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| RFA-CA-19-033 Improving Outcomes for Pediatric, Adolescent and Young Adult Cancer Survivors | |
| Mechanism | U01 |
| Leadership | Single or Multiple PI |
| Clinical Trial Requirement | Required |
| Aims | This FOA requests applications from investigators to develop and test interventions that:   * prevent, mitigate or manage adverse physical, psychosocial, and behavioral outcomes in pediatric and/or AYA cancer survivors; or * improve healthcare delivery for pediatric and/or AYA cancer survivors |
| Populations | Interventions may be   * targeted to pediatric and/or AYA cancer survivors, caregivers, providers, healthcare systems; or * multilevel interventions delivered by providers, teams, communities, and/or care delivery systems |
| Study Requirements | Proposed clinical trials must aim to develop/refine and/or test an intervention to improve physical, psychosocial, or behavioral adverse effects or to improve healthcare delivery, and may employ any one of the following trial designs:   * early phase studies to develop and preliminarily test a novel intervention; * phase II or phase III studies that focus on testing efficacy; * trials that examine intervention effectiveness in in real-world settings (e.g., in community settings, with community-based providers); and * dissemination and implementation studies (including hybrid effectiveness-implementation designs) examining the scale up and spread of empirically supported interventions in diverse healthcare settings. |
| Budget Considerations | The application budget should reflect the actual needs of the proposed project but must not exceed $500,000 (direct costs) per year. Modular budgets are allowed. |
| Scientific Contacts | Dr. Danielle Daee ([Danielle.Daee@nih.gov](mailto:Danielle.Daee@nih.gov))  Dr. Sandra Mitchell ([Sandra.Mitchell@nih.gov](mailto:Sandra.Mitchell@nih.gov)) |

Application FAQs

**Why is this mechanism a U01 (as opposed to a R01 or other type)?**

The U01 mechanism allows NCI to provide scientific support and program coordination to awardees. As such, NCI will facilitate collaboration and information sharing across the individual awards.

**Is a letter of intent required and by what deadline? What should be included?**

Yes. A letter of intent (LOI) is required for RFA-CA-19-033. LOIs assist NCI in identifying expert reviewers without conflicts of interest. **LOIs are due by February 15, 2019** for the first application due date (March 15, 2019). For the second application due date (January 3, 2020), LOIs are due December 3, 2019.

LOIs should include the following:

* Descriptive title of proposed activity
* Specific Aims for the proposed project
* Name(s), address(es), and telephone number(s) of the PD(s)/PI(s)
* Names of other key personnel
* Participating institution(s)
* Number and title of this funding opportunity

The LOI should be sent by email, with the subject "Letter of Intent for RFA-CA-19-033" to Danielle.Daee@nih.gov

**What are the new NIH clinical trials policies?**

Key policy notices are available [here](https://grants.nih.gov/policy/clinical-trials/key-dates-and-policy-notices.htm).

NIH requirements for all grant applications that propose a clinical trial are available [here](https://grants.nih.gov/policy/clinical-trials.htm).

**Will there be another set of solicitations issued?**

RFA-CA-19-033 has two receipt dates March 15, 2019 and January 3, 2020. NCI is exploring future strategies to address the priorities described in the [STAR Act](https://www.congress.gov/bill/115th-congress/senate-bill/292/text?q=%7B%22search%22%3A%5B%22S292%22%5D%7D&r=1).

**Will you accept international collaborators as subcontractors?**

Yes, international institutions and collaborators are eligible to apply to this RFA. Non-domestic (non-U.S.) Entities (Foreign Institutions) are eligible to apply.

Non-domestic (non-U.S.) components of U.S. Organizations are eligible to apply.

Foreign components, as defined in the NIH Grants Policy Statement, are allowed.

Applications from foreign organizations or international organizations will be evaluated and scored using the standard review criteria.

* Whether the project presents special opportunities for furthering research programs through the use of unusual talent, resources, populations, or environmental conditions in other countries that are not readily available in the United States or that augment existing U.S. resources.
* Whether the proposed project has specific relevance to the mission and objectives of the IC and has the potential for significantly advancing the health sciences in the United States.

**Can you say more about what should be included in the data sharing plan?**

All applications, regardless of the amount of direct costs requested for any one year, should address a Data Sharing Plan.

NCI has established a data sharing policy for projects that are funded as part of the [Beau Biden Cancer MoonshotSM Initiative](https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/blue-ribbon-panel/pediatric-cancer-working-group-report.pdf) that requires applicants to submit a Public Access and Data Sharing Plan that: (1) describes their proposed process for making resulting Publications and to the extent possible, the Underlying Primary Data immediately and broadly available to the public and; (2) if applicable, provides a justification to NCI if such sharing is not possible. NCI will give competitive preference and funding priority to applications with a data sharing plan that complies with the strategy described [here](https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/funding/public-access-policy?redirect=true). The data sharing plan will become a term and condition of award.

The Data Sharing Plan is expected to include sharing relevant resources and data through appropriate NIH-supported repositories (as applicable).

The Data Sharing Plan should address participants' Study Consents and include (whenever possible) the option to use data and/or biospecimens for future research studies.

**Is an Awaiting Receipt of Application (ARA) required for budgets that exceed $500K direct costs in any of the grant years?**

As application budgets for this RFA may not exceed $500,000 (direct costs) per year, the ARA policy does not apply.

**Does Early Stage Investigator (ESI) or New Investigator (NI) status apply to these RFAs? Will NI or ESI investigators be considered too “junior” to lead a competitive U01?**

Yes, ESI/NI statuses apply. For grant applications that involve more than one PI (e.g. multi-PI), all PD/PIs must meet the [definition](https://grants.nih.gov/policy/early-investigators/index.htm) of NI or ESI for the application to be designated as such. NCI is committed to supporting Early Stage Investigators (ESIs) and will place special emphasis on supporting ESI-designated applications.

ESI/NI investigators will not be considered as too early in their career to compete for this funding opportunity. However, for a successful grant application, it will be essential that the applicant clearly demonstrate that members of the team have both the expertise and the experience required to accomplish the study that has been proposed.

**Is a U34 Multi-Center Clinical Study Implementation Planning Cooperative Agreement needed prior to application?**

No. This RFA does not use the U34 mechanism.

**How much preliminary data about an intervention is needed prior to applying?**

Reviewers will evaluate the application for scientific merit, which includes an assessment of the rigor of the prior research (developed either by the applicant or cited from the literature) that supports the scientific premise for the proposed project. Additional preliminary data (developed by applicants as needed) should be sufficient to support any gaps in the premise of the proposed project and/or to demonstrate that your proposed research approach is potentially promising, sufficiently rigorous, and that the applicant and their team have the skills, experience, and environmental resources to address the study aims

**Should applications include multiple sites, or will single institution applications be considered competitive?**

Single institution and multiple site applications are both allowed.

**Can you speak to how important it is to submit for the first deadline of this FOA, versus the second later in 2019?**

This RFA has two receipt dates March 15, 2019 and January 3, 2020. Applicants who submit in March 2019 will be allowed to resubmit for the January 2020 submission date.  With a re-submitted application, applicants can specifically address reviewer comments from the first submission. After the January 2020 receipt date, resubmissions are not allowed, and applicants wishing to resubmit would have to submit the proposal as a new application to any applicable funding opportunity announcement.

Research Scope FAQs

**Is the development of models for risk stratification, such as identification of predisposition to additional primary tumors, within the scope of the FOA?**

Intervention development and testing using a clinical trial design is a requirement of this RFA. As such, model development for risk stratification would only be in scope if it was used in the context of testing, supporting or refining a proposed intervention.

**Are interventions delivered during treatment (i.e. while still on chemotherapy) eligible for this application if they are designed to prevent a late effect?**

This RFA specifically targets the development and testing of interventions to improve care and quality of life for pediatric and AYA cancer survivors. As such, applications that evaluate interventions delivered during cancer-directed treatment, but which are designed to prevent or mitigate long-term or late adverse physical, psychosocial, and/or behavioral outcomes in survivors would be responsive. However, applications that test interventions designed to prevent or mitigate the immediate or acute adverse effects of treatment would not responsive.

**Is there a preference for interventional strategies versus correlation of biomarkers with a clinical outcome?**

Development and testing of an intervention must be proposed for applicants to be responsive to this RFA. As such, applicants responding to this FOA should propose a clinical trial that aims to develop/refine and test an intervention to prevent or mitigate physical, psychosocial, or behavioral adverse effects or to improve healthcare delivery. Studies may include biomarkers to evaluate proximal endpoints or to understand the mechanisms of a proposed intervention.

**Will this RFA support prognostic biomarkers to direct interventions or predictive biomarkers to suggest drug sensitivities?**

Yes, studies may include biomarkers (prognostic or predictive) to evaluate proximal endpoints and/or to understand the mechanism of action underlying an intervention under study. Such mechanistic, predictive or explanatory 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, improve delivery of interventions to those at greatest risk, or optimize the components of an intervention)

**Will investigations of behavioral interventions to benefit cancer-related cognitive impairment be supported?**

Yes. Studies that are developing and testing any intervention designed to prevent or mitigate late or long-term adverse physical, psychosocial, and/or behavioral outcomes in survivors are responsive.

**Would an exploratory application that uses a descriptive design – for example, to understand how radiation doses in various brain regions contribute to long-term neurocognitive outcomes given patient demographics, tumor characteristics and other treatment variables – be responsive?**

Applications using a descriptive or correlational study design, in this case to provide insight into the natural history of a specific adverse effect or its underlying etiology would not be responsive. Similarly, applications that propose testing of interventions to address short-term or transient adverse effects or propose development or testing of cancer-directed therapies, rather than interventions to address adverse effects of treatment, would not be responsive. Responsive applications are those that propose development or testing of an intervention to prevent, mitigate or manage physical, psychosocial, or behavioral adverse effects in pediatric and/or AYA cancer survivors.

**What is the appropriate trial design for this RFA?**

Appropriate trial designs include:

* early phase studies to develop and preliminarily test a novel intervention;
* phase II or phase III studies that focus on testing efficacy;
* trials that examine intervention effectiveness in real-world settings (e.g., in community settings, with community-based providers);
* dissemination and implementation studies (including hybrid effectiveness-implementation designs) examining the scale up and spread of empirically-supported interventions in diverse healthcare settings.

**What projects will be prioritized?**

The development and testing of interventions that address/target the needs and preferences of minority or other medically underserved populations will be of high priority in all research areas.

Additionally, NCI will consider the significance of the proposed research in terms of:

* addressing a pressing need for pediatric and/or AYA survivors; or
* addressing an important knowledge gap in pediatric and/or AYA survivor research

**How would pre-clinical model systems be valued in a proposal that seeks to identify subgroups of patients that would benefit most from an intervention?**

This RFA requires that an intervention be developed and/or tested using a clinical trial design, which includes prospective assignment of human subjects to one or more study arms.  As such, pre-clinical models would only be in scope if they were employed in the context of supporting the development of the intervention, justifying its scientific premise (e.g. relationship of intervention to study endpoints), or shaping the prospective assignment of participants to an arm of the study.

**Are studies with a behavioral end point (e.g. physical activity, healthy diet, sleep) as primary outcome of interest?**

Yes. Primary endpoints used to determine intervention efficacy may be physical, psychological or behavioral, and may be measured using a patient-reported outcome measure, a clinician-reported measure, a performance-based or instrumented outcome or a biomarker. All endpoints should have some evidence of validity, reliability and responsiveness to change, and should have a well-conceptualized relationship to the intervention under study.

**Would a trial to use a pharmacologic intervention (e.g. carvedilol) DURING cancer treatment trial with the goal to prevent or mitigate late effects be considered responsive?**

Yes. This RFA is specifically targeted to improving care and quality of life for pediatric and AYA cancer survivors. As such, applications that evaluate interventions delivered during cancer-directed treatment, but which are designed to prevent or mitigate long-term or late adverse physical, psychosocial, and/or behavioral outcomes in survivors would be responsive. However, applications that test interventions designed to prevent the immediate or acute adverse effects of treatment would not responsive.

Research Population FAQs

**Please define survivor.**

An individual is considered a cancer survivor from the time of diagnosis, through the balance of his or her life. There are many types of survivors, including those living with cancer and those free of cancer.

**Would projects that improve care for AYAs with cancer also be applicable, and not just survivors?**

This RFA is specifically targeted to improving care and quality of life for pediatric and AYA cancer survivors who are post-treatment. As such, applications that propose to develop/test interventions that are delivered during cancer-directed treatment but are primarily intended to prevent or mitigate the long-term adverse physical, psychosocial, and/or behavioral outcomes in survivors,are responsive. Applications testing interventions designed to prevent or treat the acute or immediate adverse effects of cancer-directed therapies are not responsive.

**Are the eligibility criteria for the age of cancer diagnosis in survivors to be studied within this RFA 0-39 years of age?**

Yes, pediatric and AYA cancer survivors diagnosed between 0-39 years of age are the population of interest for this RFA.

**What qualifies as research focusing on pediatric/young adult survivors? Is a person eligible potentially from the time of cancer diagnosis? What is the upper age limit for this group of participants?**

Cancer survivorship begins at the day of cancer diagnosis. Pediatric and AYA cancer survivors with age of diagnosis between 0-39 years of age are the population of interest for this RFA. Applications may propose the testing of interventions for survivors of pediatric and AYA cancers who are now older than age 39, however responsive applications must propose to study individuals who were diagnosed with cancer before age 40. As such, there is no there is no upper age limit that defines a survivor of a pediatric or AYA cancer.

**Can you provide more detail about what is meant by ‘health disparities’ being of high priority?**

Health disparities are barriers to access or differences in outcomes which systematically and negatively impact less advantaged groups including, but not limited to, racial and ethnic minorities, the rural and urban poor, and other medically underserved populations. The development and testing of interventions that address known health disparities, and/or have been tailored to the specific needs and preferences of minority or other medically underserved populations will be of high priority in all research areas.

**Are interventions that specifically address AYA Latino cancer survivors responsive?**

Yes, the development and testing of interventions that focus on the needs and preferences of minority or other medically underserved populations will be of high priority in all research areas. Note that these interventions should reflect population considerations including, for example, the language that is used to deliver the intervention, comprehensibility, developmental appropriateness, and digital accessibility.

**Would interventions in another language such as Spanish or multiple languages be of value?**

Intervention materials and components should be tailored to the needs of the target population and reflect considerations that include the language that is used to deliver the intervention, comprehensibility, developmental appropriateness, and digital accessibility. The development of interventions that address/target the needs and preferences of minority or other medically underserved populations will be of high priority in all research areas.

**Can the intervention address caregivers?**

Interventions being developed or tested may be targeted to pediatric and/or AYA cancer survivors, as well as their informal caregivers (including parents and spouses) or clinical providers. Interventions that include the caregiver may be dyadic (i.e. patient and caregiver) or focused solely on the caregiver.

General Background FAQs

**What is the STAR Act?**

The Childhood Cancer Survivorship, Treatment, Access, Research (STAR) Act of 2018 was introduced as proposed legislation in the U.S. House of Representatives and the U.S. Senate during the 115th Congress (earlier versions of the bill had also been introduced in previous sessions of Congress). The STAR Act passed in both the Senate (March 2018) and House (May 2018) with bipartisan support, and the President signed the bill into law in June 2018 ([Public Law No: 115-180](https://www.congress.gov/bill/115th-congress/senate-bill/292/text?q=%7B%22search%22%3A%5B%22s292%22%5D%7D&r=1&s=2)). The STAR Act includes several provisions that aim to advance research and care for children, adolescents, and young adults with cancer. Among other provisions, the law authorizes and encourages continued research to improve the care and quality of life for survivors (Section 202). The NCI, through its Office of Cancer Survivorship, is issuing [RFA-CA-19-033](https://grants.nih.gov/grants/guide/rfa-files/RFA-CA-19-033.html) both to build upon the Institute’s ongoing commitment to childhood, adolescent and young adult cancer survivorship research, and to foster research applications that align directly with areas emphasized in Section 202 of the STAR Act.

**What is the** [**Cancer MoonshotSM**](https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative)**?**

The Cancer Moonshot to accelerate cancer research aims to make more therapies available to more patients, while also improving our ability to prevent cancer and detect it at an early stage.

Congress passed the 21st Century Cures Act in December 2016, authorizing $1.8 billion in funding for the Cancer Moonshot over 7 years. The funding must be appropriated each fiscal year over those 7 years. Congress appropriated $300 million to NCI for fiscal year (FY) 2017, $300 million for FY 2018, and $400 million for FY 2019.