Title

Participation in pediatric oncology research protocols: Racial/ethnic, language and age-based disparities

Journal

Pediatric Blood & Cancer, 62(8)

ISSN

1545-5009

Authors

Aristizabal, Paula
Singer, Jenelle
Cooper, Renee
et al.

Publication Date

2015-08-01

DOI

10.1002/pbc.25472

Peer reviewed

HHS Public Access

Author manuscript

Pediatr Blood Cancer. Author manuscript; available in PMC 2016 August 01.

Published in final edited form as:

Pediatr Blood Cancer. 2015 August ; 62(8): 1337–1344. doi:10.1002/pbc.25472.

Participation in Pediatric Oncology Research Protocols: Racial/ethnic, Language and Age-based Disparities

Paula Aristizabal, MD, MASc[1,2,3], **Jenelle Singer, MPH**[1], **Renee Cooper, MPH**[4], **Kristen J. Wells, PhD, MPH**[5,6], **Jesse Nodora, DrPH**[3,6], **Mehrzad Milburn, RN, BSN, CCRC**[1], **Sheila Gahagan, MD, MPH**[1,2], **Deborah E. Schiff, MD**[1,2], and **Maria Elena Martinez, PhD**[3,6]

[1]Department of Pediatrics, University of California San Diego, San Diego, CA

[2]Division of Pediatric Hematology/Oncology, Rady Children's Hospital San Diego, San Diego, CA

[3]Moores Cancer Center, University of California San Diego, La Jolla, CA

[4]Graduate School of Public Health, San Diego State University, San Diego, CA

[5]Department of Psychology, San Diego State University, San Diego, CA

[6]Department of Family and Preventive Medicine, University of California San Diego, La Jolla, CA

Abstract

Background—Survival rates in pediatric oncology have improved dramatically, in part due to high patient participation in clinical trials. Although racial/ethnic inequalities in clinical trial participation have been reported in adults, pediatric data and studies comparing participation rates by socio-demographic characteristics are scarce. The goal of this study was to assess differences in research protocol participation for childhood cancer by age, sex, race/ethnicity, parental language, cancer type and insurance status.

Procedure—Data on enrollment in any protocol, biospecimen, or therapeutic protocols were collected and analyzed for newly diagnosed pediatric patients with cancer from 2008–2012 at Rady Children's Hospital.

Results—Among the 353 patients included in the analysis, 304 (86.1%) were enrolled in any protocol. Enrollment in biospecimen and therapeutic protocols was 84.2% (261/310) and 81.1% (206/254), respectively. Logistic regression analyses revealed significant enrollment underrepresentation in any protocol for Hispanics compared to Non-Hispanic whites (81% vs. 91%; Odds Ratio [OR], 0.43; 95% Confidence Interval [CI], 0.21–0.90; p=0.021) and among children of Spanish-speaking vs. English-speaking parents (78% vs. 89%; OR, 0.45; 95%CI, 0.23–0.87; p=0.016). Compared to patients aged 0–4 years, significant underrepresentation was also found among patients 15–21 years old (92% vs.72%; OR, 0.21; 95% CI, 0.09–0.48; p<0.001).

Corresponding author: Paula Aristizabal, MD, MASc, Rady Children's Hospital San Diego, 3020 Children's Way, Suite 209, MC 5035, San Diego, CA, 92123, Phone: (858) 966-5811, Fax: (858) 966-8035, paristizabal@rchsd.org.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIC, NIH or ACS.

Similar trends were observed when analyzing enrollment in biospecimen and therapeutic protocols separately.

Conclusions—There was significant underrepresentation in protocol participation for Hispanics, children of Spanish-speaking parents, and patients ages 15–21. Research is urgently needed to understand barriers to research participation among these groups underrepresented in pediatric oncology clinical trials.

Keywords

Pediatric oncology; Outcomes research; Clinical trials; Race/ethnicity; Disparities

INTRODUCTION

In the United States, approximately 15,700 children under 21 years old are diagnosed with cancer each year [1, 2]. Although cancer is rare in children, the incidence of childhood cancer has been increasing approximately 1% per year for over a decade [3]. It has been reported that both non-Hispanic whites (NHWs) and Hispanics have the highest incidence rates for childhood and adolescent cancers overall [2]. While Hispanic children have a significantly higher incidence of B-cell leukemias and lymphomas [4–6], survival trends for primary cancers in children demonstrate that Hispanic, and black non-Hispanic children have poorer 5-year survival rates than their NHW counterparts (74% and 73% vs. 81%, respectively, $p<0.0001$) [5, 7]. This disparity in survival outcomes between Hispanic and NHW patients may indicate that we do not yet have a clear understanding of the underlying factors and have not yet developed effective interventions to improve outcomes specific to certain populations [8]. Factors that could potentially be associated with these survival disparities include biological differences, socioeconomic status, parental education, health insurance status, enrollment in clinical trials and knowledge about cancer [2, 9].

Over the past several decades, medical centers across the United States (U.S.) have cooperated to study and treat childhood cancer. Survival rates and quality of life for pediatric patients with cancer have improved dramatically, in part, as a result of the success in enrollment in clinical trials. Throughout the 1990s, approximately 70% of all patients with cancer under 19 years of age were enrolled in therapeutic clinical trials [10, 11]. However, patients between 15 and 19 years are less likely to enroll in cancer clinical trials compared to children younger than 15 years old [11, 12]. Overall enrollment in cancer clinical trials has declined in the past 15 years, with the current national enrollment rate estimated to be 52% of all patients with cancer under 15 years old [3]. Low enrollment of adult racial/ethnic minorities in clinical trials has been documented for more than 20 years and some racial/ethnic minorities continue to be underrepresented in cancer clinical trials, including African-American men, Hispanic/Latinos, Asian Pacific Islanders and American Indian/Alaskan Natives [11]. Low socioeconomic status and rural residence also appear to be associated with low enrollment in clinical trials. Although racial/ethnic inequalities in cancer clinical trial participation have been extensively reported in adults [8, 12–19], little work has been done to describe and understand racial/ethnic disparities in research protocol enrollment in the pediatric population [1, 3–5, 10, 11, 20–22]. To address this important gap, we conducted a retrospective cohort study to examine the participation in research protocols,

including biospecimen and therapeutic trials, of children diagnosed with cancer at Rady Children's Hospital San Diego (RCHSD) from 2008 to 2012. Specifically, our aim was to identify differences in research protocol participation by age, sex, race/ethnicity, primary parental language, cancer type and insurance status. We hypothesized that Hispanics, adolescents and young adults, children of Spanish-speaking parents, and Medicaid patients would be underrepresented in clinical protocol enrollment. Our main comparisons were between Hispanic and NHW children and adolescents, because Hispanics and NHWs are the largest racial/ethnic groups in our population.

METHODS

Study Population and Data Sources

We performed a retrospective analysis of 869 patients who were evaluated for a previously untreated cancer at RCHSD, San Diego, California, between January 1, 2008, and December 31, 2012. The Institutional Review Board for University of California San Diego/RCHSD approved this study.

Cases were identified via the RCHSD Tumor Registry. Newly diagnosed oncology patients 21 years old and under, treated at the Peckham Center for Cancer and Blood Disorders at RCHSD during the study period and eligible for an open biospecimen and/or therapeutic research protocol were considered to be eligible for the analysis. A total of 353 children met the inclusion criteria for this study. Patients with the following characteristics were not eligible for our study (n=516): research protocol not available (n=230), benign tumors (n=112), diagnosis and/or treatment outside of RCHSD (n=94), not initially seen by a pediatric hematologist/oncologist at RCHSD for diagnosis (n=61), considering transfer of care to another country (n=11) and second malignancy (n=8) [Figure 1].

The RCHSD Tumor Registry and the RCHSD Hematology/Oncology Research Center database were used to determine if subjects were enrolled in biospecimen and/or therapeutic protocols sponsored by the Children's Oncology Group (COG) or St. Jude Children's Research Hospital. We reviewed medical records from all cases identified to verify the data collected from the RCHSD Tumor Registry and the Hematology/Oncology Research Center database. We collected data on age at diagnosis, sex, race/ethnicity, parental primary language (i.e., English or Spanish), cancer type (i.e., solid or hematologic malignancy), insurance status (i.e., Medicaid, private or self-pay) and clinical protocol enrollment information. Data on race/ethnicity were initially ascertained from the medical record. However, some entries were based on self-report, and others inferred from last name information collected by administrative admission staff. In order to diminish race/ethnicity misclassification, we used several methods to ascertain this variable, including review from: 1) the hospital medical record face sheet; 2) description by social worker and/or physician in history and physical; and 3) all demographics forms, including those completed by the patient's parent or legal guardian. In the 11 remaining cases for which race/ethnicity information was not collected or discrepant information was found, the primary oncologist was consulted for verification. Race/ethnicity was compiled into 5 groups: NHW, Black Non-Hispanic, Hispanic, Asian/Pacific Islander, and mixed/multiple.

Primary parental language was determined by the language they selected for the questionnaire and, where applicable, the language used by the interpreter. Individuals were categorized as English-speaking, Spanish-speaking, or other. Age was categorized into four groups: 0–4 years, 5–9 years, 10–14 years, and 15–21 years.

Protocol Enrollment

We calculated counts of patients enrolled overall and by subgroups of interest along with a denominator count of total eligible cases for the enrollment period of January 1, 2008, to December 31, 2012. Every pediatric patient with cancer who is newly diagnosed and treated at RCHSD may be eligible for one or more protocols. Clinical protocols were divided into 2 groups which were not mutually exclusive. Thus, an eligible patient may have been enrolled in a biospecimen protocol and/or therapeutic protocol. Enrolled patients met eligibility criteria for protocol enrollment on an open protocol, and they/their parent or guardian consented to participate on one or more protocols. Patients who were eligible but did not participate in a research protocol were considered to be not enrolled in any protocol (n=49). Reasons for non-enrollment included: parent declined (n=22), physician perceived barrier (n=15), critical clinical status (n=7), protocol exclusion (n=3), and Research Center logistics (n=2) [Figure 1]. Out of the total analytic sample of patients eligible for any protocol (n=353), 310 patients were eligible to enroll in a biospecimen protocol and 254 were eligible to enroll in a therapeutic protocol.

Statistical Analyses

After obtaining counts of eligible patients for each protocol by age, sex, race/ethnicity, parental language, cancer type and insurance status, we compared the proportions of patients whose parents chose not to enroll their child in a research study compared to those who chose to enroll their child in a study. For race/ethnicity comparisons, differences in enrollment rates were primarily focused on Hispanics and NHWs due to the small number of patients from other racial groups in our cohort.

We used logistic regression to model the relationship between the log-odds for enrollment in the protocol of interest (dependent variable) according to patient age, sex, race/ethnicity, parental language, cancer type and insurance status (independent variables). We conducted these analyses for each of the three enrollment outcomes: any protocol, biospecimen protocols and therapeutics protocols. We first calculated crude odds ratios (OR) and their 95% confidence intervals (CIs) for each independent variable. We next conducted two types of multivariate models. The first model considered all the variables excluding primary language use, and the second included all variables, excluding race/ethnicity. We did not model both language use and race/ethnicity in a single model due to their high correlation (i.e., parents of NHWs all spoke only English). Cancer type and insurance status were not significant predictors of enrollment and were removed from the models. ORs and 95% CIs were generated for each variable. Significant associations were identified if the CI did not include 1. Basic descriptive statistics for the study population were calculated using SPSS statistical software (version 21.0.0.0; SPSS Inc., Chicago, IL). All other analyses were completed using R (version 3.0.1.; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Patient Characteristics

Baseline characteristics for patients included in the analysis (n=353) are shown in Table I. The largest group of patients was 4 years old and under (48%). Of the total, 41% were Hispanic and 37% were NHW; 22% of the parents were Spanish-speaking. We found similar distributions by sex and by type of cancer (solid and hematologic malignancy). The majority of patients had either private or Medicaid insurance (Medi-Cal in California).

Protocol Enrollment

The overall accrual to any protocol was 86.1% (304/353); accrual rates for biospecimen and therapeutic protocols were 84.2% (261/310) and 81.1% (206/254), respectively. We also assessed enrollment according to year of diagnosis and compared NHW vs. Hispanic participation across the study period. Overall enrollment in research protocols declined between 2008 and 2009 and increased between 2009 and 2012 (Figure 2). Enrollment for Hispanics was below that of NHWs when participation was analyzed across all five study years (OR, 0.43; 95%CI, 0.21–0.89). Fifty-three percent of the parents that declined participation in a research study were of Hispanic origin, whereas 20% were NHW.

Protocol Enrollment by Socio-demographics

Table II shows any protocol enrollment by demographic characteristics (age, sex, race/ethnicity), cancer type, primary parental language, and insurance status. In the crude model, children 5–9 and 15–21 years old were significantly less likely to be enrolled in a research protocol compared to children aged 0–4 years (81% vs. 92%; OR, 0.35; 95% CI, 0.16–0.80; p=0.010 and 72% vs. 92%; OR, 0.21; 95% CI, 0.09–0.48; p<0.001, respectively). Hispanic patients were less likely to be enrolled in research protocols compared to NHWs (81% vs. 91%; OR, 0.43; CI, 0.21–0.90; p=0.021). Furthermore, children of Spanish-speaking parents were significantly less likely to be enrolled in any protocol compared to English-speakers 78% vs. 89%; (OR, 0.45; CI, 0.23–0.87; p=0.016). We found no significant differences in protocol enrollment for other racial groups, by sex, by cancer type or by insurance status. Overall, results were similar in the multivariate adjusted models.

Tables III and IV show crude and adjusted ORs separately for the biospecimen and therapeutic protocols. Similar to the previous findings, children who were 5–9 and 15–21 years old and of Hispanic ethnicity were less likely to be enrolled in the biospecimen protocols (Table III). Likewise, a significant lower likelihood of enrolling in biospecimen protocols was found for children of Spanish-speaking parents compared to children of English-speaking parents (73% vs. 88%; OR, 0.37; CI, 0.19–0.72; p=0.003). The findings were similar for enrollment in therapeutic protocols for age and race/ethnicity.

DISCUSSION

Cancer clinical trial accrual rates remain low for racial/ethnic minority populations despite the National Cancer Institute's efforts towards and support for the inclusion of more women and minorities in cancer research [5, 12]. There is good documentation that Hispanic adults

are underrepresented in cancer clinical trials [18, 22]. In our large pediatric oncology center, the overall enrollment rate in any protocol was 86.1% for patients for whom there was an open protocol. Our study excluded 230 children for whom there was no open protocol available. When these patients are included, the enrollment rate is 52.1% (304/583), similar to a 2001 reported national rate of clinical trial enrollment in patients 0–15 years of age [3]. In our cohort, participation in pediatric oncology clinical research was significantly lower among Hispanics compared to NHWs, and for patients ages 5 to 9 years and 15 to 21 years of age compared to patients 4 years old and under. For any and biospecimen protocols, we found lower participation among children of Spanish-speaking parents. We did not observe any significant associations between insurance status and enrollment. However, lack of insurance has been previously associated with lower clinical trial participation among adolescent and Hispanic patients with cancer [8, 14, 20, 23].

We are not aware of prior research on childhood cancer clinical protocol participation comparing Hispanic to NHW patients. In fact, racial and ethnic differences in pediatric cancer clinical trial participation are understudied [19], with several studies finding that black children were underrepresented in enrollment in cancer clinical trials compared to NHWs [24–27]. A current problem in the field is that minority patients have fewer opportunities to participate in research and outcomes data are based on information obtained mostly from NHW patients. This leads to inadequate information to assess whether or not treatments or diagnostic procedures have the same benefits for underrepresented groups. The racial/ethnic disparities in research participation revealed by our study are highly relevant to the rapidly changing demographics in the U.S. According to the 2013 U.S. Census, Hispanic children comprise 46% of the total population in San Diego, compared to 33% for NHWs [28, 29]. Further, it has been projected that by 2050, Hispanics will make up 29% of the U.S. population and 50% of the California population [30]. In response to these shifting demographics, there will be a need to develop diagnostic tests and cancer treatments that are effective for this growing population. Thus, it is imperative that clinical trials and other research studies include more participation by Hispanic pediatric patients with cancer.

Ford et al. have elucidated the need for a standardized and more quantitative approach to understand barriers and related solutions to participation in clinical trials [8]. Their systematic review proposes a conceptual framework with three categories of barriers: opportunity, awareness, and acceptance. Opportunity barriers relate to socio-demographic factors which may exclude individuals from participation. Awareness barriers include a patient’s lack of knowledge and/or understanding of cancer and/or clinical trials. Acceptance barriers are those that hinder patients from accepting enrollment in a clinical trial. In our study, reasons for parents’ decline of participation in a study could have been influenced by language barriers and cultural traditions [31], such as the tradition of respect. Respect, a Hispanic cultural tradition of passivity in the presence of an authoritative figure, such as a physician, is associated with asking fewer questions even when there is a need for clarification of very difficult concepts and information [17, 32]. Unique to the setting of childhood cancer, language and cultural barriers become more pronounced in the emotionally straining situation that childhood cancer presents to parents [33]. When asked for consent during such a sensitive period, parents of racial/ethnic minority children reportedly feel more anxiety and less control over their decision-making than NHW parents

[34, 35]. Given that parent mentor programs have been found to significantly improve clinical outcomes in pediatric patients with other chronic diseases [36], similar strategies, including patient navigators could be considered to support parents of children with newly diagnosed cancer. Furthermore, offering the support of a parent mentor or a patient navigator who shares the same race/ethnicity, culture, and primary language could be explored in future studies as an intervention to facilitate clinical trial accrual procedures among Hispanic patients.

In most pediatric cancer centers in the U.S, protocols are offered to all eligible patients 21 years old and under for all cancer types. Despite this eligibility, 5–9 and 15–21 year olds were found to be underrepresented in research studies in our cohort. Consistent with the literature [23, 37], we found that adolescents and young adults (15–21 years old) were less likely to participate in clinical protocols at our institution. Adolescents have unique socio-psychological needs, tend to have a strong sense of independence, and may be mistrusting of healthcare professionals [38]. Moreover, physicians who are not specialists in adolescent medicine may lack the necessary training to care for this population [39]. Thus, when considering this underrepresentation, it may be possible to consider the use of peer-centered support groups, similar to some of the interventions used in tobacco prevention [40], given that these patients are more dependent and focused on their peers.

Determining opportunity barriers to participation in clinical research relies heavily on the quality of communication between the patient and his/her provider. Poor communication between providers and patients with limited English proficiency has a profound effect on quality of patient care [41, 42]. We suggest that communication barriers between physicians and patients when presenting a research protocol could be influenced by potential cultural, language and racial/ethnic mismatch. Nodora et al. [43] reported that physician fluency in Spanish is more important than physician ethnicity when adult Hispanic patients are presented with a clinical trial and are faced with the decision to participate. Kuo et al. found that 22% of monolingual physicians do not feel prepared to communicate with limited English proficiency individuals [42]. Clinicians may be more likely to omit information, not present consent documentation, and are less likely to use partnership-building statements when communicating with minority parents [34, 44]. Howerton et al. further found that clinicians perceive a mistrust from minority parents, which in turn negatively affects how they deliver the research protocol information [15]. The need for improved strategies to raise cultural awareness and sensitivity among healthcare providers has been reported in the literature [42, 45].

For patients with limited English proficiency, the use of interpreter services has proven to be effective in dissolving the language barrier to health care access [41] and has resulted in improved medical outcomes and increased patient satisfaction [42]. In particular, a trained in-person interpreter should be fully available to patients with limited English proficiency during conferences for cancer diagnosis and clinical trial enrollment. Furthermore, physicians and other providers may benefit from training in the use of interpretation services. Training staff on how to use interpretation services has been shown to improve odds significantly for using the services than in facilities whose staff was not trained [41].

There are few pediatric oncologists of Hispanic origin in the U.S. For example at RCHSD, only one staff physician in Pediatric Hematology/Oncology is of Hispanic origin and fluent in Spanish and only one interpreter is on staff full time to serve the Spanish-speaking patients who comprise approximately 30% of the hematology/oncology patient population at our institution. Moreover, during the study period, particularly in early years, the majority of COG consents were not routinely translated into other languages and only 60% of all cancer protocol written consent documents were translated to Spanish in our institution. Currently, 80% of phase III therapeutic protocols are translated into Spanish. Even when translated, these documents may be void of some cultural context and written consent documents may remain difficult to understand as translation is done directly from English. This may present a barrier to participation in clinical research [46]. Reducing language barriers is crucial to improving access to clinical trials.

Because our data were from a single institution, the results are not generalizable to all Hispanic patients and parents in the U.S. In addition, the limited sample size of children from other racial/ethnic groups likely impacted some of the statistical comparisons. Another limitation is that modifiable psychosocial, behavioral or environmental factors were not assessed in this study. Additionally, we did not include any ancillary research studies, such as supportive care studies designated to evaluate symptom management, since there were no such open protocols at the time of the study period. Further studies should engage Hispanic pediatric oncology patients and their caregivers to evaluate these factors with validated survey instruments in Spanish, in order to develop culturally and linguistically appropriate interventions for this underserved population, such as anticipatory guidance tools.

CONCLUSION

The majority of progress in pediatric oncology is a direct result of clinical trial participation, which has led to great improvements in cancer care, quality of life, and survival outcomes in the past decade. Clinical trials, therefore, are crucial for progress in survival rates for childhood cancer. As such, disparities in cancer treatment and survival outcomes must be addressed by adequate inclusion of underrepresented minority pediatric patients in clinical trials and other clinical research. A major objective of all research centers should be to attain accrual rates representative of the demographics of the population they serve. As the population in the U.S. continues to change from a NHW majority to a Hispanic majority, action must be taken to prepare the healthcare system for these changes to equitably accommodate patients from this and other racial/ethnic groups. For regions that serve a large segment of the Hispanic population, more focus should be placed on equal representation of children in pediatric oncology clinical research. Characterization of modifiable factors affecting trial accrual is urgently needed to understand and address barriers, including those related to patient-provider communication, health literacy and to the informed consent process in pediatric oncology.

Acknowledgments

The authors thank Courtney Thornburg, MD, MS and Amy Geddis, MD, PhD for their contributions to the revision of the manuscript, Malaika Tobias, MPH, who assisted in the formatting of the manuscript and Michael Donohoue

and Gordon Honerkamp-Smith (University of California San Diego Clinical and Translational Research Institute) for statistical support.

Grant Support:

This project was partially supported by the National Cancer Institute (NCI) Research Supplements to Promote Diversity in Health-related research to the Specialized Cancer Center Support Grant, P30CA23100 (Lippman, PI), the National Institute of Health (NIH) grant ULTR000100 (Firestein, PI) and American Cancer Society(ACS) Mentored Research Scholar grant MRSG-11-102-01-CPPB- ACS/MRSG (Nodora, PI).

Abbreviations

COG	Children's Oncology Group
CI	Confidence Interval
NHWs	Non-Hispanic Whites
RCHSD	Rady Children's Hospital San Diego
OR	Odds Ratio
U.S	United States

References

1. Liu L, Krailo M, Reaman GH, Bernstein L. Surveillance and End Results Childhood Cancer Linkage. Childhood cancer patients' access to cooperative group cancer programs: a population-based study. Cancer. 2003; 97(5):1339–45. [PubMed: 12599243]
2. Ward E, Desantis C, Robbins A, Kohler B, Jemal A. Childhood and adolescent cancer statistics, 2014. CA Cancer J Clin. 2014
3. Shochat SJ, Fremgen AM, Murphy SB, Hutchison C, Donaldson SS, Haase GM, Provisor AJ, Clive-Bumpus RE, Winchester DP. Childhood cancer: patterns of protocol participation in a national survey. CA Cancer J Clin. 2001; 51(2):119–30. [PubMed: 11577480]
4. Bhatia S. Disparities in cancer outcomes: lessons learned from children with cancer. Pediatr Blood Cancer. 2011; 56(6):994–1002. [PubMed: 21328525]
5. Bhatia S, Sather HN, Heerema NA, Trigg ME, Gaynon PS, Robison LL. Racial and ethnic differences in survival of children with acute lymphoblastic leukemia. Blood. 2002; 100(6):1957–64. [PubMed: 12200352]
6. Dores GM, Devesa SS, Curtis RE, Linet MS, Morton LM. Acute leukemia incidence and patient survival among children and adults in the United States, 2001–2007. Blood. 2012; 119(1):34–43. [PubMed: 22086414]
7. Linabery AM, Ross JA. Childhood and adolescent cancer survival in the US by race and ethnicity for the diagnostic period 1975–1999. Cancer. 2008; 113(9):2575–96. [PubMed: 18837040]
8. Ford JG, Howerton MW, Lai GY, Gary TL, Bolen S, Gibbons MC, Tilburt J, Baffi C, Tanpitukpongse TP, Wilson RF, Powe NR, Bass EB. Barriers to recruiting underrepresented populations to cancer clinical trials: a systematic review. Cancer. 2008; 112(2):228–42. [PubMed: 18008363]
9. Bhatia S. Influence of race and socioeconomic status on outcome of children treated for childhood acute lymphoblastic leukemia. Curr Opin Pediatr. 2004; 16(1):9–14. [PubMed: 14758108]
10. Lund MJ, Eliason MT, Haight AE, Ward KC, Young JL, Pentz RD. Racial/Ethnic Diversity in Children's Oncology Clinical Trials. Cancer. 2009; 115(16):3808–3816. [PubMed: 19484783]
11. Tejeda HA, Green SB, Trimble EL, Ford L, High JL, Ungerleider RS, Friedman MA, Brawley OW. Representation of African-Americans, Hispanics, and whites in National Cancer Institute cancer treatment trials. J Natl Cancer Inst. 1996; 88(12):812–6. [PubMed: 8637047]
12. Swanson GM, Ward AJ. Recruiting minorities into clinical trials: toward a participant-friendly system. J Natl Cancer Inst. 1995; 87(23):1747–59. [PubMed: 7473831]

13. Baker KS, Loberiza FR Jr, Yu H, Cairo MS, Bolwell BJ, Bujan-Boza WA, Camitta BM, Garcia JJ, Ho WG, Liesveld JL, Maharaj D, Marks DI, Schultz KR, Wiernik P, Zander AR, Horowitz MM, Keating A, Weisdorf DJ. Outcome of ethnic minorities with acute or chronic leukemia treated with hematopoietic stem-cell transplantation in the United States. J Clin Oncol. 2005; 23(28):7032–42. [PubMed: 16145067]
14. Godden S, Ambler G, Pollock AM. Recruitment of minority ethnic groups into clinical cancer research trials to assess adherence to the principles of the Department of Health Research Governance Framework: national sources of data and general issues arising from a study in one hospital trust in England. J Med Ethics. 2010; 36(6):358–62. [PubMed: 20439335]
15. Howerton MW, Gibbons MC, Baffi CR, Gary TL, Lai GY, Bolen S, Tilburt J, Tanpitukpongse TP, Wilson RF, Powe NR, Bass EB, Ford JG. Provider roles in the recruitment of underrepresented populations to cancer clinical trials. Cancer. 2007; 109(3):465–76. [PubMed: 17200964]
16. Jimenez R, Zhang B, Joffe S, Nilsson M, Rivera L, Mutchler J, Lathan C, Paulk ME, Prigerson HG. Clinical trial participation among ethnic/racial minority and majority patients with advanced cancer: what factors most influence enrollment? J Palliat Med. 2013; 16(3):256–62. [PubMed: 23384245]
17. Kagawa-Singer M, Dadia AV, Yu MC, Surbone A. Cancer, culture, and health disparities: time to chart a new course? CA Cancer J Clin. 2010; 60(1):12–39. [PubMed: 20097836]
18. Murthy VH, Krumholz HM, Gross CP. Participation in cancer clinical trials: race-, sex-, and age-based disparities. JAMA. 2004; 291(22):2720–6. [PubMed: 15187053]
19. Swanson GM, Bailar JC. Selection and description of cancer clinical trials participants--science or happenstance? Cancer. 2002; 95(5):950–9. [PubMed: 12209677]
20. Flores G. Committee on Pediatric Research. Technical report--racial and ethnic disparities in the health and health care of children. Pediatrics. 2010; 125(4):e979–e1020. [PubMed: 20351000]
21. Howell DL, Ward KC, Austin HD, Young JL, Woods WG. Access to pediatric cancer care by age, race, and diagnosis, and outcomes of cancer treatment in pediatric and adolescent patients in the state of Georgia. J Clin Oncol. 2007; 25(29):4610–5. [PubMed: 17925556]
22. Walsh C, Ross LF. Are minority children under- or overrepresented in pediatric research? Pediatrics. 2003; 112(4):890–5. [PubMed: 14523182]
23. 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(7 Suppl):1645–55. [PubMed: 16906507]
24. Pui CH, Pei D, Pappo AS, Howard SC, Cheng C, Sandlund JT, Furman WL, Ribeiro RC, Spunt SL, Rubnitz JE, Jeha S, Hudson MM, Kun LE, Merchant TE, Kocak M, Broniscer A, Metzger ML, Downing JR, Leung W, Evans WE, Gajjar A. Treatment outcomes in black and white children with cancer: results from the SEER database and St Jude Children's Research Hospital, 1992 through 2007. J Clin Oncol. 2012; 30(16):2005–12. [PubMed: 22547602]
25. Metzger ML, Castellino SM, Hudson MM, Rai SN, Kaste SC, Krasin MJ, Kun LE, Pui CH, Howard SC. Effect of race on the outcome of pediatric patients with Hodgkin's lymphoma. J Clin Oncol. 2008; 26(8):1282–8. [PubMed: 18323551]
26. Pui CH, Sandlund JT, Pei D, Rivera GK, Howard SC, Ribeiro RC, Rubnitz JE, Razzouk BI, Hudson MM, Cheng C, Raimondi SC, Behm FG, Downing JR, Relling MV, Evans WE. Results of therapy for acute lymphoblastic leukemia in black and white children. JAMA. 2003; 290(15): 2001–7. [PubMed: 14559953]
27. Rubnitz JE, Lensing S, Razzouk BI, Pounds S, Pui CH, Ribeiro RC. Effect of race on outcome of white and black children with acute myeloid leukemia: the St. Jude experience. Pediatr Blood Cancer. 2007; 48(1):10–5. [PubMed: 16642489]
28. U.S. Census Bureau. San Diego County, California. 2013. http://quickfacts.census.gov/gfd/states/06/06073.html
29. Summary: San Diego County. 2013. kidsdata.org[cited 2014 June 25]; Available at, http://www.kidsdata.org/region/368/san-diego-county/summary#6/demographics
30. Castaneda, X.; Wallace, S. Fact Sheet. University of California; Berkeley: 2010. Demographics Profile of Latinos in the United States.

31. Biedrzycki BA. Decision making for cancer clinical trial participation: a systematic review. Oncol Nurs Forum. 2010; 37(6):E387–99. [PubMed: 21059572]
32. Johns AL, Oland AA, Katz ER, Sahler OJ, Askins MA, Butler RW, Dolgin MJ. Qualitative analysis of the role of culture in coping themes of Latina and European American mothers of children with cancer. J Pediatr Oncol Nurs. 2009; 26(3):167–75. [PubMed: 19398713]
33. Simon CM, Siminoff LA, Kodish ED, Burant C. Comparison of the informed consent process for randomized clinical trials in pediatric and adult oncology. J Clin Oncol. 2004; 22(13):2708–17. [PubMed: 15226338]
34. Miller VA, Drotar D, Burant C, Kodish E. Clinician-parent communication during informed consent for pediatric leukemia trials. J Pediatr Psychol. 2005; 30(3):219–29. [PubMed: 15784918]
35. Simon C, Zyzanski SJ, Eder M, Raiz P, Kodish ED, Siminoff LA. Groups potentially at risk for making poorly informed decisions about entry into clinical trials for childhood cancer. J Clin Oncol. 2003; 21(11):2173–8. [PubMed: 12775743]
36. Flores G, Bridon C, Torres S, Perez R, Walter T, Brotanek J, Lin H, Tomany-Korman S. Improving asthma outcomes in minority children: a randomized, controlled trial of parent mentors. Pediatrics. 2009; 124(6):1522–32. [PubMed: 19948624]
37. Ferrari A, Montello M, Budd T, Bleyer A. The challenges of clinical trials for adolescents and young adults with cancer. Pediatr Blood Cancer. 2008; 50(5 Suppl):1101–4. [PubMed: 18360838]
38. Ferrari A, Bleyer A. Participation of adolescents with cancer in clinical trials. Cancer Treat Rev. 2007; 33(7):603–8. [PubMed: 17250970]
39. Shaw PH, Boyiadzis M, Tawbi H, Welsh A, Kemerer A, Davidson NE, Ritchey AK. Improved clinical trial enrollment in adolescent and young adult (AYA) oncology patients after the establishment of an AYA oncology program uniting pediatric and medical oncology divisions. Cancer. 2012; 118(14):3614–7. [PubMed: 22213134]
40. Thomas RE, Lorenzetti DL, Spragins W. Systematic review of mentoring to prevent or reduce tobacco use by adolescents. Acad Pediatr. 2013; 13(4):300–7. [PubMed: 23830017]
41. Flores G, Torres S, Holmes LJ, Salas-Lopez D, Youdelman MK, Tomany-Korman SC. Access to hospital interpreter services for limited English proficient patients in New Jersey: a statewide evaluation. J Health Care Poor Underserved. 2008; 19(2):391–415. [PubMed: 18469412]
42. Kuo DZ, O'Connor KG, Flores G, Minkovitz CS. Pediatricians' use of language services for families with limited English proficiency. Pediatrics. 2007; 119(4):e920–7. [PubMed: 17371933]
43. Nodora J, Nuno T, O'Day K, Yrun V, Garcia F. Barriers and facilitators to mexican-american participation in clinical trials: physician and patient focus group perspectives. Health. 2010; 2(7): 742–752.
44. Simon C, Eder M, Raiz P, Zyzanski S, Pentz R, Kodish ED. Informed consent for pediatric leukemia research: clinician perspectives. Cancer. 2001; 92(3):691–700. [PubMed: 11505417]
45. Seibert PS, Stridh-Igo P, Zimmerman CG. A checklist to facilitate cultural awareness and sensitivity. J Med Ethics. 2002; 28(3):143–6. [PubMed: 12042396]
46. Lakes KD, Vaughan E, Jones M, Burke W, Baker D, Swanson JM. Diverse perceptions of the informed consent process: implications for the recruitment and participation of diverse communities in the National Children's Study. Am J Community Psychol. 2012; 49(1–2):215–32. [PubMed: 21671109]

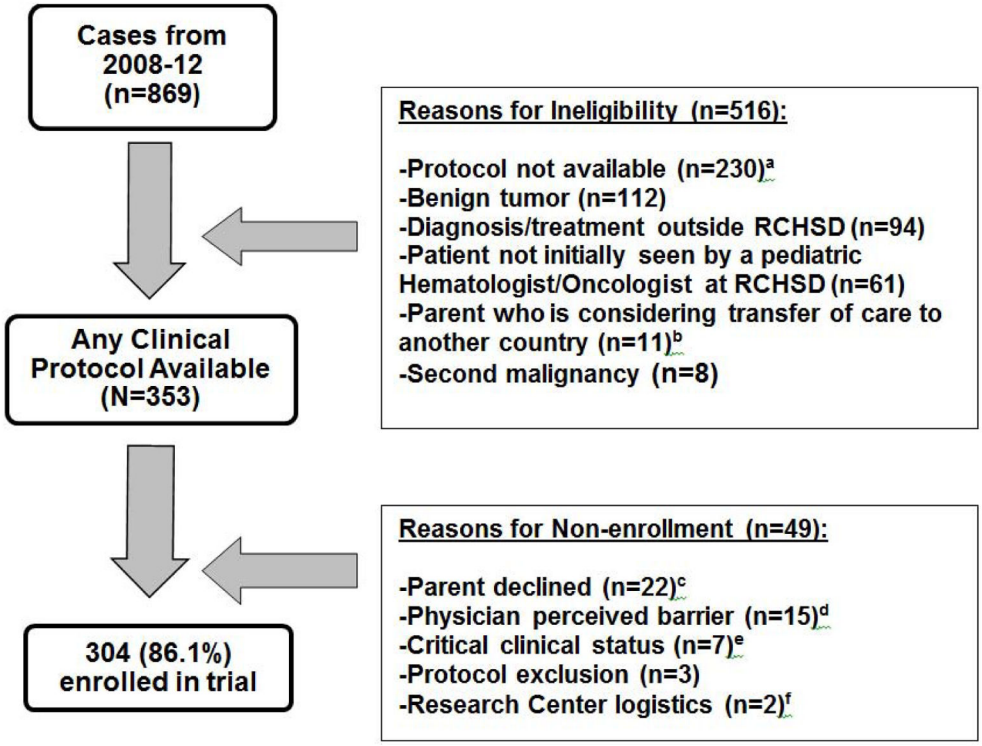

Figure 1. Flow chart of clinical protocol enrollment in any protocol at Rady Children's Hospital San Diego, 2008–2012

[a] Protocol not available- No protocol available for the specific disease, no protocol open at RCHSD, no consents available in the language of the parent. [b] Parent who is considering transfer of care to another country – Parents who were not presented with clinical trial protocols due to ineligibility for enrollment given patient's country of residency other than the U.S. [c] Parent declined – Parents who were presented with a protocol who refused to participate. [d] Physician perceived barrier - The physician's decision not to present research trial information due to perceived language and/or cultural barriers. [e] Critical clinical status - The physician's decision not to present research trial information due to the patient's critical physical health status. [f] Research Center logistics – Coordination and/or scheduling conflicts, lack of time, lack of personnel.

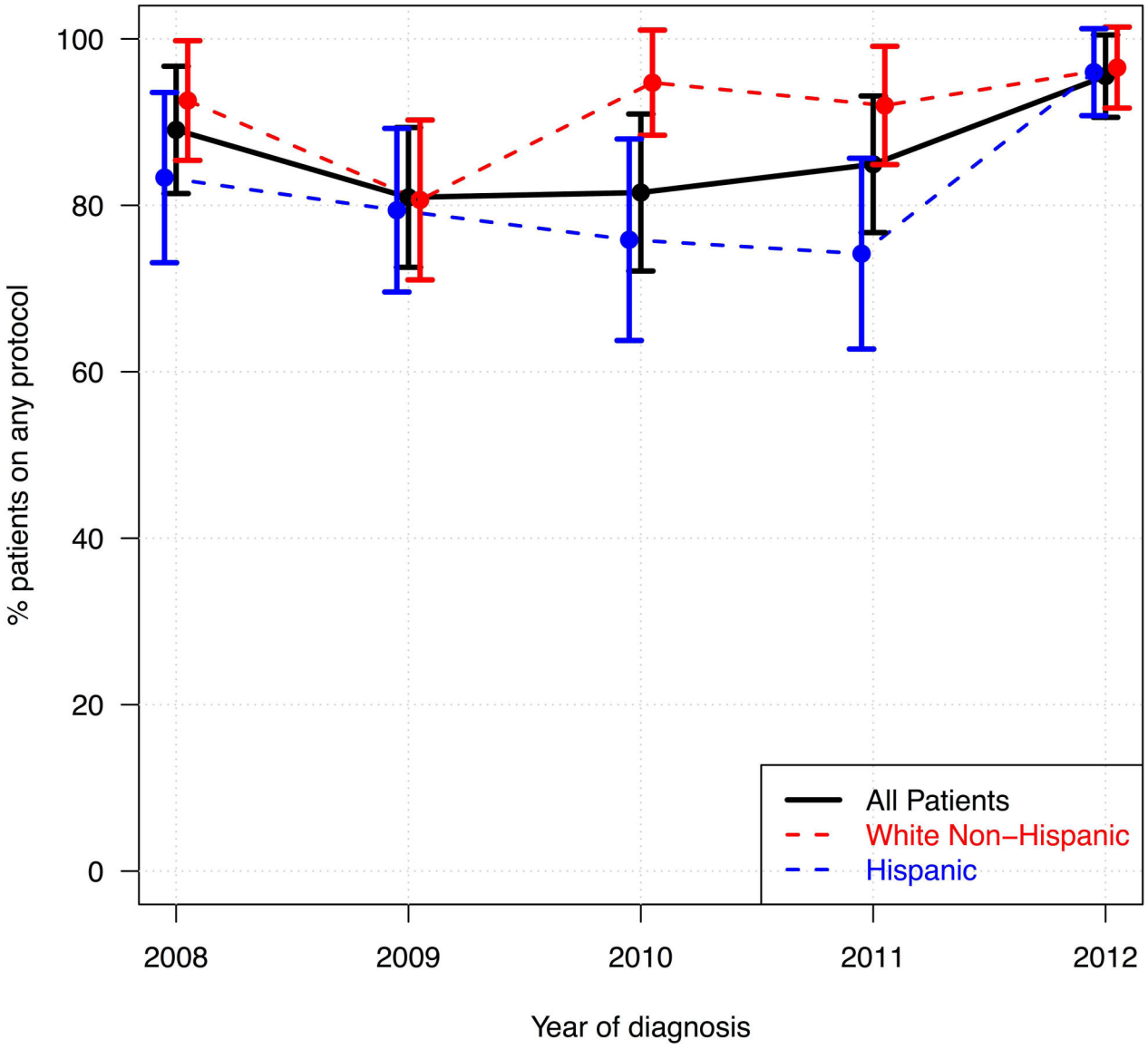

Figure 2.

Trends in enrollment in any protocol by year of diagnosis and race/ethnicity at Rady Children's Hospital San Diego, 2008–2012

Table I

Characteristics of Patients with Access to Clinical Protocols at Rady Children's Hospital San Diego, CA 2008–2012 (N=353)

Characteristic	N (%)
Age, years	
0–4	168 (48%)
5–9	73 (21%)
10–14	59 (17%)
15–21	53 (15%)
Sex	
Male	192 (54%)
Female	161 (46%)
Race/ethnicity	
Non-Hispanic white	131 (37%)
Hispanic	143 (41%)
Asian/Pacific Islander	29 (8%)
Black	13 (4%)
Mixed/multiple	37 (10%)
Primary Parental Language	
English	269 (76%)
Spanish	78 (22%)
Other	6 (2%)
Cancer type	
Hematological	187 (53%)
Solid	166 (47%)
Insurance Status	
Medicaid (Medi-Cal)	176 (50%)
Private	167 (47%)
Self-pay	10 (3%)

Table II

Crude and adjusted odd ratios for enrollment in any protocol at Rady Children's Hospital San Diego according to model including race/ethnicity and model including primary parental language (N=353)

	Not Enrolled (N=49)	Enrolled (N=304)	Crude OR (95%CI)	Adjusted OR (95%CI)	Crude OR (95%CI)	Adjusted OR (95%CI)
			Model Including Race/Ethnicity		Model including Primary Parental Language	
Age						
0–4 years	13 (8%)	155 (92%)	1.00	1.00	1.00	1.00
5–9 years	14 (19%)	59 (81%)	0.35* (0.16, 0.80)	0.33* (0.14, 0.75)	0.35* (0.16, 0.80)	0.38* (0.16, 0.88)
10–14 years	7 (12%)	52 (88%)	0.62 (0.24, 1.65)	0.62 (0.24, 1.75)	0.62 (0.24, 1.65)	0.62 (0.24, 1.74)
15–21 years	15 (28%)	38 (72%)	0.21* (0.09, 0.48)	0.22* (0.10, 0.51)	0.21* (0.09, 0.48)	0.22* (0.09, 0.51)
Sex						
Female	17 (11%)	144 (89%)	1.00	1.00	1.00	1.00
Male	32 (17%)	160 (83%)	0.59 (0.31, 1.11)	0.61 (0.31, 1.15)	0.59 (0.31, 1.11)	0.57 (0.29, 1.08)
Race/Ethnicity						
Non-Hispanic White	12 (9%)	119 (91%)	1.00	1.00		
Hispanic	27 (19%)	116 (81%)	0.43* (0.21, 0.90)	0.42* (0.19, 0.86)		
Asian/Pacific Islander	4 (14%)	25 (86%)	0.63 (0.19, 2.12)	0.66 (0.20, 2.57)		
Black Non-Hispanic	3 (23%)	10 (77%)	0.34 (0.08, 1.39)	0.41 (0.10, 2.11)		
Mixed/multiple	3 (8%)	34 (92%)	1.14 (0.31, 4.28)	0.98 (0.28, 4.58)		
Language						
English	30 (11%)	239 (89%)			1.00	1.00
Spanish	17 (22%)	61 (78%)			0.45* (0.23, 0.87)	0.45* (0.23, 0.91)
Other	2 (33%)	4 (67%)			0.25 (0.04, 1.43)	0.31 (0.05, 2.44)
Cancer Type						
Hematological	25 (13%)	162 (87%)	1.00		1.00	
Solid	24 (14%)	142 (86%)	0.91 (0.50, 1.67)		0.91 (0.50, 1.67)	
Insurance Status						
Medicaid	28 (16%)	148 (84%)	1.00		1.00	
Private	20 (12%)	147 (88%)	1.39 (0.75, 2.58)		1.39 (0.75, 2.58)	
Self-pay	1 (10%)	9 (90%)	1.70 (0.21,13.98)		1.70 (0.21,13.98)	

Author Manuscript

Author Manuscript

Author Manuscript

* p<0.05; OR, Odd Ratios; CI, Confidence Interval

Table III

Crude and adjusted odd ratios for enrollment in biospecimen protocol at Rady Children's Hospital San Diego according to model including race/ethnicity and model including primary parental language (N=310)

	Not Enrolled (N=49)	Enrolled (N=261)	Crude OR (95%CI)	Adjusted OR (95%CI)	Crude OR (95%CI)	Adjusted OR (95%CI)
			Model Including Race/Ethnicity		Model including Primary Parental Language	
Age						
0–4 years	14 (9%)	136 (91%)	1.00	1.00	1.00	1.00
5–9 years	14 (21%)	54 (79%)	0.40* (0.18,0.89)	0.35* (0.15, 1.06)	0.40* (0.18,0.89)	0.43* (0.85, 0.99)
10–14 years	7 (14%)	42 (86%)	0.62 (0.23,1.63)	0.60 (0.23, 1.70)	0.62 (0.23, 1.63)	0.61 (0.23, 1.73)
15–21 years	14 (33%)	29 (67%)	0.21* (0.09,0.50)	0.23* (0.09, 0.54)	0.21* (0.09,0.50)	0.22* (0.09, 0.52)
Sex						
Female	16 (11%)	124 (89%)	1.00	1.00	1.00	1.00
Male	33 (19%)	137 (81%)	0.54 (0.28,1.02)	0.55 (0.27, 1.06)	0.54 (0.28, 1.02)	0.52* (0.26, 0.10)
Race/Ethnicity						
Non-Hispanic White	11 (10%)	103 (90%)	1.00	1.00		
Hispanic	28 (22%)	97 (78%)	0.37* (0.18,0.78)	0.35* (0.15, 0.80)		
Asian/Pacific Islander	4 (15%)	23 (85%)	0.61 (0.18, 2.10)	0.64 (0.19, 2.55)		
Black Non-Hispanic	3 (25%)	9 (75%)	0.32 (0.08, 1.36)	0.43 (0.10, 2.26)		
Mixed/multiple	3 (9%)	29 (91%)	1.03 (0.27, 3.95)	0.887(0.24, 4.13)		
Language						
English	29 (12%)	210 (88%)			1.00	1.00
Spanish	18 (27%)	48 (73%)			0.37*(0.19, 0.72)	0.35* (0.18, 0.71)
Other	2 (40%)	3 (60%)			0.21 (0.03, 1.29)	0.24 (0.03, 2.07)
Cancer Type						
Hematological	24 (15%)	141 (85%)	1.00		1.00	
Solid	25 (17%)	120 (83%)	0.82 (0.44, 1.51)		0.82 (0.44, 1.51)	
Insurance Status						
Medicaid	29 (19%)	122 (81%)	1.00		1.00	
Private	19 (13%)	130 (87%)	1.63 (0.87, 3.05)		1.63 (0.87, 3.05)	
Self-pay	1 (10%)	9 (90%)	2.14 (0.26,17.56)		2.14 (0.26,17.56)	

Author Manuscript

Author Manuscript

Author Manuscript

* p<0.05; OR, Odd Ratios; CI, Confidence Interval

Table IV

Crude and adjusted odd ratios for enrollment in therapeutic protocol at Rady Children's Hospital San Diego according to model including race/ethnicity and model including primary parental language (N=254)

	Not Enrolled (N=48)	Enrolled (N=206)	Crude OR (95%CI)	Adjusted OR (95%CI)	Crude OR (95%CI)	Adjusted OR (95%CI)
			Model Including Race/Ethnicity		Model including Primary Parental Language	
Age						
0–4 years	14 (12%)	103 (88%)	1.00	1.00	1.00	1.00
5–9 years	13 (24%)	42 (76%)	0.44* (0.19, 1.01)	0.42* (0.18, 1.00)	0.44* (0.19, 1.01)	0.51 (0.21, 1.21)
10–14 years	8 (17%)	39 (83%)	0.66 (0.26, 1.70)	0.67 (0.26, 1.83)	0.66 (0.26, 1.70)	0.68 (0.27, 1.84)
15–21 years	13 (37%)	22 (63%)	0.23* (0.10, 0.56)	0.24* (0.10, 0.60)	0.23*(0.10, 0.56)	0.25* (0.10, 0.63)
Sex						
Female	18 (16%)	98 (84%)	1.00	1.00	1.00	1.00
Male	30 (22%)	108 (78%)	0.66 (0.35, 1.26)	0.60 (0.30, 1.18)	0.66 (0.35, 1.26)	0.63 (0.32, 1.21)
Race/Ethnicity						
Non-Hispanic White	11 (12%)	80 (88%)	1.00	1.00		
Hispanic	27 (25%)	82 (75%)	0.42* (0.19, 0.90)	0.40* (0.17, 0.86)		
Asian/Pacific Islander	5 (26%)	14 (74%)	0.39 (0.12, 1.28)	0.38 (0.11, 1.39)		
Black Non-Hispanic	2 (29%)	5 (71%)	0.34 (0.06, 1.99)	0.28 (0.05, 2.19)		
Mixed/multiple	3 (11%)	25 (89%)	1.15 (0.30, 4.44)	0.94 (0.26, 4.47)		
Language						
English	30 (16%)	159 (84%)			1.00	1.00
Spanish	16 (26%)	45 (74%)			0.53 (0.27, 1.06)	0.58 (0.28, 1.20)
Other	2 (50%)	2 (50%)			0.19 (0.03, 1.39)	0.27 (0.03, 2.53)
Cancer Type						
Hematological	25 (16%)	131 (84%)	1.00		1.00	
Solid	23 (23%)	75 (77%)	0.62 (0.33, 1.17)		0.62 (0.33, 1.17)	
Insurance Status						
Medicaid	26 (20%)	103 (80%)	1.00		1.00	
Private	20 (17%)	99 (83%)	1.25 (0.66, 2.38)		1.25 (0.66, 2.38)	
Self-pay	2 (33%)	4 (67%)	0.51(0.09, 2.91)		0.51 (0.09, 2.91)	

*p<0.05; OR, Odd Ratios; CI, Confidence Interval