Statistical Analysis Plan (SAP) for the Spark Trial

Grant Title	Optimizing self-monitoring in a digital health intervention for weight loss
Trial Registration	ClinicalTrials.gov: NCT05249465
Funding Agency	NIH/NIDDK
Grant Number	K23DK129805
CRU/Department/Division/Center	Stanford Prevention Research Center/Dept. of Medicine/Stanford University School of Medicine
IRB Number	Stanford IRB: 64716
Investigators:	
Lead Investigator	Michele L. Patel
Multiple PIs	n/a
Co-investigators	Abby C. King, Lisa G. Rosas, Gary G. Bennett
Biostatistician(s)	John Gallis
Supervising Biostatistician	n/a
Original Creation Date	07/06/2021
Version Date	09/27/2026
Project Folder Location	
Project Goal(s)	Peer-reviewed manuscript; abstract for presentation at national conference
Submission Deadline(s)	

Investigator Agreement	☒ All statistical analyses included in an abstract or manuscript should reflect the work of the biostatistician(s) listed on this SAP. No changes or additional analyses should be made to the results or findings without discussing with the project biostatistician(s). ☒ All biostatisticians on this SAP should be given sufficient time to review the full presentation, abstract, manuscript, or grant and be included as co-authors on any abstract or manuscript resulting from the analyses. ☒I have reviewed the SAP and understand that any changes must be documented. *Acknowledged by:* Michele L. Patel *Date:* June 4, 2025
Activity Log	June 4, 2025: MLP provided additional details to SAP; no modifications made to prior plan. June 9, 2025: John reviewed this specific draft for the first time and made a few minor edits and comments. September 27, 2026: MLP added winsorization details regarding the GLTEQ measure analyses.

Table of Contents

Optimizing self-monitoring in a digital health intervention for weight loss 1
1 Study Overview 3
1.1 Aims 3
2 Study Population 4
2.1 Inclusion Criteria 4
2.2 Exclusion Criteria 4
2.3 Sample Size 4
2.4 Randomization 5
2.5 Data Acquisition 5
3 Outcomes and Additional Variables of Interest 6
3.1 Primary Outcome 6
3.2 Secondary Outcomes 6
3.3 Other Outcomes 6
3.4 Other Variables of Interest 6
3.5 Independent Variables 7
4 Decision Criteria for Creating the Optimized Intervention 8
5 Statistical Analysis Plan 9
5.1 Overview of Factorial Trial Analyses 9
5.2 Characterizing the Sample 9
5.3 Analytic Plan for Primary Outcome 9
5.4 Analytic Plan for Secondary Outcomes 10
5.5 Analytic Plan for Engagement and its Association with Weight Loss 10
6 References 11
7 Appendix 13
7.1 Appendix A 13
7.2 Appendix B 14

1 Study Overview

Given high rates of overweight and obesity among U.S. adults, there is critical need to develop effective and scalable weight loss solutions.[1,2] In behavioral obesity treatments, self-monitoring is considered a core component.[3-5] Yet the optimal combination of self-monitoring strategies that maximize weight loss is unknown. Thus, we sought to address this gap in the context of a fully digital intervention, which has high potential for scalability given its standalone format, lower cost, and broad reach. To systematically determine the optimal combination of self-monitoring strategies, we leverage a framework for optimizing multicomponent behavioral interventions – the Multiphase Optimization Strategy (MOST).[6,7]

Spark is an Optimization-RCT that tests the unique and combined effects of three self-monitoring strategies (tracking dietary intake, steps, and/or body weight) in a 6-month fully digital weight loss intervention for adults with overweight or obesity. The study is fully remote and is open to participants from across the U.S. The study uses a 2^3 full factorial design (i.e., 2x2x2), whereby each participant is randomized to 1 of 8 experimental conditions that represent all possible combinations of these self-monitoring strategies. For each strategy, half of participants are assigned to receive it ("Yes") while the other half do not receive it ("No"; see **Figure**, below). All participants receive a core intervention that includes weekly evidence-based lessons and action plans to promote healthy eating and physical activity. We will recruit 176 participants (22 per condition). The trial was preregistered in February 2022 at ClinicalTrials.gov: NCT05249465. Assessments occur at baseline, 1 month, 3 months, and 6 months.

1.1 Aims

- Test the unique and combined effects of the three self-monitoring components (tracking dietary intake, tracking steps, and tracking body weight) on change in weight from baseline to 6 months (primary outcome).
- Test the unique and combined effects of the three self-monitoring components (tracking dietary intake, tracking steps, and tracking body weight) on change in secondary outcomes from baseline to 6 months, including caloric intake, physical activity, and health-related quality of life, as well as weight change from baseline to 1 and 3 months.
- Assemble an intervention made up of all active self-monitoring components (i.e., those with ≥ 2.1 kg mean weight loss at 6 months when comparing those who received vs. did not receive this component) without any inactive components (i.e., those with < 2.1 kg mean weight loss at 6 months).

2 Study Population

2.1 Inclusion Criteria

- adults aged ≥18 years
- BMI of 25.0 kg/m^2 to 45.0 kg/m^2, which corresponds to having overweight or obesity
- smartphone ownership
- willing to install the Fitbit mobile app on one's personal phone
- access to a personal email account
- proficiency in the English language
- interested in losing weight through behavioral strategies

2.2 Exclusion Criteria

- concurrent enrollment in another weight management intervention
- loss of ≥10 lbs. in the past 6 months
- current use of a weight loss medication
- prior or planned bariatric surgery
- current or planned pregnancy during the study period
- current breastfeeding
- living with someone else participating in the study
- hospitalization for a mental health condition in the past 12 months
- inability to engage in moderate forms of physical activity akin to brisk walking
- potential contraindications to losing weight due to a serious medical condition (e.g., cancer, end stage renal disease, schizophrenia, dementia) or medication (e.g., steroids, anti-psychotics)
- a history of an eating disorder or cardiovascular event or uncontrolled diabetes mellitus or uncontrolled hypertension that could predispose an individual to be better suited for a more intensive or different type of intervention
- investigator discretion for safety reasons

2.3 Sample Size

Using a power calculation, we determined that a sample size of 176 participants would be required in our factorial trial to detect a minimum clinically important difference of 2.4 kg at 6 months, which is associated with improvements in cardiometabolic risk factors.[8] We assumed a standard deviation of 4.5 kg, based on prior 6-month weight loss outcomes in digital interventions.[9-11] Thus, we sought to detect a main effect or interaction effect of d=0.53. Specifically, assuming 80% power, an alpha of 5% in a two-sided test, and 35% attrition at 6 months (a conservative estimate based on prior trials of fully digital weight loss interventions[5,12-14]), a sample size of 172 is needed. To obtain an equal number of participants in each treatment condition, we increased the sample size to 176 total participants (22 per condition). Allowing for an equal number of participants per condition permits the tests of the main effects and interactions to be uncorrelated. Even if unequal sample size across conditions occurs due to differential dropout resulting in minor imbalance, the correlations between effects should be small.[15] This power analysis was computed using the FactorialPowerPlan SAS Macro (v1.0).[16]

Our trial uses a 2^3 factorial design since it has 3 factors, each with two levels (*Yes*, *No*). In these types of 2^k factorial trial—those with k number of factors—all else being equal, the power for detecting a b-weight corresponding to an interaction effect is the same as that for detecting a b-weight corresponding to a main effect when using effect coding to represent the levels of the factors.[6] Thus, no additional participants are needed to detect interactions in 2^k factorial trials.

2.4 Randomization

This study uses a 2x2x2 (i.e., 2^3) factorial design, with 3 factors (i.e., tracking dietary intake, tracking steps, tracking body weight) each with 2 levels (received it vs. did not receive it), resulting in 8 experimental conditions. Following recommendations for factorial designs,[17] we randomized participants to 1 of 8 conditions using restricted randomization stratified by sex assigned at birth and using permuted block randomization with a block size of 8. The allocation sequence was generated using SAS by the study's statistician (JAG) and stored in REDCap.[18] Study staff used REDCap to implement the random allocation sequence (i.e., randomize a participant) once both the baseline weight and web-based surveys were submitted.

2.5 Data Acquisition

Study design	Factorial trial (2x2x2)
Number of participants	176

Data source/how the data were collected	- Primary data collection from participants across the United States
	  ○ Weight via scale (Fitbit Aria Air)
	  ○ Surveys via REDCap
	- Self-monitoring engagement data collected from Fitbit tracker, scale, and app, and retrieved via Fitabase, a software data management platform

Contact information for team member responsible for data collection/acquisition	PI, Michele Patel (michele.patel@stanford.edu)
Date or version (if downloaded, provide date)	n/a
Data transfer method and date	REDCap to Stanford Medicine Box to Duke Box
Where dataset is stored	A Duke Box folder called Spark Trial

3 Outcomes and Additional Variables of Interest

3.1 Primary Outcome

- The primary outcome is weight change from baseline to 6 months, measured in kg. Negative values indicate weight loss whereas positive values indicate weight gain.

3.2 Secondary Outcomes

- Weight change from baseline to 1 month (in kg)
- Weight change from baseline to 3 months (in kg)
- Clinically significant weight loss at 6 months: proportion of participants achieving ≥5% weight loss from baseline to 6 months
- BMI change from baseline to 6 months (in kg/m^2)
- Caloric intake change from baseline to 6 months (in kcal)
    - We will exclude from our analyses any recalls with outliers of daily caloric intake reported as <600 kcal or >4400 kcal for women and <650 kcal or >5700 kcal for men, in accordance with ASA24 recommended procedures based on NHANES data.[19]
- Physical activity change from baseline 6 months (via Godin Leisure-Time Exercise Questionnaire)
    - Specifically, the moderate-to-vigorous physical activity (MVPA) score index

3.3 Other Outcomes

- Engagement in self-monitoring dietary intake: average percentage of days in the 6-month intervention of self-monitoring dietary intake
    - Assessed only among those who were assigned to receive this component (n=88)
    - Count days as valid if they have ≥ 800 kcal recorded
- Engagement in self-monitoring body weight: average percentage of days in the 6-month intervention of self-monitoring body weight
    - Assessed only among those who were assigned to receive this component (n=88)
- Engagement in self-monitoring steps: average percentage of days in the 6-month intervention of self-monitoring steps
    - Assessed only among those who were assigned to receive this component (n=88)
    - Count days as valid only if ≥ 1000 steps are recorded
- Health-related quality of life change from baseline to 6 months
    - Summarized as the physical component score and the mental component score
- Engagement in action plans: average percentage of action plans completed in the 6-month intervention (100% = all 19 action plans completed)
- Relation between engagement in self-monitoring and 6-month weight change (kg), calculated separately for the 3 self-monitoring domains

3.4 Other Variables of Interest

- Retention rate at 1 month, 3 months, 6 months: the proportion of participants who submitted a weight entry at those timepoints
- Use of anti-obesity medication(s) during the 6-month intervention
- Baseline characteristics: sociodemographic (e.g., sex, age, education), psychosocial (e.g., health literacy), behavioral (e.g., history of self-monitoring), and clinical (e.g., type II diabetes diagnosis, hypertension diagnosis) factors

3.5 Independent Variables

The primary independent variables are the three self-monitoring components listed in the top row of the **Figure**, below. Detailed descriptions of these components are provided in the protocol paper.

Experimental Condition	Core	Track Diet	Track Steps	Track Weight
1	Yes	No	No	No
2	Yes	No	No	Yes
3	Yes	No	Yes	No
4	Yes	No	Yes	Yes
5	Yes	Yes	No	No
6	Yes	Yes	No	Yes
7	Yes	Yes	Yes	No
8	Yes	Yes	Yes	Yes

4 Decision Criteria for Creating the Optimized Intervention

Using the Multiphase Optimization Strategy (MOST) framework for intervention optimization, this study seeks to balance intervention effectiveness (i.e., weight loss) against efficiency (i.e., minimizing participant burden). Thus, our *Optimization Objective* is to create an intervention made up of all active components without any inactive components. To decide which self-monitoring strategies should comprise our newly optimized intervention, we will use the Component Screening Approach described by Collins 2018,[6] which iteratively sorts through the results of the factorial trial. A minimum threshold of 2.1 kg mean weight loss at 6 months will be used to decide whether to consider including any self-monitoring components alone or in combination. This magnitude equates to an alpha level of .10, assuming a standard deviation of 4.5 kg. We selected a higher alpha level during this decision-making phase when constructing the newly optimized intervention because we want to lower the chance of mistakenly discarding an intervention component that is actually beneficial (i.e., reduce the type II error rate). This rationale reflects the "decision-priority perspective" of MOST; in contrast, the "conclusion-priority perspective" is focused on drawing scientific conclusions from a trial using well-established conventions of alpha level ≤ .05.[6,7]

Using the Component Screening Approach, first, the main effects of each self-monitoring component on 6-month weight change will be determined. The self-monitoring strategies that meet or exceed this threshold will be tentatively included in the "screened-in" set, while those not meeting this threshold will be included in the "screened-out" set. Then, lower-level interactions will be examined, first among any components in the screened-in set, followed by those in the screened-out set. Next, we will examine the interaction among all three self-monitoring components. For interactions meeting or exceeding the 2.1 kg threshold of weight loss, their components will be considered for inclusion in the screened-in set (even if the components, by themselves, did not demonstrate main effects). To aid in interpretation of interactions, we will plot the predicted marginal means; this visualization will provide information on whether synergistic or antagonistic interactions exist. Lastly, we will review our components in the screened-in set in light of ratings of acceptability (perceived helpfulness of each type of self-monitoring) and self-monitoring engagement rates; for instance, if a component was frequently rated as "not at all helpful" and had low engagement that could indicate that it was not acceptable to participants, and therefore it is possible that their weight loss was driven by participation in weight management strategies not related to the Spark intervention.

Results of this trial will inform development of a newly optimized intervention that can be tested in a subsequent evaluation-RCT. If no self-monitoring strategies, alone or in combination, exceed our 2.1 kg weight loss threshold, then we will return to the Preparation Phase of the MOST framework to refine the conceptual model, brainstorm and pilot test new candidate components, adapt existing components, and/or strengthen the core digital health intervention.

5 Statistical Analysis Plan

5.1 Overview of Factorial Trial Analyses

Unlike an RCT that compares the means of each *arm* to one another (arm 1 vs. arm 2 vs. arm 3, and so on), in a factorial trial, the means across *combinations of conditions* are used to test main effects of components and their interactions.[15] In our 2^3 full factorial trial (i.e., a 2x2x2 with 8 conditions), we are testing whether three self-monitoring strategies, alone or in combination, improve weight loss at 6 months (our primary end point). To estimate the main effect of each self-monitoring component on weight change, we will examine the difference between the mean of conditions where the target component is present and the mean of conditions where the target component is absent.[6] For example, for 'Tracking Diet,' the mean of experimental conditions 5, 6, 7, and 8 (i.e., component is present) will be compared to the mean of conditions 1, 2, 3, and 4 (i.e., component is absent; see **Figure**, above). We will use effect coding (i.e., -1 when component is absent, +1 when component is present) for analyzing the main effects and interactions of the components, as recommended for factorial designs.[6] Thus, a main effect is interpreted as the effect of a factor averaged across all other factors. Because each main effect and interaction is based on the entire sample, the factorial design is considered efficient and economical.[20]

Outcomes will be analyzed only once all data are collected in the trial. No interim analyses are planned. The study biostatistician (JAG) will analyze primary outcomes in a masked fashion such that treatment assignment will not be revealed.

5.2 Characterizing the Sample

Descriptive statistics will be used to describe baseline characteristics, reported overall and stratified by factor (i.e., self-monitoring component) and factor level (i.e., Yes – those who received it vs. No – those who did not receive it). For categorical variables, we will report frequencies and percentages. For normally distributed continuous variables, we will report means (SD) and for non-normally distributed data, we will report medians (IQR). To determine whether any baseline variables differ by retention status (completers vs. non-completers), we will use Pearson chi-square tests for categorical variables, the Fisher exact tests for small cell counts, ANOVA for normally distributed continuous variables, and the Kruskal-Wallis test for non-normally distributed data. If we find that any covariates predict missingness, we will adjust for these variables in the model as a sensitivity analysis.

A CONSORT flow diagram will display the progress of participants through the Spark trial (see CONSORT flow diagram template in **Appendix A**). The number of participants lost to follow-up will be presented in the flow diagram, and retention rates will be presented in the text as an overall proportion of all participants and by factor level (e.g., retention rate for those assigned vs. not assigned to self-monitor dietary intake). The number who withdraw from the weight loss intervention, including both those who do and do not agree to be contacted for follow-up assessments, will be summarized, along with their reasons for withdrawal. Lastly, the number (and percentage) of participants experiencing adverse events (and their type) will be descriptively reported for each factor and factor level.

5.3 Analytic Plan for Primary Outcome

Our primary outcome is weight change, in kilograms, from baseline to 6 months. Using intent-to-treat principles, we will use linear mixed models to examine the main effects of the three self-monitoring components and all of their interactions on mean weight change at each follow-up time point. This model will include fixed effects for the following: time point (1, 3, or 6 months), sex assigned at birth (i.e., the stratification variable), self-monitoring component, pairwise interactions of each component, and the time-by-component and time-by-pairwise interactions. We will fit an unstructured covariance matrix to take into account the correlation of weight measures within person across time. We will use maximum likelihood to estimate the model parameters, allowing for missingness at random. Statistical tests will be 2-

sided. No adjustments for multiplicity will be made. Applicable outcomes will be reported with 95% confidence intervals (2-sided). Example SAS code for fitting this model is shown in **Appendix B**. Lastly, data will also be disaggregated by sex in exploratory analyses.

5.4 Analytic Plan for Secondary Outcomes

Similar linear mixed models will be used to assess the main effects and interactions on the secondary outcomes, including caloric intake, physical activity, and health-related quality of life.

Protocol update: To handle extreme outliers in the GLTEQ physical activity data, winsorization will be performed using the Median Absolute Deviation (MAD) method. A modified z-score cutoff of 3.5 units will be used to detect outliers, which will be replaced with the corresponding threshold boundary.

To assess differences in achieving clinically significant weight loss (≥5% from baseline)[8] between the 'present' vs. 'absent' levels of each factor, we will fit a log-Poisson generalized estimating equations (GEE) model[21] with robust standard errors[22,23] and an unstructured working correlation matrix to take into account repeated measures across time. From these models, we will report risk ratios comparing levels of intervention components and their interactions. As recommended by the CONSORT statement for randomized trials,[24] we will report both absolute and relative effects of these models.

5.5 Analytic Plan for Engagement and its Association with Weight Loss

We will first assess patterns of self-monitoring engagement (tracking dietary intake, steps, and body weight) over 6 months using descriptive statistics (medians and interquartile range if non-normally distributed, as is expected[12]) and via graphical presentation. Then, for each self-monitoring domain, we will use Spearman rank correlation coefficients (if engagement data are non-normally distributed) and linear regression models to examine the relation between self-monitoring engagement and weight change at 6 months.

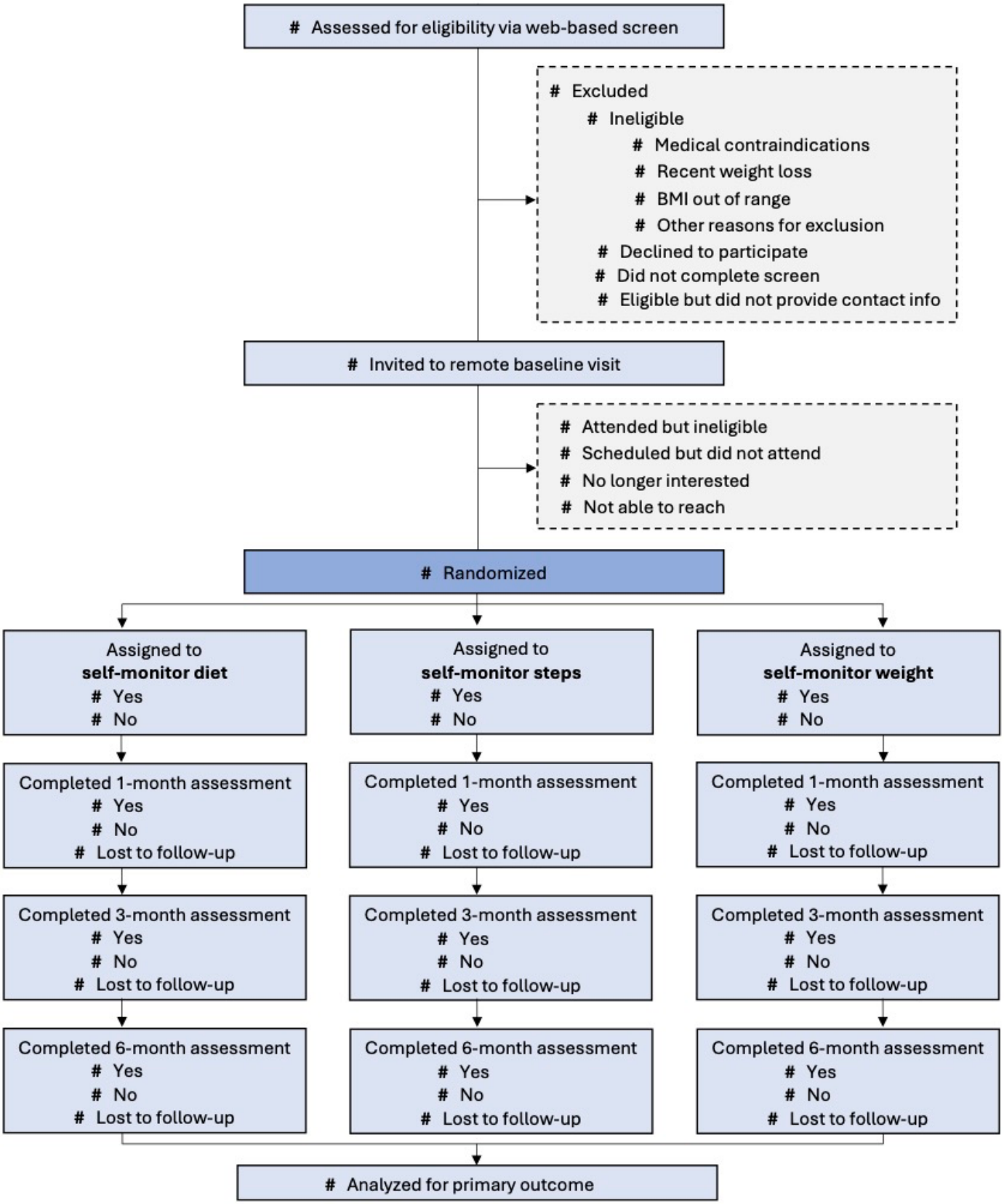
6 References

1. Emmerich SD, Fryar CD, Stierman B, Ogden CL. Obesity and severe obesity prevalence in adults: United States, August 2021–August 2023. 2024.
2. Fryar CD CM, Afful J. Prevalence of overweight, obesity, and severe obesity among adults aged 20 and over: United States, 1960–1962 through 2017–2018. *NCHS Health E-Stats* 2020.
3. Baker RC, Kirschenbaum DS. Self-monitoring may be necessary for successful weight control. *Behavior Therapy.* 1993;24(3):377-394.
4. Burke LE, Wang J, Sevick MA. Self-monitoring in weight loss: a systematic review of the literature. *Journal of the American Dietetic Association.* 2011;111(1):92-102.
5. Patel ML, Wakayama LN, Bennett GG. Self-Monitoring via Digital Health in Weight Loss Interventions: A Systematic Review Among Adults with Overweight or Obesity. *Obesity.* 2021;29(3):478-499.
6. Collins LM. *Optimization of behavioral, biobehavioral, and biomedical interventions.* Springer; 2018.
7. Collins LM, Nahum-Shani I, Guastaferro K, Strayhorn JC, Vanness DJ, Murphy SA. Intervention Optimization: A Paradigm Shift and Its Potential Implications for Clinical Psychology. *Annu Rev Clin Psychol.* 2024;20(1):21-47.
8. Jensen M, Ryan D, Apovian C, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation.* 2014;129(25 Suppl 2):S139-S140.
9. Dunn CG, Turner-McGrievy GM, Wilcox S, Hutto B. Dietary Self-Monitoring Through Calorie Tracking but Not Through a Digital Photography App Is Associated with Significant Weight Loss: The 2SMART Pilot Study—A 6-Month Randomized Trial. *Journal of the Academy of Nutrition and Dietetics.* 2019;119(9):1525-1532.
10. Crane MM, Lutes LD, Ward DS, Bowling JM, Tate DF. A randomized trial testing the efficacy of a novel approach to weight loss among men with overweight and obesity. *Obesity.* 2015;23(12):2398-2405.
11. Thomas JG, Raynor HA, Bond DS, et al. Weight loss and frequency of body-weight self-monitoring in an online commercial weight management program with and without a cellular-connected 'smart' scale: a randomized pilot study. *Obesity Science and Practice.* 2017;3(4):365-372.
12. Patel ML, Hopkins CM, Brooks TL, Bennett GG. Comparing self-monitoring strategies for weight loss in a smartphone app: Randomized controlled trial. *Journal of medical Internet research.* 2019;21(2).
13. Bennett GG, Steinberg D, Bolton J, et al. Optimizing an Obesity Treatment Using the Multiphase Optimization Strategy Framework: Protocol for a Randomized Factorial Trial. *JMIR research protocols.* 2021;10(1):e19506.
14. Turner-McGrievy GM, Wilcox S, Boutté A, et al. The Dietary Intervention to Enhance Tracking with Mobile Devices (DIET Mobile) Study: A 6-Month Randomized Weight Loss Trial. *Obesity.* 2017;25(8):1336-1342.
15. Collins LM, Dziak JJ, Kugler KC, Trail JB. Factorial experiments: efficient tools for evaluation of intervention components. *American journal of preventive medicine.* 2014;47(4):498-504.
16. Dziak J, Collins L, Wagner A. FactorialPowerPlan SAS macro suite users' guide. In: University Park: The Methodology Center, Penn State; 2013.
17. Gallis JA, Bennett GG, Steinberg DM, Askew S, Turner EL. Randomization procedures for multicomponent behavioral intervention factorial trials in the multiphase optimization strategy framework: challenges and recommendations. *Translational behavioral medicine.* 2019;9(6):1047-1056.
18. Cleland C. REDcap for MOST. 2018; https://www.methodology.psu.edu/ra/most/redcap/. Accessed September 1, 2020.
19. Automated Self-Administered 24-Hour (ASA24) Dietary Assessment Tool. 2016; https://epi.grants.cancer.gov/asa24/.
20. Collins LM, Murphy SA, Strecher V. The multiphase optimization strategy (MOST) and the sequential multiple assignment randomized trial (SMART): new methods for more potent eHealth interventions. *American journal of preventive medicine.* 2007;32(5):S112-S118.
21. Liang K-Y, Zeger SL. Longitudinal data analysis using generalized linear models. *Biometrika.* 1986;73(1):13-22.
22. Gallis JA, Turner EL. Relative measures of association for binary outcomes: challenges and recommendations for the global health researcher. *Annals of Global Health.* 2019;85(1).

23. Zou G, Donner A. Extension of the modified Poisson regression model to prospective studies with correlated binary data. *Statistical methods in medical research.* 2013;22(6):661-670.
24. Schulz KF, Altman DG, Moher D, Group C. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *Trials.* 2010;11(1):32.
25. Kraemer HC. Assessment of 2× 2 associations: generalization of signal-detection methodology. *The American Statistician.* 1988;42(1):37-49.
26. Kraemer HC, Wilson GT, Fairburn CG, Agras WS. Mediators and moderators of treatment effects in randomized clinical trials. *Archives of general psychiatry.* 2002;59(10):877-883.
27. Yesavage JA. Signal Detection Software for Receiver Operator Characteristics (ROC). https://web.stanford.edu/~yesavage/ROC.html. Accessed 04/05/2025.

7 Appendix

7.1 Appendix A



7.2 Appendix B

SAS code for fitting the general linear model with unstructured covariance and constrained so that baseline is equal.

```
PROC MIXED DATA=data METHOD=REML CL noclprint=10;
       title "cLDA model";
       CLASS id visit;
       model weight = m1 m3 m6

       /* regression coefficients at 1-month post-randomization */
       m1*c1 m1*c2 m1*c3 m1*c1*c2 m1*c1*c3 m1*c2*c3 m1*c1*c2*c3

       /* regression coefficients at 3-month post-randomization */
       m3*c1 m3*c2 m3*c3 m3*c1*c2 m3*c1*c3 m3*c2*c3 m3*c1*c2*c3;

       /* regression coefficients at 6-month post-randomization */
       m6*c1 m6*c2 m6*c3 m6*c1*c2 m6*c1*c3 m6*c2*c3 m6*c1*c2*c3;

       /* 1-month post-randomization effects (2*regression coefficient) */
       * MAIN EFFECTS;
       estimate "c1 main effect m1"     c1*m1 2;
       estimate "c2 main effect m1"     c2*m1 2;
       estimate "c3 main effect m1"     c3*m1 2;

       * TWO-WAY INTERACTIONS;
       estimate "c1,c2 interaction effect m1"  c1*c2*m1 2;
       estimate "c1,c3 interaction effect m1"  c1*c3*m1 2;
       estimate "c2,c3 interaction effect m1"  c2*c3*m1 2;

       * THREE-WAY INTERACTION;
       estimate "c1,c2,c3 interaction effect m1" c1*c2*c3*m1 2;

       /* 3-month post-randomization effects (2*regression coefficient) */
       * MAIN EFFECTS;
       estimate "c1 main effect m3"     c1*m3 2;
       estimate "c2 main effect m3"     c2*m3 2;
       estimate "c3 main effect m3"     c3*m3 2;

       * TWO-WAY INTERACTIONS;
       estimate "c1,c2 interaction effect m3"  c1*c2*m3 2;
       estimate "c1,c3 interaction effect m3"  c1*c3*m3 2;
       estimate "c2,c3 interaction effect m3"  c2*c3*m3 2;

       * THREE-WAY INTERACTION;
       estimate "c1,c2,c3 interaction effect m3" c1*c2*c3*m3 2;

       /* 6-month post-randomization effects (2*regression coefficient) */
       * MAIN EFFECTS;
       estimate "c1 main effect m6"     c1*m6 2;
       estimate "c2 main effect m6"     c2*m6 2;
       estimate "c3 main effect m6"     c3*m6 2;

       * TWO-WAY INTERACTIONS;
       estimate "c1,c2 interaction effect m6"  c1*c2*m6 2;
       estimate "c1,c3 interaction effect m6"  c1*c3*m6 2;
       estimate "c2,c3 interaction effect m6"  c2*c3*m6 2;

       * THREE-WAY INTERACTION;
       estimate "c1,c2,c3 interaction effect m6" c1*c2*c3*m6 2;

       REPEATED visit / TYPE=un SUBJECT=id R RCORR;
       ods output estimates=output;
RUN;
```