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

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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-enrolling clinics 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.
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. 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. Enrollment rates also vary across AYAs, including differences by cancer type, insurance status, age at diagnosis, and treatment setting (pediatric vs. adult). Higher participation rates among AYAs have been identified in National Cancer Institute (NCI)-designated Comprehensive Cancer Centers and other academic medical centers, 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 NCI-designated cancer centers.

The successful enrollment of an AYA patient with cancer onto a CCT requires multiple, unobstructed steps. The complexity of this process has led to institution-, provider-, and patient-level barriers. 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. 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, 18 NCORP sites (13 community, 5 minority/underserved) met the inclusion criteria, 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 (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 framework for CCT enrollment and were tailored to stakeholder roles. Each stakeholder was asked to describe their role in the CCT enrollment

| NCORP site no. | Clinic enrollment status | Site type | Presence of medical or pediatric oncology | Region |
|---------------|--------------------------|-----------|------------------------------------------|--------|
| 1             | High-enrolling clinic     | Minority/underserved | Med/ped onc Med only | East   |
| 2             | Low-enrolling clinic      | Community-based   | Med/ped onc Med only | Midwest|
| 3             | High-enrolling clinic     | Community-based   | Med onc only Med only | Midwest|
| 4             | Low-enrolling clinic      | Community-based   | Med/ped onc Med/ped onc | Midwest|
| 5             | High-enrolling clinic     | Community-based   | Med/ped onc Med only | West   |
| 6             | Low-enrolling clinic      | Community-based   | Med only Med only | West   |

*Table modified from its original publication by Siembida et al. and republished with permission. Abbreviation: NCORP, NCI Community Oncology Research Program.
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. 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 halted. 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) 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 high-enrolling 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 emphasized that high patient volume reduced physicians’ available time to discuss trials.

**Location of Trial Clinic**

A similar percentage of stakeholders from high- and low-enrolling 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   | High AYA enrolling | Low AYA enrolling |
|----------------------------------------------------------|---------|--------------------|-------------------|
| 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)             |

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

| Facilitator                                                                 | Total   | High AYA enrolling | Low AYA enrolling |
|---------------------------------------------------------------------------|---------|--------------------|-------------------|
| 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)             |

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 real-life 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 multi-level and tailor able. 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 confute 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.21 Our team has created cross-network enrollment FAQ documents.22 Finally, both our results and the results of other studies23,24 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 awareness.

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.25-27

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.28

![Figure 1](image-url)
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. 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.

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 patient-level 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, tailor able 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.

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

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**Conflict of Interest**

The authors indicated no financial relationships.

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**Data Availability**

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

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