Use of Appropriate Initial Treatment Among Adolescents and Young Adults With Cancer

Arnold L. Potosky, Linda C. Harlan, Karen Albright, Rosemary D. Cress, Debra L. Friedman, Ann S. Hamilton, Ikuko Kato, Theresa H.M. Keegan, Gretchen Keel, Stephen M. Schwartz, Nita L. Seibel, Margaret Shnorhavorian, Michele M. West, Xiao-Cheng Wu; and the AYA HOPE Study Collaborative Group

Manuscript received March 10, 2014; revised June 3, 2014; accepted August 19, 2014.

Correspondence to: Arnold L. Potosky, PhD, Georgetown University Medical Center, Harris Building, Suite 4100, 3300 Whitehaven St NW, Washington, DC 20007 (e-mail: alp49@georgetown.edu).

Background There has been little improvement in the survival of adolescent and young adult (AYA) cancer patients aged 15 to 39 years relative to other age groups, raising the question of whether such patients receive appropriate initial treatment.

Methods We examined receipt of initial cancer treatment for a population-based sample of 504 AYAs diagnosed in 2007–2008 with acute lymphoblastic leukemia (ALL), Hodgkin’s or non-Hodgkin’s lymphoma, germ cell cancer, or sarcoma. Registry data, patient surveys, and detailed medical record reviews were used to evaluate the association of patient demographic, socioeconomic, and health care setting characteristics with receipt of appropriate initial treatment, which was defined by clinical specialists in AYA oncology based on adult guidelines and published literature available before 2009 and analyzed with multivariable logistic regression. All statistical tests were two-sided.

Results Approximately 75% of AYA cancer patients in our sample received appropriate treatment, 68% after excluding stage I male germ cell patients who all received appropriate treatment. After this exclusion, appropriate treatment ranged from 79% of sarcoma patients to 56% of ALL patients. Cancer type (P < .01) and clinical trial participation (P = .04) were statistically significantly associated with appropriate treatment in multivariable analyses. Patients enrolled in clinical trials were more likely to receive appropriate therapy relative to those not enrolled (78% vs 67%, adjusted odds ratio = 2.6, 95% confidence interval = 1.1 to 6.4). Except for those with early stage male germ cell tumors, approximately 30% (or 3 in 10) AYA cancer patients did not receive appropriate therapy. Further investigation is required to understand the reasons for this potential shortfall in care delivery.

Conclusions

The past several decades have witnessed improvements in early detection and treatment of cancer, leading to overall improvements in survival from cancer for the US population as a whole. However, relative to young children and older adults, there has been far less improvement in cancer-specific survival among the adolescent and young adult (AYA) patients aged 15 to 39 years during this time (1–4). For example, adolescents aged 15–19 years diagnosed with cancer have experienced only half of the improvement in five-year survival from 1975 to 1998 compared with younger children and adults older than 45 years of age (5). Seeking explanations for the lack of improvement in survival, an expert panel noted that the proportion of AYA cancer patients who receive evidence-based, current and sometimes appropriate “cutting edge” initial cancer treatments in general community practice remains largely unknown and understudied (6, 7).

One possible barrier to receipt of appropriate initial treatment is that oncologists in community practice who primarily treat older adult cancer patients may not be as familiar with specialized treatment protocols used to treat AYA patients who have tumors biologically different from older adults (8–11). Given these barriers, it is possible that AYAs with cancer treated in community settings may be less likely to receive appropriate treatment than if they had been referred to pediatric specialists or to academic institutions or comprehensive cancer centers where access to state-of-the-art care and clinical trial participation are likely greater (10, 12, 13).

Another potential barrier to receipt of adequate treatment may be socioeconomic status (SES) and insurance coverage. Until recently, AYA patients have been among the highest uninsured group in the US (14). This may be changing with the implementation of dependent coverage to age 26 years under the Affordable Care Act of 2011. However, unemployment after age 25 years may limit the ability of some AYAs diagnosed with cancer to obtain adequate coverage. Socioeconomic status (SES) has been reported...
to account for racial-ethnic survival disparities in non-Hodgkin’s lymphoma (NHL) survivors independent of other demographic and treatment-related variables, suggesting that for one of the most common AYA cancer types nonclinical factors may be associated with underuse of appropriate treatments.

In this study, we evaluated the associations of health care setting, physician specialty, patient race/ethnicity or patient SES with receipt of appropriate initial treatment in AYAs with cancer. Our investigation is important because it is among the first to address these topics in a large, population-based cohort treated in a variety of academic and nonacademic settings.

Methods

The AYA HOPE (Health Outcomes and Patient Experiences) study has been described in greater detail elsewhere (15). Briefly, patients aged 15 to 39 years diagnosed between July 1, 2007 and October 31, 2008 with a first invasive, histologically confirmed germ cell cancer, NHL, Hodgkin’s lymphoma (HL), acute lymphoblastic leukemia (ALL), Ewing sarcoma, osteosarcoma, or rhabdomyosarcoma were identified by seven population-based Surveillance, Epidemiology, and End-Results (SEER) program cancer registries: Metropolitan Detroit, Seattle/Puget Sound area, Los Angeles County, San Francisco/Oakland Bay Area/San Jose/Monterey, Greater California (13 counties around Sacramento plus Orange County), and the states of Iowa and Louisiana. The patients must have been able to read English. Institutional Review Board (IRB) approvals were obtained from each registry’s institution and the National Cancer Institute (NCI).

Data Collection

Patients were mailed 1) a self-administered questionnaire that addressed topics such as impact of cancer, health-related quality of life, and health care delivery, 2) a request for release of medical information, and 3) a health care provider and facility form to determine where and by whom care was provided. A total of 524 eligible patients (of 1208 alive and eligible) completed the initial questionnaire (at a median of 11 months after diagnosis) and one patient completed only the medical record release, a response proportion of 43%. However, we have previously reported that only males and non-Hispanic Blacks and Hispanics were less likely to respond to the survey than females and other racial-ethnic groups, with no differences in response by age, region, ecological SES variables, and cancer type (15).

Data from the questionnaire used in this analysis included patient-reported race and Hispanic ethnicity, education, marital status, social support, participation in clinical trials, and availability and gaps in health insurance coverage for treatments sought. Ninety-five percent of patients consented to the release of their medical records for this study. Medical records were obtained for 517 cases, including 27 patients who were later determined to have died. Among these 517 cases, we excluded 13 cases for which we were unable to classify appropriateness of treatment because of insufficient information in the medical records, yielding a total study sample of 504 cases. However, because all 116 males in our sample with Stage I T1 or T2 germ cell cancer received standard primary treatment (orchiectomy plus surveillance), we excluded them from all subsequent analysis. This left a final analysis sample of 388 cases.

Information obtained from registry and medical record reviews included type of hospital where initial treatment was delivered, physician subspecialties consulted as part of initial care, tumor characteristics and staging, diagnostic procedures, insurance, and comorbid conditions. For those who received care at more than one hospital, we assigned patients to the hospital where the patient received the most definitive surgery and, if no surgery was given, the most definitive therapy. Then, the hospitals where patients received definitive therapy were classified into a single category according to the following hierarchy (since patients could have gone to more than one hospital for their care): NCI-designated cancer center, academic center, cancer centers not affiliated with either NCI or an academic center, and the remaining hospitals which were labeled as “community hospitals.” For patients younger than age 25 years, we determined whether a pediatric hematologist or oncologist was involved with initial treatment vs a medical oncologist. Participants were considered participants in a clinical trial if they reported this on the survey or it was abstracted from the medical record. Protocol numbers for medical record–derived data were verified at clinicaltrials.gov to ensure we captured treatment trials. We did not require validation of self-report for those without medical record documentation of trial participation, because of potential underreporting of trials in medical records, though we conducted a sensitivity analysis using medical record–only verification to assess the impact of this assumption. Details on cancer therapy were collected for all enrolled patients, including surgery, specific chemotherapeutic agents or standard protocols used, their start and end dates, and the timing and dose of radiation therapy. We contacted offices of treating physicians to obtain complete information on adjuvant therapies. We used the patient’s address at the time of cancer diagnosis to determine census tracts that were then linked to US Census data on median household income.

Definition of Appropriate Therapy

We defined “appropriate therapy” as the optimal treatment based on cancer type and, where relevant, Tumor, Node, Metastasis stage and other specific pathological or histological features. We followed a quasi-Delphi consensus method whereby we relied on a panel of expert coauthors to propose a set of criteria followed by critical review by independent content experts (16). Specifically, four clinician coauthors (KA, DLF, NLS, MS), each having expertise in a specific cancer included in this study, reviewed published studies and both adult and AYA-specific (created after 2010) National Comprehensive Cancer Network (NCCN) guidelines. These experts examined the state-of-the-science as it existed before 2009 (17–26), given the timing of our enrolled cohort, in order to create the initial definition of appropriate treatment according to specific clinical and pathological features. After our group proposed an initial set of criteria, an additional five oncologists not affiliated with the study reviewed these and suggested further revisions. The final categorization of therapies defined as “appropriate” is shown in Supplementary Table 1 (available online).

Statistical Analyses

We first performed bivariable analysis of appropriate therapy according to patient and health care setting characteristics. Multivariable logistic regression was used to assess the association
between each characteristic and the receipt of appropriate therapy for all patients, adjusting for other variables in the model. For the regression model, we combined all five cancers rather than fitting a model for each cancer because of small sample sizes for several of the cancer types. Analyses were conducted using SAS version 9.2 (SAS Institute Inc., Cary, NC), using a significance level of alpha = .05 (two-tailed).

**Results**

Overall, 75% of the total initial sample of 504 AYAs in our study received appropriate therapy. The estimated percent of AYA patients who received appropriate therapy declined from 75% to 68% after excluding 116 males (leaving n = 388) with Stage I T1 or T2 germ cell cancer, all of whom received standard orchectomy plus surveillance. All subsequent analyses are based on these 388 remaining cases. The percent of germ cell cases receiving appropriate therapy declined from 92% to 78% after this exclusion. ALL had the fewest patients receiving appropriate therapy at 56%, followed by 58% of HL patients, 73% of NHL patients, 78% of germ cell patients, and 79% of sarcoma patients.

Table 1 shows the distribution of patient characteristics overall and by cancer type. The most common institutional setting for initial treatment was non–NCI designated (NOS) cancer center (~42%), followed by NCI-designated cancer centers and community hospitals (~20% each) and academic centers (~13%). About 41% of both ALL and sarcoma patients under 25 had a pediatric hematologist/oncologist involved with initial treatment, likely associated with their generally younger age distribution compared with the lymphomas. Participation in clinical trials was infrequent overall, with about 13% of patients participating in a trial when using a measure combining self-report with medical record reviews, but only 7% based on medical records alone. In bivariable analyses of all patients, no patient demographic or SES characteristic was statistically significantly associated with receipt of appropriate therapy (Table 2). Patients getting care at a non-NCI affiliated cancer center had a lower use of appropriate therapy than patients seen in NCI-designated cancer centers, academic institutions, and community hospitals (61% vs 73%, 72%, and 75%). The difference between academic institutions vs non–NCI affiliated cancers centers was not statistically significant (72% vs 61%, P = .14). Only six of 58 patients aged 15 to 19 years received some initial care at a pediatric hospital (data not shown). Patients participating in clinical trials were more often recipients of appropriate therapy (78% vs 67% not in clinical trials), but this unadjusted result was not statistically significant (P = .13). Although non-Hispanic whites had the lowest use of appropriate therapy compared with Hispanics and Blacks, this difference was not statistically significant. We did not detect a statistically significant association of having at least one comorbid condition with receipt of appropriate therapy in unadjusted or adjusted comparisons (data not shown).

After adjustment for all other variables except pediatric oncologist involvement, the only two variables statistically significantly associated with receipt of appropriate therapy were cancer type (P < .01) and clinical trial participation (P = .04) (Table 3). Those patients enrolled in clinical trials were more likely to receive appropriate therapy relative to those not enrolled in trials (adjusted odds ratio [AOR] = 2.6, 95% confidence interval [CI] = 1.1 to 6.4). We observed some differences that attained borderline statistical significance. There was more frequent appropriate therapy among Hispanics (AOR = 2.0, 95% CI = 1.0 to 4.3) and non-Hispanic blacks (AOR = 2.5, 95% CI = 1.0 to 6.4) relative to non-Hispanic white (overall P value for race/ethnicity = .10). Similarly, those treated in non–NCI designated cancer centers were half as likely as those treated in NCI-designated cancer centers to receive appropriate treatment (AOR = 0.5, 95% CI = 0.2 to 1.0), though hospital type overall was not associated with appropriate therapy (P = .16).

**Discussion**

We investigated whether a large, diverse, population-based sample of AYAs diagnosed with five types of cancer and treated in the full spectrum of US health care systems received appropriate initial cancer treatment. These five cancers have been infrequently studied in AYA populations with respect to their quality of care and patient outcomes in general oncologic practice. Our study, the first of its size and scope focusing on the AYA age group, was motivated by the lack of information available and the relative lack of gains in survival over the past several decades compared with pediatric and older cancer age groups (1–4). We explored whether patient and health care setting factors were associated with receiving appropriate treatment for AYAs with cancer.

We found the lowest use of appropriate therapy in AYA with either ALL or HL. For AYA patients diagnosed with ALL (n = 27), the most common reason for not getting appropriate treatment was that they did not receive one of the multiple specific chemotherapy agents for induction, consolidation, or maintenance therapy that met our predefined criteria following diagnosis (Supplementary Table 1, available online). Most often (n = 11 case patients), they did not receive either cyclophosphamide or high-dose cytarabine when indicated. There may be reasonable clinical justification for such “deviations” from our definition of appropriate therapy for ALL and for the other cancers treated with combination chemotherapy regimens. One important factor may be the desire to balance the benefit against potential toxicity.

For AYAs with HL, the main reason for not receiving appropriate therapy was receipt of radiation therapy with doses in excess of 30 Gy (47 of 58 cases not having appropriate therapy). There have been no randomized control trials of only AYA patients comparing efficacy of multimodality therapy with radiotherapy less or more than 30 Gy. However, high cure rates have been attained in studies that included AYA as well as older HL patients with no radiation therapy or with doses of less than 30 Gy when administered with multiagent chemotherapy (27–35). Another reason we considered lower dose RT for this cancer as appropriate were the reported risks of long-term effects of radiotherapy related to higher dose, as well as volume and field (36–39). After adjustment for patient and health care setting variables, clinical trial participation was statistically significantly related to receipt of appropriate therapy. However, given the relative infrequency of clinical trial enrollment in the population, this factor is not likely a major determinant of who receives appropriate therapy.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All combined (n = 388)</th>
<th>Acute lymphoblastic leukemia (n = 27)</th>
<th>Germ cell* (n = 69)</th>
<th>Hodgkin's lymphoma (n = 137)</th>
<th>Non-Hodgkin's lymphoma (n = 126)</th>
<th>Sarcoma (n = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at initial diagnosis, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15–19</td>
<td>58 (14.9)</td>
<td>13 (48.1)</td>
<td>7 (10.1)</td>
<td>17 (12.4)</td>
<td>11 (8.7)</td>
<td>10 (34.5)</td>
</tr>
<tr>
<td>20–24</td>
<td>66 (17.0)</td>
<td>†</td>
<td>16 (23.2)</td>
<td>23 (16.8)</td>
<td>16 (12.7)</td>
<td>7 (24.1)</td>
</tr>
<tr>
<td>25–29</td>
<td>97 (25.0)</td>
<td>5 (18.5)</td>
<td>18 (26.1)</td>
<td>44 (32.1)</td>
<td>24 (19.0)</td>
<td>6 (20.7)</td>
</tr>
<tr>
<td>30–34</td>
<td>81 (20.9)</td>
<td>†</td>
<td>16 (23.2)</td>
<td>30 (21.9)</td>
<td>32 (25.4)</td>
<td>†</td>
</tr>
<tr>
<td>35–39</td>
<td>86 (22.2)</td>
<td>5 (18.5)</td>
<td>12 (17.4)</td>
<td>23 (16.8)</td>
<td>43 (34.1)</td>
<td>†</td>
</tr>
<tr>
<td><strong>Race/ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>222 (57.2)</td>
<td>12 (44.4)</td>
<td>40 (58.0)</td>
<td>86 (62.8)</td>
<td>71 (56.3)</td>
<td>13 (44.8)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>77 (19.8)</td>
<td>10 (37.0)</td>
<td>22 (31.9)</td>
<td>19 (13.9)</td>
<td>21 (16.7)</td>
<td>5 (17.2)</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>45 (11.6)</td>
<td>†</td>
<td>†</td>
<td>19 (13.9)</td>
<td>15 (11.9)</td>
<td>†</td>
</tr>
<tr>
<td>Other/unknown</td>
<td>44 (11.3)</td>
<td>†</td>
<td>†</td>
<td>13 (9.8)</td>
<td>19 (15.1)</td>
<td>7 (24.1)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>197 (50.8)</td>
<td>13 (48.1)</td>
<td>50 (72.5)</td>
<td>54 (39.4)</td>
<td>61 (48.4)</td>
<td>19 (65.5)</td>
</tr>
<tr>
<td>Female</td>
<td>191 (49.2)</td>
<td>14 (51.9)</td>
<td>19 (27.5)</td>
<td>83 (60.6)</td>
<td>65 (51.6)</td>
<td>10 (34.5)</td>
</tr>
<tr>
<td><strong>Insurance source</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Public</td>
<td>70 (18.0)</td>
<td>8 (29.6)</td>
<td>9 (13.0)</td>
<td>24 (17.5)</td>
<td>22 (17.5)</td>
<td>7 (24.1)</td>
</tr>
<tr>
<td>Private</td>
<td>305 (78.6)</td>
<td>19 (70.4)</td>
<td>57 (82.6)</td>
<td>110 (80.3)</td>
<td>97 (77.0)</td>
<td>22 (75.9)</td>
</tr>
<tr>
<td>Unknown or no insurance</td>
<td>13 (3.4)</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>7 (5.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Annual median household income in census tract at diagnosis (quartiles)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1 ($≤$40K)</td>
<td>98 (25.3)</td>
<td>5 (18.5)</td>
<td>16 (23.2)</td>
<td>34 (24.8)</td>
<td>36 (28.6)</td>
<td>7 (24.1)</td>
</tr>
<tr>
<td>Q2 ($&gt;$40K - $54K)</td>
<td>97 (25.0)</td>
<td>8 (29.6)</td>
<td>17 (24.6)</td>
<td>36 (26.3)</td>
<td>30 (23.8)</td>
<td>6 (20.7)</td>
</tr>
<tr>
<td>Q3 ($&gt;$54K - $72K)</td>
<td>98 (25.3)</td>
<td>10 (37.0)</td>
<td>21 (30.4)</td>
<td>30 (21.9)</td>
<td>28 (22.2)</td>
<td>9 (31.0)</td>
</tr>
<tr>
<td>Q4 ($&gt;$72K)</td>
<td>95 (24.5)</td>
<td>†</td>
<td>15 (21.7)</td>
<td>37 (27.0)</td>
<td>32 (25.4)</td>
<td>7 (24.1)</td>
</tr>
<tr>
<td><strong>Hospital (initial treatment)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCI-designated cancer center</td>
<td>79 (20.4)</td>
<td>13 (48.1)</td>
<td>9 (13.0)</td>
<td>34 (24.8)</td>
<td>16 (12.7)</td>
<td>7 (24.1)</td>
</tr>
<tr>
<td>Academic institution</td>
<td>50 (12.9)</td>
<td>†</td>
<td>9 (13.0)</td>
<td>†</td>
<td>29 (23.0)</td>
<td>7 (24.1)</td>
</tr>
<tr>
<td>Cancer center, NOS</td>
<td>162 (41.8)</td>
<td>10 (37.0)</td>
<td>28 (40.6)</td>
<td>62 (45.3)</td>
<td>52 (41.3)</td>
<td>10 (34.5)</td>
</tr>
<tr>
<td>Community hospital</td>
<td>79 (20.4)</td>
<td>†</td>
<td>22 (31.9)</td>
<td>28 (20.4)</td>
<td>26 (20.6)</td>
<td>†</td>
</tr>
<tr>
<td>Unknown</td>
<td>18 (4.6)</td>
<td>†</td>
<td>†</td>
<td>10 (7.3)</td>
<td>†</td>
<td>†</td>
</tr>
<tr>
<td><strong>Clinical trial participation†</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No or not recorded in medical record</td>
<td>339 (87.4)</td>
<td>15 (55.6)</td>
<td>63 (91.3)</td>
<td>122 (89.1)</td>
<td>120 (95.2)</td>
<td>19 (65.5)</td>
</tr>
<tr>
<td>Yes</td>
<td>49 (12.6)</td>
<td>12 (44.4)</td>
<td>6 (8.7)</td>
<td>15 (10.9)</td>
<td>6 (4.8)</td>
<td>10 (34.5)</td>
</tr>
<tr>
<td><strong>Pediatric oncology specialist involved in care vs medical oncologist (ages &lt; 25 only)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>95 (76.6)</td>
<td>10 (58.8)</td>
<td>23 (100.0)</td>
<td>31 (77.5)</td>
<td>21 (77.8)</td>
<td>10 (58.8)</td>
</tr>
<tr>
<td>Yes</td>
<td>29 (23.4)</td>
<td>7 (41.2)</td>
<td>†</td>
<td>9 (22.5)</td>
<td>6 (22.2)</td>
<td>7 (41.2)</td>
</tr>
<tr>
<td><strong>Summary stage at diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local</td>
<td>84 (21.6)</td>
<td>†</td>
<td>11 (15.9)</td>
<td>21 (15.3)</td>
<td>43 (34.1)</td>
<td>9 (31.0)</td>
</tr>
<tr>
<td>Regional</td>
<td>141 (36.3)</td>
<td>30 (43.5)</td>
<td>71 (51.8)</td>
<td>29 (23.0)</td>
<td>11 (37.9)</td>
<td></td>
</tr>
<tr>
<td>Distant</td>
<td>157 (40.5)</td>
<td>27 (100.0)</td>
<td>28 (40.6)</td>
<td>42 (30.7)</td>
<td>52 (41.3)</td>
<td>8 (27.6)</td>
</tr>
<tr>
<td>Unstaged</td>
<td>6 (1.5)</td>
<td>-</td>
<td>†</td>
<td>†</td>
<td>†</td>
<td>†</td>
</tr>
</tbody>
</table>
Table 1. Continued

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All combined</th>
<th>Acute lymphoblastic leukemia</th>
<th>Germ cell*</th>
<th>Hodgkin's lymphoma</th>
<th>Non-Hodgkin's lymphoma</th>
<th>Sarcoma</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surveillance, epidemiology and end-results region</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>San Francisco Bay area</td>
<td>95 (25.2)</td>
<td>26 (27.1)</td>
<td>13 (9.5)</td>
<td>6 (22.2)</td>
<td>6 (20.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Los Angeles County</td>
<td>47 (12.0)</td>
<td>15 (15.6)</td>
<td>10 (7.3)</td>
<td>6 (22.2)</td>
<td>8 (29.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Greater California</td>
<td>36 (9.8)</td>
<td>12 (12.6)</td>
<td>8 (6.2)</td>
<td>6 (22.2)</td>
<td>12 (46.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detroit Metropolitan area</td>
<td>46 (12.1)</td>
<td>21 (21.7)</td>
<td>10 (7.3)</td>
<td>6 (22.2)</td>
<td>12 (46.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iowa</td>
<td>29 (7.5)</td>
<td>10 (10.5)</td>
<td>7 (5.3)</td>
<td>6 (22.2)</td>
<td>7 (26.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seattle- Puget Sound area</td>
<td>73 (19.8)</td>
<td>32 (32.4)</td>
<td>22 (16.7)</td>
<td>6 (22.2)</td>
<td>26 (9.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Louisiana</td>
<td>63 (16.8)</td>
<td>26 (26.0)</td>
<td>12 (9.1)</td>
<td>6 (22.2)</td>
<td>32 (11.9)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Composite derived from patient self-report and medical record review.
† Data not shown because of small cell size.
‡ Data not shown because of small cell size.
†‡ From the total Adolescents and Young Adults study sample of 504 cases, we excluded 116 male germ cell (testis) cases with Tumor, Node, Metastases Stage I, T1, or T2. All 116 cases received standard primary treatment (orchiectomy and surveillance). NCI = National Cancer Institute; NOS = non-NCI designated.

Not yet established is the extent to which either structural factors, such as the relative lack of oncologists who have knowledge and experience in treating cancers in the AYA subgroup (vs pediatric or older adult cancers), or patient factors, such as knowledge of trials or willingness to enroll in available trials, contribute to the relatively low level of trial participation by AYAs with cancer. Since the time of our study, AYA trial availability may have improved with the initiation of several new ALL trials by NCI Cooperative Groups after 2007 and with the NCI’s National Clinical Trials Network (NCTN), extending age limits for selected AYA cancers (40).

Despite the hypothesized association of hospital type and physician specialty with quality of care (41,42), we did not find large differences in appropriate therapy for AYA cancer patients seen outside of NCI-designated cancer centers or academic centers compared with those seen in these facilities. No differences in appropriate therapy were observed for patients under age 25 years, whether or not they received any initial care from a pediatric oncology specialist. This may be partly because of our sample being relatively small for those cancer types (ALL and sarcomas) most likely to be managed by pediatric specialists, given their younger age distribution relative to lymphomas and germ cell cancers.

Studies of AYA cancer patients have reported poorer treatment and survival according to demographic and socioeconomic status (SES) (43–45). Several studies have reported poorer survival among lower SES patients and among AYA racial/ethnic minority cancer patients (46–50). For example, blacks and Hispanics ages 15 to 44 years had increased risks of death from HL of 74% and 43%, respectively, than white patients of the same age (48). These authors also reported that young HL patients with lower neighborhood SES had worse survival than patients with higher SES (48). Motivated by these findings, we investigated variations in appropriate therapy according to SES or demographic factors. We detected some differences consistent with the disparities literature suggesting that AYA patients living in higher SES areas more frequently received appropriate therapy, but these differences did not attain statistical significance. However, contrary to the evidence suggesting poorer survival and thus less appropriate treatment expected among racial/ethnic minorities, we found that both Hispanic and black patients were more likely than whites to receive appropriate therapy. It is not clear whether this finding reflects actual practice patterns and/or that there is only a weak correlation between appropriate treatment and improved population survival. It is also possible that
Table 2. Bivariate analysis of receipt of appropriate initial treatment according to patient and health care setting characteristics for adolescents and young adults with cancer diagnosed in 2007–2008 (n = 388*)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>No. (%), n = 388</th>
<th>Yes. (%), n = 264</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>124 (32.0)</td>
<td>264 (68.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Age at initial diagnosis, y</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15–19</td>
<td>58</td>
<td>21 (36.2)</td>
<td>37 (63.8)</td>
<td></td>
</tr>
<tr>
<td>20–24</td>
<td>66</td>
<td>17 (25.8)</td>
<td>49 (74.2)</td>
<td></td>
</tr>
<tr>
<td>25–29</td>
<td>97</td>
<td>34 (35.1)</td>
<td>63 (64.9)</td>
<td></td>
</tr>
<tr>
<td>30–34</td>
<td>81</td>
<td>25 (30.9)</td>
<td>56 (69.1)</td>
<td></td>
</tr>
<tr>
<td>35–39</td>
<td>86</td>
<td>27 (31.4)</td>
<td>59 (68.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Race/ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>222</td>
<td>82 (36.9)</td>
<td>140 (63.1)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>77</td>
<td>20 (25.8)</td>
<td>57 (74.0)</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>45</td>
<td>10 (22.2)</td>
<td>35 (77.8)</td>
<td></td>
</tr>
<tr>
<td>Other/unknown</td>
<td>44</td>
<td>12 (27.3)</td>
<td>32 (72.7)</td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>197</td>
<td>57 (28.9)</td>
<td>140 (71.1)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>191</td>
<td>67 (35.1)</td>
<td>124 (64.9)</td>
<td></td>
</tr>
<tr>
<td><strong>Insurance source</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Public</td>
<td>70</td>
<td>26 (37.1)</td>
<td>44 (62.9)</td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>305</td>
<td>96 (31.5)</td>
<td>209 (68.5)</td>
<td></td>
</tr>
<tr>
<td>Unknown/unknown‡</td>
<td>13</td>
<td>§</td>
<td>11 (84.6)</td>
<td>.36</td>
</tr>
<tr>
<td><strong>Annual median household income in census tract at diagnosis (quartiles)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1 (&lt;=$40K)</td>
<td>98</td>
<td>31 (31.6)</td>
<td>67 (68.4)</td>
<td></td>
</tr>
<tr>
<td>Q2 (&gt;40K - $54K)</td>
<td>97</td>
<td>37 (38.1)</td>
<td>60 (61.9)</td>
<td></td>
</tr>
<tr>
<td>Q3 (&gt;54K - $72K)</td>
<td>98</td>
<td>26 (26.5)</td>
<td>72 (73.5)</td>
<td></td>
</tr>
<tr>
<td>Q4 (&gt;72K)</td>
<td>95</td>
<td>30 (31.6)</td>
<td>65 (68.4)</td>
<td></td>
</tr>
<tr>
<td><strong>Hospital (initial treatment)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCI-designated cancer center</td>
<td>79</td>
<td>21 (26.6)</td>
<td>58 (73.4)</td>
<td></td>
</tr>
<tr>
<td>Academic institution</td>
<td>50</td>
<td>14 (28.0)</td>
<td>36 (72.0)</td>
<td></td>
</tr>
<tr>
<td>Cancer center, NOS</td>
<td>162</td>
<td>63 (38.9)</td>
<td>99 (61.1)</td>
<td></td>
</tr>
<tr>
<td>Community hospital</td>
<td>79</td>
<td>20 (25.3)</td>
<td>59 (74.7)</td>
<td></td>
</tr>
<tr>
<td>Unknown†</td>
<td>18</td>
<td>6 (33.3)</td>
<td>12 (66.7)</td>
<td>.09</td>
</tr>
<tr>
<td>**Clinical trial participation</td>
<td></td>
<td>**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No or not recorded in med. record</td>
<td>339</td>
<td>113 (33.3)</td>
<td>226 (66.7)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>49</td>
<td>11 (22.4)</td>
<td>38 (77.6)</td>
<td>.13</td>
</tr>
<tr>
<td><strong>Pediatric oncology specialist involved in care vs medical oncologist (aged &lt;25 y only)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>95</td>
<td>28 (29.5)</td>
<td>67 (70.5)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>29</td>
<td>10 (34.5)</td>
<td>19 (65.5)</td>
<td>.61</td>
</tr>
<tr>
<td><strong>Summary stage at diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local</td>
<td>84</td>
<td>26 (31.0)</td>
<td>58 (69.0)</td>
<td></td>
</tr>
<tr>
<td>Regional</td>
<td>141</td>
<td>49 (34.8)</td>
<td>92 (65.2)</td>
<td></td>
</tr>
<tr>
<td>Distant</td>
<td>157</td>
<td>47 (29.9)</td>
<td>110 (70.1)</td>
<td></td>
</tr>
<tr>
<td>Unstaged</td>
<td>6</td>
<td>§</td>
<td>§</td>
<td>.66</td>
</tr>
<tr>
<td><strong>Surveillance, epidemiology, and end results Region</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>San Francisco Bay area</td>
<td>95</td>
<td>31 (32.6)</td>
<td>64 (67.4)</td>
<td></td>
</tr>
<tr>
<td>Los Angeles County</td>
<td>47</td>
<td>11 (23.4)</td>
<td>36 (76.6)</td>
<td></td>
</tr>
<tr>
<td>Greater California</td>
<td>36</td>
<td>11 (30.6)</td>
<td>25 (69.4)</td>
<td></td>
</tr>
<tr>
<td>Detroit Metropolitan area</td>
<td>45</td>
<td>11 (24.4)</td>
<td>34 (75.6)</td>
<td></td>
</tr>
<tr>
<td>Iowa</td>
<td>29</td>
<td>13 (44.8)</td>
<td>16 (55.2)</td>
<td></td>
</tr>
<tr>
<td>Seattle-Puget Sound area</td>
<td>73</td>
<td>23 (31.5)</td>
<td>50 (68.5)</td>
<td></td>
</tr>
<tr>
<td>Louisiana</td>
<td>63</td>
<td>24 (38.1)</td>
<td>39 (61.9)</td>
<td>.41</td>
</tr>
<tr>
<td><strong>Cancer type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute lymphoblastic leukemia</td>
<td>27</td>
<td>12 (44.4)</td>
<td>15 (55.6)</td>
<td></td>
</tr>
<tr>
<td>Germ cell cancer*</td>
<td>69</td>
<td>15 (21.7)</td>
<td>54 (78.3)</td>
<td></td>
</tr>
<tr>
<td>Hodgkin's lymphoma</td>
<td>137</td>
<td>57 (41.6)</td>
<td>80 (58.4)</td>
<td></td>
</tr>
<tr>
<td>Non-Hodgkin's lymphoma</td>
<td>126</td>
<td>34 (27.0)</td>
<td>92 (73.0)</td>
<td></td>
</tr>
<tr>
<td>Sarcoma</td>
<td>29</td>
<td>6 (20.7)</td>
<td>23 (79.3)</td>
<td>≤.01</td>
</tr>
</tbody>
</table>

* Excludes 116 male germ cell (testis) cases with Tumor, Node, Metastases Stage I, T1, or T2: NCI = National Cancer Institute; NOS = non-NCI designated.
† P values are from two-sided chi-square tests of differences for each variable between those receiving or not receiving appropriate therapy.
‡ Missing or unknown not included in chi-square tests of differences.
§ Data not shown because of small cell size.
|| Composite derived from combination of self-report and medical record review.
our results may be biased by the somewhat lower survey participation among racial/ethnic minorities, for example, if higher SES minorities (and possibly also lower SES whites) disproportionately responded to our survey. We also investigated other previously understudied social factors collected on the patient questionnaire, including marital status, educational attainment, currently raising children, and extent of social support from family or friends; none were statistically significantly associated with receipt of appropriate therapy.

Strengths of our study include its multiregional and population-based inclusion of diverse patients treated in the full range of health care delivery systems in seven states. We employed a standardized data collection protocol across all seven registries to ensure consistency of data abstracted from medical records. Another strength

---

**Table 3. Multivariable analysis of receipt of appropriate treatment according to patient and health care setting characteristics for adolescents and young adults with cancer (n = 354*)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adj. OR(95% CI)</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at initial diagnosis, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15–19</td>
<td>1.0 (reference)</td>
<td>.70</td>
</tr>
<tr>
<td>20–24</td>
<td>2.0 (0.8 to 5.1)</td>
<td></td>
</tr>
<tr>
<td>25–29</td>
<td>1.5 (0.7 to 3.5)</td>
<td></td>
</tr>
<tr>
<td>30–34</td>
<td>1.6 (0.6 to 4.0)</td>
<td></td>
</tr>
<tr>
<td>35–39</td>
<td>1.6 (0.7 to 4.0)</td>
<td></td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>1.0 (reference)</td>
<td>.10</td>
</tr>
<tr>
<td>Hispanic</td>
<td>2.0 (1.0 to 4.3)</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>2.5 (1.0 to 6.4)</td>
<td></td>
</tr>
<tr>
<td>Other/unknown</td>
<td>1.4 (0.6 to 3.2)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.0 (reference)</td>
<td>.27</td>
</tr>
<tr>
<td>Female</td>
<td>0.8 (0.5 to 1.2)</td>
<td></td>
</tr>
<tr>
<td>Insurance source</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>1.0 (reference)</td>
<td>.40</td>
</tr>
<tr>
<td>Public</td>
<td>0.8 (0.4 to 1.4)</td>
<td></td>
</tr>
<tr>
<td>Annual median household income in census tract at diagnosis (quartiles)</td>
<td></td>
<td>.48</td>
</tr>
<tr>
<td>Q1 (≤$40K)</td>
<td>1.0 (reference)</td>
<td></td>
</tr>
<tr>
<td>Q2 ($40K – $54K)</td>
<td>0.9 (0.4 to 1.8)</td>
<td></td>
</tr>
<tr>
<td>Q3 ($54K – $72K)</td>
<td>1.5 (0.7 to 3.1)</td>
<td></td>
</tr>
<tr>
<td>Q4 ($72K)</td>
<td>1.4 (0.7 to 3.1)</td>
<td></td>
</tr>
<tr>
<td>Hospital (initial treatment)</td>
<td></td>
<td>.16</td>
</tr>
<tr>
<td>NCI-designated cancer center</td>
<td>1.0 (reference)</td>
<td></td>
</tr>
<tr>
<td>Academic institution</td>
<td>0.7 (0.2 to 2.6)</td>
<td></td>
</tr>
<tr>
<td>Cancer center, NOS</td>
<td>0.5 (0.2 to 1.0)</td>
<td></td>
</tr>
<tr>
<td>Community hospital</td>
<td>1.0 (0.4 to 2.5)</td>
<td></td>
</tr>
<tr>
<td>Clinical trial participation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No or not recorded in med. record</td>
<td>1.0 (reference)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2.6 (1.1 to 6.4)</td>
<td></td>
</tr>
<tr>
<td>Summary stage at diagnosis</td>
<td></td>
<td>.92</td>
</tr>
<tr>
<td>Local</td>
<td>1.0 (reference)</td>
<td></td>
</tr>
<tr>
<td>Regional</td>
<td>1.0 (0.5 to 2.0)</td>
<td></td>
</tr>
<tr>
<td>Distant</td>
<td>1.1 (0.6 to 2.2)</td>
<td></td>
</tr>
<tr>
<td>Surveillance, epidemiology and end results region</td>
<td></td>
<td>.45</td>
</tr>
<tr>
<td>San Francisco Bay area</td>
<td>1.0 (reference)</td>
<td></td>
</tr>
<tr>
<td>Los Angeles</td>
<td>1.1 (0.3 to 3.9)</td>
<td></td>
</tr>
<tr>
<td>Greater California</td>
<td>2.2 (0.7 to 6.3)</td>
<td></td>
</tr>
<tr>
<td>Detroit Metropolitan area</td>
<td>3.0 (1.1 to 8.3)</td>
<td></td>
</tr>
<tr>
<td>Iowa</td>
<td>1.9 (0.6 to 5.9)</td>
<td></td>
</tr>
<tr>
<td>Seattle-Puget Sound area</td>
<td>2.3 (0.9 to 5.8)</td>
<td></td>
</tr>
<tr>
<td>Louisiana</td>
<td>1.4 (0.5 to 3.8)</td>
<td></td>
</tr>
<tr>
<td>Cancer type</td>
<td></td>
<td>&lt;=.01</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>1.0 (reference)</td>
<td></td>
</tr>
<tr>
<td>Acute lymphoblastic leukemia</td>
<td>0.6 (0.2 to 1.8)</td>
<td></td>
</tr>
<tr>
<td>Germ cell cancer*</td>
<td>3.2 (1.5 to 7.1)</td>
<td></td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphoma</td>
<td>2.2 (1.1 to 4.1)</td>
<td></td>
</tr>
<tr>
<td>Sarcoma</td>
<td>2.8 (0.9 to 8.9)</td>
<td></td>
</tr>
</tbody>
</table>

* Excludes 116 testis patients with Tumor, Node, Metastases Stages I, T1, or T2 cancer, and another 34 patients with missing or unknown stage, insurance status, or hospital type. NCI = National Cancer Institute; NOS = non-NCI designated.
† P values are derived from two-sided likelihood ratio tests of the significance of the estimated coefficient (expressed as an adjusted odds ratio) for each variable as a whole, adjusting for all other variables in the table.
|| Derived from combination of self-report and medical record review.

---
is the merging of information from a patient survey with medical record and cancer registry information to examine many previously underinvestigated potential explanations for receipt of appropriate therapy.

This study also had some limitations. First, we lacked sufficient sample size to make robust comparisons of appropriate therapy among the five cancer types, or by race/ethnicity or hospital type, with selected comparisons showing differences but only attaining borderline statistical significance. Second, our definition of “appropriate care” was based on the expert clinician investigators interpreting the literature and published guidelines for adults and children, sometimes without sufficient evidence from RCTs specific to AYAs with cancer. There may be gaps in data abstraction from medical records, leading to potential underidentification of appropriate therapies used longer after the initial period of treatment. Fourth, the generalizability of our results to the United States may be limited by our sampling cases in seven states. Finally, we were unable to assess completion of planned therapies or assess patient adherence.

In summary, we found that there is a sizable and largely unexplained gap in the receipt of appropriate treatment among AYA cancer patients other than those with early stage male germ cell cancer. Subsequent studies of quality of care should identify new longitudinal AYA cohorts to facilitate a comprehensive investigation of the reason for deficits in appropriate treatment and, perhaps even more critically, whether these apparent deficits are associated with poor clinical and patient-reported outcomes.

References
7. Albritton K, Caligiuri M, Anderson B, Nichols C, Ulman D. Closing the Gap: Research and Care Imperatives for Adolescents and Young Adults with Cancer: Report of the Adolescent and Young Adult Oncology Progress Review Group. 2006.


Funding
This work was supported by the National Cancer Institute at the National Institutes of Health (HHSN2612013000041, HHSN2612013000051, HHSN261201300011I, HHSN261201300012I, HHSN261201300014I, HHSN261201300016I, HHSN261201300020I, and P01CA051008). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Cancer Institute or the National Institutes of Health.

Notes
The authors gratefully acknowledge Ms. Alexandra Bicki and Ms. Charlene Kuo (Georgetown University) for their assistance with conducting literature reviews. We also acknowledge the contribution of clinicians who reviewed our criteria for defining appropriate therapy: Brian K. Link, MD, University Hospitals and Clinics, Iowa City, IA; Douglas Hawkins, MD, Seattle Children’s Hospital, Seattle, WA; Alberto Pappo, MD, St Jude’s Medical Center, Memphis, TN; David Thomas, MBBS, PhD, Peter MacCallum Cancer Centre, Melbourne, Australia; Wendy Stock, MD, University of Chicago, Chicago, IL; and Andrea Ferrari, MD, Istituto Nazionale Tumori, Milan, Italy. The authors report no conflicts of interest.

AYA HOPE Study
Fred Hutchinson Cancer Research Center (Seattle, WA): Stephen M. Schwartz, PhD (PI); Martha Shellenberger; Tiffany Jakes
University of Iowa (Iowa City, IA): Charles F. Lynch, MD, PhD (PI); Michele M. West, PhD; Lori A. Somers, RN
Wayne State University (Detroit, MI): Ikuko Kato, MD, PhD (PI); Ann Bankowski; Marjorie Stock
California Cancer Registry/Public Health Institute (Sacramento, CA): Rosemary Cress, DrPH (PI); Gretchen Agha; Mark Cruz
Louisiana State University (New Orleans, LA): Xiao-Cheng Wu, MD, MPH (PI); Vivien Chen, PhD; Pinki K. Prasad, MD
Cancer Prevention Institute of California (Fremont, CA): Theresa Keegan, PhD (PI); Laura Allen; Zinnia Loya; Lisa Selhton-Herendeen
University of Southern California (Los Angeles, CA): Ann Hamilton, PhD (PI); Jennifer Zelaya; Urduja Trinidad
National Cancer Institute (Bethesda, MD): Linda C. Harlan, BSN, BSN, MPH, PhD (Investigator); Ashley Wilder Smith, PhD MPH (Coinvestigator);
Gretchen Keel, BS, BA; Jana Eisenstein, MS
Consultants: Arnold Potosky, PhD; Keith Bellizzi, PhD; Karen Allbritton, MD; Michael Link, MD; Debra Friedman, MD; Brad Zebrack, PhD

Affiliations of authors: Lombardi Comprehensive Cancer Center, Georgetown University Medical Center, Washington, DC (ALP); Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, MD (LCH); Cook Children’s Medical Center and University of North Texas Health Science Center Fort Worth, TX (KA); Public Health Institute/Cancer Registry of Greater California, Sacramento, CA (RDC); Monroe Carell Jr. Children’s Hospital, Vanderbilt-Ingram Cancer Center, Nashville, TN (LDL). Keck School of Medicine, University of Southern California, Los Angeles, CA (ASH); Departments of Oncology and Pathology, Wayne State University, Detroit, MI (IK); Cancer Prevention Institute of California, Fremont, CA (THMK); School of Medicine, Stanford University, Stanford, CA (THMK); Information Management Services, Inc, Silver Spring, MD (GK); Epidemiology Program, Public Health Sciences Division, Fred Hutchinson Cancer Research Center, Seattle, WA (SMS); Cancer Therapy Evaluation Program, National Cancer Institute, Bethesda, MD (NLS); Department of Urology, Division of Pediatric urology, University of Washington, Seattle Children’s Hospital, Seattle, WA (MS); Department of Epidemiology, University of Iowa, Iowa City, IA (MMW); Louisiana State University, New Orleans, LA (XCW).