

10. Specific Aims

Treatment-associated physical disability impairs quality of life, limits therapeutic options, and contributes to the social and economic burden of cancer care in the elderly⁶. Despite this, few clinical trials capture disability as an outcome and no clinical trials have focused on whether it can be ameliorated. My goal, as an oncologist trained in geriatrics, is to address this gap in knowledge. **My objective in this proposal is to conduct a pilot study of an intervention to prevent or slow the rate of decline in physical function during chemotherapy among high risk older adults.** This project will both catalyze my development as an independent investigator in geriatric oncology, and advance substantially the quest for interventions to mitigate treatment-associated disability and decrements in quality of life for older cancer survivors.

This proposal builds on my training in geriatrics, hematology, and oncology and the support of my current T. Franklin Williams award. We have good preliminary evidence that objective measures of physical function decline after chemotherapy in older patients with acute myelogenous leukemia (AML). Patients with AML in some ways represent a worst-case scenario due to the intensity of chemotherapy administered, high short-term risk for toxicity, and uncertainty about optimal management of older adults with AML. In addition, our prior experience in AML demonstrates that this population is amenable to participating in interventions of this type during active therapy. Lessons from this group could thus be adapted to other older oncology populations. This proposal is significant because of the critical role of physical disability in the life of older adults; it is innovative because it will advance our knowledge about design and implementation of tailored interventions in older adults receiving cancer therapy that could improve both physical and mental health status. Moreover, as outlined in the Career Development Plan (CDP), this research will facilitate my career by providing me with additional training in measurement, design of physical activity interventions, and leadership experience. As part of this award, I will conduct a randomized controlled trial (N=70) of an inpatient physical activity intervention that also promotes on-going lifestyle behavior change, with the goal of minimizing decline in physical function during chemotherapy. This is a pilot study which will establish design benchmarks related to feasibility, intervention delivery and effect size that are needed to develop a definitive trial. Ideally, a definitive trial in this area would use an objective, valid, reliable marker of physical function known to predict outcomes in older adults. Therefore, I will collect data on the responsiveness of the Short Physical Performance Battery (SPPB) to the intervention, to provide effect size estimates to power a larger study. The Research Plan is designed to achieve the following aims:

AIM 1. To implement a state-of-the-art, symptom-adapted, randomized behavioral intervention designed to improve physical function in older adults receiving chemotherapy for AML.

Goal: The intervention will enroll at least 60% of eligible patients. In addition, among patients without medical complications, we have a target retention rate of 85% and, in line with other exercise studies among older adults, expect that adherence to physical activity sessions will exceed 75%.

AIM 2. To estimate the effect size of the physical activity intervention on change in an objective measure of physical function, SPPB--the anticipated primary outcome for a future definitive trial.

Goal: Using these data we will be able to determine the sample size required for a future trial by providing a range of possible effect sizes consistent with the study's results.

AIM 3. To examine the effects of the intervention on self-reported physical function and quality of life, which are anticipated important secondary outcomes of a future definitive trial.

Goal: To collect data on change in self-reported physical function (measured by the Pepper Assessment Tool for Disability and the Mobility Assessment Tool-short form), health-related quality of life (measured by the Functional Assessment of Cancer Therapy-Leukemia survey), and symptoms (depression, distress and fatigue) to inform the design of a future definitive trial using these measures as secondary outcomes.

Completion of these three aims in the context of the proposed career development activities will provide the necessary experience, preliminary data, and effect sizes to generate a competitive R01 application that will test a definitive physical activity intervention among older adults receiving chemotherapy for AML. This research plan builds upon: 1) an ongoing study (supported by the T. Franklin Williams award) of a geriatric assessment for older adults receiving chemotherapy for AML; 2) a completed non-randomized pilot of an inpatient physical activity intervention for older adults receiving chemotherapy for AML; 3) an exceptional mentoring team; and 4) an outstanding environment. This project integrates well with my Career Development Plan, and is ideally suited to launch my career as a leader in geriatric oncology with a focus on behavioral intervention studies among vulnerable older adults with cancer.