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 controls 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

**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: Secondary
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