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MODIFYING AN ADULT VERSION OF A CANCER SYMPTOM INVENTORY  
TO BE USED WITH CHILDREN  
WITH CANCER

by

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## **Dedication**

To all children fighting cancer.

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## ABSTRACT

# MODIFYING AN ADULT VERSION OF A CANCER SYMPTOM INVENTORY TO BE USED WITH CHILDREN WITH CANCER

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Childhood cancer is the second most common cause of death and the first cause of disease-related death among children in the United States. Each year, approximately 15,000 children and adolescents are diagnosed with cancer. Given that children with cancer experience multiple psychological and physical symptoms and functional impairments that are associated with cancer and its treatment, it is important that these symptoms and functional impairments be identified and measured. The primary aim of the present study was to develop a self-report measure that included multiple symptoms and functional impairments. This goal was achieved by modifying the adult version of an already existing measure (MD Anderson Symptom Inventory) to be used with children 8-12 years of age. The modification process was based on the results from interviews with experts, caregivers, and children to ensure that the modified measure was developmentally appropriate for children in the age range of 8-12. Upon completion of

interviews and several revisions, the final version of the measure was used to explore the initial psychometrics of the modified measure.

This study demonstrated that the modified measure (MDASI-C) is age-appropriate and children as young as 8 years old can comprehend and respond to items on the measure. Including both symptoms and functional impairments when assessing patients' responses is essential to our understanding of how cancer affects children. The MDASI-C (8-12) is a useful measure for evaluation of the severity and impairments associated with symptoms in a pediatric oncology population.

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## CHAPTER I: INTRODUCTION

Cancer is a major public health concern worldwide. Childhood cancer is the second most common cause of death and the first cause of disease-related death among children (aged 1-14) in the United States (Siegel et al., 2019). There are more than 15,000 children diagnosed with cancer each year (Center for Disease Control, CDC, 2021). More specifically, leukemia, which accounts for 28% of cancer cases, is the most common childhood cancer. Brain and other nervous system tumors account for 26% of cases and are the second most common types of childhood cancer, followed by lymphomas (16%), thyroid cancer and melanoma (9%), germ cell tumors (7%), soft tissue sarcomas (7%), malignant bone tumors (6%), sympathetic and allied nervous system tumors (5%), renal tumors (4%), retinoblastoma (2%), and hepatic tumors (1%) (National Research Council, 2013; Siegel et al., 2019).

### **Incidence, Death, and Survival Rates of Pediatric Cancer**

Each year, approximately 15,780 children and adolescents are diagnosed with cancer in the United States (American Childhood Cancer Organization, 2022), which accounts for almost 1% of all cancer cases. Since 1975, the overall incidence rate of childhood cancer has been steadily rising slightly by 0.6-0.7% per year (American Cancer Society, 2020; Siegel et al., 2019). Despite this increase, death rates as a result of childhood cancer have decreased from 6.5 (per 100,000) in 1970 to 2.3 (per 100,000) in 2016. Although there is an overall death rate reduction of 65% in children, there are still a large number of children who die from cancer each year, as it is expected that 1,050 children under the age of 15 die from cancer in 2022 (American Cancer Society, 2022).

Associated with decreased death rate, five-year survival rate in children has improved drastically from 58% (during the mid-1970s) to 85% (during 2008-2014). In

other words, 85% of children with cancer will be living at least five years after their diagnosis (American Cancer Society, 2022; Siegel et al., 2019). Furthermore, cure rates in children with cancer have improved and are approaching 80%, although cancer remains the leading cause of disease-related death in children (Jemal et al., 2006; Mogavero et al., 2020).

## **Pediatric Cancer Symptom Experience**

### ***Symptom Severity and Functional Impairment***

Despite significant improvements in cancer care and treatment, children experience multiple psychological and physical symptoms associated with cancer and its treatment. One dimension of children's symptom experience is symptom severity, measured by the patients' rating of the intensity of their symptoms. Another dimension of children's symptom experience is functional impairments, referred to as experiencing interference and dysfunction in social, academic, and other aspects of children's lives (Uestuen & Kennedy, 2009), as well as limitations in their ability to engage in daily activities (Stein & Jessop, 1990). Within the context of pediatric cancer, experiencing symptoms impacts children's functioning in different domains of their lives (Dodd et al., 2001; Robinson et al., 2009). Of note, symptoms and functional impairment may be related to cancer itself (e.g., pain from tumor) and/or affected by the toxicities of the treatment of cancer (e.g., nausea after chemotherapy; Williams et al., 2006).

### **Symptoms Experienced**

Several studies have been done to explore the most commonly experienced symptoms in children with cancer (Bradford et al., 2021, Collins et al., 2000; Williams et al., 2012). The type of cancer can sometimes define the symptoms experienced by patients. For example, brain tumors can cause increased pressure in the skull that can subsequently lead to headaches, nausea, vomiting, and blurred vision (American Cancer

Society, 2022). In addition to cancer itself, children diagnosed with cancer frequently undergo invasive medical treatments and procedures for curative purposes that often lead to experiencing multiple symptoms (Miller et al., 2011; Torres et. al., 2019). Common treatment options to address pediatric cancer include chemotherapy, surgery, radiation therapy, immunotherapy, stem cell transplant, and alternative treatments, such as herbalism, acupuncture, and neuropathy (Clarke et al., 2005). Overall studies have shown that children receiving cancer treatment experience greater numbers of symptoms than those diagnosed with cancer but not receiving treatment (Heath et al., 2010). Treatment-related symptoms may vary depending on the type of treatment (Krull et al., 2013; Nagel, 2004). Additionally, research has indicated that almost all children undergoing cancer treatment experience bothersome symptoms, and 60% have at least one severely bothersome symptom (Johnston et al., 2018). As recommended by Williamson et al. (2021), symptoms commonly reported by children diagnosed with cancer can be further discussed in three clusters of physical (e.g., nausea, vomiting, breathing, dry mouth), psychological (e.g., depression and anxiety, memory issues, sleep difficulties, drowsiness, poor appetite), and neurological (e.g., pain, fatigue, numbness and tingling in body) symptoms.

Nausea and vomiting are two of the most bothersome symptoms often reported by children with cancer when they undergo active treatment (Ho et al., 2019; Jiyeon Lee et al, 2013). Collins et al. (2000) conducted a study on 159 children with different types of cancer and found 35-50% and 12-39% prevalence of nausea and vomiting, respectively. Regarding specific treatment effects, chemotherapy-induced nausea and vomiting (CINV) is one of the most common cancer treatment side effects even when antiemetic medications have been used (Cefalo et al., 2009; Yeh et al., 2012). In this specific type of treatment, chemotherapeutic agents that circulate in the blood stimulate the

chemoreceptor trigger zone and cause acute nausea and vomiting (O'Brien & O'Brien, 2008). Dupuis et al. (2016) indicated that nausea and vomiting are experienced in nearly 70% of pediatric oncology patients undergoing chemotherapy. Nausea as a subjective experience that is characterized by a feeling of impending vomiting, can be present without the act of vomiting (Ruggiero et al., 2018). More recently, Rawat et al. (2021) conducted a study of 75 children undergoing chemotherapy and found that nausea was reported by 87% of their participants as one of the most distressing and persisting symptoms. In addition to chemotherapy, radiotherapy can lead to nausea and vomiting, depending on the treatment sites (American Cancer Society, 2017). Research has shown that children undergoing radiotherapy in their upper abdominal region and the ones undergoing whole-brain radiation are at increased risk of experiencing these symptoms (Habibi et al., 2016; Texas Oncology, 2019). Furthermore, given that use of anesthesia is a common approach in radiotherapy for children, studies have identified vomiting as a risk of undergoing anesthesia (Anghelescu et al., 2008; Seiler et al., 2001; Stackhouse, 2013). Research has also found that anticipatory nausea and vomiting (Roscoe et al., 2011), as a conditioned response, are present in approximately 25% of pediatric patients (Dupuis et al., 2014).

Children with cancer may also experience respiratory distress (Meyer et al., 2004) that could often lead to admission to pediatric intensive care unit (Haut, 2005; Leverger & Sommelet, 1999; Nazemi & Malempati, 2009). Tumor growth and space-occupying masses that lead to airway obstruction are common factors resulting in breathing difficulties in children with cancer (Tino, 2007). Shortness of breath can also be caused by vascular damage which is a common side effect of some cancer treatments (Salido et al., 2011). Additionally, depending on the degree of immunosuppression, pediatric oncology patients are at higher risk of various infectious diseases that can lead to

respiratory dysfunction (Kelly & Wheatley, 2009). For example, major infections in the first few days after chemotherapy are not uncommon (Meyer et al., 2004). Additionally, radiotherapy and surgical procedures can lead to respiratory complications (Shibasaki et al., 2008).

Furthermore, oral complications are often experienced by children diagnosed with cancer and undergoing cancer treatment. For example, changes in taste is a symptom reported by patients receiving stem cell transplant. A study by Loves et al. (2019) indicated that 45% of these children reported bothersome changes in taste, and among them, 10% reported this symptom as severely bothersome. Oral mucositis is another symptom experienced by children undergoing stem cell transplant (Ethier et al., 2012; Patel et al., 2021) and chemotherapy (Ethier et al., 2012). A study by Qingfu et al. (2019) identified the intensity, duration, and mode of chemotherapy among the main factors leading to mucositis and further oral complications. Xerostomia (i.e., dry mouth) is another symptom reported by children with cancer (Rosenberg et al., 2016). A study by Yeh et al. (2008) revealed that 42% of 144 children in their study reported dryness in their mouth as distressing. Coulson (2007) also indicated that some treatments (e.g., radiotherapy to head and neck) can cause dryness in mouth. Other studies (Chias et al., 2019; Rawat et al., 2021) also have shown that dry mouth is often one of the most frequently reported symptoms by children who are undergoing chemotherapy.

Pain is another prevalent symptom experienced by children with cancer (Collins et al., 2000; Erickson et al., 2013; Hedén et al., 2013; Poder et al., 2010). Pain can result from the disease itself. For example, in children with a tumor, there is a close association between tumor growth and pain (Moody et al., 2021). Additionally, tumors can indirectly lead to pain by obstructing bowel and bladder and by compressing blood vessels. In addition to cancer, treatments, such as chemotherapy (Ameringer et al., 2015; Baggott et



al., 2010), stem cell transplant (Ward et al., 2020), radiotherapy, and surgery (Moody et al., 2021) can also be a source of pain. In addition to pain, sensory issues are also often reported by children with cancer. Among these difficulties, numbness and tingling in hands and feet are commonly experienced by children with cancer, as some treatments (e.g., chemotherapy) can cause sensory peripheral neuropathy (Arslan et al., 2013; Beker, 2007; Beker, 2009; Smolik et al., 2018). In a study done by Walker et al. (2010), nearly 40% of children in the age range of 7 to 12 reported these symptoms.

Fatigue is also one of the most commonly experienced symptoms, which can occur at any time throughout the disease course, prior to diagnosis, during treatment, and following the completion of therapies (Wang et al., 2014). Studies have shown that 50-70% of children with cancer experience fatigue (Baggott et al., 2010; Walker et al., 2010). Berger et al. (2015) define cancer-related fatigue as physical, emotional, and cognitive tiredness, as a result of experiencing cancer, that is not proportional to one's recent activity level and causes functional impairments. Treatment approaches can also cause fatigue (Berger et al., 2015). For example, stem cell transplant (SCT) can lead to acute and long-term fatigue (Tonosaki, 2012). Results from a study done by Tomlinson et al. (2018) indicated that 82.5% of pediatric cancer patients who were transplant recipients reported bothersome fatigue. Among those children, approximately 25% reported their fatigue to be severely bothersome. Erickson et al. (2011) also measured the severity of fatigue in 20 children receiving first-line chemotherapy. Approximately 75% of children in that study reported feeling tired during the month of chemotherapy. Those children identified cognitive fatigue as the least bothersome and physical fatigue, as a result of sleep/rest disturbances, as the most bothersome. In addition to chemotherapy, other treatments (e.g., radiotherapy) often result in fatigue (Soanes et al., 2009).

Closely related to fatigue, sleep difficulties are also frequently reported by children diagnosed with cancer (Graef et al, 2016). Approximately 95% of children in Erickson et al.'s (2011) study reported sleep-wake disturbance at least once every three days. Sleep disturbances reported by those children comprised not feeling rested and alert during the day, not feeling satisfied with sleep quality, and feeling sleepy and tired during the day. Specific treatments can also lead to sleep disturbances. For example, stem cell transplant procedures (Graef et al, 2016), or undergoing anesthesia for children who receive radiotherapy (Stackhouse, 2013) can contribute to sleepiness.

Changes in appetite are another symptom frequently reported by pediatric cancer population in treatment. Johnston et al. (2018) administered a cancer symptom inventory to 302 children with cancer in the age range of 4 to 18 and found changes in appetite as the second most commonly experienced symptom, reported by 77% of children undergoing stem cell transplant. Among those children, 25% reported their symptoms to be severely bothersome. Additionally, Loves et al. (2020) conducted a qualitative study with 50 children in the age range of 4 to 18 who were diagnosed with at least one type of cancer. They found that changes in appetite (both decreases and increases) were commonly experienced by stem cell transplant recipients. They further explained that increases in appetite are associated with the use of corticosteroids following transplants and decreases in appetite were associated with factors such as co-occurring symptoms (e.g., nausea and vomiting; Pirri et al., 2013), inactivity, and hospital environment.

Cancer can also have other psychological ramifications for children undergoing treatment. Overall, chemotherapy as a treatment option can negatively affect children's psychological adjustment and emotional regulation (Wallace et al., 2013; Zhang et al., 2019). Mood disturbance and sadness are symptoms commonly reported by children undergoing chemotherapy (Baggott et al., 2012). Linder et al. (2018) found that when

sadness is present, 50% of the time, it is of moderate and greater severity. Also, extended hospital stays to complete treatment procedures and address complications lead to withdrawal (Patenaude, 1990). Subsequently, this physical isolation can contribute to increased depressive symptoms (Pot-Mees, 1989).

Cancer treatments can also be anxiety-provoking. For example, during radiotherapy, children have to be separated from their caregivers, which can cause separation anxiety and significant distress (Bucholtz, 1994; Filin et al., 2009; Pimm et al., 1997). In a qualitative study conducted by Engvall et al. (2016), children reported that they often feel sad and afraid during radiotherapy treatment. In addition to the aftermath and side effects of radiotherapy, children reported extreme difficulty managing their anxiety prior to sedation, which is necessary for some children, as well as with the mask during the procedure and fear of the machine (Angstorm-Brannstorm et al., 2015; Engvall et al., 2016; Filin et al., 2009; Scott et al., 2002). Other types of treatment can also lead to anxiety. A study completed by Meyers et al. (1994) revealed that 40% of children experience significant anxiety during hospitalization before stem cell transplant procedure. Furthermore, some surgeries that are performed while children are awake (e.g., craniotomy while awake) can create significant anticipatory and procedural anxiety (Bajunaid & Ajlan, 2015; Riquin et al., 2017). Studies have also shown fear of relapse among children undergoing surgery (Riquin et al., 2017).

### **Functional Impairments**

Functional impairment has been defined as limitations in managing life activities in multiple domains (Erickson et al., 2020). Research has shown that functional impairment is an independent construct that needs to be distinguished from symptoms (Rapee et al., 2012). In the context of pediatric cancer, children's functioning in various domains (cognitive, social, emotional, or physical) can be impacted as a result of their

disease and/or undergoing treatments (Buckner et al., 2014). Cognitive functioning is one of the areas that is often impacted by cancer and its treatment (Benzing et al., 2018). Overall, cognitive deficits experienced by children with cancer are categorized into two groups of core deficits and secondary deficits. Core deficits involve fluid reasoning, executive functions, and processing. Secondary deficits involve crystallized knowledge. Evidence suggests that having cancer is often associated with core deficits, which subsequently result in secondary deficits in cognitive functioning (Moleski, 2000). Teachers and parents describe these deficits in children as difficulties in reading, spelling, math (Conklin et al., 2008; Kaeming et al., 2004; Reddick et al., 2003), attention deficit, and social problems over time (Butler & Copeland, 2002; Mabbott et al., 2005). To monitor children's cognitive functioning, the standard of care for pediatric cancer patients is to consistently use neuropsychological evaluation (Walsh et al., 2016) especially when children experience difficulty at school.

Additionally, there is evidence that treatment methods impact cognitive functioning (Ahles & Root, 2018). For example, brain cranial radiation therapy (RT) is associated with neurocognitive impairment in children with cancer (Pierson et al., 2016), as children with central nervous system (CNS) tumors are the most severely impacted group (Winick, 2011). The cognitive deficits experienced by children with brain tumors and treatments that directly affect the brain are often due to quantitative loss of white matter (Butler & Mulhern, 2005; Correa, 2010). This may consequently result in attention and concentration difficulties, automatic shifting difficulty, poor working memory, forgetfulness, reduced information processing speed, learning difficulties, and an overall decline in intelligence (Edelmann et al., 2016; Filley, 2015; Lockwood et al., 1999; Schatz et al., 2000). Radio therapy can also place children at a higher risk of cognitive decline (Duffner, 2004; Hutchinson et al., 2017) than those who do not receive this

treatment. Rowland et al. (1984) assessed 104 children at least 1 year following their treatment, and they found significantly lower full-scale IQ on a cognitive test, as well as lower scores on achievement tests, compared to children not undergoing treatment. Given that using sedation and anesthesia for children receiving radio therapy is common, animal studies have also shown that anesthesia exposure early in life may predispose children to neurocognitive impairments (Creeley et al., 2013; Schenning et al., 2017). Although human studies have shown inconsistent results, a recent study (Banerjee et al., 2020) has shown that exposure to anesthesia and treatment duration may be associated with neurocognitive impairments in children with leukemia. The US Food and Drug Association (FDA, 2017) has also recently issued an announcement that repeated and/or lengthy use of anesthesia for children may affect their brain development.

In addition to cognitive functioning, experiencing cancer symptoms and undergoing cancer treatment impact children's social and emotional functioning. Childhood cancer has been characterized as a stressful and arduous experience, and a disruptive life event that entails negative impacts on children's and their families' social functioning and emotional well-being (Barrera et al., 2000; D'Olivo et al. 2018; Eiser & Havermans, 1994; Parsons et al., 1999; Vannatta et al., 1998; Woodgate et al., 2003). These impacts include changes in family dynamics, changes in physical appearance, disruption of school and daily routines, reduced time spent with peers, and lower levels of social support (Brand et al., 2017; D'Olivo et al., 2018; Kazak et al., 2006; Marsland et al., 2006). Associated with social and emotional functioning, adjustment problems (e.g., adjustment with the disease, Koumarianou et al., 2021; adjustment to disruptions in daily routines, Chiang et al., 2009) are among the most common difficulties experienced by not only the child, but also caregivers, siblings, and others around the child (Patenaude & Kupst, 2005; Rafii et al., 2014; Sahler et al., 1994; Woodgate et al., 2003). In a

qualitative study, one of the commonly reported functioning problems was the adjustment to disruptions in daily routines and activities, including wanting to be normal, being restricted to home, not being able to do daily activities, and missing family and friends (Hildenbrand et al. (2011). Furthermore, among other adverse social emotional consequences of childhood cancer, it can be pointed to overdependence on caregivers, anger toward health care providers and parents, and reduced treatment adherence as difficulties commonly experienced by children diagnosed with cancer (Phipps, 2006).

Treatment of cancer may also result in a decline in children's opportunity to interact with others. Children with cancer often experience enforced isolation and missed social experiences as a result of their treatment requirements. This may later result in subsequent disruption in their social functioning, especially during the acute phase of their treatment. For example, children are frequently absent from school to participate in their treatment or due to their treatment-related side effects (French et al., 2011; Vance & Eiser, 2002). Another example would be children who are immunocompromised and have to socially isolate during and after their treatment, due to the high risk of infection (Kotecha, 2020). A study by Pot-Mees (1989) compared children's social emotional functioning 6 months after stem cell transplant with their functioning pre-transplant. Results revealed that 40% of children undergoing transplant experienced increases in anxiety, depression, peer isolation, and behavioral problems (e.g., aggression) 6 months after their transplantation. These disruptions due to treatment requirements can also impact children's academic functioning. For example, recipients of bone marrow transplants are required to stay in quarantine for approximately 1-3 months to prevent infections due to their compromised immune system. During this time, they will not be able to attend school and participate in age-appropriate activities with peers, impacting their academic performance (Golomb, 2000). As School attendance is associated with

children's social emotional skills development, treatment-related limitations can also lead to declines in social emotional competence (Phipps et al., 1995).

Moreover, peers make up a large part of children's daily lives (Christiansen et al., 2015). Peers often perceive children who have cancer as more socially isolated, less physically competent, less athletically skilled, and less attractive than their healthy peers (Vannatta et al., 1998). Negative perceptions of peers about children who have cancer could disrupt their subsequent social and emotional development. Of note, school-age children are at a developmental stage in which they are becoming interested in friendship and developing a desire to belong to a group (Brand et al., 2017; Erikson, 1950), and this relationship with peers impacts how they think about and evaluate themselves.

Another predominant impact of childhood cancer treatment is reduced day-to-day physical functioning. Reduced mobility is one of the most frequently reported functional impairments (76%; Jalmsell et al., 2006). This difficulty can be due to infections, bed rest, graft vs. host disease, etc. These impacts can be more significant in specific treatments (e.g., stem cell transplant) than in other treatments (e.g., chemotherapy). For example, children undergoing transplant can experience physical difficulties (e.g., low muscle strength and cardiorespiratory issues) in the pre-transplant, peri-transplant, and/or post-transplant phases (West et al., 2014). Oswald et al. (2019) compared children with cancer with children with no cancer diagnosis and found impaired walking speed, capacity, and balance in children with a cancer diagnosis. This can directly impact children's engagement in daily physical activities (e.g., play, sports). Immobility may also lead to other complications, such as infections, which the body may be weak to overcome due to being immunocompromised. Additionally, cancer-related fatigue can impact one's physical functioning (Hofman et al., 2007). Fatigue not only affects one's ability to complete daily tasks but also impacts their willingness to participate in and

adhere to their treatment (Wang et al., 2014). Hockenberry et al. (2003) conducted a study on 149 seven to twelve-year-old children with cancer. Most of those children endorsed intense lack of energy and difficulties such as not being able to play, being tired in the morning, and having to stop and rest when walking. Another physical complication is developing oral complications, including mucositis and the pain associated with it that can impair one's ability to eat and drink (Sonis, 1993).

## **Symptom Assessment**

### ***Importance of Symptom Assessment***

Given the presence of cognitive, affective, and physical symptoms as a result of cancer and its treatment, and the impact of these symptoms on children's functioning in different domains (i.e., cognitive, social, emotional), it is important that cancer symptoms be identified and measured. In fact, symptom management begins with a comprehensive assessment of the symptom experience reported by the individuals experiencing the symptoms. Further, cancer symptoms are the most frequently reported concerns of children and adolescents (Tseng et al., 2008). Finally, several studies have indicated that frequent and accurate assessment of cancer-related symptoms facilitates the communication between the patient, clinician, and caregivers and results in better treatment outcomes (Bainbridge, 2011; Naughton and Homsy, 2002; Velikova et al., 2004; Williams et al., 2012).

### ***Barriers to Pediatric Symptom Assessment***

Even though the importance of symptom assessment has been acknowledged, there is a lack of appropriate symptom measures in children with cancer, as symptoms are often assessed through a brief history, physical examination, or a formalized pain scale in clinical oncology settings (Skeens et al., 2019). This is concerning because these methods



are either brief or focused on a single aspect of children's experience (e.g., pain), which may result in underestimation of the impacts of the symptoms. In fact, several researchers have referred to the lack of appropriate symptom assessment as one of the main challenges in the process of cancer care (Bainbridge et al., 2011; Cleeland, 2000; Naughton & Homsy, 2002; Wang et al., 2004). For instance, several studies have indicated that physicians and health care providers consider a lack of routine and adequate assessment as the most important influencing factor in symptom management (Naughton & Homsy, 2002; Von Roenn et al., 1993).

Considering the subjective nature of symptom assessment, self-reports have been recognized as the most appropriate method of symptom assessment (McColl, 2004). However, there are general concerns with children completing self-report measures, even if there were appropriate scales to measure symptoms and adverse effects of cancer. There are several developmental reasons why symptom assessment via self-report in children is difficult. First, children's limited ability to report their symptoms and experiences is associated with their language development (Linder, 2008). Younger children often give less expansive responses to questions about their symptom experiences and health than older children (Hinds et al., 2004). Associated with their limited language skill to express themselves, children's distressing symptoms that are less observable are at high risk of being unrecognized (Linder, 2008).

Second, children's neurocognitive developmental stage is associated with their ability to recall and rate their symptoms. Although a review of research indicates that children as young as five years of age can respond to items on self-report measures (Linder, 2008; Varni et al., 2007), recall period is an area that needs to be considered. Collins et al. (2000) identify school-age children (8-12 years old) to have potential

difficulty with recall period of one week, which is used in most instruments, and recommend using a shorter period (past two days).

Third, children's developmental stage is also associated with their cognitive appraisal and their ability to form an opinion about (i.e., perceive) symptoms they experience. More specifically, before becoming distressed by cancer-related symptoms, their symptom experience has to be cognitively evaluated as potentially distressing (Algren, 2007). Compared to adolescents, younger children's tendency to be more present-focused and think more concretely (Lazarus & Folkman, 1984) may affect their perception of illness and its negative consequences. For example, in a study by Hockenberry-Eaton et al. (1998), it was shown that children, compared to adolescents, focused more on physical, rather than mental symptoms, and were able to identify fewer causes for their cancer-related distress.

Fourth, some of the existing types of symptom assessment instruments have been shown to provide unreliable results because they are not age-appropriate. For example, numerical rating scales (NRS) require children to have developed number concepts and the ability to express themselves in quantitative terms. Similarly, adjective scales require development of verbal fluency at a high school level (Von Baeyer, 2006). In addition, there is no reliable information available about the youngest age for which NRS can be used (Von Baeyer, 2009). Finally, each of the existing versions of the face scales, as the most commonly used type of scale, has disadvantages (e.g., limited to specific ethnic groups, infection control issues, anchor effects) and is not ideal for children (Von Baeyer, 2009).

### ***Lack of Specific Measures Related to Childhood Cancer***

Despite these barriers to general symptom assessments in children, some assessments have been developed; however, there is still a lack of assessments specific to

children with cancer. With regard to measures specifically developed to be used in pediatric oncology settings, there are a few scales that measure cancer or treatment effects; however, the unique and multifaceted experience of children with cancer has often been captured by using single-item measures (Huang et al., 2014; Naughton & Homsy, 2002; Redd et al., 1987; Tyc et al., 1993). Further, although the use of self-reports for symptom screening within the adult oncology setting has been well established in the literature (Cleeland et al., 2000; Ganz et al., 1995; McCorkle & Young, 1978; Rhodes et al., 2000; Tucci & Bartels, 1998), few studies have attempted to explore cancer symptoms experienced by children.

Available pediatric cancer symptom assessment measures include Memorial Symptom Assessment Scale 7-12 (MSAS, Collins et al., 2002), Therapy-Related Symptom Checklist-Children (TRSC-C, Williams et al., 2012), Play Performance Scale for Children (PPSC, Lansky et al., 1985), Rotterdam Symptom Checklist (RSCL, Eiser et al., 1995), Patient Reported Outcomes Measurement Information System (PROMIS, Menard et al., 2014), Perceived Symptom Severity Scale (PSS, Wu et al., 2014), and Symptom Screening in Pediatrics Tool (SSPedi, Tomlinson, et al., 2014). Each measure has limited advantages and several disadvantages. Advantages include the measurement of multiple symptoms (e.g., MSAS, SSPedi), multidimensionality (e.g., assessing frequency, severity, distress in MSAS), and measuring the impacts on functioning (e.g., PPSC). Some of these measures are also advantageous because they are specifically designed to be used in pediatric oncology settings (e.g., PPSC, RSCL).

Regarding the limitations of these measures, some of them assess a limited number of symptoms (e.g., MSAS) or one dimension of a symptom (e.g., PPSC, PSS), which does not capture the comprehensive picture of children's experience of the symptoms. In addition, some measures were developed by including only children in the

scale development process (e.g., MSAS), while it is also recommended to consult with experts, as well as caregivers (Devellis, 2017). Further, some measures (e.g., MSAS) do not address the impact of experiencing the symptoms on different aspects of children's lives (e.g., social relations, school performance, sports). Finally, the length (TRSC-C) and formatting of some of the measures (e.g., MSAS) are also limitations. More specifically, in some measures, the instrument is too long or the format is too complex and difficult for younger children to complete.

Some of these measures are not limited by their content, but they are limited by who completes the assessment. More specifically, some measures (e.g., PPSC, RSCL) ask only informants (e.g., caregivers, clinicians) to rate children's symptom experience, while it has been indicated that children as young as five years of age are able to report their symptoms (Linder, 2008). In addition, results from previous research have indicated that clinicians would like to include children's perceptions in the treatment process since symptoms are subjective and private experiences of individuals (Eiser et al., 1999). Research has also shown that parents experience difficulty in reporting their children's distress, especially their psychological distress (Eiser et al., 1995).

### **Literature Gap and Focus of the Present Study**

Since Engel's (1977) proposal more than four decades ago to utilize biopsychosocial model in clinical settings to address chronic illnesses, the effective integration of the approach into everyday health care practices has not happened yet (Lane, 2014). Symptom assessment has been a priority in adult cancer management and treatment, and several scales have been developed and validated to be used in the adult oncology setting (Boer-Dennert et al., 1997; Carelle et al., 2002; Griffin et al., 1996). However, in pediatric oncology settings, symptom assessment is rarely a part of routine cancer care (Cleeland, 2000), mainly due to limited research on the symptom experiences

of young children (Linder, 2008). Research on symptom assessment in pediatric cancer is still in the early stages with increasing efforts to design developmentally appropriate measures to capture thorough experiences of children with cancer (Linder, 2005).

As mentioned before, due to the subjective nature of symptom experience, children are considered to be the best judges of their own experiences (Docherty, 2003; McColl, 2004; Tomlinson et al., 2014). Thus, the use of developmentally appropriate self-reports has been recommended (Linder, 2008). However, despite the evidence that indicates high and ongoing symptomatology in children with cancer, there is no widely accepted self-report multiple symptom assessment tool in pediatric oncology settings (Huang et al., 2014). The most commonly used symptom assessment tools emphasize individual symptoms (e.g., pain, fatigue) and include numerical rating with verbal or pictorial descriptive, color scales, visual analogue scales, faces, or Likert scales (Zeltzer, et al., 1988; Zeltzer & LaBaron, 1986). To address the paucity of developmentally appropriate multi-symptom assessment tools that explore multiple dimensions of children's experiences, it is recommended to consult experts and actively include children and caregivers in the process of measure development (DeVellis, 2017). It has also been stated that because symptom experience is a subjective experience, self-report would give children an opportunity to voice their concerns, which may remain unrecognized if only rated by caregivers and/or health care providers (Linder, 2008).

### **Focus of the Present Study**

The present study closes the gap in research by addressing the limitations in the available literature, as well as in the already developed measures in the oncology setting. Given the subjective nature of a child's experiences with cancer and their limitations when they report these symptoms, the present study captures more specific features of children's symptom experience, especially those children who may struggle

developmentally and cognitively with accurately reporting their symptoms (children 8-12 years old). Thus, the present study develops a self-report measure that includes multiple symptoms and explores different dimensions of the symptoms, such as symptom presence, severity, and functional impairment (McColl, 2004; Steen et al., 1996).

Although the aforementioned purpose was the main goal, there is also a secondary goal. Currently, MD Anderson has an adult version of symptom inventory for cancer patients. However, they wanted an adaptive measure that could be used with children. Thus, the secondary goal of the present study is to modify the adult version of an already existing cancer symptom inventory (MD Anderson Symptom Inventory, MDASI, Cleeland, et al., 2000), so it could be used with children 8-12 years of age. According to Hennessy and Kind (2002), using adult measures with children may not yield adequate information, if the language and concepts in the measure are not understood by children. Thus, the present study aims to develop the children's version of the MDASI for patients in this age range. Professionals at MD Anderson wanted the original MDASI questions to be retained in the child version of the measure (MDASI-C 8-12); however, they requested that the measure be modified to ensure that children could understand and accurately complete the measure. This modification includes making the questions developmentally appropriate, using age-appropriate language, utilizing appropriate visuals, if necessary, and including children, as well as caregivers and experts in the process of measure modification (DeVellis, 2017; FDA Guidance, 2006; Patel et al., 2016).

With regard to the significance of the present study, the final version of the MDASI for Children, who are in the age range of 8-12 (MDASI-C 8-12) will have the following functions: serving as a symptom checklist, measuring symptom severity and functional impairments (interference), providing covariate measures for research,

enabling the collection of similar data in children and adults for comparative studies, and measuring treatment outcomes used in both research and clinical works.

## CHAPTER II:

### METHODS

#### **Original Scale and Professional Needs**

##### ***Original Scale***

*The MD Anderson Symptom Inventory (MDASI)* is a self-report measure that assesses the presence and severity of 13 core symptoms and six areas of interference with the patients' daily functioning in multiple aspects of their lives (see Appendix A for the MDASI; Cleeland et al., 2000; Cleeland et al., 2013). The core symptoms were recommended by the National Cancer Institute to be assessed in measures used in oncology settings with the purpose of better understanding treatment efficacy and facilitating cross-study comparisons (Reeve et al., 2014). The MDASI core symptoms are the symptoms with high prevalence and clinical relevance across cancer trials (Cleeland et al., 2013). The original MDASI has been validated for use across multiple cancer diagnoses (Armstrong et al., 2010; Fadol et al., 2008; Gning et al., 2009; Jones et al., 2014; Mendoza et al., 2011; Mendoza et al., 2013; Rosenthal et al., 2007; Sailors et al., 2013; Wang et al., 2010). The severity of each MDASI symptom and the level of interference with the patients' daily functioning is rated on a scale of 0 to 10, with 0 meaning symptom not present or no interference, and 10 meaning symptoms being as bad as it can be imagined or complete interference. Furthermore, the MDASI can be administered through various media, including paper and pencil, in-person interview, telephone systems, and electronic versions (Williams et al., 2018).

**Psychometric Properties of the Original MDASI.** The MDASI has been widely used in oncology settings for adult patients with diverse cancer diagnoses and has proved to have appropriate sensitivity, reliability, and validity to measure symptom severity and



symptom interference among cancer patients. MDASI has demonstrated sensitivity to both disease severity and treatment status (Anderson et al., 2007; Cleeland, 2000).

Regarding the validity of the MDASI, construct validity was established by factor analysis, which revealed a two-factor structure (general symptoms factor and gastrointestinal symptoms factor both in the symptom severity items). Concurrent validity was examined by correlating MDASI scores with the scores of the Short Form 12 Version 2 (SF12V2), the Eastern Cooperative Oncology Group Performance Scale, and the New York Heart Association Classification (Cleeland et al., 2000). Furthermore, known group validity was established by comparing MDASI scores between patients with good and poor performance both in their symptom severity and symptom interference (Fadol et al., 2008), between patients undergoing treatment and those not undergoing treatment, and between inpatients and outpatients.

Regarding the reliability of the MDASI, the scale and subscales show good internal consistency, with the Cronbach alpha being .85 for the general symptoms, .82 for the gastrointestinal symptoms, and .91 for the interference items (Cleeland et al., 2000). Furthermore, the test-retest reliability was .83 for the symptom severity composite score and .84 for the interference items composite score over a one-day interval.

### ***Professional Needs***

A team of professors at MD Anderson (including those that developed the original MDASI for adults) requested that the MDASI be redesigned to be used with children ages 8–12. The team at MD Anderson requested a child version of the MDASI to be developed by modifying the adult version of the measure (MDASI) and maintaining the content of each question.

## **Modification of the Original Scale**

To modify the original scale, there was a 4-step process, including initial revision of the original scale (Step 1), interviews with experts resulting in responsive revisions (Step 2), interviews with caregivers resulting in responsive revisions (Step 3), and interviews with children resulting in responsive revisions (Step 4). Then, the final version of the revised scale was filled out by several children (ages 8-12) to examine the initial psychometric properties of the modified measure.

### **Step 1: Initial Modification of the Original MDASI.**

In the first step of the study, the researcher, with the help of a pediatric psychologist and researcher, revised the original measure to make it developmentally appropriate for 8–12-year-old children. To make the measure developmentally appropriate, modifications included changing the language of the measure, providing examples and explanations in the instructions, providing practice items, writing the keyword in each item in bold font, and adding a face scale along with descriptors to the Likert scale. The format and content of the items remained consistent throughout the measure and only the symptom (e.g., pain, breathing) or area of functioning (e.g., walking, relationship with others) changed in each item. Thus, the first draft of the MDASI for Children (MDASI-C) was parallel to the original MDASI in terms of the number and order of the items.

### **Steps 2-4: Experts, Caregivers, and Children’s Interviews**

After the initial draft was completed, there were three more steps to the development of the measure. The methods for each step were similar, and only the people who were interviewed changed (experts, caregivers, and children). The methods for steps 2-4 included the identification of participants for each group of interviewees, the review of the scale by the participant, and then the interview regarding feedback about the scale

with each participant. After all interviews for each group of interviewees were completed, the researcher modified the measure based on the feedback. For each step, a new group of interviewees was sent the most recent version of the measure. It should be noted that each group of interviewees was recruited differently, and the number of participants differed by population.

**Identification of Experts.** Ten experts were identified through personal contacts of the faculty sponsor, the student researcher, and their professional colleagues. These experts were physicians or psychologists that had expertise in the area of symptom experience, child development, or child assessment. Inclusion criteria for the experts included training and professional experience in the field.

**Identification of Caregivers.** Overall, 35 caregivers participated, including seven caregivers for 8-year-olds, nine caregivers for 9-year-olds, six caregivers for 10-year-olds, six caregivers for 11-year-olds, and seven caregivers for 12-year-olds. These caregivers were identified through personal contacts of the faculty sponsor, the student researcher, and their professional colleagues. In addition, caregivers who were students at the University of Houston-Clear Lake (UHCL) were recruited through the participant pool. Inclusion criteria for the caregivers included having at least one child in the age range of 8 to 12. Having a child experiencing cancer-related symptoms was not an inclusionary criterion for caregivers, because caregivers were asked to assist the researcher to explore whether the format, language, structure, and visuals used in the questionnaire were appropriate and understandable for children aging from 8 to 12 years old.

**Identification of Children.** Overall, 29 children participated, including five 8-year-olds, eight 9-year-olds, five 10-year-olds, five 11-year-olds, and six 12-year-olds. These children were identified through personal contacts of the faculty sponsor and

student researcher. In addition, children whose caregivers were UHCL students were recruited through the participant pool. Inclusion criteria for the children included being in the age range of 8-12. Experiencing cancer-related symptoms was not an inclusion criterion for children, because they were asked to assist the researcher to explore whether the overall format, language, structure, and visuals used in the questionnaire were appropriate for children aging from 8 to 12 years old.

**Recruitment Procedure.** Once the participants for each group were identified, they were contacted via email and asked to participate. Once they agreed to participate, a consent form and an assent form for children were sent to them via email. A waiver for documentation of informed consent (i.e., no signature obtained from the participant) was requested, since the project presented no more than minimal risk of harm to participants and involved no procedures for which written consent is normally required outside the research context. Additionally, participants were asked to agree to waive their signature so that their responses were completely anonymous. The researcher provided a written explanation in the consent form about the research project to volunteering participants.

**Interviews Procedure.** Upon receipt of the consent form, participants who agreed to participate in the study notified the researcher to schedule a time for the interview. The most recent draft of the modified MDASI-C was sent to these participants via email at least one day prior to the interview day. The participants were encouraged, but not required, to briefly review the measure before the scheduled interview. The interview with experts was either via telephone or face-to-face depending on their preference and availability. All the interviews with caregivers and children were via telephone. The interviews took 15-20 minutes (see Appendix B for Questions Used for the Interview- Experts, Appendix C for Questions Used for the Interview- Caregivers, Appendix D for Questions Used for the Interview- Children).

For the caregiver and child interviews, questions were asked about their child's and their own demographics. All participants were asked open-ended questions (Lasch et al., 2010; Turner et al., 2007) about their thoughts and feedback about the instructions, items, response options, language of the questionnaire, layout, and length of the questionnaire. Participants were also asked about their suggestions to improve the measure. Experts were asked more specific questions related to children's developmental stage, such as the appropriateness of the recall period in the questionnaire and the extent to which the questionnaire can help children communicate about their symptoms. Experts were also asked to provide feedback about the inclusiveness of the questionnaire in terms of overall symptoms experienced by children with cancer. Finally, experts were asked if any symptoms or areas of impairment were under or over-represented.

In addition to open-ended questions, all participants were asked to rate some features of the questionnaire on a scale of 1 to 5, with 1 meaning not appropriate and 5 meaning very appropriate for the age range of 8-12 years old. These features included the clarity and appropriateness of instructions, items, response options, and overall language of the measure for 8–12-year-old children. Participants also rated the appropriateness of the layout and length of the measure. Experts were asked to rate some more specific areas, such as children's ability to rate their symptoms over the last 24 hours and the extent to which the measure includes diverse aspects of symptoms experienced by children who have at least one type of cancer. Finally, experts were asked to rate how much the questionnaire reflects the symptoms experienced by children suffering from cancer.

**Data Analysis Procedure.** During the interviews, the researcher recorded the responses on a word document without any identifying information. Regarding the number of caregivers and children in each age range, the researcher stopped interviewing

once the data reached saturation point. The term saturation is often used in qualitative research and refers to the situation when no additional data are being found, and as a result, collecting more data is unnecessary (Saunders et al., 2018). Upon completion of the interviews, responses to open-ended questions gathered during interviews were qualitatively analyzed to determine whether there were any patterns in the data that could help the modification process of the measure.

In addition to qualitative analysis, descriptive statistics were calculated to describe participants' ratings. The caregivers and children rated 10 items and the experts rated 13 items about different aspects of the measure (instructions, questions, response options, overall language, use of the measure for children, content, layout, and length of the measure). For each group of participants (i.e., experts, caregivers, children), the mean ratings for each item were calculated. Average rating of 3 and above on each item indicates that a specific domain of the measure (e.g., instructions) is appropriate for children in the age range of 8-12. Average ratings below 3 indicate that the researcher needed to revise that specific aspect of the measure (e.g., instructions) to make it more appropriate to be used with children in this age range.

After a thorough review of the data obtained in each step, the scale (MDASI- C) was revised according to the qualitative and quantitative feedback, and that version was used in the next step. For example, once the revisions were made according to experts' feedback, the revised version was sent to the caregivers. Then, once the revisions were made according to caregivers' feedback, the revised version was sent to the children. Finally, the researcher revised the scale (MDASI- C) according to the children's qualitative and quantitative feedback, and this version (see Appendix E for the MDASI-C 8-12) was the final version that was used in the pilot phase, where initial psychometrics of the measure were developed.

## **Pilot Phase: Development of Initial Psychometrics**

### ***Participant Recruitment and Administration***

Upon completion of the interviews and several revisions, the final version of the measure (MDASI-C 8-12) was created and used for the pilot study. To pilot the survey, 50 children in the age range of 8 to 12 were identified through convenient and snowball sampling. Inclusion criteria for these children included being in the age range of 8-12. Experiencing cancer-related symptoms was not an inclusion criterion for children.

Once children were identified, their caregivers were sent an email with a brief explanation about the study and a Qualtrics link that included a consent form for caregivers and an assent form for children. Participants were able to use the link on any type of electronic device (e.g., laptop, phone). Once the participant clicked on the link, they were presented with the consent form and the assent form for the child. If the participant agreed to participate, they clicked on the Next button to continue and began the study. On the first page, participants answered four demographic questions about the child's age, grade, gender, and ethnicity. If the participant chose to continue, they clicked on the Next button at the end of the page. On the second page, participants were presented with the MDASI-C (8-12) measure that consists of 13 symptom severity items and 6 symptom interference items. Participants had to scroll down to read the instructions and answer the items. To answer each item, the participant had to use the dropdown menu at the end of each item to insert their rating. At the end of the survey, participants clicked on the Next button to submit their responses. All items on the survey were set on forced choice response type. Thus, participants had to answer all items to be able to submit the survey. When participants submitted their responses, they were given an option of clicking another link to provide the researcher with their email address on a separate page while their responses remained anonymous. If they were selected as one of

the three winners, they were emailed a 10-dollar electronic Amazon gift card. Throughout the survey, the children could either read and answer the items themselves, or they could ask for assistance from adults.

### ***Initial Psychometrics for MDASI-C***

**Descriptive Statistics.** Means, standard deviations, and frequencies were calculated for demographics, including age, gender, education level, and ethnicity. In addition, descriptive statistics were calculated to describe the results of the questionnaire. Total mean and standard deviation of each item was calculated. To understand differences across age groups, one-way ANOVAs were conducted to determine whether there were any differences across children in different age ranges in terms of their scores in symptom severity and symptom interference.

**Psychometric Analysis.** Exploratory factor analysis was conducted to determine the underlying factor structure. Internal consistency reliability was calculated by using Cronbach  $\alpha$  coefficients for the symptom severity (first 13 items) and symptom interference items (last 6 items). The criterion for a good internal consistency (reliability) requires a Cronbach  $\alpha$  value of 0.70 or higher (Nunally & Berstein, 1994 as cited in Mendoza et al., 2019). Further, to determine whether each symptom contributed to its factor, each item in each factor was deleted in turn and Cronbach  $\alpha$  coefficients were recalculated. If the coefficients were consistently similar to the overall coefficient for that factor, it was concluded that the item contributed to the factor and should remain in its group (Li et al., 2017).



## CHAPTER III:

### RESULTS

#### **Step 1: Initial Modification of the Adult Version of MDASI**

The initial task involved modifying the original adult version of the MDASI measure in a way that was developmentally appropriate for 8-12-year-old children. This modification included changing three main components of the measure (i.e., instructions, items, response options).

Modification of the instructions included using developmentally appropriate language (e.g., what number would you give it instead of rate how severe your symptoms have been), providing synonyms for difficult keywords (e.g., body problems or symptoms), breaking the instructions into smaller pieces with shorter sentences, checking for understanding (e.g., do you know what 24 hours is?), providing explanations (e.g., 24 hours is one day), providing an opportunity to practice before answering the items.

Modification of the items included reminding children in each item to think about the last 24 hours when answering questions (Again, I want you to think about the last 24 hours). Additionally, revised items reminded children to think about each symptom at its worst (e.g., Think about when the pain was the worst. When it was at its worst, what rating would you give it?). Furthermore, developmentally appropriate words for symptoms, as shown in Table 1, were used in the modified version. Finally, modifications of response options included adding a combination of numbers (0-10), faces, colors, and descriptors for 0s and 10s in each item.

Table 1.

*Modification of the Wording of Symptoms*

Item	Wording of symptoms in the original scale	Wording of symptoms in the modified scale
Symptom Severity		
1	Pain	Pain
2	Fatigue/tiredness	Tiredness
3	Nausea	Stomach pain
4	Disturbed sleep	Trouble sleeping
5	Distressed (upset)	Upset
6	Shortness of breath	Hard time breathing
7	Remembering things	Hard time remembering things
8	Lack of appetite	Not feeling like eating
9	Drowsy (sleepy)	Sleepy
10	Dry mouth	Dryness in your mouth
11	Sad	Sad
12	Vomiting	Throw up
13	Numbness or tingling	Numbness or tingling on your body
Symptom Interference		
14	General activity	Daily activities
15	Mood	How you felt
16	Work	School work and chores
17	Relations with others	Friendships and family relations
18	Walking	Walking
19	Enjoyment of life	How you like life and living

**Readability Statistics**

Results indicate that the Flesh-Kincaid Grade Level slightly increased in the revised child version. The grade level is calculated based on the length of the words and sentences. Thus, using words with fewer syllables and shorter sentences will improve readability level. However, longer sentences were used in the revised child version to provide children with more context and reminders to only think about their symptoms within the last 24 hours (e.g., Again, I want you to think about the last 24 hours. Think about when you were sleepy. When you were the sleepest, what rating you would give

it? vs. feeling drowsy at its worst). Furthermore, although longer sentences were used in the revised child version, they were repeated throughout the questionnaire. In other words, all the items in both symptom severity and symptom interference sections were worded the same except for the specific words for symptoms or symptom interferences.

## **Step 2: Expert Interview**

### **Participants**

Of the 14 experts contacted, 10 (71%) agreed to participate in the interview. Of the 10 experts, 2 (20%) were developmental psychologists, 2 (20%) were pediatric psychologists, 5 (50%) were clinical child psychologists, and 1 (10%) was a pediatrician.

### **Qualitative Data Analysis**

**Instructions:** During interviews, experts noted instructions were mostly problem-focused and negatively worded and suggested using neutral language. For example, one expert said, “use a less negative word.” A few experts also suggested using simple bullet points instead of using multi-level bullets. In order to ensure that children understand the meaning of the keywords/concepts (e.g., 24 hours, symptoms, interfere), some experts suggested checking for understanding and providing an explanation for those words. Furthermore, a few experts stated the example item was helpful and suggested keeping that item. Additionally, most experts suggested simplifying the language, and one expert suggested ensuring children know they may not have had some of these symptoms in the past 24 hours.

**Response Options:** To improve/revise the response options, some experts noted the number options, as shown in Figure 1 below, could be confusing to children, as some (0, 2, 4, 6, 8, 10) have colored circles around them and some do not (1, 3, 5, 7, 9). They suggested unifying the format. A few experts also indicated that “very very -----” may not be an accurate descriptor for the highest severity of symptoms and suggested using “more

----- than you can imagine” as a descriptor for the highest severity (i.e., 10). Most experts also indicated that the combination of colors, faces, numbers, and descriptors for points 0 and 10 was helpful and recommended keeping these aspects in the next version of the questionnaire.

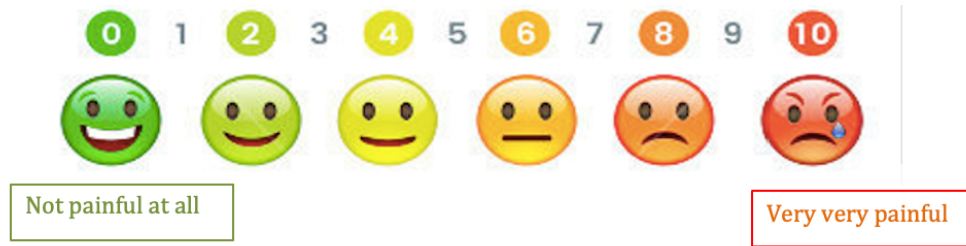


Figure 1.

*Response options in the version that was sent to experts*

**Symptom Severity Items (1-13):** A few experts noted that it was not clear how children should respond to items (verbally, pointing, writing), and they suggested specifying response modality. Experts also suggested revising the wordings of some of the items. For example, they suggested changing “stomach pain” to “upset stomach” in item 3 to refer to nausea, rather than pain. Additionally, in item 9, they suggested changing “sleepy” to “sleepy during the day” to refer to drowsiness. They also suggested changing the wordings of some of the descriptors. For example, in item 8, they suggested changing the 0 descriptor from “I could eat food as much as I wanted” to “no problems eating at all” to indicate lack of appetite.

**Symptom Interference Items (14-19):** Some experts suggested including examples in some items (e.g., for the item asking about daily activities). Most experts also suggested simplifying the items (e.g., changing “your friendship and family relations” to “relationships with others”).

## **Quantitative Data Analysis**

Experts rated 13 items about multiple aspects of the measure on a scale of 1 to 5. Means and standard deviations of their responses to each question were calculated. Overall, a mean rating of 3 or less was used as a cutoff to indicate that a specific domain (e.g., instructions) needed to be revised/modified to be more developmentally appropriate for 8-12-year-old-children. Overall, none of the means of the questions were lower than a 3; thus, in general, the experts indicated the measure was clear, developmentally appropriate, and accurate or reflective of what children experience.

### **Step 3: Caregiver Interview**

#### **Participants**

Thirty-five caregivers participated, and 6-9 caregivers were interviewed for each of the children's age groups (8, 9, 10, 11, and 12) that the assessment was targeting. With regard to gender, 45.7% (n=16) were females and 54.3% (n = 19) were males, and the mean age was 33 years of age (range = 21-45). Regarding caregivers' education level, 14.3% (n = 5) had associate degree, 40% (n=14) had bachelor's degree, 37.1% (n=13) had master's or doctoral degree (PhD and MD), and 8.6% (n=3) decided not to report the education level. Regarding caregivers' ethnicity, 57.1% (n=20) were White/Caucasian/European American, 11.4% (n=4) were Hispanic/Latino, 11.4% (n=4) were Black/African American/African, 2.8% (n=1) were Asian, and 17.1% (n=6) were from other ethnicities.

#### **Qualitative Data Analysis**

**Instructions:** During interviews, most caregivers noted instructions were straightforward, easy to understand, and a good way to orient their children to the questionnaire. They suggested to keep definitions (e.g., interfere), explanations (e.g., 24

hours), and a combination of faces and colors. For example, one caregiver said, “instructions are very good and help the child understand what the rating scale is about.”

**Items:** Most caregivers noted that the items were clear, understandable, and appropriate for their children. They suggested to keep consistency in wording and emphasis on one symptom in each item. For example, one caregiver said, “I like that you have bolded the keywords.” Some caregivers also stated that it is helpful to remind children that they only need to respond about the past 24 hours. For example, one caregiver said, “I like how in each question there is a reminder for the last 24 hours.” A few caregivers suggested adding an example or explanation for some items. For example, one caregiver suggested adding an explanation for item 13 (numbness and tingling) by adding a phrase like “like your arms and legs falling asleep.” One caregiver also suggested to ask either about chores or schoolwork in item 16 as symptoms may impact these two areas differently. A few parents also suggested emphasizing that they only need to think about the last 24 hours. For example, one caregiver said, “add the word only in the instructions.”

**Response Options:** Most caregivers noted the combination of colors, faces, numbers, and descriptors make it easy to understand for children and help them answer the questions accurately. A few parents noted that some components of the response options (e.g., faces, colors) are similar to other scales their children have filled out and this familiarity helps children better understand the task. Finally, a few parents suggested to remove the circles around numbers and only use numbers with matching colors to faces. Some parents also suggested to remove the tear drop from face 10 as having severe symptoms may not always lead to crying.

**Other areas:** Most parents noted that the overall language of the questionnaire is easy to understand for their children. Regarding the overall layout of the questionnaire,

most caregivers noted that having response options after each item is helpful. Regarding the length of the questionnaire, some caregivers noted that although it seems lengthy and time-consuming, “it goes fast” because of the repetitions in each question and having only three questions on each page.

### **Quantitative Data Analysis**

Results from descriptive statistics of caregivers’ ratings of different aspects of the measure revealed that the caregivers rated all aspects above a 4 for each aspect. In fact, none of the ratings were below 4.1. More specifically, caregivers indicated that the instructions, items, response options, and overall language of the questionnaire are clear and developmentally appropriate for their children and peers their age. Results also indicated that the measure is appealing and of appropriate length.

### **Step 4: Children Interview**

#### **Participants**

Of the 29 children recruited, 17.2% (n=5) were 8 years old, 31% (n=9) were 9 years old, 17.2% (n=5) were 10 years old, 17.2% (n=5) were 11 years old, and 20.1% (n=6) were 12 years old. Of the 29 children, 44.8% (n=14) were males and 55.2% (n=16) were females.

#### **Qualitative Data Analysis**

**Instructions:** During interviews, most children noted that instructions were clear and easy to understand. Some children noted that examples and explanations (e.g., 24 hours, interfere) helped them understand the words and how to answer the questions. For example, one child said, “I didn’t actually know what interfere means but now I do.” Some children also stated that the instructions were easy for them. A few children stated that the first instruction was lengthy but helpful to orient children to the questionnaire. For example, one child said, “it had a lot of words, but I think it was needed.” A few

children suggested adding an example of using the word “interfere” in a sentence in part 2 instruction.

**Items.** Most children noted that they understood the words/phrases used for symptoms and interference in each item (in bold). For example, one child said, “bolded fonts help me focus better.” Some children noted that the items are lengthy and repetitive and suggested making them shorter. For example, one child said, “I think that it was annoying, it kept on saying again remember the past 24 hours” and another child said, “too wordy, too much repetition.” For item 14 (interference with daily activities), some children suggested removing “sports” as an example of daily activities and to replace it with another activity that most children would do on a daily basis. For example, one child said, “playing sports may be a daily activity for some people not for all.” Another child said, “use watching TV instead of sports” and another child said, “add take a bath.” For item 17 (interference with their relationships with others), some children suggested to specify relationships by including examples. For example, one child said, “use buddy or friend to make it clear” and another child said, “add family and friends.”

**Response Options.** Most children noted that the combination of faces, colors, and numbers helped them better understand the task and rate their symptoms. Some children also stated that they were familiar with this combination and that helped them understand the task better. For example, one child said, “faces and colors help because I’m used to these questionnaires” and another child said, “they’re like what they ask at school.” All children understood the concept of the scale and the reason there are only two descriptors at 0 and 10 points. One child said, “0 means nothing and 10 means the most possible so it can’t be more than that.” Most children also stated that two descriptors are enough.

**Other areas.** Most children indicated that the overall language of the questionnaire is simple, clear, understandable, and specific. One child said, “It’s not



super complex. It is simple enough that a kid would know it unless a kid with cancer hasn't been able to go to school then they may have a more difficult time understanding things.” Additionally, most children like the overall appearance and structure of the questionnaire. One child said, “it looks really neat and organized” and another child said, “three questions in each page looks persuasive, pretty fun to answer” and another child said, “it catches kids’ attention because it’s colorful.” Regarding the length of the questionnaire, most children noted that although it looks long, it is manageable because the item structure and response options are the same for all questions and they only need to focus on one symptom or interference in each item. For example, one child said, “It's a moderate size, not super short, but it doesn't go on forever.”

### **Quantitative Data Analysis**

Descriptive statistics analysis of children’s ratings of different aspects of the measure revealed that the children rated all aspects above a 4. In fact, none of the ratings were below a 4.3. More specifically, children indicated that the instructions, items, response options, and overall language of the questionnaire were clear and developmentally appropriate for themselves and peers their age. Results also indicated that the measure is appealing and of appropriate length.

### **Pilot Phase: Development of Initial Psychometrics**

Upon completion of the interviews and several revisions, the final version of the measure (MDASI-C (8-12)) was created and used for the pilot study.

### **Participants Demographics**

Of more than 100 caregivers contacted through convenient and snowball sampling, 72 consented for their children to participate in the study. Of those children, 50 assented and returned a completed MDASI-C (8-12). Participants' demographics are described in Table 2.

Table 2.

*Demographics of Children (N = 50)*

	<i>Number</i>	<i>%</i>
Age		
8 years old	10	20
9 years old	10	20
10 years old	10	20
11 years old	12	24
12 years old	8	16
Gender		
Male	21	42
Female	28	56
Prefer not to say	1	2
Ethnicity		
Hispanic	6	12
White	38	76
Black/African American	5	10
Asian	1	2

## Descriptive Statistics for Survey

Overall, the mean and standard deviation of each item is presented in Table 3.

Table 3.

*Descriptive Statistics of MDASI-C (8-12) Items Rated by Children (N = 50)*

Items	<i>M</i>	<i>SD</i>
Symptom Severity Items		
1- Pain	1.96	1.77
2- Tiredness	3.14	2.59
3- Upset stomach	1.84	2.04
4-Trouble sleeping	2.32	1.97
5- Upset	3.18	2.71
6- Hard time breathing	1.58	1.27
7- Hard time remembering things	2.02	1.54
8- Not feel like eating	2.08	2.03
9- Sleepy during the day	2.36	1.98
10- Dryness in mouth	1.86	1.86
11- Sad	2.68	1.86
12- Throw up	1.12	0.48
13 numbness or tingling on body	1.38	1.04
Symptom Interference Items		
14- Daily activities	1.61	1.28
15- How you felt	2.38	1.82
16- Schoolwork and chores	2.00	1.88
17- Relationships with others	1.64	1.66
18- Walking	1.52	1.54
19- Enjoy life	1.94	1.92

*Note:* Symptom Severity Categories: 0 (No Symptom), 1-3 (Mild), 4-6 (Moderate), 7-10 (Severe). Symptom Interference Categories: 0 (No Interference), 1-3 (Mild), 4-6 (Moderate), 7-10 (Severe) (Tsze, et al., 2018)

The results indicate that the average ratings of all items are within the mild range. Regarding symptom severity, the symptoms rated on the higher end of mild category are item 5: Upset ( $M=3.18$ ,  $SD=2.71$ ) and item 2: Tiredness ( $M=3.14$ ,  $SD=2.59$ ). Regarding symptom interference, while still in the mild range, the impact of symptoms on how

children feel ( $M=2.38$ ,  $SD=1.82$ ) and their schoolwork and chores ( $M=2.00$ ,  $SD=1.88$ ) were rated as the highest impacts.

A one-way ANOVA revealed significant differences between 11-year old and 9-year-olds' responses to symptom severity items,  $F(4, 45) = 4.91$ ,  $p < .05$ ,  $\eta^2 = .30$ . Pairwise comparisons revealed that 11-year-old children's ratings of symptom severity items ( $M = 28.75$ ;  $SD = 21.18$ ) were significantly higher than 9-year-old children's ratings ( $M = 3.70$ ;  $SD = 4.30$ ),  $p < .05$ . Another one-way ANOVA was performed to explore differences in symptom interference ratings by children in different age groups. Results revealed that there are no statistically significant differences between age groups in their ratings of symptom interference items,  $F(4, 45) = 2.50$ ,  $p > .05$ .

### **Psychometric Analysis**

Principal component factor analysis with direct oblimin rotation was used to determine the underlying factor structure. Initial eigen values indicated that the first four factors explained 46%, 13%, 9%, and 8% of the variance respectively (Cumulative: 76%). No items were eliminated as all the 13 items met the minimum criterion of having a primary factor loading of .4 and above. The factor loading matrix is presented in Table 4.

Table 4.

*Factor Loadings of Symptom Severity Items (N = 50)*

Measure/Subscale	<i>General Physical and Psychological Symptoms</i>	<i>Oral, Neurological, and Secondary Side Effects</i>	<i>Other Side Effects</i>	<i>Gastrointestinal Issues</i>
3- Upset stomach	<b>.89</b>	.13	.19	.08
6- Breathing	<b>.88</b>	-.14	-.01	.19
11- Sad	<b>.77</b>	-.02	-.02	-.06
5- Upset	<b>.71</b>	.12	-.15	-.18
1- Pain	<b>.59</b>	.36	-.17	-.05
4- Trouble sleeping	<b>.45</b>	.32	-.24	-.01
10- Dryness in mouth	.07	<b>.93</b>	.04	.01
13- Numbness and tingling	-.07	<b>.91</b>	-.03	.14
8- Not feel like eating	.43	<b>.45</b>	-.17	-.37
7- Remembering things	-.28	.17	<b>-.91</b>	.15
9- Sleepy during daytime	.37	-.18	<b>-.65</b>	-.03
2- Tiredness	.43	.03	<b>-.54</b>	-.17
12- Throw up	.18	.14	-.12	<b>.94</b>

Results indicate that the 13 symptom severity items of the MDASI-C (8-12) measure 4 constructs: 1) a general physical and psychological symptoms factor comprised of the following items: upset stomach, breathing problems, sadness, being upset, pain, and trouble sleeping; 2) a treatment and medication side effect (oral, neurological, secondary side effects) factor comprised of the following items: dryness in mouth, numbness and tingling on body, and poor appetite; 3) other cancer/treatment side effects factor comprised of the following items: difficulty remembering things, drowsiness, and fatigue; and 4) a gastrointestinal-related item: throw up. Some of the factor labels were proposed by Cleeland et al. (2000) and were retained as they suited the extracted factors. Another factor analysis was performed for symptom interference items.

Initial eigen values indicated all six items belong to one factor and they explained 59% of the variance.

As described above, symptom severity items are comprised of three scales and one individual item, based on primary factor loadings. Internal consistency for each of the scales was examined using Cronbach's alpha. The coefficient alpha value for the first scale (General Physical and Psychological Symptoms) was 0.88. No item was eliminated from this scale. The coefficient alpha value for the second scale (Oral/Neurological/Secondary Side Effects) was 0.76, which was slightly improved when item 8 (not feel like eating) was removed from the scale. Item 8 was removed from this scale and was added to the first scale as the results from factor analysis indicated that item 8 had cross loadings on factor 1 (.43) and factor 2 (.45). Internal consistency analysis for first scale was performed again after adding item 8 to the scale. The coefficient alpha value for the first scale was improved to .90 after adding item 8 to the scale. Furthermore, the label of the second scale was changed to Oral/Neurological Side Effects to represent the two items in that scale (dryness in mouth, numbness and tingling on body). The coefficient alpha value for the third scale (Other Side Effects) was .71, which was slightly improved when item 7 (remembering) was removed. However, item 7 was retained in this scale for three reasons. First, removing item 7 only slightly improves the coefficient alpha value and the improved value will still be in the acceptable range. Second, item 7 is the only item that examines cognitive side effects of cancer and its treatment. Third, as this measure is an adapted version of the original adult MDASI measure, retaining item 7 will be helpful for future comparative studies between children and adults.

Internal consistency for symptom interference scale was also examined using Cronbach's alpha. The coefficient alpha value for this scale was .84, which was improved

to .89 when item 18 (walking) was removed from the scale. However, item 18 was retained in this scale because it only slightly improved the coefficient alpha value, and the value is still in the good range. Additionally, keeping the items on this measure parallel to the ones on the original MDASI helps future comparative studies.

Composite scores were created for each of the factors, based on the sum of items which had their primary loadings on each factor. Higher scores indicated more severe general symptoms, larger side effects (both oral/neurological side effects and other more general side effects), and more severe GI issues, specifically vomiting. Only small to moderate correlations between each of the composite scores and the individual GI item existed, indicating that these 4 scales are not redundant, and they are measuring constructs that are different from each other. These results are presented in Table 5.

*Table 5.*

*Correlations Between general physical and psychological symptoms, oral and neurological side effects, general side effects, and GI item (N = 50)*

	GS	ONSE	OGSE	GI
General physical and psychological symptoms	--	.48	.64	.13
Oral and neurological side effect		--	.35	.32
Other general side effects			--	.14
GI item				--

*Note.* GS = General Symptoms; ONSE = Oral and Neurological Side Effects; OGSE = Other General Side Effects; GI = Gastrointestinal;  $p < .05$

## CHAPTER IV: DISCUSSION

Prior research has identified several pediatric cancer assessment measures; however, these measures have some limitations, including assessing only one or a limited number of symptoms, only relying on informants' ratings, and not addressing functional impairment as a result of experiencing cancer-related symptoms. Thus, the present study was designed to develop a self-report measure for children that includes multiple symptoms and explores different dimensions of the symptoms, such as symptom presence, severity, and functional impairment (McColl, 2004; Steen et al., 1996). To do so, the adult version of an already existing measure (MD Anderson Symptom Inventory, MDASI, Cleeland, et al., 2000) was modified to be used with children 8-12 years of age. The modification process included revising the measure to make it developmentally appropriate, using age-appropriate language and appropriate visuals, and including children, as well as caregivers and experts in the process of measure development (DeVellis, 2017). The current version of the modified measure, MDASI-C (8-12), is a multidimensional instrument that consists of 13 core symptom severity and 6 symptom interference items. Thus, the primary aim of the present study was to adapt the original adult version of the MDASI to be used with children in the age range of 8-12 years old. Properties of the adapted version, MDASI-C (8-12), are discussed in more detail below.

### **Developmentally Appropriate Language and Readability**

One of the first steps in adapting the original adult version of the MDASI was to ensure the language in the measure was developmentally appropriate. Literature has outlined various ways to accomplish this goal. More specifically, interviewing potential respondents of the measure regarding the appropriateness of multiple aspects of the measure (e.g., length, appearance, language of the measure) has been suggested. The



FDA Guidance (2009) recommends conducting interviews with patients, assessing transcripts of interviews, analyzing interview results, and taking actions to remove or modify items in response to the interview. Additionally, including experts and caregivers, as well as children in the process of measure modification and measure development has been recommended (DeVellis, 2017). In addition to interviews, using a readability test is also recommended. There are different formulas to calculate text readability. One formula is Flesch-Kincaid test, which is a common metric that takes into account the length of the words and sentences in a text.

In the present study, both of the above methods (interviews and readability test) were utilized. This study used interviews with experts, caregivers, and children to ensure clarity, appropriateness, and understandability of the measure for children in the age range of 8-12 years old. In addition to interviews, the results from the readability statistics revealed that the readability level slightly increased in the modified child version, compared to the original adult version. However, that grade level increase does not necessarily translate into a more difficult to understand measure, primarily because the readability formula used in the present study takes into account the length of the words and sentences. In other words, the longer the words and sentences, the higher the grade level and the more difficult to read the text is. However, longer sentences were used in the child version to provide children with more context and remind them to only think about the last 24 hours when answering each item, as opposed to the adult version with only one prompt for all 13 symptom severity items and one prompt for all 6 functional impairment items. Furthermore, although longer prompts were used in the child version, they were repeated in each item except for the specific words for each symptom or functional impairment. Additionally, for some items in the child version, multiple words were used to refer to specific symptoms (e.g., upset stomach for

nauseous, sleepy during the daytime for drowsiness), and this also added to the length of the sentences, and as a result increased the readability statistics. Moreover, in the child version, examples were added to some of the items (e.g., daily activities, like homework, brushing teeth, watching TV, and taking a bath) to make the concept more comprehensible for children. This also significantly added to the length of some of the items.

Thus, the present study used multiple approaches to ensure the appropriateness of the MDASI-C for 8-12-year-old children. The results indicated that several aspects of the measure (e.g., language, appearance, structure, length, visuals) are developmentally appropriate for children in the age range of 8-12. The use of comprehensible format and developmentally appropriate language is consistent with recommendations from several researchers (Hennessy & Kind, 2002). More specifically, the current study chose a narrow age range for the measure, so “developmentally appropriate” language could be set for a specific age range (FDA Guidance, 2009). FDA Guidance also recommends determining the lower age limit at which children can understand the questions and concepts. The lower age limit in this study was 8 years old, which is consistent with a study by Rebok et al. (2001) that explored children’s understanding of health-related terms within different age groups. Most children 8 years old and above in that study reported understanding health-related terms (e.g., pain, nervous, healthy). Additionally, children’s understanding increased as their age increased.

Thus, this study highlights the importance of ensuring the understandability of the measure by children. Further, since a high reading level required to complete instruments can lead to health disparities in vulnerable populations, it is important to take readability into account to ensure equity in the delivery of care (Dorismond et al., 2021). Finally, this measure was not piloted with children with a cancer diagnosis, and cancer, its treatment,

and limitations associated with cancer can affect children's cognitive functioning and literacy (French et al., 2011; Vance & Eiser, 2002). Thus, the readability level needs to be re-assessed when the measure is piloted with children with cancer in the future.

### **Response Options**

Another step to modifying the adult version of the MDASI included changing the response options to make them more understandable for children. Although there is limited evidence on the advantage of picture illustrations in measures (e.g., faces), a study by Holme et al. (2003) showed that the pictures on instruments keep the child engaged and help in faster completion of measures. Faces were used in the response options in the present study. Regarding the developmentally appropriate use of faces, studies have shown that faces do not require knowing the concept of magnitude and can therefore be used for raters as young as pre-school-aged children (Walker et al., 2019). Other studies have also shown that faces scales facilitate self-report of pain in children (Malviya, 2006; Maunuksela et al., 1987) since reading, writing, and expressive abilities are not needed on faces scales (Kuttner & LePage, 1989). The appeal and popularity of faces scales have also been extensively studied in both clinical and research settings (Huguet et al., 2010; Hunter et al., 2000; Stinson et al., 2006). Results (Champion et al., 1998; Miro et al., 2009) indicate that these scales are generally appealing to and preferred by children to other self-report measures (e.g., visual analogue scales, numerical scales). Results also indicate that faces scales are popular with clinical providers, as they are relatively quick and easy to administer (Hunter et al., 2000), and they create minimum disruptions in medical routines (Kuttner & LePage, 1989).

Despite studies that support the use of faces for children, there are conceptual and psychometric concerns with these scales. For example, there is a major concern about the confounding of emotion with symptom intensity, as it is often difficult to distinguish

between acute symptoms (e.g., pain), distress, and anxiety (Taplin et al, 1999). Additionally, it is important to note that in the faces scales with numbers, the scale is ordinal as the numbers are arbitrarily assigned to each face, and as a result, only non-parametric statistical analyses can be conducted. Furthermore, regarding reliability, traditional techniques (e.g., test-retest reliability) cannot be applied to these scales as most symptoms assessed by faces scales (e.g., pain) are rarely stable over time. Therefore, most researchers have focused their studies on establishing validity for these scales, maintaining that reliability is assumed following the establishment of high validity (Beyer & Knapp, 1986; Kuttner & LePage, 1989).

Regarding different varieties of faces scales, there are two commonly used versions (Chambers & Craig, 1998). One version includes a smiling face representing no symptom/pain (e.g., Wong-Baker Faces Scale), and one version includes a neutral face representing no symptom/no pain (e.g., Bieri Faces Pain Scale). Data has suggested that faces scales with smiling face at no symptom/pain end of the scale may overestimate the symptom/pain (Chambers & Craig, 1998). The main reason is that children without pain, but with distress from other sources might be reluctant to choose a smiling face (Walker et al., 2019). However, the scale developed in this study used the smiling face to represent no symptom, as research has shown that children often report that they like the version with a smiling face more than the version with a neutral face (Ullrich et al., 2009). Also, to add clarity and to avoid overestimation of the intensity of symptoms, a short descriptor was added under extreme points (i.e., 0 and 10) on the scale.

Appropriateness of the faces and the descriptors were assessed during interviews. Experts and parents noted that the use of descriptors was helpful as they facilitated children's understanding of the scale. Children also noted that they understood how to rate their symptoms using faces and they also reported that descriptors were helpful.

Regarding the response levels at which children can distinguish and rate intensity of symptoms, Von Baeyer et al. (2000) found that the 0-10 scale was strongly favored by 70% of respondents in their study over other options (e.g., 0-5 scale). Research has also shown that 0-10 numerical self-rating scales can be used with children 8 years old and above (Von Baeyer, 2013). Consistent with these results, 0-10 rating scale was adopted in this study for the MDASI-C (8-12). Additionally, during the interviews with children, most of them noted that they were familiar with this metric and knew how to differentiate among points on the scale. Parents also reported that their children are used to using scales similar to the one used in the present measure.

Research has also shown that the use of numerical rating scales (NRS) is a valid and reliable way to assess pain/symptoms in children as young as 8 years old (Bailey et al., 2010; Page et al., 2012), as most children have developed numeracy and ability to express self in quantitative terms by this point. Moreover, research has shown that visual analogue scale (VAS) is appropriate for children 8 years old and above (Mcgrath et al., 2008; Stinson et al., 2006). Similarly, color analogue scale (CAS) is a well-established tool for self-report of pediatric pain in children as young as 5 years old (Bulloch et al., 2009). In a recent study, Van Muilekom et al. (2022) explored patients' and parents' perspectives on the use of colors in patient reported outcome measures to optimize its implementation in pediatric clinical practice. One of the themes that they found in their qualitative data analysis was that parents and children unanimously rated the use of colors as positive and stated that colors make the layout of the measure appealing. This is consistent with what caregivers and children in the present study noted. The majority of respondents suggested keeping the colors in the final version of the MDASI-C (8-12) and noted that use of colors enhances children's ability to use the scale and makes the measure more attractive. In an older study, McGrath et al (1985) pointed to the benefits

of using colors for rating the intensity of the symptoms instead of word descriptors in rating scales. However, no data has been found to support the superiority of colors to word descriptors (see Chambers & Johnston, 2002). Regarding the assignment of colors to different rating points, Van Muilekom et al. (2021) assigned colors to response options based on response category. Consistent with this study, the present study assigned different colors to different categories/levels of symptom intensity or interference (e.g., no pain, worst pain in this study, no interference).

To accommodate children's ratings and enhance judgment of their responses, the scale in this study used a combination of pictorial facial expressions, word descriptions, numbers, and color coding to help children rate their symptoms and functional impairments (Keck et al., 1996). During interviews, most experts indicated that the combination of faces, descriptors, colors, and numbers was helpful and recommended keeping these aspects in the next version of the measure. Most caregivers also noted this combination can make the scale easy to understand for children and help them answer the questions accurately. A few parents noted that some components of the response options (e.g., faces, colors) are similar to other scales their children have filled out and this familiarity helps children better understand the task. Additionally, most children noted that this combination helped them better understand the task.

### **Age Range**

Age is another important property of measures when assessing changes and improvements in health outcomes over time. Respondents' ages are commonly grouped into ranges based on stages of development (Sigelman & Rider, 2014), such as pre-school (4-7), childhood (8-12), adolescence (13-19), young adulthood (20-35), middle adulthood (36-64), and late adulthood (65 and above). FDA Guidance (2009) recommends the use of narrow age bands to ensure developmentally appropriate wordings and language.

Regarding the age range of respondents in this study, the minimum age was set at 8 years to reflect the results of the available research that children as young as 8 years old can provide reliable self-report (Tadic et al., 2020).

Research has also shown that children in the age range of 8-12 have developed the capacity to understand health concepts and self-regulatory abilities that are required to sustain efforts to complete a measure. Children in this age range have also developed cognitive processing capacities to understand the task, evaluate the questions, differentiate between response options, and choose the one that applies to them (Bevans et al., 2010). Zigler et al. (2020) noted that children younger than 10 years old may be susceptible to respondent fatigue. To limit these issues and if necessary, they recommend close supervision by a facilitator and administration of the measure early on in the day. The primary goal of the present study was to modify the original adult measure in a developmentally appropriate way to use it with children in the age range of 8-12 years old. This was the main focus of the interviews with experts, caregivers, and children to ensure the measure is appropriate for this age range. Experts and caregivers noted that the measure is appropriate for this age range. Additionally, children noted that the measure is appropriate for children their age.

### **Recall Period**

In clinical settings, recall of symptoms is used to develop initial treatment, determine symptom management, and assess treatment progress (Chogle et al., 2012). It is important to take into consideration the patient's ability to retroactively recall the information. It is recommended to choose the recall period based on the purpose, intended use of the instrument, and characteristics of the symptoms, including the duration, frequency, and intensity of the concept being measured (Matza et al., 2013; O'Sullivan et al., 2015; US Department of Health and Human Services, 2006). FDA

Guidance (2009) recommends using a very brief (e.g., 24 to 48 hours) recall period, particularly when there are co-occurring symptoms to be able to evaluate potential co-occurring problems (Baggott et al., 2009).

Retroactive recall of information is also affected by age. In fact, Broderick et al. (2008) found that lengthy recall periods impact children's ability to report symptoms accurately. Other studies have also shown that a 24-hour recall period is appropriate for children even younger than 8 years old (Coombes et al., 2021). Rebok et al. (2001) found that young children (5-6 years old) were less likely to understand the concept of last week or last month. Furthermore, Ungar et al. (2012) highlighted children's limitations in using longer recall periods. They found that children often have difficulty comprehending timeframes and remembering events and their parents often have to help them by linking the timeframe to specific events and activities.

In the present study, given that cancer-related symptoms may have day-to-day fluctuations, a 24-hour recall period was used, and the appropriateness of this timeframe was supported by results from interviews. During the interviews, experts suggested asking children if they know what 24 hours means and providing them with explanations and examples. During the interviews with caregivers, they agreed that providing explanations about 24 hours would be helpful. Children also noted in their interviews that the explanation of 24 hours helped orient them to the measure. Children also reported that they are able to recall and report information from 24 hours ago. Another attribute of the present measure is assessing each symptom severity at its worst. It is recommended to focus assessment on a salient point (e.g., pain at its worst) if fluctuations in the symptoms occur rapidly. Shi et al. (2008) supported the appropriateness of using a combination of recall period and severity descriptors (e.g., worst, least, average, current. For example, worst pain in the last 24 hours) in a sample of cancer patients with persistent symptoms.



### **Length of the Measure**

Length of the measure is another characteristic that needs to be carefully taken into consideration (Matza et al., 2013) due to wide variations in children's ability to maintain attention on task (Matza et al., 2004). Long measures may interfere with children's attentiveness, which can subsequently result in less accurate and reliable data (Eiser & Morse, 2001). International Society for Pharmacoeconomics and Outcomes Research (ISPOR) task force (Matza et al., 2013) recommends cognitive interviews with children of the target age range to determine the appropriateness of the length of the measure. During the interviews in this study, caregivers noted that although the measure may look long, the length is appropriate, and children can complete it quickly, because the items and response options are the same for all the items, and there is only the symptom or the functional impairment that changes in each item. Additionally, a few children noted that the first instruction was lengthy but helpful to orient them to the measure and what they need to do. Although most children stated that the length of the measure was appropriate, some children suggested using shorter prompts in each item. This was addressed, and the prompts for the 13 core symptom severity items were revised in the final version of the MDASI-C (8-12). In addition to qualitatively supporting the length of the measure, children also rated the length of the measure in the appropriate range.

### **Content of the Measure**

Given that content validity is a critical component of Patient Reported Outcome Measures (PROMs), it is recommended to conduct qualitative research and include direct input from the target population to establish content validity for measures (FDA Guidance, 2009; Patrick et al., 2011). In other words, when developing pediatric measures, it has been recommended to consider children as content experts and consider

their perspectives (e.g., by interviewing them) (Brod et al., 2009; Collins, 2003; Leidy & Vernon, 2008; Matza et al., 2013; Morris et al., 2007; Riesch et al., 2006; Stewart et al., 2005; Tomlinson et al., 2009). Another aspect of establishing content validity is taking other informants' (e.g., experts, caregivers) perspectives into consideration (Matza et al., 2013). During the interviews with experts in this study, they were asked about the inclusiveness of the measure. Most experts noted that the items are a good combination of affective and physical symptoms. Experts who had experience working with a pediatric oncology population also stated that there was a good association between the items and what children with cancer experience as a result of the disease and its treatment. Children who were interviewed in this study noted that only some items (e.g., sadness, tiredness) would apply to them, as they were not diagnosed with cancer. However, given that MDASI-C is going to be eventually used for children with cancer, future studies should focus on interviews with children who have a cancer diagnosis, in addition to interviews with experts. This will establish validity as children may have unique perspectives based on their symptom experience and the impacts of symptoms on different aspects of their lives. Thus, comprehensiveness and relevance of the items still need to be evaluated.

### **Development of Initial Psychometrics**

The initial analysis of symptom severity and symptom interference items indicated that most children did not report any concerns, and on average, all symptoms were rated in the mild range by most children. Given that some of the symptoms (e.g., sadness, fatigue, trouble sleeping) in the MDASI-C (8-12) may be experienced by everyone, even children who are not diagnosed with cancer, experiencing symptoms in the non-clinically significant range (no symptoms to mild symptoms) was expected.

When examining age differences in the present measure, results revealed that 11-year-olds rated the symptom severity items higher than the 9-year-olds. Further, when examining individual items, it was found that 11-year-olds rated general symptoms (e.g., tiredness, upset stomach, difficulty sleeping, poor appetite) higher than 9-year-olds. Thus, rating of symptoms that are more specific to cancer and cancer treatments (e.g., dryness in mouth, numbness and tingling, remembering things) were not different in 11 and 9-year-olds. Given that children who responded to the items were children with no cancer diagnosis, this difference in their ratings based on age could have other explanations. In general, research has shown that cognitive maturation plays an important role in internalizing experiences (e.g., worry) in children (Ellis & Hudson, 2010). In younger children, because their brain is undergoing development, cognition, concept formation, and the capacity to experience internal experiences may be limited (Beidel & Turner 2005; Vasey et al. 1994). Research has also emphasized high rates of comorbidities of multiple internalizing conditions, such as anxiety and depression in children (Alfano 2012; Masi et al., 1999). For example, Jarrett et al. (2015) indicated that older children often exhibit more anxiety (mostly school-related), higher irritability, lower mood, and more trouble paying attention, when compared to younger children (Jarrett et al., 2015). These symptoms are similar to the general symptoms rated higher by 11-year-olds in the present study when compared to 9-year-olds.

Furthermore, examining individual respondents' ratings, four 11-year-old respondents rated 40-55% of the symptom severity items in the moderate and severe range. Their ratings significantly impacted the difference between the two groups (9- and 11-year-olds). Given that respondents were children with no cancer diagnosis, these highly-rated symptoms (pain, tiredness, upset stomach, sadness, sleepiness, poor appetite) can be due to other diagnoses, conditions, or stressors. In future studies, when piloting the

measure with children who are diagnosed with cancer, it is important to monitor for differences between children from different age groups.

Regarding symptom interference items, results revealed that all children rated their functional problems in the mild range. In other words, children in different age groups (i.e., 8, 9, 10, 11, 12-year-olds) were not different in terms of their functioning in different aspects of their lives (e.g., participation in daily routines, social emotional functioning, physical functioning). This was expected as children who completed the measure were not diagnosed with cancer, and the items asked in the measure were all impairments as a result of cancer itself or cancer treatment. The items asked about social and emotional impairments (Brand et al., 2017; D’Olivo et al., 2018; Kazak et al., 2006; Marsland et al., 2006; Phipps et al., 1995), impact on academic functioning (Golomb, 2000), and impairment in physical functioning (Jalmsell et al., 2006; Oswald et al., 2019; West et al., 2014). Given the differences in how 9- and 11-year-old children rated their symptom severity, this result indicates that although older children may experience higher levels of symptoms severity, compared to younger children, they are able to function similarly in different aspects of their lives. This may be explained by the development of more complex coping skills (e.g., distraction strategies, positive self-talk, cognitive reappraisal) as children get older (Ebata & Moos, 1994; Hoffman et al., 1992; Hoffner, 1993; Losoya, 1998).

### **Factor Analysis**

Regarding the underlying factors found in the measure, there was a discrepancy in the number of factors in the original MDASI (Cleeland et al., 2000) and the modified child version (MDASI-C 8-12). This discrepancy may be related to sample size and participants who completed the measure. Although there is continued discussion about minimum sample size recommendations for conducting factor analysis, several studies

indicate that factor analysis may be subject to erroneous conclusions due to a small sample size (MacCallum et al., 1999). Additionally, the original MDASI was rated by patients diagnosed with cancer; however, the modified MDASI-C (8-12) was rated by children who are not diagnosed with cancer. Thus, results from factor analysis may be different if the items were responded to by the target population. Therefore, future studies should focus on piloting the measure with children with cancer and re-evaluating the factor loadings, as it is recommended to evaluate the psychometric properties of the scales with a specific population for whom scales are intended to be used (Huguet et al., 2010; McConahay et al., 2007). However, if this was to be used with children with cancer, caution should be used regarding using scale scores as the current scales in the MDASI-C (8-12) are from the responses of children with no cancer diagnosis.

### **Limitations**

Several limitations affect the generalizability of the findings. A major limitation in this study is the small sample size. Additionally, although no participant reported difficulty in completing the measure, some children may have experienced survey fatigue which could have impacted the results. Also, in the pilot phase of the study, there was a significant level of incomplete responses that needed to be completely removed from data. One potential explanation for incomplete responses could be the length of the survey despite children noting in the interviews that the length of the measure was appropriate. Some children reported that the measure may initially look long as response options (same for all items) after each item take some space on each page and adds to the length of the survey. Another explanation could be not reading the consent and assent forms thoroughly and not understanding the purpose of the study and discontinuing the survey as soon as they noticed the measure was designed for children with cancer. This is a limitation that may have been posed by the sampling procedure as the researcher was

not available to participants who were recruited through convenient and snowball sampling to explain the purpose of the study.

Additionally, the MDASI-C (8-12) was modified and piloted with children with no cancer diagnosis. The appropriateness of the language and format of the measure for children in the age range of 8-12 were assessed during interviews. However, the comprehensiveness and relevance of the items were not evaluated as children and parents did not have any experience with cancer symptoms and functional problems. Thus, it is recommended to conduct interviews with children who are diagnosed with cancer and further evaluate the content validity of the measure in future studies.

Furthermore, the current version of the MDASI-C (8-12) was normed in children with no cancer diagnosis. In terms of symptom experience, most respondents reported either no or mild symptoms and functional problems. However, finding a clear explanation for respondents who reported moderate to severe symptoms and functional problems was challenging as respondents were not asked to report their medical or psychiatric history and current stressors. It is hypothesized that children with cancer report higher levels of symptom severity and functional impairments than children with no cancer diagnosis. While the results from this pilot study can be used for comparative studies in the future, it is recommended to norm the measure on children who are diagnosed with cancer in future studies.

Finally, due to the recruitment method, many children were from educated families. This can consequently affect children's reading level as well as vocabulary knowledge, previous familiarity with measures, and knowing how to rate their experiences. Thus, results may be different if participants were more reflective of the general population.

## **Summary**

Overall, understanding symptom experiences and the functional impairments as a result of those symptoms are essential areas of research that could improve the outcomes in children with cancer (Torres et al., 2019). It is important that these symptoms and functional impairments are identified and measured. Furthermore, accurate understanding of these symptoms and impairments can facilitate communication between the patient, families, and providers. Moreover, better communication could lead to better treatment outcomes (Bainbridge, 2011; Williams et al., 2012). In other words, numerical ratings of symptoms and impairments should inform providers' decision making about symptom treatment. This includes early detection of symptoms that could lead to emergency room visits and hospitalizations.

Also, when validating the measure with children who are diagnosed with cancer, it is important to have a set of core symptoms and impairments that can be rated by all children, regardless of their cancer type. At the same time, if certain groups of children with a specific cancer type or treatment status have symptoms requiring monitoring that are not included in the core items, a subset of symptoms specific to their condition will need to be appended to the core items. Further, if there is functional impairment impacting children's functioning in several areas, they may benefit from psychological support through their illness and treatment. The current measure seems to provide this information.

## **Conclusion**

Symptom experience is inherently subjective and self-report measures are the gold standard method to assess symptoms (Collins et al., 2000). Self-reports play a critical role in helping providers understand the symptom experience of children diagnosed with cancer. A symptom assessment can facilitate effective teamwork and

communications across settings and providers, as well as patients and providers during cancer treatment.

This study used an iterative approach to develop a developmentally appropriate measure for children with cancer (MDASI-C 8-12). The study utilized a multidisciplinary group of experts, including pediatric, developmental, and clinical child psychologists, and a pediatrician, as well as caregivers and children, to develop the measure. This study demonstrated that the MDASI-C (8-12) is age-appropriate and children as young as 8 years old can comprehend and respond to items on the measure. This is consistent with findings from prior research (Linder, 2008; Varni et al., 2007). Including both symptoms and functional impairments when assessing patients' responses is essential to our understanding of how cancer affects children. The MDASI-C (8-12) is a useful measure for evaluation of the severity and impairments associated with symptoms in a pediatric oncology population.



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APPENDIX A:

MD ANDERSON SYMPTOM INVENTORY (MDASI)

Date: \_\_\_\_\_

Institution: \_\_\_\_\_

Subject Initials: \_\_\_\_\_

Hospital Chart #: \_\_\_\_\_

Study Subject #: \_\_\_\_\_

**M. D. Anderson Symptom Inventory (MDASI) Core Items**

**Part I. How severe are your symptoms?**

People with cancer frequently have symptoms that are caused by their disease or by their treatment. We ask you to rate how severe the following symptoms have been *in the last 24 hours*. Please fill in the circle below from 0 (symptom has not been present) to 10 (the symptom was as bad as you can imagine it could be) for each item.

	Not Present										As Bad As You Can Imagine	
	0	1	2	3	4	5	6	7	8	9	10	
1. Your <b>pain</b> at its WORST?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. Your <b>fatigue (tiredness)</b> at its WORST?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. Your <b>nausea</b> at its WORST?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. Your <b>disturbed sleep</b> at its WORST?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. Your feelings of being <b>distressed (upset)</b> at its WORST?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. Your <b>shortness of breath</b> at its WORST?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. Your problem with <b>remembering things</b> at its WORST?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. Your problem with <b>lack of appetite</b> at its WORST?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9. Your feeling <b>drowsy (sleepy)</b> at its WORST?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10. Your having a <b>dry mouth</b> at its WORST?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Date: \_\_\_\_\_

Institution: \_\_\_\_\_

Subject Initials: \_\_\_\_\_

Hospital Chart #: \_\_\_\_\_

Study Subject #: \_\_\_\_\_

	Not Present											As Bad As You Can Imagine										
	0	1	2	3	4	5	6	7	8	9	10	0	1	2	3	4	5	6	7	8	9	10
11. Your feeling <b>sad</b> at its WORST?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
12. Your <b>vomiting</b> at its WORST?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
13. Your <b>numbness or tingling</b> at its WORST?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

**Part II. How have your symptoms interfered with your life?**

Symptoms frequently interfere with how we feel and function. How much have your symptoms interfered with the following items in the last 24 hours:

	Did Not Interfere											Interfered Completely										
	0	1	2	3	4	5	6	7	8	9	10	0	1	2	3	4	5	6	7	8	9	10
14. <b>General activity?</b>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
15. <b>Mood?</b>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
16. <b>Work (including work around the house)?</b>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
17. <b>Relations with other people?</b>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
18. <b>Walking?</b>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
19. <b>Enjoyment of life?</b>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

APPENDIX B:  
QUESTIONS USED FOR THE INTERVIEW-EXPERTS

This is a scale currently used by MD Anderson to assess Pain and related symptoms in Adult Cancer Patients. We want to use it with children ages 8 - 12. Thus, we would like your expert opinion on several aspects of the scale. Each question will begin with your thoughts related to a particular concept and then end with a rating of each concept, on a scale of 1- 5, with 1 being the least and 5 being the most.

Also, as you complete the questions, please keep in mind:

- 1.) The scale is for children ages 8 – 12
- 2.) Children will be asked about each symptom separate
- 3.) Children will be asked about when their symptoms were the worst over the last 24 hours.

**Instructions:**

What are your thoughts related to the instructions?

On a scale of 1 – 5, with 1 being not clear and 5 being totally clear, how **clear** are the instructions?

1                      2                      3                      4                      5

**Questions:**



What are your thoughts related to the questions?

On a scale of 1 – 5, how **clear** are the questions?

1                      2                      3                      4                      5

On a scale of 1 – 5, how **appropriate** are the questions?

1                      2                      3                      4                      5

**Response Options:**

What are your thoughts related to the response options?

On a scale of 1 – 5, how **clear** are the response options?

1                      2                      3                      4                      5

On a scale of 1 – 5, how **appropriate** are the questions?

1                      2                      3                      4                      5

**Overall Language of the Questionnaire**

What are your thoughts about the overall language used in the questionnaire?

On a scale of 1 – 5, how **clear** is the language of the questionnaire?

1                      2                      3                      4                      5

On a scale of 1 – 5, how **appropriate** is the language of the questionnaire for children 8-12 years old?

1                      2                      3                      4                      5

### **Use of the Questionnaire for Children**

What are your thoughts about a child’s ability to accurately describe his/her symptoms over the last 24 hours?

On a scale of 1-5, how **accurate** a child can describe his/her symptoms over the last 24 hours?

1                      2                      3                      4                      5

How do you think the questionnaire helps children (8-12 years old) to **communicate about their symptoms**?

On a scale of 1-5, how much the questionnaire can **help children communicate about their symptoms**?

1                      2                      3                      4                      5

## Content of the Questionnaire

What are your thoughts about the **inclusiveness of the questionnaire**?

On a scale of 1-5, how much do you think the questionnaire **includes aspects of pain** experienced by children who have at least one type of cancer?

1                      2                      3                      4                      5

What are your thoughts about the **association between the content** of the items in the questionnaire **and the symptoms** experienced by children suffering from cancer?

On a scale of 1-5, how closely does the questionnaire **reflect the symptoms** experienced by children suffering from cancer?

1                      2                      3                      4                      5

## Appearance of the Questionnaire

What are your thoughts about the **layout of the questionnaire**? (i.e. order of the questions, sections, visuals, etc.)

On a scale of 1-5, how **appealing** is the questionnaire to children (8-12 years old)?

1                      2                      3                      4                      5

What are your thoughts about the **length of the questionnaire**?

On a scale of 1-5, how **long** is the questionnaire?

1

2

3

4

5

**IMPROVEMENTS:**

Any suggestions on how to improve the questionnaire?

**COMMENTS:**

Any other comments or suggestions?

Do you think any important symptom, problem or concern have been **missed out** in the questionnaire?

Do you feel that any area or problems in the questionnaire are **over-represented**?

Do you feel that any area or problems in the questionnaire are **under-represented**?

APPENDIX C:  
QUESTIONS USED FOR THE INTERVIEW-CAREGIVERS

This is a scale currently used by MD Anderson to assess Pain and related symptoms in Adult Cancer Patients. We want to use it with children ages 8 - 12. Thus, we would like your opinion on several aspects of the scale. Each question will begin with your thoughts related to a particular concept and then end with a rating of each concept, on a scale of 1- 5, with 1 being the least and 5 being the most.

Also, as you complete the questions, please keep in mind:

- 1.) The scale is for children ages 8 – 12
- 2.) The children will be asked about each symptom separate
- 3.) They will be asked about when their symptoms were the worst over the last 24 hours.

Age of your child? \_\_\_\_\_ Gender of your  
Child? \_\_\_\_\_

**Instructions:**

What are your thoughts related to the instructions?

On a scale of 1 – 5, how **clear** are the instructions?

1                      2                      3                      4                      5

**Questions:**

What are your thoughts related to the questions?

On a scale of 1 – 5, how **clear** are the questions?

1                      2                      3                      4                      5

On a scale of 1 – 5, how **appropriate** are the questions?

1                      2                      3                      4                      5

**Response Options:**

What are your thoughts related to the response options?

On a scale of 1 – 5, how **clear** are the response options?

1                      2                      3                      4                      5

On a scale of 1 – 5, how **appropriate** are the questions?

1                      2                      3                      4                      5

**Overall Language of the Questionnaire**

What are your thoughts about the **overall language** used in the questionnaire?

On a scale of 1 – 5, how **clear** is the language of the questionnaire?

1                      2                      3                      4                      5

On a scale of 1 – 5, how **appropriate** is the language of the questionnaire?

1                      2                      3                      4                      5

### **Appearance of the Questionnaire**

What are your thoughts about the **layout of the questionnaire?** (i.e. order of the questions, sections, visuals, etc.)

On a scale of 1-5, how **appealing** is the questionnaire to children?

1                      2                      3                      4                      5

What are your thoughts about the **length of the questionnaire?**

On a scale of 1-5, how **long** is the questionnaire?

1

2

3

4

5

**Overall**

On a scale of 1-5, how likely would it be for your child to accurately complete this questionnaire?

1

2

3

4

5

**IMPROVEMENTS:**

Any suggestions on how to improve the questionnaire?

**COMMENTS:**

Any other comments or suggestions?



APPENDIX D:  
QUESTIONS USED FOR THE INTERVIEW-CHILDREN

You will be asked questions about how you like the questionnaire and how we can change it to make it better for children your age. You will also be asked if you understand all the words in the questionnaire.

DOB of the child? \_\_\_\_\_ Gender of the  
Child? \_\_\_\_\_

**Part 1 Instruction:**

On the first page, you see a short description of what the questionnaire is about. It also teaches you what 24 hours means. Also, it gives you an example to practice how to answer the questions. What do you think about the first page?

How **clear** do you think this page is? not clear (1), so so (2), or very clear (3)?

1                      2                      3

Can you explain what this means? When your boredom was at its worst, circle the number you would give it.

**Questions:**

There are 19 questions in this questionnaire (from page 2 to 8)? What do you think about the questions?

**Q1**, when someone asks you about **pain**, what type of pain are they asking you about?

**Q3**, what does **upset stomach** mean?

**Q4**, what does it mean when someone has **trouble sleeping**?

**Q5** asks you about when you were the most **upset**. What does upset mean? Can you use it in a sentence?

**Q6**, Do you know what **breathing** means? Can you show me how you breathe (for in person interview)?

**Q10** asks you about **dryness in your mouth**. Why do you think that happens? Does it mean being thirsty?

**Q11** asks you about when you were **sad**. Question 5 asks you about when you were upset. What is the difference between being sad and being upset?

In **Q 12**, is it better to say **throw up** or **vomit**? Also, do you think this question is asking you about when you actually threw up or when you were about to throw up?

In **Q 13**, what does **numb/numbness** mean? Can you use it in a sentence? What does **tingling** mean? When do you usually feel numbness and tingling in your body?

**Part 2 Instruction:**

On page 6, you see the second part of the questionnaire. Before question 14, we teach you how to answer the questions and also teach you what the word “interfere” means. What do you think about this part?

How **clear** do you think this part is? Not clear (1), so so (2), or very clear (3)?

1

2

3

Can you use interfere in a sentence?

In **Q14**, are these good examples for **daily activities** (homework, brushing your teeth and sports)?

What is **Q15** asking about? Do you think it would be easier if we give you example? What are some examples?

**Q16** asks you about schoolwork and **chores**. Do you think chores are part of your daily activities? If yes, should we move chores to Q14 and use it as one of the examples?

In **Q17**, what does **relationship with others** mean?

What is **Q 19** asking about?

Now, I want you to think about all the 19 questions. How **clear** do you think the questions are in general? Not clear (1), so so (2), or very clear (3)?

1

2

3

**Response Options:**

Below each question, you see faces, numbers, colors and two boxes that show what 0 and 10 mean. What do you think about these?

Look at the 2 boxes below 0 and 10 in each question. Why do you think only 0s and 10s have the boxes?

For Q1, if I circle 9, what would that mean? What if I circle 5?

For Q18, if I circle 0, what would that mean? What if I circle 1? What if I circle 10?

How **clear** do you think the response options are (i.e. faces, numbers, colors, boxes)? Not clear (1), so so (2), or very clear (3)?

1                      2                      3

How **appropriate** do you think they are for children your age? Not appropriate (1), so so (2), very appropriate (3)?

1                      2                      3

### **Appearance of the Questionnaire**

What do you think about **how the questionnaire looks like?** (i.e. order of the questions, 2 parts, faces, colors, etc.)

How **interesting** is this questionnaire to children your age? Not interesting (1), so so (2), very interesting (3)?

1                      2                      3

If not 3, how can we **make it better?**

Do you think the questionnaire is too long (1), a little long and could be shorter (2), or it's appropriate (not too short, not too long) (3)?

1

2

3

**IMPROVEMENTS:**

Do you think this questionnaire is childish or appropriate for children your age?

Do you have any other suggestions for us to make the questionnaire better for children your age?

APPENDIX E:  
MDASI-C (8-12)

**MDASI for Children (8-12)**

**Part 1.**

Children with cancer often have body problems/symptoms (like tiredness, pain, trouble sleeping) that are caused by their cancer or caused by the treatment of their cancer. Today, we are going to be asking about those symptoms.

To help us with this:

We want you to think about how bad these body problems/symptoms have been over the last 24 hours.

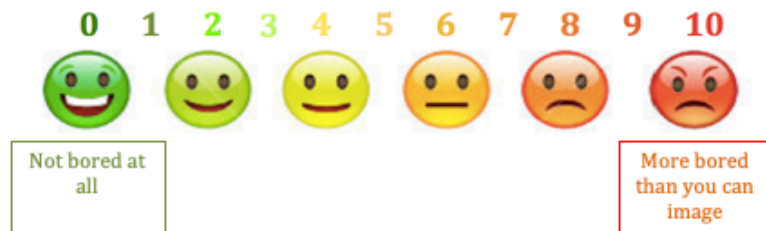
- Do you know what 24 hours is?
- 24 hours is one day. So, look at the clock.
- What time is it?
- What were you doing at this time yesterday (24 hours ago)?

Also, some of these symptoms you may not have had in the last 24 hours, so you would circle 0 (not at all). If you have had them, then you would circle one of the other numbers.

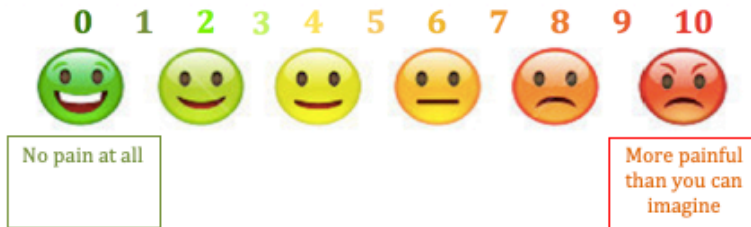
Now, as we fill out this form, I want you to think about the whole day (those 24 hours; from this time yesterday until now). Then, I want you to think about when those body problems have been the worst during the whole day.

Let's do an example:

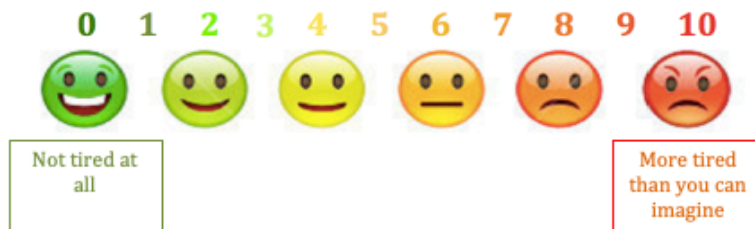
Think about when your **boredom** was the worst in the last 24 hours and circle the number you would give it.



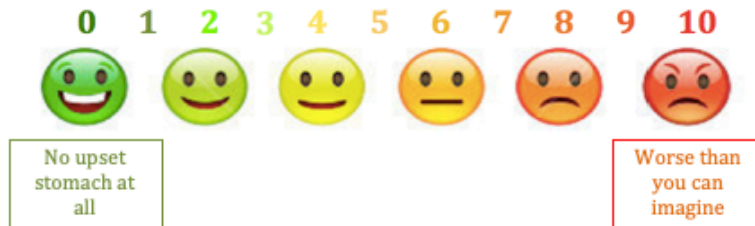
1. Think about when your **pain** was the worst in the last 24 hours and circle the number you would give it.



2. Think about when your **tiredness** was the worst in the last 24 hours and circle the number you would give it.



3. Think about when your **upset stomach** was the worst in the last 24 hours and circle the number you would give it.





4. Think about when your **trouble sleeping** was the worst in the last 24 hours and circle the number you would give it.

0 1 2 3 4 5 6 7 8 9 10




Not trouble sleeping at all

Harder than you can imagine

The scale consists of 11 smiley faces. The first face (0) is green and smiling broadly. The second (1) is light green and smiling. The third (2) is yellow and smiling. The fourth (3) is yellow and has a neutral expression. The fifth (4) is orange and has a neutral expression. The sixth (5) is orange and has a neutral expression. The seventh (6) is orange and has a neutral expression. The eighth (7) is orange and has a neutral expression. The ninth (8) is orange and has a neutral expression. The tenth (9) is orange and has a neutral expression. The eleventh (10) is red and angry.

5. Think about when you were most **upset** in the last 24 hours and circle the number you would give it.

0 1 2 3 4 5 6 7 8 9 10




Not upset at all

More upset than you can imagine

The scale consists of 11 smiley faces. The first face (0) is green and smiling broadly. The second (1) is light green and smiling. The third (2) is yellow and smiling. The fourth (3) is yellow and has a neutral expression. The fifth (4) is orange and has a neutral expression. The sixth (5) is orange and has a neutral expression. The seventh (6) is orange and has a neutral expression. The eighth (7) is orange and has a neutral expression. The ninth (8) is orange and has a neutral expression. The tenth (9) is orange and has a neutral expression. The eleventh (10) is red and angry.

6. Think about when you had the hardest time **breathing** in the last 24 hours and circle the number you would give it.

0 1 2 3 4 5 6 7 8 9 10

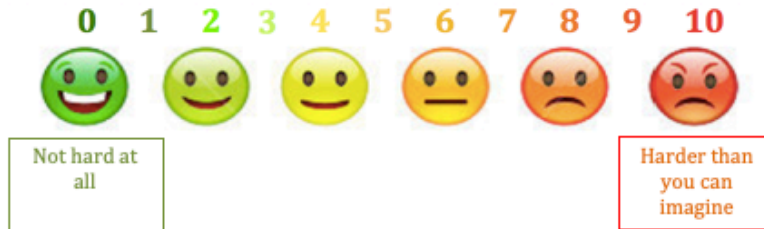


Not hard at all

Harder than you can imagine

The scale consists of 11 smiley faces. The first face (0) is green and smiling broadly. The second (1) is light green and smiling. The third (2) is yellow and smiling. The fourth (3) is yellow and has a neutral expression. The fifth (4) is orange and has a neutral expression. The sixth (5) is orange and has a neutral expression. The seventh (6) is orange and has a neutral expression. The eighth (7) is orange and has a neutral expression. The ninth (8) is orange and has a neutral expression. The tenth (9) is orange and has a neutral expression. The eleventh (10) is red and angry.

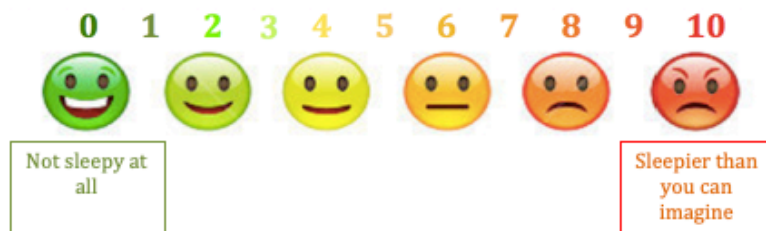
7. Think about when you had the hardest time **remembering things** in the last 24 hours and circle the number you would give it.



8. Think about when you did **not feel like eating** at all in the last 24 hours and circle the number you would give it.




9. Think about when you were the **sleepiest during the daytime** in the last 24 hours and circle the number you would give it.



10. Think about when you had the worst **dryness in your mouth** in the last 24 hours and circle the number you would give it.

0 1 2 3 4 5 6 7 8 9 10




No dry mouth at all

More dry than you can imagine

Detailed description: A horizontal scale of 11 smiley faces. The faces transition from green (happy) on the left to red (angry) on the right. The numbers 0 through 10 are positioned above each face. The number 2 is highlighted in green. Below the scale are two boxes: a green-bordered box on the left containing the text 'No dry mouth at all' and a red-bordered box on the right containing the text 'More dry than you can imagine'.

11. Think about when you were the **saddest** in the last 24 hours and circle the number you would give it.

0 1 2 3 4 5 6 7 8 9 10




Not sad at all

Sadder than you can imagine

Detailed description: A horizontal scale of 11 smiley faces, identical to the one in question 10. The number 2 is highlighted in green. Below the scale are two boxes: a green-bordered box on the left containing the text 'Not sad at all' and a red-bordered box on the right containing the text 'Sadder than you can imagine'.

12. Think about when you had the worst **throw up** in the last 24 hours and circle the number you would give it.

0 1 2 3 4 5 6 7 8 9 10

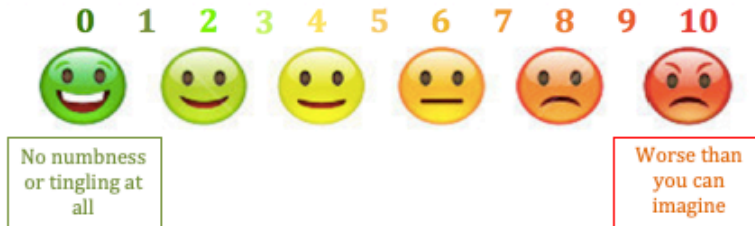


No throw up at all

Worse than you can imagine

Detailed description: A horizontal scale of 11 smiley faces, identical to the ones in the previous questions. The number 2 is highlighted in green. Below the scale are two boxes: a green-bordered box on the left containing the text 'No throw up at all' and a red-bordered box on the right containing the text 'Worse than you can imagine'.

13. Think about when you had the worst **numbness or tingling on your body** in the last 24 hours and circle the number you would give it.



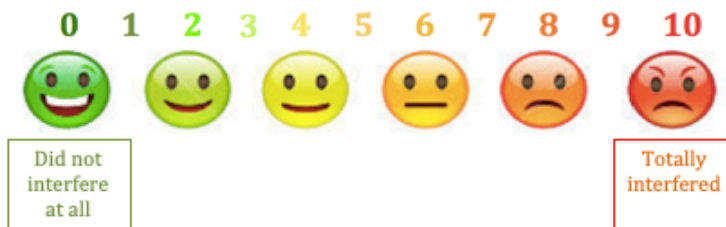
### Part 2.

We just talked about some problems and symptoms that you had in the last 24 hours. In the next section, you are going to answer some questions about how much these problems and symptoms interfered with your life.

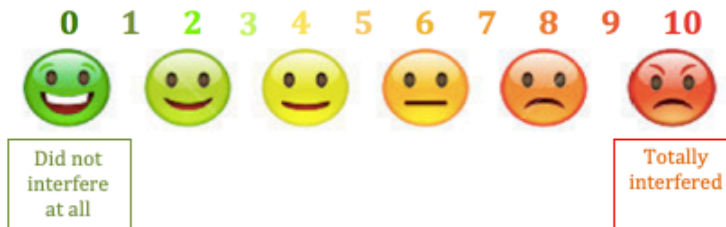
Do you know what *interfere* means?

- If no, it means “get in your way of doing things” or “make it hard to do things.” For example, you had a headache and it hurt so bad that it interfered with your schoolwork.

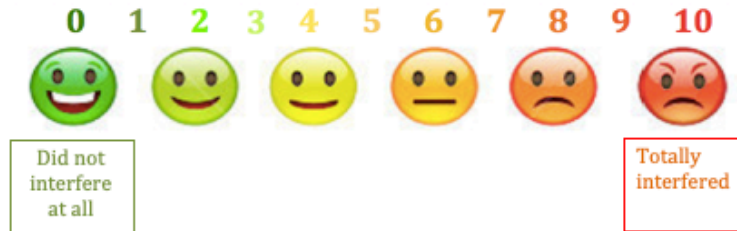
14. In the last 24 hours, how much have these body problems or symptoms interfered with your **daily activities**, like homework, brushing teeth, watching TV, and taking a bath?



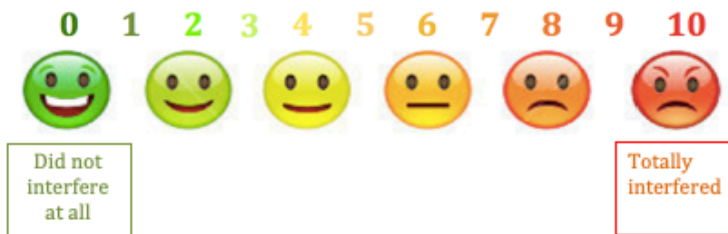
15. In the last 24 hours, how much have these body problems or symptoms interfered with how you **felt**?



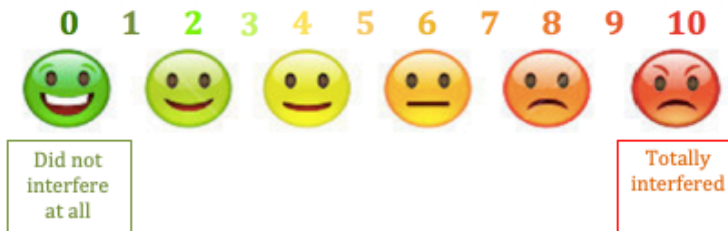
16. In the last 24 hours, how much have these body problems or symptoms interfered with your **schoolwork and chores**?



17. In the last 24 hours, how much have these body problems or symptoms interfered with your **relationships with others** (like your friends, family, teachers)?



18. In the last 24 hours, how much have these body problems or symptoms interfered with your **walking**?



19. In the last 24 hours, how much have these body problems or symptoms interfered with **how you enjoy life**?

