

Supplementary Table 1. Complete Inclusion and Exclusion Criteria for Phase 1

Inclusion Criteria: Healthy Controls

1. Males and females, 19 to 30 years of age, inclusive.
 2. Type 1 Diabetes Cohort:
 - a. Diagnosis of type 1 diabetes for greater than 1 year at screening.
 - b. Hemoglobin A1c 6.5-13%
- or**
Control Cohort without diabetes:
- a. Healthy individuals without diabetes matched to T1D cohort by BMI, and sex
3. Able to provide informed consent.
 4. BMI 18-39.9 kg/m²

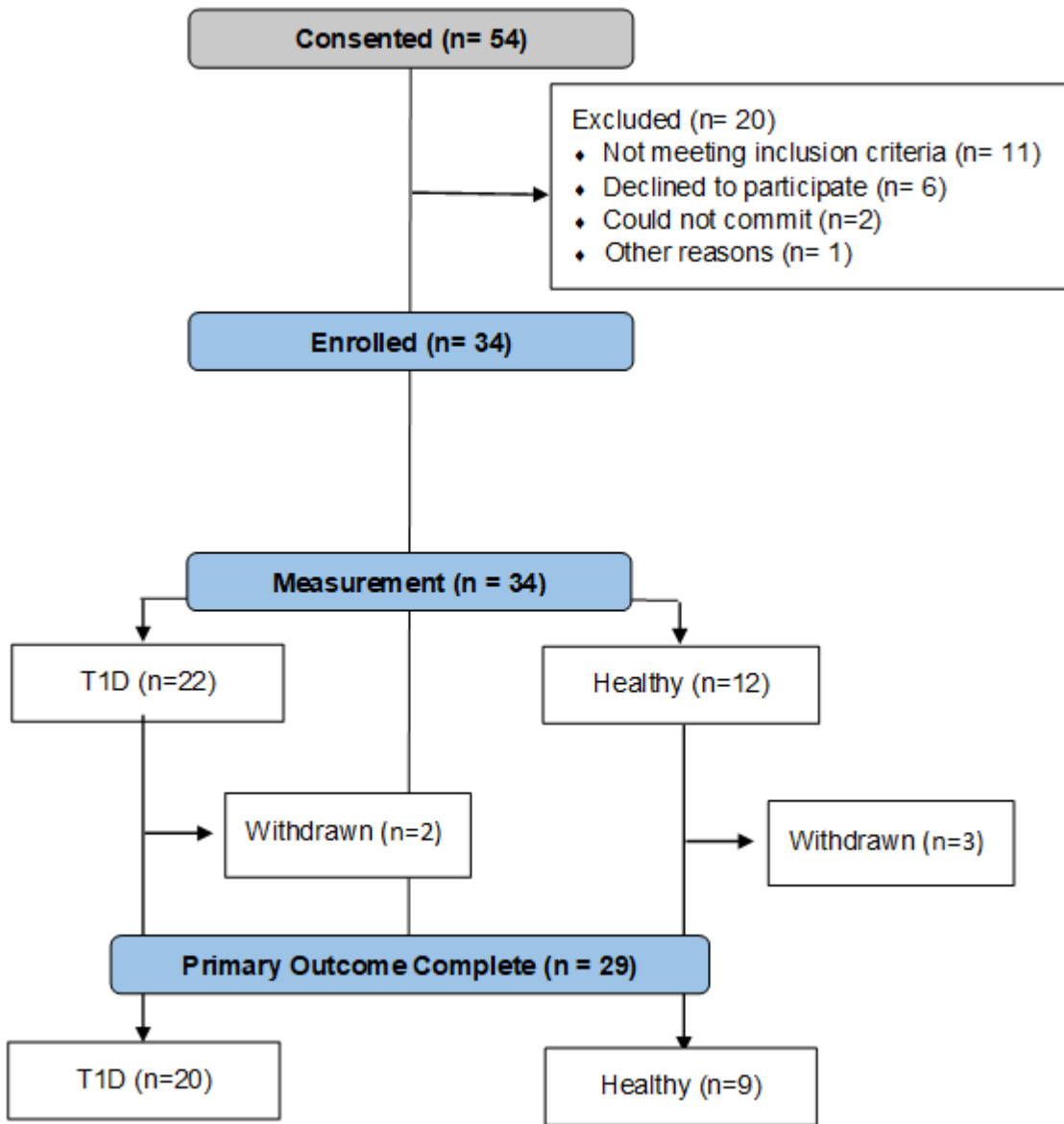
Exclusion Criteria

1. Type 2 diabetes
2. History or presence of cardiovascular disease (unstable angina, myocardial infarction or coronary revascularization within 6 months, clinically significant abnormalities on EKG, presence of cardiac pacemaker, implanted cardiac defibrillator)
3. Liver disease (AST or ALT >2.5 times the upper limit of normal), history of hepatitis
4. Kidney disease (creatinine >1.6 mg/dl or estimated GFR <60 ml/min)
5. Triglycerides >800 mg/dl, LDL >200 mg/dl
6. Anemia (hemoglobin <12 g/dl in men, <11 g/dl in women)
7. Thyroid dysfunction. Participants with a TSH > 10 μ IU or less than 0.4 μ IU are excluded. Participants on thyroid replacement medication may be enrolled providing they have been on a stable dose of medication for at least 6 weeks prior to screening and their TSH is within the range specified above.
8. Uncontrolled hypertension (BP >160 mmHg systolic or > 100mmHg diastolic)
9. History of cancer within the last 5 years (skin cancers, with the exception of melanoma, may be acceptable).
10. Initiation or change in hormone replacement therapy within the past 3 months (including, but not limited to thyroid hormone, birth control or estrogen replacement therapy)
11. History of organ transplant
12. History of HIV, active Hepatitis B or C, or Tuberculosis
13. Pregnancy, lactation, or 6 months postpartum from screening visit
14. History of major depression
15. Psychiatric disease prohibiting adherence to study protocol
16. History of eating disorders
17. Cushing's disease or syndrome
18. History of bariatric surgery
19. Tobacco use within the past 3 months
20. History of drug or alcohol abuse (≥ 3 drinks per day) within the last 5 years, except positive Tetrahydrocannabinol (THC) is acceptable.
21. Use of oral or injectable anti-hyperglycemic agents (except insulin)
22. Current use of beta-adrenergic blocking agents
23. Drugs that affect immune, weight or metabolic function, including but not limited to: oral corticosteroids, oral or injectable anti-obesity medications, oral or injectable antihyperglycemic medications other than insulin within 3 months of screening. Drugs for dyslipidemia (statins,

ezetimibe, etc.) and a daily full strength or baby aspirin for atherosclerosis prevention will be allowed, provided patients have been on stable doses for at least 6 weeks prior to screening.

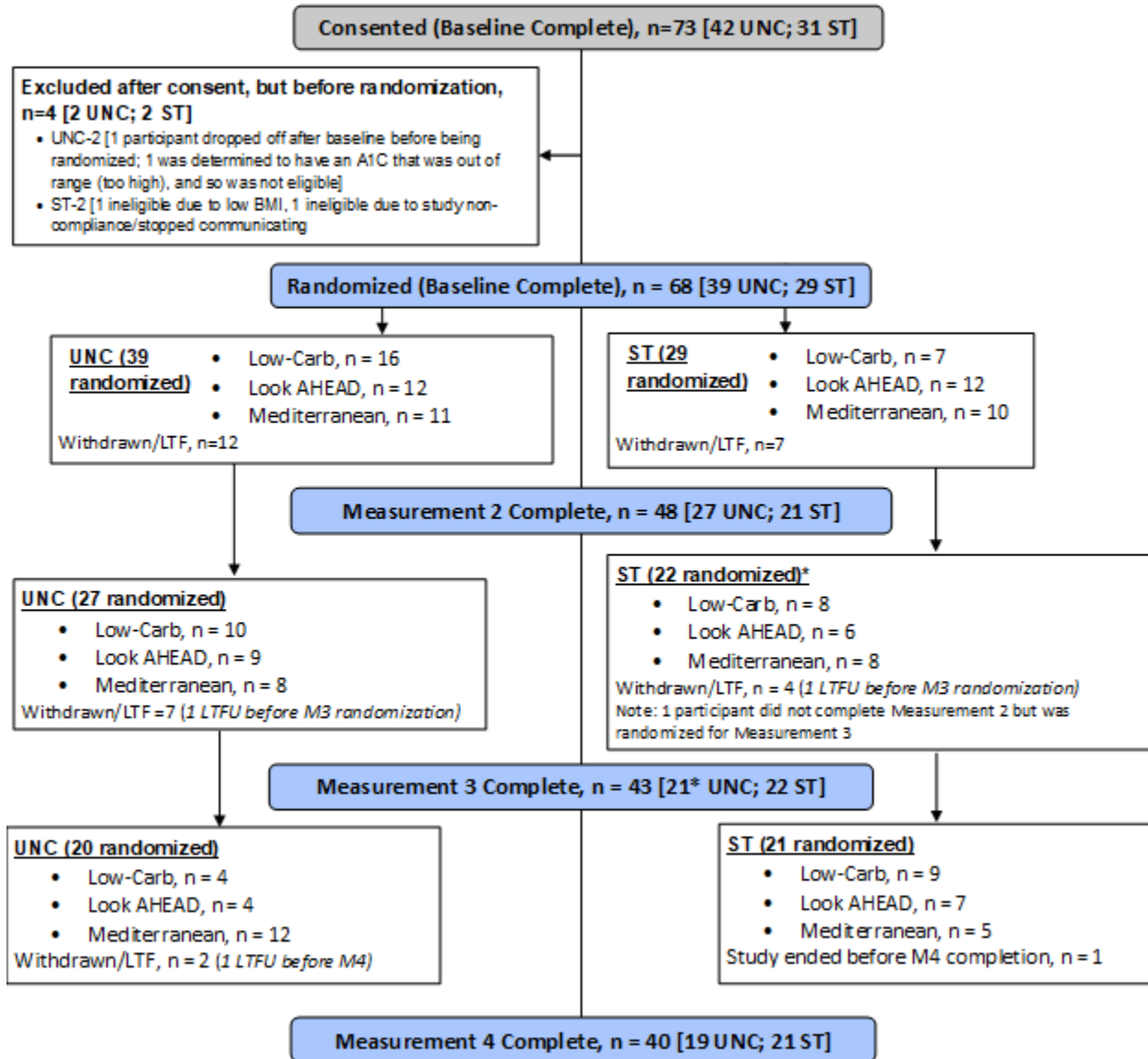
24. Use of antibiotics within the past 3 months
25. Weight >450 lbs. (This is DEXA table weight limit)
26. Metal implants (pacemaker, aneurysm clips) based on Investigator's judgment at screening
27. Unable to participate in MRI or MRS assessment based on Investigator's judgment at screening
28. Participants with strict dietary concerns (e.g., vegetarian or kosher diet, multiple food allergies, or allergies to food we will provide them during the study)
29. Gastrointestinal disorders including: inflammatory bowel disease or malabsorption, swallowing disorders, suspected or known strictures, fistulas or physiological/mechanical GI obstruction, history of gastrointestinal surgery, Crohn's disease or diverticulitis.
30. Presence of any condition that, in the opinion of the investigator, compromises participant safety or data integrity or the participant's ability to complete study visits

Supplementary Figure 1: Phase 1 CONSORT



In Phase 1, 54 participants were consented, 34 were enrolled and completed the measurement visit, and 20 completed the primary outcome.
Abbreviations: T1D = type 1 diabetes

Supplementary Figure 2. ACT1ON Phase 2 SMART Pilot CONSORT Diagram

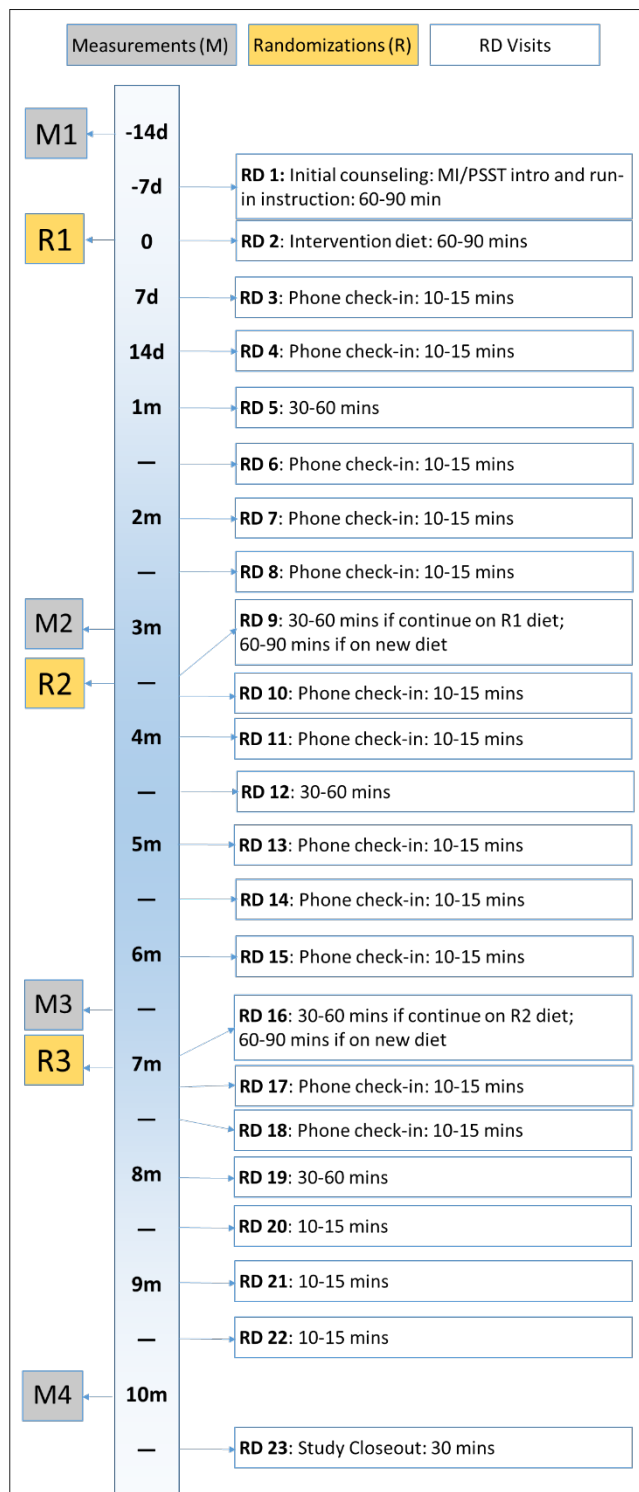


In Phase 2, 73 participants were consented, 68 were randomized, 48 completed Measurement Visit 1, and 40 completed the study. Note: the numbers screened/assessed for eligibility exclude those who were entered into CDART but who were never contacted about recruitment.

*Indicates one participant was withdrawn or lost to follow-up after completing the visit, but before randomization.

Abbreviations: M3= Measurement 3; M4 = Measurement 4; UNC – University of North Carolina at Chapel Hill; ST – Stanford; LTF – Lost to follow-up

Supplementary Figure 3. Phase 2 Schedule of Encounters with Registered Dietitian



Abbreviations: RD – Registered Dietitian. Similar to the ADA guidelines for intensive lifestyle counseling for weight management, Phase 2 study participants had 23 total encounters with a Registered Dietitian, of which eight were longer counseling and education sessions, and 10 were shorter phone “check-ins.”