Contact Information

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Project Requirements and Description

Requirements to submit AOI (all answers must be "yes" to proceed)

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 Association between voluntary increase in physical activity and future morbidity in the Childhood Cancer Survivor Study

Planned research population (eligibility criteria)

Childhood Cancer Survivors with at least two completed questionnaires including self-reported physical activity.

Proposed specific aims

Aim 1: To define the association between a voluntary increase in physical activity and the risk for individual medical conditions in childhood cancer survivors. This aim will address the following hypotheses:

- A voluntary increase in physical activity is associated with a lower risk for developing new onset medical conditions known to be associated with physical activity in the general population – cardiovascular disease, metabolic syndrome, cerebrovascular disease, musculoskeletal disease, second malignant neoplasms. The risk for those with a voluntary increase is similar to the risk for those with a constant high level of physical activity.
- A voluntary increase in physical activity is associated with a subsequent improvement of medical conditions known to be associated with physical activity in the general population, in individuals with pre-

existing medical conditions at start of follow-up.

Aim 2: To define the association between a voluntary increase in physical activity and individual mental disorders in childhood cancer survivors. This aim will address the following hypotheses:
- A voluntary increase in physical activity is associated with a lower risk for developing new onset individual mental disorders known to be associated with physical activity in the general population, e.g. depression and anxiety.
- A voluntary increase in physical activity is associated with a subsequent improvement of the same mental disorders in individuals with pre-existing mental disorders at start of follow-up.

Aim 3: To define the association between a voluntary increase in physical activity and health-related quality of life (HRQoL) in childhood cancer survivors. This aim will address the following hypothesis:
- A voluntary increase in physical activity is associated with a better trajectory for both mental and physical HRQoL.

Aim 4 (exploratory): Define a meaningful dose of increase in physical activity in terms of reduced risk for individual medical and mental health outcomes, and to explore whether this dose depends on baseline level of physical activity.

Aim 5: To determine the association between risky health behavior clusters, defined by Lown et al., and the individual outcomes defined in Aims 1-2. This aim will address the following hypothesis:
- Clustering of health risk behaviors leads to an exponential risk increase that is larger than the sum of risk for each behavior.

Aim 6: To define the population attributable fraction of health risk behaviors on the risk for developing the individual medical and mental conditions defined in Aims 1-2. This aim will address the following hypotheses:
- Poor lifestyle constitutes a significant population attributable fraction for the development of new-onset medical conditions and poor mental health in childhood cancer survivors.
- This fraction is comparable to the population attributable fraction for chemotherapy but lower than the population attributable fraction for cranial radiotherapy.

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?

Aron Onerup has already received a 3-year, USD 360,000, grant from the Swedish Research Council covering his salary for a postdoc at St Jude Children's Research Hospital for research on health benefits from physical activity in childhood cancer survivors.

Does this project require contact of CCSS study subjects for:

Additional self-reported information	No

Biological samples	No
Medical record data	No

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

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

Second Malignancy	
Chronic Disease	Secondary
Psychology/Neuropsychology	Secondary
Genetics	
Cancer Control	Primary
Epidemiology/Biostatistics	

Outcomes or Correlative Factors

Late Mortality	Secondary
Second Malignancy	Secondary

Health Behaviors

Tobacco	Correlative Factors
Alcohol	Correlative Factors
Physical Activity	Primary
Medical Screening	
Other	

If other, please specify

Psychosocial

Insurance	Correlative Factors
Marriage	Correlative Factors

Education	Correlative Factors
Employment	Correlative Factors
Other	

If other, please specify

Medical Conditions

Hearing/Vision/Speech	Secondary
Hormonal Systems	Primary
Heart and Vascular	Primary
Respiratory	Primary
Digestive	Primary
Surgical Procedures	Primary
Brain and Nervous System	Primary
Other	

If other, please specify

Medications

Describe medications

Psychologic/Quality of Life

BSI-18	Secondary
SF-36	Secondary
CCSS-NCQ	Secondary
PTS	
PTG	
Other	

If other, please specify

Other

Pregnancy and Offspring	
Family History	
Chronic Conditions (CTCAE v3)	Primary
Health Status	Correlative Factors

Demographic

Age	Correlative Factors
Race	Correlative Factors
Sex	Correlative Factors
Other	

If other, please specify

Cancer Treatment

Chemotherapy	Correlative Factors
Radiation Therapy	Correlative Factors
Surgery	Correlative Factors

Anticipated Sources of Statistical Support

CCSS Statistical Center	No
Local Institutional Statistician	Yes

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

Will this project utilize CCSS biologic samples?

No

If yes, which of the following?

If other, please explain

Other General Comments

Dr Kirsten Ness has agreed to be a senior co-investigator in this project. We aim to design Aims 1-4 as an emulated target trial comparing survivors who voluntarily increased their level of physical activity to those who remained on the same level during follow/up. We will use dose of physical activity. Thus, we will use data from follow-up 2 and onward for the original cohort to be able to use questions where we really can calculate dose.

The categories of physical activity will be defined according to the publication by Scott et al. 2018. The risky health behaviors will be defined using the publication by Lown et al. 2016.

This application of intent has been revised according to the discussions in a meeting 8/26/2022 and the revised version has today been read and approved by Drs. Nathan and Snyder of the Cancer Control Working Group.

Agree

I agree to share this information with St. Jude

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