The diagnosis, treatment, and medical late effects of childhood cancer may alter the psychosocial trajectory of survivors across their life course. This review of the literature focuses on mental health symptoms, achievement of social milestones, socioeconomic attainment, and risky health behaviors in survivors of childhood cancer. Results suggest that although most survivors are psychologically well adjusted, survivors are at risk for anxiety and depression compared with siblings. Although the absolute risk of suicide ideation and post-traumatic stress symptoms is low, adult survivors are at increased risk compared with controls. Moreover, young adult survivors are at risk for delayed psychosexual development, lower rates of marriage or cohabitation, and non-independent living. Survivors’ socioeconomic attainment also is reduced, with fewer survivors graduating college and gaining full-time employment. Despite risk for late health-related complications, survivors of childhood cancer generally engage in risky health behaviors at rates similar to or only slightly lower than siblings and peers. CNS tumors and CNS-directed therapies are salient risk factors for poor psychosocial outcomes. In addition, physical health morbidities resulting from cancer-directed therapies are associated with worse psychosocial functioning. Several studies support the effectiveness of cognitive and behavioral interventions to treat psychological symptoms as well as to modify health behaviors. Additional randomized controlled trials are needed to evaluate the efficacy and long-term outcomes of intervention efforts. Future research should focus on the identification of potential genetic predispositions related to psychosocial outcomes to provide opportunities for preventive interventions among survivors of childhood cancer.
symptoms without assessing associated impairments or the prevalence of mental disorders. Studies using both symptom rating scales and diagnostic interviews suggest many survivors of childhood cancer with elevated symptoms may not have mental health disorders,\textsuperscript{3,4} which is consistent with epidemiologic studies showing survivors are more likely to use mental health services but not more likely to have severe psychopathology.\textsuperscript{5} Moreover, beyond the absence of psychological symptoms, a substantial proportion of survivors report that cancer had a limited or even positive impact on their adjustment.\textsuperscript{6}

Nevertheless, survivors of childhood cancer as a whole are at risk for adverse psychological outcomes. Children and adolescent survivors are significantly more likely to have symptoms of anxiety and depression, inattention, antisocial behavior, and impaired social competence compared with siblings.\textsuperscript{7} Increased prevalence of depression and anxiety symptoms have been reported in adult survivors of childhood cancer many years after completion of therapy,\textsuperscript{1,2} as have post-traumatic stress symptoms (PTSS) and suicide ideation (SI).\textsuperscript{8,9} Although the absolute risk of SI and PTSS were low (6% to 8% for SI; 9% for PTSS), adult survivors were at increased risk compared with controls. Importantly, it remains unclear if risk of SI extends to increased risk for suicide attempts or deaths.\textsuperscript{10}

Several factors have been associated with adverse psychological symptoms in survivors, including low income, lower education, female sex, disability status, and unmarried status.\textsuperscript{2} However, the direction of effects is unclear, as these factors may contribute to, or be the consequences of, mental health problems. Poor physical health, including chronic health conditions, pain, and disfigurement, are consistently associated with poor mental health outcomes in survivors.\textsuperscript{1,7,9,11}

With mental health strongly tied to childhood cancer survivors' physical health, it is not surprising that cancer treatments associated with medical late effects are associated with psychological adjustment. CNS-directed therapies, especially cranial radiation therapy (CRT) have been associated with poor adjustment, and CNS tumor survivors overall are at high risk for poor adjustment.\textsuperscript{2,7,11} Intensive chemotherapy regimens and those including alkylating agents also have been associated with psychological symptoms.\textsuperscript{2,7,11} Survivors of bone tumors are at risk for psychosocial problems, likely reflecting the impact of physical mobility problems and pain on adjustment.\textsuperscript{2,11}

Little research has focused on the implementation and evaluation of interventions targeting psychological symptoms in survivors of childhood cancer (Table 1).\textsuperscript{12-15} and most existing studies are limited by small sample sizes, lack of appropriate comparison groups, and diagnostically heterogeneous samples. However, results seem to suggest that tailored cognitive-behavioral therapy can improve PTSS and anxiety as well as behavior problems in survivors of CNS tumors.

### Social Outcomes

In childhood, survivors are at risk for social difficulties marked by poor peer acceptance, isolation, and diminished leadership roles. Difficulties in the social arena are most commonly observed among survivors of CNS tumors and CNS-directed therapies.\textsuperscript{16} Critical tasks for survivors include the development of social relationships and establishing independence from primary caregivers. Attainment of these developmental tasks may be complicated by survivors' treatment history and/or the emergence of late effects. In general, results from large cohort studies suggest that survivors have lower rates of marriage or cohabitation compared with siblings,\textsuperscript{17} national cancer registry data,\textsuperscript{18} and general population data.\textsuperscript{17} Predictors of not partnering include CNS tumor diagnosis,\textsuperscript{17,18} CNS-directed therapies,\textsuperscript{17} and male sex.\textsuperscript{18} Rates of separation or divorce appear largely equivocal between survivors and comparison groups.\textsuperscript{18}

Successful negotiation of psychosexual milestones has been increasingly recognized as an important social outcome for

<table>
<thead>
<tr>
<th>Table 1. Empirically Supported Interventions for Psychological Symptoms in Survivors of Childhood Cancer</th>
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<tbody>
<tr>
<td>Primary Intervention</td>
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<tr>
<td>----------------------</td>
</tr>
<tr>
<td>Behavior problems</td>
</tr>
<tr>
<td>Posttraumatic stress, anxiety</td>
</tr>
<tr>
<td>Posttraumatic stress, uncertainty, anxiety, benefit finding, health promotion</td>
</tr>
<tr>
<td>Posttraumatic stress, anxiety, depression, fear of progression/relapse</td>
</tr>
</tbody>
</table>

Abbreviations: CBT, cognitive behavior therapy; RCT, randomized controlled trial.
survivors of childhood cancer. Female survivors have reported lower sexual function, interest, desire, arousal, satisfaction, and activity compared with female siblings, and male survivors have reported significantly less sexual activity and 2.6-fold higher relative risk of erectile dysfunction compared with male siblings. Delayed achievement of psychosexual milestones, including dating, masturbation, and sexual intercourse, also have been reported among survivors. Higher neurotoxic treatment intensity seems to be a significant risk factor for delayed and/or impaired psychosexual development. Importantly, some data indicate no differences in risky sexual behaviors between adolescent survivors and siblings, suggesting more pronounced psychosexual difficulties may not emerge until young adulthood, when the development of intimate relationships is a more salient social goal.

The ability of survivors to live independently serves an important indicator of adult autonomy. Unfortunately, survivors are twice as likely to live dependently compared with their siblings. Risk factors for nonindependent living include CNS tumor diagnosis, CRT, poor physical functioning, and neurocognitive problems. The ability of survivors to live independently may be additionally complicated by treatment-related morbidities, including hearing impairment and vision loss.

The majority of intervention research related to social functioning has involved social skills training among child and adolescent survivors of CNS tumors (Table 2). This focused effort is prudent, given the heightened risk for adverse social outcomes among survivors of CNS tumors as well the importance of early intervention to offset later deleterious social outcomes. However, these studies have been limited by small sample sizes, relatively modest effects, and discrepancies in outcomes on the basis of parent versus survivor self-report. Future work is needed to understand the long-term impact of these interventions as well as to promote social integration and independence among adult survivors of childhood cancer.

### Educational Achievement

School-age patients with cancer may miss significant educational opportunities because of their illness and treatment. This may result in survivors requiring additional educational support or grade retention. A report from the Childhood Cancer Survivor Study indicated that 23% of survivors had a history of special education services compared with 8% of siblings. Neurocognitive deficits contribute significantly to the educational difficulties experienced by survivors. Although survivors of CNS tumors and leukemia are generally at greatest risk for low educational achievement, elevated risk of not graduating high school also has been observed among survivors of non-Hodgkin lymphoma and neuroblastoma. Among survivors who did not receive CNS-directed therapies, the mechanisms underlying poor attainment have not fully been elucidated but may include individual variation in response to cancer-directed therapies, treatment-related late effects, or changes in teacher/peer behavior after school reentry. Of note, some studies suggest that subgroups of survivors achieve educational outcomes comparable to their peers, and reports from European countries indicate that survivors may surpass expected outcomes in the general population. Enhancing educational opportunities and outcomes is critical for survivors of childhood cancer, because success in the academic arena sets the stage for later vocational opportunities.

### Vocational Attainment

A recent meta-analysis revealed that the likelihood of unemployment among survivors of childhood cancer is 50% greater than observed in the general population but may be improving in comparison with earlier studies. Importantly, vocational outcomes vary by geographic region. Specifically, survivors from the United States and Canada appear to be at greater risk of

<table>
<thead>
<tr>
<th>Primary Intervention Target(s)</th>
<th>First Author</th>
<th>Intervention</th>
<th>Sample</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peer acceptance, social reputation</td>
<td>Devine26</td>
<td>Two conditions with repeated measures: peer-mediated group training or untreated comparison group</td>
<td>13 preadolescent and adolescent survivors of CNS tumors</td>
<td>No significant differences in social competence between survivors and peers. Intervention classrooms showed lower levels of social rejection and victimization.</td>
</tr>
<tr>
<td>Social skills</td>
<td>Barrera27</td>
<td>Single group with repeated measures: group social skills training</td>
<td>32 preadolescent and adolescent survivors of CNS tumors</td>
<td>Significant improvements in self-control, social skills, and quality of life.</td>
</tr>
<tr>
<td>Social skills</td>
<td>Schulte28</td>
<td>Two conditions with repeated measures: group social skills training or untreated comparison group</td>
<td>27 preadolescent and adolescent survivors of CNS tumors</td>
<td>Significant improvement in social skills in the intervention group; significant increase in social problems in untreated comparison group.</td>
</tr>
<tr>
<td>Social problem solving, social behaviors</td>
<td>Schulte29</td>
<td>Single group with repeated measures: group social skills training</td>
<td>15 preadolescent and adolescent survivors of CNS tumors</td>
<td>Significant improvements in maintaining eye contact, social conversations with peers, and cooperative play; no observed change in social problem-solving.</td>
</tr>
</tbody>
</table>
Psychosocial Outcomes of Childhood Cancer

Psychological symptoms and poor socioeconomic outcomes place survivors at risk for engagement in risky health behaviors. Importantly, risky behavior exacerbates existing health vulnerabilities and places survivors of childhood cancer at risk for adverse health outcomes. Despite these risks, survivors of childhood cancer generally engage in risky health behaviors at rates similar to or only slightly lower than siblings and peers. Few mechanisms exist for reducing risk of second cancers in survivors, but modifying risky behavior remains one such option. Although the number of randomized trials considering risky health behavior in survivors is few (Table 3), overall results confirm that health behaviors are modifiable and behavioral counseling and/or psychoeducation can result in desired behavior change.

**Tobacco Use**

Cigarette smoking has been linked to variety of adverse health outcomes, including neoplasia, cardiac, pulmonary, and other health problems. Cancer-directed therapies often result in organ compromise, which may be additionally exacerbated by tobacco use. Some 19% to 22% of survivors report smoking within the past 30 days, and 8.3% of males are smokeless tobacco users. However, these prevalence estimates may under- or overestimate the actual proportion of survivors who are tobacco users, because they are based on self-report and sensitive to secular trends. Survivors reporting psychological distress or heavy drinking are more likely to be current smokers, and those with higher income, higher education, and exposure to CRT are less likely to use tobacco. Smoking is particularly concerning among survivors, because they are less likely to successfully quit smoking after initiation compared with their peers.

**Marijuana (Cannabis) and Illicit Drug Use**

As with tobacco use, smoking marijuana has been associated with pulmonary complications, whereas cocaine and methamphetamine use has been associated with cardiac problems in survivors of childhood cancer. Fortunately, prevalence estimates of cocaine/crack use remain low (eg, 0.6%). In contrast, estimates of marijuana use range from 10% to 12%, but with increasing legalization (both medical and recreational), these rates are climbing. Risk factors for marijuana and other illicit drug use include older age, male sex, lower resiliency to peer influences, depressive symptoms, higher socioeconomic status, and drug use among friends and household members.

**Alcohol Use**

Excessive alcohol consumption has been associated with a number of malignancies, including oropharyngeal, esophageal, liver, and stomach cancers. Data from the Swiss Childhood Cancer Survivor Study indicated that frequent alcohol consumption occurred more often among survivors relative to the general population (22% vs 12%), with similar patterns observed in monthly binge drinking (18% vs 9%). Predictors of risky drinking include younger age, male sex, lower educational attainment, psychological stress, increased life stressors and dissatisfaction, activity limitations, and perceptions of poor health. Across studies, disease and treatments affecting the CNS have been associated with lower risk of alcohol use.

**Diet, Nutrition, and Physical Activity**

Healthy nutrition, diet, and physical activity can mitigate many late effects of cancer treatment, including obesity, hyperlipidemia, diabetes mellitus, cardiovascular disease, hypertension, and osteoporosis. Unfortunately, many survivors of childhood cancer do not meet recommended dietary guidelines, with 54% exceeding daily caloric consumption requirements, and only 4%, 19%, 24%, and 29% of survivors meet guidelines for vitamin D, sodium, calcium, and saturated fat intake.
Table 3. Empirically Supported Interventions for Risky Health Behaviors Among Survivors of Childhood Cancer

<table>
<thead>
<tr>
<th>Primary Intervention Target(s)</th>
<th>First Author</th>
<th>Intervention</th>
<th>Sample</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco use, self-reported smoking cessation</td>
<td>Emmons</td>
<td>RCT with two conditions: self-help condition or survivorship peer counseling, tailored and targeted written educational materials, and free nicotine replacement therapy</td>
<td>796 adult survivors of childhood cancer who smoked</td>
<td>The quit rate was significantly higher in the peer counseling condition (18.6% vs 8.5%) and 12 (15% vs 9%) months.</td>
</tr>
<tr>
<td>Tobacco use, self-reported smoking cessation</td>
<td>Emmons</td>
<td>Same study as above; consideration of cessation outcomes at 2 to 6 years post baseline</td>
<td>796 adults of childhood cancer who smoked</td>
<td>Quit rates at long-term follow-up were significantly higher in the peer counseling condition (20.6% vs 17.6%).</td>
</tr>
<tr>
<td>Tobacco use, self-reported smoking cessation</td>
<td>Emmons</td>
<td>RCT with two conditions: Web-based intervention or print materials condition that included the provision of self-help materials</td>
<td>374 adult survivors of childhood or young adult cancer</td>
<td>Equivalent rates of cessation were reported for both groups (16%) at the 15-month follow-up.</td>
</tr>
<tr>
<td>Illicit drug use, risk motivation</td>
<td>Hollen</td>
<td>RCT with two conditions: enhanced care/decision aid intervention psychoeducational modules, an educational CD-ROM, tailored substance use risk behavior counseling delivered by nurse practitioners and telephone boosters; or standard care</td>
<td>243 adolescent survivors of childhood cancer</td>
<td>At 6 months post intervention, there was a significant change in risk motivation for low risk takers.</td>
</tr>
<tr>
<td>Diet nutrition, knowledge of disease and treatment, risk perceptions, protective/risky health behaviors</td>
<td>Cox</td>
<td>RCT with two conditions: a multicompartment risk counseling intervention or standard care.</td>
<td>267 adolescent survivors of childhood cancer</td>
<td>In the intervention group, self-reported junk food consumption significantly decreased.</td>
</tr>
<tr>
<td>Physical activity, body mass index, body weight, Functional Assessment of Cancer Therapy—General Survey, physical well-being, social well-being, emotional well-being, functional well being</td>
<td>Valle</td>
<td>RCT with two conditions: a 12-week Facebook-based intervention (FITNET) or a 12-week Facebook-based self-help condition</td>
<td>86 young adult survivors of cancer</td>
<td>Over 12 weeks, increases in light physical activity were 135 min/wk greater in the FITNET group relative to the self-help condition, and the FITNET group reported significant weight loss over time (~2.1 kg).</td>
</tr>
<tr>
<td>Physical activity, exercise behavior, levels of physical activity, self-efficacy, quality of life</td>
<td>Lipton</td>
<td>RCT with two conditions: 4-day integrated adventure-based training and health education program or attention-only group</td>
<td>71 preadolescent and adolescent survivors of childhood cancer</td>
<td>Those in the experimental group reported significant differences in physical activity stages of change, higher levels of physical activity, and self-efficacy as compared with those in the control group. There were also statistically significant mean differences in physical activity levels, self-efficacy, and quality of life of participants in the experimental group from baseline to 9 months after starting the intervention.</td>
</tr>
<tr>
<td>Sun exposure, sun safety practices</td>
<td>Mays</td>
<td>RCT with two conditions: a multiple health behavior change intervention designed to increase sun safety practices or wait-list control</td>
<td>75 adolescent survivors of childhood cancer</td>
<td>Survivors in the intervention arm reported significantly more sun safety practices at 1 month post intervention than control participants.</td>
</tr>
<tr>
<td>Sun protection</td>
<td>Recklitis</td>
<td>Repeated measures; stratified assignment to two conditions: UVP or education-only comparison</td>
<td>58 adolescent and young adult survivors of childhood cancer</td>
<td>UVP was found to be acceptable and not distressing to survivors. UVP resulted in significantly improved sun protective behaviors (ie, reduced sun exposure, increased sunscreen use, and increased hat wearing).</td>
</tr>
</tbody>
</table>

Abbreviations: RCT, randomized controlled trial; UVP, UV light photography.

respectively. Furthermore, 52% of adult survivors of childhood cancer do not meet physical activity guidelines. Consistent with population factors, predictors of healthy diet among survivors include younger age, female sex, higher education, higher socioeconomic status, greater social support, and fewer depressive symptoms. Although female sex, low parent education, CRT, and
mobility restrictions predict low physical activity in adolescence, poor diet and low self-esteem in adolescence have been associated with nonadherence to physical activity guidelines in adults. Although empirical support for diet, nutritional, and physical activity interventions among survivors remains in its nascency, preliminary evidence suggests that psychoeducational and physical activity interventions have the potential to improve these behaviors.

**Sun Exposure**

Nonmelanoma skin cancer is the most prevalent subsequent malignant neoplasm in survivors of childhood cancer. Because UV radiation from the sun is a well-recognized cause of skin cancer, efforts have been made to understand sun exposure and related behaviors in survivors. A minority of survivors of childhood cancer always or often use sunscreen (44%) or sun-protective clothing (18%), wear a hat when outside (36%), limit sun exposure (35%), stay in the shade (32%), or complete recommended skin examinations (18%).

Older attained age and CNS tumors have been associated with increased engagement in sun protection, whereas overweight or obese survivors were less likely to report receiving a skin examination.

**Risky Sexual Behavior**

Risky sexual behavior has recently been included in the cluster of risky behaviors studied among survivors, in part because of its association with genital human papillomavirus (HPV) and anogenital and oropharyngeal cancers. Although prevention of specific HPV-related cancers can occur via the HPV vaccine, survivors of childhood cancer initiate the HPV vaccine at rates significantly lower than their population peers (23.8% vs 40.5%). Because survivors are more likely to experience an HPV-related cancer in adulthood, a better understanding of sexual behavior in survivors is needed.

As the population of survivors of childhood cancer continues to grow, research into their long-term psychosocial adjustment will be critical. Although most studies to date are limited by cross-sectional designs, tumor location within the CNS and CNS-directed therapies have emerged as salient risk factors for poor psychosocial outcomes. As front-line therapeutic protocols aim to reduce potentially neurotoxic treatment exposures (eg, reduced-dose craniospinal radiation for subtypes of medulloblastoma, elimination of prophylactic CRT for acute lymphoblastic leukemia), continued follow-up to assess long-term outcomes is needed to determine if an expected reduction in psychosocial morbidities occurs. In addition, the impact of therapeutic changes in other groups of survivors (ie, limb-sparing approaches in survivors of bone tumor) should be examined in relation to psychological outcomes. Unfortunately, recent research suggests that changes to front-line therapies in more contemporarily treated cohorts of survivors have not yielded reductions in poor mental health, pain, or cancer-related anxiety in adult survivors.

**CONCLUSION**

An important area of future research centers on the understanding of survivors’ mental health needs and help inform the development of intervention programs to meet those unique needs. Although most intervention efforts to date have been small, many suggest potential efficacy and should begin to be incorporated and disseminated as part of standard clinical care.

As front-line therapeutic protocols aim to reduce potentially neurotoxic treatment exposures (eg, reduced-dose craniospinal radiation for subtypes of medulloblastoma, elimination of prophylactic CRT for acute lymphoblastic leukemia), continued follow-up to assess long-term outcomes is needed to determine if an expected reduction in psychosocial morbidities occurs. In addition, the impact of therapeutic changes in other groups of survivors (ie, limb-sparing approaches in survivors of bone tumor) should be examined in relation to psychological outcomes. Unfortunately, recent research suggests that changes to front-line therapies in more contemporarily treated cohorts of survivors have not yielded reductions in poor mental health, pain, or cancer-related anxiety in adult survivors. Incorporation of mental health and behavioral measures in established and new cohort studies will support research across a broader range of survivors and new cancer therapies. In addition, longitudinal studies will serve to enhance understanding of the time course of these outcomes as well as specific temporal causes. Assessing psychiatric diagnoses and impairment because of psychological symptoms in outcomes research will significantly improve our understanding of survivors’ mental health needs and help inform the development of intervention programs to meet those unique needs. Although most intervention efforts to date have been small, many suggest potential efficacy and should begin to be incorporated and disseminated as part of standard clinical care.

An important area of future research centers on the identification of potential genetic predispositions related to psychosocial outcomes among survivors of childhood cancer. Data from the Childhood Cancer Survivor Study indicated that among survivors of medulloblastoma, those with homozygous GSTM1 gene deletion reported greater symptoms of anxiety, depression, and global distress compared with survivors of medulloblastoma with the GSTM1 non-null genotype. This work could be extended to outcomes such as post-traumatic stress disorder, where evidence supporting a genetic predisposition has been reported in other populations. However, among survivors, understanding interactions between therapeutic exposures that place survivors at risk for adverse outcomes and genetic predispositions will be critical. Moreover, pharmacogenetics studies may be useful to promote understanding of survivor engagement in risky health behaviors, such as tobacco and alcohol abuse (eg, dopamine receptor gene DRD2). Identification of survivors who are at risk for adverse

<table>
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<tr>
<th>Table 4. Psychosocial Standards of Care for Survivors of Childhood Cancer</th>
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<tbody>
<tr>
<td><strong>Standard of Care</strong></td>
</tr>
<tr>
<td>Routine and systematic assessment of psychosocial needs</td>
</tr>
<tr>
<td>Monitoring of neuropsychological deficits in survivors of brain tumor and other high-risk groups</td>
</tr>
<tr>
<td>Annual psychosocial screening of long-term survivors for educational/vocational progress; social relationships; anxiety, depression, and distress symptoms; and risky health behaviors</td>
</tr>
<tr>
<td>Access to psychosocial support and interventions</td>
</tr>
<tr>
<td>Assessment of financial hardship with targeted referrals</td>
</tr>
<tr>
<td>Education and anticipatory guidance related to late effects provided throughout the trajectory of cancer care</td>
</tr>
<tr>
<td>Opportunities for social interaction</td>
</tr>
<tr>
<td>School-reentry support that includes provision of information and recommendations to school personnel</td>
</tr>
<tr>
<td>Open, respectful communication and collaboration among families and providers</td>
</tr>
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</table>

**NOTE.** Adapted from Wiener et al. Table only includes standards specific to survivors, moderate or greater quality of evidence, and strong recommendation.
psychosocial outcomes secondary to genetic variations will provide opportunities for preventative interventions.

Timely identification of psychosocial issues is critical to offset potential deleterious effects across the developmental life course of survivors. Recent evidence-based standards for the psychosocial care of children with cancer identify services that are essential for comprehensive care (Table 4). Unfortunately, many pediatric oncology programs lack the multidisciplinary teams necessary to implement the full set of standards. Despite this potential barrier, psychosocial programming must be prioritized in pediatric oncology and survivorship settings as a means of promoting prosocial development and physical and mental health outcomes across the cancer continuum.

REFERENCES


AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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AUTHOR CONTRIBUTIONS

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Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors
Psychosocial Outcomes of Childhood Cancer


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