I. Background and Objectives for the Technical Brief

Childhood cancer survivors (CCS) face many challenges regarding long-term health outcomes, many of which are poorly understood or unknown. Despite gains in survival, CCS are at risk for adverse physical, psychosocial, and behavioral outcomes. These late effects could range in severity and complexity, and commonly include cardiovascular disease and heart failure, decreased pulmonary function, infertility, hormonal changes, kidney failure, liver disease, osteopenia and osteoporosis, neurocognitive deficits, and secondary malignancies. Moreover, CCS exhibit disparities and effects in social, economic, and health-related quality of life outcomes in comparison to healthy peers, including poor academic or professional performance, lower income, and higher prevalence of mental health disorders have been reported. 

Survivorship care is the clinical approach to address the health and wellbeing of cancer survivors, ideally using risk-based methods of surveillance, screening, management, and prevention of late effects. Many CCS do not receive recommended survivorship care, particularly after transitioning into adulthood. Barriers to survivorship care are seen at many levels, including the patient and caregiver (lack of knowledge of late effects and need for follow-up care), provider (inability to care for the complexity needed or lack of perceived content expertise), health system (absence of adequate referral network including survivorship care), payer (inadequate or no reimbursement), and many others. As a result of these barriers, disparities exist among CCS and this complexity poses unique challenges for the research base.

While disparities are increasingly recognized in the pediatric survivorship field, practitioners are often at a loss for how to avoid or mitigate disparities. The lack of rigorous assessment of strategies to reduce barriers, and the fragmented nature of existing research, hinders healthcare providers from establishing appropriate policies. Effective and efficient access to care for CCS is critical to minimize and alleviate disparities due to the adverse sequelae of their prior malignancy and treatment. As a result of the passage of the Childhood Cancer Survivorship, Treatment, Access, and Research (STAR) Act, the Childhood Cancer Data Initiative, and other policy and funding opportunities, the evidence base is growing and there is enhanced support for pediatric, adolescent, and young adult cancer research, including ongoing efforts to address pediatric cancer survivorship disparities.

This technical brief was commissioned by the National Cancer Institute to better assess the state of the science and properly inform future research needs; thus, it will provide an
overview of the existing evidence and forthcoming research relevant to disparities and barriers for pediatric cancer survivorship care, outline open questions and offer concrete guidance for future research in a user-friendly format.

II. Guiding Questions

The brief will be facilitated by guiding questions (GQs), documenting research and Key Informant input.

GQ1. What are the disparities in survivorship care for pediatric cancer survivors?

GQ2. What are the barriers to survivorship care for pediatric cancer survivors who experience disparities?

GQ3. What are proposed strategies for addressing those barriers?

GQ4. What published and unpublished studies have assessed these strategies?

GQ5. What are future directions for research in addressing barriers to survivorship care for pediatric cancer survivors?

III. Methods

The methods for this technical brief will follow the Methods Guide for Evidence-based Practice Center (EPC) Program. The guiding questions will help formulate the overarching methods and facilitate the search strategy for this technical brief, which are outlined in this protocol. This technical brief and answers to the guiding questions will be informed by interviews with key informants, grey literature searches, and published literature searches, as detailed below.

The key questions address observed disparities and barriers to survivorship care, as well as the existing strategies and their effects to address barriers and disparities. Table 1 below describes the eligibility criteria in a modified PICOTSS (Population; Independent variable / intervention; Comparator; Outcomes; Timing; Setting; Study design, analysis, and other limiters) framework.
<table>
<thead>
<tr>
<th>Table 1. Criteria for Inclusion/Exclusion of Studies in the Review</th>
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<td><strong>PICOTSS</strong></td>
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<td><strong>Population</strong></td>
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<td><strong>Independent variables and interventions</strong></td>
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<td><strong>Outcomes</strong></td>
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<td>GQ3:</td>
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### PICOTSS

<table>
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<tr>
<th>PICOTSS</th>
<th>Inclusion</th>
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<tr>
<td>Strategies will be documented regardless of any information on outcome effects, but strategies need to aim to prevent, reduce, or mitigate disparities and barriers to survivorship care. GQ4: Changes (reduction) in disparities between comparison groups for outcomes listed in GQ1 and GQ2 GQ5: Ongoing and upcoming studies need to indicate that the study will report on outcomes eligible for GQ1, GQ2, or GQ4.</td>
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| Timing | All GQs: No timing restriction apply. Studies may address CCS who recently or long in the past experienced pediatric cancer and are now in remission. | All GQs: No exclusions apply |

| Setting(s) | All GQs: All care settings applicable to US settings will be eligible, including primary, secondary, and tertiary care; inpatient and outpatient care; pediatric and adult care context. | All GQs: Studies in resource-limited settings such as developing countries will be reviewed for comparability with US settings |

| Study design and other limiters | All GQs: English-language publications. GQ1, GQ2, GQ4, GQ5: Primary studies reporting empirical data (including both quantitative and qualitative data). GQ1, GQ2: Studies may either report on distinct subgroups, e.g., dividing the sample by geographic characteristic and reporting data separately for rural and for urban participants or studies may report associations with participant characteristics, e.g., reporting correlations with a factor of interest such as gender differences. GQ3: Strategies have to have been empirically tested in a research study reporting on the outcomes of interest or have been suggested by an authoritative source such as a clinical practice guideline or relevant professional organization. GQ 4: Studies with concurrent (e.g., randomized controlled trial) or historic comparator (e.g., organizational pre-post studies). Studies with results published in clinicaltrials.gov will be included regardless of whether a journal publication is available. GQ5: Ongoing and upcoming studies have to have a published protocol or are registered in a research registry. | All GQs: Evaluations reported only in abbreviated format (e.g., in a conference abstract) with the exception of trial records. Studies exclusively reported in non-English publications. Systematic reviews will be retained for reference mining but are not eligible for inclusion. |

### 1. Data Collection:

#### A. Discussions with Key Informants

The Key Informants have expertise in at least one of the following areas: patient, family, or caregiver perspective; clinical implications, patient care, and disparities.
research; health services research and access to care for disparate populations; and administrative and payer strategy, operations, finance, and communication. Key informants will be asked to provide feedback regarding topics related to pediatric cancer survivor disparities and barriers to survivorship care, in particular those that have been insufficiently covered in formal research studies. Table 2 shows the draft questions for the interviews.

Table 2. Potential Key Informant Questions

<table>
<thead>
<tr>
<th>GQ</th>
<th>Question</th>
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<tr>
<td>GQ1 Disparities</td>
<td>• What types of disparities impact survivorship care for pediatric survivors?</td>
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<td>• What disparities do you think are most significant in impacting outcomes to pediatric cancer survivorship care?</td>
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<td>• Which domains of disparities should be distinguished?</td>
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<td>GQ2 Barriers</td>
<td>• What are the most influential barriers to pediatric cancer survivorship care? How do those barriers change as survivors transition from pediatric to adult survivorship care?</td>
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<td>• How do barriers to survivorship care vary by subgroups of pediatric cancer survivors? How do barriers effecting specific subgroups change over time, specifically as they transition from pediatric to adult care?</td>
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<tr>
<td>GQ3 Proposed Strategies</td>
<td>• What strategies to address barriers to survivorship care that lead to disparities are most promising?</td>
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<td>• Do those strategies need to be implemented using different strategies for different groups of survivors?</td>
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<td>• Which professional bodies have proposed strategies?</td>
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<td>GQ4 Assessment of Strategies</td>
<td>• How effective are strategies that you are familiar with?</td>
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<td>• What confounding factors pose a challenge to interpreting research and evaluation studies?</td>
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<td>GQ5 Future Research</td>
<td>• Where do you think are the most important gaps in our current knowledge, and how would you recommend filling those?</td>
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<td>• How can future research be designed to minimize the confounding factors influencing barriers, and ultimately, disparities?</td>
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<td>• Are you aware of any important ongoing studies addressing disparities in CCS?</td>
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The key informants will help identify key subgroups that may experience a disparity and map which outcomes of interest that may have caused the disparity (e.g., survivorship care utilization, morbidity, mortality, quality of life, satisfaction, cost and resource utilization, late effects). Lastly, key informant input will be used to refine the systematic literature search, identify grey literature resources, provide information about ongoing research, and potentially recommend approaches to help fill these gaps.

B. Gray Literature Search

Key to identifying strategies that have been proposed to reduce or mitigate disparities is a gray literature search. We will review guidance published in clinical practice guideline clearing houses such as the ECRI Guideline Trust.
Furthermore, we will screen the website of relevant professional organizations. The list of organizations are documented in the appendix.

We will also search ClinicalTrials.gov and NIH RePORTER for ongoing research using search terms outlined in the appendix.

**C. Published Literature Search**

The published literature search will address all guiding questions. Literature searches targeted to each guiding question will be designed, executed, and documented by the Evidence-based Practice Center (EPC) Medical Librarian. For GQ1 to GQ4, we will search PubMed, CINAHL, and PsycINFO. Searches will use controlled vocabulary and text words as not to miss newer studies not indexed yet and searches will be conducted without date restriction.

For GQ1, we will identify studies in CCS that address disparities directly (either in the title, abstract, or key word). In addition to using synonyms for the term disparity, we will also search for disparate populations specifically using the NIH definition of disparate populations: racial/ethnic minorities (including those who are Blacks/African Americans, Hispanics/Latinos, American Indians/Alaska Natives, Asian Americans, Native Hawaiians and other Pacific Islanders); socioeconomic status; underserved rural populations; gender; sexual and gender minorities; and educational attainment. In addition, we will use an unselected sample of publications in CCS that does not highlight disparities but that use a suitable study design (long-term follow up). We will screen the full text of the publications to identify subgroup results that suggest disparities. For GQ5 we will screen the research registries clinicaltrials.gov and Open Science Framework. The appendix shows the draft search strategies.

Literature screening and data abstraction will be conducted in an online database designed for systematic reviews (DistillerSR). Two independent reviewers will screen citations. All citations that at least one reviewer determines to be potentially relevant to the Technical Brief will be obtained as full text. Full text studies will be screened by two independent reviewers against the explicit eligibility criteria; disagreements will be resolved by consensus. The literature searches will be updated during the Peer Review process, before finalization of the Technical Brief.

**2. Data Organization and Presentation:**

**A. Information Management**

We will abstract data from published studies and online research registries using online software for literature reviews. Variables will include study ID, country, participant characteristics, disparity category (e.g., gender) and description, barrier category (e.g., access to care) and description, strategy category (e.g., care
coordination) and description, study design (e.g., cohort study) and analysis type, and the expected date of study completion in the case of ongoing research.

Informed by key informants, we will organize areas of disparities and barriers to survivorship care and map research studies and findings to the applicable categories to serve as a framework to help organize the current state of pediatric cancer survivorship research and identify gaps in the field. Key informant interviews will be documented during each call by a designated member of the project team. Notes will be reviewed and discussed by the investigators to evaluate how the input provides insight regarding disparities and barriers encountered by CCS.

B. Data Presentation

Individual study characteristics will be documented in concise evidence tables. Information across identified studies will be organized in a framework to document the available research content and volume. We used the Cancer Survivorship Research Framework developed for the purposes of survivors of adult cancer as a starting point to develop the framework. The framework includes dynamic features pertaining to factors of individuals, interpersonal factors, organizational factors, community factors, and policy factors. We will build upon the interactions of the domains of survivorship care, including prevention and surveillance for recurrence and new cancers, surveillance and management of physical effects, surveillance and management of psychosocial effects, surveillance and management of chronic medical conditions, and health promotion and disease prevention. We will group outcomes into categories of:

- **Survivorship Care Domain:**
  - Any patient outcomes related to utilization of survivorship care services, care plans, or models of care

- **Biomedical Domain:**
  - Intermediate health outcomes and adverse events (short-term)
  - Late effects and morbidity
  - Mortality (long-term, not related to cancer)

- **Psychosocial Domain:**
  - Psychological
  - Education attainment/employment
  - Substance use

- **Health Services and Economic Domain:**
  - Quality of life and satisfaction with care
  - Financial hardship, costs, and resource utilization

We will use the NIH definition of disparate populations to stratify the evidence base. The draft categorization of barriers includes access to care, insurance coverage, patient/provider knowledge, health literacy, and cultural aspects. Strategies will be grouped by whether they are targeted to the survivor, caregiver or family member, healthcare provider, or healthcare system. The framework and
the categories will be further refined by the literature review findings and key informant input. Table 3 shows the basic framework that will be used to document disparities, barriers, and strategies to address barriers and disparities. The framework will be tailored further for each guiding question.
Table 3. Proposed Framework to Evaluate Disparities and Barriers to Pediatric Cancer Survivorship Care

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<tr>
<td>Racial/ethnic minorities</td>
<td>Access to care</td>
<td>Patient/Provider Knowledge</td>
<td>Cultural</td>
<td>Other barriers</td>
<td>Utilization of survivorship care services, care plans, or models of care</td>
<td>Intermediate health outcomes and adverse events</td>
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<tr>
<td>Socioeconomic status</td>
<td>Access to care</td>
<td>Insurance coverage</td>
<td>Other barriers</td>
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<td>Underserved rural populations</td>
<td>Access to care</td>
<td>Other barriers</td>
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<td>Sexual and gender minorities</td>
<td>Access to care</td>
<td>Other barriers</td>
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<tr>
<td>Education</td>
<td>Access to care</td>
<td>Healthcare literacy</td>
<td>Patient/Provider knowledge</td>
<td>Other barriers</td>
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We will address each guiding question with a visualization of the evidence (or upcoming research in the case of GQ5) using the documented framework, summarized in a narrative synthesis. We will highlight the features of the existing and forthcoming research relevant to disparities and barriers to survivorship care, outline open questions and important evidence gaps that require further study and assessment. The synthesis will integrate the literature review results and insights from key informants.

The project data will be shared via SRDRPlus.

IV. References

V. Definition of Terms

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
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<tr>
<td>CCS</td>
<td>Childhood Cancer Survivor</td>
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<tr>
<td>GQ</td>
<td>Guiding Questions</td>
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<tr>
<td>STAR Act</td>
<td>Childhood Cancer Survivorship, Treatment, Access, and Research Act</td>
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</table>

VI. Summary of Protocol Amendments

There are no amendments.

VII. Key Informants

Within the Technical Brief process, Key Informants serve as a resource to offer insight into the clinical context of the technology/intervention, how it works, how it is currently used or might be used, and which features may be important from a patient of policy standpoint. They may include clinical experts, patients, manufacturers, researchers, payers, or other perspectives, depending on the technology/intervention in question. Differing viewpoints are expected, and all statements are crosschecked against available literature and statements from other Key Informants. Information gained from Key Informant interviews is identified as such in the report. Key Informants do not do analysis of any kind nor contribute to the writing of the report and will not review the report, except as given the opportunity to do so through the public review mechanism. Key Informants must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals are invited to serve as Key Informants and those who present with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

VIII. Peer Reviewers

Peer reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodologic expertise. Peer review comments on the draft report are considered by the EPC in preparation of the final report. Peer reviewers do not participate in writing or editing of the final report or other products. The synthesis of the scientific literature presented in the final report does not necessarily represent the views of individual reviewers. The dispositions of the peer review comments are documented and may be published three months after the publication of the Evidence report.
Potential Reviewers must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Invited Peer Reviewers may not have any financial conflict of interest greater than $5,000. Peer reviewers who disclose potential business or professional conflicts of interest may submit comments on draft reports through the public comment mechanism.

**IX. EPC Team Disclosures**

EPC core team members must disclose any financial conflicts of interest greater than $1,000 and any other relevant business or professional conflicts of interest. Related financial conflicts of interest that cumulatively total greater than $1,000 will usually disqualify EPC core team investigators.

**X. Role of the Funder**

This project was funded under Contract No. 75Q80120D00009 from the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services through an interagency agreement with the National Cancer Institute. The AHRQ Task Order Officer reviewed contract deliverables for adherence to contract requirements and quality. The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.
Appendix 1. Draft Search Strategy

PubMed [GQ1 Disparities]
Results on 5 Jun 2020: 4,077 citations
AND
(“child”[MeSH] OR “adolescent”[MeSH] OR “Minors”[Mesh] OR “Pediatrics”[Mesh] OR “Pediatricians”[Mesh] OR “Hospitals, Pediatric”[Mesh] OR “Intensive Care Units, Pediatric”[Mesh] OR “Intensive Care, Neonatal”[Mesh] OR “neonat*” OR “newborn” OR “newborns” OR “infant*” OR “baby” OR “babies” OR “nursery” OR “nurseries” OR “toddler” OR “toddlers” OR “preschool*” OR “pre school*” OR “child*” OR “kid” OR “kids” OR “juvenile” OR “juveniles” OR “minor” OR “minors” OR “youth” OR “youths” OR “youngster” OR “youngsters” OR “girl” OR “girls” OR “boy” OR “boys” OR “elementary school*” OR “grade school*” OR “preadolescent*” OR “pre adolescent*” OR “preteen*” OR “preteen” OR “middle school*” OR “adolescent*” OR “teen*” OR “high school*” OR “pediatric*” OR “PICU” OR “NICU” OR “young adult” OR “young adults”)
AND
(“Social Determinants of Health”[MeSH] OR “Health Status Disparities”[MeSH] OR “Sociology, Medical”[MeSH] OR “Healthcare Disparities”[MeSH] OR “Sociological Factors”[MeSH] OR “social determinants of health” OR “socioeconomic” OR “access to healthcare” OR “Barriers to healthcare” OR (“Black” OR “African American” OR “Alaskan Native” OR “native American” OR “white” OR “Asian” OR “Native Hawaiian” OR “Pacific Islander” OR “Hispanic” OR “Hispanics” OR “Latino” OR “Latina” OR “LatinX” OR “Latinos” OR “Latinas” OR “Blacks” OR “African Americans” OR “Alaskan Natives” OR “native Americans” OR “whites” OR “Asians” OR “Native Hawaiians” OR “Pacific Islanders” OR “health*” OR “medic*” OR “insurance” OR “insurances” OR “education*”) AND (“inequit*” OR “disparit*” OR “inequal*”)) OR ((“social*” OR “sociolog*” OR “sociology*”) AND (“factor” OR “factors” OR “trait” OR “traits” OR “attribute” OR “attributes” OR “characteristic” OR “characteristics” OR “phenomen*”)))
AND

PubMed [GQ1, Disparities, unselected US long-term studies only]
PubMed [GQ2-4 Barriers, Strategies to address barriers]

Results on 5 Jun 2020: 639 citations

("Neoplasms"[Mesh] OR "Medical Oncology"[Mesh] OR "Oncology Service, Hospital"[Mesh] OR "Oncology Nursing"[Mesh] OR "Cancer Care Facilities"[Mesh] OR "National Cancer Institute (U.S.)"[Mesh] OR "American Cancer Society"[Mesh] OR "antineoplastic*" OR "anti-neoplastic*" OR "anti neoplastic*" OR "oncolog*" OR "neoplasm" OR "neoplasms" OR "tumor" OR "tumors" OR "cancer" OR "cancers" OR "malignan*" OR "carcinoma" OR "carcinomas")

AND

("child"[MeSH] OR "adolescent"[MeSH] OR "Minors"[Mesh] OR "Pediatrics"[Mesh] OR "Pediatricians"[Mesh] OR "Hospitals, Pediatric"[Mesh] OR "Intensive Care Units, Pediatric"[Mesh] OR "Intensive Care, Neonatal"[Mesh] OR "neonat*" OR "newborn" OR "newborns" OR "infan*" OR "baby" OR "babies" OR "nursery" OR "nurseries" OR "toddler" OR "toddlers" OR "preschool*" OR "pre school*" OR "child*" OR "kid" OR "kids" OR "juvenile" OR "juveniles" OR "minor" OR "minors" OR "youth" OR "youths" OR "younger" OR "youngsters" OR "girl" OR "girls" OR "boy" OR "boys" OR "elementary school*" OR "grade school*" OR "preadolesce*" OR "pre adolesce*" OR "preteen*" OR "pre teen*" OR "middle school*" OR "adolesce*" OR "teen*" OR "high school*" OR "pediatric*" OR "PICU" OR "NICU" OR "young adult" OR "young adults")

AND

("Survivors"[Mesh] OR "Survivorship"[Mesh] OR "Population Surveillance"[Mesh] OR "Aftercare"[Mesh] OR "Survivor" OR "survivors" OR "survivorship" OR "surveillance" OR "aftercare" OR "post-treatment" OR "post treatment" OR "post-treatments" OR "post treatment" OR "follow up care" OR "follow-up care" OR "Long term follow up" OR "long-term follow-up")

AND

("Follow-Up Studies"[Mesh] OR "Longitudinal Studies"[Mesh])

AND

"Unities States" (Mesh)
“high school*” OR “pediatric*” OR “PICU“ OR “NICU“ OR “young adult” OR “young adults”)
AND
AND
("Health Services Accessibility"[Mesh] OR "Standard of Care"[Mesh] OR "Case Managers"[Mesh] OR “access to healthcare” OR “access to health care” OR “healthcare access” OR “health care access” OR “health service access” OR “health services access” OR “access to health service” OR “access to health services” OR “Barriers to healthcare” OR “standard of care” OR “standards of care” OR “care standard” OR “care standards” OR “case manager” OR “case managers” OR “facilitator” OR “facilitators”)

**ClinicalTrials.gov [GQ3-5 Strategies]**
(5June2020): 409 results
AREA[ConditionSearch] Cancer
AND
(neonate OR neonatal OR newborn OR newborns OR infant OR baby OR babies OR nursery OR nurseries OR toddler OR toddlers OR preschool OR pre school OR child OR children OR childhood OR kid OR kids OR juvenile OR juveniles OR minor OR minors OR youth OR youths OR youngster OR youngsters OR girl OR girls OR boy OR boys OR elementary school OR elementary schools OR grade school OR grade schools OR preadolescent OR preadolescents OR preadolescence OR pre adolescent OR pre adolescents OR pre adolescence OR preteen OR preteens OR preteenager OR preteenagers OR pre teen OR pre teens OR pre teenager OR pre teenagers OR middle school OR middle schools OR middle schooling OR adolescent OR adolescents OR adolescence OR teen OR teens OR teenager OR teenagers OR high school OR high schools OR high schooling OR pediatric OR pediatrics OR PICU OR NICU OR young adult OR young adults)
AND
(social determinants of health OR socioeconomic OR access to healthcare OR Barriers to healthcare OR ((Black OR African American OR Alaskan Native OR native American OR white OR Asian OR Native Hawaiian OR Pacific Islander OR Hispanic OR Hispanics OR Latino OR Latina OR LatinX OR Latinos OR Latinas OR Blacks OR African Americans OR Alaskan Natives OR native Americans OR whites OR Asians OR Native Hawaiians OR Pacific Islanders OR health OR medic OR medicine OR medical OR insurance OR insurances OR education OR educations) AND (inequity OR inequities OR disparity OR disparities OR inequality OR inequalities)) OR ((social OR sociological OR sociology) AND (factor OR factors OR trait OR traits OR attribute OR attributes OR characteristic OR characteristics OR phenomenon OR phenomena )))
AND
grey literature search websites [gq3]
- centers for disease control and prevention (cdc)
- national academies of medicine
- national cancer institute (nci)
- children’s oncology group (cog)
- american cancer society (acs)
- american academy of pediatrics (aat)
- american society of pediatric hematology and oncology (aspho)
- american society of clinical oncology (asco)
- national comprehensive cancer network (nccn)
- leukemia and lymphoma society (lls)
- st. baldrick’s foundation
- american society of blood and marrow transplantation (asbmt)
- center for international blood and marrow transplantation research (cibmtr)

search terms: childhood or pediatric cancer survivor and (disparit* or barrier*), alone or in combination

nih reporter [gq5 ongoing studies]
(5june2020):
- text search
- limit to: publications 1995-2020

search terms:
"childhood cancer survivor" and disparities: 7 publications supported by 9 core projects
"childhood cancer survivor" and barriers: 20 publications supported by 17 core projects
"childhood cancer survivor" and care and barriers: 12 publications supported by 12 core projects
"childhood cancer survivor" and care and disparities: 4 publications supported by 5 core projects
"adolescent cancer survivor": no results
"pediatric cancer survivor": no results