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Pediatric sarcoma survivorship: A call for a developmental cascades approach

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Abstract

Survivors of pediatric sarcomas often experience greater psychological and psychosocial difficulties than their non-afflicted peers. We consider findings related to poorer outcomes from a developmental cascade perspective. Specifically, we discuss how physical, neurocognitive, psychological, and psychosocial costs associated with pediatric sarcomas and their treatment function transactionally to degrade well-being in long-term pediatric sarcoma survivors. We situate the sarcoma experience as a broad developmental threat – one stemming from both the presence and treatment of a life-imperiling disease, and the absence of typical childhood experiences. Ways in which degradation in one developmental domain spills over and effects other domains are highlighted. We argue that the aggregate effect of these cascades is two-fold: first, it adds to the typical stress involved in meeting developmental milestones and navigating developmental transitions; and second, it deprives survivors of crucial coping strategies that mitigate these stressors. This position suggests specific moments of intervention and raises specific hypotheses for investigators to explore.

Keywords: developmental cascades, chronic conditions, pediatric sarcoma, quality-of-life, survivorship

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With advances in technology leading to improved survival rates among cancer patients, attention has turned to quality-of-life research and the survivorship experience. This attention has largely focused on survivors of adult cancers; less is clear about the long-term fallout of surviving cancer as a child, adolescent, or young adult. An even greater dearth of research exists for survivors of rare cancers, such as sarcomas – a form of cancer that occurs in both bone and soft tissue and requires aggressive treatment. Storey et al. (2019) recently addressed this gap, highlighting the well-being costs of pediatric sarcoma survivorship. In addition, a longitudinal investigation by Marina et al. (2017) showed that many outcomes for sarcoma survivors worsen over time as survivors age. We build on these insights, recognizing pediatric[1] sarcomas as posing both immediate physical threats and long-term developmental obstacles.

We suggest that the impact of pediatric sarcoma is best conceptualized with a "developmental cascade" model (Masten & Cicchetti, 2010). Such a model highlights how particular insults or benefits in one domain, at one point in time, "cascade" or spill over into other domains and across time. This approach frames the sarcoma experience as a broad developmental threat, reverberating through multiple domains of functioning (physical, psychological, neurocognitive, and psychosocial), extending across time, and reshaping the developmental trajectory of the young person.

Thinking about pediatric sarcoma as a developmentally cascading event – one affecting seemingly unrelated intrapersonal and interpersonal constructs (e.g., executive functions, peer group interactions) and doing so into the future – provides a structure for understanding the less than optimal outcomes of long-term survivors. What follows is not an exhaustive review of the pediatric sarcoma survivor literature; rather it is a proposal to encourage researchers and clinicians to consider the long-term outcomes of survivors as a function of developmentally cascading processes that increase stress and overwhelm coping resources at developmentally sensitive moments.

Below, we discuss the utility of a developmental cascades approach, briefly contrasting it with a biopsychosocial framework. We define "developmental tasks" and "developmental transitions" that we argue are affected by sarcoma and its treatment. We then outline common physical, psychological, neurocognitive, and psychosocial correlates of sarcoma survivorship. We indicate how these costs may interact with other domains, accumulating across time, increasing the stress of developmental tasks and transitions, reducing coping strategies for managing this stress, and degrading long-term quality of life. We end by highlighting the clinical and research implications of adopting a developmental cascade understanding of pediatric sarcoma survivorship.

[1]In this paper, "pediatric" refers to patients diagnosed in childhood, adolescence, and young adulthood (under 25). We chose this age range because of the rapid developmental changes that occur during this time.

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The Utility of a Developmental Cascades Approach

Understanding long-term outcomes related to pediatric sarcomas requires us to recognize the developmental context of the disease. Osteosarcoma and Ewing's sarcoma are predominately diagnosed in children and adolescents and are among the most common forms of bone cancer (Weber, Damron, Frassica, & Sim, 2008). In general, sarcomas account for roughly 15% of all pediatric malignant tumors (National Foundation for Cancer Research, 2019). Compared to more common childhood cancers, overall survivability is worse (Lim et al., 2015) and subsequent limitations on survivors' physical functions and daily activities are greater (Ness et al., 2005, 2008). Moreover, cognitive and psychosocial outcomes for sarcoma survivors are less than ideal (Tonning Olsson et al., 2020; Storey et al., 2019). These compromised outcomes in turn raise additional challenges, the sum of which can prove overwhelming – a recent analysis (Siracuse, Gorgy, Ruskin, & Beebe, 2017) of survivors ranging 0 and 30 years since their diagnosis indicated that they were twice as likely to die by suicide than the national average.

Biopsychosocial approaches guide clinicians and researchers in understanding contextual variables (biological, psychological, social) contributing to children's adjustment and disease outcomes during and following sarcoma treatment. Researchers informed by a biopsychosocial perspective have emphasized the importance of appreciating the developmental tasks and psychosocial milieu of adolescence and young adulthood in determining quality of life and disease outcomes (e.g., Zebrack, Santacroce, Patterson, & Gubin, 2016). However, profound physical threats encountered in childhood and adolescence carry developmental costs. The sequelae of sarcoma and its treatment interact to influence whether and how survivors accomplish developmental tasks and successfully manage the psychosocial milieu of developmental transitions. A developmental cascade approach extends the insights afforded by a biopsychosocial perspective; it closely examines transactions among domains which serve to enhance or impede survivors' abilities to effectively meet the demands of typical developmental tasks and transitions.

Researchers and clinicians have long recognized "late effects" – or negative physical and psychosocial outcomes – in childhood cancer survivors (e.g., Byrd, 1985; Mulhern, 1994). The consequences of intensive therapies and these late effects have been shown to lower the life expectancy of childhood cancer survivors (Yeh et al., 2020), particularly that of Ewing sarcoma survivors (Yeh, Nekhlyudov, Goldie, Mertens, & Diller, 2010). A developmental cascades approach offers a way of thinking about mechanisms involved in such late effects and their cumulative impact. This perspective recognizes that competent adulthood – one characterized by social connection, economic autonomy, and freedom from chronic mental health struggles – relies on a series of probabilistic developmental successes. With typical experiences, children often successfully assimilate an ocean of information from social and academic environments. In these environments, children acquire and practice skills necessary for navigating adulthood. They also practice retrieving and distilling insights from their knowledge base to help them manage novel environments. Children developing within more typical contexts and experiences learn social norms germane to their peer group; they form social identities and self-concepts conducive to success in adulthood.

Pediatric sarcoma, a highly atypical experience, removes children from the opportunities of developmentally normative contexts. Survivors have missed – and due to subsequent physical limitations, may continue to miss – many experiences key to successful development. Moreover, a cancer diagnosis is a traumatic stressor for children and families (Goldwin, Lee, Afzal, Drossos, & Karnik, 2014; Landolt, Vollrath, Ribi, Gnehm, & Sennhauser, 2003); it derails plans and routines, upends life narratives, and threatens structures of meaning children and families rely on to organize their lives and identity. The developmental cascade model, with its view of development as a dynamic set of processes, poses questions for researchers to pursue longitudinally, such as: how do the *presence* of atypical stressors (e.g., threat to life, cancer-related fatigue, chronic pain, heightened psychological distress) the *absence* of typical experiences (e.g., normative learning in social and academic environments), and the potential cost to coping resources (e.g., due to reduced mobility, smaller social networks, compromised executive functions), combine and accumulate to affect survivors' well-being (e.g., stress levels, quality of life).

A developmental cascade approach also suggests to clinicians and researchers specific moments for support and intervention. For many survivors, stress related to secondary complications – and to the sarcoma experience generally – plays out endlessly across the developmental trajectory. Each typical developmental transition – to elementary, middle and high school settings, to intimate relationships, to college, to work environments, and so on – carries more stress with fewer coping resources for sarcoma survivors than for their healthy peers. A cascade approach points to this type of recurrent stress and concomitant decrements in coping, and these moments of transition, as critical foci in need of clinical and research attention. Presently, cancer-care protocols do not appear to recognize nor address the recurrent and cumulative nature of stress – and compromised coping abilities – which may contribute to the lower well-being and poorer quality-of-life outcomes of pediatric sarcoma survivors.

Developmental Tasks and Transitions

A pediatric sarcoma diagnosis during childhood and adolescence disrupts a period of intense developmental change, one which sets the stage for adult functioning. As such, sarcomas and their treatment interfere with the accomplishment of developmental tasks and the navigation of developmental transitions. Here, "developmental tasks" refers to widely recognized tasks of middle childhood, adolescence, and young adulthood; "developmental transitions" refers to common, culturally recognized movement into psychosocial spaces (e.g., the middle school, high school, college, and work milieu) that bring greater complexity of stimuli, responsibilities, and relationships, and thus place greater demands on the developing young person. That is, researchers recognize that successfully meeting typical developmental tasks and managing typical developmental transitions invariably carry a relatively typical amount of stress (Elias, Gara, & Ubriaco, 1985; Marcia, 2010).

Developmental tasks of middle childhood include the development of a self-concept of competence and connectedness in relation to peers (Erikson, 1968), forming friendships, and managing oneself behaviorally and academically within the school environment and in accordance with prosocial goals (Hartup, 1992; Markus & Nurius, 1984). Tasks of adolescence and young adulthood include academic attainment, engagement in romantic relationships, and acquiring work competence and economic autonomy (Roisman, Masten, Coatsworth, & Tellegen, 2004; Schulenberg, Bryant, & O'Malley, 2004).

Researchers and theorists have emphasized the centrality of peer experiences in successfully meeting these tasks and navigating

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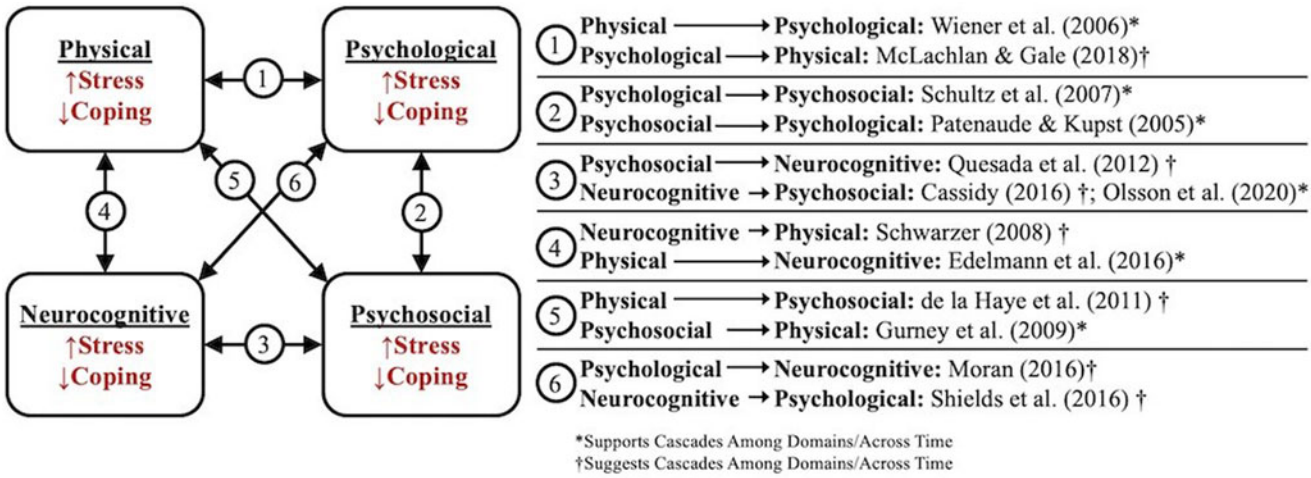

Figure 1. Domains of functioning, six cross-domain interactions with contributors to unhealthy stress and insufficient coping resources/strategies with examples from prior research (Patenaude & Kupst, 2005; Wiener et al., 2006; Schultz et al., 2007; Schwarzer, 2008; Gurney et al., 2009; de la Haye et al., 2011; Quesada et al., 2012; Cassidy, 2016; Edelmann et al., 2016; Moran, 2016; Shields et al., 2016; McLachlan & Gale, 2018; Olsson et al., 2020).

transitions. They observe that essential interpersonal and social problem-solving skills are acquired and practiced in the context of peer relationships (Connolly, Furman, & Konarski, 2000; Masten, Juvonen, & Spatzier, 2009). Further, Hay and Ashman (2003) note the importance for adolescents of extrafamilial social networks, particularly insofar as the development of self-concept, coping strategies, and emotional stability are concerned.

Successfully managing developmental transitions carries a typical level of stress. We suggest that the stress encountered by pediatric sarcoma survivors, many of whom carry the sequelae of sarcoma treatment, as they encounter developmental tasks and transitions is far greater than that encountered by their non-afflicted peers. We propose that survivors confront unhealthy levels of stress, that cascade across domains of function and overwhelm efforts and abilities to cope.

In the following sections, we highlight common physical, psychological, neurocognitive, and psychosocial correlates of survivorship. We do so with an eye towards the interactive and developmentally cascading nature of these costs, noting how disruption in one domain can undermine functioning in others. For example, treatments that even slightly degrade executive functions can negatively affect a survivor's academic performance, self-concept, social functioning, and coping strategies. We then consider development, pointing to ways in which compromised functioning – related to sarcoma and its treatment – and lack of typical experiences interfere with developmental tasks and transitions, thus affecting survivors across time. Figure 1 illustrates linkages – or cascades – among domains of functioning, noting connections which have been supported by data and relations suggested by reviews. Figure 1 also highlights the increased stress and diminished coping skills and resources that may follow from disruptions within each domain.

We propose that survivors endure heightened stress as a result of both the presence of atypical stressors and the absence of typical developmental experiences, and that this stress is exacerbated by a reduced ability to cope. We suggest that both factors contribute to lower quality of life. We further propose that a developmental cascade approach is most suited to guiding research and clinical interventions aimed at documenting, understanding, and bolstering well-being in pediatric sarcoma survivors.

Common Correlates of Sarcoma Survivorship

Physical costs

Pediatric sarcoma treatment often includes a combination of surgeries, chemotherapies, and radiation sessions that – while lifesaving – are taxing, exacting both short- and long-term tolls. Gerrand and Furtado (2017) observed that patients can be left with reduced mobility, which impedes activities of daily life (walking, dressing), reduces participation in developmentally typical activities such as sports or employment, and culminates in a lower health-related quality of life score. On average, sarcoma survivors engage in less activity and reach lower peak exertion levels compared to age/sex matched norms (Mansky et al., 2007). Hamilton and colleagues (Hamilton, Carlson, Hasan, Rassekh, & Goddard, 2017) reported that 77% of their sample of long-term sarcoma survivors (≥5 years) struggled with long-term physical complications. Accordingly, a report from the Childhood Cancer Survivor Study (Gibson et al., 2018), found childhood sarcoma survivors to have the highest cumulative incidence for a number of chronic conditions. Pediatric sarcoma survivors are often left with pain (Gerrand & Furtado, 2017) which is resistant to amelioration (Kuo et al., 2011), chronic health conditions such as heart disease, diabetes, kidney and endocrine-related problems, secondary malignancies (Marina et al., 2017; Weiss & Zimel, 2018), poorer sleep quality (Mulrooney et al., 2008), infertility, and premature menopause (Mansky et al., 2007) – all of which appear to speed the aging process (Baker, Reinke, Boonstra, & Antalis, 2019).

Such health concerns are problematic in their own right. They also serve to isolate the sarcoma survivor from their non-afflicted peers – potentially removing them from playground games, team sports, and physical hobbies (e.g., dance, exercise classes, etc.) that provide rich opportunities for social learning. Even when not physically isolating, the late effects of sarcoma treatment can be psychologically isolating. Sarcoma survivors trying to create a social identity post-treatment may be "damned if they do, damned if they don't" – few peers want to be around someone consumed by health concerns; yet if such concerns are hidden from close others, one experiences a different type of loneliness and isolation (Fantozzi, personal communication, 2019). In other words, loneliness and isolation may result from coping

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mechanisms aimed at protecting the survivor from social rejection rooted in compromised physical functioning and aimed at protecting close others from worry or harm. This particular hypothesis reflects developmental cascade thinking with respect to psychosocial functioning and psychological distress.

Echoing these observations, Maes et al. (2017) revealed links between chronic health conditions and loneliness in children and adolescents. Despite recent findings that social isolation degrades mental and physical health (Leigh-Hunt et al., 2017), this area has been only minimally addressed in the oncology literature. In qualitative interviews with 30 adult survivors of childhood cancer, Howard et al. (2014) found that nearly 2/3 grappled with some form of significant social isolation.

Amputation

Due to the etiology of sarcoma tumors, many patients undergo amputation of the affected extremity. Of cancer patients requiring amputation, Parsons et al. (2012) noted that sarcomas are the most common cancer subtype. Studies examining outcomes associated with amputation versus limb-salvage surgeries show mixed results; investigations of diminished quality of life, material well-being, and relationship satisfaction among amputees versus limb-salvage patients have been inconclusive (Aksnes et al., 2008; Barrera, Teall, Barr, Silva, & Greenberg, 2011; Mason, Mason, Meyers, & Healey, 2013; Robert, Ottaviani, Huh, Palla, & Jaffe, 2010). Although limb-salvage patients score higher than amputee patients in social desirability measures, limb-salvage patients still score lower than non-afflicted peers, suggesting widespread self-esteem issues (Mason et al., 2013).

In addition to a variety of ecological variables that influence post-amputation outcomes (e.g., family support, parent education), the developmental context plays an important role as well. Amputation in a 6-year-old, versus a 16-year-old, will have very different consequences. The limited mobility and changes in physical appearance in the 6-year-old will set the stage for the developing self-concept and peer interactions. In a 16-year-old, amputation may involve a loss of activities, social interactions, and physical competencies on which the teen's self-concept rested. These losses, in turn, may threaten identity and prior peer relationships, with subsequent consequences for mental health and well-being. Thus, the impact of amputation will cascade over time, affecting each child's psychological and social domains in very different ways as a result of the developmental context.

Cancer-related fatigue and reduced physical activity

Cancer-related fatigue (CRF), defined by its impact on one's ability to participate in both mentally taxing and physically demanding sports or academic activities, pervades the pediatric sarcoma community (LaVoy, Fagundes, & Dantzer, 2016). Though not as conspicuous as other physical impairments, CRF can markedly impair functioning during routine chores, recreational activities, social engagements, and vocational demands (Hofman, Ryan, Figueroa-Moseley, Jean-Pierre, & Morrow, 2007). CRF may also exacerbate preexisting conditions such as attention-deficit/hyperactivity disorder (ADHD). Because it permeates all aspects of life, CRF may undermine survivors' ability to concentrate in the classroom, support and sustain peer relationships, and exert effort to achieve typical developmental tasks (e.g., dating, graduating from high school, becoming financially independent). Van Dijk-Lokkart et al. (2019) noted that physical activity reduces CRF. Regrettably, such a coping strategy is less available to survivors with resected limbs, reduced mobility, and pain. CRF demands careful assessment, given its influence on academic, social, and coping processes. However, identifying causes of CRF has proven challenging because they are multifactorial, stemming from the myriad challenges related to survivorship (Tobias & Gillis, 2015).

Reduced physical activity – secondary to pain, mobility issues, CRF, or a combination of all three – can degrade quality of life and well-being by limiting opportunities for peer engagement. Such a reduction compromises social development, as well as the sense of industry, autonomy, and self-confidence that accompany the participation in sports, exercise, and hobbies (Oberle et al., 2019). Furthermore, diminished engagement in sports and exercise deprives survivors of a key strategy for managing stress, mood, and anxiety (Otto & Smits, 2011; Szuhany & Otto, 2019). Thus, in addition to stress generated by reduced physical activity, pain, and CRF, an effective means for coping with such distress is often unavailable to sarcoma survivors.

Again, the developmental context of pediatric sarcoma is highly relevant. As noted, physical impairments associated with sarcoma treatment readily cascade into the peer and psychological domain and do so across time. Harter (2012) showed that the domain of physical appearance is central to children and young adolescents' global self-esteem, and that athletic competence is a key contributor to the developing self-concept. This is important. Disruptions in physical functioning thus cascade into disruptions in psychological and psychosocial functioning, calling into question matters of identity and where one fits in the social milieu.

Investigations into child and adolescent social experiences point to the centrality of self-concept in terms of organizing behavior (Markus & Nurius, 1984), quality of peer relationships (Swann, Chang-Schneider, & Larsen McClarty, 2007) romantic relationships (Chen, Yuan, Yang, & Lai, 2020), and risky behavior (Dudovitz, Li, & Chung, 2013). Recent work also suggests that over middle childhood and adolescence, self-concept becomes a stable individual-difference variable, influencing life trajectories into young adulthood (Putnick, Hahn, Hendricks, & Bornstein, 2020). In sum, changes in physical appearance and/or the loss of typical social learning experiences due to the physical effects of sarcoma and its treatment, have repercussions for the developing self-concept, spilling into psychological and social domains, and doing so into the future. The physical cost of sarcoma treatment extends beyond the physical domain and into the future by altering socialization experiences, shaping the self-concept, self-esteem, and developing beliefs about self-efficacy.

Psychological costs. Pediatric sarcoma survivors are prone to experiencing chronic stress given the uncertainty of physical outcomes and the additive developmental challenges survivors must manage. In a study of long-term sarcoma survivors (averaging 17.4 years post-treatment), over threequarters met criteria for psychological distress (Wiener et al., 2006). Wiener et al. (2006) also found that most respondents noted persistent fear and concern for their health, while a significant minority met criterion for posttraumatic stress disorder (PTSD). Zeltzer et al. (2009) observed that, of the various cancer subtypes in their study of survivors of childhood cancer, sarcoma survivors endorsed more psychological distress than their siblings or comparison population norms. Tang, Castle, and Choong (2015) corroborated these findings of significant psychological sequelae within sarcoma-specific cohorts, finding that the prevalence of depression and anxiety range from 14% to 33% and from 12% to

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47%, depending on the study. Tang et al. further reported that elevated distress among survivors was correlated with poorer physical functions. In a related vein, Kosir and colleagues (Kosir, Wiedemann, Wild, & Bowes, 2019), in their review of psychiatric disorders in adolescent cancer survivors, note that whereas not all survivors struggle with clinically significant distress, a significant proportion do. Those at risk for developing psychiatric disorder included those burdened with greater levels of late effects. As noted, sarcoma patients are likely to encounter numerous late effects, as well as mobility and functional limitations, making them vulnerable to elevated levels of distress. Kosir et al. also raise the issue of subthreshold levels of psychopathology; that is, distress that may be elevated but not sufficiently so to receive a particular diagnosis.

Another psychological burden, particularly for adolescents, is related to struggles concerning identity, self-esteem, understanding oneself in relation to others, and the need to meet developmental milestones while carrying sarcoma-related costs (Zebrack & Zeltzer, 2001). The additional developmental demand to become more autonomous and competent while struggling with late effects of sarcoma and its treatment carries additional stress for the pediatric sarcoma survivor.

Neurocognitive costs. The adverse impact of the sarcoma experience on survivors' physical and psychological well-being is clear. However, the adverse impact on neurocognitive functioning typically is not considered in understanding long-term psychosocial outcomes. Here, we raise the possibility that even subtle neurocognitive changes secondary to life-saving sarcoma treatment also increase stress and erode coping abilities.

There appear to be at least three groups of factors contributing to neurocognitive decrements among sarcoma survivors: neurotoxicity of chemotherapy agents; chronic medical conditions resulting from cancer treatment; and cancer-related fatigue, chronic pain, and mood disorders resulting from treatment. Ikonomidou (2018) reviewed the significant effects of chemotoxicity on neurological structures and functions, noting that chemotherapy may at times result in brain injury or disruption of typical developmental processes such as myelination, neurogenesis, or the formation of neuronal networks. Among effects of chemotherapy, Ikonomidou (2018) noted disruption/decline of neurogenesis in the hippocampus, reduction in white matter volume, and problems with white matter integrity. These changes appear to be related to decrements in cognitive performance. In addition to reductions in IQ, Ikonomidou (2018) highlights evidence of problems with executive functions, memory, and attention. Similarly, Tonning Olsson and colleagues (2020) reported poorer verbal reasoning, mathematics, and long-term memory in adult survivors of childhood soft tissue sarcomas. These researchers also reported links between higher cognitive performance and higher social attainment, further observing that both chemotoxicity and chronic conditions were associated with impaired cognitive functioning.

Others have reported similar links between chronic medical conditions – secondary to chemotherapy – and poorer performance on cognitive tasks. Edelmann et al. (2016) identified lower reading scores, poorer short-term memory, attentional deficits, slower motor processing speed, and poorer cognitive fluency among adult survivors of pediatric osteosarcoma treated with high-dose methotrexate (HDMTX). This is noteworthy because HDMTX is just one drug used to treat osteosarcoma patients; HDMTX is typically administered in combination with doxorubicin, cisplatin, and ifosfamide (Hawkins, Rajendran, Conrad, Bruckner, & Eary, 2002; Miser et al., 1994). Although some sarcoma patients (i.e., those with Ewing Sarcoma Family Tumors) do not receive HDMTX as part of their treatment protocol, they do receive a similar cocktail of medications (Felgenhauer et al., 2000; Grier et al., 1994; Hawkins et al., 2002), all shown to be potentially neurotoxic (Alhowail et al., 2019; Fortin, Mccormick, Remsen, Nixon, & Neuwelt, 2000; Ikonomidou, 2018). Despite the potential harm these agents hold for the developing brain, Edelmann et al. (2016) tie the cognitive deficits of osteosarcoma survivors to the chronic medical conditions caused by cancer treatment, and not to chemotherapy. Regardless of whether the neurocognitive functions above are directly degraded by treatment, or by treatment's subsequent chronic conditions, findings indicate disruption of neurocognitive processes crucial for readily achieving developmental tasks and effectively managing developmental transitions.

The third group of factors contributing to poorer neurocognitive function includes cancer-related fatigue, chronic pain, and mood challenges secondary to treatment. In addition to the toll described earlier, CRF can also affect cognition. Feng et al. (2019) observed that patients with CRF were slower than healthy controls on a task of executive function. Diamond (2013) observes that executive functions are the "canary in the coal mine" of cognitive function – the first of cognitive abilities to suffer in the face of organismic adversity. Moreover, chronic pain and mood challenges such as depression, anxiety, and overall psychological distress – not uncommon among sarcoma survivors – have been shown to degrade cognitive functioning in other populations (Eysenck, Derakshan, Santos, & Calvo, 2007; Matthews, 2016; Mccracken & Iverson, 2001; Moriarty, Mcguire, & Finn, 2011; Paelecke-Habermann, Pohl, & Leplow, 2005; Shields, Moons, Tewell, & Yonelinas, 2016; Van den Berg, Deeg, Lindeboom, & Portrait, 2010).

Again, the developmental context is important for understanding the neurocognitive toll of cancer. Both the cerebellum and the frontal lobes, structures shown to be affected in long-term pediatric sarcoma survivors (Sleurs et al., 2020), undergo significant growth and change from childhood through young adulthood (Moore, D'Mello, McGrath, & Stoodley, 2017; Sowell et al., 1999; Sowell, Trauner, Gamst, & Jernigan, 2002; Tiemeier et al., 2010). Moreover, both structures have been implicated in multiple cognitive functions, including executive functions (Hunter & Sparrow, 2012). Given the developmentally sensitive context of pediatric sarcoma, it seems reasonable to expect that age of neural exposure to chemotoxicity will play an important role in understanding the cognitive correlates of sarcoma survivorship.

Insults to the development and functioning of cognitive – particularly executive – skills (e.g., attention regulation, working memory, cognitive flexibility, inhibitory control) undermine people's ability to manage themselves, academic and work demands, and complex social relationships (Mccracken & Iverson, 2001). In light of the role played by executive functions in emotion- and self-regulation (Liew, 2012), a developmental cascade approach to sarcoma survivorship raises specific hypotheses, such as: survivors burdened by executive dysfunction should – all other relevant variables being held constant – demonstrate smaller social networks, greater difficulties with peers, and higher levels of loneliness than survivors not similarly burdened.

Psychosocial costs. Information is limited regarding the specific psychosocial experiences of sarcoma survivors in adolescence

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and young adulthood. However, we begin to get some idea in looking at work focused on the broader population of young cancer survivors. Quinn, Gonçalves, Sehovic, Bowman, and Reed (2015) report that – compared to the general population – these adolescent and young adult survivors report worse quality of life, with concerns centered on image dissatisfaction, difficulty establishing relationships, and financial worries. Smaller studies of young cancer survivors reveal that among their peers, survivors have a social reputation of being more socially isolated (Noll, Bukowski, Davies, Koontz, & Kulkarni, 1993) and enjoy markedly fewer social activities (Pendley, Dahlquist, & Dreyer, 1997).

We argue that the aggregate and cascading effects of compromised physical functioning, heightened psychological distress, and decrements in neurocognition combine to interfere with the psychosocial experiences of pediatric sarcoma survivors. Storey et al. (2019) discovered that, among survivors, although physical functioning improved over time, psychosocial well-being did not. These researchers point out that whereas literature related to psychosocial functioning is mixed – some investigators report no differences in psychosocial outcomes despite clear differences in health-related quality of life – the preponderance of the data point to an overall reduction in well-being. A developmental cascade approach to pediatric sarcoma survivorship underscores ways in which intrapersonal domains (i.e., physical, psychological, neurocognitive), negatively impacted by sarcoma treatment, may in turn influence psychosocial attainment and subsequent wellbeing.

Stress and Coping

The challenge of moving successfully through development – accomplishing developmental tasks and navigating capably through developmental transitions – is stressful. Managing life effectively in the aftermath of pediatric sarcoma is even more stressful. We propose that the added task of managing effects related to the sarcoma experience, in the face of typical developmental demands, can readily create unhealthy stress levels in survivors. More specifically, we suggest that the presence of atypical burdens (e.g., cancer-related fatigue, post-traumatic stress symptoms, attentional difficulties), and the temporary absence from the typical social milieu as children undergo treatment, undermine coping abilities in survivors. Removal for weeks or months from the typical social milieu – in which, day to day, children build psychosocial competencies – reduces opportunities to learn and practice social skills, conflict resolution, and coping strategies. Put plainly, we argue that survivors face unhealthy levels of stress and have fewer coping resources than their unafflicted peers.

Figure 2(a) depicts how cumulative and atypical levels of stress – emerging from decrements in physical and cognitive functioning, concerns about self-efficacy, cancer-related anxieties, and so on – coupled with the typical stress of growing up, compound over time and exceed available coping strategies and resources. Figure 2(b) provides an example of how negatived developmental cascades might serve to increase stress. In this hypothetical cascade, CRF at the entry to high school subsequently undermines functioning in other domains, degrading well-being over time and increasing stress while reducing opportunities to develop coping resources and practice adaptive coping strategies.

Entry to high school requires adolescents to navigate new and more complex social hierarchies and relationships, manage increased academic expectations, and become more adept at organizing their own time. The stress of these demands can be offset by using adaptive coping strategies such as social support, attention regulation, and exercise. However, a young person burdened with CRF, may not have the energy to join extracurricular groups (a potential source of social support and identity), to regulate attention effectively (to manage academic demands and attend to less anxiety-producing events or stimuli), or to exercise (to reduce the arousal of stress or increase opportunities to form social connections). Opportunities missed and academic demands that are poorly met have consequences for self-concept and stress levels – survivors may encounter more anxiety at the realization that their participation and success in high school is not meeting the standard set by their peers. In other words, CRF may cascade into the neurocognitive and psychosocial domains, undermining competencies and reducing opportunities to develop and practice adaptive coping strategies. Figure 2 (bottom) could easily have additional arrows of influence – for example, reduced working memory might further degrade academic performance leading to avoidance of academic challenges; however, we have limited these for the sake of clarity. What we wish to highlight in Figure 2(b) are the ways in which difficulties in one domain cascade can cascade into others and broaden over time.

We acknowledge that not all pediatric sarcoma survivors will experience CRF. Similarly, not all will experience recurrent pain, reduced mobility, posttraumatic stress, or neurocognitive difficulties. In addition, not all will experience any number of the post-cancer struggles or late-effects that have been described. However, what is key to understanding and supporting survivors' quality of life is for clinicians and researchers to consider carefully the ways in which a decrement in one domain (e.g., physical) may cascade into other domains, particularly at moments of salient developmental transitions or when confronted with typical developmental tasks. These cascades may increase stress and overwhelm – or undermine – the coping resources and strategies available to survivors. Researchers have noted that some survivors engage in passive avoidance or other "maladaptive coping." We raise the possibility that some survivors' coping skills may be simply ill-matched for the task at hand.

In the absence of focused efforts to prevent and relieve the considerable stressors confronting pediatric sarcoma survivors, adolescent and young adult survivors may come to manage as best they can or cannot. Siracuse et al. (2017) noted the increased suicide rate among sarcoma survivors; however, the prevalence and potential role of maladaptive or insufficient coping behaviors in this relation have yet to be thoroughly investigated. Results from a recent study of adult cancer survivors by Hall et al. (2019) found that the physical effects of cancer and fear of recurrence were associated with unhelpful coping behaviors, including substance abuse behaviors and social isolation.

Limitations

Readers should keep in mind the limitations of our proposal while considering our appeal. First, this is not an exhaustive review of the pediatric sarcoma literature. We framed our paper using relevant literature reviews and seminal studies, but it is likely, even certain, that we missed studies and variables at each level of the cascade. Second, we do not address important genetic factors, nor contextual factors (e.g., temperament, socioeconomic status, the parent–child relationship) which undoubtedly play a role in survivor outcomes and likely moderate many of the proposed relations we highlight. Third, and relatedly, the role of ecological and cultural factors that influence patient outcomes are only minimally addressed in this paper. Protective factors and variables that amplify negative effects such as temperament, family

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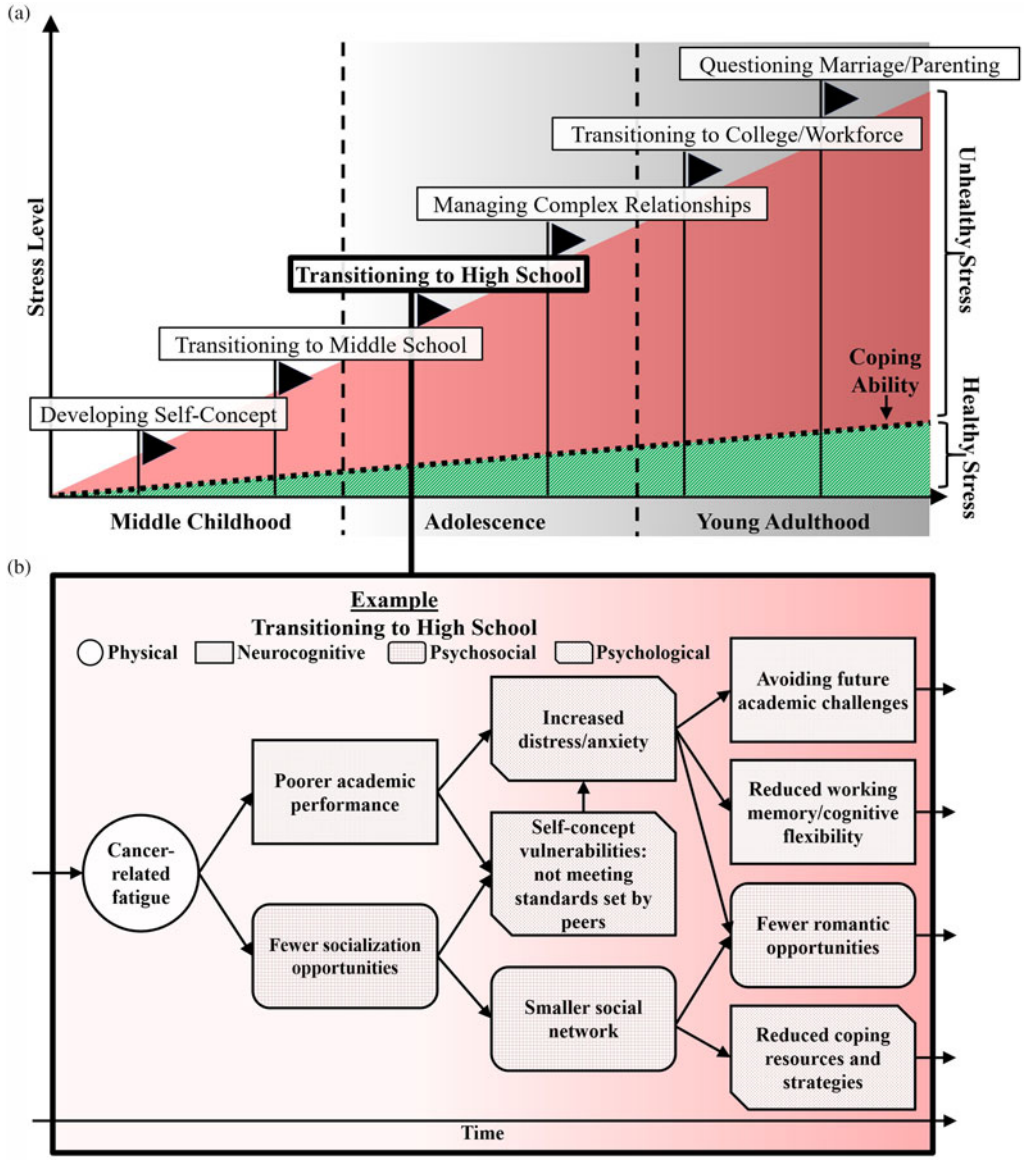

Figure 2. (a) Stress and coping across developmental tasks and transitions – contrasting typical youth versus pediatric sarcoma survivor experience. (b) Possible developmental cascades resulting from cancer-related fatigue (CRF) at the high school transition.

functioning, socioeconomic status, experiences prior to cancer, culture, and the child's macroenvironment should each be examined in future theory building and research. Finally, this application of the developmental cascade model has not been tested. Unlike other developmental cascade models (Dodge et al., 2009; Sitnick, Shaw, & Hyde, 2014), specific tests of a developmental cascades approach with respect to pediatric sarcoma survivorship remain to be conducted. Our intention with this proposal is to highlight the utility of conceptualizing survivorship using a developmental cascades approach to capture transactional and cascading processes we think are at play in influencing survivor outcomes, and to suggest specific moments of focus – that is developmental transitions – for researchers and clinicians.

Conclusion

Although more individuals are surviving pediatric sarcoma, the path towards well-being and competent adulthood remains challenging. Conceptualizing survivorship using a developmental cascades approach highlights particular moments of increased stress and vulnerability. As a general framework, a developmental cascade approach posits that decrements in physical, psychological, neurocognitive and/or psychosocial domains, and the loss of typical day-to-day experiences, interact and function to increase stress and undermine coping resources for survivors, particularly when faced with specific developmental tasks (e.g., the need to graduate high school as part of achieving autonomous adulthood) or specific developmental transitions (e.g., the entry into middle school or high school). These relations lend themselves to specific hypotheses to be tested (e.g., survivors experience more stress during developmental transitions relative to other time points and in comparison to their non-afflicted peers) and suggest that additional support for survivors are needed at specific time points (i.e., developmental transitions). Thus, a developmental cascades approach is useful for both clinicians and researchers, shedding light on the singular outcomes of each survivor and suggesting

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particular moderators and mediators for the relation between a pediatric sarcoma diagnosis and reduced well-being. Historically, routine scans that detect the recurrence of disease and assessments targeting the physical side-effects have been the cornerstone of survivorship care. Careful assessment of survivors' experiences over the last several decades suggest that late effects extend well beyond the physical domain. Adopting a developmental cascades perspective sheds light on the heterogeneity of outcomes for this population. This approach provides a useful framework for clinicians and researchers working to understand and support quality of life and well-being in pediatric sarcoma survivors.

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References

Aksnes, L. H., Bauer, H. C. F., Jebsen, N. L., Follerås, G., Allert, C., Haugen, G. S., & Hall, K. S. (2008). Limb-sparing surgery preserves more function than amputation. *Journal of Bone and Joint Surgery – Series B*, *90*, 786–794. doi:10.1302/0301-620X.90B6.19805

Alhowail, A. H., Bloemer, J., Majrashi, M., Pinky, P. D., Bhattacharya, S., Yongli, Z., … Suppiramaniam, V. (2019). Doxorubicin-induced neurotoxicity is associated with acute alterations in synaptic plasticity, apoptosis, and lipid peroxidation. *Toxicology Mechanisms and Methods*, *29*, 457–466. doi:10.1080/15376516.2019.1600086

Baker, L. H., Reinke, D., Boonstra, P., & Antalis, E. P. (2019). Detection of premature aging among adolescent and young adult osteosarcoma and Ewings sarcoma survivors [abstract]. In: Proceedings of the American Association for Cancer Research Annual Meeting 2019; 2019 Mar 29–Apr 3; Atlanta, GA. Philadelphia (PA): AACR; Cancer Res 2019;79(13 Suppl): Abstract nr 3145.

Barrera, M., Teall, T., Barr, R., Silva, M., & Greenberg, M. (2011). Health related quality of life in adolescent and young adult survivors of lower extremity bone tumors. *Pediatric Blood & Cancer*, *58*, 265–273. doi:10.1002/pbc.23017

Byrd, R. L. (1985). Late effects of treatment of cancer in children. *Pediatric Clinics of North America*, *32*, 835–857. doi:10.1016/S0031-3955(16)34839-8

Cassidy, A. R. (2016) Executive function and psychosocial adjustment in healthy children andadolescents: A latent variable modelling investigation, *Child Neuropsychology*, *22*(3), 292–317. doi:10.1080/09297049.2014.994484

Chen, W. W., Yuan, H., Yang, X., & Lai, S. K. (2020). Parenting, self-concept, and attitudes about romantic relationships. *Journal of Adolescence*, *82*, 41–49.

Connolly, J., Furman, W., & Konarski, R. (2000). The role of peers in the emergence of heterosexual romantic relationships in adolescence. *Child Development*, *71*, 1395–1408.

De La Haye, K., Robins, G., Mohr, P., & Wilson, C. (2011). How physical activity shapes, and is shaped by, adolescent friendships. *Social Science & Medicine*, *73*, 719–728.

Diamond, A. (2013). Executive functions. *Annual Review of Psychology*, *64*, 135–168. doi:10.1146/annurev-psych-113011-143750

Dodge, K. A., Malone, P. S., Lansford, J. E., Miller, S., Pettit, G. S., & Bates, J. E. (2009). A dynamic cascade model of the development of substance-use onset. *Monographs of the Society for Research in Child Development*, *74*, vii–119.

Dudovitz, R. N., Li, N., & Chung, P. J. (2013). Behavioral self-concept as predictor of teen drinking behaviors. *Academic Pediatrics*, *13*, 316–321.

Edelmann, M. N., Daryani, V. M., Bishop, M. W., Liu, W., Brinkman, T. M., Stewart, C. F., … Krull, K. R. (2016). Neurocognitive and patient-reported outcomes in adult survivors of childhood osteosarcoma. *JAMA Oncology*, *2*, 201–208. doi:10.1001/jamaoncol.2015.4398

Elias, M. J., Gara, M., & Ubriaco, M. (1985). Sources of stress and support in children's transition to middle school: An empirical analysis. *Journal of Clinical Child Psychology*, *14*, 112–118.

Erikson, E. H. (1968). *Identity: Youth and crisis* (No. 7). New York: WW Norton & Company.

Eysenck, M. W., Derakshan, N., Santos, R., & Calvo, M. G. (2007). Anxiety and cognitive performance: Attentional control theory. *Emotion*, *7*, 336–353. doi:10.1037/1528-3542.7.2.336

Felgenhauer, J., Hawkins, D., Pendergrass, T., Lindsley, K., Conrad, E. U., & Miser, J. S. (2000). Very intensive, short-term chemotherapy for children and adolescents with metastatic sarcomas. *Medical and Pediatric Oncology*, *34*), doi:10.1002/(SICI)1096-911X(200001)34:1<29::AID-MPO6>3.0.CO;2-7

Feng, L. R., Regan, J., Shrader, J. A., Liwang, J., Ross, A., Kumar, S., & Saligan, L. N. (2019). Cognitive and motor aspects of cancer-related fatigue. *Cancer Medicine*, *8*, 5840–5849. doi:10.1002/cam4.2490

Fortin, D., Mccormick, C. I., Remsen, L. G., Nixon, R., & Neuwelt, E. A. (2000). Unexpected neurotoxicity of etoposide phosphate administered in combination with other chemotherapeutic agents after blood-brain barrier modification to enhance delivery, using propofol for general anesthesia, in a rat model. *Neurosurgery*, *47*, 199–207. doi:10.1097/00006123-200007000-00041

Gerrand, C., & Furtado, S. (2017). Issues of survivorship and rehabilitation in soft tissue sarcoma. *Clinical Oncology*, *29*, 538–545. doi:10.1016/j.clon.2017.04.001

Gibson, T. M., Mostoufi-Moab, S., Stratton, K. L., Leisenring, W. M., Barnea, D., Chow, E. J., … Nathan, P. C. (2018). Temporal patterns in the risk of chronic health conditions in survivors of childhood cancer diagnosed 1970–99: A report from the childhood cancer survivor study cohort. *The Lancet Oncology*, *19*, 1590–1601.

Goldwin, M., Lee, S., Afzal, K., Drossos, T., & Karnik, N. (2014). The relationship between patient and parent posttraumatic stress in pediatric oncology: A theoretical framework. *Children's Health Care*, *43*, 1–15. doi:10.1080/02739615.2014.850855

Grier, H., Krailo, M., Link, M., *et al.* (1994). Improved outcome in non-metastatic Ewing's sarcoma and PNET of bone with the addition of ifosfamide and etoposide to vincristine, Adriamycin, cyclophosphamide, and actinomycin: A children's cancer group and pediatric oncology group report. *Proceedings of American Society of Clin Oncology*, *13*, 421.

Gurney, J. G., Krull, K. R., Kadan-Lottick, N., Nicholson, H. S., Nathan, P. C., Zebrack, B., … Ness, K. K. (2009). Social outcomes in the childhood cancer survivor study cohort. *Journal of Clinical Oncology*, *27*, 2390.

Hall, D. L., Jimenez, R. B., Perez, G. K., Rabin, J., Quain, K., Yeh, G. Y., … Peppercorn, J. M. (2019). Fear of cancer recurrence: A model examination of physical symptoms, emotional distress, and health behavior change. *Journal of Oncology Practice*, *15*, e787–e797.

Hamilton, S. N., Carlson, R., Hasan, H., Rassekh, S. R., & Goddard, K. (2017). Long-term outcomes and complications in pediatric Ewing sarcoma. *American Journal of Clinical Oncology*, *40*, 423–428.

Harter, S. (2012). *The construction of the self: Developmental and sociocultural foundations* (2nd ed.). New York: The Guilford Press.

Hartup, W. W. (1992). Friendships and their developmental significance. In H. McGurk (Ed.), *Childhood social development: Contemporary perspectives* (pp. 175–205). East Sussex, UK: Lawrence Earlbaum.

Hawkins, D. S., Rajendran, J. G., Conrad, E. U., Bruckner, J. D., & Eary, J. F. (2002). Evaluation of chemotherapy response in pediatric bone sarcomas by [F-18]- fluorodeoxy- D-glucose positron emission tomography. *Cancer*, *94*, 3277–3284. doi:10.1002/cncr.10599

Hay, I., & Ashman, A. F. (2003). The development of adolescents' emotional stability and general self-concept: The interplay of parents, peers, and gender. *International Journal of Disability, Development and Education*, *50*, 77–91.

Hofman, M., Ryan, J. L., Figueroa-Moseley, C. D., Jean-Pierre, P., & Morrow, G. R. (2007). Cancer-related fatigue: The scale of the problem. *The Oncologist*, *1*, 4–10. doi:10.1634/theoncologist.12-s1-4

Howard, A. F., Tan de Bibiana, J., Smillie, K., Goddard, K., Pritchard, S., Olson, R., & Kazanjian, A. (2014). Trajectories of social isolation in adult survivors of childhood cancer. *Journal of Cancer Survivorship: Research and Practice*, *8*, 80–93. doi:10.1007/s11764-013-0321-7

Hunter, S. J., & Sparrow, E. P. (2012). *Executive function and dysfunction: Identification, assessment and treatment.* New York: Cambridge University Press.

Ikonomidou, C. (2018). Chemotherapy and the pediatric brain. *Molecular and Cellular Pediatrics*, *5*, 8. doi:10.1186/s40348-018-0087-0

Kosir, U., Wiedemann, M., Wild, J., & Bowes, L. (2019). Psychiatric disorders in adolescent cancer survivors: A systematic review of prevalence and predictors. *Cancer Reports*, *2*, e1168.

Kuo, P. Y., Yen, J. T. C., Parker, G. M., Chapman, S., Kandikattu, S., Sohanpal, I., … Williams, J. E. (2011). The prevalence of pain in patients attending sarcoma outpatient clinics. *Sarcoma*, *2011*, 813283. doi:10.1155/2011/813483

Landolt, M. A., Vollrath, M., Ribi, K., Gnehm, H. E., & Sennhauser, F. H. (2003). Incidence and associations of parental and child posttraumatic stress symptoms in pediatric patients. *Journal of Child Psychology and Psychiatry*, *44*, 1199–1207.

LaVoy, E. C., Fagundes, C. P., & Dantzer, R. (2016). Exercise, inflammation, and fatigue in cancer survivors. *Exercise Immunology Review*, *22*, 82–93. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4755327/

Leigh-Hunt, N., Bagguley, D., Bash, K., Turner, V., Turnbull, S., Valtorta, N., & Caan, W. (2017). An overview of systematic reviews on the public health consequences of social isolation and loneliness. *Public Health*, *152*, 157–171. doi:10.1016/j.puhe.2017.07.035

Liew, J. (2012). Effortful control, executive functions, and education: Bringing self-regulatory and social-emotional competencies to the table. *Child Development Perspectives*, *6*, 105–111.

Lim, S. M., Yoo, C. J., Han, J. W., Cho, Y. J., Kim, S. H., Ahn, J. B., … Kim, H. S. (2015). Incidence and survival of pediatric soft tissue sarcomas: Comparison between adults and children. *Cancer Research and Treatment*, *47*, 9–17. doi:10.4143/crt.2013.157

Maes, M., Noortgate, W. V. D., Fustolo-Gunnink, S. F., Rassart, J., Luyckx, K., & Goossens, L. (2017). Loneliness in children and adolescents with chronic physical conditions: A meta-analysis. *Journal of Pediatric Psychology*, *42*, 622–635. doi:10.1093/jpepsy/jsx046

Mansky, P., Arai, A., Stratton, P., Bernstein, D., Long, L., Reynolds, J., … Mackall, C. (2007). Treatment late effects in long-term survivors of pediatric sarcoma. *Pediatric Blood & Cancer*, *48*, 192–199. doi:10.1002/pbc.20871

Marcia, J. E. (2010). Life transitions and stress in the context of psychosocial development. In T. W. Miller (Ed.), *Handbook of stressful transitions across the lifespan* (pp. 19–34). New York, NY: Springer.

Marina, N. M., Liu, Q., Donaldson, S. S., Sklar, C. A., Armstrong, G. T., Oeffinger, K. C., … Ness, K. K. (2017). Longitudinal follow-up of adult survivors of Ewing sarcoma: A report from the childhood cancer survivor study. *Cancer*, *123*, 2551–2560. doi:10.1002/cncr.30627

Markus, H. J., & Nurius, P. S. (1984). Self-understanding and selfregulation in middle childhood. In W. A. Collins (Ed.), *Development during middle childhood: The years from six to twelve* (pp. 147–183). Washington, DC: National Academy Press.

Mason, G. E., Mason, G. E., Meyers, P. A., & Healey, J. H. (2013). Quality of life following amputation or limb preservation in patients with lower extremity bone sarcoma. *Frontiers in Oncology*, *3*, 210. doi:10.3389/fonc.2013.00210

Masten, A., & Cicchetti, D. (2010). Developmental cascades. *Development and Psychopathology*, *22*, 491–495. doi:10.1017/S0954579410000222

Masten, C. L., Juvonen, J., & Spatzier, A. (2009). Relative importance of parents and peers: Differences in academic and social behaviors at three grade levels spanning late childhood and early adolescence. *The Journal of Early Adolescence*, *29*, 773–799.

Matthews, G. (2016). Distress. In G. Fink (Ed.), *Stress: Concepts, cognition, emotion, and behavior: Handbook of stress series volume 1* (pp. 219–226). San Diego, CA, USA: Elsevier Science.

Mccracken, L. M., & Iverson, G. L. (2001). Predicting complaints of impaired cognitive functioning in patients with chronic pain. *Journal of Pain and Symptom Management*, *21*, 392–396. doi:10.1016/s0885-3924(01)00267-6

McLachlan, K., & Gale, C. R. (2018). The effects of psychological distress and its interaction with socioeconomic position on risk of developing four chronic diseases. *Journal of psychosomatic research*, *109*, 79–85. doi:10.1016/j.jpsychores.2018.04.004

Miser, J., Arndt, C., Smithson, W., Gilchrist, G., Edmonson, J., Sim, F., … Conrad, E. (1994). Treatment of high-grade osteosarcoma (OGS) with ifosfamide (IFOS), MESNA (MES), Adriamycin (ADR), high-dose methotrexate (HDMTX), with or without cisplatin (CDDP); results of two pilot trials [meeting abstract]. *Proceedings of American Society of Clinical Oncology*, *13*, 41.

Moore, D. M., D'Mello, A. M., McGrath, L. M., & Stoodley, C. J. (2017). The developmental relationship between specific cognitive domains and grey matter in the cerebellum. *Developmental Cognitive Neuroscience*, *24*, 1–11.

Moriarty, O., Mcguire, B. E., & Finn, D. P. (2011). The effect of pain on cognitive function: A review of clinical and preclinical research. *Progress in Neurobiology*, *93*, 385–404. doi:10.1016/j.pneurobio.2011.01.002

Mulhern, R. K. (1994). Neuropsychological late effects. In D. J. Bearison, & R. K. Mulhern (Eds.), *Pediatric psychooncology: Psychological perspectives on children with cancer* (pp. 99–121). New York: Oxford University Press.

Mulrooney, D. A., Ness, K. K., Neglia, J. P., Whitton, J. A., Green, D. M., Zeltzer, L. K., … Mertens, A. C. (2008). Fatigue and sleep disturbance in adult survivors of childhood cancer: A report from the childhood cancer survivor study (CCSS). *Sleep*, *31*, 271–281. doi:10.1093/sleep/31.2.271

National Foundation for Cancer Research: Sarcoma. (2019). Retrieved from https://www.nfcr.org/cancer-types/sarcoma/.

Ness, K. K., Gurney, J. G., Zeltzer, L. K., Leisenring, W., Mulrooney, D. A., Nathan, P. C., … Mertens, A. C. (2008). The impact of limitations in physical, executive, and emotional function on health-related quality of life among adult survivors of childhood cancer: A report from the childhood cancer survivor study. *Archives of Physical Medicine and Rehabilitation*, *89*, 128–136. doi:10.1016/j.apmr.2007.08.123

Ness, K. K., Mertens, A. C., Hudson, M. M., Wall, M. M., Leisenring, W. M., Oeffinger, K. C., … Gurney, J. G. (2005). Limitations on physical performance and daily activities among long-term survivors of childhood cancer. *Annals of Internal Medicine*, *143*, 639–647. doi:10.7326/0003-4819-143-9-200511010-00007

Noll, R. B., Bukowski, W. M., Davies, W. H., Koontz, K., & Kulkarni, R. (1993). Adjustment in the peer system of adolescents with cancer: A two-year study. *Journal of Pediatric Psychology*, *18*, 351–364.

Oberle, E., Ji, X. R., Magee, C., Guhn, M., Schonert-Reichl, K. A., & Gadermann, A. M. (2019). Extracurricular activity profiles and wellbeing in middle childhood: A population-level study. *PLoS One*, *14*), doi:10.1371/journal.pone.0218488

Otto, M. W., & Smits, J. A. J. (2011). *Exercise for mood and anxiety: Proven strategies for overcoming depression and enhancing well-being*. New York, NY: Oxford University Press.

Paelecke-Habermann, Y., Pohl, J., & Leplow, B. (2005). Attention and executive functions in remitted major depression patients. *Journal of Affective Disorders*, *89*, 125–135. doi:10.1016/j.jad.2005.09.006

Parsons, C. M., Pimiento, J. M., Cheong, D., Marzban, S. S., Gonzalez, R. J., Johnson, D., … Zager, J. S. (2012). The role of radical amputations for extremity tumors: A single institution experience and review of the literature. *Journal of Surgical Oncology*, *105*, 149–155. doi:10.1002/jso.22067

Patenaude, A. F., & Kupst, M. J. (2005). Psychosocial functioning in pediatric cancer. *Journal of Pediatric Psychology*, *30*, 9–27.

Pendley, J. S., Dahlquist, L. M., & Dreyer, Z. (1997). Body image and psychosocial adjustment in adolescent cancer survivors. *Journal of Pediatric Psychology*, *22*, 29–43.

Putnick, D. L., Hahn, C. S., Hendricks, C., & Bornstein, M. H. (2020). Developmental stability of scholastic, social, athletic, and physical appearance self-concepts from preschool to early adulthood. *Journal of Child Psychology and Psychiatry*, *61*, 95–103.

Quesada, A. A., Wiemers, U. S., Schoofs, D., & Wolf, O. T. (2012). Psychosocial stress exposure impairs memory retrieval in children. *Psychoneuroendocrinology*, *37*, 125–136. doi:10.1016/j.psyneuen.2011.05.013

Quinn, G. P., Gonçalves, V., Sehovic, I., Bowman, M. L., & Reed, D. R. (2015). Quality of life in adolescent and young adult cancer patients: A systematic review of the literature. *Patient Related Outcome Measures*, *6*, 19.

Robert, R. S., Ottaviani, G., Huh, W. W., Palla, S., & Jaffe, N. (2010). Psychosocial and functional outcomes in long-term survivors of osteosarcoma: A comparison of limb- salvage surgery and amputation. *Pediatric Blood & Cancer*, *54*), doi:10.1002/pbc.22419

Roisman, G. I., Masten, A. S., Coatsworth, J. D., & Tellegen, A. (2004). Salient and emerging developmental tasks in the transition to adulthood. *Child Development*, *75*, 123–133. doi:10.1111/j.1467-8624.2004.00658.x

Schultz, K. A., Ness, K. K., Whitton, J., Recklitis, C., Zebrack, B., Robison, L. L., Zeltzer, L., & Mertens, A. C. (2007). Behavioral and social outcomes in adolescent survivors of childhood cancer: a report from the childhood cancer survivor study. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, *25*(24), 3649–3656. doi:10.1200/JCO.2006.09.2486

Schulenberg, J. E., Bryant, A. L., & O'Malley, P. M. (2004). Taking hold of some kind of life: How developmental tasks relate to trajectories of well-being during the transition to adulthood. *Development and Psychopathology*, *16*, 1119–1140. doi:10.1017/s0954579404040167

Schwarzer, R. (2008) Modeling Health Behavior Change: How to Predict and Modify the Adoption and Maintenance of Health Behaviors. *Applied Psychology: An International Review*, *57*, 1–29. doi:10.1111/j.1464-0597.2007.00325.x

Shields, G. S., Moons, W. G., Tewell, C. A., & Yonelinas, A. P. (2016). The effect of negative affect on cognition: Anxiety, not anger, impairs executive function. *Emotion*, *16*, 792–797. doi:10.1037/emo0000151

Siracuse, B., Gorgy, G., Ruskin, J., & Beebe, K. (2017). What is the incidence of suicide in patients with bone and soft tissue cancer? *Clinical Orthopaedics and Related Research*, *475*, 1439–1445. doi:10.1007/s11999-016-5171-y

Sitnick, S., Shaw, D. S., & Hyde, L. (2014). Precursors of adolescent substance use from early childhood and early adolescence: Testing a developmental cascade model. *Development and Psychopathology*, *26*, 125–140. doi:10.1017/S0954579413000539

Sleurs, C., Blommaert, J., Batalle, D., Verly, M., Sunaert, S., Peeters, R., … Deprez, S. (2020). Cortical thinning and altered functional brain coherence in survivors of childhood sarcoma. *Brain Imaging and Behavior*, doi:10.1007/s11682-020-00276-9

Sowell, E. R., Thompson, P. M., Holmes, C. J., Batth, R., Jernigan, T. L., & Toga, A. W. (1999). Localizing age-related changes in brain structure between childhood and adolescence using statistical parametric mapping. *Neuroimage*, *9*, 587–597.

Sowell, E. R., Trauner, D. A., Gamst, A., & Jernigan, T. L. (2002). Development of cortical and subcortical brain structures in childhood and adolescence: A structural MRI study. *Developmental Medicine & Child Neurology*, *44*, 4–16.

Storey, L., Fern, L. A., Martins, A., Wells, M., Bennister, L., Gerrand, C., … Taylor, R. M. (2019). A critical review of the impact of sarcoma on psychosocial wellbeing. *Sarcoma*, *2019*, 1–18. doi:10.1155/2019/9730867

Swann, W. B. Jr, Chang-Schneider, C., & Larsen McClarty, K. (2007). Do people's self-views matter? Self-concept and self-esteem in everyday life. *American Psychologist*, *62*, 84.

Szuhany, K. L., & Otto, M. W. (2019). Efficacy evaluation of exercise as an augmentation strategy to brief behavioral activation treatment for depression: A randomized pilot trial. *Cognitive Behaviour Therapy*, *49*, 228–241. doi:10.1080/16506073.2019.1641145

Tang, M. H., Castle, D. J., & Choong, P. F. M. (2015). Identifying the prevalence, trajectory, and determinants of psychological distress in extremity sarcoma. *Sarcoma*, *2015*, 745163. doi:10.1155/2015/745163

Tiemeier, H., Lenroot, R. K., Greenstein, D. K., Tran, L., Pierson, R., & Giedd, J. N. (2010). Cerebellum development during childhood and adolescence: A longitudinal morphometric MRI study. *Neuroimage*, *49*, 63–70.

Tobias, K., & Gillis, T. (2015). Rehabilitation of the sarcoma patient-enhancing the recovery and functioning of patients undergoing management for extremity soft tissue sarcomas. *Journal of Surgical Oncology*, *111*, 615–621. doi:10.1002/jso.23830

Tonning Olsson, I., Brinkman, T. M., Wang, M., Ehrhardt, M. J., Banerjee, P., Mulrooney, D. A., Huang, I. C., Ness, K. K., Bishop, M. W., Srivastava, D., Robison, L. L., Hudson, M. M., & Krull, K. R. (2020). Neurocognitive and psychosocial outcomes in adult survivors of childhood soft-tissue sarcoma: A report from the St. Jude Lifetime Cohort. *Cancer*, *126*(7), 1576–1584. doi:10.1002/cncr.32694

Van den Berg, G. J., Deeg, D. J. H., Lindeboom, M., & Portrait, F. (2010). The role of early-life conditions in the cognitive decline due to adverse events later in life. *The Economic Journal*, *120*, 411–428. doi:10.1111/j.1468-0297.2010.02396.x

Van Dijk-Lokkart, E. M., Steur, L., Braam, K. I., Veening, M. A., Huisman, J., Takken, T., … Van Litsenburg, R. (2019). Longitudinal development of cancer-related fatigue and physical activity in childhood cancer patients. *Pediatric Blood & Cancer*, *66*, e27949. doi:10.1002/pbc.27949

Weber, K., Damron, T. A., Frassica, F. J., & Sim, F. H. (2008). Malignant bone tumors. *Instructional Course Lectures*, *57*, 673–688.

Weiss, K., & Zimel, M. (2018). Considerations for the long term treatment of pediatric sarcoma survivors. *Indian Journal of Orthopaedics*, *52*, 77–80. doi:10.4103/ortho.ijortho_248_17

Wiener, L., Battles, H., Bernstein, D., Long, L., Derdak, J., Mackall, C. L., & Mansky, P. J. (2006). Persistent psychological distress in long-term survivors of pediatric sarcoma: The experience at a single institution. *Psycho-Oncology*, *15*, 898–910. doi:10.1002/pon.1024

Yeh, J. M., Nekhlyudov, L., Goldie, S. J., Mertens, A. C., & Diller, L. (2010). A model-based estimate of cumulative excess mortality in survivors of childhood cancer. *Annals of Internal Medicine*, *152*, 409–417.

Yeh, J. M., Ward, Z. J., Chaudhry, A., Liu, Q., Yasui, Y., Armstrong, G. T., … Leisenring, W. M. (2020). Life expectancy of adult survivors of childhood cancer over 3 decades. *JAMA Oncology*, *6*, 350–357.

Zebrack, B., Santacroce, S. J., Patterson, P., & Gubin, A. (2016). Adolescents and young adults with cancer: A biopsychosocial approach. In A. N. Abrams, A. C. Muriel, & L. Wiener (Eds.), *Pediatric psychosocial oncology: Textbook for multidisciplinary care* (pp. 199–217). Cham: Springer.

Zebrack, B. J., & Zeltzer, L. K. (2001). Living beyond the sword of Damocles: Surviving childhood cancer. *Expert Review of Anticancer Therapy*, *1*, 163–164. doi:10.1586/14737140.1.2.163

Zeltzer, L. K., Recklitis, C., Buchbinder, D., Zebrack, B., Casillas, J., Tsao, J. C., … Krull, K. (2009). Psychological status in childhood cancer survivors: A report from the childhood cancer survivor study. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology*, *27*, 2396–2404. doi:10.1200/JCO.2008.21.1433