RFA-CA-20-027/RFA-CA-20-028 Research to Reduce Morbidity and Improve Care for Pediatric and Adolescent and Young Adult (AYA) Cancer Survivors	
Mechanism	R01(RFA-CA-027) and R21 (RFA-CA-028) mechanisms
Leadership	Single or Multiple PI
Clinical Trial Requirement	Optional
Aims	This FOA requests applications from investigators focused on improving care and health-related quality of life for childhood and AYA cancer survivors. This FOA specifically solicits mechanistic, observational, and intervention applications that focus on one or more of the following six key domains: 1. Disparities in survivor outcomes 2. Barriers to follow-up care 3. Impact of familial, socioeconomic, and other environmental factors on survivor outcomes 4. Indicators for long-term follow-up needs related to risk for late effects, recurrence, and subsequent cancers 5. Risk factors and predictors of late/long-term effects of cancer treatment 6. Development of targeted interventions to reduce the burden of cancer for pediatric/AYA survivors
Populations	Research must focus on a subset of the pediatric and/or AYA cancer survivor population (age at primary diagnosis 0-39). Research may also focus on relevant populations in addition to pediatric and/or AYA survivors, including informal cancer caregivers and clinicians/healthcare providers.
Study Requirements	To be responsive to this FOA, proposed projects must have all of the following attributes: • Focus on a subset of the pediatric and/or AYA cancer survivor population (age at primary diagnosis 0-39). • Focus on understanding and/or addressing physical, psychosocial, and/or behavioral adverse effects or improving healthcare delivery in survivors of pediatric and/or AYA cancers. • Applications must address one or more of the six key domains: (1) disparities in survivor outcomes; (2)

	barriers to follow-up care (e.g. access, adherence); (3) impact of familial, socioeconomic, and other environmental factors on survivor outcomes; (4) indicators for long-term follow-up needs related to risk for late effects, recurrence, and subsequent cancers; (5) risk factors and predictors of late/long-term effects of cancer treatment; or (6) development of targeted interventions to reduce the burden of cancer for pediatric/AYA survivors. Additionally, applications with the following characteristics will be considered nonresponsive and will not be reviewed: • Applications addressing short-term, transient adverse effects (e.g., nausea due to cancer treatment). • Applications that propose development or testing of cancer-directed therapies.
Budget Considerations	The application budget needs to reflect the actual needs of the proposed project.
Scientific Contacts	Danielle Daee: danielle.daee@nih.gov Michelle Mollica: michelle.mollica@nih.gov

Application FAQs

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

Yes. A letter of intent (LOI) is strongly encouraged for RFA-CA-20-027 and RFA-CA-20-028. LOIs assist NCI in preparing and planning for review. With this information we can assess workload (e.g. how many applications will be reviewed) and allow us to begin identifying expert reviewers without conflicts of interest. **Letters of intent are due 30 days prior to the receipt date.**

Letters of intent 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-20-027" or Letter of Intent for RFA-CA-20-028" to Danielle.Daee@nih.gov.

What are the new NIH clinical trials policies?

Please note that this FOA is clinical trials optional. Key policy notices are available here. Clinical trial requirements for grants are available here.

Will there be another set of solicitations issued?

RFA-CA-20-027 and RFA-CA-20-028 have two receipt dates. The first receipt has been revised to allow applicants more time to prepare applications given the delays and complications caused by the COVID-19 pandemic. The receipt dates are October 1, 2020 and July 30, 2021. Please see NOT-CA-20-057 for additional information about the revised dates.

Will there be any adjustments to the timeline considering the delays associated with the COVID-19 pandemic?

Yes, the first receipt has been revised to allow applicants more time to prepare applications given the delays and complications caused by the COVID-19 pandemic. The receipt dates are October 1, 2020 and July 30, 2021. Please see NOT-CA-20-057 for additional information about the revised dates.

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.

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. This plan should detail the sharing of final research data[1] for research purposes, or state why data sharing is not possible. The Data Sharing Plan should also include plans for sharing relevant resources[2]. As applicable, resources and data should be shared through appropriate NIH-supported repositories.

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.

[1]Final research data is defined as recorded, factual material commonly accepted in the scientific community as necessary to document and support research findings. This does not mean summary statistics or tables; rather, it means the data on which summary statistics and tables are based. Please see the NIH policy for additional information.

[2]NIH has separate guidance on the sharing of research resources, which can be found here.

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

No. The policy does not apply to applications submitted in response to Requests for Applications (RFAs).

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. In grant applications that involve more than one PI (e.g. multi-PI), all PD/PIs must meet the definition 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.

No, ESI/NI investigators are not too junior to compete for this RFA. For a successful grant application, it is imperative to clearly demonstrate that the named key personnel have the expertise required to accomplish the studies proposed.

How much preliminary data on an intervention is needed prior to application?

For RFA-CA-20-027 (R01 mechanism):
The R01 mechanism is meant for well-developed projects supported by preliminary data. Reviewers will evaluate the application for scientific merit, which includes an assessment of the rigor of the prior research that serves as the scientific premise for the proposed project. Preliminary data should be sufficient to support gaps in the premise of the proposed project and/or demonstrate that

your proposed research is promising and that your ability to carry it out is credible (e.g. demonstrating a proof of concept or expertise for a technique).

For RFA-CA-20-028 (R21 mechanism):
The R21 mechanism is meant for pilot/exploratory projects. No preliminary data are required for R21 applications but may be included if available.

Can one team of researchers submit BOTH an R21 and an RO1?
Yes, an investigator team could submit both an R21 and an R01 application to this RFA. The aims in each application, however, should be independent of each other.

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

Single institution and multiple site applications are both allowed and will be considered competitive.

Will the same review panel review the R21 and R01 applications?

Yes, an NCI Special Emphasis Panel will review all applications to this RFA.

Research Scope FAQs

What is the difference between the previous pediatric and AYA RFA (RFA-CA-19-033) and this current set of RFAs?

The previous pediatric and AYA RFA, RFA-CA-19-033, focused on intervention research to address adverse physical and psychosocial effects in survivors of pediatric and AYA cancer survivors.

The current set of RFAs, RFA-CA-20-027 and RFA-CA-20-028, extends to mechanistic, observational, and intervention research and includes all six domains of the Childhood Cancer Survivorship, Treatment, Access, and Research (STAR) Act:

1. Disparities in survivor outcomes
2. Barriers to follow-up care
3. Impact of familial, socioeconomic, and other environmental factors on survivor outcomes

4. Indicators for long-term follow-up needs related to risk for late effects, recurrence, and subsequent cancers
5. Risk factors and predictors of late/long-term effects of cancer treatment
6. Development of targeted interventions to reduce the burden of cancer for pediatric/AYA survivors

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

Yes, model development for risk stratification that identifies risk for recurrence, second primary malignancies, or late effects of cancer and its treatment, are within the scope of this RFA.

Are applications focused on patients/survivors that are undergoing active treatment (i.e. while still on chemotherapy) eligible for this application if they are designed to understand or address survivor outcomes?

This RFA is specifically targeted to reducing morbidity and improving care and quality of life for pediatric and AYA cancer survivors. As such, applications that occur during the time of treatment designed to understand or address the long-term adverse physical, psychosocial, and/or behavioral outcomes in survivors **are** responsive. Research designed to prevent the acute adverse effects of treatment **are not** responsive.

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 or to understand the mechanisms of a proposed intervention. Biomarker development related to survivor-relevant outcomes is also allowed. Biomarker development to determine efficacy of a cancer-directed therapy is not considered responsive to this RFA.

Will investigations of behavioral studies to understand or address cancer-related cognitive impairment be supported?

Yes. Research designed to understand or address long-term adverse physical, psychosocial, and/or behavioral outcomes in survivors are responsive.

Would an exploratory proposal -- 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?

Yes. This proposal would provide insight into how and why a particular adverse effect happens, and as such is considered responsive to this RFA.

What projects will be considered non-responsive to this RFA?

Applications that do not address one or more of the six key domains of research, applications addressing short-term, transient adverse effects, and applications that propose development or testing of cancer-directed therapies are not considered responsive to this RFA.

What projects will be prioritized?

Applications that aim to understand and/or address health disparities (e.g., racial/ethnic, geographic, socioeconomic) and/or the needs/preferences of a minority or medically underserved population.

Additionally, NCI will consider the significance of the proposed research intervention 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

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Research Population FAQs

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

Yes, studies must focus on a subset of pediatric and AYA cancer survivors with age of diagnosis between 0-39 years of age.

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 starts at the day of cancer diagnosis. Pediatric and AYA cancer survivors with age of diagnosis between 0-39 years of age are of interest for this RFA. Survivors of pediatric and AYA cancers may be older than age 39

but would still be a population of interest for this RFA. The upper age limit for age at diagnosis is 39. There is no upper age limit for survivors of pediatric and AYA cancers.

Are applications that specifically focus on AYA Latino cancer survivors responsive?

Yes, 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. Note that application components should consider how the proposed study meets the needs of the target population in regard to language, comprehension and accessibility.

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

Health disparities are differences 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. Applications that aim to understand and/or address/target known health disparities and/or 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?

Proposed studies must focus on pediatric and/or AYA survivors, however they may also include a focus on other relevant populations, including informal cancer caregivers and clinicians/healthcare providers.

Please define survivor.

The National Cancer Institute's Office of Cancer Survivors defines a cancer survivor as any individual from the time of cancer 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.

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). 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 is issuing RFA-CA-20-027 and RFA-CA-20-028 to build upon RFA-CA-19-033 and demonstrate 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.