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 : **Effect of Hypothetical Lifestyle Interventions on Major Cardiovascular Events among Childhood Cancer Survivors**
Planned research population (eligibility criteria) :
Inclusion criteria:
- We will include all childhood cancer survivors in the CCSS cohort (diagnosed 1970-99) who participated in the baseline questionnaire.
- As comparators, we will additionally include all siblings in the CCSS cohort.

Exclusion criteria:
- Major cardiac event prior to date of return of baseline questionnaire.
- Missing values for risk factors on baseline questionnaire.
Proposed specific aims :
In conducting this analysis, we will estimate the population risk of disease under each of the below interventions (i.e., smoking cessation, exercise, moderate alcohol consumption, and weight loss). Because these interventions may vary over time and may have effects which depend on one another, standard analytic techniques may not be able to estimate this risk. Techniques such as the parametric g-formula can be adopted to account for time-varying exposure and confounding. In addition to answering an important public health question for childhood cancer survivors, this is a unique opportunity to apply an analytic technique which allows adjustment for time-varying confounders, which may have other useful applications in the Childhood Cancer Survivor Study.

Specific aim 1. To estimate the effect of lifestyle interventions on the population risk of major cardiac events (i.e., CTCAE grade 3-5 coronary artery disease, heart failure, valve

disease, and arrhythmia) among childhood cancer survivors.
- Hypothesis 1A: Had all survivors quit smoking, the rate of major cardiac events would be decreased, compared with if all survivors had not quit smoking.
- Hypothesis 1B: Had all survivors initiated moderate or greater exercise, the rate of major cardiac events would be decreased, compared with if all survivors had not initiated moderate or greater exercise.
- Hypothesis 1C: Had all survivors consumed moderate (5g/day) alcohol, the rate of major cardiac events would be decreased, compared with if all survivors had not consumed moderate alcohol.
- Hypothesis 1D: Had all overweight survivors lost 5% of BMI, the rate of major cardiac events would be decreased, compared with if all overweight survivors had not lost 5% of BMI.
Hypothesis 1E: Had all survivors subscribed to a combination of the above interventions (i.e., smoking cessation, exercise, moderate alcohol consumption, and weight loss), the rate of major cardiac events would be decreased, compared with if all survivors had not subscribed to the above interactions.

Specific aim 2. To estimate the effect of lifestyle interventions on the population risk of major cardiac events (i.e., CTCAE grade 3-5 coronary artery disease, heart failure, valve disease, and arrhythmia) among siblings.
- Hypothesis 2A: Had all siblings quit smoking, the rate of major cardiac events would be decreased, compared with if all siblings had not quit smoking.
- Hypothesis 2B: Had all siblings initiated moderate or greater exercise, the rate of major cardiac events would be decreased, compared with if all siblings had not initiated moderate or greater exercise.
- Hypothesis 2C: Had all siblings consumed moderate (5g/day) alcohol, the rate of major cardiac events would be decreased, compared with if all siblings had not consumed moderate alcohol.
- Hypothesis 2D: Had all overweight siblings lost 5% of BMI, the rate of major cardiac events would be decreased, compared with if all overweight siblings had not lost 5% of BMI.
Hypothesis 1E: Had all siblings subscribed to a combination of the above interventions (i.e., smoking cessation, exercise, moderate alcohol consumption, and weight loss), the rate of major cardiac events would be decreased, compared with if all siblings had not subscribed to the above interactions.

Will the project require non-CCSS funding to complete? : **No**

If yes, what would be the anticipated source(s) and timeline(s) for securing funding? :

Group: 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. :

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

Second Malignancy :

Chronic Disease : **Secondary**

Psychology / Neuropsychology :

Genetics :

Cancer Control : **Secondary**
Epidemiology / Biostatistics : **Primary**

Section: Outcomes or Correlative Factors

Late mortality : **Secondary**
Second Malignancy :

Group: Health Behaviors

Tobacco : **Correlative Factors**
Alcohol : **Correlative Factors**
Physical activity : **Correlative Factors**
Medical screening :
Other : **Correlative Factors**
If other, please specify : **Body mass index**

Group: Psychosocial

Insurance : **Correlative Factors**
Marriage :
Education : **Correlative Factors**
Employment : **Correlative Factors**
Other :
If other, please specify :

Group: Medical Conditions

Hearing/Vision/Speech :
Hormonal systems :
Heart and vascular : **Correlative Factors**
Respiratory :
Digestive :
Surgical procedures : **Correlative Factors**
Brain and nervous system :
Other :
If other, please specify :

Group: Medications

Describe medications :
Statin use

Group: Psychologic/Quality of Life

BSI-18 :
SF-36 :
CCSS-NCQ :
PTS :
PTG :
Other :
If other, please specify :

Group: Other

Pregnancy and offspring :

Family history :
Chronic conditions (CTCAE v3) : **Primary**
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 : **Yes**
Local institutional statistician : **Yes**
If local, please provide the name(s) and contact information of the statistician(s) to be involved. : **Statistical analysis will be conducted by Arin Madenci, in conjunction with Miguel Hernan (faculty at Harvard T.H. Chan School of Public Health) and Yutaka Yasui. This project, and its focus on methodology, has been discussed with Dr. Yasui over the past months.**
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 :
I agree to share this information with St. Jude : **Yes**