

Online Platform to Assess Complex Social Relationships and Patient-Reported Outcomes Among Adolescent and Young Adult Cancer Survivors

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PURPOSE Social integration and relationship issues have been understudied among adolescent and young adult (AYA) cancer survivors. This study compared social relationships (social networks, support, and isolation) between AYA cancer survivors and noncancer controls, and identified social integration mechanisms through which the cancer experience influences patient-reported outcomes (PROs).

MATERIALS AND METHODS One hundred two AYA cancer survivors and 102 age, sex, and race-matched noncancer controls from a national Internet panel completed an online survey to identify up to 25 of closest friends and relatives whom they have contacted within the past 2 years. Participants' interpersonal connections were used to create a social network index. The Duke-UNC Functional Social Support Questionnaire, UCLA Loneliness Scale, and PROMIS-29 Profile were used to measure social support, perceived isolation or loneliness, and PROs (physical functioning, pain interference, fatigue, anxiety, and depression domains), respectively. Path analysis tested effects of cancer experience on PROs using serial social relationship variables as mediators.

RESULTS Compared with controls, survivors of lymphoma, leukemia, and solid tumor had better social networks; however, survivors of solid tumor and central nervous system malignancies had higher perceived loneliness (all *P* values < .05). Cancer experience was directly associated with poor PROs (*P* values < .05 for all domains except fatigue) and indirectly associated through the social network-support-loneliness pathway (all *P* values < .05). Survivors with higher loneliness had lower physical functioning and higher pain interference, fatigue, anxiety, and depression versus controls with lower loneliness (all *P* values < .05).

CONCLUSION Compared with controls, survivors were more socially connected but experienced greater loneliness, which was associated with poorer PROs. Screening social integration issues during follow-up care and providing appropriate interventions are warranted.

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INTRODUCTION

Nearly 89,000 adolescents and young adults (AYAs) between age 15 and 39 years are diagnosed with cancer in the United States annually.¹ This number is eight times that of individuals diagnosed with cancer between age 0 and 14 years.¹ The AYA HOPE study found poorer self-reported physical and mental health in survivors age 25-44 years compared with the US general population.² In contrast to noncancer controls, AYA survivors are more likely to experience various late effects.^{3,4} AYAs are in a critical developmental stage,^{5,6} inclusive of completing education, pursuing employment, establishing economic independence, finding a life partner, and forming a family. However, cancer experience during young adulthood may delay the achievement of these milestones, which require a great degree of connection to the society.⁷

The Childhood Cancer Survivor Study (CCSS) and St Jude Lifetime Cohort Study (SJLIFE) have reported

poorer social outcomes of childhood cancer survivors compared with noncancer siblings and community controls, typically lower educational attainment, higher unemployment, higher proportion not married, and more likely to be living dependently.^{8,9} Survivors diagnosed with CNS tumors age between 15 and 20 years were more likely to attend special education programs compared with their siblings.¹⁰ A previous study by Kirchoff et al¹¹ found that AYA cancer survivors were at an increased risk of divorce compared with noncancer controls. However, social integration that involves connections and interactions between AYA cancer survivors and society and the associations with health outcomes are understudied.

To bridge the gap, we adopted a framework proposed by Berkman et al¹² (Appendix Fig A1) to investigate the influence of serial social integration variables (social network, social support, and perceived loneliness) on health outcomes among AYA cancer survivors. This

ASSOCIATED CONTENT

Appendix

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

Previous studies have reported poorer social outcomes in adolescent and young adult (AYA) cancer survivors (eg, lower educational attainment and higher unemployment) compared with noncancer controls. Instead, this study explored social integration issues (social network, social support, and perceived loneliness) and the associations with patient-reported outcomes (PROs) in AYA cancer survivors and evaluated different social integration as pathways through cancer experience impacts PROs.

Knowledge Generated

Using a novel online platform to measure social integration, we found that compared with noncancer controls, AYA cancer survivors have better social networks; however, they perceived greater loneliness, which was associated with poorer PROs. In addition, cancer experience was directly and indirectly (through complex social integration pathways) associated with poor PROs.

Relevance

Screening social isolation and integration issues from the early stage throughout the follow-up care and providing appropriate psychosocial interventions to strengthen social integration might help to improve PROs in AYA cancer survivors.

framework articulates that appropriate ties or connections among individuals are the cornerstones to form social relations,¹³ which influence the health of an individual either directly or indirectly through mechanisms including more social supports and perceived less social isolation. Evidence suggests higher perceived intimacy and connectedness as key elements of social bonding have been associated with better physical and mental well-being and adherence to healthy behaviors,¹⁴ whereas lack of social ties, disconnectedness, and disintegration are associated with poorer health outcomes.^{12,15} In fact, adolescent cancer survivors have reported feeling socially disconnected or isolated.¹⁶ To our knowledge, some previous studies have applied the Berkman's framework, consisting of marital status, frequency of contact with friends and relatives, and membership in church and community organizations, to measure social network status for cancer populations, including survivors of colorectal^{17,18} and breast^{19,20} cancer.

Loneliness is a perceived social isolation and has received great attention recently,^{21,22} particularly relevant to suicidal ideation in the general population.²³ A meta-analysis found that loneliness is associated with 26% elevated risk of premature mortality.²⁴ Lonelier individuals are more likely to have pain, poorer physical functioning, depression, and fatigue in contrast to socially connected individuals.²¹ Longitudinal studies suggest that lonely cancer survivors have persistent clusters of multiple symptoms compared with less lonely individuals²⁵ and that persistent symptoms occur through the altering of body physiology or neuro-immune pathways.²⁶ Feelings of loneliness accompanied by anxiety, stress, and low self-confidence can trigger behavioral and neurobiologic pathways, leading to adverse health consequences.²⁷

Previous studies have explored social integration issues in aging cancer survivors^{28,29}; however, the social relationships

in AYA cancer survivors and their influence on patient-reported outcomes (PROs) require thorough investigations. PROs, especially symptoms and poor quality of life, are prognostic factors for early onset of clinically ascertained health conditions and reduced survival in cancer populations.^{30,31} This study aimed to investigate social relationships and associations with PROs in AYA cancer survivors, with an inclusion of age, sex, and race-matched noncancer AYAs as a control group. Specifically, we (1) compared three social relationship variables (social network, social support, and perceived loneliness) between two AYA groups and (2) evaluated the contribution of social relationship variables to poor PROs.

MATERIALS AND METHODS

Study Design and Participants

This cross-sectional study included 102 AYA cancer survivors and 102 age, sex, and race-matched noncancer controls. We recruited participants from a national Internet survey panel maintained by Opinions 4 Good (Portsmouth, NH). Through the database of panel members, Opinions 4 Good identified a random sample of AYAs and sent an invitation e-mail with enclosed screening items to determine their eligibility. During the screening, survivors self-reported the type of cancer diagnosis, age at diagnosis, type of cancer treatment, and years from therapy completion. The enrollment criteria for survivors were individuals age 18-29.9 years at the time of survey, diagnosed with cancer at age 15-29.9 years as defined by the US National Cancer Institute's SEER program,³² and received no cancer therapy in the past 3 years. Our age criterion³² to define AYA cancer survivors is slightly different from the criteria (eg, age 15-39 years) used by various professional organizations.^{33,34} The enrollment criteria for noncancer controls were age 18-29.9 years at the time of survey with no history of cancer.

We used a quota sampling approach to recruit participants on the basis of age at enrollment, sex, race and ethnicity, and cancer diagnosis per the distribution of AYA cancer survivors in the CCSS. We used the same age, sex, and race and ethnicity criteria to select the matched noncancer controls. Data from survivors and controls were collected at the same period. If the eligible participants did not respond to our invitation, they were replaced by alternative participants with similar age, sex, race and ethnicity, and cancer diagnosis. This process was repeated until all prespecified slots were fulfilled. The participants were rewarded points when their survey was completed. The points earned from this and other studies could be redeemed if the threshold was reached. This study was approved by the IRB of St Jude Children's Research Hospital.

Data Collection

Data were collected between March and May 2015 through an online platform designed for social network research. Participants who were consented to this study completed a self-administered survey via smartphones, tablets, or desktop computers. The average survey length time was 30 minutes. The ordering of the survey includes demographics, cancer history, health habits, medical conditions, personal social network status, tangible and intangible support, loneliness, and PROs. If some items were not completed, the data collection platform will prompt a reminder for completion. We collected social network data using an egocentric approach, where participants reported their social relationship with friends and relatives without a confirmation from friends and relatives. Participants identified up to 25 close friends and relatives with whom they frequently contacted in the past 2 years and reported whether any of those friends and relatives knew and contacted each other. Each participant was asked about the type of relationship, type of communication used, and frequency of contact with each identified friend and relative. Additionally, participants reported resources available to them for emotional support, tangible support, physical activity advice, and weight management advice from each of the identified friends and relatives. A social network index created in our previous publication was used for each individual, with a higher score representing a stronger social network status.³⁵ Approximately 5,000 social connectedness data elements were collected from 204 participants and included in the analysis (Fig 1).

Measures

PROs were collected using the Patient-Reported Outcomes Measurement Information System-29 Profile (PROMIS-29)³⁶ with a focus on five domains of interest: physical functioning, pain interference, fatigue, anxiety, and depression. Higher scores in the physical functioning domain indicated better PROs, whereas higher scores in other domains indicated poorer PROs. Perceived social support was assessed using the Duke-UNC Functional Social

Support Questionnaire (8 items),³⁷ with higher domain scores indicating better satisfaction with social support. Perceived loneliness was assessed using the UCLA Loneliness Scale (20 items),³⁸ with higher domain scores indicating more perceived isolation. We further defined high level of loneliness if domain scores were ≥ 30 and low loneliness if scores were < 30 .³⁸

Participants self-reported their sociodemographic characteristics (age, sex, race and ethnicity, educational attainment, annual household income, and marital status) and the presence of 15 chronic health conditions on the basis of a checklist (footnote of Table 1). Race and ethnicity was categorized as non-Hispanic White, non-Hispanic Black, Hispanic, and others; educational attainment as high school or below, college, and graduate levels; annual household income as $< \$40,000$, $\$40,000$ - $\$75,999$, and $\geq \$80,000$ (US dollars); and marital status as not married and married (ie, married or living with partner).

Statistical Analysis

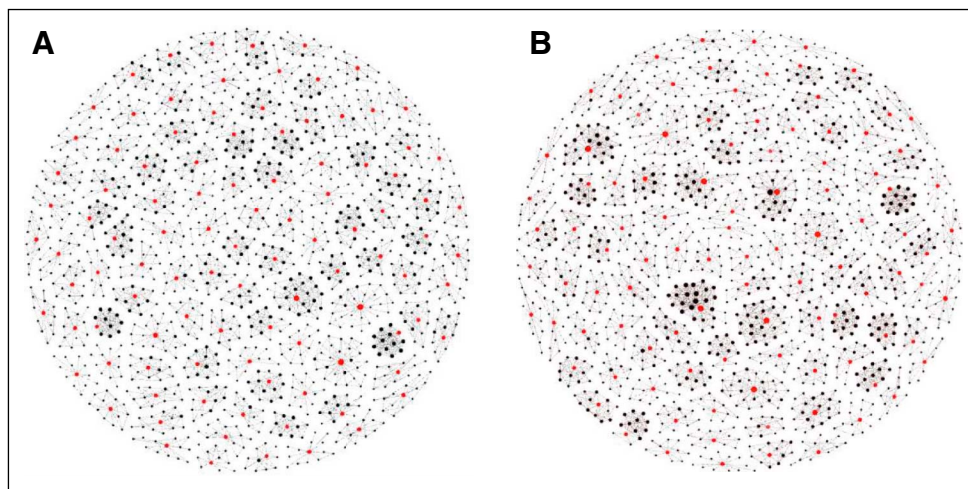
Chi-square tests were used to compare sociodemographic characteristics between survivors and controls. Multivariable linear regression analysis, adjusting for the number of chronic health conditions, was used to compare social network, social support, and perceived loneliness between survivors and controls. Path analysis was used to quantify total, direct, and indirect effects of cancer experience (*v* noncancer) on each of the PRO domains using serial social relationship variables (social network, social support, and perceived loneliness) as mediators. Total effect was estimated by the sum of direct and indirect effects. Mplus version 8 was used for path analysis³⁹ and Stata version 15 for the remaining analyses.

RESULTS

Table 1 summarizes the characteristics of participants (N = 204). Sociodemographic characteristics did not significantly differ between survivors and noncancer controls (*P* values $> .05$), except for marital status (*P* value = .046). A lower proportion of survivors were married or living with partners compared with controls (34.3% *v* 48.0%; *P* value = .046). Among survivors, 69.6% were diagnosed with cancer at age 19-26 years and 30.4% at age 15-18 years; 41.2% were treated for a non-CNS solid tumor, 26.5% for leukemia, 23.5% for lymphoma, and 8.8% for a CNS malignancy. Survivors had a higher total number of chronic health conditions compared with controls (4.7 *v* 1.1; *P* value $< .001$).

Appendix Table A1 compared social relationship variables between survivors and controls, adjusting for the number of present chronic health conditions. In contrast to controls, survivors of lymphoma, leukemia, and non-CNS solid tumor had significantly higher social network scores (β 1.978, 95% CI 0.600 to 3.355; β 1.670, 95% CI 0.379 to 2.961; and β 1.221, 95% CI 0.117 to 2.326, respectively). However, solid tumor and CNS malignancy survivors

FIG 1. Social connectedness map representing (A) 102 AYA cancer survivors and (B) 102 age, sex, and race-matched noncancer controls. Note: Red dots represent participants and black dots represent participants' friends and relatives. AYA, adolescent and young adult.



reported significantly higher loneliness scores compared with controls (β 10.833, 95% CI 5.095 to 16.571 and β 15.651, 95% CI 4.646 to 26.655, respectively). Perceived social support among cancer survivors and noncancer controls were comparable (P value $>$.05).

Figure 2 visualizes the significant direct effect from one variable to another variable, and Table 2 reports the total effect and indirect effect of one variable on another variable through the mediators by specific PRO domains. For physical functioning, survivors reported significantly poorer domain scores (β -7.495, 95% CI -9.511 to -5.422) compared with controls. Cancer experience directly explained 84.5% of variance in poor physical functioning. For pain interference, survivors had significantly poorer domain scores (β 7.140, 95% CI 4.584 to 9.466) compared with controls. Cancer experience directly explained approximately 85% of variance in pain interference. For fatigue, survivors reported significantly poorer domain scores (β 4.542, 95% CI 1.510 to 7.296) compared with controls, with no statistically significant direct effect of cancer experience. For anxiety, survivors had significantly poorer domain scores (β 6.015, 95% CI 3.221 to 8.573) compared with controls, with 68.3% of variance in anxiety directly explained by cancer experience. For depression, survivors had significantly poorer domain scores (β 6.155, 95% CI 3.492 to 8.738) compared with controls, with 62.3% of variance in depression directly explained by cancer experience.

Table 2 shows the effect of cancer experience on PRO domains indirectly through the influence of social relationship variables (ie, different indirect effects or pathways). Cancer experience was indirectly associated with poor physical functioning through all three social relationship variables (β -1.163, 95% CI -2.323 to -0.024) and perceived loneliness alone (β -1.614, 95% CI -2.589 to -0.715). Poor social networks were indirectly associated with poor physical functioning through both poor social support and loneliness (β 0.095, 95% CI 0.026 to 0.207).

Cancer experience was indirectly associated with fatigue, anxiety, and depression through all three social relationship variables (β 1.802, 1.905, and 2.321, respectively; all P values $<$.05). Furthermore, cancer experience was indirectly associated with pain interference, fatigue, anxiety, and depression through perceived loneliness (β 1.183, 2.231, 2.488, and 2.975, respectively; all P values $<$.05). Additionally, poor social networks were indirectly associated with anxiety and depression through both poor social support and loneliness.

Table 3 shows associations of cancer experience and levels of loneliness with PROs. Compared with controls having low loneliness, survivors having high loneliness had poorest PROs, typically in physical functioning, anxiety, and depression, followed by controls having high loneliness and survivors having low loneliness. The decreased PROs between survivors with high loneliness and controls with low loneliness were up to 2-fold the minimal important difference or MID (note, 1 MID is 5 points) including depression (β 12.199, 95% CI 8.787 to 15.611), anxiety (β 10.166, 95% CI 6.290 to 14.042), poor physical functioning (β -8.710, 95% CI -11.422 to -5.997), pain interference (β 7.384, 95% CI 3.899 to 10.869), and fatigue (β 6.820, 95% CI 2.613 to 11.027).

DISCUSSION

This study used an established social integration framework¹² to elucidate the mechanistic influence of the AYA cancer experience on PROs through three social relationship variables (social network connection, social support, and perceived loneliness). We found that experiencing cancer had both direct and indirect associations (via three social relationship variables) with poor PROs in AYAs. Having better social network connection was significantly associated with more social supports and lower levels of loneliness, leading to better PROs.

Although poor social outcomes (eg, educational attainment, income, employment, and insurance status) have

TABLE 1. Characteristics of the Study Participants (N = 204)

Characteristic	Cancer Survivors (n = 102)	Noncancer Controls (n = 102)	P
Participants' age (years) at study	24.64 ± 3.44	24.64 ± 3.46	1.00
Sex (%)			.779
Male	50 (49.0)	52 (51.0)	
Female	52 (51.0)	50 (49.0)	
Race and ethnicity (%)			.959
White, non-Hispanic	71 (69.6)	70 (68.6)	
Black, non-Hispanic	13 (12.8)	13 (12.8)	
Hispanic	11 (10.8)	10 (9.8)	
Others	7 (6.9)	9 (8.8)	
Educational attainment (%)			.139
High school or below	44 (43.1)	31 (30.4)	
College degree	23 (22.6)	32 (31.4)	
Graduate degree	35 (34.3)	39 (38.2)	
Annual household income (US dollars), %			.289
< \$40,000	41 (40.2)	29 (29.9)	
\$40,000-\$79,999	41 (40.2)	48 (49.5)	
≥ 80,000	20 (19.6)	20 (20.6)	
Marital status (%)			.046
Not married	67 (65.7)	53 (52.0)	
Married or living with partner	35 (34.3)	49 (48.0)	
Age (years) at cancer diagnosis (%)			
15-18	31 (30.4)	—	
19-26	71 (69.6)	—	
Cancer diagnosis (%)			
Non-CNS solid tumor	42 (41.2)	—	
Leukemia	27 (26.5)	—	
Lymphoma	24 (23.5)	—	
CNS malignancy	9 (8.8)	—	
Chemotherapy (%)			
Yes	63 (61.8)	—	
No	39 (38.2)	—	
Radiation therapy (%)			
Yes	30 (29.4)	—	
No	72 (70.6)	—	
Total No. of chronic health conditions	4.67 ± 5.10	1.05 ± 1.97	< .001

NOTE. Total No. of chronic health conditions is a summation of 15 chronic health conditions based on a self-reported checklist; these conditions include kidney conditions (kidney stones and need for dialysis), gastrointestinal conditions (chronic nausea or vomiting, chronic abdominal pain, and gallstones), endocrine and growth conditions (thyroid problems, diabetes, poor growth, osteoporosis or fragile or weak bones, and fertility issues), and heart and lung conditions (heart diseases, stroke or cerebrovascular accident, asthma, chronic cough or shortness of breath, and emphysema).

been well-characterized in childhood cancer survivors, the social relationship issue is understudied.⁴⁰ Among the limited literature, Tremolada et al⁴¹ found that survivors often lacked social support from family, friends, and significant others compared with controls; however, survivors declared better health-related quality of life potentially

because of increased resiliency over time. In addition, Soares et al⁴² found significant associations of social network and social support with lower levels of fatigue among cancer survivors. Although previous studies found the impact of cancer therapy on different PROs among AYA cancer survivors,^{43,44} these studies did not elucidate the

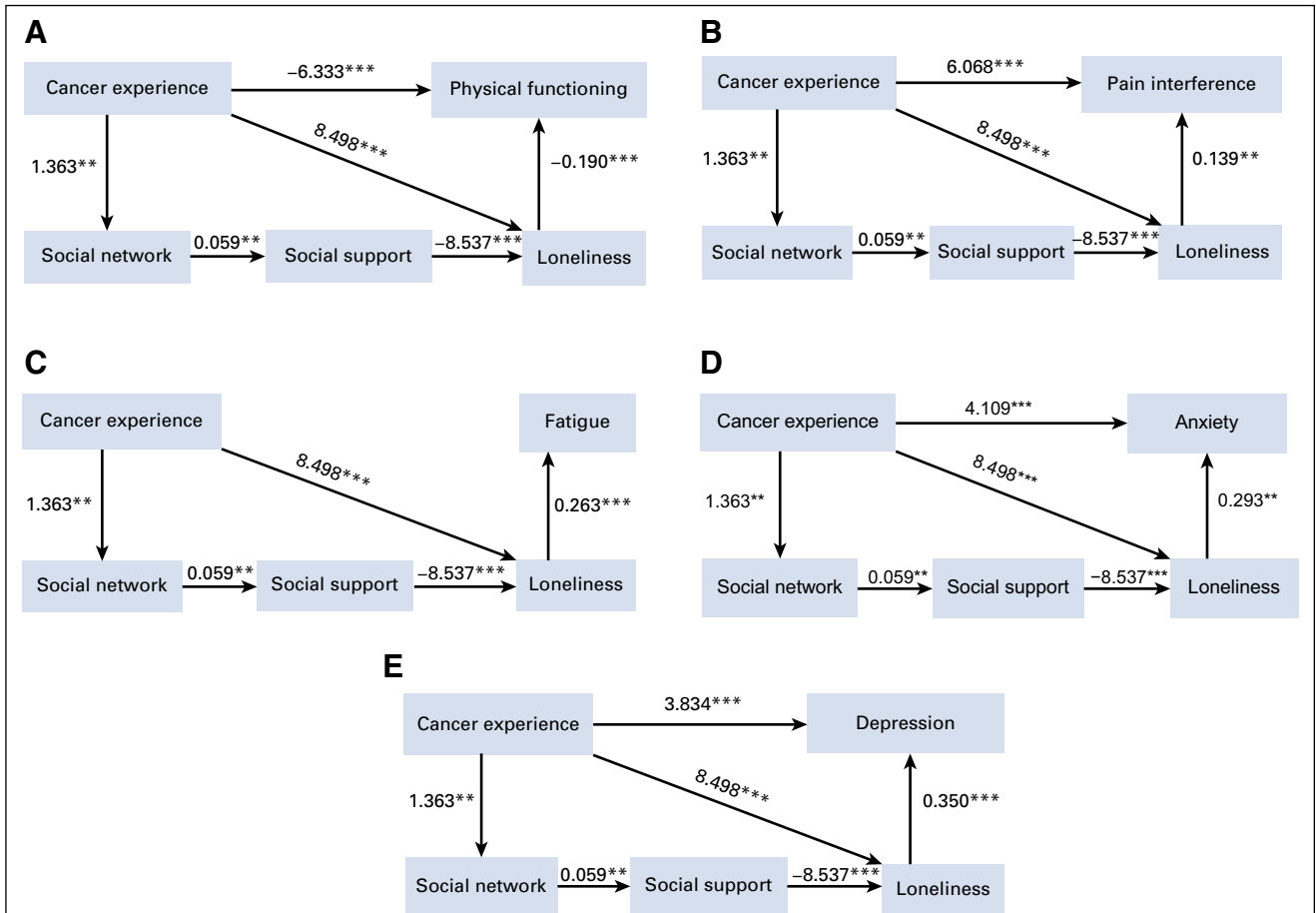


FIG 2. Direct effects of one variable on another variable by specific PRO domains (eg, cancer experience on physical functioning, cancer experience on loneliness, loneliness on physical functioning, etc): (A) all significant direct effects between variables within physical functioning domain, (B) all significant direct effects between variables within pain interference, (C) all significant direct effects between variables within fatigue domain, (D) all significant direct effects between variables within anxiety domain, and (E) all significant direct effects between variables within depression domain. Values alongside the lines represent significant direct effects; * $P < .05$; ** $P < .01$; *** $P < .001$. PRO, patient-reported outcome.

social network pathway through which cancer therapy affects PROs.

Of the social relationship variables we studied, perceived social isolation or loneliness is of particular concern among cancer populations and deserves additional attention. Prevalence of perceived loneliness is increasing in our society across all ages, and lonelier individuals are at risk for premature mortality.²⁴ Adams et al⁴⁵ observed that social constraints increase cancer-specific loneliness, which in turn elevates symptom perception (pain interference, fatigue, sleep disturbance, and cognitive complaints). Among adult survivors of childhood cancer, those experiencing loneliness were found to have elevated risk for suicidal ideation and early mortality.^{46,47} In our study, as compared with controls with low loneliness, AYA cancer survivors with high loneliness had significantly poorer physical functioning and higher pain interference, fatigue, anxiety, and depression, followed by survivors with low loneliness and then controls with high loneliness. Our findings suggest the effect of cancer experience on PROs depends upon the levels of social isolation or

loneliness. From a physiologic aspect, stressful situations associated with loneliness can affect immune function and elevate proinflammatory cytokines.⁴⁸ Future studies are warranted to elucidate biologic and physiologic pathways by which loneliness affects late effects in cancer survivors.

Social integration challenges may vary among survivors experiencing different types of cancers. We found that solid tumor and CNS AYA cancer survivors had greater loneliness compared with survivors of other cancers. One previous study found that AYA survivors of CNS tumor reported poorer peer relations in contrast to general population.⁴⁹ Strikingly, socially isolated breast cancer survivors have 1.7-fold and 2.1-fold elevated risk of all-cause and breast cancer-specific mortalities compared with socially integrated survivors.¹⁹ These studies suggest that screening social isolation and integration issues from the early stage throughout the follow-up, on the basis of the type of cancer, should be part of risk assessment. Health care providers may provide appropriate psychosocial interventions to strengthen survivors' social integration skill.

TABLE 2. Effects of Cancer Experience on Patient-Reported Outcomes (PROs) Through the Influence of Social Relationship Variables

PRO Domain	Total Effect		Indirect Effect (through social relationship variables)		Variance of Total Effect Explained by Indirect Effect (%)
	β (95% CI)	P	β (95% CI)	P	
Physical functioning					15.5
Cancer experience to physical functioning through social network, social support, and loneliness	-7.495 (-9.511 to -5.422)	< .001	-1.163 (-2.323 to -0.024)	.045	
Cancer experience to social support through social network	.112 (-0.137 to 0.354)	.364	.080 (0.025 to 0.171)	.037	
Social network to loneliness through social support	-.643 (-1.372 to 0.068)	.086	-.502 (-1.011 to -0.139)	.022	
Social support to physical functioning through loneliness	2.594 (1.438 to 3.676)	< .001	1.622 (0.892 to 2.524)	< .001	
Social network to physical functioning through social support and loneliness	.272 (-0.053 to 0.602)	.098	.095 (0.026 to 0.207)	.042	
Cancer experience to physical functioning through loneliness	-7.495 (-9.511 to -5.422)	< .001	-1.614 (-2.589 to -0.715)	.001	
Pain interference					15.0
Cancer experience to pain interference through social network, social support, and loneliness	7.140 (4.584 to 9.466)	< .001	1.072 (-0.016 to 2.426)	.090	
Cancer experience to social support through social network	.112 (-0.137 to 0.354)	.364	.080 (0.025 to 0.171)	.037	
Social network to loneliness through social support	-.643 (-1.372 to 0.068)	.086	-.502 (-1.011 to -0.139)	.022	
Social support to pain interference through loneliness	-2.408 (-3.855 to -1.050)	.001	-1.189 (-2.058 to -0.464)	.003	
Social network to pain interference through social support and loneliness	-.026 (-0.414 to 0.345)	.896	-.070 (-0.176 to -0.019)	.065	
Cancer experience to pain interference through loneliness	7.140 (4.584 to 9.466)	< .001	1.183 (0.357 to 2.221)	.013	
Fatigue					39.7
Cancer experience to fatigue through social network, social support, and loneliness	4.542 (1.510 to 7.296)	.002	1.802 (0.078 to 3.499)	.042	
Cancer experience to social support through social network	.112 (-0.137 to 0.354)	.364	.080 (0.025 to 0.171)	.037	
Social network to loneliness through social support	-.643 (-1.359 to 0.073)	.086	-.502 (-1.011 to -0.139)	.022	
Social support to fatigue through loneliness	-2.899 (-4.380 to -1.053)	.001	-2.242 (-3.618 to -1.198)	< .001	
Social network to fatigue through social support and loneliness	-.248 (-0.691 to 0.253)	.307	-.132 (-0.429 to 0.014)	.042	
Cancer experience to fatigue through loneliness	4.542 (1.510 to 7.296)	.002	2.231 (0.987 to 3.911)	.003	
Anxiety					31.7
Cancer experience to anxiety through social network, social support, and loneliness	6.015 (3.221 to 8.573)	< .001	1.905 (0.005 to 3.787)	.040	
Cancer experience to social support through social network	.112 (-0.137 to 0.354)	.364	.080 (0.025 to 0.171)	.037	
Social network to loneliness through social support	-.643 (-1.372 to 0.068)	.086	-.502 (-1.011 to -0.139)	.022	
Social support to anxiety through loneliness	-4.435 (-5.943 to -2.978)	< .001	-2.499 (-3.884 to -1.429)	< .001	

(Continued on following page)

TABLE 2. Effects of Cancer Experience on Patient-Reported Outcomes (PROs) Through the Influence of Social Relationship Variables (Continued)

PRO Domain	Total Effect		Indirect Effect (through social relationship variables)		Variance of Total Effect Explained by Indirect Effect (%)
	β (95% CI)	P	β (95% CI)	P	
Social network to anxiety through social support and loneliness	-.325 (-0.743 to 0.150)	.145	-.147 (-0.320 to -0.040)	.041	
Cancer experience to anxiety through loneliness	6.015 (3.221 to 8.573)	< .001	2.488 (1.282 to 4.079)	< .001	
Depression					37.7
Cancer experience to depression through social network, social support, and loneliness	6.155 (3.492 to 8.738)	< .001	2.321 (0.327 to 4.227)	.020	
Cancer experience to social support through social network	.112 (-0.137 to 0.354)	.364	.080 (0.025 to 0.171)	.037	
Social network to loneliness through social support	-.643 (-1.372 to 0.068)	.086	-.502 (-1.011 to -0.139)	.022	
Social support to depression through loneliness	-4.473 (-6.010 to -2.940)	< .001	-2.989 (-4.170 to -1.873)	< .001	
Social network to depression through social support and loneliness	-.377 (-0.786 to 0.033)	.077	-.176 (-0.350 to -0.055)	.024	
Cancer experience to depression through loneliness	6.155 (3.492 to 8.738)	< .001	2.975 (1.455 to 4.521)	< .001	

NOTE. This table reports the total effect and indirect effect of one variable on another variable through the mediators by specific PRO domains; the direct effect of one variable on another variable by specific PRO domains appears in Figs 2A-2E; total effect represents direct effects plus indirect effects; referent group: noncancer controls.

Abbreviation: PRO, patient-reported outcome.

AYA cancer survivors often require support from different sources to address their health needs given the unique developmental stage. Parents, caregivers, or family members may be sources of emotional and economic support, whereas peer survivors may share experiences and provide emotional and informational support.⁵⁰ AYA patients with cancer often look for resources that can help mitigate isolation, build a sense of community or inclusive environment, or provide opportunities to connect with other AYA patients with cancer or cancer survivors.⁵¹ Since the structure of social network data is complex, electronic platforms will facilitate the collection of social relationship data and further integration into informatic systems under the Big Data initiatives for assessing social determinants.

Cancer survivors commonly use online support via social media to gain a sense of empowerment and solve problems or concerns by sharing with other cancer survivors.^{52,53} However, limited interventions have been implemented to address social integration among AYA cancer survivors. Basically, technology-based health platforms can facilitate access to psychosocial and health support for AYA cancer survivors.⁵⁴ Survivors with opportunities to communicate through Web-based channels (eg, discussion board, chat, e-mail, and blog) are likely to expand their social networks and receive useful social support.⁵⁵ AYA patients with cancer and cancer survivors who participate in online support communities reported a greater sense of connectedness and

felt less lonely.⁵⁶ A recent study suggests that using Facebook as a communication platform may increase engagement in physical activities among young adult survivors through information sharing, increased motivation, and provision of tangible or intangible support.⁵⁷ Although social networking and connections among survivors via chat groups or social media seem promising, the use of technology-based interventions is challenging for individuals who lack appropriate communication skills or mHealth literacy, especially survivors with cognitive impairment. In fact, medically relevant information shared on social media (eg, Facebook) could be inaccurate or misleading,^{58,59} and AYA cancer survivors may not discuss such information with family members because of concern of burdening them.⁵⁹ Thus, clinicians need to recommend specific online resources that are appropriate to address medical and psychosocial needs of AYA cancer survivors. Future studies are needed to evaluate the effectiveness of platform-based social integration interventions to improve social connections and health outcomes for AYA cancer survivors.

This study has several limitations. First, the study design is cross-sectional, which precludes causal inferences; however, our social relationship variables were collected on the basis of a retrospective longitudinal design (ie, the past 2 years for social network status and 1 month for social isolation evaluation) and PROs were based on the past 7 days. Second, the use of cross-sectional design cannot

TABLE 3. Associations of Cancer Experience and Loneliness With Patient-Reported Outcomes

Cancer Experience and Loneliness	Domains of Patient-Reported Outcomes									
	Physical Functioning		Pain Interference		Fatigue		Anxiety		Depression	
	β (95% CI)	<i>P</i>	β (95% CI)	<i>P</i>	β (95% CI)	<i>P</i>	β (95% CI)	<i>P</i>	β (95% CI)	<i>P</i>
Controls with low loneliness	Ref		Ref		Ref		Ref		Ref	
Survivors with low loneliness	-5.382 (-7.671 to -3.094)	< .001	4.937 (1.997 to 7.878)	.001	0.500 (-3.049 to 4.049)	.782	2.412 (-0.858 to 5.682)	.147	2.324 (-0.554 to 5.202)	.113
Controls with high loneliness	-5.923 (-8.738 to -3.107)	< .001	3.487 (-0.131 to 7.105)	.059	3.786 (-0.581 to 8.153)	.089	7.399 (3.376 to 11.423)	< .001	9.060 (5.521 to 12.604)	< .001
Survivors with high loneliness	-8.710 (-11.422 to -5.997)	< .001	7.384 (3.899 to 10.869)	< .001	6.820 (2.613 to 11.027)	.002	10.166 (6.290 to 14.042)	< .001	12.199 (8.787 to 15.611)	< .001

NOTE. β coefficient obtained after adjusting for age, sex, education, and total number of chronic health conditions.

fully address the confounding issues for the complex pathways between cancer experience, social integration, and PROs. These confounders include ones' fear about cancer reoccurrence, coping strategy, resiliency, and personality or optimism trait. Third, our social network data were collected through an egocentric approach, meaning a reliance on study participants to report their social relationships with friends and relatives without further validation. As a result, we were not able to investigate bidirectional relationships between survivors and their friends and relatives. Fourth, the response or no-response rate cannot be accurately estimated because the members of the Internet survey panel are changing on a daily basis. However, in line with previous study,⁶⁰ we used a quota sampling approach to recruit study participants whose characteristics (age at

enrollment, sex, race and ethnicity, and cancer diagnosis) are consistent with a target marginal distribution of the CCSS cohort. Fifth, we only evaluated PROs as proxies for late medical effects (eg, neurocognitive functioning and chronic health conditions) rather than through clinical ascertainment. These late medical outcomes may be affected by social integration variables (social network and social isolation), which require further investigation.

In conclusion, although AYA cancer survivors have better social networks, they experience greater loneliness than noncancer controls, which in turn is associated with poor PROs. Cancer experience was directly and indirectly (through social network, social support, and perceived loneliness) associated with poor PROs.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians ([Open Payments](http://OpenPayments)).

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APPENDIX

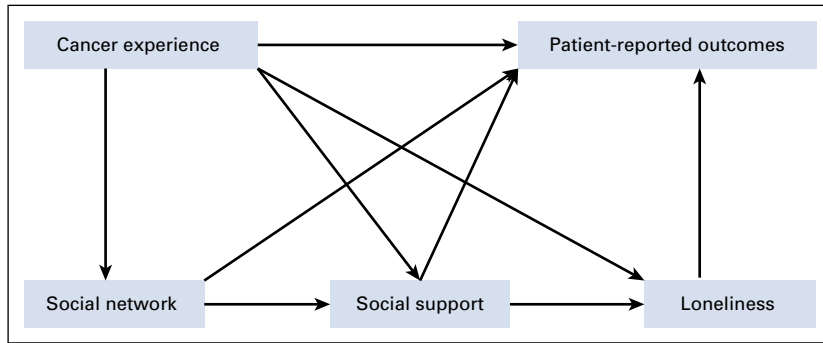


FIG A1. Conceptual framework showing the influence of social relationships on patient-reported outcomes.

TABLE A1. Social Network, Social Support, and Loneliness by Cancer Survivors and Noncancer Controls

	Social Network		Social Support		Loneliness	
	β (95% CI)	<i>P</i>	β (95% CI)	<i>P</i>	β (95% CI)	<i>P</i>
Noncancer controls	Ref		Ref		Ref	
Cancer survivors						
Lymphoma	1.978 (0.600 to 3.355)	.005	0.356 (−0.040 to 0.751)	.078	0.054 (−7.104 to 7.211)	.988
Leukemia	1.670 (0.379 to 2.961)	.012	0.141 (−0.229 to 0.512)	.453	5.850 (−0.858 to 12.558)	.087
Solid tumor	1.221 (0.117 to 2.326)	.030	0.014 (−0.303 to 0.331)	.931	10.833 (5.095 to 16.571)	< .001
CNS malignancy	−1.090 (−3.209 to 1.026)	.311	−0.299 (−0.908 to 0.309)	.333	15.651 (4.646 to 26.655)	.006

NOTE. β coefficient obtained after adjusting for total number of chronic health conditions.