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Systematic review of barriers and facilitators to clinical trial enrollment among adolescent and young adults with cancer: Identifying opportunities for intervention

Elizabeth J. Siembida, PhD, MPH^{1,2,*}, Holli A. Loomans-Kropp, PhD, MPH^{1,3,*}, Neha Trivedi, PhD, MPH^{4,5}, Ann O'Mara, PhD, RN, MPH⁶, Lillian Sung, MD, PhD^{7,8,9}, Irene Tami-Maury, DMD, MSc, DrPH¹⁰, David R. Freyer, DO, MS^{11,12,13}, Michael Roth, MD¹⁴

¹Cancer Prevention Fellowship Program, Division of Cancer Prevention, National Cancer Institute, Rockville, MD, USA

²Outcomes Research Branch, Division of Cancer Control and Population Sciences. National Cancer Institute, Rockville, MD, USA

³Gastrointestinal and Other Cancers Branch, Division of Cancer Prevention, National Cancer Institute, Rockville, MD, USA

⁴Department of Behavioral and Community Health, School of Public Health, University of Maryland, College Park, MD, USA

⁵Health Communication and Informatics Research Branch, Division of Cancer Control and Population Sciences, National Cancer Institute, Rockville, MD, USA

⁶Consultant, Potomac, MD, USA

⁷Research Institute, The Hospital for Sick Children, Toronto, Ontario, Canada

⁸Department of Paediatrics, The Hospital for Sick Children, Toronto, Ontario, Canada

⁹Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada

¹⁰Department of Behavioral Science, Division of Cancer Prevention and Population Sciences, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

¹¹Children's Center for Cancer and Blood Diseases, Children's Hospital Los Angeles, Los Angeles, CA, USA

¹²Departments of Pediatrics and Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

¹³Children's Hospital Los Angeles and USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA

*Corresponding Author: Elizabeth J. Siembida, PhD, MPH, 9609 Medical Center Drive, Room 3E502, Rockville, MD, 20850, Phone: 240-276-7585, elizabeth.siembida@nih.gov.

*Authors (E.J.S., H.A.L.) contributed equally to the manuscript and are co-first authors

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

¹⁴Department of Pediatrics, Division of Pediatrics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Abstract

Background: Adolescents and young adults (AYA) are underrepresented in cancer clinical trials (CCTs). Limited trial enrollment slows progress in improving survival rates and prevents the collection of valuable biospecimens. A systematic literature review was conducted to assess barriers and facilitators to AYA enrollment onto CCTs and identify opportunities to improve enrollment.

Methods: PubMed Medline, Web of Science, Scopus, and PsychInfo databases were searched to identify studies relevant to AYA CCT enrollment. Eligibility criteria included qualitative and/or quantitative evaluation of barriers and facilitators to AYA enrollment.

Results: One-hundred and fifty-five unique manuscripts were identified; 13 manuscripts were included in the final analysis. Barriers to AYA enrollment on CCTs included lack of existing trials applicable to the patient population, limited access to available CCTs, and lack of physician awareness of relevant trials. Facilitators to enrollment included optimization of research infrastructure, improving awareness of available CCTs amongst providers, and enhancing communication about CCTs between providers and patients.

Conclusions: The limited available research reports institution- and patient-level barriers and facilitators to AYA CCT enrollment. Given persistent disparities in AYA enrollment, there is an urgent need to further identify the barriers and facilitators to AYA CCT enrollment to determine actionable areas for intervention.

PRECIS SUMMARY

Adolescents and young adults (AYAs) remain underrepresented in cancer clinical trials. This systematic review summarizes evidence-based barriers and facilitators to AYA enrollment at all steps in the clinical trial enrollment process.

Keywords

Adolescents and young adults; Cancer; Clinical Trials; Barriers; Facilitators; Community-based

INTRODUCTION

Approximately 70,000 adolescents and young adults (AYAs; ages 15-39 at diagnosis) are diagnosed with cancer each year in the United States, and cancer is the leading cause of disease-related death in this age group.^{1, 2} AYA cancer biology, the ability to tolerate intensive anti-cancer treatment, and the survival outcomes for specific malignancies among AYAs differ compared to older adults and younger children, strongly supporting the need to study optimal approaches to treatment separately in the AYA population.³⁻⁶

Cancer clinical trials (CCTs) help determine the most effective treatments to improve patient survival and health-related quality of life.^{7, 8} Lack of enrollment of specific patient populations on CCTs prevents determination of optimal treatment regimens and collection of

essential biospecimens needed to target the underlying disease biology in future studies. AYA enrollment on CCTs has significantly lagged behind enrollment of pediatric patients.⁹ Enrollment is estimated to range between 3-14% for all AYAs, but enrollment rates vary within the AYA population.⁷⁻⁹ Previous research has consistently found higher enrollment rates in adolescent patients compared with patients in their 20s and 30s.^{8, 10}

The reasons for low AYA enrollment numbers compared to other patient subgroups are not well understood.¹¹ Suggested barriers include treatment institution, lack of available trials for cancer types or certain age groups (older AYAs), and insurance status.¹² Two previous reviews have examined barriers and/or facilitators to CCT enrollment in AYA patients.^{13, 14} The first review examined trends in CCT enrollment among AYAs across time and included a brief overview of facilitators and barriers to CCT enrollment in AYAs.¹⁴ That review was conducted in May 2015 and did not include keywords for “facilitator” or “barrier” in the literature search. Therefore, an updated and more comprehensive review of the barriers and facilitators to CCT enrollment is warranted. The second review examined AYA patients’ perceptions and attitudes towards CCTs and found that extended hospital stays and concerns about treatment side effects were common barriers.¹³ This systematic review focused exclusively on patients’ attitudes and beliefs towards CCT enrollment, and did not consider systemic or site-level barriers or facilitators that are operative before a patient is even presented the option of a CCT (e.g. a CCT does not exist for the patient’s cancer). Therefore, the current systematic review sought to describe the multilevel barriers and facilitators to AYA CCT enrollment and summarize those amenable to intervention.

METHODS

Search Strategy

We conducted a systematic review of the literature following the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines.^{15, 16} We searched PubMed, Web of Science (including both science and social science citation indexes), Scopus, and PsychInfo databases for all studies indexed before July 11, 2019. The search strategy utilized a combination of keywords focused on AYAs and clinical trial enrollment. The keywords; were tailored to each database (e.g. using MeSH terms in PubMed; Supplemental Table 1).

Eligibility Criteria

Studies were eligible for inclusion if: (1) full-text publication was written in English, (2) included quantitative or qualitative data analysis, (3) examined measured or perceived barriers and/or facilitators to CCT enrollment, and (4) the target population was AYAs with cancer. AYA cancer patients were defined as a first cancer diagnosis between the ages of 15 to 39.¹ To allow for the most comprehensive review of relevant articles, samples were considered for inclusion if: (1) at least 75% of the sample fell within the 15-39 year age range, or (2) the mean/median age of the sample fell within the 15-39 year range. Studies were excluded if they were a review, commentary, or not peer-reviewed (e.g. dissertation).

Study Selection, Conceptual Framework, and Data Abstraction

All article titles and abstracts identified were reviewed by one reviewer (E.J.S., N.S.T., or H.A.L.), and all potentially relevant articles were retrieved. The retrieved full-text articles were reviewed by at least one reviewer and 5% were reviewed by at least two reviewers to limit bias in study inclusion and disagreements were resolved by consensus.¹⁷ We utilized the kappa (κ) statistic to describe agreement for study inclusion between each pair of reviewers. Using a predefined table, one reviewer (E.J.S., N.S.T., H.A.L.) extracted the following for each study: (1) cancer type, (2) study location, (3) population (e.g. healthcare providers, AYA patients, etc.) and sample size, (4) type of study design and data collection methods, and (5) barriers and facilitators to CCT enrollment.

We utilized a narrative approach to synthesize the data identified in this review. The conceptual framework of the CCT enrollment process proposed by Freyer et al. was utilized to organize the results.¹² This framework details the CCT enrollment process as a series of steps, where at each step potential barriers may prevent a cancer patient from enrolling on a CCT. To successfully enroll on a CCT, a trial must exist for the cancer patient's diagnosis (Step 1), the patient must have access to the CCT (Step 2), the patient must be eligible for the CCT (Step 3), the patient must be presented the CCT (Step 4), and the patient must decide to enroll in the CCT (Step 5).

To reduce the potential for bias in assigning the extracted barriers and facilitators to steps within the conceptual framework, all three reviewers independently reviewed each article and assigned the barriers/facilitators to the appropriate step in the conceptual framework. Following independent review, the three reviewers met multiple times to discuss and resolve discrepancies by consensus.

RESULTS

Figure 1 describes, in detail, the literature search process. The initial search yielded a total of 332 citations (date range: 1976-2019), and we ultimately included 13 manuscripts in our review. A detailed description of the reasons for exclusion for each reviewed manuscript is included in Supplemental Table 2. Agreement on study inclusion between reviewers was high (N.S.T., E.J.S.: $\kappa=100\%$; N.S.T., H.A.L.: $\kappa=100\%$; E.J.S., H.A.L.: $\kappa=100\%$). Table 1 provides detailed information about each manuscript. The barriers and facilitators to CCT enrollment among AYA patients identified in the literature search are summarized in Figures 2A (barriers) and 2B (facilitators).

Does the clinical trial exist?

Barriers.—Four of the thirteen AYA CCT studies discussed trial existence as a possible barrier. Two studies found that lack of an existing trial was a primary barrier for between 16-57% of AYA patients.^{7, 18} However, two articles found that the proportion of AYAs and children treated at a children's hospital with an existing CCT were similar (48.3% AYAs vs. 53.8% children).¹⁹ Additionally, the existence of a CCT for AYA patients was similar between a children's hospital (52.9%) and their affiliated adult institution (53.6%).²⁰

Facilitators.—The literature search did not identify any facilitators to improving CCT enrollment at this step.

Is a clinical trial accessible?

Barriers.—Six of thirteen AYA CCT studies addressed accessibility of clinical trials and found that institutional- or system-level barriers to CCT enrollment made it difficult for AYAs to access trials.^{8, 18-22} In one study comparing AYA CCT at a children’s hospital and its affiliated adult hospital, only 4.1% of AYAs treated at the adult institution enrolled in a CCT compared with 26.4% at the children’s hospital.²¹ Additionally, AYAs treated at the adult institution for “AYA” cancers (e.g. Hodgkin lymphoma) were not enrolled in any CCTs, but 27.3% of AYAs treated for the same disease at the children’s hospital were enrolled in a CCT.²¹ Thomas et al. (2018) found that although AYAs treated at a children’s institution and the affiliated adult hospital had similar proportions of existing trials, a significantly lower proportion of AYAs treated at the adult hospital had the existing trials activated at their treating institution (16.7%) compared to AYAs treated at the children’s hospital (44.1%).²⁰ In contrast, when AYAs and children (< 14 years) were both treated at a children’s hospital, the accessibility of CCTs was similar (39.7% AYAs vs. 47.5% children).¹⁹ Additional barriers to CCT accessibility included lack of IRB approval at the treating institution, the study was suspended at the institution, the patients’ age prevented them from receiving care at the institution with the CCT (e.g. too old for care at a children’s hospital), or they lacked a referral to an institution with the CCT open.^{8, 18, 22} Collins et al. examined AYA CCT enrollment across three affiliated institutions – a local children’s hospital and two adult institutions (a cancer hospital and a public hospital).⁸ They noted that Children’s Oncology Group (COG) trials were only available to AYAs being treated at the children’s hospital, and not available to those being treated at any of the adult institutions examined.⁸

Facilitators.—Three of thirteen AYA CCT studies addressed efforts to increase trial accessibility.^{19, 23, 24} Two single institution studies reported that the creation of AYA-specific oncology programs improved research/CCT participation after the implementation of dedicated staff to aid in connecting AYA patients with open CCTs.^{23, 24} Following establishment of an AYA oncology program at the University of Pittsburgh Cancer Institute and Children’s Hospital of Pittsburgh, participation in CCTs by referred AYA patients significantly improved (4% versus 32%, $p<0.01$).²³ The results of this study highlight the importance of how clinical settings (e.g. pediatric, adult academic) may influence accessibility of CCTs. However, we cannot draw specific inferences because the program components responsible for the improvement in CCT enrollment were not described.

Is the patient eligible?

Barriers.—Three of the thirteen AYA studies addressed barriers to patient eligibility.^{7, 18, 23, 25} In their study, Shaw and Ritchey found that 6% of patients (8/139) age 15-22 were not enrolled onto a study due to ineligibility. Reasons for ineligibility included: patient began treatment at a different institution, did not complete the tests required for CCT enrollment prior to initiation of treatment, treatment was delayed, or the patient had low functional status.^{7, 18, 23}

Facilitators.—We did not identify studies describing any facilitators to overcoming barriers to enrollment related to AYA patient eligibility.

Is the CT presented to the patient?

Barriers.—Two of thirteen AYA CCT studies addressed the extent to which lack of presentation of CCTs to eligible patients was a barrier to enrollment.^{7, 18} Physicians are commonly responsible for presenting patients with CCT options. However, AYA patients treated by pediatric oncologists or a pediatric oncology team were more likely to enroll on CCTs (verified by medical record extraction and treating physician), compared to AYA patients treated by medical oncologists only (pediatric oncology only: OR 7.39, 95% CI 2.49, 21.93; pediatric oncology and other: OR 3.69, 95% CI 1.63, 8.36).⁷

Facilitators.—The establishment of a formalized AYA Oncology Program at the University of Pittsburgh overcame barriers to enrollment related to lack of clinical trial presentation. Investigators met regularly to discuss trials available at the children’s hospital and/or adult cancer center, total accrual, and consider new means to improve enrollment.²³

Is the CT accepted by the patient?

Barriers.—Nine of thirteen AYA CCT studies addressed the extent to which lack of AYA acceptance of a CCT was a barrier to enrollment.^{7, 18, 23-29} CCT enrollment discussions that occurred close to diagnosis were overwhelming and impaired decision-making.^{24, 26, 28} The time of CCT randomization was seen as the point where the most imperative decisions were made.²⁵ Three studies indicated patient disinterest and parental preference as barriers.^{18, 23, 29} Additionally, the terminology used when describing the cancer or treatment, such as “poor response” and “rare cancer”, directed AYAs’ perception of CCTs.⁸ Other reasons cited by AYA patients for not enrolling in CCTs were a parent or other member of their social support network suggesting against enrolling, interference of the presented CCT with other studies, other life commitments (e.g. employment), emotional or symptom distress, and cost or lack of adequate health insurance coverage.^{18, 23-25, 27, 29, 30} In two included studies, multivariate analysis demonstrated that uninsured individuals were about 75% less likely to enroll as individuals with private insurance (OR: 0.25, 95% CI 0.08, 0.76⁷; OR: 0.3, 95% CI 0.20, 0.43²⁵).^{7, 25} Furthermore, age at diagnosis/enrollment and gender were significantly associated with the likelihood of AYA participation in CCTs.⁷ In the population-based National Cancer Institute’s Patterns of Care study, AYAs ages 25-29 (OR: 0.28, 95% CI 0.11, 0.73), 30-34 (OR: 0.43, 95% CI 0.19, 0.96), and 35-39 (OR: 0.32, 95% CI 0.15, 0.69) were less likely to enroll compared to AYAs ages 15-19.⁷

Concerns about toxicity or potential side effects from the experimental treatment and overall burden of the trial were also commonly reported barriers in AYA cancer.^{24, 26, 27, 31} AYA cancer patients were concerned that the trial may cause more side effects than the standard of care and worsen their health-related quality of life.^{24, 27}

Facilitators.—Patient-level facilitators to CCT enrollment among AYAs focused on including them in the CCT enrollment decision, building strong, trusting relationships between AYAs and their healthcare providers, altruism, having a form of distraction while at

the hospital, and the desire to further science.^{24, 26-29} Providers reported that supporting AYAs' growing autonomy, being sensitive to AYAs' concerns regarding trial enrollment, and providing opportunities for AYAs to ask questions were important for establishing trusting provider-patient relationships.^{24, 26, 28} Including the AYA in the decision making process facilitated enrollment.²⁶

DISCUSSION

CCTs are an essential component to studying disease biology and improving survival and health-related quality of life outcomes; however, only between 3-14% of all AYAs with cancer enroll on a CCT.^{7, 8, 10, 32} Previous reviews on this topic have identified patient-level barriers to CCT enrollment, including concerns about treatment side effects and a lack of patient awareness.^{13, 14} Our review extended this body of literature to encompass site-level barriers that may arise before the patient is ever presented with a CCT (e.g. physician preference to present trial).²¹ Despite a growing focus on AYA cancer patients and disparities in care and outcomes, few studies have adequately addressed factors contributing to the low enrollment of AYAs onto CCTs and even fewer studies have assessed the efficacy of interventions enhancing AYA enrollment. The current systematic review identified only thirteen eligible AYA CCT studies, ten of which were single institution reports. Given the importance of CCTs in improving patient treatment options and overall outcomes, additional research is needed to fully understand the barriers and facilitators to AYA CCT enrollment. However, this review identified several barriers to enrollment and potential areas for intervention.

AYA access to CCTs is limited by the lack of existence of trials for this age group, institutional barriers, and restrictive age of eligibility. With the relative rarity of AYA cancers and the challenges of lower-resourced settings, recruiting AYAs to CCTs faces numerous challenges.^{33, 34} The reorganization of the NCI National Clinical Trials Network (NCTN) and the development of the NCI Cancer Trials Support Unit (CTSU) have the potential to foster cross enrollment of patients through consolidation of the cooperative groups, increasing collaboration, maximizing patient access to trials, and expanding or eliminating age eligibility criteria.³⁵⁻³⁷ However, cross-enrollment of AYAs has been limited, and the development of intergroup trials (e.g. ARST1321) has been challenging due to differences in historical treatment approaches and institutional limits on patient age (e.g. pediatric hospitals).³⁸⁻⁴⁰ Additionally, the impact of CT networks improving enrollment in smaller, lower-resourced settings has been mixed.²³ Our review identified the development of AYA-specific programs as one method for improving AYA CCT enrollment, however, this program was developed in an academic medical center and may not be reproducible in settings with fewer resources or different organizational priorities.²³

Provider and patient factors may be more challenging to address given the diversity of clinical practices and patient populations. However, these barriers are critical to address because provider-patient discussions are one of the most common ways in which patients learn about CCTs. Lack of time and resources often prevent physicians from regularly participating in CCT enrollment.^{7, 18, 21, 41, 42} Incentivizing physicians, improving educational resources, learning how to best advise AYA patients about CCTs, and

conducting trials in line with the physician's interests may help overcome some of these barriers.^{43, 44} A means to alleviate the initial pressure on the physician may be the development of a nurse navigator program or a formalized AYA program.^{8, 23, 25} Previous research has found that nurse navigator programs work as a conduit for identifying eligible patients for CCTs.^{45, 46} Formalized AYA oncology programs increase communication between pediatric and medical oncology and has facilitated AYA CCT enrollment.⁵¹ These approaches may be particularly helpful because physicians may not initially be aware of trials for which their AYA patient is eligible. However, improving physician knowledge and awareness of trials does not alleviate patient burden. Studies assessing barriers to CCTs for older adults (ages 65 and older) and racial/ethnic minority populations suggest that life constraints and obligation of travel to the study site may substantially influence patient enrollment.⁴⁷⁻⁴⁹ These barriers may also impact AYA populations.

The current review has a few limitations. First, there is a paucity of studies that have assessed barriers and facilitators to AYA enrollment, and most assessed enrollment factors at single institutions, limiting our ability to draw generalizable conclusions. Second, due to the limited existing evidence, it is likely that not all barriers and facilitators to CCT enrollment have been captured. This may be a result of restricted response options in surveys or questionnaires, or qualitative assessment of barriers and facilitators gathered from small, targeted focus groups. Finally, many of the studies reviewed were conducted prior to or right after the initiation of the NCTN or centralized IRBs, and these systemic changes may improve AYA CCT enrollment. The current review, however, lays the groundwork to perform a further, in-depth analysis of barriers, as well as identify initial targetable areas for intervention.

CONCLUSIONS

Few studies examining the barriers and facilitators to AYA CCT enrollment currently exist in the literature. The few existing studies suggest that the barriers to AYA CCT enrollment are multifactorial and include system-, institution-, and individual-level factors. These barriers need to be further understood with the goal of identifying interventions with high potential to enhance AYA enrollment, particularly for those cancers with the most need (e.g. sarcomas, brain tumors). The NCTN and the NCI Community Oncology Research Program, a well-resourced community research network, are well-positioned to conduct this research.^{50, 51} Increasing enrollment of AYAs onto CCTs is urgently needed to determine optimal treatment approaches and maximize outcomes for AYAs with cancer.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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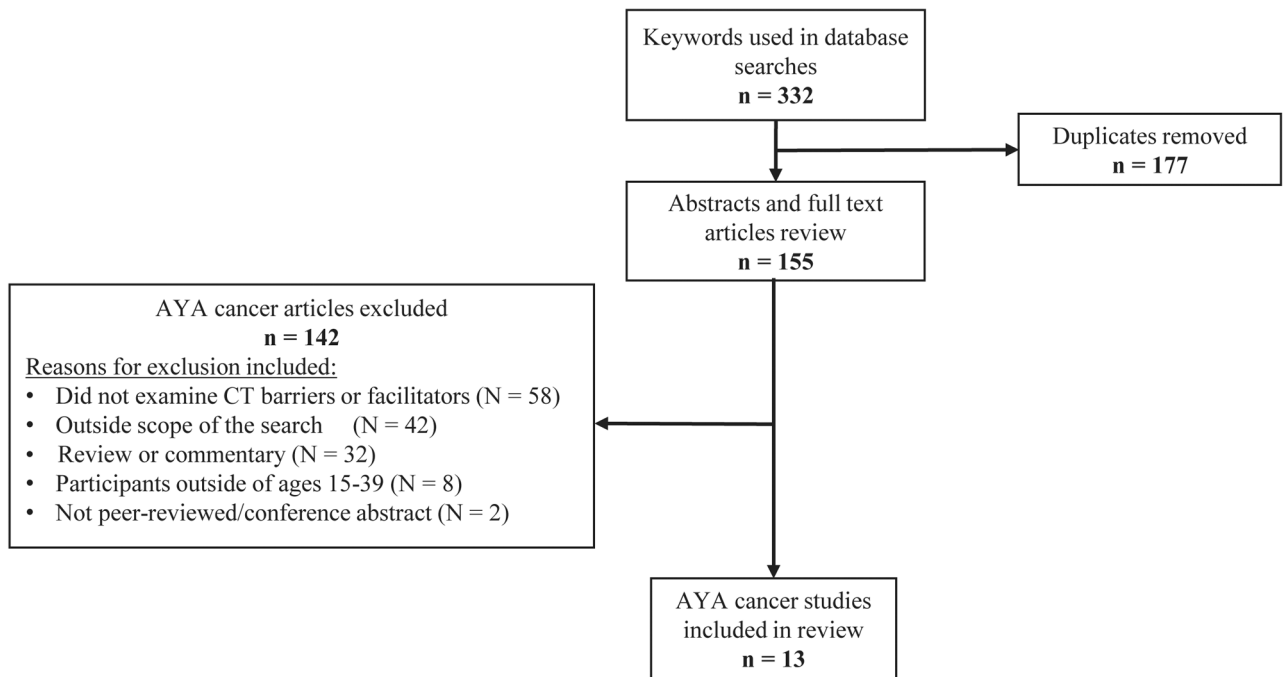


Figure 1.
Flow diagram of study selection for the systematic analysis.



Figure 2. Identified cancer clinical trial barriers (A) and facilitators (B) identified in the systematic review. No studies were found addressing facilitators for clinical trial existence or eligibility.

Table 1.

Descriptive information for included articles (N=13)

Citation	Study Location	Study Population	Study Objective	Data Collection Method	Type of Cancer
Shaw, P. H., & Richey, A. K. (2007) ¹⁸	Children's Hospital of Pittsburgh (USA)	Adolescents age 15 to 22 (n=139)	To determine if and why pediatric patients over the age of 15 had a low clinical trial enrollment rate	Secondary analysis of Children's Hospital of Pittsburgh database	Mixed (majority acute lymphoblastic leukemia, Ewing sarcoma, Hodgkin disease, non-Hodgkin lymphoma)
Downs-Canner, S., & Shaw, P. H. (2009) ²¹	Children's Hospital of Pittsburgh, University of Pittsburgh Cancer Institute (USA)	New AYA diagnosis age 15 to 22 (n=91); Patients enrolled (n=24)	To determine if and why pediatric patients over the age of 15 had a low clinical trial enrollment rate	Secondary analysis of University of Pittsburgh Cancer Institute clinical trial database	Acute lymphoblastic leukemia, acute myelogenous leukemia, central nervous system tumors, chronic myelogenous leukemia, Ewing sarcoma, Hodgkin lymphoma, melanoma, non-Hodgkin lymphoma, osteosarcoma, sarcomas
Parsons, H. M., Harlan, L. C., et al. (2011) ⁷	National Cancer Institute Patterns of Care Study, Surveillance, Epidemiology, and End Results (SEER) program data (USA)	AYA patients age 15 to 39 (n=1,358)	To examine patterns of clinical trial participation, time to treatment, and provider characteristics in a population-based sample of AYA patients with cancer	Secondary analysis of SEER cancer registry and National Cancer Institute Patterns of Care study	Multiple cancers, including acute lymphoblastic leukemia and sarcoma
Shaw, P. H., Boyiadzis, M., et al. (2012) ²³	Children's Hospital of Pittsburgh, University of Pittsburgh Cancer Institute (USA)	AYA patients age 15 to 22 (n=57)	To determine if clinical trial enrollment improved among AYA patients who attended both pediatric and adult cancer centers since the inception of a joint AYA Oncology Program	Secondary analysis of University of Pittsburgh Cancer Institute clinical trial database	Mixed (majority: acute lymphoblastic leukemia, Ewing sarcoma, osteosarcoma, rhabdomyosarcoma)
Hendricks-Ferguson, V. L., et al. (2013) ²⁹	Six pediatric and three adult hospitals across six medical centers throughout the Midwest and southern portions of the United States	AYA patients age 11-24 (n=118)	To describe recruitment strategies, participants' reasons for consent or refusal, and the final recruitment rates of AYA with cancer into a research study called "Stories and Music for Adolescent/Young Adult Resilience during Transplant" (SMART)	Intervention recruitment to understand strategies to improve recruitment of AYA	Allogeneic or autologous HSCT for cancer with a myeloablative regimen
Barakat, L. P., Schwartz, L. A., et al. (2014) ²⁶	East coast children's hospital at a large cancer center (USA)	AYA patients age 15 to 23 (n=13); Caregivers (n=16); Healthcare providers (n=11)	To describe key components of phase III clinical trial enrollment and evaluate a measure of attitudes	One-on-one interviews; focus groups	Acute lymphoblastic leukemia, acute promyelocytic leukemia, non-Hodgkin lymphoma, osteosarcoma, rhabdomyosarcoma
Collins, C. L., Malvar, J., et al. (2015) ⁸	Los Angeles County (USA)	USC Norris Comprehensive Cancer Center by institution (n=1699) versus Los Angeles County SEER incidence (n=11,358)	To compare the percentage of AYAs, children, and older adults enrolled onto cancer clinical trials and determine predictors of enrollment	Secondary analysis of California Cancer Registry and institutional trial enrollment database	Acute leukemia, breast carcinoma, central nervous system malignancies, cervical carcinoma, colorectal cancer, lymphoma, melanoma, sarcoma, thyroid carcinoma
Bell, J. A., Forcina, V., et al. (2018) ²⁷	AYA Program at Princess Margaret Cancer Centre (Canada)	AYA patients age 18 to 39 (n=21)	To explore unique factors influencing the cancer clinical trial decision-making process, AYA perceptions, and attitudes towards cancer clinical trials	One-on-one interviews	Breast cancer, leukemia, lymphoma, sarcoma, testicular cancer

Citation	Study Location	Study Population	Study Objective	Data Collection Method	Type of Cancer
Pearce, S., Brownsdon, A., et al. (2018) ²⁴	AYA Cancer	Teenage and Young Adult treatment center in the UK	AYA patients (n=21); Health professionals (n=18)	Qualitative; interpretive interviews	Ewing's sarcoma, Osteosarcoma
Sreeraman Kumar, R., Thapa, R., et al. (2018) ²⁵	Moffitt Cancer Center in Tampa, FL (USA)	AYA patients age 15-39 (n=1,831)	To examine AYA enrollment into therapeutic melanoma clinical trials at Moffitt and examine relevant factors impacting enrollment	Retrospective review of de-identified records of patients	Melanoma
Thomas, S. M., Malvar, J., et al. (2018) ¹⁹	Children's Hospital Los Angeles (USA)	Total participants (n=216); children age 14 and younger (n=158), early AYA age 15 to 21 (n=58)	To assess whether differences in cancer clinical trial availability explain low cancer clinical trial enrollment for early AYAs	Quantitative analysis of an observational cohort	Mixed (majority for early AYA: leukemia/lymphoma, non-brain solid tumor, solid tumors)
Thomas, S. M., Malvar, J., et al. (2018) ²⁰	Children's Hospital Los Angeles (USA)	Children age 0 to 14; eAYAs age 15 to 21	To compare the proportions of eAYAs and children for whom an appropriate CCT existed, was available locally, and was used for enrollment; secondary objectives were to evaluate the effects of age and other factors on CCT enrollment.	Secondary analysis of pathology reports from CHLA and Norris Cancer Hospital, and available trials listed on clinicaltrials.gov	Leukemia/lymphoma and solid tumor
Lavender, V., Gibson, F., et al. (2019) ²⁸	Large AYA treatment center (UK)	Healthcare professionals who care for AYAs age 15 to 24 years (n=18)	To explore professional expertise, specialist knowledge and skill development and strategies described by the health professionals for communicating with AYAs about participating in clinical trials	Semi-structured narrative interviews	Osteosarcoma