Investigating Racial Differences in Diet Benefits for Knee Osteoarthritis

Study Protocol & Statistical Analysis Plan

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Study Protocol

A telephone screening interview will be used to assess each participant's OA status and assessment of the reported duration of knee OA, current and past treatments, comorbid conditions, current medication use, dietary conditions and other exclusion criteria. Eligible, participants will be invited to the testing facilities in Campbell Hall for informed consent and baseline measures. Following this visit, participants will record daily food consumption for one week as well as daily pain ratings. After one week, participants will visit the Clinical Research Unit for fasted blood draw and additional testing. Immediately following this session, participants will be asked to select one week of meals and snacks from a menu of commercially-available meals. Study personnel will record the choices and order the meals to be delivered to the participants to initiate the intervention. During the 6-week intervention, participants will be contacted by study personnel weekly to place food orders and be instructed to record any beverages consumed during the week. Every three weeks, participants will return for testing. At the end of 6 weeks, blood will be taken prior to testing/debriefing.

Participants. The investigators will recruit 20 adult women (55-75) with knee OA with equal representation across racial groups (10 AA, 10 NHW). Peak prevalence rates for OA are at the 55-75 years of age, so the investigators feel confident that there will be no trouble recruiting this population. Participants will be recruited using existing databases, community flyers and community outreach. The feasibility trial used prescribed diets and had an attrition rate of 0% in the LCD group. Here, provision of all of the food for the intervention is expected to have lower rates of attrition.

Inclusion criteria will include:

- diagnosis of knee OA;
- pain in at least 4/7 days/week for the past 3 months;
- age between 65-75;
- average daily consumption of >100 g carbohydrates;
- understanding of verbal and written English;
- self-identification as either AA or NHW;
- BMI between 25 and 40 kg/m2.

Exclusion criteria will be the following:

- diabetes;
- unwillingness to follow prescribed diets;
- recent weight change (>4 kg in past month);
- currently on a diet;
- history of eating disorders or other psychiatric disorders;
- digestive diseases;
- difficulty chewing or swallowing;
- reliance on others for meal preparation;
- cardiovascular or pulmonary disease;
- daily opioid pain medications;
- use of medications known to alter metabolism or digestion (e.g., proton-pump inhibitors);
- use of anti-hypertensive medications that affect glucose tolerance;

- use of tobacco;
- participation in extreme exercise,
- knee replacement.

Diet Intervention. All foods will be provided under the direction of study personnel and will be delivered weekly to participants' home address. Weekly contact will maintain retention in the intervention and improve adherence. The Dietary Guidelines for Americans suggests 225-325 g of carbohydrates/day. Therefore, those participants consuming less than 100 g/day would be considered as consuming a reduced-carbohydrate diet and will be excluded. Participants are directed to reduce their total (not net) carbohydrate intake to ≤ 40 g/day. Meals will be offered such that no combination of chosen meals will exceed our limit. Fats will not be restricted, nor will protein (meats, eggs). Fruits will be restricted and vegetables permitted in limited quantities (2 cups/day of leafy greens, 1 cup/day non-starchy vegetables, etc.). Participants will be instructed as to the types and quantities of beverages that are permitted to accompany the LCD. Daily or almost-daily consumption of sugar-sweetened beverages was associated with lowered optimism in chronic pain sufferers and greater risk for depression in healthy women. Artificial carbohydrate-free sweeteners (stevia or sucralose) will be permitted, but powdered sweeteners (aspartame, saccharin, stevia, sucralose) can only be used in limited quantities as they contain maltodextrin (1 g of rapidly digesting carbohydrate). LCDs are known to be safe and first-line treatments for diabetes. LCDs are also known to reduce inflammatory biomarkers to a greater extent than low-fat diets. In fact, a LCD resulted in improved insulin sensitivity as well as reduced triglycerides even when weight loss was accounted for.

Anthropocentric Measures. Body weight, height, waist circumference, blood pressure, and heart rate will be assessed.

Pain-Specific Questionnaires. Pain and disability will be measured using the Brief pain Inventory (BPI) short form and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). The BPI is used to assess the severity of pain and the degree to which that pain interferes with daily activities. This inventory also allows for reports on medications used to treat pain. The WOMAC is commonly used in studies of arthritis and has been validated in numerous clinical trials. Specifically, the WOMAC allows for assessment of pain and interference, but also is specific to aspects of stiffness in the joints not accessed by other surveys. The investigators have previously utilized these measures for chronic pain sufferers. These assessments will be given at baseline and every 3 weeks.

Evoked Pain Testing. Functional tests will be carried out by study personnel. Participants will rate the intensity and unpleasantness of the pain in their affected knee (0-100 scale) prior to and immediately following the tests. The numerical rating scale will be anchored at 0 (no pain) and 100 (worst pain imaginable). Questionnaires will be given between each task to allow for a rest period. Task order will be randomized.

Temporal summation will be assessed on the patellar of the affected knee using a nylon monofilament (Touch test Sensory Evaluator 6.65) calibrated to bend at 300 g of pressure. Participants will provide a pain rating following a single contact of the monofilament, after which they will provide another pain rating following a series of 10 contacts (at a rate of one contact

per second). The change in pain ratings for single versus multiple contacts reflects temporal summation.

Repeated chair stands is a portion of the Short Performance Physical Battery. Participants are asked to stand from a sitting position five times in a row as fast as possible with arms crossed. The time to completion and number of successful stands is scored as the degree of ability.

Timed Up-and-Go is a common task for evaluating pain interference of everyday activities. From a seated position, participants will be asked to get up, walk 10 feet, turn and return to the chair. Time to complete the task will be recorded.

Timed walk will be the final task included. As in the Short Performance Physical Battery, a distance of 15 feet will be marked out on the floor. Participants will complete the distance walking at normal gait speed twice and the time to complete each walk will be recorded.

Quality of Life and Emotional State. Quality of Life will be measured using the short form 36 (SF-36) every 3 weeks. The SF- 36 measures general health status and quality of life across eight domains that are relevant for assessment of a diet intervention. The domains include physical functioning, role limitations due to physical health, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and mental health. The SF-36 has demonstrated reliability and validity in older adult populations and in diet intervention studies. Depression and mood will be assessed using the Patient Health Questionnaire (PHQ-9), which assesses the DSM-IV criteria for depression and can measure depression severity and response to intervention. Participants with PHQ-9 scores >15 will be referred to University of Alabama at Birmingham (UAB) Psychiatry Services for evaluation, as will participants identifying suicidal ideation of any duration on question 9.