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 : **Changes in long-term outcomes among survivors of childhood acute lymphoblastic leukemia**

Planned research population (eligibility criteria) :
Survivors within the CCSS with a primary diagnosis of acute lymphoblastic leukemia

Proposed specific aims :
1) Evaluate late mortality (death > 5 years after diagnosis) among ALL survivors in the CCSS cohort compared to the US population overall and among survivors treated with cranial radiation (None, >0 to 20 Gy, >20 Gy), anthracycline (None, >0 and <120 mg/m2, ≥120 mg/m2 and <250 mg/m2, ≥250 mg/m2), alkylator (CED None, >0 to 1000 mg/m2, >1000 mg/m2), dexamethasone (Yes, No) and methotrexate (None, IT exposure, IV exposure).
2) Describe the incidence of subsequent neoplasms (benign and malignant) among ALL survivors in the CCSS cohort compared to the US population overall and among survivors treated with cranial radiation (None, >0 to 20 Gy, >20 Gy), anthracycline (None, >0 and <120 mg/m2, ≥120 mg/m2 and <250 mg/m2, ≥250 mg/m2), alkylators (CED None, >0 to 1000 mg/m2, >1000 mg/m2), dexamethasone (Yes, No) and methotrexate (None, IT exposure, IV exposure).
3) Describe late neurocognitive outcomes among ALL survivors in the CCSS

cohort compared to siblings using the NCQ to report the frequency of impairment overall and among survivors treated with cranial radiation (None, >0 to 20 Gy, >20 Gy).
4) Describe the prevalence of chronic health conditions among ALL survivors in the CCSS cohort compared to sibling controls. Chronic health conditions will be classified using the Common Terminology Criteria for Adverse Events version 4.0, separated by organ system (i.e. cardiac, endocrine, metabolism and nutrition, neurologic, musculoskeletal etc.) and scored based on the CTCAE grading system (with grades ranging from 1-5, mild to fatal). We will describe results for any CHC and separated by grade 1-2 and grade 3-5 conditions. We will specifically examine bone health (fracture, osteoporosis, osteopenia, osteonecrosis, joint replacement) with regard to type of steroid exposure, endocrine/metabolic outcomes such as obesity and diabetes with respect to radiation to the brain, stroke with respect to radiation to the brain, cardiac conditions with respect to anthracycline exposure and dose given changes in therapy over time which may lead to differential effects by treatment exposure.
5) Describe overall health status among ALL survivors compared to sibling controls including general health, mental health, functional status and activity limitations overall and among survivors treated with cranial radiation (None, >0 to 20 Gy, >20 Gy), anthracycline (None, >0 and <120 mg/m2, ≥120 mg/m2 and <250 mg/m2, ≥250 mg/m2), alkylators (CED None, >0 to 1000 mg/m2, >1000 mg/m2), dexamethasone (Yes, No), and methotrexate (None, IT exposure, IV exposure).
6) Describe socioeconomic factors among ALL survivors compared to sibling including marriage, employment, education and insurance status overall and among survivors treated with cranial radiation (None, >0 to 20 Gy, >20 Gy), anthracycline (None, >0 and <120 mg/m2, ≥120 mg/m2 and <250 mg/m2, ≥250 mg/m2), alkylators (CED None, >0 to 1000 mg/m2, >1000 mg/m2), dexamethasone (Yes, No) and methotrexate (None, IT exposure, IV exposure).
Exploratory Aim: As an exploratory outcome, we will evaluate the above aims by treatment era, stratifying by 5 year time blocks (i.e. 1970-74, 1975-89, 1980-84, 1985-89, 1990-94 and 1995-99).

*** Dosing thresholds described above may change**

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 : **Secondary**

Chronic Disease : **Primary**

Psychology / Neuropsychology : **Secondary**
Genetics :
Cancer Control : **Secondary**
Epidemiology / Biostatistics : **Secondary**

Section: Outcomes or Correlative Factors

Late mortality : **Primary**
Second Malignancy : **Secondary**

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 : **Secondary**
Marriage : **Secondary**
Education : **Secondary**
Employment : **Secondary**
Other :
If other, please specify :

Group: Medical Conditions

Hearing/Vision/Speech : **Secondary**
Hormonal systems : **Secondary**
Heart and vascular : **Secondary**
Respiratory : **Secondary**
Digestive : **Secondary**
Surgical procedures : **Secondary**
Brain and nervous system : **Secondary**
Other : **Secondary**
If other, please specify : **Endocrine/Metabolic, Musculoskeletal/Bone Health. Correlative: Relapse status**

Group: Medications

Describe medications :

Group: Psychologic/Quality of Life

BSI-18 : **Secondary**
SF-36 : **Secondary**
CCSS-NCQ : **Secondary**

PTS :
PTG :
Other :
If other, please specify :

Group: Other

Pregnancy and offspring :
Family history :
Chronic conditions (CTCAE v3) : **Secondary**
Health status : **Secondary**

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 :

Section: Anticipated Sources of Statistical Support

CCSS Statistical Center : **Yes**
Local institutional statistician :
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 :

Section: Other General Comments

Other General Comments :
Senior Author/Mentor: Paul Nathan