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Clinical research participation among adolescent and young adults at an NCI-designated Comprehensive Cancer Center and affiliated pediatric hospital

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Abstract

Purpose—Minimal clinical trial participation among adolescents and young adults (AYAs) with cancer limits scientific progress and ultimately their clinical care and outcomes. These analyses examine the current state of AYA clinical research participation at a Midwestern comprehensive cancer center and affiliated pediatric hospital to advise program development and increase availability of trials and AYA participation. Enrollment is examined across all diagnoses, the entire AYA age spectrum (15–39), and both cancer therapeutic and supportive care protocols.

Methods—This study was a retrospective review of electronic medical records via existing databases and registries for all AYAs. Data were collected for AYAs seen by an oncologist at the adult outpatient cancer center or at the pediatric hospital between the years 2010 and 2014. Descriptive statistics and logistic regression analyses were conducted to characterize this sample.

Results—In the pediatric setting, 42.3% of AYAs were enrolled in a study compared to 11.2% in the adult setting. Regression analyses in the pediatric setting revealed that AYAs with private insurance or Caucasian race were more likely to participate. Within the adult setting, ethnicity, race, insurance, and diagnosis were associated with study participation; 54.8% of study enrollments were for cancer therapeutic and 43.4% for supportive care studies.

Conclusions—These results are comparable to previously published data and support the need for new local and national AYA initiatives to increase the availability of and enrollment in therapeutic clinical trials. The same is true for supportive care studies which play a crucial role in improving quality of life.

Compliance with ethical standards

Conflict of interest There are no financial disclosures from the authors. This work was unfunded and there are no conflicts of interest. The authors have full control of all primary data and agree to allow review of the data upon request.

Keywords

Adolescents; Young adults; Clinical trials; Cancer survivors

Introduction

The field of adolescent and young adult (AYA) oncology emerged with the realization that, unlike older and younger groups, persons diagnosed with cancer between 15 and 39 years of age had not benefited from significant improvements in survival rates over more than two decades. In 2005–2006, the National Cancer Institute and the LIVESTRONG Foundation conducted a progress review group which published a report (PRG report) highlighting the unique clinical and research needs of AYAs and formulated a strategic plan for improving quality of life and outcomes. The PRG identified multiple plausible factors that may contribute to the lack of improvement in survival rates such as access to care, poor continuity of care, and notably, low participation in cancer clinical trials [1].

An examination of published data on AYA participation rates in clinical trials reveals clear room for improvement. Indeed, fewer gains in survival improvements and lower accrual rates to trials have been observed not only in the USA but internationally including Europe, Canada, and Australia [2]. Early studies in the USA have noted that within institutions that participate in National Cancer Institute (NCI) sponsored trials, two thirds of children under 15 years of age are enrolled on trials. Adolescents (ages 15–19) are less likely to be treated at these institutions (20–35%) and, even in these settings, are less likely to be enrolled on clinical trials (10%) [3, 4]. Further, AYAs between the ages of 20 and 39 are under-represented in pediatric and adult NCI Cooperative Group trials with only 1–2% being enrolled. The majority of 20–39-year-olds are treated in community-based oncology settings where the availability of clinical trials is much more variable [5, 6]. Correlation data suggests that participation in NCI-funded trials for diagnoses such as sarcomas is strongly associated with improvements in 5-year survival rates [7]. Therefore, low rates of participation in clinical trials among AYAs are alarming as clinical trials further the knowledge base that ultimately accelerates treatment advances.

Since publication of the PRG report, experts have proposed solutions regarding the low rate of clinical trial enrollment for AYAs. The University of Pittsburgh Cancer Institute and Children's Hospital of Pittsburgh demonstrated improvements in AYA clinical trial enrollments after initiating an AYA oncology program that fosters collaboration between pediatric and medical oncologists and the opening of new AYA-relevant clinical trials via a joint Institutional Review Board [8]. Others have suggested a strategy for improving enrollment statistics for AYAs via influencing referrals to centers known to have relatively higher proportions of AYA enrollment including pediatric cancer centers, AYA oncology programs, and NCI-designated Cancer Centers [9]. Freyer and Seibel recently published a review of the “clinical trial gap” for AYAs, including a conceptual framework for research and discussion of how recent developments in the NCI-funded enterprise (e.g., National Clinical Trials Network and NCI Community Oncology Research Program) provide opportunity for improvement with emphasis on greater opportunity for trial enrollment in

community oncology settings [10]. These authors denote the interacting processes of trial availability nationally and within individual institutions, as well as the role of the provider presenting the trial and the patient's reception to participation.

Similarly, a recent review published by investigators in the UK highlights their success with improving AYA accrual rates via a combination of health-care policy directives, advocacy, and dedicated staff within their National Health Service [2]. Despite significant gains, they note that deficits remain when compared to recruitment of younger survivors. They proposed the "5 A's model" moving forward which notes five factors that influence AYA clinical trial enrollment (available, accessible, aware, appropriate, and acceptable) while placing emphasis on their observation that there was no scientific basis for many historical age-related inclusion and exclusion criteria. They assert that these five factors provide a systemic framework for designing and conducting clinical trials for AYAs [2]. Additionally, behavioral scientists within the Children's Oncology Group (COG) note the importance of accounting for patient characteristics when designing AYA studies, recruitment strategies, and training recruitment staff, with emphasis on developmental considerations and parental perspectives [11].

In light of these proposals, the primary aim of this study was to examine the current state of clinical trial enrollment of AYAs at a major adult-based comprehensive cancer center and pediatric affiliate in the USA as a means to advise program development and methods for tailoring existing innovations, ultimately increasing the availability of trials and study participation of AYAs at these institutions. Both cancer therapeutic and supportive care studies were examined. Based on the existing literature, we anticipated that our rates of enrollment would be equal to or greater than previously published rates, with higher rates of study enrollment in our pediatric setting. We also hypothesized that study enrollment would vary by disease and patient demographics. We are hopeful that this investigation will provide useful information for other institutions with similar aims.

Methods

Study design and procedures

This study was a retrospective review of electronic medical records for all AYAs seen at the Ann and Robert H. Lurie Children's Hospital of Chicago (ARHLCH) and our NCI-designated adult cancer center, the Robert H. Lurie Comprehensive Cancer Center of Northwestern University (RHLCCC). Institutional Review Board approval was obtained from each institution. Data from electronic medical records were obtained for patients between the ages of 15 and 39 that completed a new patient encounter with one of our surgical or medical/pediatric oncologists at either of the two institutions over a 5-year time period; 2010–2014. Records for patients diagnosed with a neoplasm that was benign, of uncertain behavior, or of unspecified nature were excluded for these analyses.

Being distinct institutions, data is housed differently at the ARHLCH and the RHLCCC. Within the pediatric setting, data from the ARHLCH were extracted via the Ann and Robert H. Lurie Children's Hospital Cancer Registry. Within the adult setting of the RHLCCC, data were extracted via the Northwestern Medicine® Enterprise Data Warehouse (EDW). The

EDW provides a single, comprehensive, and integrated repository of all clinical and research data sources on the campus to facilitate research, clinical quality, healthcare operations, and medical education. Patient data including demographics, insurance information, diagnosis, and if the patient had ever been enrolled on a trial were extracted via these sources. Finally, patient data from both institutions were matched with clinical trial information via Northwestern's Oncology Trial Information System (NOTIS), which is a web-based clinical trial management system used to track cancer protocols and patients enrolled on clinical trials within the cancer center and its affiliates. It also includes an electronic case report form module used to capture patient data while patients are participating in studies.

Statistical analyses

Chi-square tests were used to test the association between patient characteristics and clinical study participation. Because patients are clustered within providers and certain providers may have greater or lesser tendencies to recommend study participation to patients, the observations are not strictly independent as the chi-square test assumes. Therefore, we also used mixed effects logistic regression models, with a random effect for provider, to test these comparisons adjusted for the non-independence of patients with the same provider. Finally, significant variables were entered into a single mixed effects logistic regression model.

Results

Participants

Within the pediatric setting of the ARHLCH, records were identified for a total of 208 AYAs. The average age was 17.1 years (SD = 2.5; range 15–33) and 90.4% were under the age of 20 years. The majority were male (55.3%), White (85.6%) and privately insured (75.9%). The most common diagnoses were brain/CNS cancer (21.7%) and lymphoma (21.3%), followed by leukemia (17.9%) and sarcoma (17.4%). Additional details about demographics and diagnoses across settings are provided in Table 1.

Within the adult setting of the RHLCCC, records were identified for a total of 1946 AYAs. The average age in this setting was 31.7 years (SD = 5.7; range 15–39) and 32.6% were less than 30 years of age. The majority were female (65.3%), White (74.7%), and privately insured (74.6%). The most common diagnosis was breast cancer (24.9%), followed by lymphoma (15.1%), skin cancer (11.6%), gynecologic cancer (10.1%), and brain/CNS cancer (8.5%).

AYAs enrolled on study

Of the 208 AYAs treated at the pediatric hospital, 88 or 42.3% were enrolled in a clinical study. Unfortunately, we were unable to match NOTIS data on type of protocol for the majority of our pediatric sample (65.9%) as the NOTIS data files lacked patient identifying information. For this 65.9% of patients, we were unable to determine the details of the type of study they were enrolled on. Of the remaining cases ($n = 30$), the majority were enrolled on Children's Oncology Group (COG) trials (46.7%; additional details in Table 2). In examining study participation by diagnosis, patients with leukemia had the largest

percentage participating in a study (65%) followed by lymphoma (45%), brain/CNS cancer (38%), and sarcoma (33%).

Of the 1946 AYAs at the RHLCCC, 218 or 11.2% were enrolled in a clinical study. We were more successful at matching NOTIS data to individual cases in the adult setting; however, we were still unable to identify protocol details for approximately 24% of our sample. Of the remaining cases that we were able to match, the majority (62%) were enrolled in investigator-initiated trials, followed by 24% on industry trials, and nearly 14% on cooperative group trials (more details in Table 2). In examining study participation by diagnosis, patients with leukemia/myeloma had the largest percentage enrolled on study (19.4%), followed by head/neck/sarcoma (18.4%), GI cancer (14.0%), breast cancer (12.8%), brain/CNS cancer (12.6%), and lymphoma (11.3%). Furthermore, we looked at the type of study that participants were enrolled in and found 54.8% of enrollments were for cancer therapeutic studies and 43.4% were for supportive care studies. An additional three participants were enrolled in early detection or screening studies.

Mixed effects logistic regression

Within the pediatric setting of the ARHLCH, race, insurance, and diagnosis were significantly associated with whether or not a patient participated in a study via chi-square tests. Age, ethnicity, and sex were not significantly associated with participation. After adjustment for correlated data within providers, diagnosis was no longer significant; however, race and insurance remained so (see Table 3). More specifically, AYAs of Black or other race were significantly less likely to be enrolled on study than those of White race (OR = 0.25). Patients with private insurance were more likely to be enrolled on study than patients with Medicaid (OR = 2.80).

Within the adult setting of the RHLCCC, ethnicity, race, insurance, and diagnosis were significantly associated with whether or not a patient participated in a study (see Table 4). Even after adjustment for correlated data within providers, the same variables were statistically significant. More specifically, Hispanic patients were more likely to participate than non-Hispanic patients (OR = 2.71). However, patients with other or unknown race were less likely to participate than White patients (OR = 0.42). Patients with financial assistance were less likely to participate than patients with private insurance (OR = 0.56). Finally, with leukemia/myeloma as the reference group, several other diagnosis groups were less likely to participate, particularly gynecologic cancers (OR = 0.16) and skin cancers (OR = 0.28). Age and sex were not associated with study participation.

Discussion

This study examined adolescent and young adult clinical trial enrollment at a large Midwestern metropolitan cancer center and affiliated pediatric hospital in the USA. We are aware of only one other recent study from the west coast that is inclusive of the entire NCI-defined AYA age range, all diagnostic groups, and supportive care protocols in addition to cancer therapeutic trials. The west coast investigators conducted a case-linked analysis of enrollment, comparing AYAs to both pediatric and older adult patients and found cancer therapeutic trial enrollment rates to be comparable to older adults (6%) but less than children

(22%) [12]. Enrollment in any study including supportive care studies was also higher for children (54%) compared to AYAs (20%) and older adults (17%). Of note, this study differs from ours in that they excluded participants with recurrent disease, phase 1 protocols and they were able to make comparisons to older adults. A direct comparison to many other previously published rates is confounded by methodological differences; however, as predicted, our total enrollment rates varied by demographic and disease characteristics. Further, data from this study were comparable to all previous studies in that higher rates of enrollment were observed in the pediatric vs. adult setting (42.3 vs. 11.2%).

Downs-Canner and Shaw compared AYA trial enrollment at affiliated pediatric and adult cancer centers in Pittsburgh, a situation analogous to the one described in our study [13]. They found 26% of AYAs treated in the pediatric setting were enrolled compared to only 4% in the adult setting. Using data from the National Cancer Institute Patterns of Care Study, Parson's et al. found that 14% of AYAs (ages 15–39) were enrolled in a clinical trial and that adolescents were significantly more likely to be enrolled at 34.3% with percentages being much smaller for older age groups (8.8% for ages 20–24, 3.4% for ages 25–29, 5.0% for ages 30–34, and 3.7% for ages 35–39) [14]. Our rates appear higher than these prior studies, yet again, these previous studies had differing inclusion criteria such as only examining patients between the ages of 15 and 22 years or only patients with cancers common in childhood [13, 14]. Also, rates in this investigation may appear inflated due to our inclusion of supportive care protocols. For example, if we simply subtract those participants in the adult setting identified as participating in supportive care studies, the 11.2% rate decreases to 7.5%; also assuming those 52 missing data on protocol type are not participating in supportive care studies. Finally, the 2008 NCCN® benchmark study examined data from 17 participating NCCN member institutions and cited a range of 10–24% total accrual for all ages and diagnoses [15]. The 2010 follow-up to this study cited a 15.1% rate of accrual over a 12-month time period for 20 participating institutions [16]. These studies only examined therapeutic trials. With this in mind, there is clear room for improvement at our institution but also nationally in the context of historically reported AYA accrual.

Even so, for those participants for which we were able to extract trial information from NOTIS, approximately 67% in the pediatric setting, and 26% in the adult setting, were enrolled in cooperative group or NCI-sponsored studies. Taken together, these results are supportive of prior suggestions that referral to NCI-designated and pediatric cancer centers may impact AYA clinical trial participation [9]. Given evidence that trial participation is associated with improvements in 5-year survival rates, such an approach may be paramount to accelerating treatment advances for this historically under-represented subset of cancer survivors [7]. It is also worth noting that in the adult setting, more than 43% of AYAs participating in clinical studies were enrolled in supportive care studies which is indicative of AYAs' willingness to engage in such studies when available. While increasing survival rates for AYAs is a primary goal, so too is improving the quality of life of AYA survivors over the continuum of care; thus, access to supportive care studies should not be overlooked.

The 2008 NCCN® benchmarking study cites clinical trial accrual rates from 6 to 28% for minority groups [15]. Enrollment of minority young adults on cancer therapeutic trials at the RHLCCC fell within this range, including a 13.2% enrollment rate for Hispanic survivors

and 7.9% rate for Black or African Americans. In the pediatric setting, 23% of Black or African Americans were enrolled as were 49% of Hispanic survivors. However, regression analyses revealed sociodemographic differences in both settings with some racial minorities being less likely to be enrolled on a study than patients identifying as White. Also, patients that were receiving financial aid or had Medicaid were less likely to be enrolled than those with private insurance. Buchanan et al. published a review of psychosocial barriers and facilitators to AYA trial enrollment including sociodemographic factors [17]. They note that such discrepancies have been routinely examined and observed in the adult literature but less data exists for AYA survivors. They also suggest that enrollment of Hispanic survivors may be higher or equal to non-Hispanic white survivors. Interestingly, in the Collins et al. sample of AYAs, Hispanic or Asian/Pacific Islanders were more likely to enroll on “non-therapeutic” studies (e.g., epidemiologic, biologic, psychosocial, or supportive care studies) than non-Hispanic AYAs [12]. The same was not found for cancer therapeutic studies. Data from this current investigation support the suggestion of Buchanan et al. in that analyses revealed Hispanic survivors to be nearly three times as likely to be enrolled in a clinical study in the adult oncology setting [17].

After controlling for provider, variability in enrollment rates by diagnostic group was not observed in the pediatric setting but was significant in the adult setting. Survivors with diagnoses more common in childhood including leukemia or sarcoma were more likely to be enrolled on study while others such as gynecological cancers and melanoma were far less likely to participate in a study. We were unable to draw conclusions about the reasons for this variability based on the existing data, but this is not inconsistent with prior published concerns about access to trials for certain diagnostic groups including those reported by the PRG. In fact, at the time the PRG was conducted, there were no phase III melanoma trials accessible to AYAs [1]. Additionally, Collins et al. observed that their institution had cancer therapeutic trials open for 8 of the most common AYA cancer diagnoses (none for thyroid and melanoma) compared to 10/10 of the most common cancers in childhood and 9/10 of those most common to older adults [12].

There are limitations to this study, most notably that our results cannot be generalized outside of the two institutions at which the investigation was conducted. However, we believe that these results reinforce data previously published by investigators in other regions of the country and provide a broad perspective of AYA study enrollment inclusive of supportive care trials as well as the full age and diagnostic spectrum. We were not able to match NOTIS data to patient data in many cases which makes it difficult to fully characterize the types of studies in which AYAs participated. This may have resulted in an underestimation of the percentage of patients enrolled on NCI or cooperative group sponsored studies. However, our institution has since corrected this limitation by requiring linkage of NOTIS and EDW data via consistent entry of patient identifiers, thus fostering future investigations. We also do not know the reasons some patients were not enrolled on studies (e.g., refusals, lack of available trials; lack of eligibility for available trials). This is a broader concern and limitation as noted by Freyer and Seibel [10]. These authors called for national-level mechanisms that would link incident cancer cases with clinical trial enrollment to more accurately track enrollment proportions with aims of measuring the

impact of new strategies for increasing AYA study participation. This mechanism would have potential to capture reasons for non-enrollment, including trial availability.

In summary, these analyses provided a greater understanding of the current state of AYA enrollment rates in clinical studies at a major adult-based comprehensive cancer center and pediatric affiliate in the Midwestern United States. A greater awareness of strengths and limitations will advise program development and methods for tailoring existing innovations to increase the availability of trials and participation of AYAs at our institutions and may have implications for other institutions and cancer practices who are also seeking to improve AYA clinical trial participation. For example, awareness of such limitations was the impetus for creating a clinical role at the RHLCCC entitled Clinical Research and Education Specialist. This position was created to implement innovative methods to promote clinical trial enrollment among marginalized and understudied populations such as AYAs and racial/ethnic minorities. Methods include providing education about clinical trials and related resources to patients and referring physicians, cultivating and expanding community partnerships, and stimulating new trials and novel discoveries via collaborations with pharmaceutical companies, peer institutions, and clinicians. A multimedia campaign is also utilized to promote trial awareness via social media, patient and provider newsletters, clinical trial awareness days for referring physicians, an online clinical trial database, and a mobile app. We are already taking steps to tailor the broader initiatives to AYAs as well as ongoing clinical programming with the potential to improve clinical outcomes such as provision of psychosocial support and fertility services. We are also currently planning to develop a shared AYA tumor board across sites as well as collaborations within the Northwestern Developmental Therapeutics Institute.

Finally, strategies for fostering clinical trial availability and AYA enrollment in the USA have been published previously with in-depth discussions of both local and systemic approaches, including but not limited to AYA medical education, development of AYA programs, and addressing referral patterns and expansion of national cooperative group initiatives [9, 10, 17, 18]. The proposed strategy of influencing referrals to cancer centers with AYA programs, NCI-designated centers or pediatric cancer centers may be a necessary but not sufficient approach to meeting the greater needs of AYAs with cancer. Greater emphasis must be placed on community engagement as a key component to adequately reach a population of patients that are largely treated in community oncology settings. Opportunity for such engagement is greater than it has been previously with the establishment of the National Clinical Trials Network and NCI Community Oncology Research Program which is designed to help increase access to clinical research for populations like AYAs [9, 10, 18]. Interestingly, a recent examination of AYA enrollment on COG trials within the Community Clinical Oncology Program (CCOP now named NCI Community Oncology Research Program) found proportional AYA enrollments at CCOP sites to be lower than non-CCOP sites [19]. While this outcome is certainly discouraging, it elucidates the complexity of the challenge we face as AYA advocates. While challenges differ from one institution to the next and from one country to the next, there are certainly commonalities that exist and we can often learn from the work of others. Clearly, the way forward is not merely as individual institutions but collectively as a community of AYA advocates.

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Table 1Patient demographics ($N = 2154$)

	RHLCCC ($n = 1946$)		ARHLCH ($n = 208$)	
	Mean (SD)	Median (range)	Mean (SD)	Median (range)
Age, years	31.7 (5.7)	33 (15–39)	17.1 (2.5)	16 (15–33)
	<i>N</i>	%	<i>N</i>	%
Less than 30 years old	634	32.6	206	99.0
Female	1271	65.3	93	44.7
Hispanic or Latino	182	11.9	53	25.5
Race				
White	1155	74.7	178	85.6
Black or African American	151	9.8	22	10.6
Asian	84	5.4	4	1.9
Other	156	10.1	4	1.9
Private insurance (HMO, PPO, etc.)	1452	74.6	151	75.9
Diagnosis				
Brain/central nervous system cancers	166	8.5	45	21.7
Head/neck/sarcoma	141	7.2	36	17.4
Leukemia/myeloma	108	5.6	37	17.9
Lymphoma	293	15.1	44	21.3
Other	111	5.7	44	21.4
Breast cancer	485	24.9		
Gastrointestinal cancers	143	7.4		
Genitourinary cancers	78	4.0		
Gynecological cancers	196	10.1		
Skin cancers	225	11.6		

Ethnicity information missing for $n = 415$; race missing for $n = 400$

HMO health maintenance organization, *PPO* preferred provider organization

Table 2

Protocol details

RHLCCC		ARHLCH		
Protocol type	N	%	Protocol type	N %
Investigator initiated trials	103	62.05	Investigator initiated trials	10 33.3
NCI	20	12.05	NCI	2 6.7
NU	83	50.00	CMH	8 26.7
Cooperative group trials	23	13.86	Cooperative group trials	18 60.0
Alliance	4	2.41	COG	14 46.7
CALGB	2	1.20	PBTC	4 13.3
ECOG	6	3.61		
GOG	1	0.60		
RTOG	3	1.81		
SWOG	7	4.22		
Industry trials	40	24.10	Industry trials	2 6.7
Study type			Study type	
Early detection	1	0.6		
Screening	2	1.2		
Supportive care	72	43.4	Supportive care	3 10.0
Therapeutic	91	54.8	Therapeutic	27 90.0
Frequency missing = 52 (23.85%)		Frequency missing = 58 (65.90%)		

Alliance Alliance for Clinical Trials in Oncology; CALGB Cancer and Leukemia Group B; CMH Children's Memorial Hospital or ARHLCH; COG Children's Oncology Group; ECOG Eastern Cooperative Oncology Group; GOG Gynecologic Oncology Group; NCI National Cancer Institute; NU Northwestern University; PBTC Pediatric Brain Tumor Consortium; RTOG Radiation Therapy Oncology Group; SWOG Southwest Oncology Group

Table 3

Predictors of trial participation, bivariate tests—ARHLCH

	Odds ratio (95% CI)	Mixed model <i>p</i> value^a
Female (vs male)	1.10 (0.52, 2.30)	0.793
Not Hispanic or Latino (vs Hispanic)	0.55 (0.23, 1.34)	0.162
Black or other (vs White)	0.25 (0.08, 0.81)	0.026
HMO/PPO (vs Medicaid)	2.80 (1.11, 7.08)	0.033
Diagnosis name		0.221
Brain (vs other)	0.68 (0.18, 2.59)	
Leukemia (vs other)	1.55 (0.41, 5.88)	
Lymphoma (vs other)	0.88 (0.24, 3.23)	
Sarcoma (vs other)	0.38 (0.10, 1.47)	

HMO health maintenance organization, *PPO* preferred provider organization^aMixed model included a random effect for oncologist name to account for correlated data within providers

Table 4

Predictors of trial participation, multivariable model—RHLCCC

	Odds ratio (95% CI)	Mixed model <i>p</i> value ^a
Ethnicity		<0.001
Declined (vs not Hispanic)	0.71 (0.40, 1.25)	
Hispanic or Latino (vs not)	2.71 (1.65, 4.45)	
Race		0.001
Black (vs White)	0.82 (0.48, 1.40)	
Other/unknown (vs White)	0.42 (0.27, 0.66)	
Payer name		0.047
Financial assistance (vs private)	0.56 (0.32, 1.00)	
Medicaid (vs private)	1.45 (0.94, 2.24)	
Medicare (vs private)	1.12 (0.23, 5.42)	
Diagnosis name ^b		0.010
Brain/central nervous system cancers	0.64 (0.28, 1.47)	
Breast cancer	0.66 (0.33, 1.32)	
Gastrointestinal cancers	0.89 (0.40, 1.97)	
Genitourinary cancers	0.44 (0.15, 1.34)	
Gynecologic cancers	0.16 (0.06, 0.46)	
Head/neck/sarcoma	1.16 (0.48, 2.82)	
Lymphoma	0.70 (0.33, 1.46)	
Skin cancers	0.28 (0.11, 0.72)	
Other	0.48 (0.20, 1.20)	

^aMixed model included a random effect for provider name to account for correlated data within providers^bReference group for diagnosis = leukemia/myeloma