

Pre-Application Webinar

Improving Outcomes for Pediatric, Adolescent and Young Adult Cancer Survivors RFA-CA-19-033 (U01 Clinical Trial Required)

Danielle Dae, PhD, Epidemiology and Genomics Research Program

Sandra Mitchell, PhD, CRNP, Healthcare Delivery Research Program

Wendy Nelson, PhD, MPH, Behavioral Research Program

Nonniekaye Shelburne, CRNP, MS, AOCN, Epidemiology and Genomics Research Program

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<https://grants.nih.gov/grants/guide/rfa-files/RFA-CA-19-033.html>



Division of Cancer Control & Population Sciences

Webinar Presenters



[Sandra Mitchell, Ph.D.](#)

Program Director

Healthcare Delivery Research Program



[Danielle Dae, Ph.D.](#)

Program Director

Epidemiology and Genomics Research Program



[Wendy Nelson, Ph.D.](#)

Program Director

Behavioral Research Program



[Nonniekaye Shelburne, C.R.N.P., M.S., A.O.C.N.](#)

Program Director

Epidemiology and Genomics Research
Program

Webinar Outline

- I. Background and Scope of the Problem
- II. Goals of the Request for Applications (RFA)
- III. Application Requirements
- IV. Questions

Background & Scope of the Problem

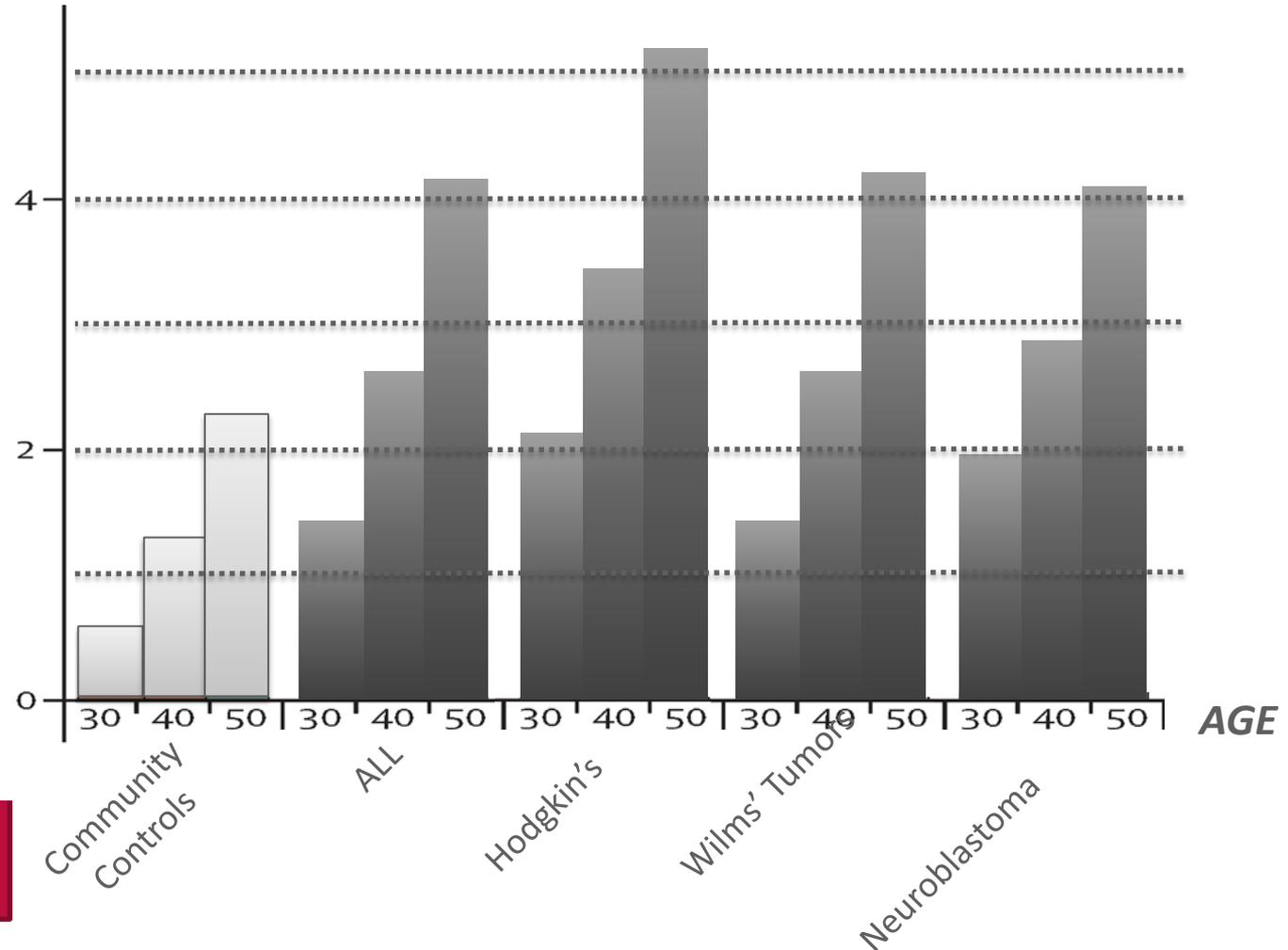
Late and Long-Term Effects
Childhood Cancer Survivorship Treatment and Research (STAR) Act
Beau Biden Cancer MoonshotSM Initiative
Blue Ribbon Panel Recommendation

Long-Term and Late Effects

St. Jude Lifetime Cohort
10+ Year Survivors¹

Cumulative Burden of
CTCAE Grade 3-5 Chronic Conditions by Age

- Survivors have significantly more chronic health conditions compared to controls
- Cumulative burden increases as survivors age
- Wide range of organ system complications and comorbid conditions



The Childhood Cancer Survivorship, Treatment, Access and Research (STAR) Act [*Public Law No: 115-180*](#)

- **Recently enacted law designed to advance pediatric/AYA cancer survivor research and care**
- Among other provisions, the STAR Act authorizes:
 - Enhancements to biospecimen collection and infrastructure (Section 101, directed to NIH/NCI)
 - Improvements to cancer registry infrastructure (Section 102, directed to CDC)
 - **Research to improve the care of and quality of life for survivors (Section 202, directed to NIH/NCI)**

Six key research areas to improve the care of and quality of life for childhood and AYA cancer survivors

1. Survivor outcomes
2. Barriers to follow-up care
3. Impact of familial, socioeconomic, and environmental factors on treatment outcomes and survivorship
4. Development of indicators used for long-term follow-up and analysis of the late effects
5. Identification of risk factors, predictors and molecular basis of adverse outcomes
6. Development of targeted interventions to reduce the burden of morbidity in survivors

health disparities, minorities or other medically underserved populations are high priority

Beau Biden Cancer MoonshotSM Initiative

GOAL: Accelerate progress in preventing, diagnosing, and treating cancer by accomplishing a decade's worth of work in 5 years



\$1.8 billion in funding for Cancer Moonshot Initiatives over the next 7 years



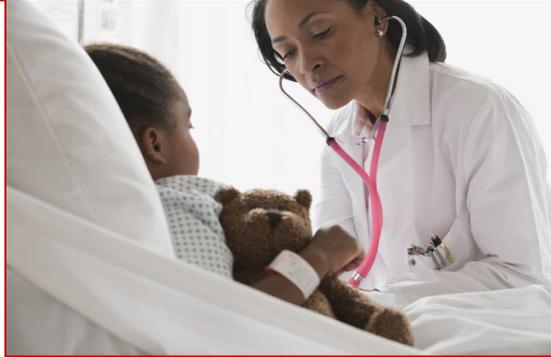
RECOMMENDATION: Minimize cancer treatment's debilitating side effects

- Accelerate the development of effective interventions to evaluate and manage symptoms and side effects

Goals of the RFA

Goals of the RFA to Address STAR Act

- Support the scientific development of **interventions** to address adverse biomedical and psychosocial effects in survivors of pediatric/AYA cancers



Interventions Leverage Insights From Observational Studies

Improve Care Delivery	Address Adverse Effects	
<ul style="list-style-type: none">▪ As survivors transition out of pediatric settings, only a minority are seen by a provider familiar with late effects¹▪ Survivors express unmet needs for organized long-term follow-up services²▪ Increased risk for physical, psychosocial and behavioral adverse effects³▪ Accelerated aging and physiologic frailty are prevalent⁴	<p><u>Physical</u></p> <ul style="list-style-type: none">▪ Symptoms (fatigue, sleep disturbances, peripheral neuropathy)▪ Impaired physical function▪ Neurocognitive impairments▪ Late treatment effects (endocrine, cardiopulmonary, 2^o malignancies)▪ Accelerated aging, frailty and comorbidity▪ Fertility concerns▪ Adverse body composition	<p><u>Psychosocial</u></p> <ul style="list-style-type: none">▪ Psychological distress▪ Disrupted social development▪ Financial hardship, insurance coverage, school/employment difficulties <p><u>Behavioral</u></p> <ul style="list-style-type: none">▪ Reduced physical activity▪ Potential for risky behaviors (alcohol, tobacco, non-adherence)

¹Tonorezos et al. (2018). *J Clin Oncol*. 36(21):2223-2230

²White et al. (2018). *Psychooncology*. 27(8):1979-1986

³Hudson et al. (2017). *Cancer Epidemiol Biomarkers Prev*. 26(5):666-674

⁴Ness et al. (2013). *J Clin Oncol*. 31(36):4496-503

Interventions to Improve Outcomes in Pediatric/AYA Cancer Survivorship: **Aims**

- Develop *feasible, effective and scalable interventions* to address biomedical and psychosocial effects in survivors of pediatric/AYA cancers:
 - Test interventions to prevent, mitigate and manage adverse long-term disease- and treatment-related effects, including interventions to promote self-management and adoption of healthy behaviors
 - Develop and test models of healthcare delivery that strengthen coordination, continuity and quality and improve outcomes
- Applicants must propose a clinical trial

Interventions to Improve Outcomes in Pediatric/AYA Cancer Survivorship: **Trial Designs**

- Trial designs may include:
 - Early phase studies to develop and preliminarily test a novel intervention
 - Phase II or III studies testing efficacy
 - Pragmatic trials to confirm intervention effectiveness in real-world settings
 - Dissemination and implementation studies (including hybrid effectiveness-implementation designs) examining scale and spread of empirically-supported interventions in diverse settings

Interventions to Improve Outcomes in Pediatric/AYA Cancer Survivorship: **Populations**

- Population focus for this RFA:
 - Pediatric and/or AYA cancer survivors who were diagnosed before age 39
 - At risk for or experiencing long-term and late adverse physical , psychosocial and/or behaviors outcomes in the post-treatment period
 - Their caregivers/parents/spouses
- Prioritize applications that address health disparities, minorities and/or medically underserved populations
- Interventions may be targeted at the individual, provider or system level; may include multi-level interventions

Interventions to Improve Outcomes in Pediatric/AYA Cancer Survivorship: **Approach**

- Address access barriers including geographic distance, literacy, functional deficits, and preferences to engage
- Examine meaningful proximal endpoints
- Mechanistic study aims (e.g. how and why an intervention works) should also address the pragmatic implications of that explanatory knowledge (e.g. can it be used to amplify intervention effects or optimize an intervention)
- Encourage applications that leverage advances in digital and mobile health solutions
- Interventions tested for effectiveness and/or implementation in pragmatic trials should have demonstrated feasibility and efficacy

Interventions to Improve Outcomes in Pediatric/AYA Cancer Survivorship: **Potential Research Topics**

- Develop, test and refine interventions to:
 - Improve access and decision-making about the use of fertility services before and after treatment
 - Prevent or mitigate late effects (e.g., secondary malignancies; comorbidities) or persistent/long-term effects (e.g., fatigue, cognitive dysfunction, functional impairment, frailty, and emotional distress)
 - Mitigate adverse outcomes in subgroups at higher risk or who are most likely to derive greatest benefit from early intervention
 - Expand the reach, adoption, effectiveness, and/or maintenance of healthy lifestyle changes
 - Support caregivers/parents/spouses, mitigate the adverse sequelae of their caregiving role, and/or improve survivor outcomes

Interventions to Improve Outcomes in Pediatric/AYA Cancer Survivorship: **Potential Research Topics**

- Comparatively evaluate the components, features, costs and value of care models that optimize key transitions in care (e.g. between pediatric and adult care settings, specialty and primary care settings, or transitions based on geographic relocation)
- Identify care delivery approaches that strengthen self-management, improve clinical outcomes and/or access, and achieve guideline concordant care
- Evaluate the outcomes of risk-based healthcare delivery targeted to specific subgroups who warrant more intensive intervention and/or follow-up
- Test novel approaches to care coordination and communication. Outcomes might include cost, quality, and experiences of care or other relevant endpoints

U01 Awardee Network Interactions

- Each U01 award will be based on an independent project
- Awardees will engage in trans-network interactions and participate in an annual investigator meeting; budgets should reflect inclusion of these activities
- NCI staff will provide scientific support and coordinate interactions among grantees, facilitating collaboration and information sharing

Non-Responsive Applications

- Applications must propose development/testing of interventions addressing physical, psychosocial, or behavioral adverse effects in pediatric and/or AYA survivors
 - Descriptive and observational studies are not responsive to this RFA
- Applications that propose testing of interventions to address short-term or transient adverse effects of treatment are non-responsive
- Applications that propose development or testing of cancer-directed therapies are non-responsive

Application Requirements

Application Requirements: Review

- Two receipt dates:
 - March 15, 2019
 - January 3, 2020
- Special emphasis panel
- Please note and address the Special Review Criteria:
 - Significance of proposed intervention in addressing priority need and/or knowledge gap for pediatric/AYA survivors
 - Relevant and meaningful proximal endpoints
- Letter of Intent to Danielle Dae (daeed@mail.nih.gov) due:
 - February 15, 2019 (for 2019 receipt date)
 - December 3, 2019 (for 2020 receipt date)

Application Requirements: Clinical Trials

- NIH requirements for clinical trials research applications were updated in January 2018. Please be sure to learn about and understand the following policies:
 - Application form now consolidates all Human Subjects and Clinical Trial related information into one place and also expands the information required for applications that include a clinical trial (FORMS-E)
 - Investigators and staff must receive training in Good Clinical Practice
 - All sites participating in multi-site studies research will use a single IRB
 - All NIH-funded clinical trials are expected to register and submit results to [Clinicaltrials.gov](https://clinicaltrials.gov)
- Information about the NIH Clinical Trial Requirements:
<https://grants.nih.gov/policy/clinical-trials.htm>

Application Requirements: Budget

- Budget should reflect the actual needs of the proposed project
- May not exceed 500K in direct costs per year
- Modular budgets are permitted

Summary

■ *Aims* reflect:

- Testing interventions to prevent, mitigate and manage adverse long-term disease- and treatment-related effects, including interventions to promote self-management and adoption of healthy behaviors
- Development and testing of models of healthcare delivery that strengthen coordination, continuity and quality and improve outcomes
- Clinical trial required (note NIH requirements for clinical trials applications)

■ *Target populations*:

- Pediatric and/or AYA cancer survivors at risk for or experiencing long-term and late adverse physical , psychosocial and/or behaviors outcomes in the post-treatment period, and their caregivers/parents/spouse
- Interventions may be targeted at the individual, provider or system level; may include multi-level interventions

Summary

■ *Approach* should reflect:

- Considerations such as access barriers including geographic distance, literacy, functional deficits, and preferences to engage
- Inclusion of meaningful proximal endpoints
- Mechanistic study aims should address the pragmatic implications of that explanatory knowledge (e.g. can it be used to amplify intervention effects or optimize an intervention?)
- Encourage applications that leverage advances in digital and mobile health solutions
- Interventions tested for effectiveness and/or implementation in pragmatic trials should have demonstrated feasibility and efficacy

■ *Budget*:

- May not exceed \$500K in direct costs per year; modular budgets permitted

Resources

- Read the FOA very carefully!
 - <https://grants.nih.gov/grants/guide/rfa-files/RFA-CA-19-033.html>
- Be sure to note the access and data sharing plans required for projects funded as part of the Cancer Moonshot
 - <https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/funding/public-access-policy>
- Today's webinar and FAQ will be posted on our website:
 - <https://healthcaredelivery.cancer.gov/media>
- **Connect with us early!**
- Scientific contacts:
 - Dr. Danielle Dae (Danielle.dae@nih.gov)
 - Dr. Sandra Mitchell (mitchlls@mail.nih.gov)

Questions?

Please type your questions in the Q & A section on
WebEx

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