|  |  |
| --- | --- |
| RFA-CA-19-033 Improving Outcomes for Pediatric, Adolescent and Young Adult Cancer Survivors | |
| Mechanism | U01 |
| LOI Due Date | December 3, 2019 |
| Application Due Date | January 3, 2020 |
| Leadership | Single or Multiple PI |
| Clinical Trial Requirement | Required |
| Aims | This FOA solicits applications from investigators to develop and test interventions to:   * 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 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. **For the January 3, 2020 due date, 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

**Do applicants who applied to the first receipt date in March 2019 and who plan to resubmit their application for the second receipt date need to submit an LOI?**

Yes. All applicants, including those who are resubmitting an application, must submit an LOI.

**How are LOIs evaluated?**

LOIs are reviewed by program staff for general responsiveness by the Scientific Contacts of the RFA. Submitting PIs will receive an email acknowledging receipt of the LOI and confirming NCI’s interest in receiving the full application

**I would like to use the NCI Community Oncology Research Program (NCORP) network to conduct my clinical trial in response to this funding announcement. Is there anything special I need to do if I am going to use the NCORP network?**

There are additional steps that must occur if you are proposing to use the NCORP network to conduct your study, and this process will take additional time. All Letters of Intent must indicate if you plan to use the NCORP network.  In addition, at least 5-6 weeks prior to submitting your application, you must speak with NCI NCORP staff and be in contact with the NCORP Research Base staff that you will be working with. Please send an email to Dr. Sandra Mitchell at [sandra.mitchell@nih.gov](mailto:sandra.mitchell@nih.gov) as soon as possible to let us know you are planning to conduct your proposed study in NCORP. We will work with NCI NCORP staff to set up a call and further outline the process to be followed.

**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 had 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?**

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 ESIs and will place special emphasis on supporting ESI-designated applications.

ESI/NI investigators will not be considered too early in their careers to compete for this funding opportunity. However, for a successful grant application, it will be essential that the applicant clearly demonstrates 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?**

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 support any gaps in the premise of the proposed project and/or demonstrate that the 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?**

RFA 19-033 has two receipt dates: March 15, 2019 and January 3, 2020. Applicants who submitted in March 2019 are encouraged to resubmit for the January 2020 submission date.  With a re-submitted application, applicants must still submit an LOI by December 3, 2019, and applicants have the opportunity to address reviewer comments about their first submission. After the January 2020 receipt date, resubmissions are not allowed, and applicants will have to submit their proposal as a new application to any applicable funding opportunity announcement.

**Will RFA-CA-19-033 be reissued?**

No, this RFA will not be reissued.

**Are there opportunities for revision of applications?**

Applications from the first receipt date (March 15, 2019) may be resubmitted for the second receipt date. However, new applications to the second receipt date cannot subsequently be resubmitted. After the January 3, 2020 receipt date, applicants who are not selected for funding will have to submit the proposal as a new application to any available funding opportunity announcement. Please see the NIH guide for available funding opportunities https://grants.nih.gov/funding/searchguide/index.html#/.

Research Scope FAQs

**Are interventions that propose development or testing of cancer-directed therapies responsive to this RFA?**

No. Applications that propose development or testing of cancer-directed therapies are not responsive. See https://grants.nih.gov/grants/guide/notice-files/NOT-CA-19-058.html.

**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 used in the context of testing, supporting or refining an 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 and are designed to prevent or mitigate long-term or late adverse physical, psychosocial, and/or behavioral effects 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? Does this RFA support the development of prognostic biomarkers to direct interventions or predictive biomarkers to suggest drug sensitivities? Does this RFA support the development of assessment tools, surveys or questionnaires?**

To be responsive to this RFA, applicants must be proposing a clinical trial to develop and test an intervention to prevent or mitigate physical, psychosocial, or behavioral adverse effects or to improve healthcare delivery. As such correlational studies, such as those evaluating the validity and predictive utility of a biomarker, or developing an outcome measure would not be responsive. Studies may include biomarkers to evaluate proximal endpoints in the trial or to understand the mechanism of action for the intervention being tested. However, 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?**

Studies that develop and test interventions to prevent or mitigate late or long-term adverse physical, psychosocial, and/or behavioral outcomes in survivors are responsive to this RFA.

**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 and testing of interventions to prevent, mitigate or manage physical, psychosocial, or behavioral adverse effects in pediatric and/or AYA cancer survivors.

**What kinds of trials designs are appropriate 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 applications will be prioritized?**

Development and testing interventions that address/target the needs and preferences of minority or other medically underserved populations is high priority.

Additionally, NCI will consider the significance of the proposed research in terms of the extent to which it addresses:

* a priority concern or need of pediatric and/or AYA cancer survivors
* an important knowledge gap in pediatric and/or AYA survivorship 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 that 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 and testing its efficacy, justifying the study’s scientific premise (e.g., relationship of intervention to study endpoints), or structuring the prospective assignment of participants to an arm of the study.

**Are studies with psychosocial or behavioral endpoints (e.g., physical activity, diet quality, sleep-wake patterns) acceptable as primary outcomes?**

Primary endpoints used to determine intervention efficacy may be physical, psycholosocial 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 established measurement properties with respect to validity, reliability, and responsive to change, and should have a well-conceptualized, highly interpretable and proximal relationship to the intervention being tested.

**Would a trial of a pharmacologic intervention DURING cancer treatment, with the goal of preventing or mitigating specific late effects, be considered responsive?**

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 immediate or acute adverse treatment effects are not responsive. Responsive applications must also include meaningful proximal endpoints.

**Please define would you mean by relevant and meaningful proximal endpoints?**

Proximal endpoints refer to endpoints that can be measured and analyzed within the time frame of the proposed award. The relevancy and meaningfulness of endpoints depends on the intervention being evaluated. All endpoints should have established measurement properties with respect to validity, reliability, and responsive to change, and should have a well-conceptualized and highly interpretable relationship to the intervention being tested.

**Are Phase 1 trials that involve development and preliminary testing of a novel intervention encouraged?**

Early phase trials to develop a novel intervention and examine it’s preliminary efficacy in prevening the preliminary efficacy of novel interventions to prevent, mitigate and manage physical, psychosocial and behavioral late and long-term effects or to improve healthcare delivery for pediatric and/or AYA cancer survivors are responsive to this RFA and are encouraged.

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 who are still undergoing cancer treatment be responsive to this RFA?**

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.

**Please clarify the population of interest for this RFA. Is there a specific range of time since diagnosis and treatment for study participants?**

The population focus for this RFA is pediatric and/or AYA cancer survivors who were diagnosed before age 39, and who are at risk for or experiencing long-term and late adverse physical, psychosocial and/or behavioral effects at any point in the post-treatment period.

**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 time 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 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. Developing and testing interventions that address known health disparities, and/or have been tailored to the specific needs and preferences of minority or other medically underserved populations, is high priority.

**Are interventions that specifically address AYA Latino cancer survivors responsive? Would interventions in another language such as Spanish or multiple languages be of value?**

Developing and testing interventions that focus on the needs and preferences of minority or other medically underserved populations is high priority.

Intervention materials and components should be tailored to the needs and preferences of the target population and should 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 is high priority.

**Can the intervention being tested include caregivers?**

Interventions being developed and 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 family-focused or dyadic interventions that include the survivor together with their parent, caregiver, siblings or spouse.

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.