First Name: Stephanie
Last Name: Kovalchik
Institution: National Cancer Institute
Address 1: 6120 Executive Blvd, EPS 8047
Address 2:
City: Rockville
State/Province: MD
Country: USA
Zip: 20852
Phone: 626-319-9890
Alternate Phone:
Email: kovalchiksa@mail.nih.gov

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

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Project Title: Influence of lifestyle on site-specific cumulative incidence for second primary malignancies in five-year survivors of a childhood cancer
Planned research population (eligibility criteria): Five-year childhood cancer survivors from the original Childhood Cancer Survivor Study cohort
Proposed specific aims: Compared to the general population, survivors of a childhood cancer are at an elevated risk of developing a second primary malignancy and a number of other life-threatening events (1-2). Several studies have assessed the increased risk of subsequent malignancies among childhood cancer survivors (3-6) and previous risk association studies have examined the risk associated with basic demographic and treatment variables (5-6). The role of lifestyle on a survivor's risk of developing a subsequent primary malignancy has been fully explored. It is also unclear how lifestyle factors might interact with treatment-related risk factors. We propose to evaluate the impact of modifiable lifestyle factors on the absolute risk of site-specific second primary cancers using the most recent follow-up data for the original Childhood Cancer Survivor Study cohort (7). We plan to expand on the work of Friedman et al. (5) and Reulen et al. (6) using data with a longer follow-up period and by conducting multivariable risk association studies of site-specific cumulative second primary cancer incidence. For each major second cancer site, we will assess the significance of the lifestyle variables body mass index, physical activity, smoking, and alcohol consumption on the absolute risk of second primary cancer in models with basic demographic and treatment variables and accounting for impact of competing risks. We will also use these models to examine interactions among the lifestyle factors and treatment-related risk factors for the absolute

risk of second primary cancer. References 1. Hudson MM, Mertens AC, Yasui Y, et al. Health status of adult long-term survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. JAMA 2001; 290(12):1583-1592. 2. Mertens AC, Yasui Y, Neglia JP, et al. Late mortality experience in five-year survivors of childhood and adolescent cancer: the Childhood Cancer Survivor Study. J Clin Oncol 2001; 19(13):3163-3172. 3. Neglia JP, Friedman DL, Yasui Y, et al. Second malignant neoplasms in five-year survivors of childhood cancer: childhood cancer survivor study. J Natl Cancer Inst 2010; 93(8):618-629. 4. Bassal M, Mertens AC, Taylor L, et al. Risk of selected subsequent carcinomas in survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. J Clin Oncol 2001; 24(3):476-483. 5. Reulen RC, Frobisher C, Winter DL, et al. Long-term risks of subsequent primary neoplasms among survivors of childhood cancer. JAMA 2011; 305(22):2311-2319. 6. Friedman DL, Whitton J, Leisenring W, et al. Subsequent neoplasms in 5-year survivors of childhood cancer: the Childhood Cancer Survivor Study. J Natl Cancer Inst 2001; 102(14):1083-1095. 7. Reulen RC, Frobisher C, Winter DL, et al. Long-term risks of subsequent primary neoplasms among survivors of childhood cancer. JAMA 2011; 305(22):2311-2319. 8. Robison LL. Treatment-associated subsequent neoplasms among long-term survivors of childhood cancer: the experience of the Childhood Cancer Survivor Study. Pediatr Radiol 2001; 39 Suppl 1:32-37.
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?: The work of the principal investigators will be supported by the intramural research program at the National Cancer Institute.

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? (Check all that apply)

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

To describe the anticipated scope of the study, please indicate the specific CCSS data to be included as outcome (primary or secondary) or correlative factors. (Check all that apply)

Late mortality: Secondary
Second Malignancy: Primary

Health Behaviors

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

Psychosocial

Insurance:
Marriage:
Education:
Employment:
Other:
If other, please specify:

Medical conditions

Hearing/Vision/Speech:
Hormonal systems:
Heart and vascular:
Respiratory:
Digestive:
Surgical procedures:
Brain and nervous system:
Other: Correlative Factors
If other, please specify: Age at childhood cancer diagnosis; Type of childhood cancer

Medications

Describe medications:

Pregnancy and offspring:
Family History:

Psychologic/Quality of Life

BSI-18:
SF-36:
CCSS-NCQ:
PTS:

PTG:
Other:
If other, please specify:

Chronic conditions (CTCAE v3):
Health status:

Demographic

Age: Correlative Factors
Race: Correlative Factors
Sex: Correlative Factors
Others:
If others, please specify:

Cancer treatment

Chemotherapy: Correlative Factors
Radiation therapy: Correlative Factors
Surgery:

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.: Dr. Kovalchik will be the statistical lead of the project. Some assistance from the CCSS Statistical Center could be required for the formulation of the analytic data set.
Will this project utilize CCSS biologic samples?: No

If yes, which of the following?

Buccal cell DNA:
Peripheral blood:
Lymphoblastoid cell lines:
Second malignancy pathology samples:
Other requiring collection of samples:
If other, please explain:

Other general comments: