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Understanding and Addressing the Lack of Clinical Trial Enrollment Among Adolescents With Cancer

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Abstract

Despite overall improvement in survival, morbidity, and quality of life of US patients with cancer, this progress is less prevalent in the population of adolescent and young adult patients with cancer, including those between the ages of 15 and 19 years. Evidence suggests that participation in clinical trials is associated with better survival outcomes among children and adolescents with cancer; however, adolescents have lower clinical trial participation rates compared with younger age cohorts. To better understand the unique concerns among adolescent patients with cancer, the Division of Cancer Prevention and Control at the Centers for Disease Control and Prevention convened a workgroup of researchers and health care providers in the field of adolescent and young adult oncology and cancer survivorship to examine the barriers and challenges limiting the participation of adolescents in clinical trials and to define ways to improve upon these concerns. This article summarizes the activities of the workgroup and their suggestions for enhanced accrual.

Keywords

adolescents; cancer; clinical trial enrollment; oncology; teens; youth

The number of cancer survivors in the United States has increased from 3 million to nearly 12 million over the past 35 years, with marked improvements in cancer survival, morbidity,

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and quality of life.¹ These improvements, however, are less prevalent among adolescent patients with cancer who are between the ages of 15 and 19 years.^{2–6} Overall 5-year survival rates of adolescent patients diagnosed with cancer have remained stagnant since the mid-1980s.²⁴ Despite evidence supporting the association between increased clinical trial participation and improved survival outcomes among patients with cancer,^{3,7–9} adolescents have lower clinical trial enrollment and participation rates (5%–34%) compared with younger children (>90%)^{3,10–12}

Referral patterns may contribute to lower enrollment rates among adolescents. Due to overlapping age criteria, cancer type, and geographic accessibility, adolescents suspected of having cancer can be referred to either pediatric or adult oncologists. However, the data suggest that older adolescents are more likely to be referred to adult oncologists,¹³ and indeed patients with cancer who are in this age group are more often treated at adult cancer centers than at pediatric cancer centers^{2,3,14–17} However, adolescents treated by adult oncologists are less likely to enroll in clinical trials compared with those treated by pediatric oncologists^{2–4,14,17,18} The overall low participation rates in clinical trials for adolescents may partially explain poor survival outcomes in this age group.¹⁹ For certain pediatric-type cancers, such as acute lymphoblastic leukemia, rhabdomyosarcoma, and Ewing's sarcoma, evidence suggests that adolescents treated on pediatric protocols have better outcomes compared with those on adult protocols.^{20–24} In addition, treating adolescent patients who have cancer can be complicated due, in part, to the unique psychosocial considerations during this developmental stage. These challenges may include self-image, peer relationships, social and financial issues, and changes in autonomy versus dependency that can affect treatment decisions.^{25–27} Health care providers may lack awareness of these psychosocial issues and how they can negatively affect adherence to therapy, quality of life,²⁸ and long-term outcomes.^{25,26,29,30}

In response to the Carolyn Pryce Walker Conquer Childhood Cancer Act of 2008,³¹ which calls for “expansion and widespread implementation of activities that provide available information on treatment protocol to ensure early access to the best available therapies and clinical trials for pediatric cancers,” the Division of Cancer Prevention and Control at the Centers for Disease Control and Prevention (CDC) convened a workgroup of adolescent and young adult (AYA) cancer providers and researchers to examine the association between provider specialty (pediatric versus adult oncologist), clinical trial enrollment, and subsequent medical and psychosocial outcomes among adolescents between 15 and 19 years of age who have cancer. The main purpose of the workgroup was to identify practical issues and barriers that contribute to the limited participation of adolescent patients with cancer in clinical trials and to determine specific, actionable priorities to address these problems. The present article summarizes workgroup proceedings and highlights potential actions to improve clinical trial participation rates among adolescent patients with cancer and ultimately improve long-term outcomes.

METHODS

Convening the Workgroup

Between March and May 2012, the CDC convened a group of 20 US- and Canadian-based participants from a number of clinical and academic institutions, nonprofit organizations, and governmental agencies representing multiple fields, including pediatric and adult oncology, clinical research, behavioral science, health informatics, and clinical trials expertise. An invitation to participate in the workgroup was initially extended to 29 individuals who were selected based on their history of first-authored, peer-reviewed manuscripts on related topics and area of expertise. A total of 18 experts, in addition to the workgroup chair and co-chair who were previously identified by CDC staff, accepted the invitation and participated in the workgroup meetings. CDC staff served as observers of the meeting and provided clarification on CDC-related activities for all participating workgroup members. After searches of the published literature on the topics, weekly discussions of the organizing committee, and development of review materials, three 2-hour Web-based meetings were convened on March 19, April 24, and May 23, 2012.

Webinar Sessions

To maximize interaction during the webinars, workgroup members were assigned specific topics related to clinical trial enrollment among adolescent patients with cancer. Each webinar session was divided into multiple discussion segments or subtopics. The topics were selected based on a literature review conducted on clinical trial enrollment and related outcomes among adolescents and further defined by the workgroup's chair and co-chair with input from CDC staff. During the March and April webinars, discussions were preceded by presentations from selected workgroup members on current knowledge or projects relevant to a subtopic of the discussion. In addition, topics were assigned to members of the workgroup who were then responsible for crafting responses to specific questions in preparation for the webinar.

The March 2012 webinar focused on potential barriers to clinical trial enrollment among adolescents with cancer. The discussions centered around trends in clinical trial enrollment among 15-to 19-year-old patients with cancer, current and developing AYA oncology programs and their potential impact on clinical trial enrollment, and the unique psychosocial needs of adolescent patients. The April 2012 webinar explored the issue of where adolescent patients with cancer receive their diagnosis and treatment. Specifically, the discussion addressed the influence of geography on where adolescent patients with cancer seek care, differences between adult and pediatric centers in providing professional care, and the challenges impeding the enrollment into clinical trials of adolescent patients treated at adult cancer centers. The issue of adolescent patients with cancer and their psychosocial needs was revisited during the April webinar. The final webinar session in May 2012 focused on defining and discussing priority areas and future directions aimed toward improving clinical trial enrollment rates and subsequent outcomes of adolescents with cancer.

RESULTS AND DISCUSSION

Challenges and Suggested Priorities for Action

Discussions in all 3 sessions focused extensively on the various barriers and challenges that impede enrollment of adolescent patients with cancer into clinical trials. The workgroup members discussed a range of issues encompassing patient-, provider-, and institution-related challenges that hinder adolescent patients from receiving comprehensive cancer care associated with clinical trial participation. The workgroup participants also provided input on how to address the identified challenges and suggested actions that could be pursued by oncologists, nurses, mental health providers, patients, organizations, and agencies to improve clinical trial enrollment rates and care for adolescent patients with cancer.

The workgroup identified 5 issues as the most important barriers: (1) low referral rates of adolescent patients with cancer to pediatric cancer centers; (2) limited availability of clinical trials for certain cancers; (3) physician-related barriers limiting clinical trial accrual; (4) institutional barriers impeding collaboration between pediatric and adult oncologists on clinical trials; and (5) unique psychosocial needs of adolescent patients with cancer.

Low Referral Rates—The first barrier identified by the workgroup was low referral rates of adolescent patients with cancer to pediatric cancer centers and other centers with qualified clinical trials for these patients.

Workgroup participants reported that policymakers, cancer center directors, community health professional leaders, and AYA specialists may use the National Comprehensive Cancer Network guidelines on AYA oncology that were published in February 2012.³² These guidelines begin by recommending consideration of referral to an appropriate National Cancer Institute (NCI)-sponsored medical institution. Specialists in the AYA oncology field may benefit by developing effective outreach messages targeting primary care providers (PCPs) and patients in their communities to promote services and treatment options available to adolescent patients with cancer through their programs and cancer centers. These messages may consider important factors that influence the PCP's referral decisions and highlight the unique medical and psychosocial needs of adolescent patients who require additional support; this support may be available through pediatric cancer centers. Outreach efforts can also increase general awareness about clinical cancer trials and the availability of trials in the communities where these oncologists practice. It may be of benefit for oncologists, organizations, and agencies working on AYA-related issues to expand clinical trial educational efforts beyond practicing PCPs. The "Stop A Doc" campaign, which encourages greater engagement of AYA cancer patients with their health care providers, may provide a good model for these efforts.³³ AYA organizations can use popular Web sites and other social media tools managed by prominent cancer organizations and professional provider organizations to target adolescent patients and PCPs and to increase awareness about the care options available for adolescent patients with cancer. The AYA organizations can also use Web site advertising tools to direct traffic to appropriate AYA cancer Web sites.

Clinical Trial Availability—The second barrier identified by the workgroup was the limited availability of clinical trials for certain cancers that are common among adolescent patients. In an effort to increase demand for more clinical trials available to adolescent patients with cancer, workgroup members recommended that AYA organizations and agencies engage adolescent patients and patient rights groups in informing health care providers to consider and participate in clinical trials for adolescent patients with cancer. As more evidence becomes available on the pharmacodynamics, pharmacokinetics, and effects of therapy on young patients, the 18-year lower age limit for adult clinical trials may need to be reevaluated. For cancers with highly favorable treatment outcomes in the adolescent population (eg, Hodgkin’s lymphoma, germ cell tumors), new clinical trials can be designed with a focus on reducing therapy-related toxicities. Treatment protocols of clinical trials appropriate for adolescent patients should include goals specific to this population. Collaboration between pediatric and adult oncologists may be leveraged to design AYA-focused clinical trials for cancers common among this group. The reorganization of the NCI-sponsored clinical trial enterprise³⁴ may consider including a focus on AYA clinical trials and specifically those with potential application to adolescents. The annual renewal of NCI-designated cancer centers that are recipients of Cancer Center Support Grants may also require the reporting of the age of patients accrued to clinical trials, with a specific metric for the 15- to 19-year-old and 20- to 39-year-old age groups.

Physician-Related Barriers—The third barrier identified by the workgroup was physician-related barriers limiting clinical trial accrual among adolescent patients with cancer. This barrier may include issues such as the lack of standards of care for the common cancers in adolescents and limited participation of adult oncologists in pertinent adolescent cancer clinical trials. Workgroup participants recommended increasing collaboration between pediatric and adult oncologists to increase clinical trial enrollment for adolescent patients with cancer. Barriers currently limiting physician participation and collaboration on clinical trials relevant to adolescent patients, such as the lack of financial incentives and low accrual rates, need to be taken into consideration when planning these efforts. Differences in pediatric and adult oncologists’ views on the purposes of clinical trials may also need to be reconciled to increase clinical trial enrollment. Similar to increasing awareness among PCPs and in local communities, the specific needs of adolescent patients must be realized in the oncology arena. Reaching treatment consensus among pediatric and adult oncologists must be prioritized for AYA common cancers to establish standard of care. In addition, increased collaboration between pediatric and adult oncologists may be more effective if undertaken at the time when AYA-relevant clinical trials are designed. Elements of successful collaborative clinical trial efforts between pediatric and adult cooperative groups should be thoroughly examined to understand existing barriers and challenges so that future partnerships and models of care can be developed.

Institutional Barriers—The fourth barrier identified by the workgroup was institutional barriers impeding collaboration of pediatric and adult oncologists in clinical trials and limiting accrual of adolescents in clinical trials. An example of this barrier was the lack of recognition of centralized institutional review boards (IRBs) by individual cancer institutions. Academic institutions involved in collaborative multisite research often obtain

approval from their own individual IRBs. However, many institutions are unwilling to defer IRB approval to centralized IRBs for various reasons.³⁵ This action results in the use of excessive resources on IRB applications, reviews, and duplication of efforts at multiple institutions. Workgroup members discussed potential solutions, which may include modification of clinical trial IRB issues (eg, single IRB of record, recognition of centralized IRBs by cancer institutions), reimbursement of adult specialists participating in pediatric clinical trials, and examination of geographic barriers to trial implementation (eg, location of treatment versus location of principal trial investigator).

Unique Psychosocial Needs of Adolescent Patients With Cancer—The fifth barrier identified by the workgroup was the unique psychosocial needs of adolescent patients with cancer. Although it is well recognized that adolescents have unique psychosocial needs, it is not clear how these issues have an impact on clinical trial participation. Overall, more recent research on AYA psycho-oncology tends to have focused on the “young adults” of this spectrum, and there is much to learn about adolescent patients with cancer, especially in terms of their input regarding treatment choices and adherence to treatment. Integration of psychosocial goals into the treatment protocols of clinical trials relevant to adolescent patients is needed and could help explain how participation of adolescents in clinical trials affects the psychosocial outcomes of participants compared with nonparticipants. An example of this process is the distress screening mandate that all Commission on Cancer-approved hospitals must adhere to.³⁶ Clinicians may benefit from receiving training on how to have developmentally relevant discussions with their adolescent patients about issues related to their care, including presenting information on clinical trials. AYA groups and organizations may work with cancer organizations to identify and engage public figures who were diagnosed with cancer during adolescence to share their experience with adolescent cancer patients.

The workgroup also recommended additional efforts to support the development of AYA cancer peer groups to offer psychosocial support to adolescent patients with cancer through existing networks of cancer survivors or by forming new groups at NCI-designated cancer centers. AYA organizations may consider developing training materials for peer support specific to AYA that can be disseminated to cancer peer support groups.

The role of parents in decision-making for adolescents with cancer was also discussed. An adolescent’s transition from dependent to autonomous decision making may depend on his or her level of cognitive and emotional maturity. Although panelists noted that an adolescent may have the desire and/or developmental maturity to assume more responsibility in decision-making, there are ethical and legal complications regarding consent and assent that may arise when parents and adolescents do not agree about clinical trial enrollment. Although it was noted that parents have the legal right to make clinical trial enrollment decisions, with or without the adolescent’s assent, increased communication and collaboration between clinicians, adolescent patients, and parents are needed to ensure cooperation and adherence to treatment and clinical trial enrollment, as well as to alleviate emotional concerns associated with relinquishing or assuming decision-making responsibilities.

CONCLUSIONS

Adolescent patients with cancer have unique experiences as they face the dual stress of having a life-threatening disease while dealing with the challenges of transitioning from childhood to adulthood.³⁷ Despite significant progress in cancer care and survivorship, adolescent patients have seen less improvement compared with other age groups. Poor outcomes among adolescent patients with cancer may ultimately be attributed to the limited awareness about their distinctive treatment and care needs among the medical community in addition to the lack of an organized body of research and a well-formulated discipline in medicine devoted to this specific group of patients.^{3,7,28} Even within the expanding AYA oncology field, the focus on young adults may overshadow the issues that uniquely affect the adolescent cancer population.³⁴ The limited knowledge about issues relevant to the care of adolescent patients with cancer emphasizes the need for more initiatives focusing on this population. Convening this workgroup offered an opportunity for researchers and providers working in the AYA oncology field to discuss this frequently overlooked group. The suggestions put forth by workgroup members highlight the importance of engaging various stakeholders of the AYA community to address the problems and barriers hindering the participation and enrollment of adolescents with cancer into clinical trials and hence limiting the care options for these patients.

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ABBREVIATIONS

AYA	adolescent and young adult
CDC	Centers for Disease Control and Prevention
IRB	institutional review board

NCI National Cancer Institute

PCPs primary care providers

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