# **UC Davis**

# **UC Davis Previously Published Works**

# **Title**

Comparing Barriers and Facilitators to Adolescent and Young Adult Clinical Trial Enrollment Across High- and Low-Enrolling Community-Based Clinics

#### **Permalink**

https://escholarship.org/uc/item/72z3h2w3

# **Journal**

The Oncologist, 27(5)

#### **ISSN**

1083-7159

#### **Authors**

Siembida, Elizabeth J Loomans-Kropp, Holli A Tami-Maury, Irene <u>et al.</u>

### **Publication Date**

2022-05-06

# DOI

10.1093/oncolo/oyac030

Peer reviewed



# Comparing Barriers and Facilitators to Adolescent and Young Adult Clinical Trial Enrollment Across High- and Low-Enrolling Community-Based Clinics

Elizabeth J. Siembida<sup>1,\*,</sup>, Holli A. Loomans-Kropp<sup>2,3</sup>, Irene Tami-Maury<sup>4</sup>, David R. Freyer<sup>5,6,7</sup>,, Lillian Sung<sup>8</sup>, Howland E. Crosswell<sup>9</sup>,, Brad H. Pollock<sup>10</sup>,, Michael E. Roth<sup>11</sup>,

<sup>1</sup>Institute of Health System Science, Northwell Health, Manhasset, NY, USA

#### **Abstract**

**Background:** Adolescent and young adult (AYA) patients with cancer are underrepresented on cancer clinical trials (CCTs), and most AYAs are treated in the community setting. Past research has focused on individual academic institutions, but factors impacting enrollment vary across institutions. Therefore, we examined the patterns of barriers and facilitators between high- and low-AYA enrolling community-based clinics to identify targets for intervention.

**Materials and Methods:** We conducted 34 semi-structured interviews with stakeholders employed used at National Cancer Institute Community Oncology Research Program (NCORP) affiliate sites ("clinics"). Stakeholders (eg, clinical research associates, patient advocates) were recruited from high- and low-AYA enrolling clinics. We conducted a content analysis and calculated the percentage of stakeholders from each clinic type that reported the barrier or facilitator. A 10% gap between high- and low-enrollers was considered the threshold for differences.

**Results:** Both high- and low-enrollers highlighted insufficient resources as a barrier and the presence of a patient eligibility screening process as a facilitator to AYA enrollment. High-enrolling clinics reported physician gatekeeping as a barrier and the improvement of departmental collaboration as a facilitator. Low-enrollers reported AYAs' uncertainty regarding the CCT process as a barrier and the need for increased physician endorsement of CCTs as a facilitator.

**Conclusions:** High-enrolling clinics reported more barriers downstream in the enrollment process, such as physician gatekeeping. In contrast, low-enrolling clinics struggled with the earlier steps in the CCT enrollment process, such as identifying eligible trials. These findings highlight the need for multi-level, tailored interventions rather than a "one-size-fits-all" approach to improve AYA enrollment in the community setting.

Key words: adolescent and young adult; clinical trial enrollment; barriers; facilitators; NCORP.

#### **Implications for Practice**

The current analysis demonstrates both shared and distinct patterns in the barriers and facilitators to adolescent and young adult (AYA) cancer clinical trial enrollment experienced by high- and low-AYA enrolling National Cancer Institute Community Oncology Research Program clinics. We found that high-enrolling clinics were more likely to experience downstream barriers, like physician gatekeeping, and that low-enrolling clinics were more likely to experience upstream barriers, like lack of local trial opening. Taken together, these results show that any interventions developed to improve AYA clinical trial enrollment cannot be "one-size-fits-all." Instead, interventions need to be multi-level and tailorable to the unique needs and resources of individual institutions.

<sup>&</sup>lt;sup>2</sup>Cancer Prevention Fellowship Program, Division of Cancer Prevention, National Cancer Institute, Rockville, MD, USA

<sup>&</sup>lt;sup>3</sup>Gastrointestinal and Other Cancers Research Group, Division of Cancer Prevention, National Cancer Institute, Rockville, MD, USA

<sup>&</sup>lt;sup>4</sup>Department of Epidemiology, Human Genetics, and Environmental Sciences, The University of Texas Health Science Center at Houston School of Public Health, Houston, TX, USA

<sup>&</sup>lt;sup>5</sup>Department of Pediatrics, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

Department of Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

<sup>&</sup>lt;sup>8</sup>Department of Pediatrics, Hospital for Sick Children, Toronto, ON, Canada

<sup>&</sup>lt;sup>9</sup>Bon Secours Mercy, St. Francis Cancer Center, Greenville, SC, USA

<sup>&</sup>lt;sup>10</sup>Department of Public Health Sciences, School of Medicine, University of California, Davis, Davis, CA, USA

<sup>&</sup>lt;sup>11</sup>Department of Pediatrics, Division of Pediatrics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

<sup>\*</sup>Corresponding author: Elizabeth J. Siembida, Institute of Health System Science, Northwell Health, 600 Community Drive, Suite 403, Manhasset, NY 11030, USA. Tel: (516) 600-1757; Email: esiembida@northwell.edu

#### Introduction

Enrollment in cancer clinical trials (CCTs) is associated with better survival outcomes, improves access to novel therapeutics and supportive care, and provides biospecimens for future research.<sup>1,2</sup> However, adolescent and young adults (AYAs; diagnosed ages 15-39) with cancer enroll onto CCTs at much lower rates than those with childhood cancer and similar to older adults with cancer.3-7 Enrollment rates also vary across AYAs, including differences by cancer type, insurance status, age at diagnosis, and treatment setting (pediatric vs. adult).8-9 Higher participation rates among AYAs have been identified in National Cancer Institute (NCI)-designated Comprehensive Cancer Centers and other academic medical centers, 4,5,10 but the majority of AYAs are treated in community cancer centers and rates of enrollment in these settings lags behind those in academic medical settings like NCIdesignated cancer centers.11

The successful enrollment of an AYA patient with cancer onto a CCT requires multiple, unobstructed steps. <sup>12</sup> The complexity of this process has led to institution-, provider-, and patient-level barriers. <sup>13</sup> Recent systematic reviews have identified AYA patient-level barriers to CCT enrollment, including concerns about side effects, and institution- and provider-level barriers, including lack of available trials and physician awareness of CCTs. <sup>14,15</sup> However, most prior research has been conducted in single institutions, most of which have been academic medical centers. This likely reduces the generalizability of study findings, misses the experiences of community-based institutions where most AYAs receive their cancer care, and limits the ability to compare experiences across institutions.

Community-based clinics vary in their clinical trial office staffing, resources, and patient populations. Therefore, it is likely that some community-based clinics are performing better than others in successfully recruiting AYAs onto clinical trials. We recently conducted a multi-site, qualitative study to overcome the limitations of these previous studies, and identified barriers and facilitators to AYA CCT enrollment at 5 NCI Community Oncology Research Program (NCORP) sites. The NCORP currently comprises 46 sites (32 community sites, 14 minority/underserved sites). Each NCORP site is a network of multiple community-based clinics, referred to as affiliate sites. For clarity, we will refer to these affiliate sites

as "clinics" and the overall network of individual clinics as the "NCORP site." The parent study used qualitative coding to identify institution-, provider-, and patient-level barriers and facilitators common across all participating clinics and NCORP sites, such as insufficient staff and resources and the need for institutional AYA "champions." In the current study, we conducted an in-depth analysis exploring how these previously identified barriers and facilitators to AYA CCT enrollment differed between high- and low-AYA enrolling clinics. Our purpose in undergoing this in-depth analysis was to identify potential targets for future intervention efforts to improve AYA enrollment.

#### **Materials and Methods**

#### Site Selection, Recruitment, and Data Collection

Details of site selection, recruitment, data collection, and interview questions for the parent study were previously described. To be eligible, an NCORP site must have at least one clinic defined as high-AYA enrolling and at least one clinic defined as low-AYA enrolling. A clinic was defined as high enrolling if >10% of total enrollments onto National Clinical Trials Network (NCTN) trials in the past 2 years were AYAs, and low enrolling if <3% of the total enrollments were AYAs. Eighteen NCORP sites (13 community, 5 minority/underserved) met the inclusion criteria, representing all NCTN research bases. The research team contacted 15 eligible NCORP sites, and the first 5 to return complete stakeholder contact information were selected (Table 1). Enrollment data were obtained from the NCORP enrollment database.

We consented and remotely interviewed (<60 minutes) up to 5 stakeholders at each of the 10 clinics using the video-conferencing software, Zoom (Zoom Video Communications, Inc., San Jose, CA). These stakeholders included a (1) lead clinical research associate or research nurse (CRA/CRN); (2) physician involved in enrollment; (3) nurse navigator, if available; (4) regulatory research associate (RRA), if available; and (5) Patient Advocate, if available. Interview questions covered each domain of the Freyer and Seibel<sup>12</sup> framework for CCT enrollment and were tailored to stakeholder roles. Each stakeholder was asked to describe their role in the CCT enrollment

Table 1. Characteristics of the selected community-based clinics, separated by NCORP site.<sup>a</sup>

NCORP site no.	Clinic enrollment status	Site type	Presence of medical or pediatric oncology	Region
1	High-enrolling clinic	Minority/underserved	Med/ped onc	East
	Low-enrolling clinic		Med onc only	
2	High-enrolling clinic	Community-based	Med/ped onc	Midwest
	Low-enrolling clinic		Med onc only	
3	High-enrolling clinic	Community-based	Med onc only Med onc only	Midwest
	Low-enrolling clinic			
4	High-enrolling clinic	Community-based	Community-based Med/ped onc	Midwest
	Low-enrolling clinic		Med/ped onc	
5	High-enrolling clinic	Community-based	Med/ped onc	West
	Low-enrolling clinic		Med onc only	

process (eg, CRA/CRN asked about screening procedures), if they perceived more or less difficulty enrolling AYAs compared to other patients with cancer, and what they believed to be the most significant barriers/facilitators to AYA enrollment. Interviews were recorded, transcribed, and de-identified.

#### Qualitative Analysis

The sociodemographic characteristics of the stakeholders were described with univariate statistics. The transcripts were independently coded by an outside vendor, Adept Word Management Inc., using a structured analytic approach.<sup>17</sup> Coding was conducted on an iterative basis. After every 10 interviews, Adept Word Management Inc. and the research team reviewed the transcripts for preliminary codes. If additional codes were identified, the study team continued recruitment Findings were progressively reviewed in this manner until code saturation (defined as no new identified codes) was reached and additional recruitment was halted. This process was key for sample size resolution, which was assessed on an ongoing basis and as a concurrent process to qualitative data analysis. 18 Once the codebook was created by Adept Word Management Inc., members of the study team reviewed it, made modifications, and discussed any discrepancies until agreement was reached. The final themes were identified across all interview data and organized into barriers and facilitators.

The current content analysis focused on a subset (N=34) of the original 43 interviews to focus only on the stakeholders employed at individual clinics. To align with our original qualitative analysis and allow for comparisons by enrollment status, stakeholder responses were organized first by one of the 11 barriers or one of the 11 facilitators identified in the parent study (full definitions for each barrier and facilitator can be found in the previous manuscript<sup>16</sup>) and then categorized by clinic enrollment status. We calculated the percentage of stakeholders from each clinic type who reported the barrier or facilitator. We considered barriers/facilitators reported by high- versus low-enrolling clinics similar if the percentage of respondents reporting that barrier/facilitator were within 10%. We considered barriers/facilitators different if the percentage of stakeholders reporting the barrier/facilitator across clinics differed by >10%.

#### Results

The final sample included 21 stakeholders from highenrolling clinics and 13 from low-enrolling clinics. The sociodemographic characteristics of stakeholders varied slightly by clinic type (Table 2), and the patterns of barriers/ facilitators differed by level of enrollment activity (Tables 3 and 4).

# Barriers Reported by Both High- and Low-Enrolling Clinics

#### Insufficient Staff and Resources

Thirty-eight percent of stakeholders in both clinic types reported insufficient staff and resources as a barrier. Limited staff reduced the number of trials opened and number of patients screened for enrollment, and also reduced the speed of these processes: "...if perhaps they had another coordinator or 2 they could potentially handle a higher volume..." (Regulatory Research Nurse, High-Enrolling, Female, 35-44 years). Stakeholders from low-enrolling clinics also

**Table 2.** Sociodemographic characteristics of stakeholders from highand low-enrolling clinics.

	High AYA enrolling N = 21 (%)	Low AYA enrolling $N = 13$ (%)
Age		
<25 years	0 (0)	0 (0)
25-34 years	3 (14)	0 (0)
35-44 years	9 (43)	4(31)
45-54 years	8 (38)	3 (23)
55+ years	1 (5)	6 (46)
Gender		
Male	3 (14)	2 (15)
Female	18(86)	11 (85)
Stakeholder role		
Clinical research associate/nurse	6 (29)	5 (38)
Physician involved in enrollment	3 (14)	4 (31)
Regulatory research nurse	4 (19)	1 (8)
Nurse navigator	4 (19)	2 (15)
Patient advocate	4 (19)	1 (8)
Years used at clinic		
<1 year	5 (24)	2 (15)
2-4 years	4 (19)	0 (0)
5-9 years	6 (29)	2 (15)
10+ years	6 (29)	9(69)

Abbreviation: AYA, adolescent and young adult.

emphasized that high patient volume reduced physicians' available time to discuss trials.

#### Location of Trial Clinic

A similar percentage of stakeholders from high- and lowenrolling clinics (29% vs. 23%) reported that the trial's location was a barrier. Most stakeholders highlighted that their clinics often treated rural patients who had to travel multiple hours. Many AYA patients chose not to enroll in studies that would require extra travel.

#### Regulatory Burden

Few stakeholders (10% high, 8% low) explicitly discussed regulatory burden as a barrier. Those that did highlighted potential issues of re-consenting AYA patients after they turn 18 and the chance that having a joint trial between 2 NCTN groups could lead to multiple audits.

#### Barriers More Frequently Reported by High-Enrolling Clinics

#### Physician Gatekeeping

Almost half of the stakeholders from high-enrolling clinics (43%) mentioned physician gatekeeping as a barrier. Stakeholders felt that many physicians are not interested in research, are unlikely to refer younger patients to trials for standard diseases to not delay quick initiation of treatment, or do not feel comfortable working with younger patients.

Table 3. Percentage of barriers reported by high- and low-enrolling clinics.

Barrier	Total $N = 34$	High AYA enrolling $N = 21$ (%)	Low AYA enrolling $N = 13$ (%)
Trial availability and eligibility	15	8 (38)	7 (54)
Insufficient staff and resources	13	8 (38)	5 (38)
Uncertainty regarding the CCT process	13	7 (33)	6 (46)
Physician gatekeeping	12	9 (43)	3 (23)
Location of trial clinic	9	6 (29)	3 (23)
Time	9	7 (33)	2 (15)
Communication between pediatric and adult oncology	8	6 (29)	2 (15)
Finances	7	6 (29)	1 (8)
Regulatory burden	3	2 (10)	1 (8)
Adherence	2	2 (10)	0 (0)
Contacting AYAs	2	2 (10)	0 (0)

Abbreviations: AYA, adolescent and young adult; CCT, cancer clinical trial.

**Table 4.** Percentage of facilitators reported by high- and low-enrolling clinics.

Facilitator	Total $N = 34$	High AYA enrolling N = 21 (%)	Low AYA enrolling $N = 13$ (%)
Use of a screening process	19	11 (52)	8 (62)
Physician endorsement	12	6 (29)	6 (46)
Community and staff education	10	6 (29)	4 (31)
Incentivize enrollment	7	5 (24)	2 (15)
Updated communication methods	7	4 (19)	3 (23)
Departmental collaboration	6	5 (24)	1 (8)
Simplified interaction with the Children's Oncology Group	5	3 (14)	2 (15)
More AYA trials	4	2 (10)	2 (15)
AYA coordinators and navigators	4	4 (19)	0 (0)
Advocates and mentors	3	1 (5)	2 (15)
Increasing awareness	2	0 (0)	2 (15)
AYA working groups	1	1 (5)	0 (0)

Abbreviation: AYA, adolescent and young adult.

#### Patient Time

Thirty-three percent of stakeholders from high-enrolling clinics (vs. 15% of low-enrolling clinics) reported limited patient time as a barrier. Most responses highlighted the additional burdens on AYAs' time due to their current life stage (eg, working full-time), making it difficult for AYAs to consider enrolling on trials that required more appointments: "...having to go to the clinic as many times as this study requires...if you [AYA patients] are on standard of care, you would go once a month, but on trial, you go weekly" (CRA/CRN, High-Enrolling, Female, 45-54 years).

# Communication Between Pediatric/Medical Oncology

Approximately one-third of stakeholders from high-enrolling clinics reported poor communication between the pediatric and medical oncology groups as a barrier. When the two departments did not communicate adequately, stakeholders reported that neither group was aware of open trials or of eligible patients in the other group.

#### Patient Finances

More stakeholders from high-enrolling clinics (29%) reported patient finances as a barrier (8% low-enrolling clinics). A few stakeholders mentioned the financial challenges faced by AYAs who were just entering financial independence. However, most stakeholders focused on lack of insurance: "...[the] AYA...may not have a full-time job...if they don't have new insurance and we're not giving them any additional incentives to participate, then they might not be able to sign up..." (CRA/CRN, High-Enrolling, Female, 35-44 years).

#### Communication With AYAs and Adherence

A small percentage of stakeholders from high-enrolling clinics, and no stakeholders from low-enrolling clinics,

reported challenges in communicating with AYAs (10%) by phone and AYAs' noncompliance to study protocols (10%), primarily through missed appointments, as barriers.

# Barriers More Frequently Reported by Low-Enrolling Clinics

#### Trial Availability/Eligibility

Fifty-four percent of stakeholders from low-enrolling clinics (vs. 38% high-enrolling clinics) reported trial availability or eligibility as a barrier. Most stakeholders emphasized the lack of their clinic opening available trials: "...our patients get penalized by not being able to get on clinical trials because we can't open them because we won't put enough on..." (Patient Advocate, High-Enrolling, Female, 45-54 years).

Stakeholders also reported patient eligibility as a barrier. In some cases stakeholders suggested AYAs were not eligible due to their age: "...we don't do kids, so most of the trials that we do, the enrollment inclusion-exclusion is greater than or equal to 18 years of age..." (Physician, Low-Enrolling, Female, 65-74 years). In other cases, stakeholders highlighted tumor characteristics or the rarity of AYA diagnoses as eligibility barriers.

#### Patient Uncertainty Regarding CT Process

Forty-six percent of the stakeholders from low-enrolling clinics (vs. 33% high-enrolling) reported that patients' uncertainty regarding clinical trials (CTs) was a barrier. Many stakeholders stated that patients were apprehensive about receiving unproven, "experimental" treatment. Although most common among low-enrolling clinics, when high-enrolling clinics reported this barrier, stakeholders reported that AYAs may be overwhelmed by the quick enrollment decision-making process.

# Facilitators Reported by Both High- and Low-Enrolling Clinics Use of a Screening Process

More than half of the stakeholders discussed instituting a timely process to screen and identify eligible patients (possibly utilizing technology) and having access to open studies in both pediatric and adult departments. Stakeholders also emphasized the importance of collaboration between departments, service lines (inpatient vs. outpatient), and research staff and physicians in this process.

#### Improving Community and Staff Education

Stakeholders from both high- and low-enrolling clinics (29% vs. 31%, respectively) believed that improving community and staff education would increase AYA enrollment. This facilitator included increasing the knowledge of CCTs available at these clinics and educating providers on the enrollment process. Stakeholders noted that multidisciplinary meetings (eg, joint tumor boards) were prime opportunities for education.

#### Incentivizing Enrollment

Twenty-four percent of stakeholders from high-enrolling clinics and 15% from low-enrolling clinics reported incentivizing AYA enrollment as a facilitator. However, stakeholders from high-enrolling clinics primarily discussed patient-directed incentives (eg, gas cards), while stakeholders from low-enrolling clinics discussed institution-directed incentives (eg, increased reimbursement).

# Simplify Interactions With Children's Oncology Group

Fourteen percent of stakeholders from high-enrolling clinics and 15% from low-enrolling clinics suggested simplifying interactions with the Children's Oncology Group (COG) for staff not affiliated with COG. Stakeholders believed that AYA patients could not be enrolled on COG trials unless the enrolling physician was a COG member. This was problematic as few medical oncologists are COG members. Stakeholders suggested streamlining the process to become COG members and make website navigation easier.

#### Greater Number of and More Flexible AYA Trials

Developing more AYA-specific trials or trials flexible to reallife challenges (eg, childcare responsibilities) was reported as a facilitator by 10% and 15% of stakeholders from high- and low-enrolling clinics, respectively. Stakeholders primarily discussed the need to create flexible protocols that allowed for community-based clinics to accommodate the needs of their patients (eg, reduce the number of appointments, use telemedicine).

#### **Update Patient Communication Methods**

Nineteen percent of stakeholders from high-enrolling clinics and 23% from low-enrolling clinics felt that modifying communication methods with AYAs would facilitate enrollment. Stakeholders from high-enrolling clinics reported that conversations with AYAs needed to be "rapport-building" and ensure "their autonomy." Stakeholders also emphasized the importance of technology-based communication.

#### Patient Mentors/Advocates

A few stakeholders from high- and low-enrolling clinics (5% vs. 15%) felt that peer mentoring and/or a lay navigation program would facilitate AYA CCT enrollment: "...we actually have someone in person who has succeeded...a survivor to actually spin them and, kind of, help navigate them through their opening months..." (Patient Advocate, High-Enrolling, Male, 25-34 years).

# Facilitators Reported by High-Enrolling Clinics AYA Coordinators/Navigators

Only stakeholders from high-enrolling clinics felt that having AYA-specific coordinators/navigators on staff would facilitate enrollment. Having a staff member dedicated to this population that works in tandem with research coordinators would increase knowledge of the AYA population and possible trials.

# Improving Departmental Collaboration

Twenty-four percent of stakeholders at high-enrolling clinics, compared to 8% at low-enrolling clinics, suggested that improving collaboration between pediatric and medical oncology groups would facilitate AYA enrollment. Having adult and pediatric providers work together to enroll patients and creating AYA clinics or shared tumor boards that include staff from both groups are two possible approaches.

# Facilitators Reported by Low-Enrolling Clinics Physician Endorsement and Awareness

Forty-six percent of stakeholders from low-enrolling clinics believed that increasing physician endorsement for trials would improve enrollment: "If a physician is recommending that...is the most obvious seal of approval that patients need to make the decision to proceed or not." (CRA/CRN, Low-Enrolling, Female, 55-64 years). Stakeholders also emphasized that AYA enrollment may improve if physicians are aware of the AYA population and available trials when deciding which trials to open.

#### Increasing Patient Awareness

Only stakeholders from low-enrolling clinics believed that increasing patient awareness of the availability of CTs would improve AYA enrollment. Stakeholders felt that any advertisement or marketing strategy should clearly highlight that "...research is part of the care that [clinic] offers..." (CRA/CRN, Low-Enrolling, Female, 55-64 years), and it should be targeted to AYAs.

#### **Discussion**

Previous research on AYA CCT enrollment has focused only on single, academic medical institutions, likely missing critical barriers experienced by community-based organizations. Our study overcomes these limitations by examining barriers and facilitators to AYA CCT across 10 different community-based clinics. We identified shared and distinct patterns in the barriers (Fig. 1) and facilitators to AYA CCT enrollment across high- and low-enrolling NCORP clinics. High-enrolling clinics appeared to have fewer challenges opening and activating AYA-relevant trials. Instead, they reported barriers further downstream, such as physician gatekeeping. In contrast, low-enrolling clinics struggled with earlier steps in the enrollment process, like local trial availability and the need for institution-level financial incentives for targeting AYA enrollment. These findings highlight that barriers to AYA CCT enrollment are not uniform across community-based institutions, and, therefore, future interventions need to be multilevel and tailorable. A "one-size-fits-all" approach will not work. Our discussion will focus on three intervention targets and discuss key variations in how high- and low-enrolling clinics may approach addressing these targets (Fig. 2).

Improving institution and staff knowledge of the AYA population and available CCTs will require multi-pronged

approaches. First, providing staff with an accurate definition of AYA is critical. Multiple stakeholders from both high- and low-enrolling clinics appeared to conflate AYA patients with pediatric patients (<18 years). Most AYA patients are over 18 and treated in adult institutions. 19,20 If staff believe they lack available CCTs because most AYAs are <18 years, they are likely missing out on potential CCTs focused on adult cancers that are also common among AYAs. Second, education efforts should increase knowledge of cross-network enrollment procedures. Stakeholders incorrectly perceived that COG AYA studies were only accessible to COG members. In fact, members of adult NCTN network groups can enroll patients onto COG-led AYA trials, and COG members can enroll on AYA trials led by the adult NCTN groups.<sup>21</sup> Our team has created cross-network enrollment FAQ documents.<sup>22</sup> Finally, both our results and the results of other studies<sup>23,24</sup> suggest that the limited availability of CCTs for AYAs is likely due to the lack of local trial opening, rather than national availability. Distributing a list of nationally available CCTs for common AYA cancer diagnoses at regular intervals to both research staff and oncologists may be one option for increasing clinic

Creating an effective screening process of AYA patients and potential CCTs was identified by both clinic types as critical to improving enrollment but emphasized differently. Low-enrolling clinics emphasized the need to streamline collaboration between departments/service lines, and high-enrolling clinics indicated the need for a list of available trials in both pediatrics and adult oncology. All clinics emphasized the benefits of using electronic medical record (EMR) systems or other technology to improve screening processes. Technology-enabled screening systems benefit from being easier to tailor to local institutions. For low-enrolling clinics, screening can be supplemented with feedback and auditing, which has been shown to improve other care delivery outcomes.<sup>25-27</sup>

Finally, improving communication with AYA patients about CCTs and helping them understand the process are critical targets. High-enrolling clinics discussed the need for rapport-building and supporting autonomy in AYAs. This approach aligns with developmental science as increasing autonomy is a critical milestone in this stage of life.<sup>28</sup>

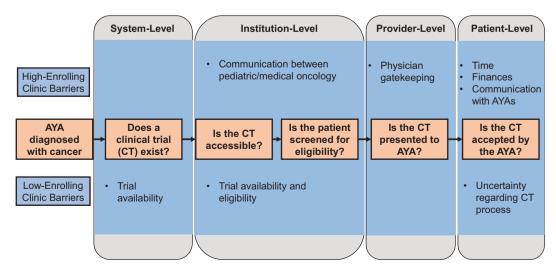
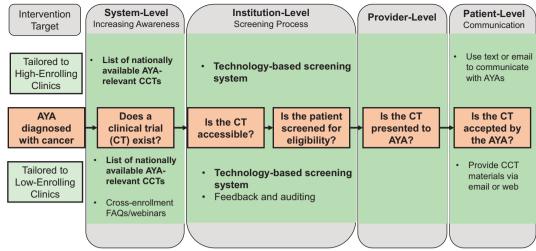


Figure 1. Barriers predominantly reported by high- or low-enrolling clinics.



Note. Intervention targets that are bolded are shared across high- and low-enrolling clinics.

Figure 2. Suggested intervention targets tailored to high- or low-enrolling clinics.

Low-enrolling clinics were more concerned about AYAs' uncertainty of the CCT process. Providing patient-centered, developmentally appropriate information to AYAs about CCTs to supplement discussions with providers supports autonomy building and increases understanding without undermining the importance of patient-provider communication.<sup>29,30</sup> Finally, using digital communication, such as email and/or text messages, to communicate with AYAs about CCTs, both during and after recruitment, will likely improve enrollment and retention.<sup>31</sup>

There are limitations with our approach. We presented our results as percentages to overcome the lower number of stakeholders from low-enrolling clinics due to fewer navigators and patient advocates at these clinics. Therefore, barriers/ facilitators in low-enrolling clinics may have been missed. However, we believe that the lower number of stakeholders recruited from low-enrolling clinics reflects the challenges faced in AYA enrollment. The lack of staff in certain key roles for CCT enrollment is likely contributing to these clinics' low enrollment. Future research should focus on systematically studying the differing perspectives of stakeholders holding various roles in the CCT enrollment process to allow for comparison across roles. Despite this limitation, our study is the first to compare barriers/facilitators across high- and low-enrolling clinics. Second, due to our anonymous study design we cannot confirm if the lack of endorsement of a specific barrier/facilitator by a stakeholder meant it was not present or the accuracy of any reported barriers/facilitators. Third, although we included patient advocates, the lack of AYA patients' perspectives likely led to some missed patientlevel factors influencing CCT enrollment. Finally, our sample included diverse NCORP sites, but participation bias may have occurred.

Improving AYA CCT enrollment is a complex, multi-step process that will require novel approaches to developing and testing interventions. We believe our results suggest the importance of creating dynamic, tailorable intervention packages that include a core set of components, but provides additional optional components that clinics can elect to implement if it fits their current resources. This approach will allow diverse settings to improve AYA enrollment, addressing a critical need of this patient population.

#### **Funding**

This work was supported by grants U10-CA180886 (M.E.R., D.R.F.), P30 CA016672 (M.E.R., I.T.-M.), UG1-CA189955 (B.H.P., M.E.R., I.T.-M.), and UG1-CA189955 (B.H.P.) from the National Cancer Institute at the National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

#### **Conflict of Interest**

The authors indicated no financial relationships.

#### **Author Contributions**

Conception/design: M.E.R., I.T.-M., E.J.S., H.A.L.-K., D.R.F., L.S., H.E.C., B.H.P. Collection and/or assembly of data: M.E.R., I.T.-M., E.J.S., H.A.L.-K. Data analysis and interpretation: M.E.R., I.T.-M., E.J.S., H.A.L.-K. Manuscript writing: M.E.R., I.T.-M., E.J.S., H.A.L.-K., D.R.F., L.S., H.E.C., B.H.P. Final approval of manuscript: All authors

# **Data Availability**

The data underlying this article will be shared on reasonable request to the corresponding author.

#### References

- Burke ME, Albritton K, Marina N. Challenges in the recruitment of adolescents and young adults in cancer clinical trials. *Cancer*. 2007;110(11):2385-2393. https://doi.org/10.1002/cncr.23060
- Unger JM, Cook E, Eric T, et al. The role of clinical trial participation in cancer research: Barriers, evidence, and strategies. Am Soc Clin Oncol Educ Book. 2016;35:185-198.
- Bleyer A, Budd T, Montello M. Adolescents and young adults with cancer: the scope of the problem and criticality of clinical trials. Cancer. 2006;107(suppl 7):1645-1655. https://doi.org/10.1002/ cncr.22102
- 4. Collins CL, Malvar J, Hamilton AS, et al. Case-linked analysis of clinical trial enrollment among adolescents and young adults at a

- National Cancer Institute-designated comprehensive cancer center. Cancer. 2015;121(24):4398-4406. https://doi.org/10.1002/cncr.29669
- Sanford SD, Beaumont JL, Snyder MA, et al. Clinical research participation among adolescent and young adults at an NCIdesignated Comprehensive Cancer Center and affiliated pediatric hospital. Support Care Cancer. 2017;25(5):1579-1586. https://doi. org/10.1007/s00520-016-3558-7
- Shaw PH, Ritchey AK. Different rates of clinical trial enrollment between adolescents and young adults aged 15 to 22 years old and children under 15 years old with cancer at a children's hospital. J Pediatr Hem Oncol. 2007;29(12):811-814.
- Downs-Canner S, Shaw PH. A comparison of clinical trial enrollment between adolescent and young adult (AYA) oncology patients treated at affiliated adult and pediatric oncology centers *J Pediatr Hem Oncol*. 2009;31(12):927-929.
- Parsons HM, Harlan LC, Seibel NL, et al. Clinical trial participation and time to treatment among adolescents and young adults with cancer: does age at diagnosis or insurance make a difference?
   J Clin Oncol. 2011;29(30):4045-4053. https://doi.org/10.1200/ JCO.2011.36.2954
- Parsons HM, Penn DC, Q L, et al. Increased clinical trial enrollment among adolescent and young adult cancer patients between 2006 and 2012-2013 in the United States. *Pediatr Blood Cancer*. 2019;66(1):e27426.
- Roth ME, Unger JM, O'Mara AM, et al. Enrollment of adolescents and young adults onto SWOG cancer research network clinical trials: a comparative analysis by treatment site and era. Cancer Med. 2020;9(6):2146-2152. https://doi.org/10.1002/cam4.2891
- Roth ME, O'Mara AM, Seibel NL, et al. Low enrollment of adolescents and young adults onto cancer trials: insights from the Community Clinical Oncology Program. J Oncol Pract. 2016;12(4):e388-e395. https://doi.org/10.1200/JOP.2015.009084
- Freyer DR, Seibel NL. The clinical trials gap for adolescents and young adults with cancer: Recent progress and conceptual framework for continued research. *Curr Pediatr Rep.* 2015;3(2):137-145. https://doi.org/10.1007/s40124-015-0075-y
- Tai E, Buchanan N, Eliman D, et al. Understanding and addressing the lack of clinical trial enrollment among adolescents with cancer. *Pediatrics*. 2014;133(suppl 3):S98-S103. https://doi.org/10.1542/ peds.2014-0122D
- Forcina V, Vakeesan B, Paulo C, et al. Perceptions and attitudes toward clinical trials in adolescent and young adults with cancer: a systematic review. Adol Heal Med Ther. 2018;9:87-94.
- Siembida EJ, Loomans-Kropp HA, Trivedi N, et al. Systematic review of barriers and facilitators to clinical trial enrollment among adolescents and young adults with cancer: identifying opportunities for intervention. *Cancer.* 2020;126(5):949-957. https://doi.org/10.1002/cncr.32675
- Siembida EJ, Loomans-Kropp HA, Tami-Maury I, et al. Barriers and facilitators to adolescent and young adult cancer trial enrollment: NCORP site perspectives. *JNCI Cancer Spectr.* 2021;5(3). https://doi.org/10.1093/jncics/pkab027.

- Vaismoradi M, Turunen H, Bondas T. Content analysis and thematic analysis: Implications for conducting a qualitative descriptive study. Nurs Health Sci. 2013;15(3):398-405. https://doi.org/10.1111/nhs.12048
- 18. Sebele-Mpofu FY. Saturation controversy in qualitative research: complexities and underlying assumptions. A literature review. *Cogent Soc Sci.* 2020;6(1):1838706. https://doi.org/10.1080/23311886.2020.1838706
- Albritton KH, Wiggins CH, Nelson HE, et al. Site of oncologic specialty care for older adolescents in Utah. J Clin Oncol. 25. 2007;25:4616-4621.
- Yeager ND, Hoshaw-Woodard S, Ruymann FB, et al. Patterns of care among adolescents with malignancy in Ohio. *Pediatr Hematol* Oncol I. 2006;28(1):17-22.
- National Clinical Trials Network. NCTN Participation and Crediting Rules. Accessed August 19, 2021. https://www.ctsu.org/master/simplepage.aspx?ckey=CRED-RULES.
- Cancer Trials Support Unit website. Accessed July 26, 2021. https://www.ctsu.org/Public/Default.aspx?ReturnUrl=%2f.
- Thomas SM, Malvar J, Tran HH, et al. A prospective comparison of cancer clinical trial availability and enrollment among adolescents/young adults treated at an adult cancer hospital or affiliated children's hospital. *Cancer.* 2018;124(20):4064-4071. https://doi. org/10.1002/cncr.31727
- 24. Thomas SM, Malvar J, Tran H, et al. A prospective, observational cohort study comparing cancer clinical trial availability and enrollment between early adolescents/young adults and children. *Cancer*. 2018;124(5):983-990. https://doi.org/10.1002/cncr.31127
- Petrick AF, Green BB, Vollmer WM, et al. The validation of electronic health records in accurately identifying patients eligible for colorectal cancer screening in safety net clinics. Fam Pract. 2016;33(6):639-643.
- Bird JA, McPhee SJ, Jenkins C, et al. Three strategies to promote cancer screening. How feasible is wide-scale implementation? *Med Care*. 1990;28(11):1005-1012. https://doi.org/10.1097/00005650-199011000-00003
- Cataldi JR, Kerns ME, O'Leary ST. Evidence-based strategies to increase vaccination uptake: a review *Curr Opin Pediatr.* 2020;32(1): 151-159. https://doi.org/10.1097/MOP.0000000000000843
- 28. Berger KS. *The Developing Person: Through the Life Span*. Worth Publishers; 2005.
- 29. Coyne I, Amory A, Kiernan G, Gibson F. Children's participation in shared decision-making: children, adolescents, parents, and healthcare professionals' perspectives and experiences. *Eur J Oncol Nurs*. 2014;18:273-280. https://doi.org/doi:10.1016/j.ejon.2014.01.006
- Weaver MS, Baker JN, Gattuso JS, et al. Adolescents' preferences for treatment decisional involvement during their cancer. *Cancer*. 2015;121:4416-4424. https://doi.org/10.1002/cncr.29663
- Casillas J, Goyal A, Bryman J, et al. Development of a text messaging system to improve receipt of survivorship care in adolescent and young adult survivors of childhood cancer. J Cancer Surviv Res Pract. 2017;11(4):505-516.