EXPLORING THE INTERPLAY OF SOCIAL DETERMINANTS OF HEALTH, PSYCHOLOGICAL DISTRESS, CANCER-RELATED WORRY, AND PHYSICAL ACTIVITY IN PREDICTING PAIN AMONG SURVIVORS OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA: INSIGHTS FROM THE ST. JUDE COHORT DATASET

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ABSTRACT

Background: Acute lymphoblastic leukemia (ALL) is diagnosed more often in children than any other form of cancer. Survivors of ALL often face long-term effects such as chronic pain, psychological distress, and cancer-related worry (CRW). While treatment-related effects are well documented, far less is known about how Social Determinants of Health (SDoH) shape pain outcomes in this population. Adverse SDoH may contribute to increased pain, and these effects may be further intensified by psychological distress, including CRW. Physical activity is widely recognized for its potential to promote health and resilience, often helping to offset the influence of social and psychological challenges on physical symptoms like pain. Given these factors, the current study investigated how SDoH, psychological distress, CRW, and physical activity together predict pain among pediatric ALL survivors.

Methods: The study utilized cross-sectional data from the St. Jude LIFE study and included 1,433 survivors of pediatric ALL. Structural equation modeling (SEM) was employed to test five hypotheses involving mediation and moderation pathways between the variables of interest.

Results: The moderated mediation model showed good convergence. Greater adverse SDoH were associated with a lower likelihood of reporting pain (β = −0.104, 95% CI [−0.135, −0.074]). Physical activity significantly moderated this relationship (β = 0.044, 95% CI [0.026, 0.061]), weakening the inverse association among those with higher activity levels. Similarly, more adverse SDoH predicted a lower likelihood of psychological distress (β = −0.100, 95% CI [−0.163, −0.036]) and CRW; β = −0.093, 95% CI [−0.147, −0.039]). Psychological distress and CRW interacted to increase pain likelihood (β = 1.369, 95% CI [1.179, 1.551]). Physical activity moderated these effects by amplifying the distress–pain link (β = 0.035, 95% CI [0.004, 0.068]) and buffering the CRW–pain link (β = −0.203, 95% CI [−0.242, −0.164]). A three-way interaction showed physical activity reduced the compounded effect of co-occurring CRW and distress on pain (β = −0.248, 95% CI [−0.282, −0.216]). Significant moderated indirect effects through psychological distress (β = −0.011) and CRW (β = 0.010) were also found.

Conclusion: This study elucidates how adverse SDoH, psychological distress, CRW, and physical activity interact to influence pain experiences in survivors of pediatric ALL. Contrary to expectations, survivors facing greater social adversity reported less pain, psychological distress, and CRW, suggesting potential resilience or alternative coping strategies within this group. Importantly, psychological distress and CRW jointly amplified pain, highlighting the substantial burden of co-occurring psychological symptoms. Physical activity played a nuanced role, sometimes intensifying the distress–pain link but buffering the impact of CRW on pain, and reducing the combined effect of distress and CRW on pain. These findings underscore the necessity for pain management interventions that move beyond biological treatment alone.

Exploring the Interplay of Social Determinants of Health, Psychological Distress, Cancer-Related Worry, and Physical Activity in Predicting Pain Among Pediatric Acute Lymphoblastic Leukemia Survivors: Insights from the St. Jude LIFE Cohort Dataset

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CHAPTER 1: INTRODUCTION

Acute lymphoblastic leukemia (ALL) is diagnosed more often in children than any other form of cancer. Advancements in care have led to major improvements in survival, with approximately 85% of children expected to survive five or more years (American Cancer Society, 2024). Despite these medical successes, survivors continue to face long-term effects such as persistent pain, fatigue, decreased physical function, as well as anxiety and depression symptoms (Shaulov et al., 2018; Van Asselt et al., 2024). Survivors also frequently encounter challenges related to cognitive and behavioral change, such as inattention and learning difficulties (Liu et al., 2018). These effects significantly impact academic performance and how they interact socially.

In addition to these challenges, the environments in which survivors live shape long term health outcomes. Adverse SDoH, including factors like socioeconomic disadvantage, reduced access to reliable healthcare, limited educational opportunities, and fewer available social support systems, can compound the detrimental effects of cancer. Studies have shown that survivors from lower socioeconomic backgrounds, particularly those covered by Medicaid or uninsured, experience poorer survival outcomes than children who have private insurance (Fine et al., 2023; Bona et al., 2016). Geographic location is another important factor, as children from rural communities or areas with economic disadvantage may face barriers to accessing specialized care, which can lead to less effective treatment and a decline in overall quality of life (Tran et al., 2022; Larson et al., 2020). Moreover, educational attainment servers as an important indicator of long-term health outcomes, as individuals with more education often report better physical and emotional well-being, including improved coping abilities and better access to needed healthcare services (Kimbro et al., 2008; Walsemann et al., 2013).

Beyond the physical and medical aspects, mental health concerns, such as CRW, are a significant issue for survivors. Many survivors experience ongoing fear related to potential recurrence, ongoing effects that appear after treatment has ended, and worries about their long term health and well-being (Wang et al., 2015; Ware et al., 2023). Additionally, the emotional distress associated with cancer survivorship is compounded by challenges related to chronic pain, which can interfere with daily activities, thereby hindering recovery and resulting in a decline in overall quality of life (Coluzzi et al., 2020). Studies indicate that survivors who participate in regular physical activity often demonstrate better emotional health and improved physical functioning, including lower rates of depression, less fatigue, and better cognitive function (Tonorezos et al., 2019; Coombs et al., 2020). However, pain, fatigue, and limited mobility often hinder physical activity, underscoring the need for effective pain management strategies (Cox et al., 2009).

Survivors of pediatric ALL face a range of complex challenges extending beyond the immediate physical effects of treatment. Issues such as chronic pain, CRW, and the lasting emotional burden of childhood cancer can meaningfully affect survivors' quality of life. In addition, factors such as physical activity levels, social support, and socioeconomic status further contribute to overall health and well-being. To better understand these diverse influences, conducting research and reviewing the existing research body is essential.

CHAPTER 2: LITERATURE REVIEW

Social Determinants of Health and Inequities

SDoH describes the social and environmental conditions into which people are born, reared, and live, all of which ultimately influence health outcomes (World Health Organization: WHO, 2019). Health inequalities occur when these systems are distributed inequitably, resulting in unequal access to resources (e.g., healthcare, nutritious food, safe housing). Among the various SDoH, Socioeconomic Status (SES) plays an important role in health outcomes. SES includes factors such as income, education attainment, job standing, and how individuals perceive their own social position, which reflect an individual's opportunities and overall life quality (Socioeconomic Status, n.d.). Additionally, lower SES resources can restrict a person's ability to access quality healthcare or adopt healthier lifestyle behaviors. In addition to SES, access to quality education includes not only formal schooling but also skills such as literacy and language proficiency, which are essential for individuals to engage with and benefit fully from educational opportunities (Education Access and Quality | Prepare Your Health | *CDC*, 2023). Education also shapes health literacy and influences how effectively individuals can navigate the healthcare system. Another key domain of SDoH is access to healthcare, which refers to how easily individuals can obtain necessary medical services, with various social, economic, cultural, and geographic factors influencing this access (Health Care Access, n.d.). Access to healthcare ensures an early diagnosis and timely treatment. Beyond institutional systems, interpersonal factors such as social support networks serve an important role in shaping well-being. Social support consists of the help or comfort provided by individuals within one's social network, such as family, friends, colleagues, or community groups, to support individuals in managing physical, psychological, and social difficulties (APA Dictionary of Psychology, n.d.). The

presence or absence of social support networks can also greatly influence coping mechanisms and well-being. Lastly, aspects of the neighborhood and built environment including the quality of housing, availability of transportation, and levels of crime or community violence, play a significant role in influencing residents' overall health and well-being. (Neighborhood and Built Environment | Prepare Your Health | CDC, n.d.). Where individuals live can affect their overall safety, as it may lead to environmental hazards and influence the availability of healthy food options. Together, these structural and social conditions interact in multiple ways to shape health and perpetuate health inequities.

Notably, SDoH are not equitably distributed across the population. Specifically, individuals who are racial and/or ethnic minorities often face disproportionately lower access to resources, resulting in intensified health inequities. For example, research suggests that racial minorities are at risk of lower cancer survival rates. From 2000 to 2003, the 10-year survival rate for Hispanic children with ALL were 79.1% (95% CI, 74.9%-82.7%), compared to 90.9% (95% CI, 88.2%-93.0%) for non-Hispanic white children (Kahn et al., 2016). This disparity in survival rates may be influenced by several contributing factors, including SDoH, that impact both access to care and the ability to adhere to treatment protocols.

Medication adherence is a particularly well-researched area at the intersection of pediatric cancer and SDoH. Medication adherence is especially critical in the context of cancer care, where adherence to prescribed treatments can directly influence the effectiveness of therapy and overall patient outcomes. Specifically, poor adherence to oral 6-mercaptopurine (6-MP) has been associated with a higher likelihood of relapse. For example, patients who receive fewer than 85 percent of prescribed 6-MP doses face a relapse risk almost six times higher than those with higher adherence rates (Bhatia et al., 2012). Notably, approximately 20% of pediatric ALL

patients fail to adhere to at least one in every ten prescribed 6-MP, underscoring the magnitude of adherence challenges in this population (Bhatia et al., 2014). Furthermore, adverse social determinants such as housing instability (aOR = 0.64; 95% CI 0.44–0.93), food insecurity (aOR = 0.56; 95% CI 0.42–0.7), and social determinants overall (aOR = 0.75; 95% CI 0.65–0.88) have been found to meaningfully influence medication adherence among individuals with chronic health conditions (Wilder et al., 2021). This gap in adherence as a function of SDoH may contribute significantly to the observed disparities in survival rates. However, a comprehensive understanding of health inequalities in pediatric cancer requires a thorough examination of the five key SDoH and how each contributes to health inequities.

Health Care Access and Quality

Access to reliable and high-quality healthcare is essential for good health. The accessibility to healthcare can be affected by geographic location, income level, and health insurance status. Individuals in underserved areas or with lower incomes often encounter challenges in obtaining timely and effective medical care; this can result in significant consequences, especially in the context of pediatric oncology. Research has shown that children with Medicaid insurance have worse survival outcomes compared to their privately insured peers (Fine et al., 2023). Medicaid patients had a 23.3% lower 5-year recurrence-free rate and a 16.5% lower 5-year overall survival rate than those with private insurance. Despite receiving similar treatment modalities in terms of radiation and chemotherapy, these patients had lower survival rates, indicating that factors beyond the hospital's setting may contribute to poorer outcomes. Furthermore, delayed diagnosis, potentially due to insufficient access to primary care or preventative screenings, could lead to later-stage cancer diagnoses, which can be more challenging to treat.

Education Access and Quality

Educational access and quality are important predictors of health outcomes. Research has shown that individuals who receive higher education typically have better job opportunities, higher incomes, and increased access to healthcare. A meta-analysis found that pediatric cancer survivors had a notably lower likelihood of graduating from high school (OR = 0.74, 95% CI [0.60, 0.92]) and university (OR = 0.74, 95% CI [0.58, 0.94]) compared to their peers without a cancer history. However, this was not true for all cancer types. Children who survived central nervous system (CNS) cancers showed marked educational disadvantages, including a substantially reduced likelihood of finishing high school (OR = 0.34, 95% CI [0.25, 0.47]) and university graduation (OR = 0.50, 95% CI [0.41, 0.62]) compared to controls. In contrast, survivors of non-CNS cancers did not show significant differences in graduation rates. This analysis also explored the impact of age at diagnosis, revealing that survivors diagnosed before 10 years of age were less likely to graduate from high school (OR = 0.73, 95% CI [0.59, 0.89]). However, no significant effect was found for university graduation (OR = 0.78, 95% CI [0.46, 1.34]). Notably, research on educational attainment in pediatric cancer survivors is limited, partly due to traditional metrics, such as high school and university rates of completing school, which are inherently age dependent. Since these outcomes are often measured at specific ages, they may not accurately reflect the long-term academic pathways of younger survivors or those who experience delayed educational milestones due to their illness. These educational inequities are shaped by individual attainment and structural factors, such as the unequal distribution of educational resources and systemic barriers within educational systems.

Neighborhood and Built Environment

The neighborhood and built environment are essential factors that influence health. These determinants include aspects such as housing quality, access to recreational spaces, and exposure to environmental hazards. For example, children living in neighborhoods with fewer amenities (e.g., parks or recreational facilities) are more likely to face health concerns including obesity, which is a risk factor for developing health conditions like cancer (Engemann et al., 2019). Furthermore, children living in neighborhoods with abundant green spaces have been shown to have a reduced likelihood of mental health diagnoses later in life (Engemann et al., 2019). Conversely, the lack of such spaces contributes to experiences of stress, depression symptoms, and anxiety. Environmental hazards like air pollution also significantly affect children's health. Previous research has shown that roughly one in five children in the United States live in areas with unsafe levels of air pollution, contributing to higher rates of asthma and other respiratory issues (Anenberg et al., 2022). Moreover, children in rural areas face unique challenges that impact a child's overall health. Nearly 20% of U.S. children live in rural communities, where 1 in 3 rural counties lack a pediatrician (Larson et al., 2020). These children have an elevated risk of obesity, injuries, and infant mortality. This may be partially due to the community's design of high vehicular speed, fewer walking destinations, and reduced access to grocery stores. For instance, between 1990 and 2015, the proportion of counties with fewer than eight grocery stores per 10,000 residents rose from 11 percent to 27 percent, which limits access to healthy food and contributes to higher obesity rates (Stevens et al., 2021).

Additionally, exposure to chemicals such as pesticides poses another environmental hazard, particularly for children in rural areas. In 2018, 35,000 children aged five and under were reported to have been exposed to toxic pesticides, making up 4% of all toxic ingestions in young

children that year (Gummin et al., 2019). Importantly, these environmental disadvantages extend beyond general health outcomes to affect access to critical survivorship care. Recent research reveals that rural pediatric cancer survivors were significantly more likely to not initiate or discontinue follow-up survivorship care compared to their urban counterparts (Strange et al., 2025). Specifically, rural survivors living 25 miles from a clinic nearly doubled the odds of not continuing care compared to urban-near survivors. However, neighborhood-level SDoH may not fully explain disparities in all contexts. An investigation of childhood cancer survivors treated at two urban hospitals found no significant associations between neighborhood-level SDoH and care received over longer-term follow-up periods. Instead, follow-up was instead more strongly associated with individual-level factors, such as age at diagnosis, race/ethnicity, and cancer type (Suntum et al., 2025). For instance, non-Hispanic Black survivors and those diagnosed in adolescence were less likely to attend follow-up care. Survivors of CNS cancers had the lowest survivorship clinic attendance despite high rates of other ambulatory care. These findings suggest that while neighborhood-level disadvantage is important in rural environments, it may not capture the full range of barriers in urban populations. Understanding how neighborhood and environmental conditions influence child health outcomes is essential for shaping future research and policy efforts aimed at reducing these disparities.

Social and Community Context

The social and community context significantly influences individuals' health. This includes elements such as social networks and community support. Tran et al. (2022) highlighted a significant gap in research, noting that no studies have specifically examined social and community contexts concerning pediatric cancer survivorship. However, strong social connections and active community involvement have been shown to enhance mental health,

provide emotional support, and enhance overall quality of life. Research has indicated that family and peer support significantly predict higher physical activity engagement among pediatric cancer survivors. For instance, research by Gilliam et al. (2011) reported that support from family members ($p = 0.004$) and support from peers ($p = 0.013$) were important indicators of higher physical activity levels. Conversely, social isolation, lack of support networks, and experiences of discrimination can increase stress levels and contribute to poorer health outcomes. Experiencing social isolation and loneliness have been linked with a 43 percent increase in mortality for those in the highest loneliness group (95% CI [1.17, 1.76]) and a 74% higher risk for those in the highest isolation group (95% CI [1.25, 2.42]) (Hong et al., 2023). Additionally, loneliness was linked to a 25 percent greater chance of developing lung disease (95% CI [1.04, 1.51]) and chronic pain (13% higher risk, 95% CI [1.02, 1.25]), while social isolation was linked to a 30 percent increased probability of experiencing stroke (95% CI [1.01, 1.67]) and a 22% increased likelihood of cognitive impairment (95% CI [1.02, 1.46]). This is important in the context of cancer because nearly half (49.7%) of adolescent cancer survivors report at least one instance of peer exclusion at school (Kim et al., 2018). Given how essential social support is for overall health and the frequent occurrence of peer exclusion among pediatric cancer survivors, further research on the role of social and community contexts in their well-being is essential.

Economic Stability

Financial barriers also contribute to these disparities. Tran et al. (2022) carried out a systematic review between 2009 and 2021 to explore the relationship between SES and survival rates in pediatric cancer. The findings indicate that patients from areas with the highest levels of poverty face a substantially elevated risk of mortality. The review also highlighted that geography, including rural versus urban settings, did not affect survival. Furthermore, research

on ALL patients has shown that children living in high-poverty communities have a 5-year overall survival rate of about 85%, whereas those from low-poverty communities have a rate closer to 92% (Bona et al., 2016). Moreover, 92% of relapses in high-poverty children occurred within 36 months of achieving complete remission, compared to 48% in low-poverty children ($p = 0.008$). The study suggests that the earlier relapse in high-poverty children may explain the observed poorer survival outcomes. No significant differences in treatment-related mortality were detected. These results underscore the importance of continued research on how socioeconomic factors influence health outcomes.

Pediatric Cancer Survivorship

Prevalence and Survival of Pediatric Cancer

In 2024, about 9,620 U.S. children younger than 15 years old received a cancer diagnosis. Over the last five decades, advances in pediatric cancer treatments have led to substantial gains in overall survival. Approximately 85% of children diagnosed with cancer are expected to live five years or longer, whereas in the mid-1970s when the five-year survival rate stood at 58% (American Cancer Society, 2024). With advancements in the efficacy of cancer treatments, the total population of pediatric cancer survivors has grown. There are approximately 495,739 survivors of childhood cancer residing in the United States, spanning ages 0 to 19 years old at the time of diagnosis (National Childhood Cancer Registry Explorer, 2020).

Psychosocial Impact of Pediatric Cancer

The psychosocial impact of pediatric oncology on children and their families is both complex and far-reaching. For children, being diagnosed with cancer and going through treatment introduces a variety of stressors that can influence their mental health. The disruption of typical childhood activities and social interactions due to frequent hospital visits and

treatment-related side effects can lead to symptoms of anxiety and depression (Nadel, 2021). The side effects of treatment, including fatigue and physical limitations, may also heighten psychological distress (Kennard et al., 2004; Nathan et al., 2009; Walsh et al., 2024). The psychosocial challenges faced by children are particularly pronounced in the case of ALL, where the intensity and duration of treatment can exacerbate emotional and social stressors.

Acute Lymphoblastic Leukemia

Prevalence

In 2024, it is anticipated that around 6,550 individuals received a diagnosis of ALL (American Cancer Society, 2024). Within these cases, an estimated 1,330 deaths occurred. Most new diagnoses occur in children younger than five years old. While its prevalence slowly decreases through the mid-twenties, it starts to increase again after age 50. ALL is classified as a rare cancer, making up under 0.5% of all cancer diagnoses in the United States. An individual's lifetime likelihood of developing ALL is roughly 1 in 1,000. Risk factors show slight variations, being slightly more common in males than in females, and more prevalent in White individuals compared to African Americans (American Cancer Society, 2024). Despite the higher incidence in children, most deaths occur in adults. Despite its rarity, the psychosocial aspects of ALL are critical to explore. As the population of survivors increases, there is a need for psychological support, coping mechanisms, and resources designed to enhance long-term well-being and quality of life following a life-threatening diagnosis in childhood and an intensive treatment course.

Etiology

The etiology of ALL remains unknown, prompting ongoing research to uncover its causative factors (Tebbi, 2021). Environmental influences have been identified as potential

contributors, including exposure to ionizing radiation, benzene, or earlier chemotherapy or radiation treatment. Genomic studies further point to somatic polymorphic variants in genes like ARD5B, IKZF1, and CDKN2A as associated with an elevated risk of ALL. In rare instances, germline mutations, particularly in PAX5, ETV6, and p53, can also predispose individuals to leukemia development. Importantly, ALL is generally not considered a familial disease, and no routine screening programs are recommended for childhood testing (Puckett & Chan, 2023).

Symptom Presentation

The clinical presentation of ALL varies widely, encompassing a spectrum of symptoms that can meaningfully affect patients' quality of life (American Cancer Society, 2024). Symptoms frequently arise from a low number of healthy blood cells. These can include fatigue, weakness, dizziness, breathing difficulties, and pale skin resulting from insufficient red blood cells. A reduced white blood cell count can manifest as recurrent or persistent infections. Additionally, insufficient platelets may lead to a tendency to bruise and bleed easily**,** such as recurring nosebleeds or gum bleeding, or heavy menstruation. Patients with ALL may also experience symptoms like unexplained weight loss, fever, night sweats, or decreased appetite. Additionally, the accumulation of leukemia cells in the liver and spleen can lead to abdominal swelling, appearing as increased fullness or discomfort, leading individuals to feel satiated after consuming only small amounts of food.

Assessment and Treatment Approaches

Diagnosing ALL involves a series of specialized tests, including blood tests, bone marrow evaluations, diagnostic imaging, and spinal fluid analysis ("What Is Acute Lymphocytic Leukemia (ALL)?," 2018). Blood tests are crucial for evaluating white and red blood cell counts, platelet levels, and identifying the detection of blast cells, which are undeveloped cells typically

found only in bone marrow. During a bone marrow evaluation, a sample of bone marrow is removed from the hipbone or breastbone. Once doctors receive the sample, they look for leukemia cells and sort the blood cells into categories according to their size, shape, and molecular characteristics. Image testing, such as computerized tomography (CT) scans, ultrasound scans, and X-rays, can assist in identifying the extent of cancer spread. Lastly, a lumbar puncture, commonly referred to as a spinal tap, may be used to assess whether cancer cells have entered the spinal fluid.

Treatment for ALL typically progresses through three distinct phases (Acute lymphocytic leukemia - Diagnosis and treatment - Mayo Clinic, 2022). The initial phase, induction therapy, aims to eliminate the majority of leukemia cells within the bloodstream and bone marrow and reestablish normal blood production. This is followed by consolidation therapy, often referred to as post-remission treatment, designed to eradicate any remaining leukemia cells remaining in the body. The final phase, maintenance treatment, works to inhibit the return of leukemia cells. During this stage, treatment is usually given in smaller doses over multiple years. Additionally, a preventative treatment specifically targeting the central nervous system (CNS) may be provided during any of the three phases. This involves injecting chemotherapy directly into the spinal cord fluid to eliminate leukemia cells that may have spread to the CNS.

Pain in Acute Lymphoblastic Leukemia

Among pediatric ALL patients, many factors influence pain, such as experiencing emotional distress, fear of the future, and increased CRW. Research indicated that 49.2% of ALL patients reported pain, with 35.3% experiencing severe or very severe pain (Shaulov et al., 2018). Pain was strongly correlated with psychological symptoms like sleep difficulties, worrying, and irritability. Additionally, factors that influence pain include being at a young age,

poor functional status, and a longer duration since chemotherapy (with pain peaking around 4-5 weeks after treatment). The most common pain sites were the oropharynx (40%), head (21.8%), and abdomen (20%). Despite the high pain burden, less than 1% of patients were referred to palliative care. Furthermore, these findings are supported by Coluzzi et al. (2020), who found that 48% of children undergoing therapy reported pain, leading to decreased health-related quality of life (HRQoL). Pain often occurs along with symptoms of fatigue, depression, poor cognitive function, and low physical activity. Long-term survivors of childhood leukemia also experience persistent pain, with 41% of survivors reporting pain after treatment ends. Chronic fatigue is a significant predictor, with fatigued survivors being five times more likely to experience pain. Specifically, various types of pain, such as back pain and headaches, are also prevalent, with 44% of ALL survivors reporting back pain compared to 22% of siblings (Coluzzi et al., 2020). Pain is an important symptom to address patients and survivors of ALL, given its impact on HRQoL and daily functioning.

Pain and Social Determinants of Health

SDoH can significantly influence pain management for survivors of ALL. Notably, no published studies have examined the role of SDoH and pain in pediatric cancer survivors, let alone among ALL patients specifically. However, studies examining the association among other populations have found significant associations between chronic pain and across the five SDoH domains. For example, youth living in households with food scarcity had a 46% higher likelihood of experiencing pain (Chen et al., 2024). Low school engagement and unsafe school environments were associated with a 33% and 65% higher likelihood of chronic pain, respectively. Additionally, disparities in healthcare availability may result in inconsistent pain management for those in underserved areas. Lack of access to quality healthcare was correlated

to a 156% higher likelihood of reporting chronic pain, and frequent hospital visits were correlated to a 376% higher likelihood of reporting chronic pain. The impact of neighborhood and community context on chronic pain was also significant, with youth living in neighborhoods with fewer amenities (1-2 amenities) showing a 38% higher likelihood of experiencing chronic pain. While no studies specifically target pediatric cancer survivors, the evidence from Chen et al. (2024) focused on broader youth populations underscores the importance of addressing these social determinants in the care and pain management strategies for ALL survivors.

Physical Activity and Mental Health

Physical activity is essential for supporting and improving mental health. A large body of literature shows that participating in physical activity is linked to better mental health outcomes, including reduced depression and anxiety, improved self-esteem, and enhanced cognitive functioning (Biddle et al., 2018). These associations are seen to benefit children with ALL, where exercise interventions have demonstrated benefits for both mental and physical health. For example, engaging in individualized and supervised exercise programs during treatment phases can mitigate fatigue and improve overall strength (Coombs et al., 2020). Additionally, survivors who met national exercise guidelines had a 20% reduced risk of depression and somatization relative to those who did not meet the guidelines (Tonorezos et al., 2019). Exercise was also associated with improved HRQoL, with those meeting exercise guidelines showing better physical functioning and vitality. Similarly, Wright et al. (2013) reported a moderate positive relationship between social support and physical activity ($r = 0.35$, $p = 0.02$). However, pain, fatigue, and anxiety have been identified as substantial obstacles to physical activity among childhood cancer survivors; specifically, fatigue was inversely related to physical activity, and greater cancer-related pain was linked to heightened fatigue and anxiety (Cox et al., 2009). More

recently, Ware et al. (2023) reported that 75.3% of childhood cancer survivors failed to meet CDC's physical activity recommendations. Body-focused CRW showed a significant negative association with physical activity at follow-up ($\beta = -19.6$, $p = 0.012$), as did pain interference ($\beta = -27.7$, $p = 0.002$) and diagnoses of CNS tumors ($\beta = -41.3$, $p = 0.0003$) or non-CNS solid tumors ($\beta = -19.4$, $p = 0.02$). To further support this concern, a recent study by Lee et al. (2025) found that although long-term cancer survivors were generally more active than health-related peers, 76.1% of survivors still did not meet the physical activity guidelines for aerobic exercise. These studies suggest that physical activity and mental health are strongly correlated among children with ALL.

Pain and Physical Activity

Beyond the physical symptoms, pain can markedly influence a patient's overall well-being and quality of life, and mental health. Chronic pain not only limits a child's ability to engage in physical activity but also contributes to emotional distress, withdrawal, and developmental delays (Van Asselt et al., 2024). Chronic pain in childhood leukemia survivors frequently coexist with other health challenges, including neuropathic pain, musculoskeletal problems, and fatigue. Chronic pain in survivors can lead to a limited ability to engage in physical activity. As noted by caregivers of youth with ALL, 94% reported that symptoms such as pain, fatigue, and general malaise directly impacted their child's ability to be physically active during treatment. When pain was present, survivors were less likely to engage in physical activity, with caregivers noting that their child's physical activity was low or restricted due to these concurrent symptoms. Lack of physical activity may lead to muscle atrophy, reduced mobility, and further physical deconditioning, making it harder for the child to recover or maintain a healthy level of functioning. As noted by Van Asselt et al. (2024), emotional distress

is compounded by the frustration of not being able to participate in physical activity or sports, which can impact a child's social development.

Mental Health and ALL

Individuals diagnosed with ALL may face significant challenges with their mental health. For example, research suggests ALL survivors have a higher prevalence of inattention, learning, and oppositional behavior challenges (Liu et al., 2018). These cognitive and behavioral difficulties can impact academic performance and social interactions. In addition to cognitive and behavioral challenges, ALL survivors may also experience higher levels of psychological distress and poor self-image when compared to their siblings, which may lead to lower overall quality of life (Baytan et al., 2016). However, studies also indicate that childhood cancer survivors may experience posttraumatic growth (PTG), finding positive changes in their lives despite the hardships they face. Many childhood cancer survivors report enhanced appreciation for life, improved relationships, and a greater sense of purpose (Barakat, 2006). Yet this growth often coexists with challenges such as anxiety and depression, making the mental health landscape complex for survivors.

Psychological Distress

Survivors of ALL are at an increased risk of developing psychological distress. Psychological distress includes symptoms of anxiety, depression, and somatization. Studies have shown that as many as 40% of childhood cancer survivors experience symptoms of anxiety and depression (Raguindin et al., 2024). Furthermore, the Swiss Childhood Cancer Survivor Study (SCCSS) found a significant increase in the prevalence of psychological distress over time, with 25% of survivors experiencing distress at follow-up, compared to only 13% at baseline. The increase was seen across various distress scales, including somatization, depression symptoms,

anxiety, and elevations on the Global Severity Index (GSI). Elements that contribute to greater distress among survivors of ALL included older age, female sex, longer time since diagnosis, and a history of late effects from treatment. Notably, survivors who were unemployed at baseline were also more likely to develop or persist in psychological distress.

Cancer-Related Worry (CRW)

CRW is a significant concern for pediatric cancer survivors. Research reveals that female survivors reported significantly higher levels of cancer worry than males ($\beta = -9.4$, $p < 0.001$), with higher treatment intensity also linked to increased worry ($\beta = -18.5$, $p = 0.004$) (Wang et al., 2015). Additionally, 31.5% of survivors exhibited disproportionate worry about late effects, particularly fertility (26%) and second malignancies (13%), despite not being at risk of these effects. Female survivors were more likely to experience excessive worry. Furthermore, 25% of survivors endorsed body-focused cancer-related worry, while 40% reported general cancer-related worry (Ware et al., 2023). Furthermore, Pain intensity was significantly associated with increased fear of cancer recurrence (FCR) in survivors. Pain catastrophizing was a strong predictor of FCR. Specifically, child pain catastrophizing explained 7% of the variance in child FCR (Tutelman et al., 2022). These findings highlight the interplay between cancer-related worry and pain in pediatric cancer survivors.

Summary of the Current Literature

The current literature underscores the significant impact of SDoH on the well-being and health outcomes among ALL survivors. Access to quality healthcare is crucial, with disparities in treatment access often contributing to poor outcomes. For example, children from low-income backgrounds or those covered by Medicaid face worse survival rates than their privately insured peers (Fine et al., 2023; Bona et al., 2016; Tran et al., 2022). Education also plays a significant

role, as higher education attainment is associated with better health outcomes. Specifically, children with lower educational attainment may experience greater difficulty coping with the long-term effects of cancer and treatment, with age considered in the analysis to account for their potential confounding effects on health outcomes (Walsemann et al., 2013; Kimbro et al., 2008). Children with ALL face a range of physical and emotional challenges, including pain, fatigue, anxiety, depression, and a reduced quality of life (Biddle et al., 2019; Coluzzi et al., 2020). Chronic pain is a common side effect experienced by survivors, with many reporting persistent symptoms even after treatment ends (Van Asselt et al., 2024). Furthermore, engaging in physical activity benefits both physical and mental health by reducing depression and fatigue. Yet, many survivors struggle to exercise because of pain and mobility limitations (Coombs et al., 2020; Tonorezos et al., 2019). Social support has likewise been recognized as an important factor in enhancing mental health and encouraging physical activity, while social isolation and lack of social networks can exacerbate emotional distress (Gilliam et al., 2011; Wright et al., 2013). Furthermore, environmental factors, such as neighborhood safety and community amenities, contribute to the overall health of pediatric cancer survivors, with children living in neighborhoods with fewer resources being at higher risk of poor health outcomes (Engemann et al., 2019; Anenberg et al., 2022; Larson et al., 2020; Stevens et al., 2021; Gummin et al., 2019). In sum, the intersection of SDoH, Physical Activity, pain, and psychological distress is vital when considering survivorship care for ALL cancer survivors.

Gaps in the Current Literature

Despite the advancements in pediatric cancer survivorship, several critical gaps remain in the literature. While studies have explored the physical and psychological challenges faced by ALL, there is a lack of research on how SDoH influences pain. Similarly, although Physical

Activity has been shown to benefit pain outcomes in chronic conditions, its specific role in mitigating the negative effects of adverse SDoH on pain in pediatric ALL survivors are not well understood. Addressing these gaps may enhance the current understanding of complex factors influencing pain in pediatric ALL survivors.

Research Aims

Study aims are summarized and depicted in Figure 1 below.

Hypothesis 1a. Pediatric ALL survivors with a history of more adverse SDoH will report higher pain compared to those with fewer adverse SDoH.

Hypothesis 1b. Physical Activity is expected to moderate the relationship between adverse SDoH and pain, such that among individuals who report more adverse SDoH, higher levels of activity will be associated with lower pain. While individuals with fewer adverse SDoH may also experience lower pain with higher Physical Activity, the expected effect will be less pronounced.

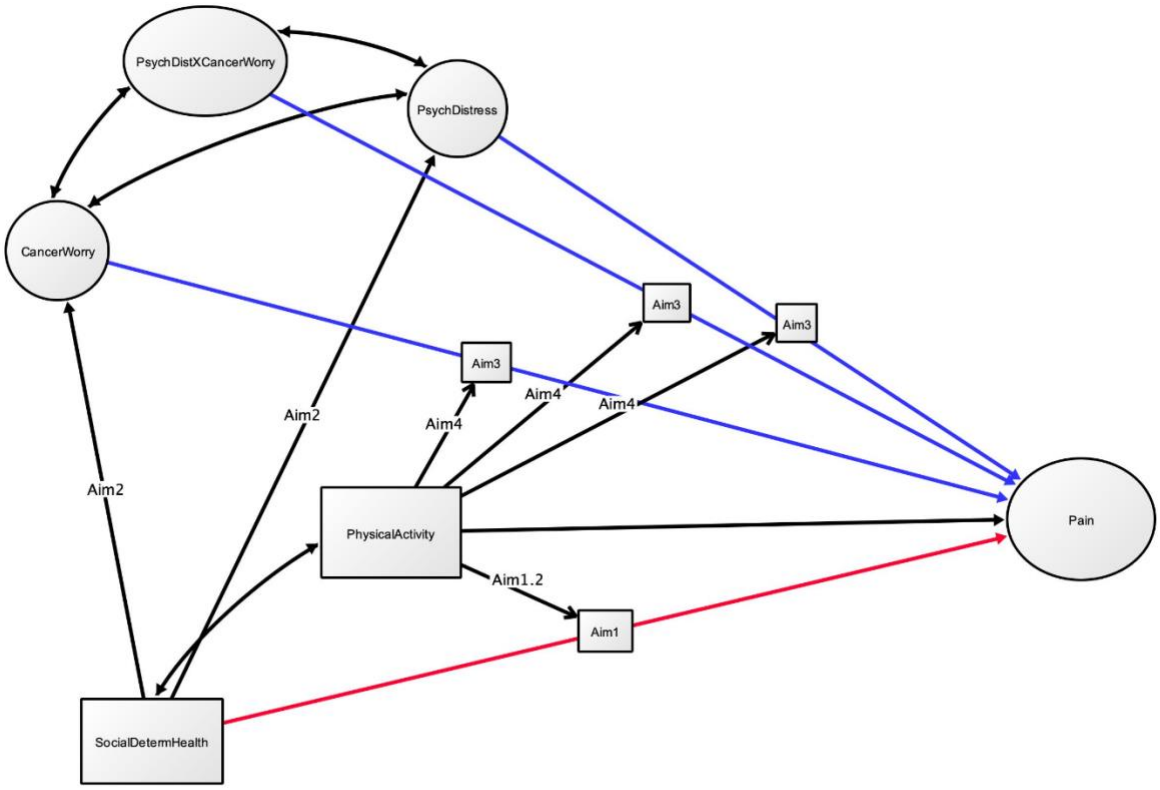
Hypothesis 2. Survivors with more adverse SDoH will be more likely to report both psychological distress and CRW.

Hypothesis 3. CRW and PD will interact, such that the difference in reported pain between those reporting psychological distress and those who aren't will be larger for participants who are also experiencing CRW.

Hypothesis 4. PA is expected to moderate the distal meditational paths between psychological distress, CRW, their interaction and pain, such that among individuals with elevated psychological distress or who are experiencing CRW, Physical Activity will have a weaker negative association with pain.

Hypothesis 5. Psychological distress, CRW, and their interaction will mediate the relationship between SDoH and pain.

Figure 1: Hypothesized Model & Study Aims



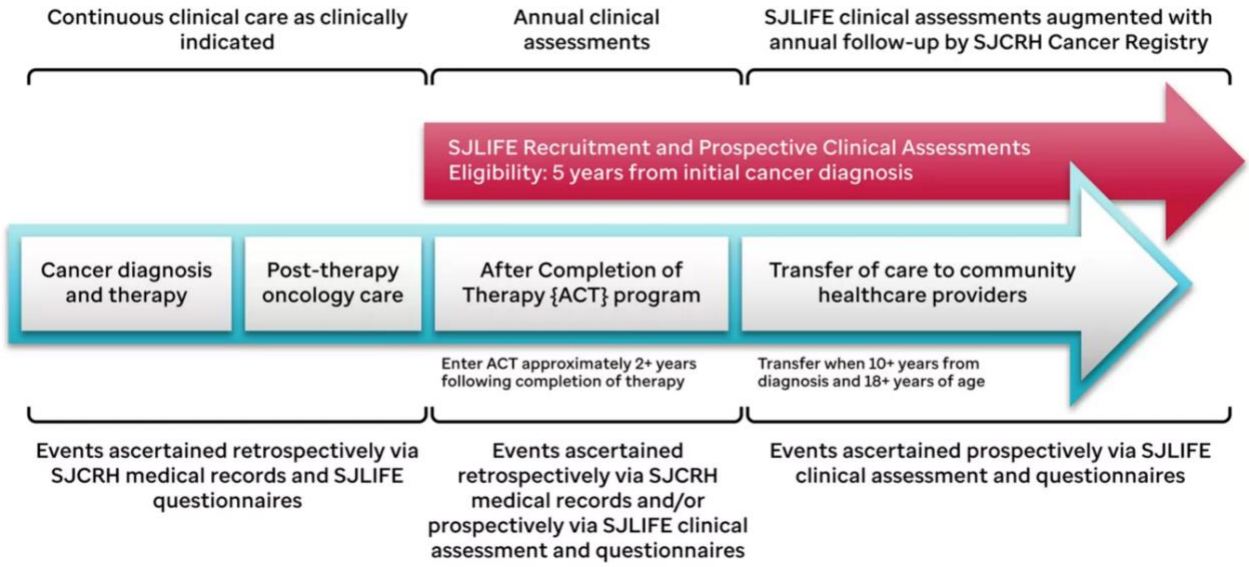
Note: This figure depicts the hypothesized relationships between psychological distress, CRW, SDoH, physical activity, and pain. Blue lines represent moderated paths involved in mediation; red lines represent moderated paths not involved in mediation.

CHAPTER 3: RESEARCH METHODS

Data Source

This research is being conducted using data provided by the *St. Jude LIFE* study, which is focused on the long-term effects of childhood cancer. The *St. Jude LIFE* study aims to learn how frequently late effects occur, how long it takes for long-term effects to develop, how to predict who will experience long-term effects, what health screenings should be conducted, and discover what actions survivors can take to prevent and manage late effects. It includes three to four days of testing, approximately every five years, with adult survivors of pediatric cancer and a control group of adults who did not experience cancer (Figure 2). The data used in this study is cross-sectional and from 2025 data freeze.

Figure 2: Study Design and Recruitment Timeline (Study Design, n.d.)



Participants

The participants in this study are survivors of pediatric ALL who were treated or followed at St. Jude Children's Research Hospital and participated in the SJLIFE study. The eligibility criteria for this study are that participants must be at least 18 years old and at least five

years after being diagnosed with pediatric cancer, with diagnoses occurring on or before June 30, 2012.

Variables of Interest:

SDoH

In this study, demographic variables are used both to describe participant characteristics and to operationalize SDoH. Descriptive variables include factors such as age at diagnosis, sex, and race. These variables are important for understanding individual characteristics but do not directly reflect broader social and environmental influences on health. In contrast, demographic factors such as type of insurance, educational attainment, employment status, rural-urban commuting area (RUCA) codes, and marital status are used to operationalize SDoH, as these factors reflect the social, economic, and environmental conditions in which individuals live. For example, low income, unemployment, and low educational attainment are considered adverse SDoH, as they can create barriers to healthcare access, healthy living conditions, and overall well-being. In this study, SDoH are coded as 0 – 5, with 0 representing that no adverse SDoH and 5 being that all components of SDoH are considered adverse. Based on the U.S. Census Bureau, the income ranges are categorized into three broad socioeconomic status groups: Lower Class – Income less than or equal to $39,999; Middle Class – Income between $40,000 and $99,999; Upper Class – Income greater than or equal to $100,000. Participants who reported being in the lower-class category were coded as adverse, while participants who reported being in the middle- or upper-class category were coded as non-adverse. Educational attainment was categorized as follows: adverse education levels include “less than high school”, “some high school, but did not graduate”, and “high school/GED”, while non-adverse education levels include “Some college”, “College graduate”, and “Post-graduate education.” To categorize

healthcare access and quality, insurance status was assessed based on the responses to questions regarding how insurance is provided (e.g., through employment, spouse/parent's policy, purchased personally, Medicaid/Medicare, military benefits, or other sources). Adverse health insurance included Medicaid or other public assistance programs, which have limitations in coverage and access to services; health insurance plans with exclusions or restrictions based on a participant's health history, such as pre-existing conditions; and policies that impose extra premiums due to health status. Additionally, having no health insurance coverage was categorized as adverse. Non-adverse health insurance included coverage obtained through employment, a spouse or parent's policy, or self-purchased plans without exclusions or surcharges based on health status. To further assess the impact of these factors on health, RUCA Codes were used. These codes were created using participants' residential zip codes and reflect population density and urbanization. Codes ranging from 1-10 delineate metropolitan, micropolitan, small town, and rural community areas. For the purposes of this study, RUCA codes were dichotomized to reflect potential disparities in structural and environmental access. Codes 1-3 were not adverse as they represent metropolitan cores and surrounding areas with substantial commuting flow to urbanized areas. In contrast, codes 4-10 were considered adverse as they represent micropolitan, small towns, and rural areas. These codes allowed for an assessment of how the built environment may influence pain intensity, psychological distress, and physical activity levels. Lastly, marital status was utilized for the social and community context, including being divorced, widowed, separated, or no longer living as married, as an adverse SDoH. Non-adverse social and community context included never married, married, and living with a partner as married.

Pain

To assess the extent to which pain interferes with various aspects of life, the study used the Medical Outcome Study 36-item Short Form Health Survey (SF-36). The SF-36 is a widely recognized measure to evaluate health-related quality of life (HRQoL) across eight domains. The measure aims to capture health status and functioning within the past four weeks. The domains include 1) Physical Functioning, 2) Role Limitations – Physical, 3) Bodily Pain, 4) General Health Perceptions, 5) Vitality, 6) Social Functioning, 7) Role Limitations – Emotional, and 8) Mental Health. The Bodily Pain subscale assesses pain intensity and interference. Pain intensity was assessed using a single item that asked participants to rate the intensity of pain. The item is measured using a 6-point Likert scale, with responses ranging from "1 = None" to "6 = Very severe." In addition to this, respondents were asked to indicate the specific location of the pain with options including head, neck, chest, abdomen, back, pelvis, legs/feet, or other areas. Finally, a single item assessed the impact of pain interference by asking participants how much their pain interfered with their normal work (within and outside the home). The responses ranged from "1 = Not at all" to "6 = Extremely." In this study, pain was assessed using the Bodily Pain scaled score. As part of the standard SF-36 scoring, raw Bodily Pain scores were transformed to a 0–100 scale using the formula: [(Observed Score – Lowest Possible Score) / (Possible Score Range)] × 100, where higher scores reflect less pain. Participants were then categorized into two groups: those with significant pain (t-scores <40) and those with nonsignificant pain (t-scores ≥ 40). The SF-36 is reliable and valid for assessing pain intensity and interference in pediatric cancer survivors. Reulen et al. (2006) examined the psychometric properties of the SF-36 in a cohort of over 10,000 adult survivors of childhood cancer. For the Bodily Pain subscale, the

Cronbach's alpha coefficient for leukemia survivors was 0.87, reflecting high correlation between items.

Cancer-Related Worry (CRW)

CRW was measured using three body-focused items assessing participants' concerns about their health following treatment. Specifically, participants were asked to report their level of worry with physical problems related to their cancer, worries about their appearance, and current anxieties stemming from their cancer or its treatment. Responses were recorded on a 5-point Likert Scale, ranging from "Strongly Disagree" to "Strongly Agree." A mean score was calculated across the three items with scores ≥ 3 categorized as indicating cancer-related worry (Ware et al., 2023).

Physical Activity

To assess participants' physical activity levels, the International Physical Activity Questionnaire – Short Form (IPAQ-SF) was administered. The IPAQ-SF is a widely used and validated self-report measure designed to capture the frequency, duration, and intensity of physical activities within the last seven days (Craig, Marshall, Sjöström, et al., 2003). The measure has demonstrated strong reliability and validity across diverse populations, with correlation values typically around 0.80 for reliability and 0.30 for criterion validity. The IPAQ-SF computes total physical activity by converting reported physical activity into Metabolic Equivalent of Task (MET)-minutes per week using established values for each activity type. Specifically, walking is assigned a value of 3.3 METs, moderate-intensity activities are assigned 4.0 METs, and vigorous-intensity activities are assigned 8.0 METs. The resulting total physical activity score is used to classify participants into three categories based on their weekly MET-minutes. Individuals are classified as having high physical activity if they accumulate at least

3000 MET-minutes per week. Moderate physical activity includes those with weekly MET-minutes between 600 and 2999. Scores below 600 MET-minutes per week fall into the low physical activity category.

Psychological Distress

To assess psychological distress, the Brief Symptom Inventory - 18 (BSI-18) was utilized (Derogatis, 2000). The BSI-18 included 18 questions designed to measure symptoms of anxiety, depression, and somatization. Participants were asked to rate their experiences with various symptoms over the past week, such as nervousness or shaking inside, faintness or dizziness, chest pain, thoughts of ending life, and feelings of fear, loneliness, or hopelessness. Other items assess physical manifestations of psychological distress, including nausea, trouble breathing, numbness, and weakness in parts of the body. Each item is rated on a 5-point Likert scale, ranging from 0 = "Not at all" to 4 = "Extremely." This measure is known for its strong psychometric properties. The instrument demonstrates high internal consistency, with Cronbach's alpha ranging from 0.75 to 0.88 for the subscales and 0.90 for the Global Severity Index (GSI)**.** Recklitis et al. (2006) suggest that the BSI-18 is a valid and reliable measure for assessing psychological distress in adult survivors of childhood cancer. The responses to these items were used to calculate T scores for depression, somatization, and anxiety GSI T-score will also be derived from the overall symptom burden, offering a comprehensive measure of psychological distress. The GSI T-score was used to dichotomize psychological distress; a T-score of 63 or higher is considered indicative of clinically significant psychological distress, while a score below 63 represents the individual is not reporting clinically significant distress.

Data Analysis

Model Estimation:

All data management was performed in R Version 4.4.2 (R Core Team, 2024), while model estimations were performed via Blimp Version 3.2.20 (Keller & Enders, 2023). Missing data was addressed at the scale level within the Fully-Bayesian model estimation via full conditional Metropolis-Hastings sampler of a fully factored specification for the proposed Structural Equations Model, including simultaneously fitting nuisance models for all predictor variables with missing data (Enders, 2023; Keller, In Press). Two parallel chains were run for a burn-in of 20,000 iterations, followed by 60,000 iterations. Model convergence is established via Potential Scale Reduction (PSR) values for all parameters remaining close to 1, (e.g. 1.1 or 1.05, (Gelman & Rubin, 1992), as well as visual inspection of the of the MCMC chains to ensure convergence to a stable distribution for all parameters. Statistical significance is assessed via examination of the 95% Credible Intervals for all parameters of primary interest.

Model Specification:

Sex and Race were included as covariate predictors for all endogenous variables and both SDoH and age at diagnosis were grand-mean centered. Consistent with the proposed model, shown in Figure 1, categorical dependent variables were treated as latent response variables (i.e. estimated via probit regression), with residual variances set to 1 for identification. To preserve variables common metric across predictor and criterion, latent response variables are employed for all predictor instances of endogenous variables (e.g. CRW, and Psychological Distress) (Breen et al., 2013). Indirect effects are known to be non-constant on the probability metric for categorical exogenous variables and therefore do not fully capture changes in dependent variables. Thus, the indirect effects are evaluated via parameters computed within the Bayesian

model estimation for the conditional probability of the dependent variable (e.g. Pain) at predetermined predictor values, consistent with recommendations for specification of indirect (Muthén et al., 2016) and moderated indirect effects (Nguyen et al., 2016) in mediation models with categorical mediators and dependent variables.

CHAPTER 4: RESULTS

Descriptive Statistics

The sample comprised 1,433 adult survivors of pediatric ALL. The majority of participants identified as White (n = 1,252; 87.4%), followed by Black (n = 144; 10.0%) and other racial groups (n = 37; 2.6%). The average age at diagnosis was 6.51 years, with a range from 2 months to 20 years old. Examination of SDoH revealed varied exposure to adverse conditions across the sample. 28.1% (n = 402) reported no adverse indicators, 29.0% (n = 415) endorsed one adverse factor, 22.4% (n = 321) reported two, 14.8% (n = 212) reported three, 5.0% (n = 72) reported four, and 0.8% (n = 11) experienced all five adverse SDoH indicators. Educational attainment data was available for 1,291 participants. The sample demonstrated diverse educational backgrounds: approximately a quarter (24.1%) had completed some college, 18.6% were college graduates, 16.1% held a high school diploma or GED, and 10.1% had not finished high school. Smaller proportions included 7.3% with 1-8 years of formal schooling, 5.2% with postgraduate education, 3.5% with training after high school other than college, 2.8% reported other education levels, and 11.1% of the educational data was missing. Regarding healthcare access, a significant majority of the sample experienced non-adverse conditions (56.5%; n=810). Conversely, 34.2% (n=490) reported adverse healthcare access. Insurance data was unavailable for 9.3% of the sample.

RUCA codes were available for 1,298 participants (90.6% of the total sample), with 9.4% of the sample missing this data. Of those with data, most survivors resided in metropolitan cores (53.2%) or metropolitan areas with high commuting into urbanized areas (17.0%). A smaller number lived in metropolitan low commuting areas (0.5%). Micropolitan areas accounted for 14.9% of participants (across core, high, and low commuting zones), while 10.2% lived in small

towns, and 4.1% resided in rural regions. Overall, the majority of the sample lived in urban or urban-adjacent locations, with fewer from rural or isolated small towns. In terms of social and community context, marital status was diverse: 34.6% were married, 7.1% cohabitating as married, 4.3% separated, 7.0% divorced, and 0.4% widowed. The largest group (46.6%) was single, never married, or never cohabited as married. Marital status data were missing for 21.2% (n = 304). Economic stability among participants showed considerable variation, with 14.9% reporting incomes below $19,999, 20.2% between $20,000 -$39,999, 14.4% earning $40,000-$59,999, 10.9% earning $60,000-$79,999, 7.7% earning $80,000-$99,999, and 9.1% accounted for over $100,000. Finally, Physical Activity levels were assessed across the sample. The majority of participants (48.4%; n=694) reported Low Activity. Moderate Activity was observed in 33.1% (n=475) of the sample, while 10.6% (n=152) engaged in High Activity. Data on physical activity was unavailable for 7.8% (n=112) of participants.

Model Results

The model met convergence criteria, as indicated by PSR values remaining below the required threshold (e.g. PSR<1.05) and the MCMC chains demonstrating good mixing and convergence to a stable distribution for all parameters. Further, only one of the residual correlations was significant, though small (r_{CRWxPD}=.091, SD=.035, 95%CI[.023,.159]). 59.2% of the data was complete, with 7 missing data patterns that consisted of at least 1% of the data. The three most prevalent (accounting for 14.6%, 7.7% and 6.2%) were univariate missingness on Psychological Distress, Pain and Physical Activity respectively. Coefficients accounted for the majority of variance for Pain (proportion of variance explained=.620, SD=.049, 95%CI[.519,.709]), but only a small amount of variability in CRW (Variance explained=.045,

se=.013, 95%CI[.023,.073]) and Psychological Distress (Variance explained=.037, SD=.014, 95%CI[.015,.069]).

Hypothesis 1a

To assess the hypothesis that pediatric ALL survivors with a history of more adverse SDoH will be more likely to report Pain compared to those with fewer adverse SDoH, SDoH was significantly associated with Pain, $\beta = -0.104$ (*SD* = 0.015, 95% CI [−0.135, −0.074]).

Hypothesis 1b

We hypothesized that Physical Activity would moderate the relationship between adverse SDoH and probability of reporting Pain, such that for those who report more Physical Activity, the association between SDoH and the probability of reporting Pain would be weaker. This moderation was significant, $\beta = 0.044$, (*SD* = .009, 95% CI [.026, 0.061]). While this is not the exact predicted pattern of moderation – due to the unexpected direction of the main effect for SDoH – this is still consistent with the predicted buffering effect of Physical Activity. Those reporting higher Physical Activity levels will have a weaker negative association between SDoH and the probability of reporting Pain. Specifically, for individuals with higher physical activity, the impact of adverse SDoH on the likelihood of experiencing pain is less pronounced, suggesting that physical activity may buffer the harmful effect of adverse SDoH on pain reporting.

Hypothesis 2

We hypothesized that survivors with more adverse SDoH would be more likely to report both Psychological Distress and CRW. Adverse SDoH was significantly associated with the probability of reporting psychological distress, $\beta = -0.100$ (*SD* = 0.033, 95% CI[−0.163, -0.036]). However, contrary to expectations, the probability of experiencing Psychological

Distress decreases by .100 for each additional adverse SDoH a survivor experiences. Adverse SDoH were also significantly associated with likelihood of reporting CRW, β = −0.093 (*SD* = 0.028, 95% CI [−0.147, −0.039]). Again, contrary to expectations, the probability of experiencing CRW decreases by 0.093 for each additional adverse SDoH a survivor experiences.

Hypothesis 3

We hypothesized that CRW and psychological distress would interact, such that the difference in probability of reporting Pain between those experiencing Psychological Distress versus those who are not will be larger for participants who are also experiencing CRW. The interaction between the latent-response Psychological Distress and latent-response CRW was β = 1.369 (*SD* = 0.095, 95%CI[1.179,1.551]), consistent with the expected compounding effect for those experiencing both CRW and Psychological Distress on the probability of reporting Pain.

Hypothesis 4

The hypothesized moderating role of Physical Activity on the distal meditational paths involving Psychological Distress, CRW, and their interaction in relation to reporting Pain, predicted that for those reporting Psychological Distress or CRW, the association between Physical Activity and the probability of reporting Pain will be weaker. While the interaction between Physical Activity and the latent-response Physical Distress showed a significant moderating effect on Pain, β = 0.035 (*SD* = 0.016, 95% CI [.004, 0.068]), this was not in the expected direction. Higher Physical Activity weakly increased the strength of the relationship between Psychological Distress and the probability of reporting Pain.

The interaction of latent CRW and manifest Physical Activity also demonstrated a significant moderating effect on Pain, β = −0.203 (*SD* = 0.020, 95% CI [−0.242, −0.164]), but

this time in the expected direction. Higher Physical Activity served as a protective buffer, reducing the likelihood that those experiencing CRW will report experiencing Pain.

Finally, the three-way interaction among manifest Physical Activity, Psychological Distress, and CRW on Pain was significant, $\beta = -0.248$ (*SD* = 0.017, 95% CI [−0.282, −0.216]), as expected. Physical Activity again serves as a buffer – almost fully countering the compounding effects observed between CRW and Psychological Distress on probability of experiencing Pain.

Hypothesis 5

To evaluate the hypothesis that Psychological Distress, CRW, and the interaction there-between will mediate the relationship between SDoH and Pain, various indirect effects from the number of adverse SDoH to Pain were examined. The indirect effect of the number of adverse SDoH on Pain via CRW was significant, $\beta = -0.009$ (*SD* = 0.004, 95% CI [−0.017, −0.003). To interpret the conditional impact of the indirect effect, the conditional probability of reporting Pain is computed at different values of grand-centered SDoH (e.g. low: -.5, mean: 0 and high:.5). The conditional indirect probability of reporting Pain for $SDoH_{low}$=.913 (SD=.106, 95%CI[.597,.992]), for $SDoH_{mean}$ = .872 (SD=.120, 95%CI[.537,.985]) and $SDoH_{high}$ = .820 (SD=.134, 95%CI[.683,.996]).

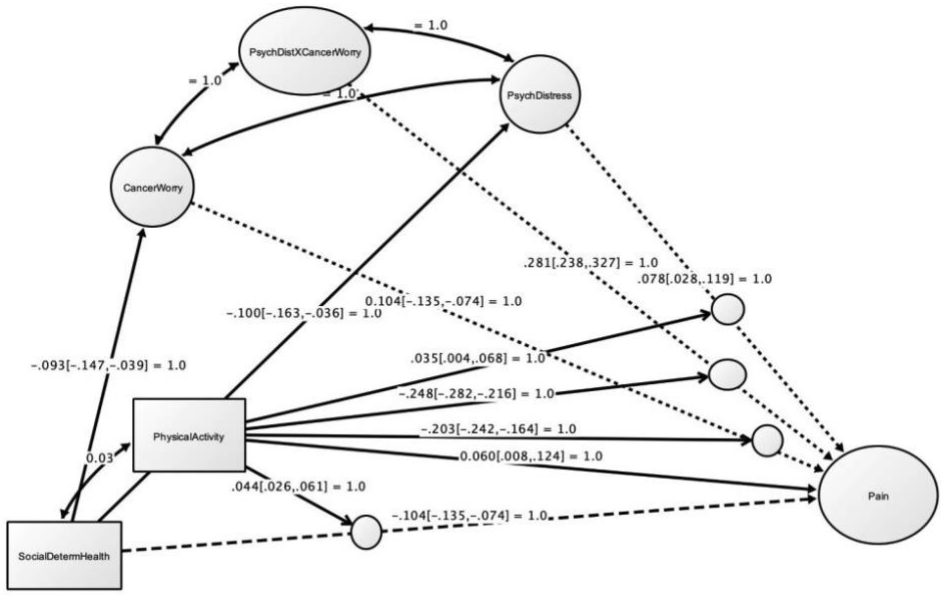
The indirect effect of the number of adverse SDoH on Pain via Psychological Distress was also significant, $\beta = -0.007$ (*SD* = 0.004, 95% CI [−0.016, −0.002]). The indirect probability of reporting Pain for $SDoH_{low}$=.945 (SD=.084, 95%CI[.683,.996]), for $SDoH_{mean}$ = .934 (SD=.074, 95%CI[.719,.992]) and $SDoH_{high}$ .895 (SD=.094, 95%CI[.632,.984]).

Additionally, several moderated indirect effects related to the interaction were observed. The indirect effect of the number of adverse SDoH on Pain via CRW, conditionally moderated by

Physical Activity, was significant, β = 0.010 (*SD* = 0.003, 95% CI [0.004, 0.016]). The moderated indirect probability of reporting Pain for $SDoH_{low}$=.936 (SD=.080, 95%CI[.697,.994]), for $SDoH_{mean}$ = .904 (SD=.091, 95%CI[.646,.987]) and $SDoH_{high}$ .860 (SD=.103, 95%CI[.587,.976]).

Similarly, the indirect effect of the number of adverse SDoH on Pain via latent Psychological Distress, conditionally moderated by Physical Activity, was significant, β = −0.011 (*SD* = 0.004, 95% CI [−0.020, −0.004]). The indirect probability of reporting Pain for $SDoH_{low}$=.934 (SD=.076, 95%CI[.719,.992]), for $SDoH_{mean}$ = .930 (SD=.100, 95%CI[.709,.994]) and $SDoH_{high}$ .924 (SD=.094, 95%CI[.642,.994]).

Figure 3: Model & Study Aims Results



Note: This figure displays the results of the statistical model. Solid lines represent moderated paths involved in mediation pathways, while dashed lines represent moderated paths not part of a mediation pathway.

CHAPTER 5: DISCUSSION

Principal Results & Comparisons with Prior Work

This study aimed to investigate the complex interplay among adverse SDoH, psychological distress, CRW, physical activity, and their influence on pain in pediatric ALL survivors. The findings from the analysis revealed several significant relationships. First, contrary to hypothesis 1, a greater number of adverse SDoH was significantly associated with lower reported pain. This result contrasts the findings from prior literature. For example, Youn et al. (2024) synthesized findings from 20 studies and concluded that adverse SDoH are consistently associated with increased cancer-related pain. However, their review also highlighted a lack of attention to the intersectionality and dynamic interactions among different SDoH domains. One possible explanation for the current study's unexpected result is that individuals who experience multiple stressors may develop adaptive coping mechanisms over time. These coping skills might attenuate the subjective experience of pain through increased psychological resilience. While there have not been specific studies that have investigated these relationships within survivors of childhood cancer, Vieira et al. (2020) found that resilience partially mediated the relationship between childhood trauma and the presence and severity of mood disorders in a community sample of young adults. Their findings suggest that resilience functions as a protective factor, reducing the negative psychological impact of early adversity. In the context of pain perception, it is plausible that similar resilience mechanisms contribute to a form of emotional regulation that dampens the intensity of reported pain. The importance of resilience in pediatric populations facing adversity is further underscored by a recent study that highlighted its critical role in mitigating acute stress symptoms after pediatric traumatic injury (Bonanno, 2012). Nevertheless, further research is needed to explore the role of resilience in

attenuating pain severity among pediatric ALL survivors who have experienced adverse SDoH. Additionally, future work should investigate whether this unexpected finding reflects a true effect or is a result of model over-parameterization or misspecification.

While a significant moderating effect of physical activity on the relationship between adverse SDoH and pain was found, this finding was also contrary to the specific direction of hypothesis 1b. The hypothesis predicted that the buffering effect of physical activity would be more pronounced among individuals with greater adverse SDoH. Instead, the results suggest that while engaging in more physical activity was associated with lower likelihood of reporting pain, its mitigating effect was distinctly less pronounced in the high-adversity group. This interaction implies that while physical activity remains an important factor for pain management, its protective capacity may be more context-dependent than hypothesized. While not all of our hypotheses were supported, this study contributes to the existing literature by thoroughly examining this complex interaction within pediatric ALL survivors, highlighting a nuanced interplay between physical activity and SDoH in influencing pain outcomes in this specific population. Our findings align with previous research showing physical activity as a promising approach for managing chronic pain (Liska & Kolen, 2020; Wang et al., 2024). However, few studies have focused specifically on survivors of childhood cancer (Malysse et al., 2021), and even fewer have investigated how contextual factors like SDoH may influence these relationships. Therefore, there is a need for future studies to explore the role of physical activity to manage pain in survivors of childhood cancer.

Hypothesis 2, which posited that more adverse SDoH would be associated with higher psychological distress and CRW, was not supported. Instead, individuals with more adverse SDoH were significantly less likely to report psychological distress and less likely to report

CRW. Similar to our findings for Hypothesis 1, these inverse relationships suggest that survivors facing a greater cumulative burden of SDoH may exhibit unexpected patterns of psychological adjustment, possibly reflecting enhanced resilience or different coping strategies. The pattern may align with work by Palmer et al. (2019), who emphasize that adverse social conditions affect people differently. They suggest that resilience processes and protective social supports can interrupt the pathway from social disadvantage to poor health. From this perspective, the findings from the current study could reflect how some individuals harness strengths and external supports to adapt over time.

Hypothesis 3, which predicted the interaction between CRW and psychological distress on pain was supported. A significant positive interaction was observed, where the effect of psychological distress on pain was amplified by higher levels of CRW. This indicates that the combined burden of these two psychological factors does not simply add up but rather intensifies their individual effects on pain. This finding aligns with literature recognizing CRW as a prevalent issue for cancer survivors. For instance, a study among adult survivors of childhood cancer found that a substantial portion reported CRW, which was associated with increased psychological symptoms, inadequate physical activity, and increased healthcare utilization (McDonnell et al., 2021). The results from the current study extend this understanding by specifically demonstrating how CRW, in conjunction with psychological distress, significantly increases the experience of pain in pediatric ALL survivors. Despite the prevalence of pain in this population, few interventions have been specifically developed or tested for survivors of childhood cancer. Recent efforts from Patton's (2024) evaluated the use of WebMAP, a web-based CBT program originally developed for youth with chronic pain, to explore the feasibility of the intervention for adolescent survivors of childhood cancer. While the program was not

adapted for this group, it provided encouraging preliminary evidence that digital interventions may help manage pain in this population. Survivors and caregivers reported improvements in pain, sleep, stress regulation, and communication skills. However, participant feedback also revealed important limitations, including low engagement with lengthy, text-heavy modules and the absence of content tailored to the broader psychosocial and medical challenges faced by childhood cancer survivors. Thus, clinical interventions targeting Pain management should not address pain alone but rather adopt a holistic approach that addresses the concurrent and amplifying effects of CRW and psychological distress. Given the limited number of interventions specifically designed for this population, there is a pressing need for integrated, survivorship-focused treatments that simultaneously address the emotional and physical dimensions of pain.

Hypothesis 4 further explored the moderating role of physical activity on distal mediational paths to pain. The interaction between physical activity and psychological distress showed a significant positive moderating effect on likelihood of reporting ain. This indicates that when psychological distress is high, the potential pain-reducing benefits of physical activity are reduced. This suggests that the emotional burden of psychological distress can interfere with the therapeutic potential of physical activity. A cross-sectional study of adult cancer survivors showed that individuals reporting higher anxiety or depressive symptoms were less likely to meet recommended physical activity levels. The authors noted that distress-related depletion of motivation and energy may impede engagement in exercise (Miller et al., 2024). This provides a plausible mechanism for how heightened psychological distress might impede an individual's ability to fully benefit from physical activity in pain management. In contrast, the interaction of CRW with physical activity showed a significant negative moderating effect on the probability of reporting pain. This indicates that when CRW was high, physical activity was associated with a

lower likelihood of reporting pain. A recent study that also utilized the St. Jude Lifetime Cohort conducted a longitudinal analysis that examined CRW at baseline as a predictor of objectively assessed physical activity 5 years later in childhood cancer survivors (Ware et al., 2023). They identified Body-Focused CRW as being significantly associated with decreased subsequent physical activity ($\beta = -19.6$, $p = 0.012$). While their longitudinal study observed a predictive negative association between CRW and levels of physical activity, the present study extends the literature by indicating the concurrent presence of CRW enhances the pain-reducing effect of physical activity. For individuals burdened by CRW, physical activity might serve as a powerful coping mechanism, offering distraction, a sense of control over one's body, or an outlet for anxiety. The significant three-way moderation among physical activity, psychological distress, and CRW on pain further highlights the combinations of psychological states where physical activity is most or least effective. These results imply that the effectiveness of physical activity as a pain management strategy may be highly contingent on the specific psychological landscape of the individual. Clinical interventions should be tailored, perhaps prioritizing the management of psychological distress before or alongside physical activity recommendations, while leveraging physical activity as a potent tool for those primarily experiencing CRW.

Finally, Hypothesis 5 explored the mediational role of psychological distress, CRW, and their interaction in the relationship between SDoH and pain. The analysis revealed several significant indirect effects, indicating that these psychological factors serve as pathways through which adverse SDoH influence pain. First, a greater number of adverse SDoH indirectly led to lower Pain through CRW. Similarly, more adverse SDoH indirectly led to lower pain through psychological distress. These findings align with the earlier observation that more adverse SDoH were directly associated with lower pain (Hypothesis 1). The analyses conducted to evaluate

Hypothesis 5 help us understand why this might be the case, by showing that these psychological factors are part of the mechanism.

The indirect effect of SDoH on pain via CRW was significantly moderated by physical activity. This means that while the pathway from adverse SDoH through CRW generally contributes to lower pain, higher levels of physical activity led to less pain reduction via this specific pathway**.** As previously discussed, Ware et al. (2023) highlighted body-focused CRW as a significant concern for childhood cancer survivors, emphasizing its connection to physical function and appearance. One possible explanation for this unexpected result may stem from the impact of an individuals' awareness of their own bodies. For some childhood cancer survivors, particularly those facing social disadvantages or experiencing bodily-focused CRW, a coping strategy for managing chronic pain might involve a degree of mental detachment from physical sensations. However, engaging in more physical activity inherently draws attention to bodily cues and sensations (e.g., muscle fatigue, breathing, exertion). This heightened focus on the body, rather than offering a coping mechanism, could inadvertently interfere with or disrupt their existing strategy of mental detachment.

Limitations

This study offers a novel contribution by applying a moderated mediation model to understand how psychosocial and behavioral factors influence pain in survivors of pediatric ALL. However, several limitations must be acknowledged. Notably, the marginal distributions of many of these variables were heavily skewed. Over 91% of the sample reported experiencing pain, while only 14% of the sample reported psychological distress and 52.5% of the sample engaged in low levels of physical activity. This variance compression is most concerning for pain, since there is minimal variance to account for, especially under the complexity of the

proposed model. While the marginal proportions do raise some concerns, it is well established that both sparsity in the conditional distributions, variance attenuation or over-fitting to a limited subset of atypical cases can artificially induce spurious results, which proffer an alternative potential explanation for some of the unexpected findings. Finally, it should be noted that both CRW and psychological distress had minimal proportions of variance accounted for by the estimated coefficients, especially relative to the markedly high proportion of pain variance accounted for. At minimum, the proposed model did not account for the bulk of CRW's and psychological distress' (markedly attenuated) variance, indicating that much is missing from this picture. Future sensitivity analyses should attempt to 1) determine if the findings are driven by sparsity in the conditional distributions, and 2) if the findings are still present across either simplified models or alternative specifications (e.g. logit rather than probit specifications). These limitations should temper the interpretation of this model, and further sensitivity analyses should seek to determine how robust the findings are across alternative parameterizations of the associations of interest.

Finally, the nature of the data also introduced some potential limitations. The cross-sectional design prevents conclusions about temporal relationships between the variables. Second, all key constructs were assessed via self-reported measures. While these measures are validated and widely used, self-reports are subject to recall bias, social desirability bias, and potential misunderstanding of items. In particular, physical activity may be over or under reported due to misestimates of duration or intensity. Additionally, data captured in a single snapshot often fails to represent the dynamic and fluctuating nature of activity patterns over time. Third, although SDoH was operationalized using established indicators, the compression of this complex experience into a single ordinal variable may have oversimplified the nuances within

each domain. Lastly, the distribution of variables across the sample was not balanced. For example, the majority of participants identified as White, lived in metropolitan areas, and reported non-adverse insurance coverage, while a relatively small proportion reported multiple adverse SDoH indicators or rural residency.

Conclusions

This study highlights the intricate relationships among adverse SDoH, psychological functioning, physical activity, and Pain in survivors of pediatric ALL. Despite the surprising direction of some direct effects, the study supports a more nuanced understanding of how pain is shaped by the interplay of social context, psychological processes, and health behaviors. The interaction between psychological distress and CRW significantly predicted increased pain, emphasizing the compounded burden of co-occurring psychological concerns. Notably, physical activity emerged as a complex moderator, sometimes enhancing and other times diminishing the effects of distress and worry on pain. For instance, while physical activity appeared less beneficial in the context of high distress, it showed a more protective role when CRW was elevated. The findings also confirm that both psychological distress and CRW mediate the relationship between SDoH and pain, with additional conditional effects depending on levels of physical activity. These results reinforce that pain in pediatric cancer survivors is not merely a biological outcome but is shaped by a web of psychosocial and contextual influences. Taken together, this study supports the importance of integrated care models that consider a survivor's psychological state, physical habits, and social background when addressing chronic pain. These findings may reflect resilience within this population, suggesting that survivors who have faced cumulative life adversity may develop adaptive coping mechanisms that buffer against future psychological and physical challenges. Alternatively, these results may point to measurement

limitations or model misspecification obscuring the true relationships. Future research should continue to explore these complex interactions over time, identify protective factors that promote resilience, and tailor interventions to an individual's unique psychosocial profile to enhance well-being and quality of life in survivorship.

References

Acute lymphocytic leukemia - Diagnosis and treatment - Mayo Clinic. (2022). https://www.mayoclinic.org/diseases-conditions/acute-lymphocytic-leukemia/diagnosis-treatment/drc-20369083

American Cancer Society. (2024). *Cancer Facts & Figures 2024*. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2024/2024-cancer-facts-and-figures-acs.pdf

Anenberg, S. C., Mohegh, A., Goldberg, D. L., Kerr, G. H., Brauer, M., Burkart, K., Hystad, P., Larkin, A., Wozniak, S., & Lamsal, L. (2022). Long-term trends in urban NO2 concentrations and associated paediatric asthma incidence: estimates from global datasets. *The Lancet Planetary Health*, *6*(1), e49–e58. https://doi.org/10.1016/s2542-5196(21)00255-2

APA Dictionary of Psychology. (n.d.). https://dictionary.apa.org/social-support

Barakat, L. P., Alderfer, M. A., & Kazak, A. E. (2005). Posttraumatic growth in adolescent survivors of cancer and their mothers and fathers. *Journal of Pediatric Psychology*, *31*(4), 413–419. https://doi.org/10.1093/jpepsy/jsj058

Baytan, B., Aşut, Ç., Kantarcıoğlu, A. Ç., Evim, M. S., & Güneş, A. M. (2016). Health-Related quality of Life, Depression, Anxiety, and Self-Image in acute lymphocytic leukemia survivors. *Turkish Journal of Hematology*, *33*(4), 326–330. https://doi.org/10.4274/tjh.2015.0356

Bhatia, S., Landier, W., Hageman, L., Kim, H., Chen, Y., Crews, K. R., ... & Maloney, K. W. (2014). 6MP adherence in a multiracial cohort of children with acute lymphoblastic leukemia: a Children's Oncology Group study. Blood, 124(15), 2345-2353.

Bhatia, S., Landier, W., Hageman, L., Kim, H., Hanby, C., Nancy, K., ... & Mascarenhas, L. (2012). Nonadherence to Oral 6-Mercaptopurine (6MP) in a Multi-Ethnic Cohort of Children with Acute Lymphoblastic Leukemia (ALL) and Its Impact On Relapse–a Children's Oncology Group (COG) Study (AALL03N1).

Biddle, S. J., Ciaccioni, S., Thomas, G., & Vergeer, I. (2018). Physical activity and mental health in children and adolescents: An updated review of reviews and an analysis of causality. *Psychology of Sport and Exercise*, *42*, 146–155. https://doi.org/10.1016/j.psychsport.2018.08.011

Bona, K., Blonquist, T. M., Neuberg, D. S., Silverman, L. B., & Wolfe, J. (2016). Impact of socioeconomic status on timing of relapse and overall survival for children treated on Dana-Farber Cancer Institute ALL Consortium Protocols (2000–2010). *Pediatric Blood & Cancer*, *63*(6), 1012–1018. https://doi.org/10.1002/pbc.25928

Bonanno, G. A., & Diminich, E. D. (2012). Annual Research Review: Positive adjustment to adversity–trajectories of minimal–impact resilience and emergent resilience. *Journal of Child Psychology and Psychiatry*, *54*(4), 378–401. https://doi.org/10.1111/jcpp.12021

Breen, R., Karlson, K. B., & Holm, A. (2013). Total, direct, and indirect effects in logit and probit models. Sociological Methods & Research, 42(2), 164-191.

Chen, Y., Liu, Z., Werneck, A. O., Huang, T., Van Damme, T., Kramer, A. F., Cunha, P. M., Zou, L., & Wang, K. (2024). Social determinants of health and youth chronic pain. *Complementary Therapies in Clinical Practice*, 101911. https://doi.org/10.1016/j.ctcp.2024.101911

Coluzzi, F., Rocco, M., Gladden, R. G., Persiani, P., Thur, L. A., & Milano, F. (2020). Pain management in childhood leukemia: diagnosis and available analgesic treatments. *Cancers*, *12*(12), 3671. https://doi.org/10.3390/cancers12123671

Coombs, A., Schilperoort, H., & Sargent, B. (2020). The effect of exercise and motor interventions on physical activity and motor outcomes during and after medical intervention for children and adolescents with acute lymphoblastic leukemia: A systematic review. *Critical Reviews in Oncology/Hematology*, *152*, 103004. https://doi.org/10.1016/j.critrevonc.2020.103004

Cox, C. L., Montgomery, M., Oeffinger, K. C., Leisenring, W., Zeltzer, L., Whitton, J. A., Mertens, A. C., Hudson, M. M., & Robison, L. L. (2009). Promoting physical activity in childhood cancer survivors. *Cancer*, *115*(3), 642–654. https://doi.org/10.1002/cncr.24043

Craig, C. L., Marshall, A. L., Sjöström, M., Bauman, A. E., Booth, M. L., Ainsworth, B. E., Pratt, M., Ekelund, U., Yngve, A., Sallis, J. F., & Oja, P. (2003). International Physical Activity Questionnaire: 12-Country Reliability and Validity. *Medicine & Science in Sports & Exercise*, *35*(8), 1381–1395. https://doi.org/10.1249/01.mss.0000078924.61453.fb

Derogatis, L. R. (2000). Brief Symptom Inventory-18 [Dataset]. In *PsycTESTS Dataset*. https://doi.org/10.1037/t07502-000

Education Access and Quality | Prepare your Health | CDC. (2023). https://www.cdc.gov/prepyourhealth/discussionguides/education.htm

Enders, C. K. (2023). Missing data: An update on the state of the art. Psychological Methods. Advanced online publication.

Engemann, K., Pedersen, C. B., Arge, L., Tsirogiannis, C., Mortensen, P. B., & Svenning, J. (2019). Residential green space in childhood is associated with lower risk of psychiatric disorders from adolescence into adulthood. *Proceedings of the National Academy of Sciences*, *116*(11), 5188–5193. https://doi.org/10.1073/pnas.1807504116

Fine, J. R., Ransdell, J. M., Pinheiro, P. S., Kwon, D., Reis, I. M., Barredo, J. C., & Isrow, D. M. (2023). The effect of health insurance on pediatric cancer survival: An analysis of children evaluated for radiation therapy in diverse multicenter health systems. *Journal of Pediatric Hematology/Oncology*, *45*(6), e662–e670. https://doi.org/10.1097/mph.0000000000002678

Gelman, A., & Rubin, D. B. (1992). Inference from Iterative Simulation Using Multiple Sequences. *Statistical Science*, *7*(4). https://doi.org/10.1214/ss/1177011136

Gilliam, M. B., Madan-Swain, A., Whelan, K., Tucker, D. C., Demark-Wahnefried, W., & Schwebel, D. C. (2011). Social, demographic, and medical influences on physical activity in child and adolescent cancer survivors. *Journal of Pediatric Psychology*, *37*(2), 198–208. https://doi.org/10.1093/jpepsy/jsr085

Gummin, D. D., Mowry, J. B., Spyker, D. A., Brooks, D. E., Beuhler, M. C., Rivers, L. J., Hashem, H. A., & Ryan, M. L. (2019). 2018 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 36th Annual Report. *Clinical Toxicology*, *57*(12), 1220–1413. https://doi.org/10.1080/15563650.2019.1677022

Health care access. (n.d.). RAND. https://www.rand.org/topics/health-care-access.html

Hong, J. H., Nakamura, J. S., Berkman, L. F., Chen, F. S., Shiba, K., Chen, Y., Kim, E. S., & VanderWeele, T. J. (2023). Are loneliness and social isolation equal threats to health and

well-being? An outcome-wide longitudinal approach. *SSM - Population Health*, *23*, 101459. https://doi.org/10.1016/j.ssmph.2023.101459

Larson EH, Andrilla CHA, Garberson LA. Supply and Distribution of the Primary Care Workforce in Rural America: 2019. Policy Brief #167. WWAMI Rural Health Research Center, University of Washington; June 2020.

Lee, M. K., Park, D., Lee, D. H., Yu, J., Park, J. S., & Jeon, J. Y. (2025). Physical activity levels among long-term cancer survivors of more than 5 years: a propensity score matching analysis. *Supportive Care in Cancer*, *33*(4), 340. https://doi.org/10.1007/s00520-025-09366-0

Liska, T. M., & Kolen, A. M. (2020). The role of physical activity in cancer survivors' quality of life. Health and Quality of Life Outcomes, 18(1). https://doi.org/10.1186/s12955-020-01448-3

Liu, W., Cheung, Y. T., Brinkman, T. M., Banerjee, P., Srivastava, D., Nolan, V. G., Zhang, H., Gurney, J. G., Pui, C., Robison, L. L., Hudson, M. M., & Krull, K. R. (2018). Behavioral symptoms and psychiatric disorders in child and adolescent long-term survivors of childhood acute lymphoblastic leukemia treated with chemotherapy only. *Psycho-Oncology*, *27*(6), 1597–1607. https://doi.org/10.1002/pon.4699

Kahn, J. M., Keegan, T. H., Tao, L., Abrahão, R., Bleyer, A., & Viny, A. D. (2016). Racial disparities in the survival of American children, adolescents, and young adults with acute lymphoblastic leukemia, acute myelogenous leukemia, and Hodgkin lymphoma. *Cancer*, *122*(17), 2723–2730. https://doi.org/10.1002/cncr.30089

Keller, B.T. (In press). A factored regression approach to modeling latent variable interactions and nonlinear effects. Psychological Methods.

Keller, B. T., & Enders, C. K. (2023). Blimp user's guide (Version 3). Retrieved from www.appliedmissingdata.com/blimp

Kennard, B. D., Stewart, S. M., Olvera, R., Bawdon, R. E., Lewis, C. P., & Winick, N. J. (2004). Nonadherence in adolescent oncology patients: preliminary data on psychological risk factors and relationships to outcome. Journal of Clinical Psychology in Medical Settings, 11(1), 31-39.

Kim, M. A., Park, J. H., Park, H. J., Yi, J., Ahn, E., Kim, S. Y., Shin, D. W., Park, M., Lim, Y., Park, E. S., Park, K. D., & Hong, J. S. (2018). Experiences of peer exclusion and victimization, cognitive functioning, and depression among adolescent cancer survivors in South Korea. *American Journal of Orthopsychiatry*, *88*(4), 441–449. https://doi.org/10.1037/ort0000292

Kimbro, R. T., Bzostek, S., Goldman, N., & Rodríguez, G. (2008). Race, ethnicity, and the education gradient in health. *Health Affairs*, *27*(2), 361–372. https://doi.org/10.1377/hlthaff.27.2.361

Malysse, C., Romero-Galisteo, R. P., Merchán-Baeza, J. A., Durán-Millán, J. I., González-Sánchez, M., & Galan-Mercant, A. (2021). Physical activity promotion programmes in childhood cancer patients and their Impact on fatigue and Pain: a Systematic review. Children, 8(12), 1119. https://doi.org/10.3390/children8121119

McDonnell, G. A., Brinkman, T. M., Wang, M., Gibson, T. M., Heathcote, L. C., Ehrhardt, M. J., Srivastava, D. K., Robison, L. L., Hudson, M. M., & Alberts, N. M. (2021). Prevalence and predictors of cancer-related worry and associations with health behaviors in adult survivors of childhood cancer. *Cancer*, *127*(15), 2743–2751. https://doi.org/10.1002/cncr.33563

Muthén, B., Muthén, L., & Asparouhov, T. (2016). Regression and mediation analysis using Mplus. Los Angeles, CA.: Muthén & Muthén.

Miller, N. E., Lally, P., Conway, R., Steptoe, A., Frank, P., Beeken, R. J., & Fisher, A. (2024). Psychological distress and health behaviours in people living with and beyond cancer: a cross-sectional study. *Scientific Reports*, *14*(1). https://doi.org/10.1038/s41598-024-66269-6

Nadel, A. (2021). Psychosocial factors impacting children with cancer and their families. In *Elsevier eBooks* (pp. 735–748). https://doi.org/10.1016/b978-0-12-821671-2.00028-3

Nathan, P. C., Wasilewski-Masker, K., & Janzen, L. A. (2009). Long-term outcomes in survivors of childhood acute lymphoblastic leukemia. *Hematology/Oncology Clinics of North America*, *23*(5), 1065–1082. https://doi.org/10.1016/j.hoc.2009.07.003

National Childhood Cancer Registry Explorer (NCCR*Explorer). (2020). https://nccrexplorer.ccdi.cancer.gov/

Neighborhood and Built Environment | Prepare your Health | CDC. (n.d.). https://www.cdc.gov/prepyourhealth/discussionguides/neighborhood.htm

Nguyen, T. Q., Webb-Vargas, Y., Koning, I. M., & Stuart, E. A. (2016). Causal mediation analysis with a binary outcome and multiple continuous or ordinal mediators: Simulations and application to an alcohol intervention. *Structural equation modeling: a multidisciplinary journal*, *23*(3), 368-383.

Palmer, R. C., Ismond, D., Rodriquez, E. J., & Kaufman, J. S. (2019). Social Determinants of Health: Future Directions for Health Disparities Research. *American Journal of Public Health*, *109*(S1), S70–S71. https://doi.org/10.2105/ajph.2019.304964

Patton, M. (2024, September 20). Internet-Delivered Cognitive Behavioral Treatment for Chronic pain in adolescent survivors of childhood Cancer: a Single-group feasibility trial. https://hdl.handle.net/1880/119869

Puckett, Y., & Chan, O. (2023). Acute lymphocytic leukemia. StatPearls - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK459149/

R Core Team. 2024. *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing. https://www.R-project.org/.

Raguindin, P. F., Rueegg, C. S., Kälin, S., Bergstraesser, E., Von Der Weid, N. X., Tinner, E. M., Kuehni, C. E., & Michel, G. (2024). Longitudinal changes of psychological distress among childhood cancer survivors: The Swiss Childhood Cancer Survivor Study. *Pediatric Blood & Cancer*, *71*(8). https://doi.org/10.1002/pbc.31095

Recklitis, C. J., Parsons, S. K., Shih, M., Mertens, A., Robison, L. L., & Zeltzer, L. (2006). Factor structure of the Brief Symptom Inventory--18 in adult survivors of childhood cancer: Results from the Childhood Cancer Survivor Study. *Psychological Assessment*, *18*(1), 22–32. https://doi.org/10.1037/1040-3590.18.1.22

Reulen, R. C., Zeegers, M. P., Jenkinson, C., Lancashire, E. R., Winter, D. L., Jenney, M. E., & Hawkins, M. M. (2006). The use of the SF-36 questionnaire in adult survivors of childhood cancer: evaluation of data quality, score reliability, and scaling assumptions. *Health and Quality of Life Outcomes*, *4*(1). https://doi.org/10.1186/1477-7525-4-77

Shaulov, A., Rodin, G., Popovic, G., Caraiscos, V. B., Le, L. W., Rydall, A., Schimmer, A. D., & Zimmermann, C. (2018). Pain in patients with newly diagnosed or relapsed acute leukemia. *Supportive Care in Cancer*, *27*(8), 2789–2797. https://doi.org/10.1007/s00520-018-4583-5

Socioeconomic status. (n.d.). https://www.apa.org. https://www.apa.org/topics/socioeconomic-status/

Strange, L. F., Lewis, R. S. W., Ji, X., & Effinger, K. E. (2025). Rurality of Residence and Distance to Clinic is a Risk Factor for Non-Engagement in Childhood Cancer Survivor Care. *Cancer Epidemiology Biomarkers & Prevention*. https://doi.org/10.1158/1055-9965.epi-25-0023

Stevens, Alexander, Clare Cho, Metin Çakır, Xiangwen Kong, and Michael Boland June 2021. The Food Retail Landscape Across Rural America, EIB-223, U.S. Department of Agriculture, Economic Research Service.

Study design. (n.d.). St. Jude LIFE. https://sjlife.stjude.org/investigators/study-design.html

Suntum, T. K., Ahn, J., Lobo, T., Alaoui, A., Appel, B. E., Pudela, C., Beight, L., Heller, C., Bryant, S. L., Tercyak, K. P., Dash, C., Potosky, A. L., & Kadan-Lottick, N. S. (2025). Patient Characteristics and Neighborhood-Level Social Determinants of Health Associated with Childhood Cancer Survivor Follow-Up at Urban Cancer Centers. *Pediatric Blood & Cancer*. https://doi.org/10.1002/pbc.31784

Tebbi, C. K. (2021). Etiology of Acute Leukemia: A review. *Cancers*, *13*(9), 2256. https://doi.org/10.3390/cancers13092256

Tonorezos, E. S., Ford, J. S., Wang, L., Ness, K. K., Yasui, Y., Leisenring, W., Sklar, C. A., Robison, L. L., Oeffinger, K. C., Nathan, P. C., Armstrong, G. T., Krull, K., & Jones, L. W. (2019). Impact of exercise on psychological burden in adult survivors of childhood cancer: A report from the Childhood Cancer Survivor Study. *Cancer*, *125*(17), 3059–3067. https://doi.org/10.1002/cncr.32173

Tran, Y. H., Coven, S. L., Park, S., & Mendonca, E. A. (2022). Social determinants of health and pediatric cancer survival: A systematic review. *Pediatric Blood & Cancer*, *69*(5). https://doi.org/10.1002/pbc.29546

Tutelman, P. R., Chambers, C. T., Noel, M., Heathcote, L. C., Fernandez, C. V., Flanders, A., MacLeod, J., Sherry, S. B., Simard, S., Stern, M., Stewart, S. H., & Urquhart, R. (2022). Pain and fear of cancer recurrence in survivors of childhood cancer. *Clinical Journal of Pain*, *38*(7), 484–491. https://doi.org/10.1097/ajp.0000000000001049

Van Asselt, A. E., Gibler, R. C., Tokala, M., Gillette, M. L. D., Klages, K. L., Gilbert, R., Weber, J., & Bates, C. R. (2024). Exploring the role of pain on physical activity among youth with acute lymphoblastic leukemia using the biopsychosocial model. *Pediatric Blood & Cancer*. https://doi.org/10.1002/pbc.31276

Vieira, I. S., Moreira, F. P., Mondin, T. C., De Azevedo Cardoso, T., Branco, J. C., Kapczinski, F., Jansen, K., De Mattos Souza, L. D., & Da Silva, R. A. (2020b). Resilience as a mediator factor in the relationship between childhood trauma and mood disorder: A community sample of young adults. *Journal of Affective Disorders*, *274*, 48–53. https://doi.org/10.1016/j.jad.2020.04.011

Walsemann, K. M., Gee, G. C., & Ro, A. (2013). Educational attainment in the context of social inequality. *American Behavioral Scientist*, *57*(8), 1082–1104. https://doi.org/10.1177/0002764213487346

Walsh, S., Mulraney, M., McCarthy, M., & De Luca, C. R. (2024). Fatigue in children who have recently completed treatment for acute lymphoblastic leukemia: a longitudinal study. *Health and Quality of Life Outcomes*, *22*(1). https://doi.org/10.1186/s12955-024-02241-2

Wang, J., Lv, M., Li, H., Guo, D., & Chu, X. (2024). Effects of Exercise in Adults with Cancer Pain: A Systematic Review and Network Meta-Analysis. Journal of Pain and Symptom Management, 69(1), 82–101. https://doi.org/10.1016/j.jpainsymman.2024.08.033

Wang, R., Syed, I. A., Nathan, P. C., Barr, R. D., Rosenberg-Yunger, Z. R., & Klassen, A. F. (2015). Exploring cancer worry in adolescent and young adult survivors of childhood cancers. *Journal of Adolescent and Young Adult Oncology*, *4*(4), 192–199. https://doi.org/10.1089/jayao.2015.0029

Ware, M. E., Delaney, A., Krull, K. R., Brinkman, T. M., Armstrong, G. T., Wilson, C. L., Mulrooney, D. A., Wang, Z., Lanctot, J. Q., Krull, M. R., Partin, R. E., Shelton, K. C., Srivastava, D. K., Hudson, M. M., Robison, L. L., & Ness, K. K. (2023). Cancer-Related worry as a predictor of 5-yr physical activity level in childhood cancer survivors. *Medicine & Science in Sports & Exercise*, *55*(9), 1584–1591. https://doi.org/10.1249/mss.0000000000003195

Wilder, M. E., Kulie, P., Jensen, C., Levett, P., Blanchard, J., Dominguez, L. W., Portela, M., Srivastava, A., Li, Y., & McCarthy, M. L. (2021). The Impact of Social Determinants of Health on Medication Adherence: a Systematic Review and Meta-analysis. *Journal of General Internal Medicine*, *36*(5), 1359–1370. https://doi.org/10.1007/s11606-020-06447-0

World Health Organization: WHO. (2019, May 30). *Social determinants of health*. https://www.who.int/health-topics/social-determinants-of-health#tab=tab_1

Wright, M., Bryans, A., Gray, K., Skinner, L., & Verhoeve, A. (2013). Physical Activity in Adolescents following Treatment for Cancer: Influencing Factors. *Leukemia Research and Treatment*, *2013*, 1–7. https://doi.org/10.1155/2013/592395

Youn, N., Sorensen, J., Howland, C., & Gilbertson-White, S. (2024). Social Determinants of Health and Cancer Pain in the US: Scoping review. *Clinical Nursing Research*, *33*(5), 416–428. https://doi.org/10.1177/10547738241232018

Appendix A: Table of Results

Parameter	Estimate	SD	95% CI	χ^2	P-Value
Residual Correlations					
CRW, PD	0.091	0.035	[0.023, 0.159]	6.789	0.009
CRW, Pain	0.037	0.037	[-0.035, 0.110]	1.014	0.314
PD, Pain	-0.001	0.037	[-0.074, 0.072]	0.000	0.984
Direct Effects					
SDoH --> Pain	-0.104	0.015	[-0.135, -0.074]	45.890	<0.001
SDoH --> CRW	-0.093	0.028	[-0.147, -0.039]	11.388	0.001
SDoH --> PD	-0.100	0.033	[-0.163, -0.036]	9.357	0.002
PD --> Pain	0.078	0.023	[0.028, 0.119]	11.051	0.001
CRW --> Pain	0.100	0.025	[0.049, 0.149]	15.406	<0.001
PA --> Pain	0.060	0.029	[0.008, 0.124]	4.446	0.035
Interaction Effects					
SDoH * PA --> Pain	0.044	0.009	[0.026, 0.061]	22.456	<0.001
PD * CRW --> Pain	0.281	0.023	[0.238, 0.327]	153.397	<0.001
PA * PD --> Pain	0.035	0.016	[0.004, 0.068]	4.746	0.029
PA * CRW --> Pain	-0.203	0.020	[-0.242, -0.164]	105.692	<0.001

PA * PD * CRW --> Pain	-0.248	0.017	[-0.282, -0.216]	214.398	<0.001
Indirect Effects					
SDoH --> CRW --> Pain	-0.009	0.004	[-0.017, -0.003]	6.419	0.011
SDoH --> PD --> Pain	-0.007	0.004	[-0.016, -0.002]	4.585	0.032

Appendix B: Participant Characteristics

Participant Characteristic	Category	N	%
Total Participants		1,433	100.0
Race			
	White (reference)	1,252	87.4%
	Black	144	10.0%
	Other	37	2.6%
Age at Diagnosis			
	Average (years)	6.51	
	Range (years)	0.17 - 20	
SDoH Indicators			
	No Adverse Indicators	402	28.1%
	One Adverse Factor	415	29.0%
	Two Adverse Factors	321	22.4%
	Three Adverse Factors	212	14.8%
	Four Adverse Factors	72	5.0%
	Five Adverse Factors	11	0.8%
Educational Attainment			
	Some College	311	24.1%
	College Graduate	240	18.6%
	High School Diploma or GED	208	16.1%
	Had not Finished High School	130	10.1%

	1-8 Years of Formal Schooling	94	7.3%
	Postgraduate Education	67	5.2%
	Training after High School Other than College	45	3.5%
	Other	36	2.8%
	Missing Data	143	11.1%
Healthcare Access			
	Non-Adverse Conditions	810	56.5%
	Adverse Healthcare Access	490	34.2%
	Insurance Data Unavailable	133	9.3%
RUCA Codes			
	Metropolitan Cores	691	53.2%
	Metropolitan Areas with High Commuting into Urbanized Areas	221	17.0%
	Metropolitan Low Commuting areas	6	0.5%
	Micropolitan Areas (Core, High, and Low Commuting Zones)	193	14.9%
	Small Towns	132	10.2%
	Rural Regions	53	4.1%
	Missing Data	135	9.4%

Social and Community Context			
	Married	496	34.6%
	Cohabitating as Married	102	7.1%
	Separated	62	4.3%
	Divorced	100	7.0%
	Widowed	6	0.4%
	Single, Never Married, or Cohabitated as Never Married	668	46.6%
	Missing Data	304	21.2%
Economic Stability			
	Below $19,999	214	14.9%
	$20,000 - $39,999	289	20.2%
	$40,000 - $59,999	206	14.4%
	$60,000 - $79,999	156	10.9%
	$80,000 - $99,999	110	7.7%
	Over $100,000	130	9.1%
Physical Activity			
	Low Activity	694	48.4%
	Moderate Activity	475	33.1%
	High Activity	152	10.6%
	Missing Data	112	7.8%