	x	x	x	x	
--Food insecurity[11] and material need insecurities[21]	8	x				
--Predictors of behavioral change						
--Exercise self-efficacy,[22] weight loss self-efficacy,[12] self-regulation,[13] eating behaviors,[14] and *self-weighing behaviors*[15]	30	x	x	x	x	
--Medications for high BP, high blood lipids, diabetes, and weight loss (self-report with EHR review)	5	x	x	x	x	
--Adverse outcomes, CVD events, ER visits, and hospitalizations (follow-up only)	5		x	x	x	
--Acceptability (follow-up only)	5-10		x	x	x	
Diet and PA goals and success achieving goals (collected by web-based intervention platform)	NA					Collected after each counseling session in intervention group.
Exploratory Outcome						
Stool microbiome (participants may elect not to complete this measure)	NA	x	x	x	x	First sample will be collected in the 2 week period immediately after randomization. (These are the only baseline data collected after randomization.) The follow-up samples will be collected w/n a 2 week window of follow-up visit date.
Other						
--EHR to assess/confirm adverse health outcomes	NA		x	x	x	To confirm information collected by questionnaire at these visit time points