



Pre-Application Webinar

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

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



Division of Cancer Control & Population Sciences

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Webinar Presenters



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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

Beau Biden Cancer MoonshotSM Initiative
Blue Ribbon Panel Recommendation
Long-Term and Late Effects

Childhood Cancer Survivorship Treatment and Research (STAR) Act



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

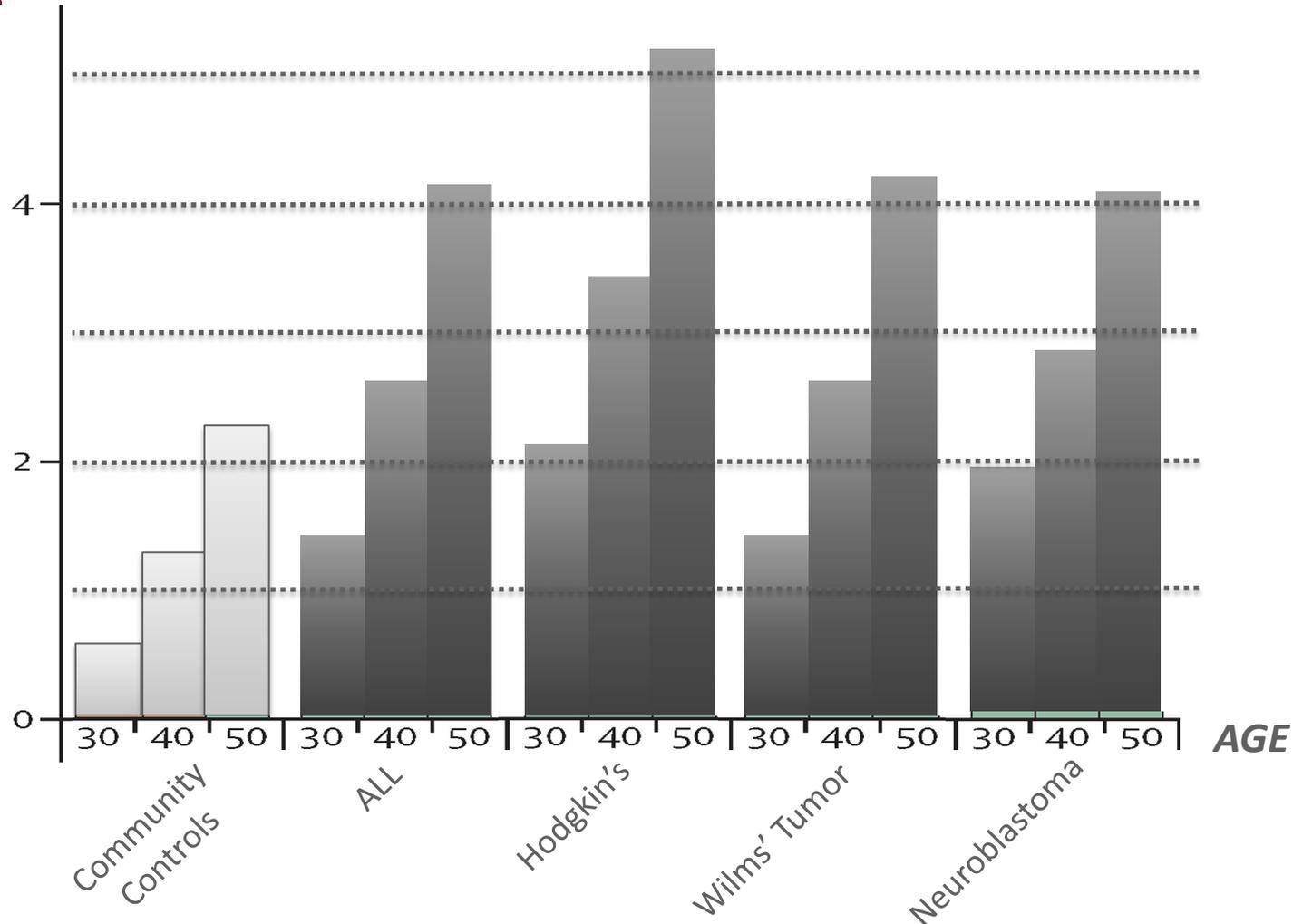
- Accelerate the development of effective interventions to evaluate and manage symptoms and side effects

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 survivor ages
- Wide range of organ system complications and comorbid conditions





The Childhood Cancer Survivorship, Treatment, Access and Research (STAR) Act

- Recently enacted law ([*Public Law No: 115-180*](#)) designed to advance pediatric/AYA cancer survivor research and care
- 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

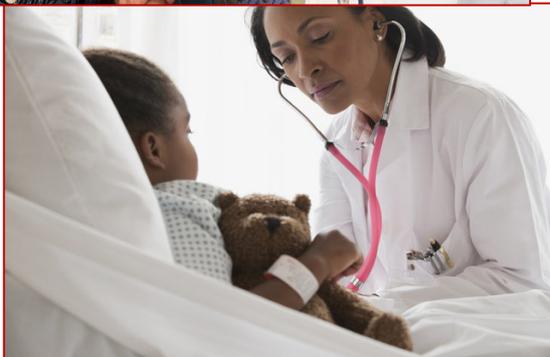
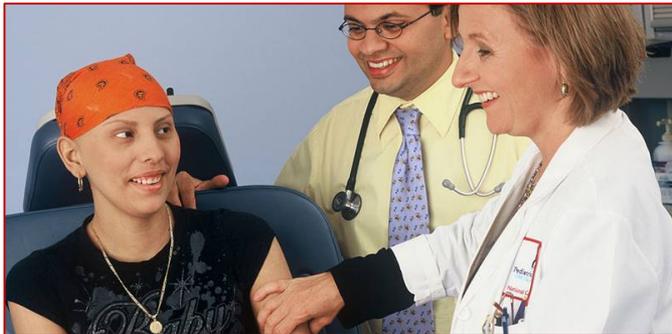
1. Survivor outcomes
2. Barriers to follow-up care
3. Impact of familial, socioeconomic, and environmental factors on treatment outcomes and survivorship
4. Development of indicators used for long-term follow-up and analysis of the late effects
5. Identification of risk factors, predictors and molecular 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]

Goals of the RFA

RFA-CA-19-033: Overall Goal

- Support the scientific development of interventions to address adverse biomedical and psychosocial effects in survivors of pediatric/AYA cancers
- RFA issued in January, 2019:
 - First receipt date: March 15, 2019 (3 awards made)
 - **Second receipt date: January 3, 2020**



Interventions Leverage Insights From Observational Studies

Improve Care Delivery

- 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

Address Adverse Effects

Physical

- Symptoms (fatigue, sleep disturbances, peripheral neuropathy)
- Impaired physical function
- Neurocognitive impairments
- Late treatment effects (endocrine, cardiopulmonary, 2nd malignancies)
- Accelerated aging, frailty and comorbidity
- Fertility concerns
- Adverse body composition

Psychosocial

- Psychological distress
- Disrupted social development
- Financial hardship, insurance coverage, school/employment difficulties

Behavioral

- 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

RFA-CA-19-033: 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 lifestyle behaviors
 - Develop and test models of healthcare delivery that strengthen coordination, continuity and quality and improve outcomes
- Applicants must propose a clinical trial

RFA-CA-19-033: Population Focus

- Population focus for this RFA:
 - Survivors of pediatric and/or AYA cancer who were diagnosed before age 39, and who are at risk for or experiencing long-term and late adverse physical, psychosocial and/or behavioral outcomes in the post-treatment period
 - Interventions may be family-focused or dyadic interventions that include the survivor together with their parent, caregiver, siblings or spouse
- 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

RFA-CA-19-033: Potential 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

RFA-CA-19-033: Scientific Approach

- Address access barriers including geographic distance, literacy, functional deficits, and preferences to engage in self-management
- 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



RFA-CA-19-033: 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 behaviors
 - Support caregivers/parents/spouses, mitigate the adverse sequelae of their caregiving role, and/or improve survivor outcomes



RFA-CA-19-033: Potential Research Topics

- Comparatively evaluate the components/features, outcomes, costs, and value of care delivery models that:
 - Optimize transitions in care (e.g. between pediatric and adult care settings, specialty and primary care settings, or transitions based on geographic relocation)
 - Strengthen self-management, improve clinical outcomes and/or access, and achieve guideline concordant care
 - Offer novel approaches to optimize care coordination and communication, focusing on outcomes such as cost, quality, experiences of care or other relevant endpoints
 - Deliver risk-based care targeted to specific subgroup of survivors who warrant more intensive intervention and/or follow-up

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

- Descriptive and observational studies are not responsive to this RFA
 - Applications must propose development/testing of interventions
 - 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
- <https://grants.nih.gov/grants/guide/notice-files/NOT-CA-19-058.html>



Application Requirements

Application Requirements

- Application receipt date:
 - January 3, 2020
- Special emphasis panel
- Please be sure to 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
- Investigators planning to utilize NCORP (CCDR or CPC) must have their application to this RFA approved by NCI-NCORP prior to submission (allow 6 week lead time)
- Letter of Intent to Danielle Dae (daeed@mail.nih.gov) due:
 - Due December 3, 2019
 - LOI required both for resubmissions and for new applications

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 consolidates all Human Subjects and Clinical Trial related information into one place and 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
- 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
- Up to 5 years of support may be requested

RFA-CA-19-033: Highlights

■ *Aims* reflect:

- Testing intervention efficacy in preventing, mitigating and managing 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 population*:

- Pediatric and/or AYA cancer survivors at risk for or experiencing long-term and late adverse physical , psychosocial and/or behavioral outcomes
- Interventions may be targeted at the individual, provider or system level; may include multi-level interventions

RFA-CA-19-033: Highlights

- *Approach* should reflect:
 - Significance of proposed intervention in addressing priority need and/or knowledge gap for pediatric/AYA survivors
 - Inclusion of meaningful proximal endpoints
 - Considerations such as access barriers including geographic distance, literacy, functional deficits, and preferences to engage
 - Opportunities to leverage digital and mobile health solutions, where possible
- Interventions proposed for testing in effectiveness and/or implementation studies (including pragmatic trials) should have demonstrated feasibility and efficacy
- Applicants planning to use the NCORP network must have prior approval from NCI

Resources

- Read the FOA very carefully!
 - <https://grants.nih.gov/grants/guide/rfa-files/RFA-CA-19-033.html>
- Be sure to note the public 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. Sandra Mitchell (Sandra.Mitchell@nih.gov)
 - Dr. Danielle Dae (Danielle.dae@nih.gov)

Questions?

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

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