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ORIGINAL REPORT

# Health-Related Quality of Life of Adolescent and Young Adult Patients With Cancer in the United States: The Adolescent and Young Adult Health Outcomes and Patient Experience Study

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## ABSTRACT

### Purpose
Adolescents and young adults (AYAs) diagnosed with cancer face numerous physical, psychosocial, and practical challenges. This article describes the health-related quality of life (HRQOL) and associated demographic and health-related characteristics of this developmentally diverse population.

### Patients and Methods
Data are from the Adolescent and Young Adult Health Outcomes and Patient Experience (AYA HOPE) study, a population-based cohort of 523 AYA patients with cancer, ages 15 to 39 years at diagnosis from 2007 to 2009. Comparisons are made by age group and with general and healthy populations. Multiple linear regression models evaluated effects of demographic, disease, health care, and symptom variables on multiple domains of HRQOL using the Pediatric Quality of Life Inventory (PedsQL) and the Short-Form Health Survey 12 (SF-12).

### Results
Overall, respondents reported significantly worse HRQOL across both physical and mental health scales than did general and healthy populations. The greatest deficits were in limitations to physical and emotional roles, physical and social functioning, and fatigue. Teenaged patients (ages 15 to 17 years) reported worse physical and work/school functioning than patients 18 to 25 years old. Regression models showed that HRQOL was worse for those in treatment, with current/recent symptoms, or lacking health insurance at any time since diagnosis. In addition, sarcoma patients, Hispanic patients, and those with high school or lower education reported worse physical health. Unmarried patients reported worse mental health.

### Conclusion
Results suggest that AYAs with cancer have major decrements in several physical and mental HRQOL domains. Vulnerable subgroups included Hispanic patients, those with less education, and those without health insurance. AYAs also experienced higher levels of fatigue that were influenced by current symptoms and treatment. Future research should explore ways to address poor functioning in this understudied group.

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## INTRODUCTION

Nearly 69,200 adolescents and young adults (AYAs) ages 15 to 39[1] were diagnosed with cancer in 2008,[2] almost seven times the number of incident cases in those younger than 15 years at diagnosis that year.[3] Cancer is also the leading cause of disease-related death among AYAs.[2] Historically, AYA patients with cancer have poorer cancer outcomes than pediatric and older adult patients.[4] Further, although there have been numerous health-related quality of life (HRQOL) studies among children, adolescent, and

adult survivors of childhood cancer,[5-7] less is known about the HRQOL of patients diagnosed with cancer during adolescence or young adulthood. The few studies that have examined AYAs have demonstrated extensive psychosocial[8] and long-term symptom burden of disease.[9,10] Given the developmental transitions experienced by AYAs (eg, movement toward increasing autonomy financially and in family and personal relationships, as well as changes in school/work settings and insurance coverage) while navigating diagnosis, treatment, and health care decisions, it is important to understand

HRQOL outcomes to determine relevant services and resources required to serve them.

Our article describes HRQOL outcomes from the Adolescent and Young Adult Health Outcomes and Patient Experience (AYA HOPE) study sponsored by the National Cancer Institute (NCI), with support from LIVESTRONG, and conducted by NCI Surveillance, Epidemiology, and End Results (SEER) registries. To date, this is the first population-based study in the United States that characterizes HRQOL of recently diagnosed AYA oncology patients. The aim of our analysis is to examine physical, emotional, social, cognitive, and psychological functioning of AYA patients/survivors with cancer, and to determine potential disease, demographic, health care and symptom correlates of HRQOL.

## PATIENTS AND METHODS

Details regarding recruitment and study methods have been published previously.[8,11] Briefly, AYA HOPE respondents were diagnosed with a histologically confirmed non-Hodgkin lymphoma, Hodgkin lymphoma, germ cell cancer, acute lymphocytic leukemia, or sarcoma (Ewing's, osteosarcoma, or rhabdomyosarcoma) between July 2007 and August 2009. Patients were ages 15 to 39 years at diagnosis, 6 to 14 months postdiagnosis at study entry, and were able to read and write in English. Participants were recruited from one of seven SEER registries: Detroit, Seattle/Puget Sound, Los Angeles County, San Francisco/Oakland, Greater California, Iowa, and Louisiana. Study approval was obtained by each of the registries' and NCI's institutional review boards. Of the 1,208 patients identified as eligible, 525 patients responded to the study (one respondent only consented to release of medical record data and one survey was lost, leaving 523 surveys), and medical records were obtained for 490 respondents. There was a 43% response rate for the overall study, with male patients, Hispanic patients, and non-Hispanic black patients less likely to participate.[11]

The AYA HOPE patient survey asked about demographic characteristics; barriers to and the quality of health care; treatment and symptoms; insurance status, information, and service needs; the impact of cancer; and HRQOL including psychosocial and physical functioning domains. The survey took approximately 15 to 20 minutes to complete.

### Measures

*HRQOL.* Two instruments were used to assess physical and psychosocial functioning across the wide age/developmental range in AYA HOPE; the 12-item Short-Form Health Survey (SF-12, version 2) and the Pediatric Quality of Life Inventory study (PedsQL). The SF-12 has been validated for use in adults 18 and older and includes eight subscales: physical functioning, physical role limitations, bodily pain, general health, vitality, social functioning, emotional role limitations, and mental health.[12] Weighted subscale scores are used to compute physical component summary (PCS) and mental component summary (MCS) scores. Population norms by age have been published.[13] The PedsQL 4.0, which was designed for children and adolescents, has a young adult version designed for individuals up to age 25 years,[14] validated in young adults with cancer[15] and adult survivors of pediatric cancer.[16] It includes the following scores: total, physical health summary, psychosocial health summary, emotional functioning, social functioning, and work/school functioning. We also included the PedsQL fatigue module.[14] Higher scores on the PedsQL and SF-12 indicate better HRQOL.

*Covariates.* Demographic data including age, sex, race/ethnicity, education level, and marital status were collected from the survey. Disease-related variables, including cancer type, American Joint Committee on Cancer stage, treatment type (surgery alone, radiation, chemotherapy, or combined chemotherapy and radiation), whether participants were receiving treatment at the time of the study, and comorbid conditions were obtained from SEER and medical records. Severe and/or chronic comorbid conditions (ie, conditions serious enough they were expected to affect treatment, outcomes, or create

significant health burden) were categorized into condition groups and were summed to create comorbidity scores (0, 1, or $\geq 2$) done previously for AYA survivors.[17] Health insurance data (including whether respondents lacked health insurance at any time since diagnosis) and data on symptoms were collected from the survey. Based on consultation with clinical experts, we included symptoms common to the cancer types being studied. Participants reported whether they experienced the following symptoms in the past 4 weeks: nausea/vomiting, frequent/severe stomach pain, diarrhea/constipation, pain in joints/bones, weight loss, weight gain, frequent/severe fevers, hot flashes, tingling/weakness/clumsiness of the hands/feet, frequent/severe headaches, frequent/severe mouth sores that affected eating/drinking, problems with memory/attention/concentration. The number of symptoms was summed and categorized as 0, 1 to 2, 3 to 4, or $\geq 5$.

### Statistical Analysis

Comparisons between SF-12 scores and age-matched population norms[13] were analyzed using *t* tests for AYAs ages 18 years and older. AYA HOPE participants were categorized into age groups matching the age ranges from published norms (18 to 24, 25 to 34, 35 to 44 years), though our study only went to age 41 years. Comparisons with healthy adolescents were not possible because there are no SF-12 population norms for individuals younger than 18 years. Notably, statistically significant differences were identified by medium (0.50) to large ($\geq 0.80$) effect sizes.[18] Similar analyses compared PedsQL outcomes to similarly aged healthy AYAs[14,19] and examined age group differences within the AYA HOPE group. We then developed hierarchical multiple regression models to examine associations between HRQOL outcomes (total; physical and mental summary scores; physical, emotional, social, and work/school functioning scores; and fatigue) and potential demographic, cancer-related, comorbidities, and symptom correlates, each added in blocks to examine their impact. Because 39 participants had missing responses on covariates or outcomes, the analytic sample for regression models was n = 484. However, the unadjusted analyses comparing outcomes with population norms made use of the maximal number of available responses.

## RESULTS

The majority of the cohort was made up of male patients, who worked full-time, were unmarried, had early-stage cancer, and were not currently in treatment (Table 1). In addition, 20% of the sample was Hispanic, 35% had at least one comorbidity, and 51% had three or more symptoms. Table 2 lists that young adults with cancer age 25 years and older reported significantly lower scores on the PCS, MCS, and all subscales, compared with population norms.[13] Survey respondents ages 18 to 24 years reported significantly worse scores for General Health, Physical Functioning, Physical Role Limitations, and Emotional Role Limitations compared with population norms. The greatest effect sizes were seen among 25- to 34-year-olds on the Physical Functioning and Social Functioning subscales, across all age groups on the Physical Role Limitations subscale, among those $\geq 35$ years on the General Health subscale, and among the 25-to-34 years and $\geq 35$ years age groups on the Emotional Role Limitations subscale.

PedsQL results showed that AYA HOPE participants reported substantially worse HRQOL than healthy young adults[19] on the total score (effect size, 0.6) and on physical functioning (effect size, 0.9; Table 3). Significant differences were also seen for social functioning, though the effect size was small (effect size, 0.4). Results were comparable between our sample and age-matched young adults on psychosocial summary, emotional functioning, and work/school functioning. Comparisons within the AYA HOPE cohort showed that 18- to 25-year-olds reported better physical functioning and better work/school functioning than their younger counterparts. AYA

**Table 1.** AYA HOPE Sample Characteristics (N = 523)

| Characteristic | No. of Patients | % |
|---|---|---|
| Background variables | | |
| Age at survey, years | | |
| 15-17 | 23 | 4.4 |
| 18-24 | 115 | 22.0 |
| 25-29 | 126 | 24.1 |
| 30-34 | 124 | 23.7 |
| 35-41 | 135 | 25.8 |
| Sex | | |
| Male patients | 331 | 63.3 |
| Female patients | 192 | 36.7 |
| Race/ethnicity | | |
| Hispanic | 108 | 20.7 |
| White | 310 | 59.3 |
| Black | 45 | 8.6 |
| Other | 60 | 11.5 |
| Education, prediagnosis | | |
| High school or less | 149 | 28.5 |
| Some college | 138 | 26.4 |
| College graduate | 235 | 44.9 |
| Missing | 1 | 0.2 |
| Employment status, prediagnosis | | |
| Full-time work | 316 | 60.4 |
| Full-time school | 119 | 22.8 |
| Part-time work | 24 | 4.6 |
| Part-time school | 22 | 4.2 |
| Homemaker | 17 | 3.3 |
| Unemployed/disabled | 23 | 4.4 |
| Other/unknown | 2 | 0.4 |
| Marital status | | |
| Married | 219 | 41.9 |
| Not married | 303 | 57.9 |
| Missing | 1 | 0.2 |
| Raising children | | |
| No | 316 | 60.4 |
| Yes | 207 | 39.6 |
| Lack of health insurance, any time since diagnosis with no coverage | | |
| No | 435 | 83.2 |
| Yes | 75 | 14.3 |
| Missing | 13 | 2.5 |
| Disease-related variables | | |
| Cancer type | | |
| Acute lymphoblastic leukemia | 21 | 4.0 |
| Germ cell cancer | 204 | 39.0 |
| Hodgkin lymphoma | 142 | 27.2 |
| Non-Hodgkin lymphoma | 131 | 25.0 |
| Sarcoma | 25 | 4.8 |
| AJCC cancer stage | | |
| I | 206 | 39.4 |
| II | 127 | 24.3 |
| III | 73 | 14.0 |
| IV | 67 | 12.8 |
| N/A | 28 | 5.4 |
| Unknown | 22 | 4.2 |
| Location of care | | |
| Cancer center | 309 | 59.1 |
| Community hospital | 116 | 22.2 |
| (continued in next column) | | |

**Table 1.** AYA HOPE Sample Characteristics (N = 523) (continued)

| Characteristic | No. of Patients | % |
|---|---|---|
| Pediatric hospital | 1 | 0.2 |
| Academic institution | 43 | 8.2 |
| Outpatient only/unknown | 20 | 3.8 |
| Missing/no consent | 34 | 6.5 |
| Treatment type | | |
| Surgery only | 60 | 11.5 |
| Radiation | 52 | 9.9 |
| Chemotherapy | 249 | 47.6 |
| Radiation and chemotherapy | 121 | 23.1 |
| Missing/unknown/no treatment | 41 | 7.8 |
| Currently undergoing treatment | | |
| No | 419 | 80.1 |
| Yes | 91 | 17.4 |
| Missing | 13 | 2.5 |
| Severe comorbidity | | |
| 0 | 342 | 65.4 |
| 1 | 84 | 16.1 |
| ≥ 2 | 63 | 12.0 |
| Missing/no consent | 34 | 6.5 |
| Current/recent symptoms | | |
| 0 | 81 | 15.5 |
| 1 or 2 | 175 | 33.5 |
| 3 or 4 | 121 | 23.1 |
| ≥ 5 | 146 | 27.9 |

Abbreviation: AJCC, American Joint Committee on Cancer; AYA HOPE, Adolescent and Young Adult Health Outcomes and Patient Experience study; N/A, not applicable.

HOPE participants reported significantly more fatigue (lower scores indicate poorer HRQOL, ie, more fatigue) than healthy AYAs,[14] but there were no significant differences in reports of fatigue by age within the AYA HOPE cohort.

Multiple regression model results for the SF-12 PCS showed that the combined variables in the overall model accounted for 38% (adjusted $R^2$) of the variance in physical HRQOL (Table 4); demographics and health insurance status accounted for 14%, cancer-related variables for 15%, severe comorbidity for 1%, and symptoms for 8%. Worse HRQOL was reported among those with high school or less education, those without health insurance, and among Hispanic respondents (compared with white respondents). For the disease-related variables, sarcoma patients reported significantly worse PCS scores compared with germ cell cancer patients. Those respondents currently undergoing treatment reported worse PCS scores, and those who had chemotherapy reported worse PCS scores than those who only had surgery. Before symptoms were added to the models, age (continuous) was also significant, with younger respondents reporting worse HRQOL ($\beta = -0.18$; SE, 0.08; $P = .02$). Symptoms were associated with worse PCS scores, with increasing numbers of symptoms having a greater negative effect.

For the SF-12 MCS, the combined variables accounted for 27% of the variance in mental HRQOL (Table 4); demographics and health insurance status accounted for 7%, cancer-related variables for 5%, comorbidity for 2%, and symptoms for 13%. Specific correlates of mental HRQOL included marital status (unmarried respondents reported worse HRQOL than married respondents), health insurance (lacking insurance was associated with worse MCS scores), cancer type

**Table 2.** SF-12 Health Survey Outcomes Among AYA HOPE Participants and US Population Norm Scores by Age at Survey

| Age Group (years) | AYA HOPE | | | General US Norm Score | | | t Test | P | Effect Size (Cohen's d) |
|---|---|---|---|---|---|---|---|---|---|
| | No. of Patients | Mean | SD | No. of Patients | Mean | SD | | | |
| Physical component summary by age group, years | | | | | | | | | |
| 15-17 | 22 | 45.90 | 12.18 | N/A | | | | | |
| 18-24 | 109 | 49.68 | 10.16 | 214 | 53.02 | 9.24 | −2.88 | **.001** | 0.4 |
| 25-34 | 242 | 49.66 | 10.91 | 1,062 | 53.27 | 9.56 | −4.75 | **< .001** | 0.4 |
| 35-44* | 133 | 50.03 | 9.15 | 1,557 | 52.00 | 8.07 | −2.41 | **.02** | 0.2 |
| Mental component summary by age group, years | | | | | | | | | |
| 15-17 | 22 | 48.91 | 9.77 | N/A | | | | | |
| 18-24 | 109 | 46.81 | 10.95 | 215 | 46.00 | 12.80 | 0.59 | .55 | 0.1 |
| 25-34 | 242 | 44.89 | 12.26 | 1,065 | 48.90 | 12.30 | −4.59 | **< .001** | 0.3 |
| 35-44* | 133 | 44.68 | 10.94 | 1,558 | 48.80 | 9.60 | −4.21 | **< .001** | 0.4 |
| Physical function by age group, years | | | | | | | | | |
| 15-17 | 23 | 46.38 | 11.77 | N/A | | | | | |
| 18-24 | 114 | 49.61 | 9.91 | 215 | 52.99 | 9.67 | −2.97 | **< .01** | 0.4 |
| 25-34 | 248 | 48.15 | 11.30 | 1,072 | 53.64 | 9.00 | −7.14 | **< .001** | **0.6** |
| 35-44* | 134 | 50.06 | 9.92 | 1,567 | 52.36 | 7.66 | −2.62 | **.01** | 0.3 |
| Role physical by age group, years | | | | | | | | | |
| 15-17 | 23 | 44.16 | 10.73 | N/A | | | | | |
| 18-24 | 113 | 46.90 | 11.20 | 215 | 52.63 | 9.65 | −4.61 | **< .001** | **0.6** |
| 25-34 | 249 | 47.22 | 11.30 | 1,074 | 52.80 | 10.62 | −7.10 | **< .001** | **0.5** |
| 35-44* | 135 | 47.28 | 9.95 | 1,563 | 52.16 | 8.37 | −5.53 | **< .001** | **0.6** |
| Bodily pain by age group, years | | | | | | | | | |
| 15-17 | 23 | 47.25 | 10.19 | N/A | | | | | |
| 18-24 | 113 | 50.32 | 10.27 | 214 | 51.45 | 10.13 | −0.95 | .34 | 0.1 |
| 25-34 | 249 | 49.67 | 11.30 | 1,063 | 51.95 | 11.38 | −2.87 | **< .01** | 0.2 |
| 35-44* | 135 | 49.97 | 9.82 | 1,557 | 50.88 | 9.07 | −1.04 | .30 | 0.1 |
| General health by age group, years | | | | | | | | | |
| 15-17 | 23 | 43.90 | 14.24 | N/A | | | | | |
| 18-24 | 113 | 47.72 | 10.61 | 213 | 50.97 | 10.71 | −2.63 | **< .01** | 0.3 |
| 25-34 | 248 | 47.94 | 11.39 | 1,066 | 52.59 | 10.84 | −5.84 | **< .001** | 0.4 |
| 35-44* | 135 | 46.82 | 10.48 | 1,555 | 51.37 | 8.82 | −4.90 | **< .001** | **0.5** |
| Vitality by age group, years | | | | | | | | | |
| 15-17 | 22 | 50.04 | 10.73 | N/A | | | | | |
| 18-24 | 114 | 48.63 | 10.59 | 212 | 48.50 | 11.77 | 0.10 | .92 | 0.0 |
| 25-34 | 250 | 47.79 | 10.80 | 1,056 | 50.68 | 12.31 | −3.70 | **< .001** | 0.2 |
| 35-44* | 135 | 46.93 | 9.84 | 1,542 | 50.26 | 9.58 | −3.78 | **< .001** | 0.4 |
| Social function by age group, years | | | | | | | | | |
| 15-17 | 23 | 46.91 | 9.86 | N/A | | | | | |
| 18-24 | 112 | 47.19 | 11.15 | 213 | 48.65 | 12.99 | −1.06 | .29 | 0.1 |
| 25-34 | 248 | 45.45 | 12.23 | 1,062 | 50.86 | 12.08 | −6.28 | **< .001** | **0.5** |
| 35-44* | 135 | 46.54 | 10.58 | 1,556 | 50.22 | 9.71 | −3.90 | **< .001** | 0.4 |
| Role emotional by age group, years | | | | | | | | | |
| 15-17 | 23 | 46.60 | 9.45 | N/A | | | | | |
| 18-24 | 113 | 46.03 | 11.72 | 216 | 49.85 | 12.48 | −2.74 | **< .01** | 0.3 |
| 25-34 | 250 | 45.21 | 13.12 | 1,068 | 51.44 | 11.29 | −6.93 | **< .001** | **0.5** |
| 35-44* | 135 | 45.81 | 11.93 | 1,560 | 50.99 | 8.82 | −4.93 | **< .001** | **0.6** |
| Mental health by age group, years | | | | | | | | | |
| 15-17 | 22 | 48.47 | 10.57 | N/A | | | | | |
| 18-24 | 113 | 47.93 | 11.21 | 215 | 46.97 | 12.56 | 0.70 | .48 | 0.1 |
| 25-34 | 250 | 45.72 | 11.54 | 1,071 | 49.45 | 13.01 | −4.49 | **< .001** | 0.3 |
| 35-44* | 134 | 45.62 | 10.68 | 1,566 | 49.20 | 9.91 | −3.75 | **< .001** | 0.4 |

NOTE. From Ware et al.[13] Higher scores represent better HRQOL. Sample size differences by rows are due to missing item responses; physical function (n = 519), role physical (n = 520), bodily pain (n = 520), general health (n = 519), vitality (n = 521), social function (n = 518), role emotional (n = 521), and mental health (n = 519). Bold font indicates significance at $P < .05$ in P column and medium or large effect size in Effect Size column.

Abbreviations: AYA HOPE, Adolescent and Young Adult Health Outcomes and Patient Experience study; HRQOL, health-related quality of life; N/A, not applicable; SD, standard deviation; SF-12, Short-Form Health Survey 12.

*From the AYA HOPE age group, ages 35-41 years.

**Table 3.** PedsQL Outcomes Among AYA HOPE Participants by Age at Survey Compared With Healthy Young Adults

| Participant Group | No. of Patients | Mean | SD | Groups Compared | t Test* | P | Effect Size (Cohen's d) |
|---|---|---|---|---|---|---|---|
| Total score | | | | | | | |
|   1. Reference, AYA HOPE, ages 18-25 years | 135 | 71.17 | 20.42 | | | | |
|   2. Healthy young adults, ages 18-25 years† | 1,171 | 78.18 | 9.20 | 1 v 2 | **3.94** | **.001** | **0.6** |
|   3. AYA HOPE, ages 15-17 years | 23 | 64.54 | 18.89 | 1 v 3 | 1.54 | .14 | 0.3 |
|   4. AYA HOPE, ages ≥ 26 years | 363 | 67.61 | 21.03 | 1 v 4 | 1.71 | .09 | 0.2 |
| Psychosocial summary | | | | | | | |
|   1. Reference, AYA HOPE, ages 18-25 years | 134 | 71.70 | 20.96 | | | | |
|   2. Healthy young adults, ages 18-25 years† | 1,171 | 73.87 | 10.53 | 1 v 2 | 1.18 | .24 | 0.2 |
|   3. AYA HOPE, ages 15-17 years | 23 | 66.26 | 18.02 | 1 v 3 | 1.30 | .21 | 0.3 |
|   4. AYA HOPE, ages ≥ 26 years | 363 | 69.48 | 20.07 | 1 v 4 | 1.06 | .29 | 0.1 |
| Physical functioning | | | | | | | |
|   1. Reference, AYA HOPE, ages 18-25 years | 136 | 75.60 | 23.24 | | | | |
|   2. Healthy young adults, ages 18-25 years† | 1,171 | 86.25 | 10.63 | 1 v 2 | **5.28** | **< .001** | **0.9** |
|   3. AYA HOPE, ages 15-17 years | 23 | 64.69 | 26.06 | 1 v 3 | **1.88** | .07 | **0.5** |
|   4. AYA HOPE, ages ≥ 26 years | 364 | 70.00 | 25.76 | 1 v 4 | **2.32** | **.02** | 0.2 |
| Emotional functioning | | | | | | | |
|   1. Reference, AYA HOPE, ages 18-25 years | 135 | 66.21 | 25.24 | | | | |
|   2. Healthy young adults, ages 18-25 years† | 1,171 | 66.68 | 15.00 | 1 v 2 | 0.21 | .83 | 0.0 |
|   3. AYA HOPE, ages 15-17 years | 23 | 68.04 | 21.99 | 1 v 3 | −0.36 | .72 | 0.1 |
|   4. AYA HOPE, ages ≥ 26 years | 363 | 63.61 | 22.59 | 1 v 4 | 1.05 | .29 | 0.1 |
| Social functioning | | | | | | | |
|   1. Reference, AYA HOPE, ages 18-25 years | 133 | 80.70 | 23.47 | | | | |
|   2. Healthy young adults, ages 18-25 years† | 1,171 | 85.48 | 11.90 | 1 v 2 | **2.31** | **.02** | 0.4 |
|   3. AYA HOPE, ages 15-17 years | 23 | 75.36 | 22.54 | 1 v 3 | 1.04 | .31 | 0.2 |
|   4. AYA HOPE, ages ≥ 26 years | 362 | 78.78 | 22.07 | 1 v 4 | 0.82 | .41 | 0.1 |
| Work/school functioning | | | | | | | |
|   1. Reference, AYA HOPE, ages 18-25 years | 129 | 72.96 | 23.76 | | | | |
|   2. Healthy young adults, ages 18-25 years† | 1,171 | 69.47 | 13.94 | 1 v 2 | −1.64 | .10 | 0.2 |
|   3. AYA HOPE, ages 15-17 years | 22 | 58.86 | 19.70 | 1 v 3 | **3.00** | **.01** | **0.6** |
|   4. AYA HOPE, ages ≥ 26 years | 347 | 70.72 | 23.54 | 1 v 4 | 0.91 | .36 | 0.1 |
| Fatigue‡ | | | | | | | |
|   1. Reference, AYA HOPE, ages 18-25 years | 136 | 61.31 | 26.90 | | | | |
|   2. Healthy young adults, ages 18-25 years‡ | 391 | 70.92 | 16.94 | 1 v 2 | 3.91 | **.001** | **0.6** |
|   3. AYA HOPE, ages 15-17 years | 23 | 59.78 | 23.75 | 1 v 3 | 0.28 | .78 | 0.1 |
|   4. AYA HOPE, ages ≥ 26 years | 363 | 57.01 | 25.27 | 1 v 4 | 1.61 | .11 | 0.2 |

NOTE. Sample size differences for AYA HOPE by rows are owing to missing item responses; total score (n = 521), psychosocial summary (n = 520), physical functioning (n = 523), emotional functioning (n = 521), social functioning (n = 518), work/school functioning (n = 498), and fatigue (n = 522). Higher scores represent better HRQOL. Bold font indicates significance at $P < .05$ in P column and medium or large effect size in Effect Size column.

Abbreviations: AYA HOPE, Adolescent and Young Adult Health Outcomes and Patient Experience study; HRQOL, health-related quality of life; PedsQL, Pediatric Quality of Life Inventory; SD, standard deviation.

*Based on independent samples' t tests.
†Published in Varni et al.[19]
‡Published in Varni et al.[14]

(patients with non-Hodgkin lymphoma and acute lymphocytic leukemia reported better MCS scores than those with germ cell cancer), and symptoms.

Before symptoms were included in the model, significant differences were also seen for age ($\beta = -0.26$; SE, 0.10; $P < .01$), comorbidity, and treatment. Individuals with two or more severe comorbid conditions reported worse MCS scores ($\beta = -4.42$; SE, 1.72; $P = .01$) than those without. Respondents who had both radiation and chemotherapy reported worse MCS than those who only had surgery ($\beta = -5.23$; SE, 2.37; $P = .03$), and those respondents currently receiving current treatment reported worse mental HRQOL than those who were not ($\beta = -4.28$; SE, 1.54; $P < .001$).

Similar results were seen for PedsQL outcomes (Table 5). Results indicated that the inclusion of symptoms was significant in all scales. Additional variance explained by symptoms in the models was sub-

stantial and ranged from 18% on the Emotional Functioning subscale to 30% on the Total Score. After accounting for the impact of symptoms, other significant covariates included older age (associated with fatigue and physical functioning), lacking health insurance (associated with fatigue and emotional functioning), and current treatment (associated with all outcomes except emotional functioning). However, similar to the SF-12 findings, before symptoms were entered into the models, covariates such as age, female sex, Hispanic ethnicity, having less than a high school education, being unmarried, lacking health insurance, having radiation and chemotherapy, and having two or more severe comorbid conditions were significantly associated with worse HRQOL on several PedsQL subscales and the total score (Appendix Table A1 [online-only]). The strongest and/or most consistent predictors (when symptoms were not in the models) were age, lacking health insurance, and having severe comorbidities.

**Table 4.** Multivariate Linear Regression Models Examining Demographic and Clinical Factors With SF-12 Outcomes

| Factor Model summary | No. of Patients | Physical Component Summary | | | | | Mental Component Summary | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | $F$ | $R^2$ | Beta | SE | $P$ | $F$ | $R^2$ | Beta | SE | $P$ |
| Demographics | 484 | **8.49** | **0.38** | | | **< .001** | **5.04** | **0.27** | | | **< .001** |
| Age at survey, continuous | 484 | | | −0.10 | 0.07 | .16 | | | −0.13 | 0.09 | .15 |
| Sex | | | | | | | | | | | |
| Male patients | 311 | | | 0.47 | 0.95 | .62 | | | 0.45 | 1.19 | .70 |
| Female patients | 173 | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Race/ethnicity | | | | | | | | | | | |
| White | 285 | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Hispanic | 100 | | | **−2.56** | **1.01** | **.01** | | | 0.61 | 1.26 | .63 |
| Black | 43 | | | −1.84 | 1.51 | .22 | | | 1.88 | 1.89 | .32 |
| Other | 56 | | | −0.97 | 1.26 | .44 | | | 0.91 | 1.57 | .56 |
| Education, prediagnosis | | | | | | | | | | | |
| High school or less | 130 | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Some college | 127 | | | **2.37** | **1.11** | **.03** | | | −0.82 | 1.39 | .55 |
| College graduate | 226 | | | **3.09** | **1.07** | **< .01** | | | −2.50 | 1.34 | .06 |
| Missing | 1 | | | | | | | | | | |
| Marital status | | | | | | | | | | | |
| Married | 205 | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Not married | 278 | | | 0.95 | 0.90 | .29 | | | **−2.69** | **1.12** | **.02** |
| Missing | 1 | | | | | | | | | | |
| Lack of health insurance at any time since diagnosis | | | | | | | | | | | |
| No | 407 | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Yes | 70 | | | **−2.42** | **1.12** | **.03** | | | **−4.09** | **1.40** | **< .01** |
| Missing | 7 | | | | | | | | | | |
| Disease-related variables | | | | | | | | | | | |
| Cancer type | | | | | | | | | | | |
| Acute lymphoblastic leukemia | 16 | | | −3.81 | 4.43 | .39 | | | **10.98** | **5.54** | **.05** |
| Germ cell cancer | 193 | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Hodgkin lymphoma | 135 | | | −0.04 | 1.40 | .98 | | | 0.63 | 1.74 | .72 |
| Non-Hodgkin lymphoma | 121 | | | −0.69 | 1.36 | .61 | | | **3.76** | **1.70** | **.03** |
| Sarcoma | 19 | | | **−8.02** | **2.43** | **.001** | | | 2.98 | 3.03 | .33 |
| AJCC cancer stage | | | | | | | | | | | |
| I | 200 | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| II | 117 | | | 0.68 | 1.15 | .55 | | | 0.10 | 1.43 | .94 |
| III | 69 | | | −0.83 | 1.28 | .52 | | | −0.48 | 1.60 | .76 |
| IV | 59 | | | 0.22 | 1.43 | .88 | | | 1.64 | 1.79 | .36 |
| N/A | 21 | | | −0.85 | 3.81 | .82 | | | −3.29 | 4.76 | .49 |
| Unknown | 18 | | | −1.42 | 2.33 | .54 | | | −0.74 | 2.91 | .80 |
| Treatment type | | | | | | | | | | | |
| Surgery only | 59 | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Radiation | 50 | | | −1.48 | 1.64 | .37 | | | −1.33 | 2.05 | .52 |
| Chemotherapy | 227 | | | **−3.55** | **1.46** | **.02** | | | −1.25 | 1.82 | .49 |
| Radiation and chemotherapy | 108 | | | **−3.36** | **1.76** | **.06** | | | −2.81 | 2.20 | .20 |
| Missing/unknown/no treatment | 40 | | | −1.53 | 2.48 | .54 | | | −3.98 | 3.10 | .20 |
| Currently in treatment | | | | | | | | | | | |
| No | 396 | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Yes | 78 | | | **−4.75** | **1.16** | **< .001** | | | −1.68 | 1.45 | .25 |
| Missing | 10 | | | | | | | | | | |
| Comorbidity | | | | | | | | | | | |
| 0 | 315 | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| 1 | 77 | | | −1.27 | 1.11 | .25 | | | 1.26 | 1.39 | .36 |
| ≥ 2 | 59 | | | −0.93 | 1.28 | .47 | | | −2.34 | 1.60 | .15 |
| Missing/no consent | 33 | | | | | | | | | | |
| Current/recent symptoms | | | | | | | | | | | |
| 0 | 78 | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| 1 or 2 | 166 | | | −0.48 | 1.18 | .68 | | | **−3.99** | **1.47** | **.01** |
| 3 or 4 | 108 | | | **−4.22** | **1.29** | **.00** | | | **−8.12** | **1.61** | **< .001** |
| ≥ 5 | 132 | | | **−8.08** | **1.34** | **< .001** | | | **−13.9** | **1.67** | **< .001** |

NOTE. Bold font indicates significance at $P < .05$.
Abbreviations: AJCC, American Joint Committee on Cancer; N/A, not applicable; SF-12, Short-Form Health Survey 12; Ref, reference.

**Table 5.** Multivariate Linear Regression Models Examining Demographic and Clinical Factors With PedsQL Outcomes

| Factors Predicting HRQOL | No. of Patients | Total Score | | | | | Fatigue | | | | | Physical Functioning | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | F | $R^2$ | Beta | SE | P | F | $R^2$ | Beta | SE | P | F | $R^2$ | Beta | SE | P |
| Model Summary | 484 | 15.79 | 0.54 | | | < .001 | 12.11 | 0.47 | | | < .001 | 13.44 | 0.50 | | | < .001 |
| Demographics | | | | | | | | | | | | | | | | |
| Age at survey | | | | −0.23 | 0.13 | .06 | | | **−0.36** | **0.17** | **.03** | | | **−0.51** | **0.16** | **.001** |
| Sex | | | | | | | | | | | | | | | | |
| Male patients | 311 | | | 2.31 | 1.63 | .16 | | | 4.31 | 2.20 | .05 | | | 3.59 | 2.07 | .08 |
| Female patients | 173 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Race/ethnicity | | | | | | | | | | | | | | | | |
| White | 285 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Hispanic | 100 | | | −1.34 | 1.73 | .44 | | | 0.92 | 2.33 | .69 | | | −3.03 | 2.20 | .17 |
| Black | 43 | | | 0.98 | 2.59 | .71 | | | 2.30 | 3.50 | .51 | | | 0.62 | 3.30 | .85 |
| Other | 56 | | | −0.89 | 2.16 | .68 | | | −0.95 | 2.91 | .75 | | | −1.02 | 2.75 | .71 |
| Education | | | | | | | | | | | | | | | | |
| High school or less | 130 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Some college | 127 | | | −0.46 | 1.91 | .81 | | | −2.43 | 2.57 | .35 | | | 2.94 | 2.43 | .23 |
| College graduate | 226 | | | −0.85 | 1.84 | .64 | | | −3.49 | 2.48 | .16 | | | 3.82 | 2.34 | .10 |
| Missing | 1 | | | | | | | | | | | | | | | |
| Marital status | | | | | | | | | | | | | | | | |
| Married | 205 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Not married | 278 | | | −1.76 | 1.55 | .26 | | | −3.01 | 2.08 | .15 | | | −0.91 | 1.97 | .64 |
| Missing | 1 | | | | | | | | | | | | | | | |
| Lack of health insurance | | | | | | | | | | | | | | | | |
| No | 407 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Yes | 70 | | | −3.06 | 1.93 | .11 | | | **−5.27** | **2.60** | **.04** | | | −2.34 | 2.46 | .34 |
| Missing | 7 | | | | | | | | | | | | | | | |
| Disease-related variables | | | | | | | | | | | | | | | | |
| Cancer type | | | | | | | | | | | | | | | | |
| Acute lymphoblastic leukemia | 16 | | | 4.56 | 7.62 | .55 | | | 9.19 | 10.27 | .37 | | | −3.47 | 9.69 | .72 |
| Germ cell cancer | 193 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Hodgkin lymphoma | 135 | | | −0.42 | 2.40 | .86 | | | −0.30 | 3.24 | .93 | | | −2.74 | 3.05 | .37 |
| Non-Hodgkin lymphoma | 121 | | | 1.48 | 2.33 | .53 | | | 3.27 | 3.15 | .30 | | | 0.64 | 2.97 | .83 |
| Sarcoma | 19 | | | −1.57 | 4.17 | .71 | | | 4.86 | 5.62 | .39 | | | **−16.2** | **5.31** | **.002** |
| AJCC cancer stage | | | | | | | | | | | | | | | | |
| I | 200 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| II | 117 | | | −1.65 | 1.97 | .40 | | | 0.22 | 2.66 | .93 | | | 0.28 | 2.51 | .91 |
| III | 69 | | | −2.89 | 2.20 | .19 | | | −4.17 | 2.97 | .16 | | | −3.51 | 2.80 | .21 |
| IV | 59 | | | −2.30 | 2.47 | .35 | | | −0.66 | 3.32 | .84 | | | −3.00 | 3.13 | .34 |
| N/A | 21 | | | −7.43 | 6.55 | .26 | | | −10.71 | 8.83 | .23 | | | −5.10 | 8.33 | .54 |
| Unknown | 18 | | | −7.49 | 4.00 | .06 | | | −5.65 | 5.39 | .30 | | | −4.76 | 5.09 | .35 |
| Treatment type | | | | | | | | | | | | | | | | |
| Surgery only | 59 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Radiation | 50 | | | −2.01 | 2.81 | .48 | | | **−7.80** | **3.79** | **.04** | | | −2.28 | 3.58 | .53 |
| Chemotherapy | 227 | | | −2.89 | 2.50 | .25 | | | −3.80 | 3.38 | .26 | | | −4.48 | 3.18 | .16 |
| Radiation and chemotherapy | 108 | | | −3.22 | 3.03 | .29 | | | −4.37 | 4.09 | .29 | | | −3.32 | 3.85 | .39 |
| Missing/unknown/no treatment | 40 | | | −6.81 | 4.26 | .11 | | | −8.03 | 5.74 | .16 | | | −8.21 | 5.42 | .13 |
| Currently in treatment | | | | | | | | | | | | | | | | |
| No | 396 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Yes | 78 | | | **−6.20** | **2.00** | **.002** | | | **−7.77** | **2.69** | **.004** | | | **−8.45** | **2.54** | **.001** |
| Missing | 10 | | | 1.20 | 4.75 | .80 | | | 1.72 | 6.40 | .79 | | | 0.08 | 6.04 | .99 |
| Severe comorbidity | | | | | | | | | | | | | | | | |
| 0 | 315 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| 1 | 77 | | | −0.49 | 1.91 | .80 | | | 2.19 | 2.58 | .40 | | | 0.47 | 2.43 | .85 |
| ≥ 2 | 59 | | | −2.48 | 2.21 | .26 | | | 0.05 | 2.98 | .99 | | | −3.88 | 2.81 | .17 |
| Missing/no consent | 33 | | | 5.22 | 3.97 | .19 | | | 5.14 | 5.35 | .34 | | | 5.24 | 5.05 | .30 |
| Current/recent symptoms | | | | | | | | | | | | | | | | |
| 0 | 78 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| 1 or 2 | 166 | | | **−8.39** | **2.02** | **< .001** | | | **−11.9** | **2.73** | **< .001** | | | **−7.50** | **2.57** | **.004** |
| 3 or 4 | 108 | | | **−21.2** | **2.21** | **< .001** | | | **−28.8** | **2.98** | **< .001** | | | **−21.5** | **2.81** | **< .001** |
| ≥ 5 | 132 | | | **−34.3** | **2.30** | **< .001** | | | **−42.0** | **3.10** | **< .001** | | | **−34.9** | **2.92** | **< .001** |

**Table 5.** Multivariate Linear Regression Models Examining Demographic and Clinical Factors With PedsQL Outcomes (continued)

| Factors Predicting HRQOL | No. of Patients | Emotional Functioning | | | | | Social Functioning | | | | | Work/School Functioning | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | F | R² | Beta | SE | P | F | R² | Beta | SE | P | F | R² | Beta | SE | P |
| Model Summary | 484 | 6.31 | 0.32 | | | < .001 | 8.80 | 0.39 | | | < .001 | 7.21 | 0.35 | | | < .001 |
| Demographics | | | | | | | | | | | | | | | | |
| Age at survey | | | | −0.23 | 0.18 | .20 | | | −0.09 | 0.15 | .55 | | | 0.23 | 0.17 | .18 |
| Sex | | | | | | | | | | | | | | | | |
| Male patients | 311 | | | 3.22 | 2.29 | .16 | | | −2.87 | 1.98 | .15 | | | 0.93 | 2.24 | .68 |
| Female patients | 173 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Race/ethnicity | | | | | | | | | | | | | | | | |
| White | 285 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Hispanic | 100 | | | −1.10 | 2.43 | .65 | | | −3.02 | 2.10 | .15 | | | 0.25 | 2.38 | .91 |
| Black | 43 | | | 2.51 | 3.64 | .49 | | | −0.54 | 3.15 | .86 | | | −0.27 | 3.57 | .94 |
| Other | 56 | | | 1.62 | 3.04 | .59 | | | −0.28 | 2.63 | .92 | | | −3.56 | 2.98 | .23 |
| Education | | | | | | | | | | | | | | | | |
| High school or less | 130 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Some college | 127 | | | −3.26 | 2.68 | .22 | | | −0.97 | 2.32 | .68 | | | −1.18 | 2.62 | .65 |
| College graduate | 226 | | | −3.30 | 2.58 | .20 | | | −2.34 | 2.23 | .30 | | | −2.89 | 2.53 | .25 |
| Missing | 1 | | | **−53.6** | **20.89** | **.01** | | | 24.46 | 18.08 | .18 | | | 7.99 | 20.48 | .70 |
| Marital status | | | | | | | | | | | | | | | | |
| Married | 205 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Not married | 278 | | | −2.43 | 2.17 | .26 | | | −2.27 | 1.88 | .23 | | | −1.11 | 2.13 | .60 |
| Missing | 1 | | | 14.56 | 20.45 | .48 | | | 25.57 | 17.69 | .15 | | | 37.34 | 20.04 | .06 |
| Lack of health insurance | | | | | | | | | | | | | | | | |
| No | 407 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Yes | 70 | | | **−5.84** | **2.71** | **.03** | | | 0.59 | 2.35 | .80 | | | −2.04 | 2.66 | .44 |
| Missing | 7 | | | 4.68 | 7.77 | .55 | | | 4.87 | 6.72 | .47 | | | −1.19 | 7.62 | .88 |
| Disease-related variables | | | | | | | | | | | | | | | | |
| Cancer type | | | | | | | | | | | | | | | | |
| Acute lymphoblastic leukemia | 16 | | | 8.92 | 10.69 | .40 | | | −9.25 | 9.25 | .32 | | | 15.37 | 10.48 | .14 |
| Germ cell cancer | 193 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Hodgkin lymphoma | 135 | | | 0.47 | 3.37 | .89 | | | 0.47 | 2.91 | .87 | | | 1.67 | 3.30 | .61 |
| Non-Hodgkin lymphoma | 121 | | | 2.17 | 3.28 | .51 | | | −1.69 | 2.84 | .55 | | | 2.57 | 3.21 | .42 |
| Sarcoma | 19 | | | 5.66 | 5.86 | .33 | | | −2.67 | 5.07 | .60 | | | 9.79 | 5.74 | .09 |
| AJCC cancer stage | | | | | | | | | | | | | | | | |
| I | 200 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| II | 117 | | | −3.15 | 2.77 | .26 | | | −4.01 | 2.39 | .09 | | | −3.25 | 2.71 | .23 |
| III | 69 | | | −1.95 | 3.09 | .53 | | | −4.21 | 2.68 | .12 | | | −1.05 | 3.03 | .73 |
| IV | 59 | | | 0.69 | 3.46 | .84 | | | −0.31 | 2.99 | .92 | | | **−6.74** | **3.39** | **< .05** |
| N/A | 21 | | | −6.52 | 9.19 | .48 | | | −2.82 | 7.95 | .72 | | | −9.86 | 9.01 | .27 |
| Unknown | 18 | | | −6.67 | 5.62 | .24 | | | **−11.7** | **4.86** | **.02** | | | **−11.5** | **5.51** | **.04** |
| Treatment type | | | | | | | | | | | | | | | | |
| Surgery only | 59 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Radiation | 50 | | | 1.58 | 3.95 | .69 | | | −0.12 | 3.42 | .97 | | | −1.80 | 3.87 | .64 |
| Chemotherapy | 227 | | | −0.56 | 3.52 | .87 | | | −2.84 | 3.04 | .35 | | | −1.92 | 3.45 | .58 |
| Radiation and chemotherapy | 108 | | | −1.76 | 4.25 | .68 | | | −4.07 | 3.68 | .27 | | | −2.96 | 4.17 | .48 |
| Missing/unknown/no treatment | 40 | | | −3.69 | 5.98 | .54 | | | −6.07 | 5.17 | .24 | | | −7.14 | 5.86 | .22 |
| Currently in treatment | | | | | | | | | | | | | | | | |
| No | 396 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Yes | 78 | | | −1.84 | 2.80 | .51 | | | **−6.83** | **2.43** | **.01** | | | **−5.45** | **2.75** | **< .05** |
| Missing | 10 | | | | | | | | | | | | | | | |
| Severe comorbidity | | | | | | | | | | | | | | | | |
| 0 | 315 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| 1 | 77 | | | 0.68 | 2.69 | .80 | | | −2.04 | 2.32 | .38 | | | −4.24 | 2.63 | .11 |
| ≥ 2 | 59 | | | −1.31 | 3.10 | .67 | | | −4.90 | 2.68 | .07 | | | −1.91 | 3.04 | .53 |
| Missing/no consent | 33 | | | 5.38 | 5.57 | .33 | | | 1.86 | 4.82 | .70 | | | 7.13 | 5.46 | .19 |
| Current/recent symptoms | | | | | | | | | | | | | | | | |
| 0 | 78 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| 1 or 2 | 166 | | | **−8.82** | **2.84** | **.002** | | | **−5.81** | **2.46** | **.02** | | | **−8.03** | **2.78** | **.004** |
| 3 or 4 | 108 | | | **−18.6** | **3.10** | **< .001** | | | **−16.8** | **2.68** | **< .001** | | | **−19.7** | **3.04** | **< .001** |
| ≥ 5 | 132 | | | **−31.4** | **3.23** | **< .001** | | | **−28.8** | **2.79** | **< .001** | | | **−33.5** | **3.16** | **< .001** |

NOTE. Bold font indicates significance at $P < .05$.
Abbreviations: AJCC, American Joint Committee on Cancer; HRQOL, health-related quality of life; N/A, not applicable; PedsQL, Pediatric Quality of Life Inventory; Ref, reference.

## DISCUSSION

Results from the AYA HOPE study indicate that AYA patients with cancer have significantly worse HRQOL than similarly aged population norms and healthy populations. HRQOL subdomains of physical and social functioning, limitations to physical and emotional roles, and fatigue were worse than reference populations and young adult survivors of pediatric cancer,[16] suggesting that cancer is disruptive to daily activities and functioning among newly diagnosed AYAs. These results may also be considered clinically relevant, as differences exceeded minimally important difference thresholds of four to five points, half a standard deviation on the SF-12.[20] We also found several important correlates of poorer HRQOL, including younger age, high school or less education, current symptoms, treatment, and lacking health insurance. In combination, these data suggest major HRQOL decrements experienced by subgroups of AYA patients with cancer.

Data from the current study suggest that cancer among AYAs has a major impact on fatigue and physical functioning. Though AYA HOPE participants reported worse fatigue than healthy college students, compared with pediatric cancer patients (ages 2 to 18 years)[21] AYA HOPE patients' fatigue scores were substantially worse (10 to 20 points lower, depending on treatment status). However, 18- to 25-year-old adults with chronic disease have reported similar levels of fatigue[14] to those found in AYA HOPE patients, suggesting that AYAs in general may be reporting higher levels of fatigue than children.[7] With respect to physical functioning, AYAs are in a period characterized by tremendous physical and cognitive growth and development with significant hormone-related changes. Decrements in physical functioning and fatigue among AYAs may in part be a result of these physical changes. They may also be the result of cumulative effects of normal developmental challenges in young adults (eg, college, work, relationships, starting families) coupled with a cancer diagnosis. Research suggests that school, work, and families are negatively affected by cancer,[8,22] though it is not clear whether there are direct effects on fatigue. The strongest correlates of fatigue and physical functioning in AYA HOPE were current symptoms, being in treatment, and being treated with radiation, thus highlighting the need for clinicians to pay particular attention to symptom management during acute and post-treatment periods to help attenuate debilitating fatigue and physical outcomes experienced by AYA cancer survivors.

AYA HOPE results also highlight that AYAs are at risk for poor psychosocial functioning compared with the general population of AYAs. Specific differences were seen for social functioning, limitations in emotional roles, and mental health. Though work/school functioning was not different between young adults ages 18 to 25 years with or without cancer, the lower work/school functioning scores reported by 15- to 17-year-olds with cancer (compared with patients 18 to 25 years old) are consistent with current literature.[23] These data indicate that adolescents may need additional educational support during and after treatment as they transition back to school. Taken together, effects of cancer and age on psychosocial outcomes suggest the importance of interventions to promote social integration for AYAs, for whom friendships and social roles are key components of identity and mental health.

Several important correlates of HRQOL emerged from our study. Current symptoms, cancer type, and treatment status/type were strongly associated with HRQOL, consistent with previous studies in both older[24,25] and younger patients.[26] Symptoms were by far the overwhelming contributor to HRQOL outcomes across domains. The list of symptoms in the AYA HOPE survey included several debilitating conditions that are often associated with treatment. However, both current treatment and reported symptoms were significantly associated with HRQOL in adjusted models, suggesting that treatment alone does not account for the symptom experience. We know of no other studies of AYAs with cancer that have specifically investigated symptom burden. It is not clear from these data whether AYAs have more symptoms than older/younger cancer populations or whether their symptoms are not being addressed well. These results suggest the need for more targeted attention to AYAs to address cancer-related symptoms.

Poorer HRQOL in this study was reported for Hispanic patients, those lacking health insurance, and those with less education, suggesting socioeconomic effects and highlighting the need to explore these disparities relative to health care delivery to better understand whether symptoms and HRQOL are poorly addressed in these subgroups (eg, because of possible communication, cost, or language barriers). Though research in adult survivors of childhood cancer have reported somewhat similar findings,[6] to our knowledge our study is the first to report such associations among patients diagnosed in this age group and in Hispanic patients. It is interesting that lack of health insurance was associated with both physical and mental functioning; suggesting that financial strains may have effects that influence physical outcomes (eg, treatment adherence) and that associated stress may affect mental health. Though we know that AYAs are less likely than many other age groups to have health insurance[27] and that health care costs affect treatment decision-making,[28] changes in health care policy and coverage specifically for young adults will hopefully reduce this burden in the future.[27]

Study limitations include generalizability, given the modest response rate (though those who participated do reflect the population of AYA cancer survivors[11]) and small sample size for cancer type and treatment, making disease-specific comparisons difficult. Further, we could not explore health care system components (location of care in adult *v* pediatric facilities) on HRQOL outcomes owing to sample size constraints. We were also limited by the restricted age ranges on assessment tools to measure HRQOL; neither of the gold-standard instruments had demonstrated evidence of validity or reliability for the entire AYA age range. It would be helpful to have appropriate instruments for the entire AYA population and, fortunately, there are efforts underway to develop such tools for patients diagnosed as AYAs.[29,30] Nevertheless, it is encouraging that similar results were seen for SF-12 and PedsQL outcomes, two prominent instruments validated in age ranges that overlap this population.

Our study has several strengths. Participants were recruited from seven population-based registries, providing a larger sample of Hispanic respondents and geographic diversity than has been presented previously. In addition, with self-report, cancer registry, and medical record data, we obtained a comprehensive perspective on factors affecting patient experiences and outcomes. Though we have learned from studies on long-term survivors of childhood cancer about experiences important to AYAs, it has also been argued that the impact of cancer in a young adult is different from the experiences of those patients diagnosed during childhood,[31] and we need to better understand those differences.

Data from our study suggest several areas for future research in AYAs. Further examination of the persistence of fatigue is needed in this population, plus its longer-term effects on HRQOL outcomes, to better inform interventions. Future work could also focus on specific symptoms or clusters of symptoms that adversely affect HRQOL in AYAs to better manage or attenuate these effects. Though we know of no other known data sets with sufficiently large samples of AYA patients with cancer to explore differences in our patients' experiences, our results indicate a need to develop future studies that can better examine demographic and health insurance issues.

In summary, our study highlights major decrements in physical and psychosocial HRQOL experienced by AYAs recently diagnosed with cancer in the United States. Clinicians need to be aware of the influence that current symptoms and treatment may have on fatigue in AYA patients. Further, patient care teams need to attend to vulnerable subgroups, such as Hispanic patients, those with less education, and those without health insurance, as they may be at greatest risk for poorer HRQOL. With the increasing number of patients diagnosed with cancer in this age range each year,[2] future research should explore ways to address poor functioning in this understudied population of AYA cancer survivors.

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## *Acknowledgment*

## Appendix

**Table A1.** Demographic and Clinical Factors Associated With PedsQL Outcomes Excluding Symptoms

| Factors Predicting HRQOL | No. of Patients | Total Score | | | | | Fatigue | | | | | Physical Functioning | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | $F$ | $R^2$ | Beta | SE | $P$ | $F$ | $R^2$ | Beta | SE | $P$ | $F$ | $R^2$ | Beta | SE | $P$ |
| Model summary | 484 | 4.85 | 0.24 | | | < .001 | 3.72 | 0.20 | | | < .001 | 6.01 | 0.28 | | | < .001 |
| Demographics | | | | | | | | | | | | | | | | |
|   Age at survey | | | | −0.55 | 0.16 | < .001 | | | −0.75 | 0.20 | < .001 | | | −0.84 | 0.19 | < .001 |
|   Sex | | | | | | | | | | | | | | | | |
|     Male patients | 311 | | | 7.52 | 2.04 | < .001 | | | 10.73 | 2.65 | < .001 | | | 8.99 | 2.42 | < .001 |
|     Female patients | 173 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
|   Race/ethnicity | | | | | | | | | | | | | | | | |
|     White | 285 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
|     Hispanic | 100 | | | −3.56 | 2.20 | .11 | | | −1.63 | 2.85 | .57 | | | −5.32 | 2.61 | .04 |
|     Black | 43 | | | −2.22 | 3.29 | .50 | | | −1.37 | 4.27 | .75 | | | −2.65 | 3.90 | .50 |
|     Other | 56 | | | −3.62 | 2.75 | .19 | | | −4.15 | 3.56 | .24 | | | −3.86 | 3.26 | .24 |
|   Education | | | | | | | | | | | | | | | | |
|     High school or less | 130 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
|     Some college | 127 | | | −1.32 | 2.42 | .59 | | | −3.25 | 3.15 | .30 | | | 2.00 | 2.87 | .49 |
|     College graduate | 226 | | | 2.92 | 2.32 | .21 | | | 1.24 | 3.01 | .68 | | | 7.63 | 2.75 | .01 |
|     Missing | 1 | | | −4.10 | 18.90 | .83 | | | −9.43 | 24.53 | .70 | | | −0.78 | 22.41 | .97 |
|   Marital status | | | | | | | | | | | | | | | | |
|     Married | 205 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
|     Not married | 278 | | | −3.61 | 1.96 | .07 | | | −5.11 | 2.55 | < .05 | | | −2.82 | 2.33 | .23 |
|     Missing | 1 | | | 21.92 | 18.49 | .24 | | | 16.88 | 24.01 | .48 | | | 21.62 | 21.93 | .32 |
|   Lack of health insurance | | | | | | | | | | | | | | | | |
|     No | 407 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
|     Yes | 70 | | | −7.6 | 2.44 | .002 | | | −10.8 | 3.16 | .001 | | | −7.00 | 2.89 | .02 |
|     Missing | 7 | | | 5.60 | 7.03 | .43 | | | 5.34 | 9.13 | .56 | | | 5.83 | 8.34 | .48 |
| Disease-related variables | | | | | | | | | | | | | | | | |
|   Cancer type | | | | | | | | | | | | | | | | |
|     Acute lymphoblastic leukemia | 16 | | | 6.86 | 9.70 | .48 | | | 11.68 | 12.59 | .35 | | | −1.12 | 11.50 | .92 |
|     Germ cell cancer | 193 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
|     Hodgkin lymphoma | 135 | | | 2.76 | 3.05 | .37 | | | 3.42 | 3.95 | .39 | | | 0.54 | 3.61 | .88 |
|     Non-Hodgkin lymphoma | 121 | | | 3.96 | 2.96 | .18 | | | 6.13 | 3.85 | .11 | | | 3.18 | 3.52 | .37 |
|     Sarcoma | 19 | | | −1.95 | 5.31 | .71 | | | 4.64 | 6.90 | .50 | | | −16.6 | 6.30 | .01 |
|   AJCC cancer stage | | | | | | | | | | | | | | | | |
|     I | 200 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
|     II | 117 | | | −2.41 | 2.51 | .34 | | | −0.65 | 3.26 | .84 | | | −0.49 | 2.98 | .87 |
|     III | 69 | | | −3.27 | 2.80 | .24 | | | −4.56 | 3.63 | .21 | | | −3.81 | 3.32 | .25 |
|     IV | 59 | | | −2.53 | 3.14 | .42 | | | −1.03 | 4.07 | .80 | | | −3.15 | 3.72 | .40 |
|     N/A | 21 | | | −7.36 | 8.34 | .38 | | | −10.7 | 10.83 | .32 | | | −5.00 | 9.89 | .61 |
|     Unknown | 18 | | | −6.92 | 5.05 | .17 | | | −5.26 | 6.56 | .42 | | | −3.84 | 5.99 | .52 |
|   Treatment type | | | | | | | | | | | | | | | | |
|     Surgery only | 59 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
|     Radiation | 50 | | | −3.54 | 3.57 | .32 | | | −9.77 | 4.64 | .04 | | | −3.72 | 4.24 | .38 |
|     Chemotherapy | 227 | | | −7.22 | 3.16 | .02 | | | −9.19 | 4.10 | .03 | | | −8.82 | 3.75 | .02 |
|     Radiation and chemotherapy | 108 | | | −9.31 | 3.83 | .02 | | | −11.7 | 4.97 | .02 | | | −9.60 | 4.54 | .04 |
|     Missing/unknown/none | 40 | | | −5.33 | 5.42 | .33 | | | −6.23 | 7.04 | .38 | | | −6.57 | 6.43 | .31 |
|   Currently in treatment | | | | | | | | | | | | | | | | |
|     No | 396 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
|     Yes | 78 | | | −12.9 | 2.49 | < .001 | | | −15.7 | 3.23 | < .001 | | | −15.4 | 2.95 | < .001 |
|     Missing | 10 | | | −6.47 | 5.99 | .28 | | | −6.85 | 7.77 | .38 | | | −8.09 | 7.10 | .26 |
| Severe comorbidity | | | | | | | | | | | | | | | | |
|   0 | 315 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
|   1 | 77 | | | −3.16 | 2.43 | .19 | | | −1.07 | 3.15 | .74 | | | −2.34 | 2.88 | .42 |
|   ≥ 2 | 59 | | | −7.83 | 2.78 | .01 | | | −6.21 | 3.61 | .09 | | | −9.46 | 3.29 | .004 |
|   Missing/no consent | 33 | | | −3.29 | 5.02 | .51 | | | −5.33 | 6.51 | .41 | | | −3.54 | 5.95 | .55 |

(continued on following page)

**Table A1.** Demographic and Clinical Factors Associated With PedsQL Outcomes Excluding Symptoms (continued)

| Factors Predicting HRQOL | No. of Patients | Emotional Functioning | | | | | Social Functioning | | | | | Work/School Functioning | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | F | $R^2$ | Beta | SE | P | F | $R^2$ | Beta | SE | P | F | $R^2$ | Beta | SE | P |
| Model summary | 484 | 2.52 | 0.14 | | | < .0001 | 3.78 | 0.20 | | | < .001 | 2.42 | 0.14 | | | < .001 |
| Demographics | | | | | | | | | | | | | | | | |
| Age at survey | | | | **−0.52** | **0.19** | **.01** | | | **−0.36** | **0.17** | **.03** | | | −0.09 | 0.19 | .66 |
| Sex | | | | | | | | | | | | | | | | |
| Male patients | 311 | | | **7.80** | **2.51** | **.002** | | | 1.56 | 2.22 | .48 | | | **5.96** | **2.52** | **.02** |
| Female patients | 173 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Race/ethnicity | | | | | | | | | | | | | | | | |
| White | 285 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Hispanic | 100 | | | −3.12 | 2.70 | .25 | | | **−4.96** | **2.39** | **.04** | | | −1.96 | 2.71 | .47 |
| Black | 43 | | | −0.43 | 4.04 | .92 | | | −3.32 | 3.59 | .35 | | | −3.46 | 4.06 | .40 |
| Other | 56 | | | −0.79 | 3.38 | .82 | | | −2.66 | 2.99 | .38 | | | −6.24 | 3.39 | .07 |
| Education | | | | | | | | | | | | | | | | |
| High school or less | 130 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Some college | 127 | | | −4.00 | 2.98 | .18 | | | −1.81 | 2.64 | .49 | | | −2.06 | 2.99 | .49 |
| College graduate | 226 | | | 0.14 | 2.85 | .96 | | | 0.77 | 2.53 | .76 | | | 0.76 | 2.86 | .79 |
| Missing | 1 | | | −46.2 | 23.24 | .05 | | | 31.18 | 20.60 | .13 | | | 15.83 | 23.35 | .50 |
| Marital status | | | | | | | | | | | | | | | | |
| Married | 205 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Not married | 278 | | | −4.12 | 2.41 | .09 | | | −3.89 | 2.14 | .07 | | | −2.96 | 2.42 | .22 |
| Missing | 1 | | | 15.10 | 22.74 | .51 | | | 25.75 | 20.16 | .20 | | | 37.72 | 22.85 | .10 |
| Lack of health insurance | | | | | | | | | | | | | | | | |
| No | 407 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Yes | 70 | | | **−9.89** | **3.00** | **.001** | | | −3.26 | 2.65 | .22 | | | **−6.45** | **3.01** | **.03** |
| Missing | 7 | | | 7.48 | 8.64 | .39 | | | 8.01 | 7.66 | .30 | | | 2.16 | 8.69 | .80 |
| Disease-related variables | | | | | | | | | | | | | | | | |
| Cancer type | | | | | | | | | | | | | | | | |
| Acute lymphoblastic leukemia | 16 | | | 11.07 | 11.93 | .35 | | | −7.20 | 10.57 | .50 | | | 17.71 | 11.99 | .14 |
| Germ cell cancer | 193 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Hodgkin lymphoma | 135 | | | 3.34 | 3.75 | .37 | | | 3.22 | 3.32 | .33 | | | 4.80 | 3.76 | .20 |
| Non-Hodgkin lymphoma | 121 | | | 4.44 | 3.65 | .22 | | | 0.46 | 3.23 | .89 | | | 5.04 | 3.66 | .17 |
| Sarcoma | 19 | | | 5.23 | 6.53 | .42 | | | −3.07 | 5.79 | .60 | | | 9.33 | 6.56 | .16 |
| AJCC cancer stage | | | | | | | | | | | | | | | | |
| I | 200 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| II | 117 | | | −3.86 | 3.09 | .21 | | | −4.67 | 2.74 | .09 | | | −4.01 | 3.10 | .20 |
| III | 69 | | | −2.44 | 3.44 | .48 | | | −4.50 | 3.05 | .14 | | | −1.48 | 3.46 | .67 |
| IV | 59 | | | 0.39 | 3.86 | .92 | | | −0.42 | 3.42 | .90 | | | **−6.97** | **3.87** | **.07** |
| N/A | 21 | | | −6.48 | 10.26 | .53 | | | −2.72 | 9.09 | .77 | | | −9.77 | 10.31 | .34 |
| Unknown | 18 | | | −6.59 | 6.22 | .29 | | | **−10.9** | **5.51** | **.05** | | | −10.9 | 6.25 | .08 |
| Treatment type | | | | | | | | | | | | | | | | |
| Surgery only | 59 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Radiation | 50 | | | 0.04 | 4.39 | .99 | | | −1.30 | 3.89 | .74 | | | −3.31 | 4.41 | .45 |
| Chemotherapy | 227 | | | −4.61 | 3.88 | .24 | | | −6.40 | 3.44 | .06 | | | −6.16 | 3.90 | .12 |
| Radiation and chemotherapy | 108 | | | −7.24 | 4.71 | .13 | | | **−9.28** | **4.18** | **.03** | | | −8.93 | 4.73 | .06 |
| Missing/unknown/no treatment | 40 | | | −2.55 | 6.67 | .70 | | | −4.73 | 5.91 | .42 | | | −5.74 | 6.70 | .39 |
| Currently in treatment | | | | | | | | | | | | | | | | |
| No | 396 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| Yes | 78 | | | **−7.74** | **3.06** | **.01** | | | **−12.6** | **2.71** | **< .001** | | | **−12.0** | **3.08** | **.001** |
| Missing | 10 | | | −4.78 | 7.36 | .52 | | | −7.02 | 6.53 | .28 | | | −5.18 | 7.40 | .48 |
| Comorbidity | | | | | | | | | | | | | | | | |
| Missing/no consent | 33 | | | −2.16 | 6.17 | .73 | | | −5.35 | 5.47 | .33 | | | −1.10 | 6.20 | .86 |
| 0 | 315 | | | Ref | Ref | Ref | | | Ref | Ref | Ref | | | Ref | Ref | Ref |
| 1 | 77 | | | −1.59 | 2.98 | .59 | | | −4.35 | 2.64 | .10 | | | **−6.80** | **3.00** | **.02** |
| 2 | 59 | | | −6.03 | 3.42 | .08 | | | **−9.58** | **3.03** | **.002** | | | **−7.16** | **3.43** | **.04** |

NOTE. Bold font indicates significance at $P < .05$.
Abbreviations: AJCC, American Joint Committee on Cancer; HRQOL, health-related quality of life; N/A, not applicable; PedsQL, Pediatric Quality of Life Inventory; Ref, reference.