

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 : **Long-Term Cost-Effectiveness of the Identification of Cancer Predisposition Syndromes in Survivors of Pediatric Leukemia, Brain Tumors and Bone/Soft-Tissue Sarcomas**

Planned research population (eligibility criteria) :

Survivors of pediatric acute lymphoblastic leukemia, bone/soft-tissue sarcoma or brain tumors between 1987-1999 who have undergone germline sequencing in the CCSS cohort.

Proposed specific aims :

To leverage the CCSS data in order to fulfil the following overall study goal: Develop and inform a long-term cost-effectiveness model comparing three genetic evaluation strategies in survivors of acute lymphoblastic leukemia (ALL), bone/soft-tissue sarcomas (bone/STS) and brain tumors. The three genetic evaluation strategies are: physician-based (standard of care), MIPOGG-based and universal genetic testing.

We will estimate a set of clinical, cost, and cost-effectiveness outcomes.

Clinical outcomes include: frequency and time to CPS detection, frequency/type of SMN, SMN-related and overall survival, and quality-adjusted life years (composite metric of life-expectancy and quality of life (QoL) used in economic evaluation).

Cost-related outcomes include: healthcare costs associated with genetic counselling/testing, cancer surveillance and SMN diagnosis/treatment.

Cost-effectiveness outcomes include: cost per additional CPS diagnosis, cost per life-year gained, cost per QALY gained.

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 :

Psychology / Neuropsychology : **Secondary**

Genetics : **Primary**

Cancer Control : **Secondary**

Epidemiology / Biostatistics :

Section: Outcomes or Correlative Factors

Late mortality : **Correlative Factors**

Second Malignancy : **Primary**

Group: Health Behaviors

Tobacco :

Alcohol :

Physical activity :

Medical screening :

Other : **Primary**

If other, please specify : **Genetics - germline sequencing**

Group: Psychosocial

Insurance :

Marriage :

Education :

Employment :

Other :

If other, please specify :

Group: Medical Conditions

Hearing/Vision/Speech :

Hormonal systems :

Heart and vascular :

Respiratory :

Digestive :

Surgical procedures :

Brain and nervous system :

Other :

If other, please specify :

Group: Medications

Describe medications :

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 : **Correlative Factors**

Chronic conditions (CTCAE v3) :

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 :

Local institutional statistician : **Yes**

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

Nandini Dendukuri, Senior Biostatistician

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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 :

Between 8-10% of childhood cancers are attributed to one of over 125 known cancer predisposition syndromes (CPS). A CPS diagnosis carries a risk of developing multiple cancers over a lifetime. CPS identification can lead to direct treatment modifications and implementation of tumor surveillance strategies which can result in earlier cancer detection.

Currently, genetic evaluation for a CPS in a child diagnosed with cancer is performed at the discretion of their physician. There is no standardized approach for clinicians to decide which children require genetic evaluation for a CPS. This physician-guided approach leads to missed opportunities for early intervention. In contrast, some experts advocate for genetic testing in all children with cancer. This universal genetic testing approach requires significant healthcare resources.

To improve physician detection of a CPS, our team developed an evidence-based CPS decision-support tool called the McGill Interactive Pediatric OncoGenetic Guidelines (MIPOGG). MIPOGG consists of 140 tumor-specific decisional algorithms that generate a recommendation for referral or no referral for genetic evaluation based on the likelihood of a CPS. MIPOGG uses clinical, family history and tumor-specific features to streamline genetic referrals and testing. MIPOGG is the first evidence-based tool that incorporates all known CPS types for all pediatric cancers.

A variety of actions follow the detection of a CPS in a child with cancer. These include adapting cancer therapy, the implementation of tumor surveillance protocols, and genetic counselling/testing of at-risk family members. The use of tumor surveillance protocols was shown to decrease morbidity and mortality in certain CPS. Nevertheless, quantifying long-term clinical and economic impacts of CPS detection on patients and families is challenging due to the prolonged follow-up needed to observe the benefits of surveillance on outcomes such as SMN occurrence. This is complicated by heterogeneity of patient populations and CPS subtypes, and limited evidence regarding effectiveness of many tumor surveillance strategies considering this field's novelty. In situations like such, the state-of-the-art approach is the use of mathematical modeling to synthesize the evidence on long term consequences from a variety of sources and project outcomes over the patients' and families' lifetime. Usually, in a health economics context, the outcomes of interest include healthcare and societal costs as well as the length and quality of life. The findings of these models can in turn inform decision-makers on the value of healthcare interventions.

I agree to share this information with St. Jude : Yes