

Section: Contact Information

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Section: Project Requirements and Description

Group: Requirements to submit AOI

A comprehensive review of previously published data has been completed. : **Yes**

The specific aims are clear and focused. : **Yes**

The investigator has appropriate experience and expertise to develop the concept proposal; if not, has identified a mentor or senior co-investigator. : **Yes**

The investigator agrees to develop an initial draft of the concept proposal within 6 weeks of approval of the AOI and to finalize the concept proposal within 6 months. : **Yes**

Project Title : **Prevalence and Risk of Frailty in Survivors of Childhood Cancer**

Planned research population (eligibility criteria) :

CCSS participants who completed the baseline questionnaire, are alive, and have not refused further participation.

Proposed specific aims :

Frailty, a physical phenotype that signifies a reduced physiologic reserve and increased susceptibility to chronic disease and disability, is characterized by the presence of three or more of the following impairments: 1) low lean muscle mass; 2) muscle weakness; 3) slow walking speed; 4) self-reported exhaustion; and 5) low levels of physical activity. Recent evidence suggests that early onset of frailty is an important contributor to adverse health outcomes and reduced quality of life in childhood cancer survivors. It is therefore important to determine the age- and sex-specific prevalence of frailty in a large, geographically diverse cohort of survivors, and to comprehensively characterize treatment exposures that increase risk.

Because frailty often occurs prior to onset of clinical disease and may not have recognizable symptoms, systematic assessment is required both for determining prevalence and for using the phenotype as a predictive marker of risk. Childhood cancer survivors are geographically dispersed and most are not involved in

dedicated survivorship care, precluding systematic clinical assessment of this population. We have demonstrated in a pilot study that the five distinguishing characteristics of frailty are now amenable to remote assessment via mHealth modalities, which will allow us to characterize frailty on a larger scale, in a population of survivors with well-characterized treatment exposures. Through the following specific aims, we propose to use the unique resources of the Childhood Cancer Survivor Study to characterize the prevalence and predictors of frailty in a large population of adult survivors of childhood cancer, and to evaluate how frailty impacts quality of life in this unique group:

Aim 1. To determine the prevalence of frailty and pre-frailty in a geographically diverse population of adult 5-year survivors of childhood cancer. We hypothesize that the prevalence of frailty in survivors will be comparable to that observed at much older ages in the general population.

Aim 2. To identify associations between treatment exposures and risk of frailty and pre-frailty. We hypothesize that there will be dose-dependent increases in risk of frailty associated with both site-specific radiation and agent-specific chemotherapeutic exposures.

Aim 3. To evaluate associations between frailty, pre-frailty, or individual components of the frailty phenotype and quality of life. We hypothesize that frailty will be independently associated with decreased quality of life, independent of chronic disease.

Will the project require non-CCSS funding to complete? : **Yes**

If yes, what would be the anticipated source(s) and timeline(s) for securing funding? : **Planned NIH R01 grant proposal, targeting submission in October 2017**

Group: Does this project require contact of CCSS study subjects for:

Additional self-reported information : **Yes**

Biological samples : **No**

Medical record data : **Yes**

If yes to any of the above, please briefly describe. :

After providing informed consent, participants will be mailed instructions and equipment required to perform in-home measurements of each of the five criteria used to determine frailty. Frailty will be defined using the phenotype described by Fried et al; participants who meet two or more of the criteria will be considered “pre-frail” and those who meet three or more will be considered “frail”. Measures will capture sarcopenia, muscle weakness, slow walking speed, decreased endurance and low activity. A concurrent questionnaire will obtain information on quality of life and relevant health behaviors. Participants with a smart phone will be able to view instructional videos, collect data and transmit it automatically to the study team via the CCSS-Eureka app. Remote data collection via mHealth modalities will be encouraged, but manual data collection will also be an option for those participants who do not have a compatible smart phone. With the exception of physical activity monitoring, which will occur over seven consecutive days, all study measures can be completed in a single session lasting about one hour.

Group: What CCSS Working Group(s) would likely be involved? (Check all that apply)

Second Malignancy :

Chronic Disease : **Primary**

Psychology / Neuropsychology : **Secondary**

Genetics :

Cancer Control :

Epidemiology / Biostatistics :

Section: Outcomes or Correlative Factors

Late mortality :

Second Malignancy :

Group: Health Behaviors

Tobacco : **Correlative Factors**

Alcohol : **Correlative Factors**

Physical activity : **Correlative Factors**

Medical screening : **Correlative Factors**

Other :

If other, please specify :

Group: Psychosocial

Insurance : **Correlative Factors**

Marriage : **Correlative Factors**

Education : **Correlative Factors**

Employment : **Correlative Factors**

Other :

If other, please specify :

Group: Medical Conditions

Hearing/Vision/Speech : **Correlative Factors**

Hormonal systems : **Correlative Factors**

Heart and vascular : **Correlative Factors**

Respiratory : **Correlative Factors**

Digestive : **Correlative Factors**

Surgical procedures : **Correlative Factors**

Brain and nervous system : **Correlative Factors**

Other :

If other, please specify : **Aim 3 proposes identifying the independent association between frailty and quality of life, so models will account for chronic conditions reported on prior CCSS questionnaires.**

Group: Medications

Describe medications :

Group: *Psychologic/Quality of Life*

BSI-18 :

SF-36 : **Secondary**

CCSS-NCQ :

PTS :

PTG :

Other :

If other, please specify :

Group: *Other*

Pregnancy and offspring :

Family history :

Chronic conditions (CTCAE v3) : **Correlative Factors**

Health status :

Group: *Demographic*

Age : **Correlative Factors**

Race : **Correlative Factors**

Sex : **Correlative Factors**

Other :

If other, please specify :

Group: *Cancer treatment*

Chemotherapy : **Correlative Factors**

Radiation therapy : **Correlative Factors**

Surgery : **Correlative Factors**

Section: *Anticipated Sources of Statistical Support*

CCSS Statistical Center :

Local institutional statistician : **Yes**

If local, please provide the name(s) and contact information of the statistician(s) to be involved. :

Dr. Kumar Srivastava, Chair of Biostatistics at St. Jude Children's Research Hospital, will be included as a coinvestigator on the grant application.

Will this project utilize CCSS biologic samples? : **No**

If yes, which of the following? :

If other, please explain :

Section: *Other General Comments*

Other General Comments :

Dr. Kiri Ness will be a co-PI on this grant application.