

## Health-related quality of life in survivors of adolescent cancer: An integrative literature review

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### Abstract:

**Problem:** Adolescence is a critical developmental period, but little research is available on the quality of life for individuals ages 10–19, especially those who have faced a life-threatening illness. This integrative review examines factors related to quality of life among survivors of a childhood cancer that occurred during adolescence.

**Eligibility Criteria:** The Garrard Matrix Method guided this review of studies that were conducted from 1990 to 2017. Studies were eligible if participants were diagnosed with cancer during adolescence, the studies followed survivorship from cancer diagnosis to treatment completion, and health-related quality of life measures were taken.

**Sample:** Fifteen articles met the inclusion criteria.

**Results:** Most survivors of a childhood cancer that occurred during adolescence reported physical and psychological health-related quality of life scores similar to, or higher than, healthy controls. Risk factors for poorer quality of life were type of cancer, type of treatment, late effects, and time since diagnosis. Factors for better quality of life were older age, positive feelings such as happiness and optimism, social support, and coping strategies. Most studies used the Short Form-36 and the PedsQL Generic Core Scales to measure quality of life.

**Conclusions:** Protective factors such as social support and subjective feelings positively affected quality of life.

**Implications:** In order to promote the best patient outcomes, relevant protective factors that improve quality of life should be incorporated in long-term care plans for survivors of a childhood cancer that occurred during adolescence.

**Keywords:** Adolescence | Childhood cancer | Quality of life | Review | Survivors

## Article:

### Introduction

The overall five-year survival rate for children and adolescents with cancer has increased to almost 85% due to advanced cancer protocols and treatments (O'Leary, Krailo, Anderson, & Reaman, 2008). From 1975 to 1979, the five-year survival rate for leukemia, the most common type of cancer in children and adolescents, was 48%. However, from 2003 to 2009, the rate leapt to 84% (Ward, DeSantis, Robbins, Kohler, & Jemal, 2014), prompting an increased interest in measuring health-related quality of life (HRQOL) among survivors, research that is typically limited to adults (Veenhoven & Den Buitelaar, 1993).

What is quality of life? The World Health Organization (WHO) defines health as “a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity.” This definition has been used to construct the quality of life concept. In this article, health-related quality of life is defined as a multidimensional concept that includes the physical, mental, emotional, and social functioning of survivors (Anthony et al., 2014; Eiser, 2007). Unlike adult cancer patients, adolescent cancer patients need detailed survivorship plans that take into account this life stage of rapid physical, cognitive, and psychosocial changes (Berk & Meyers, 2015). It is a time during which they establish personal identities, peer relationships, and family roles (Mavrides & Pao, 2014). For these reasons, adolescents need plans that address their unique needs across these stages of growth and development.

The most common types of cancer in children include acute lymphoblastic leukemia, brain and central nervous system (CNS) tumors, neuroblastoma, and non-Hodgkin's lymphoma. In adolescents, common cancers are Hodgkin's lymphoma, thyroid carcinoma, brain and CNS tumors, and testicular germ cell tumors (Ward et al., 2014). Even when a child or adolescent survives cancer and treatment, he or she faces a number of complications, such as gastrointestinal issues, cardio-vascular problems, psychological stress, disfigurement, and pain (Barnett et al., 2016; Goldsby et al., 2011; McCarthy et al., 2016; Nolan et al., 2014). Most of the literature reports that survivors of childhood and adolescent cancers have similar or better quality of life (QOL) than healthy controls. However, a subgroup of survivors reports significant psychological stress and poor QOL (Kazak et al., 2010; Meeske, Patel, Palmer, Nelson, & Parow, 2007; Zeltzer et al., 2008). Because adolescents view life differently than adults, it is important to understand what QOL or HRQOL means from their perspective (Clarke & Eiser, 2004).

Adolescent and adult survivors of childhood cancer are affected by several factors known to reduce QOL, including late effects, low income, gender, and type of cancer (Maunsell, Pogany, Barrera, Shaw, & Speechley, 2006; Meeske et al., 2007; Zebrack, Yi, Petersen, & Ganz, 2008). Late effects—adverse outcomes of cancer or cancer treatments—can arise or persist five years after diagnosis (Bhatia & Landier, 2005; National Cancer Institute, 2016). Survivors of childhood cancer that occurred during adolescence report late effects including physical symptoms, fatigue, and psychological stress, which adversely affects their QOL (Huang et al., 2013; Meeske et al., 2007). Identifying these factors is important to tailoring a survivorship plan that helps them achieve their optimal levels of health and wellness (Lipscomb, Gotay, & Snyder,

2007). This integrative literature review examines HRQOL studies focused solely on survivors of cancer in adolescence and aims to: (1) identify the HRQOL status of survivors of cancer in adolescence, (2) identify predictive factors of HRQOL, and (3) assess HRQOL measurements for survivors to determine whether they are a good fit.

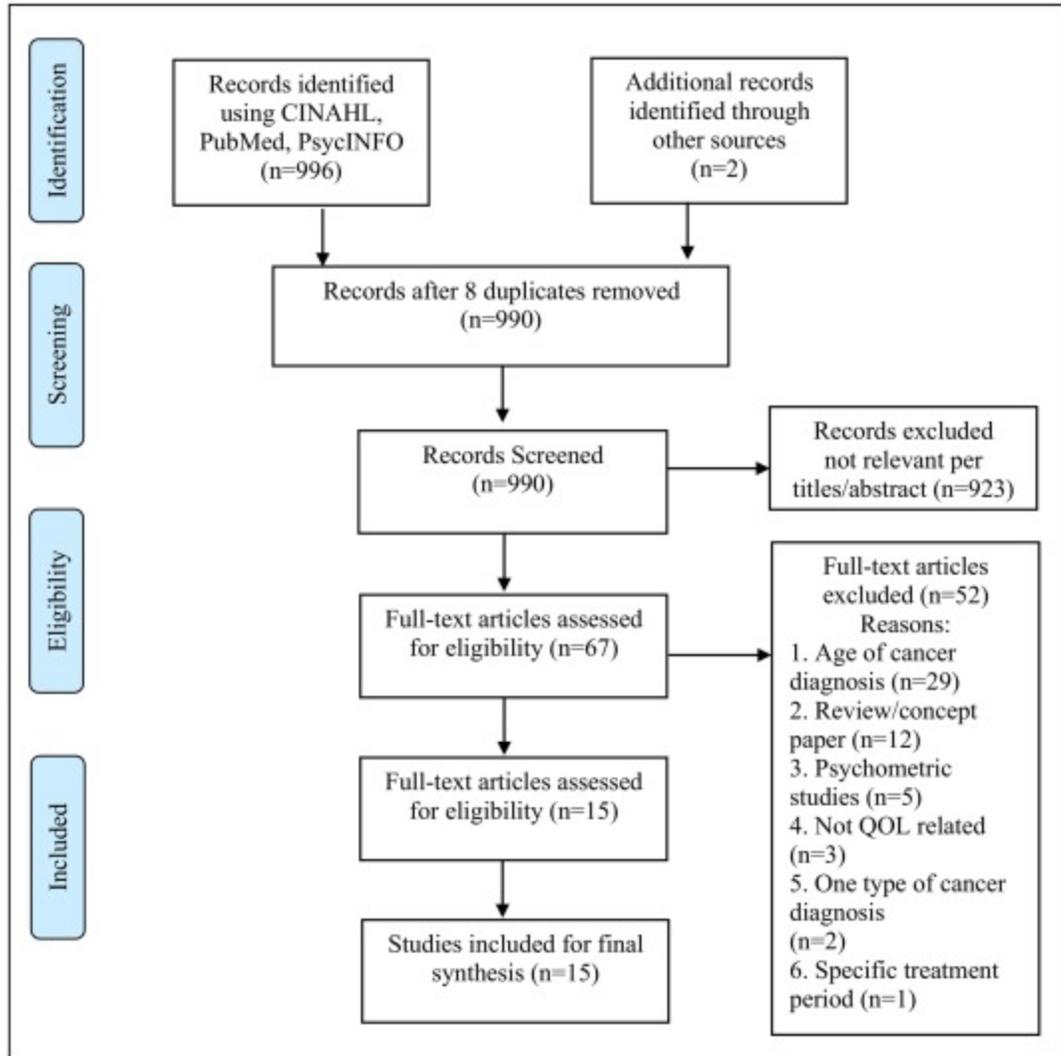
## Methods

### Search Strategy

This integrative literature review synthesizes outcomes from research articles. The review process utilized Garrard's Matrix Method for health science literature review (Garrard, 2016). Garrard defines a literature review as an analysis of scientific materials about a specific topic. Researchers need to evaluate the purpose of each study, determine the quality of the scientific methods, and examine the analysis of the findings to answer the research questions, summarize the findings, and synthesize the results. To find eligible studies, we searched three databases: the Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsycINFO, and PubMed, from 1990 until August 2017. Additional articles were identified through library searches. Search terms included: *quality of life, health-related quality of life, psychological distress, pediatric cancer survivors, adolescents with cancer, and adolescent cancer survivors*. A research librarian helped find related articles using the keywords. The search strategy is detailed in Appendix A.

Inclusion criteria were: (1) original empirical studies published in English-language, peer-reviewed journals; (2) studies of participants diagnosed with childhood cancer in adolescence, between 10 and 19 years of age based on the World Health Organization definition of adolescence; (3) studies in which adolescents comprised at least half of the total sample; (4) research in which participants met a broad definition of survivorship from diagnosis to completion of cancer treatment; (5) papers that assessed HRQOL or relationships between HRQOL and predictive factors, and (6) publications that reported measuring adolescents' HRQOL. Studies were excluded if: participants received a cancer diagnosis before or beyond adolescence, research focused on only one type of cancer diagnosis, studies examined a specific treatment period (e.g., post stem-cell transplantation), and if publication centered on something other than HRQOL or reported only validation of psychometric measures.

A Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart (Moher, Liberati, Tetzlaff, Altman, and Prisma Group, 2009) illustrates the search strategy used to identify articles for this review (see Fig. 1). The search yielded a total of 998 articles: 996 articles from CINAHL, PubMed, and PsycINFO, and 2 articles from ProQuest. A total of 923 articles were excluded because they failed to meet the inclusion criteria. The remaining 67 articles were retrieved for full examination, and 52 articles were excluded (see Fig. 1 for information).



**Figure 1.** The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flow Diagram of the studies retrieved and selection process.

## Results

Table 1 provides a summary of the 15 articles included in this integrative review study. The majority of articles concerned survivors diagnosed with cancer in adolescence, but two studies covered a broader age range (13–45 years) because they dealt with long-term survivors and adolescent comprised at least half of the sample (Maunsell et al., 2006; Nolan et al., 2014). Fourteen articles used quantitative methods, and only one study used qualitative methods (Yeh, 2001). Of the studies using a quantitative method, nine used a cross-sectional design (Arpawong, Oland, Milam, Ruccione, & Meeske, 2013; Barakat, Marmer, & Schwartz, 2010; Bitsko, Stern, Dillon, Russell, & Laver, 2008; Gordijn et al., 2013; Mannix, Feldman, & Moody, 2009; Maunsell et al., 2006; Maurice-Stam, Oort, Last, & Grootenhuis, 2009; Nolan et al., 2014; Yeh, 2001) and six used a longitudinal design (Ander et al., 2016; Jörngården, Mattsson, & von Essen, 2007; Larsson, Mattsson, & von Essen, 2010; Ruccione, Lu, & Meeske, 2013; Spangler, 2009; Vlachioti et al., 2016). Three of the studies were guided by a theoretical

perspective: Roy's adaptation model (Yeh, 2001), an integrative framework from the Pediatric Medical Traumatic Stress Model and the Adolescent Resilience Model (Ruccione et al., 2013), and the Wilson & Cleary and Wallander & Varni models (Maurice-Stam et al., 2009). Two studies (Maurice-Stam et al., 2009; Ruccione et al., 2013) used theory to identify factors related to HRQOL. Yeh (2001) applied Roy's adaptation model to determine whether the HRQOL construct included *focal and contextual stimuli*, a *physiologic mode*, and a *self-concept mode*.

Overall, the selected studies used instruments previously validated in studies of adolescent cancer. Detailed information about the internal consistency reliability of the instruments is listed in Table 1. Among the studies reviewed, the SF-36 (Ware, Kosinski, & Keller, 1994) was the most often used measurement of HRQOL (Ander et al., 2016; Jörngården et al., 2007; Larsson et al., 2010; Mannix et al., 2009; Maunsell et al., 2006). The PedsQL Generic Core Scale (Varni, Seid, & Kurtin, 2001) was used twice (Arpawong et al., 2013; Spangler, 2009). The older version, the PedsQL inventory (Varni, Seid, & Rode, 1999), was used once (Barakat et al., 2010). The Peds QL Generic Core Scale (Varni et al., 2001), the Peds QL Cancer Module (Varni, Burwinkle, Katz, Meeske, & Dickinson, 2002), and the Minneapolis-Manchester Quality of Life Instrument (MMOL) (Bhatia et al., 2002) were used in one study (Vlachioti et al., 2016). The QOL for Children with Cancer questionnaires, based on qualitative study results (Yeh, 2001), was also used in one.

Five factors relevant to this review emerged: (1) HRQOL status, (2) risk factors, (3) protective factors, (4) mediating factors, and (5) current measurements of adolescent HRQOL.

### HRQOL Status

Overall, the majority of adolescents and long-term survivors of cancer in adolescence reported physical and psychological summary HRQOL scores similar to those of healthy control groups (Ander et al., 2016; Gordijn et al., 2013; Mannix et al., 2009; Maunsell et al., 2006; Ruccione et al., 2013). In three studies, survivors showed a higher psychological summary score as well as higher social and emotional functioning scores than healthy control groups (Gordijn et al., 2013; Jörngården et al., 2007; Larsson et al., 2010).

### Risk Factors

Risk factors for poor HRQOL among survivors of cancer in adolescence are related to the type of cancer, type of treatment, chronic symptoms, late effects, and patient demographics including: age, gender, education, and household income. A lower income (less than \$20,000) was negatively associated with low physical HRQOL (Nolan et al., 2014). Also, a high school education was associated with decreasing physical and mental HRQOL compared to survivors who had obtained a college degree (Nolan et al., 2014). Interestingly, time since diagnosis was both a risk and a protective factor for HRQOL. For example, survivors with a shorter time since diagnosis (two years or less) reported lower HRQOL (Jörngården et al., 2007; Larsson et al., 2010), but survivors with a longer time since diagnosis (more than two to four years) reported similar or higher HRQOL than control groups (Bitsko et al., 2008; Gordijn et al., 2013; Jörngården et al., 2007; Larsson et al., 2010; Mannix et al., 2009; Maunsell et al., 2006; Maurice-Stam et al., 2009; Nolan et al., 2014; Ruccione et al., 2013).

**Table 1.** Summary of studies on health-related quality of life in survivors of childhood cancer that occurred during adolescence (N = 15).

|   | Study (year).<br>Country              | Design                           | Sample size (n)<br>(age range,<br>M ± SD) | Time since diagnosis<br>(mean)   | Measurements  | Purpose   | Major findings   |
|---|---------------------------------------|----------------------------------|---|--|---|---|--|
| 1 | Arpawong et al. (2013).<br>USA        | Quantitative,<br>cross-sectional | n = 94 (11–21,<br>12.3 ± 3.1)             | Within 6 months (m)<br>completing cancer<br>treatment (tx)                   | Peds QL 4.0 Generic Core<br>Scales-Adolescent and<br>young adult self-report:<br>Cronbach's<br>$\alpha = 0.89$ (physical)<br>$\alpha = 0.87$ (Psychosocial)                               | To delineate the relationship<br>between optimism and<br>Health-related quality of life<br>(HRQOL) and quality of life<br>(QOL) in adolescents with<br>cancer.                    | <ul style="list-style-type: none"> <li>• The majority of participants reported positive changes as a result of their cancer experience.</li> <li>• Posttraumatic growth (PTG) was significantly lower among survivors of bone tumors (vs. survivors of other cancers) and Hispanic survivors who primarily spoke English at home (vs. Hispanics who primarily spoke Spanish at home and non-Hispanics).</li> </ul> |
| 2 | Barakat et al. (2010). USA            | Quantitative,<br>cross-sectional | n = 102<br>(13–19,<br>15.8 ± 1.8)         | 20 m   | PedsQL 4.0 Generic Core<br>Scales:<br>Cronbach's<br>$\alpha = 0.91$ (Overall)<br>$\alpha = 0.82$ (Physical)<br>$\alpha = 0.88$ (Psychosocial)   | To evaluate the relative<br>contribution of treatment<br>intensity, family socio-<br>demographic risk, and family<br>resources to HRQOL.  | <ul style="list-style-type: none"> <li>• Teens' and parents' report of teens' physical QOL and psycho-social QOL indicated impairment.</li> <li>• Teen-report QOL: Better family functioning (e.g., clearer family roles and responsibilities) predicted better physical QOL.</li> </ul>   |
| 3 | Ander et al. (2016).<br>Sweden        | Quantitative,<br>longitudinal    | n = 61<br>(13–19)                         | T1 to T8<br>(6 m, 12 m, 18 m, 2<br>yr, 3 yr, 4 yr, & 10<br>yr)               | The Medical Outcomes<br>Short Form-36 (SF-36):<br>Without mentioning<br>reliability. SF-36 is valid<br>and reliable for use with<br>survivors of childhood<br>cancer in previous studies. | To investigate the<br>development of HRQOL and<br>symptoms of anxiety and<br>depression   | <ul style="list-style-type: none"> <li>• HRQOL mental summary did not change from 2 to 10 years after dx. The SF-36 physical summary showed an increase from 2 years after dx which declined overtime.</li> <li>• Increasing HROL and a decreasing level of depression and anxiety continued up to 4 years after dx.</li> <li>• After 10 years cancer dx, 29% survivors reported anxiety.</li> </ul>               |
| 4 | Bitsko et al. (2008). USA             | Quantitative,<br>cross-sectional | n = 50<br>(10–21, 20.2, no<br>SD)         | Time since dx (5 yr 6<br>m ± 29.4 m)<br>Time since tx (4 yr 9<br>m ± 30.5 m) | PedsQL4.0: Cronbach's<br>$\alpha = 0.95$  | To investigate how happiness<br>and time perspective mediate<br>the relationship between<br>gender and treatment<br>intensity in the HRQOL<br>outcomes and depressive<br>symptoms | <ul style="list-style-type: none"> <li>• Treatment intensity was negatively associated with survivors' QOL.</li> <li>• Subjective happiness to the model significantly reduced the relationship between treatment intensity and survivor QOL.</li> <li>• Happiness significantly mediated the relationship between gender and treatment intensity with QOL.</li> </ul>   |
| 5 | Gordijn et al. (2013).<br>Netherlands | Quantitative,<br>cross-sectional | n = 62<br>(5–17, 9.7 ± 3.2)               | 3 yrs  | Dutch version of the Child<br>Health Questionnaire<br>(CHQ):<br>Cronbach's $\alpha = 0.80$  | To determine sleep, fatigue,<br>depression, and QOL in<br>survivors of childhood Acute<br>Lymphoblastic Leukemia  | <ul style="list-style-type: none"> <li>• Parents rated the acute lymphoblastic leukemia survivors as having poorer physical QOL than the norm.</li> </ul>  |

|   | Study (year).<br>Country            | Design                        | Sample size (n)<br>(age range,<br>M ± SD) | Time since diagnosis<br>(mean)   | Measurements   | Purpose   | Major findings   |
|---|-------------------------------------|-------------------------------|---|--|--|---|--|
|   |                                     |                               |   |  |  | compared to Dutch norm references   | <ul style="list-style-type: none"> <li>• Acute lymphoblastic leukemia survivors reported better psychosocial QOL compared to the Dutch norm.</li> <li>• Female acute lymphoblastic leukemia survivors reported fewer depressive symptoms compared to the Dutch Norm.</li> </ul>  |
| 6 | Jörngården et al. (2007).<br>Sweden | Quantitative, longitudinal    | n = 56<br>(13–19, 15.7)                   | T1:After dx,<br>T2:6 m,<br>T3:12 m,<br>T4:18 m after dx.                                     | SF-36: Without mentioning reliability. SF-36 is valid and reliable for use with survivors of childhood cancer. | To investigate if and how the HRQOL, anxiety and depression of a group of adolescents with cancer differ from those of a reference group. | <ul style="list-style-type: none"> <li>• A steady increase in psychological well-being from the time of dx, when the cancer patients' ratings were significantly worse than those of the general population.</li> <li>• 1.5 yrs after cancer dx, the differences were reversed, with the cancer group reporting significantly better HRQOL and lower levels of anxiety and depression than the reference group.</li> </ul>   |
| 7 | Larsson et al. (2010).<br>Sweden    | Quantitative, longitudinal    | n = 61<br>(13–19, 15.5 ± 1.7)             | T1:After dx,<br>T2:6 m,<br>T3:12 m,<br>T4:18 m,<br>T5:24 m,<br>T6:36 m,<br>T7:48 m after dx. | SF-36: Cronbach's $\alpha = 0.68–0.72$ (mental health) & $\alpha = 0.68–0.90$ (vitality)                       | To investigate aspects of QOL, anxiety, and depression of cancer during adolescence up to 4 years after diagnosis.                        | <ul style="list-style-type: none"> <li>• The means differ over time (T1–T7) for all variables for the total cancer group, illustrating increasing improvement in QOL and decreasing levels of anxiety and depression.</li> <li>• At T1 and T2, the cancer group reported lower levels of mental health and vitality and a higher level of depression than the references.</li> <li>• At T3, there was no difference between the groups. From T4 to T7, the cancer group reported lower levels of anxiety and depression than the reference group.</li> </ul> |
| 8 | Mannix et al. (2009). USA           | Quantitative, cross-sectional | n = 23<br>(13–21, 16.1 ± 2.5)             | 13 m   | SF-36: Cronbach's $\alpha = 0.72$  | To delineate the relationship between optimism and HRQOL in adolescent with cancer.   | <ul style="list-style-type: none"> <li>• The mean of optimism score: 17.2, quite high.</li> <li>• QOL total score (72.3) was similar to the norms for teens with cancer.</li> <li>• Optimism was correlated with less pain and fewer problems with communication and the total QOL score.</li> <li>• The longest time since diagnosis was associated with the highest reported levels of physical functioning.</li> </ul>  |
| 9 | Maunsell et al. (2006).<br>Canada   | Quantitative, cross-sectional | n = 1334<br>(13–37, 23.0 ± 5.2)           | Cancer dx > 20 age, survived >5 yrs  | SF-36: no mentioned Cronbach's $\alpha$  | To assess the long-term effects of having had cancer during childhood/adolescence   | <ul style="list-style-type: none"> <li>• Fewer survivors (62.1%) than controls (71.1%) reported very good or excellent general health.</li> </ul>  |

|    | Study (year), Country                   | Design                        | Sample size (n) (age range, M ± SD) | Time since diagnosis (mean)                 | Measurements  | Purpose  | Major findings   |
|----|---|-------------------------------|-------------------------------------|---|---|--|--|
|    |   |                               |                                     |   |   | on several indicators of QOL by comparing survivors with controls who have never had cancer  | <ul style="list-style-type: none"> <li>• Having had CNS or bone cancer, more than one treatment series, and 2 organs with a dysfunction were independently associated with poorer QOL in the physical dimensions.</li> <li>• Female survivors had poorer outcomes than male survivors.</li> </ul>  |
| 10 | Maurice-Stam et al. (2009). Netherlands | Quantitative, cross-sectional | n = 353 (18–30, 24.3 ± 4.0)         | 17 yrs                                      | RAND-36, the Dutch version of SF-36: The validity and reliability of the RAND scales are satisfactory based on the original measurement: Cronbach's $\alpha = 0.90$ | To examine factors that affect survivors' HRQOL, using a theoretical model in which demographic and medical characteristics explain HRQOL mediated by course of life, coping and social support                      | <ul style="list-style-type: none"> <li>• Being female had a negative impact on HRQOL.</li> <li>• Patients with brain tumors had worse HRQOL than survivors of leukemia/lymphoma.</li> <li>• Those treated with chemotherapy, radiation therapy (RT) or without RT reported worse HRQOL than those treated with surgery only.</li> <li>• Both disease-related and generic coping strategies affected HRQOL.</li> </ul>  |
| 11 | Nolan et al. (2014). USA                | Quantitative, cross-sectional | n = 2064 (25–45, 37.2 ± 5.0)        | No mentioned (pts were long-term survivors) | SF-36: no mentioned Cronbach's $\alpha$   | To test whether sociodemographic characteristics, disfigurement is associated with an increased risk of reporting poorer HRQOL.  | <ul style="list-style-type: none"> <li>• Disfigurement of the head/neck and limb and race/ethnicity were associated with poorer mental health outcomes.</li> <li>• Sex, education, household income, current age, obesity, head/neck or limb disfigurement, and exposure to alkylating agents and/or radiation to the pelvis as associated with poor physical HRQOL.</li> </ul>  |
| 12 | Ruccione et al. (2013). USA             | Quantitative, longitudinal    | n = 102 (11–21, 14.8 ± 2.7)         | Within 6 m of completing tx                 | PedsQL 4.0 Generic Core Scales Young and adolescent and Young Adult Self-Report: Cronbach's $\alpha = 0.89$ (physical), $\alpha = 0.87$ (psychosocial)              | To assess adolescent cancer survivors' psychosocial HRQOL within 6 months after treatment completion and to evaluate the relationships among demographic and clinical factor, coping skills, and psychosocial HRQOL. | <ul style="list-style-type: none"> <li>• The mean PedsQL psychosocial functioning summary score was 76.9 (good). But 18% of participants whose PedsQL psychosocial functioning scores were equal or less than the mean of norm.</li> <li>• Pain, fatigue, depression, and posttraumatic stress were associated with lower psychosocial functioning scores. Higher self-rated physical functioning scores were associated with higher psychosocial functioning scores.</li> </ul> |
| 13 | Spangler (2009). USA                    | Quantitative, longitudinal    | n = 94 (11–21, 14.8 ± 2.7)          | Age at dx: 12.83 ± 3.14                     | PedsQL Generic Core Scale: Cronbach's $\alpha = 0.92$ (physical), $\alpha = 0.87$ (psychosocial)  | To investigate the relationship between the overall level of social support and QOL.   | <ul style="list-style-type: none"> <li>• Global social support was found to be significantly correlated with Psychosocial QOL but not with Physical QOL</li> <li>• The direct effects of cancer and its treatment may play a more significant role in contributing to Physical QOL than does social support.</li> </ul>  |

| Study (year).<br>Country                    | Design                          | Sample size (n)<br>(age range,<br>M ± SD) | Time since diagnosis<br>(mean)  | Measurements  | Purpose   | Major findings  |
|---|---------------------------------|---|---|---|---|---|
|   |                                 |   |   |   |   | <ul style="list-style-type: none"> <li>• Close friends were a source of perceived social support that contributed significantly to the prediction of Physical QOL.</li> </ul>   |
| 14<br>Yeh (2001).<br>Taiwan                 | Qualitative,<br>cross-sectional | n = 34<br>(4–17, 11.4 ± 3.9)              | From newly<br>diagnosed to terminal<br>stage  | QOL for Children with<br>Cancer (QOLCC): the<br>instrument demonstrated<br>good construct validity in<br>previous study of<br>Taiwanese children with<br>cancer.<br>Cronbach's $\alpha = 0.55–0.83$             | To undertake to establish a<br>conceptual framework for<br>adaptation of Taiwanese<br>children with cancer.   | <ul style="list-style-type: none"> <li>• Age and physical maturity have a significant impact on adaptation.</li> <li>• Physiologic and psychological aspects were interdependent parts of participant response while undergoing cancer treatment.</li> <li>• (Physiological QOL) Adolescents older than 12 years old accept intrusive procedures passively and kept their anger.</li> <li>• (Physiological QOL) Distressing symptoms reported, including oral and anal ulcers, vomiting and nausea.</li> <li>• (Role QOL) Adolescents were more likely to attach to peers and were concerned about their peers' thoughts about them.</li> </ul>   |
| 15<br>Vlachioti et<br>al. (2016).<br>Greece | Quantitative,<br>longitudinal   | n = 82<br>(13–20,<br>15.3 ± 1.7)          | Based on types of<br>cancer<br>T1: beginning of the<br>tx<br>T2: middle of tx (3<br>m–12 m from T1)<br>T3: completion of tx<br>(6 m–24 m from T1) | The Minneapolis-<br>Manchester Quality of<br>Life instrument: Many<br>studies have checked<br>validity and reliability of<br>the Minneapolis-<br>Manchester QoL<br>questionnaire. Cronbach's<br>$\alpha = 0.78$ | To evaluate the QOL of<br>adolescents with cancer<br>including various types of<br>cancer and in all phases of<br>their treatment and adolescent<br>survivors of childhood<br>cancer. | <ul style="list-style-type: none"> <li>• The QOL is comparable to healthy adolescents in the community.</li> <li>• Types of cancer, the chemotherapeutic treatment with strong cytotoxic drugs were negatively correlated with QOL.</li> <li>• The QOL of adolescent patients did not significantly change from during treatment and they showed a satisfactory QOL. Boys scored higher than girls in psychological function and body image.</li> <li>• Adolescents with solid tumors reported lower QOL scores compared to their peers who had hematologic cancer.</li> <li>• Survivors with brain tumor treated with radiotherapy present a significantly lower level of QOL, having any changes in their physical, emotional, and social functioning.</li> </ul> |

Survivors with central nervous system tumors or bone tumors reported poorer physical functioning compared to leukemia or lymphoma survivors (Maunsell et al., 2006; Maurice-Stam et al., 2009; Nolan et al., 2014; Vlachiotei et al., 2016). In addition, CNS tumorsurvivors reported poorer psychological functioning than leukemia survivors (Ruccione et al., 2013; Vlachiotei et al., 2016). Potential complications from cancer treatment including physical health problems (e.g., endocrine, hormonal, cardiovascular, neurologic, and renal), obesity, disfigurement of the head/neck and limb, and organ dysfunction are also associated with poor physical functioning (Maunsell et al., 2006; Maurice-Stam et al., 2009; Nolan et al., 2014). After cancer treatment, fatigue, generalized pain, depression, posttraumatic stress, and sleep disturbances are factors in lower psychosocial functioning scores associated with HRQOL (Gordijn et al., 2013; Ruccione et al., 2013). Survivors of cancer in adolescence report that QOL improves with time up to four years after their cancer diagnosis (Jörngården et al., 2007; Larsson et al., 2010). In two studies that examined HRQOL from cancer diagnosis to six months after, survivors scored lower on measures of HRQOL than a healthy control group. By 18 months post-diagnosis to four years after, survivors reported higher HRQOL than the healthy controls (Jörngården et al., 2007; Larsson et al., 2010).

When Arpawong et al. (2013) measured HRQOL and post-traumatic growth in these survivors, they found that physical and mental HRQOL mean scores were higher, and there was a positive relationship between HRQOL and post-traumatic growth. Zeltzer et al. (2008) described post-traumatic growth (PTG) as evidence of positive perspectives and more resilience to cope with difficulties after surviving cancer. Another study examined HRQOL in survivors of cancer in adolescence using a longitudinal design (Ander et al., 2016). For two years after a cancer diagnosis, participants' mental health scores gradually increased, but from 2 to 10 years after diagnosis, the mental summary HRQOL gradually decreased (Ander et al., 2016). Vlachiotei et al. (2016) conducted a longitudinal study that included adolescent cancer patients and survivors who had completed cancer treatment; both showed satisfactory QOL.

Many studies also report that treatment intensity has a negative impact on adolescent survivors' HRQOL (Bitsko et al., 2008; Vlachiotei et al., 2016). Treatment types such as radiation, chemotherapy, and bone marrow transplantation are associated with poorer physical functioning, and subsequently poor HRQOL (Maurice-Stam et al., 2009; Nolan et al., 2014; Ruccione et al., 2013; Vlachiotei et al., 2016). With regard to demographic variables, female survivors of childhood cancer that occurred during adolescence report poorer HRQOL (Maurice-Stam et al., 2009; Nolan et al., 2014; Vlachiotei et al., 2016). This seems to be true for healthy females, as they also report poorer HRQOL than males (Maunsell et al., 2006). In another study, demographic variables (e.g., gender, age) were not associated with QOL (Barakat et al., 2010). However, in that study, participants had survived only 20 months since cancer diagnosis (Barakat et al., 2010). By comparison, Maunsell's participants had survived for >10 years (Maunsell et al., 2006).

### Protective Factors

Factors related to higher HRQOL in survivors of cancer in adolescence include age, education level, subjective feelings (e.g., happiness, optimism, self-concept), social support, the use of coping strategies, and family functioning (Bitsko et al., 2008; Mannix et al., 2009; Maurice-Stam

et al., 2009; Nolan et al., 2014; Ruccione et al., 2013; Spangler, 2009; Vlachioti et al., 2016; Yeh, 2001). As noted earlier, a longer time since diagnosis (more than two to four years) was found to be associated with higher HRQOL (Ander et al., 2016; Jörngården et al., 2007; Larsson et al., 2010). Survivors ages 18 and older had more positive psychosocial functioning than survivors who were 17 years or younger (Ruccione et al., 2013). Subjective feelings, including happiness and a strong self-concept, were associated with better QOL and fewer depressive symptoms, regardless of cancer treatment (Bitsko et al., 2008). Survivors also reported higher optimism scores, and this was associated with fewer physical symptoms (Mannix et al., 2009). The use of passive coping strategies had a negative impact on physical and mental HRQOL, whereas active coping strategies had a positive effect (Maurice-Stam et al., 2009).

Participants' global social support (sum of social support from family, friends, and healthcare staff) was correlated with better psychosocial QOL, but not physical QOL (Spangler, 2009). In particular, close friends were a source of perceived social support that contributed significantly to the prediction of better physical QOL (Spangler, 2009). Higher family functioning scores and higher parental overprotection scores predicted higher psychosocial QOL in teenagers (Barakat et al., 2010; Vlachioti et al., 2016). In one study, good communication between parent and adolescent during cancer treatment was one of the best predictors of the adolescent's positive HRQOL (Yeh, 2001). Higher physical functioning was linked with higher psychosocial functioning (Ruccione et al., 2013). In three studies, most survivors reported QOL similar to the average scores for the instrument (Arpawong et al., 2013; Mannix et al., 2009; Ruccione et al., 2013). These survivors also reported higher post-traumatic growth (PTG), and this was positively related to psychosocial functioning but negatively related to physical functioning (Arpawong et al., 2013).

### Mediating Factors

Factors mediating the relationship between demographic variables, chronic illness, or symptoms of cancer or treatments and HRQOL included stage of life (e.g., autonomy, psychosexual, and social development), coping, social support, and family functioning (Maurice-Stam et al., 2009; Spangler, 2009). Identifying and understanding mediating variables allows healthcare providers to better understand and facilitate adjustment after cancer diagnosis and treatment (Zebrack & Zeltzer, 2003). Mediating factors may play a significant role in HRQOL, for example, by decreasing post-traumatic stress following diagnosis and treatment for cancer.

Social support did not play a mediating role between medical and demographic variables and the HRQOL of survivors (Maurice-Stam et al., 2009), but having close friends was found to have mediating effects on physical functioning (Spangler, 2009). Cancer and treatment-related variables were found to have about three times as much impact on predicting physical QOL than perceived social support. However, after controlling for the effects of CNS tumor diagnosis and radiation, perceived social support from parents and psychiatrists significantly predicted better psychosocial HRQOL (Spangler, 2009).

### Discussion

This integrative review examined risk and predictive factors related to health-related quality of life among survivors of childhood cancer that occurred during adolescence. This study's findings were compared with results from national data and large datasets that included survivors of childhood cancer. This was done in order to examine for differences in findings based on different survivors' ages since there are few studies about survivors of a childhood cancer that occurred during adolescence. With regard to demographic variables, female survivors of cancer in adolescence reported poorer QOL than male survivors. Our findings support another U.S. study of 271 adolescent cancer survivors (Mort, Salantera, Matomaki, Salmi, & Lahteenmaki, 2011). In other studies of long-term survivors of childhood cancer, other demographic factors associated with HRQOL include employment status (O'Leary, Diller, & Recklitis, 2007) and living alone, which have negative effects on HRQOL (Mort et al., 2011). Positive effects include having more than a high school education, according to the St. Jude Children's Life Time Cohort study, a survey of 1667 survivors of childhood and adolescent cancer (Huang et al., 2013).

Several factors seemed to be protective of better HRQOL including the time passed since cancer diagnosis, social support, and subjective feelings such as happiness or positive self-concept. Survivors report similar or better HRQOL than healthy control groups from six months to four years after a cancer diagnosis and >15 years after a diagnosis (Arpawong et al., 2013; Jörngården et al., 2007; Larsson et al., 2010; Maunsell et al., 2006). Few studies have examined the HRQOL of survivors of cancer in adolescence specifically for the time frame of 5 to 10 years after a diagnosis. One study (Ander et al., 2016) examined HRQOL, anxiety, and depression among adolescent survivors using a longitudinal design. This study followed survivors more than nine years after cancer diagnosis and found that HRQOL was lower than that of the healthy control group (Chan et al., 2014). Thus, assessing distress among survivors and intervening early (within a short time period after cancer diagnosis) may support vulnerable survivors in maintaining their health-related quality of life. Furthermore, more studies of survivors between 5 and 10 years after cancer diagnosis might aid in understanding the unique developmental needs related to HRQOL for survivors of cancer in adolescence.

Several studies have mentioned social support as a protective factor associated with better HRQOL (Spangler, 2009; Vlachioti et al., 2016; Yeh, 2001). Good communication between parents and their sick child (Yeh, 2001) and support from best friends were both predictors of good HRQOL (Spangler, 2009). Social support, however, was a predictor of better psychological HRQOL in childhood cancer survivors except for CNS tumor survivors (Spangler, 2009). There was an exception. Maurice-Stam et al. (2009) employed the Social Support Questionnaire for Transactions (Suurmeijer et al., 1995), which consisted of 41 questions to assess social networks. The researchers did not find a positive relationship between social support and better HRQOL. Their sample size was relatively large ( $n = 353$ ). The Social Support Questionnaire for Transactions measures broad social support of Maurice-Stam et al.'s (2009) study including *social companionship*, *daily emotional support*, *problem-oriented emotional support*, *daily instrumental support*, and *problem-oriented instrumental support*, and this may be different from the social support identified in the reviewed studies that considered family and friends only (Barakat et al., 2010; Spangler, 2009; Yeh, 2001). More research is needed that measures various types of social support to understand the relationship between social support and HRQOL among adolescents.

In this review, studies indicated that a subjective feeling such as happiness or a positive self-concept was associated with better HRQOL. This finding corresponds with a number of other studies on survivors of childhood cancer (Mort et al., 2011; Rhee et al., 2014). Feelings of happiness explained as much as 17% of the variance in the psychological portion of HRQOL in survivors of childhood cancer (Mort et al., 2011). Rhee et al. (2014) found that a positive self-concept had physical and psychological benefits and explained as much as 27% of the variance in the final HRQOL model.

Some survivors of cancer in adolescence had positive perspectives on their cancer experiences and their current HRQOL (Arpawong et al., 2013; Bitsko et al., 2008). Most survivors reported that they had better HRQOL than their healthy siblings. Based on two systematic reviews, most siblings of children with cancer did not report more psychological disorders, but subsets of them reported experiencing post-traumatic distress symptoms, such as anxiety, depression, and poor quality of life (Alderfer et al., 2010). Furthermore, siblings who engage in risky health behaviors exhibit more symptoms of cancer-related posttraumatic (Long et al., 2018). More than 60% of survivors reported positive changes in their perspectives on self and social relationships (Arpawong et al., 2013), high optimism scores (Mannix et al., 2009), and high rates of happiness (Bitsko et al., 2008). Post-traumatic growth has positive effects on psychosocial functioning (Arpawong et al., 2013). Thus, it is important to identify the factors related to cancer survivors' PTG, how the PTG process affects HRQOL, and whether self-reported HRQOL status matches current health status as verified by healthcare providers. Understanding these predictors of HRQOL might allow healthcare providers to detect vulnerable cancer patients and survivors who are at risk for poorer HRQOL later on, and to provide early intervention for them.

Researchers used various instruments to measure HRQOL and included various ages of cancer survivors. Thus, the ability to determine the generalizability of HRQOL measurement findings is limited in our population. Among the 15 studies, the SF-36 (Ware et al., 1994) and the PedsQL Generic Core Scale (Varni et al., 2001) were the most often used measurements. However, two systematic reviews of QOL instruments used with childhood cancer survivors noted that the Pediatric Quality of Life (PedsQL) 3.0 cancer module (Varni et al., 2002) was one of the most often used cancer-specific measurements (Anthony et al., 2014; Eiser, 2007). Eiser suggests that, in general, cancer-specific questionnaires are appropriate to use with cancer patients, but they are more suitable if questions concern the impact of the illness and treatment on the patient's life (Eiser, 2007). Generic measurements such as the SF-36 or PedsQL scale are excellent if the aim is to compare survivors to the average population. Thus, measurements should be chosen based on the research purpose (Anthony et al., 2014; Eiser, 2007). In one study of childhood cancer survivors, QOL was measured using the SF-36 (commonly used in the United States) and the 15D (commonly used in Finland). Results were similar. More research is necessary for measuring the holistic aspects of HRQOL in cancer survivors (Mort et al., 2011).

While most survivors reported good HRQOL scores, some researchers questioned whether the scores were elevated due to measurement issues or response bias (Mort et al., 2011; O'Leary et al., 2007). O'Leary et al. (2007) measured self-deception enhancement (SDE). They found that survivors of cancer in adolescence had a mean SDE score higher than the norm (7.5 vs. 5.8) for both genders and estimated that 40% of those surveyed were biased respondents. That is, they rated their psychological and subjective well-being as better than the normative population,

while non-biased responders rated their QOL as equal to the normative population. Thus, survivors may overestimate their positive attributes due to a lack of insight or denial of current problems. We hypothesized that there might be distinctive HRQOL instruments for survivors of cancer in adolescence to measure their unique developmental tasks, but we found none in the studies chosen for review. We anticipated that social functioning of HRQOL in adolescents might be different from adults or younger children with cancer since they might have missed school or been isolated from their peers during their treatment period. We could not determine this given the paucity of papers that focus on survivors of cancer in adolescence. This remains an area for future study.

Researchers have tried to identify and develop appropriate measurements for HRQOL among survivors of cancer in adolescence using mixed methods and qualitative designs (Nightingale et al., 2011; Quinn, Huang, Murphy, Zidonik-Eddelton, & Krull, 2013). For example, Quinn et al. (2013) used a mixed-method design with survivors ages 15–40 to verify whether current HRQOL instruments fit for those in this age group; 151 participants completed three commonly used HRQOL measurements, and researchers interviewed 30 of the participants to identify missing content from the HRQOL measurements. Participants identified that perceived sense of self, relationships, and parenthood were related to their HRQOL, and these were not measured using the HRQOL instruments (Quinn et al., 2013). In light of these findings, Quinn et al. (2013) suggested that future HRQOL measurements should include items that address self-concept, relationships, and parenthood. Similarly, qualitative studies of adult survivors of childhood cancer have yielded findings comparable to the PedsQOL measurement, including the relationship between physical and psychological functioning and social relationships. However, additional themes were identified including fertility/sexual functioning, body appearance, spirituality, and resilience (Nightingale et al., 2011). These additional items are not included in the often-used HRQOL measurements such as SF-36 or PedsQOL, suggesting a need for their inclusion in measures of HRQOL for survivors of cancer in adolescence. HRQOL is a broad construct where no clinical difference may be discerned by using a general measurement of the construct. Thus, while using current HRQOL measurements it may be important to include additional items or a brief interview to address aspects the specific developmental period of those being assessed.

While cancer survival and treatment are priorities, quality of life issues must also be addressed. This review suggests that protective or mediating factors that contribute to better HRQOL in this population should be promoted among adolescent survivors. Social skills training programs, encouraging good communication between patients and their parents, and teaching strategies to improve survivors' self-concept could help survivors of cancer in adolescence. The Children's Oncology Group has long-term follow-up guidelines for survivors of childhood and adolescent cancer, which consider physical complication issues and emotional issues, but nothing related to the quality of life of survivors (Children's Oncology Group, 2013). While these guidelines cover physical complications and emotional issues, they do not address survivors' QOL. The Institute of Medicine (2007) suggests that QOL should be addressed in survivorship plans for adult survivors but makes no mention of HRQOL or survivorship plans for adolescents. For future research and clinical care, healthcare providers should regularly measure HRQOL of survivors of cancer in adolescence both during and after cancer treatment. This would allow for the detection of problems earlier and the development of tailored survivorship plans. In addition, more

research is needed about the impact of timely interventions for survivors of cancer in adolescence, preferably in the early stages of survivorship (5 to 10 years post-diagnosis). Providing tailored interventions for those at risk for poor outcomes could greatly improve HRQOL for this population.

### **Limitations**

This review focused on survivors of a childhood cancer that occurred during adolescence. However, since there are few studies devoted to survivors of cancer in adolescence, these findings might not be representative of HRQOL in this population. Also, we focused on psychosocial distress and HRQOL, but did not include physical complications as search keywords. Physical complications are of great importance and should be added in future studies. Finally, most of the studies reviewed were conducted in the United States, limiting exploration of the effect of cultural differences, and the use of articles published only in English may have excluded important work.

### **Conclusion**

While many studies focus on adult and pediatric cancer survivors, relatively few focus on survivors of childhood cancer that occurred during adolescence. Given the unique developmental tasks of adolescence, adding a life-threatening illness to the mix is especially burdensome. Without knowledge of the particular factors affecting QOL in this population, it is difficult to impossible to devise a survivorship plan that will ensure optimal outcomes. Protective factors for HRQOL identified in the current research include: familial support and subjective feelings such as happiness, optimism, and self-concept. Risk factors include: gender, types of cancer and treatment, late effects, and a shorter time since cancer diagnosis. We know that social support and coping strategies positively affect QOL. Future research should add more comprehensive measures of mediating effects, as well as other concepts including parenthood, fertility/sexual functioning, and spirituality.

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### **Appendix A. Replicable Search Strategy**

PubMed

((("quality of life"[MeSH Terms] OR ("quality"[All Fields] AND "life"[All Fields]) OR "quality of life"[All Fields]) AND (("adolescent"[MeSH Terms] OR "adolescent"[All Fields]) AND

("neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "cancer"[All Fields])) AND (psychological[All Fields] AND distress[All Fields]) AND (("Childhood"[Journal] OR "childhood"[All Fields]) AND ("neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "cancer"[All Fields])) AND ("quality of life"[MeSH Terms] OR ("quality"[All Fields] AND "life"[All Fields]) OR "quality of life"[All Fields] OR ("health"[All Fields] AND "related"[All Fields] AND "quality"[All Fields] AND "life"[All Fields]) OR "health related quality of life"[All Fields])

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