UNIVERSITÀ DEGLI STUDI DI PADOVA

Dipartimento di Psicologia dello Sviluppo e della Socializzazione

Corso di Laurea in Scienze Psicologiche dello Sviluppo, della Personalità e delle Relazioni interpersonali

Elaborato finale

Exploring the correlation between separation anxiety and COVID-19 related worries in children and adolescents with cancer and T1D

Relatrice:
Prof.ssa Daniela Di Riso

Laureanda: Clea Fantini
Matricola n. 1220676

Anno Accademico 2021-2022

SUMMARY:

ABSTRACT:

Covid-19 is a respiratory illness caused by the SARS-Co-2 virus. It was first discovered in China in November 2019, but it soon spread all over the world, causing the WHO to declare it a pandemic. From the 9th of March 2020 to the 18th of May 2020, the Italian government established a national lockdown to stop the virus from spreading. This research was born to explore the psychological impact of COVID-19 on chronically ill children and their mothers. This study takes into consideration children between the ages of 7 and 15 years suffering from various types of cancer and Type 1 Diabetes Mellitus (T1D). The control group comprised healthy children of the same age and gender and their mothers. 33 patients with cancer, 56 patients with T1D and their mothers compiled a survey about COVID-19 and a booklet of questionnaires, assessing general mental health and anxiety. We used a normality test, an analysis of variance and a Pearson's correlation coefficient to explore the data. The results show a correlation between SAAS-C scores and the survey variables. The children's psychological well-being didn't seem to correlate with the general mental health of their mothers. This study's objective was to fill the gap in the literature regarding the correlation between the pandemic and the psychological well-being of chronically ill children.

RIASSUNTO IN ITALIANO:

Il presente studio si è occupato di indagare l'impatto psicologico della pandemia causata dal virus SARS-Co-2 su bambini che soffrono di malattie oncologiche e diabete di tipo 1. Abbiamo raccolto un campione di 148 bambini di età compresa tra 7 e 15 anni, esaminandone primariamente i sintomi internalizzanti, esternalizzanti, l'ansia di separazione, la preoccupazione per il contagio e per il ritorno alle normali attività dopo la pandemia. Successivamente, abbiamo utilizzato un test di normalità, un test ANOVA e l'indice di correlazione di Pearson per analizzare i dati ed esplorare come le variabili fossero correlate fra loro. I risultati mostrano una relazione fra i livelli di ansia di separazione e le preoccupazioni riguardanti il COVID-19. L'obiettivo di questo studio è di colmare la mancanza di ricerche riguardo l'impatto della pandemia sul funzionamento psicologico di bambini che soffrono di malattie croniche.

CHAPTER 1: THEORETICAL BACKGROUND

1.1 Type 1 diabetes

Type 1 diabetes (T1D) is an autoimmune disease determined by insufficient insulin production in the islets of Langerhans in the pancreas. Insulin is a hormone required to regulate normal glucose levels in the bloodstream (glycemia). Normally, after eating a meal, glycemia rises and the pancreas secretes insulin, which stimulates the uptake of sugar into the cells, lowering its presence in the bloodstream. As the glucose present in the blood drops, so does the secretion of insulin from the pancreas. In diabetic patients, the β-cells responsible for the secretion of insulin are mistakenly destroyed by the immune system, causing a detrimental lack of insulin in the bloodstream and a state of hyperglycemia (high blood sugar levels in the bloodstream). If left untreated, this can commonly lead to frequent urination, increased thirst, increased hunger, weight loss, and other serious lifelong complications (Norris et al., 2020). When the body experiences a lack of insulin for a prolonged period of time, diabetic ketoacidosis can occur, which is characterized by persistent fatigue, dry or flushed skin, abdominal pain, nausea or vomiting, confusion, and trouble breathing and can rapidly progress to loss of consciousness, coma and death. (DiMeglio et al., 2018). Type 1 diabetes begins suddenly, usually in childhood or adolescence, and symptoms develop over a short period of time. The major sign of T1D is very high glycemia, which typically manifests in children as a few days to weeks of increased urination, increased thirst, and weight loss. Other common symptoms in children are: increased appetite, blurred vision, involuntary urination during sleep, recurrent skin infections, irritability, and performance issues at school (Atkinson et al., 2020). At the moment, the cause of type 1 diabetes is unknown, although recent studies point to a combination of genetic and environmental factors as a possible cause (National Institute of Diabetes and Digestive and Kidney Diseases, 2014). However, more research needs to be done and many possible environmental factors remain unknown.

1.1.1 Epidemiology

Type 1 diabetes makes up an estimated 10–15% of all diabetes cases (Katsarou et al., 2017) or 11–22 million cases worldwide. Although symptoms can begin at any age, onset is most common in children, especially around the age of puberty. T1D is slightly more present in males than in females (Atkinson et al., 2020). In 2006, T1D affected 440,000 children less than 14 years of age and was the primary type of diabetes in those under 15 years (Katsarou et al., 2017). The number of reported cases has been increasing in the past decades, supporting the hypothesis that the development of T1D could be influenced by environmental causes. Since the 1950s, the incidence of T1D has been gradually rising across the world by an average 3–4% per year (Norris et al., 2020). The number of individuals suffering from T1D varies sensibly across the world. For example, in the Environmental Determinants of Diabetes in the Young (TEDDY) study (Krischer et al., 2017), Finnish centers reported an incidence of T1D that was 78% higher than that in the US, even after adjusting for genotype and family history. Other geographical differences reported include the course of the illness: in Europe and North America, 15% of children begin the course of T1D with an episode of diabetic ketoacidosis; this number reaches 80% in developing countries (Delli & Lernmark, 2016). This data further raises the question of whether T1D could be influenced by environmental factors, on top of genetic ones.

1.1.2 Risk factors

Although the exact cause of type 1 diabetes is still unknown, there are some factors that may signal an increased risk of developing it, including a family history of T1D, environmental factors (such as exposure to a viral illness), presence of autoantibodies (which are immune system cells that target a person's own tissues or organs) and geography (countries like Finland and Sweden have higher risks of T1D) (Mayo Clinic, 2020). The increasing number of cases of T1D in the past decades supports the role of environmental factors in the prevalence of the disease. Although variations in incidence between different countries might be partially explained by genetic differences, large variations that have been reported between neighboring countries with similar genetic compositions are most likely explained by environmental factors (Norris et al., 2020). Some environmental factors believed to influence the genetic predisposition in developing T1D include maternal perinatal factors,

like higher age at delivery, obesity during gestation and cesarean section (Waernbaum et al., 2019). Childhood obesity has also been linked to a higher risk of T1D (Verbeeten et al., 2011), likely influencing β-cell stress, as well as a higher birthweight. The increased intake of cow's milk in children's diets is associated with islet autoimmunity and progression to T1D (Lamb et al., 2015), although the correlation seems small. Omega-3 acids might be associated with a lower risk of islet autoimmunity, given their anti-inflammatory properties (Calder et al., 2002), however, it's not clear whether these fatty acids can actually be a protective factor against T1D. The increased consumption of dietary sugars seems associated with progression to T1D, but not to islet autoimmunity, meaning it can accelerate the later stages of the illness, but not initial development. Higher sugar intake leads to a higher insulin demand – this could cause stress to β-cells and explain why dietary sugars increase the risk of T1D (Calder et al., 2008). Other environmental factors have been taken into consideration, but results are often unclear or contradictory and need further research to be thoroughly proven to influence T1D onset.

1.1.3 Diagnosis and treatment

Diabetes is typically diagnosed when a blood test is done and shows abnormally high glycemia. The World Health Organization defines diabetes as glucose levels at or above 7.0 mmol/L (126 mg/dL) after fasting for at least eight hours (World Health Organization, 2006). Once diabetes is diagnosed, a blood test for the presence of autoantibodies that target β-cells can differentiate T1D from other types of diabetes. Before the onset of the illness, there is an asymptomatic phase, termed islet autoimmunity, in which multiple autoantibodies to β-cell antigens are detectable in serum and it is highly predictive of type 1 diabetes. Nearly 70% of children in this stage progress to T1D within 10 years of seroconversion (Norris et al., 2020). It's important that general practitioners and nurses watch out for signs of islet autoimmunity since an early diagnosis could potentially avoid diabetic ketoacidosis. However, studies report that one in three newly diagnosed children was seen by a healthcare professional with symptoms of diabetes in the weeks prior to diagnosis (Sundaram et al., 2009), indicating that early signs can sometimes go unnoticed. Treatment is lifelong and includes taking insulin about four times a day to ensure the

absorption of glucose in the cells, monitoring glucose levels in the blood, a healthy diet and an active lifestyle (Mayo Clinic, 2020).

1.2 Cancer

The term cancer refers to a group of various diseases involving abnormal cell growth with the potential to spread to other parts of the body. Over 100 types of cancers affect humans, and they all have specific symptoms, risk factors and treatments. We will focus on childhood cancers, as this study concerns individuals between 7 and 15 years of age. The causes of most childhood cancers are unknown. About 5% of all cancers in children are caused by an inherited mutation, present since birth. The rest are thought to develop as a result of genetic mutations, incurred during the child's lifespan, that lead to uncontrolled cell growth and eventually cancer (National Institutes of Health, 2021). However, it's been difficult to identify the environmental factors that can potentially influence the incidence of childhood cancer, as it isn't easy to determine what children might have been exposed to during their early development. The most common types of cancer diagnosed in children ages 0 to 14 years are leukemias, brain and other central nervous system tumors, and lymphomas (National Institutes of Health, 2021). The most common symptoms associated with childhood cancer include: fever, severe and persistent headaches, bone pain and weight loss (World Health Organization, 2021).

1.2.1 Epidemiology

Cancer is a leading cause of death for children and adolescents: each year, an estimated 400.000 children and adolescents from 0 to 19 years of age develop some form of cancer. The likelihood of surviving the illness depends on the country in which the child lives: in high-income countries, more than 80% of children with cancer are cured, while in developing countries, less than 30% survive (World Health Organization, 2021). According to the International Classification of Childhood Cancer, the largest diagnostic groups among children 15 years and younger are leukemias, with a prevalence of 34%, brain tumors, at 23%, and lymphomas, at 12%, although considerable variations in incidence have been

reported between different countries. Incidence rates among children in developed countries have been rising in the past decades, accompanied by an improvement in the likelihood of survival (Kaatsch, 2010).

1.2.2 Risk factors

Although many studies have tried to identify the possible causes of childhood cancer, the majority of the latter don't have a known cause and very few are influenced by environmental or lifestyle factors. (World Health Organization, 2021). A recent review of 47 studies obtained a small consensus on four categories of risk factors: air pollution, chemical exposures, geographical location and radiation (July et al., 2022). However, the results were mixed and the relationship between childhood cancer and environmental risk factors remains inconclusive, therefore further research is needed.

1.2.3 Diagnosis and treatment

Early diagnosis is fundamental to increase the chance of survival for many forms of cancer. Cancer is more likely to respond well to treatment when treated in its early stages, which is often less expensive and less intensive. According to the Pan-American Health Organization (2014), early diagnosis consists of three components. One is awareness of symptoms by families and primary care providers, essential to identify the first signs of cancer and avoid delays in care, as they can sometimes be fatal. On top of that, an accurate and timely clinical evaluation is needed to determine the correct diagnosis and the extent to which the cancer has spread. The last component is prompt access to proper treatment. A correct diagnosis is extremely important because each form of cancer requires a specific kind of treatment, depending also on the stage of the illness. There are many types of cancer treatment, and children aren't always treated like adults. The types of care that a child with cancer receives will depend on the site and the stage of the illness. Some of the treatments available for children include: surgery, chemotherapy, radiation therapy, immunotherapy, and stem cell transplant. During their cancer treatment, as well as after competition and after remission, children can face unique issues. They may respond differently to drugs than their adult counterparts and treatments can have a different effect on a body that is still growing and

developing. Sometimes, children receive more intense treatments. Survivors can also be affected by long-term side effects, such as fatigue, or late effects, which do not occur until months or years after treatment. This is especially true for children, whose bones, tissues and organs are growing and can be negatively affected by cancer and its treatment, depending on the age of the child (National Institutes of Health, 2021).

1.3 Psychological health of chronically ill children

Chronic medical problems pose a significant risk factor for anxiety disorders in children and adolescents (Cruz et al, 2009), and the prevalence rate of anxiety disorders among chronically ill youths is higher compared to their healthy counterparts, with rates ranging from 7 to 40% (Lavigne et al., 1992). Many factors play a role in the development of an anxiety disorder in this population, for example, predisposing biological mechanisms related to the specific medical illness, as well as other genetic factors; anxiety may also be triggered by the preoccupation with the illness, invasive treatments, or permanence in the hospital, which can be a threatening environment for the child (Pao & Bosk, 2011). Anxiety symptoms can be difficult to diagnose in children with chronic illnesses, as they have to worry about their health status, on top of everyday worries typical of childhood and adolescence. This factor can make it harder to determine what should be considered clinical levels of anxiety in chronically ill children and when intervention is needed (Pao & Bosk, 2011). In addition, anxiety disorders in this population often have comorbid psychiatric and physical illnesses which make the distinction between physiological and psychological components of anxiety more difficult (Pao & Bosk, 2011). Moreover, a study from 2008 (Chavira, et al, 2008) found that somatic symptoms related to an actual physical illness may lead to more frequent triggers for panic attacks and anxiety disorders. The same research also reported that around half of the sampled children with anxiety disorders had a comorbid physical illness, furtherly establishing that anxiety and physical illness might influence each other and likely have a bidirectional relationship. In fact, anxiety, chronic worry and stress may weaken the immune system, rendering an individual more prone to infections, and increasing the severity of the preexisting physical condition (Richardson et al., 2006). Chronic illnesses that need constant monitoring and could result in a medical crisis, such as ketoacidosis in diabetes, may also

cause a child to be more anxious about being away from their caregivers, explaining the higher rates of separation anxiety in children with medical conditions (Chavira, et al, 2008). Other factors that may contribute to a chronically ill child's mental health are the side effects of the medications prescribed, which can, at times, result in anxiety symptoms (Guite & Kazak, 2018), as well as other psychosocial factors, such as parental adjustment, intelligence and social support (Snell & DeMaso, 2010). Additionally, moderate to severe anxiety levels are believed to affect how well a child adheres to treatment, manages the symptoms and copes with the illness, inevitably influencing the medical outcome (Richardson et al., 2006). A metanalysis carried out by Bennet (1994) found that children with a chronic illness are at a slightly more elevated risk for depressive symptoms, although most are not clinically depressed. However, some chronic conditions seem to be associated with greater depressive symptoms, while others, like cancer and type 1 diabetes, appear to be at lower risk (Bennet, 1994).

1.3.1 Psychological health of diabetic children

Children with Type 1 Diabetes Mellitus experience a series of additional stressors compared to healthy children. They have to perform an intensive daily treatment regimen, that requires insulin injections multiple times a day and often need to follow a diet and stick to specific mealtimes (Mayo Clinic, 2020). Additionally, as reported by Hanson and colleagues (1989) sudden changes in daily activities require the youth to adjust their dietary intake and insulin dosages to maintain metabolic control, limiting the child's ability to enjoy unexpected social events and other opportunities that stray from routine. Moreover, we need to take into account the preoccupation with hypoglycemia and ketoacidosis, feelings of guilt and shame for possible mistakes and fear of possible future medical complications (Hanson et al., 1989). Another factor to consider when examining the mental health of adolescents with T1D is how the illness hinders the developmental challenges of adolescence. During this stage, where identification with the peer group is fundamental, dealing with the stressors of self-management and the preoccupation over the illness can make adolescents feel different from their peers. In addition, emancipation from parents becomes more difficult when the youth feels dependent on them and vulnerable to the illness (Hanson et al., 1989).

A longitudinal study on mental health in youths with T1D (Grey et al., 1995) found that, right after diagnosis, children and adolescents experience higher symptoms of depression, withdrawal and dependency. After one year from diagnosis, the diabetic group's symptoms subsided, and scores were similar to controls; however, two years post-diagnosis, the initial differences presented again. Depression levels were especially significant, as twice as many children with diabetes scored in the clinical range compared to non-diabetic children. The researchers hypothesized that this second period of psychological distress might be due to the children's realization that diabetes is something they must deal with on a daily basis and for the rest of their lives. Grey also found that diabetic youths reported higher levels of hostility than healthy controls, and the difference widened with time. However, no differences were found in anxiety levels over time between the two groups in this specific study. Another research investigating anxiety disorders found that females had higher scores in anxiety-related disorders and fear of hypoglycemia than males, while older teens (16-18 years) had higher levels of social anxiety and fear of hypoglycemia compared to younger teens (13-15 years) (Al Hayek et al., 2015). The same study found that children who used an insulin pump instead of insulin injections had significantly lower levels of anxiety-related disorders and school avoidance compared to the multiple-dose injection group. Additionally, adolescents with a longer duration of diabetes reported higher scores in all of the subscales for fear of hypoglycemia and anxiety-related disorders (Al Hayek et al., 2015). A different study highlighted the correlation between coping style and health in diabetic children (Henson et al., 1989). Two different coping styles were defined: "Utilizing Personal and Interpersonal Resources" and "Ventilation and Avoidance". The former included behaviors that seek social and emotional support and assistance from family and friends, diversion of attention from problems to positive interests and self-reliance; the latter involved getting angry and blaming others, avoiding the problem by minimization and substance abuse. The researchers found that older adolescent age, long duration of T1D and poor adherence to treatment were correlated with ventilation and avoidant coping. Moreover, this negative strategy was predicted by high stress and low family cohesion. Adolescents with a shorter duration of T1D tended to cope by utilizing personal and interpersonal resources, however, no correlation was found between this coping strategy and health outcomes (Hanson et al.,

1989). Additionally, Wysocki and colleagues (1993) found that parent-adolescent relationship was a strong predictor of health outcomes, especially when evaluating variables like family communication and conflict resolution skills.

1.3.2 Psychological health of children suffering from cancer

Children and adolescents with pediatric cancer not only have to face the typical challenges of their age, but they also have to cope with difficulties in their physical and psychosocial development and must deal with complex, invasive and onerous treatment, which can last from 6 months to several years (Decker, 2007). Cancer often comes with factors that can pose a risk to children's psychological adjustment, like painful procedures, hospitalization and uncertain prognosis (Sloper, 2000). Different studies about pediatric cancer survivors' mental health have found heterogeneous results. Some researchers have found that self-esteem among this population seems to be comparable to or even higher than that of healthy controls (Richie, 2001), however, others have reported a decline in self-esteem overtime during adolescence and/or after the conclusion of treatment (Von Essen et al., 2000). In spite of all the difficulties and stressors encountered by pediatric oncology patients, several studies have found that most survivors are well adjusted to the illness and self-report test scores don't diverge significantly from those of healthy peers (Eiser et al., 2000). On the contrary, a study by Eilersten and colleagues (2011) examined internalizing and externalizing symptoms in pediatric cancer patients and found that the latter had higher scores in emotional symptoms and reported more academic difficulties than their peers. Additionally, they found internalizing and externalizing behaviors to be more common in patients suffering from late effects and those who received a brain tumor diagnosis. Children younger than 12 years old who suffer from cancer were found to have significantly more internalizing problems and somatic complaints than healthy controls, but no differences were reported in externalizing behaviors (Tsai et al., 2013). Furthermore, Thompson and colleagues (2009) reported a correlation between a diagnosis in adolescence and higher scores in internalizing and externalizing symptoms. The relationship was particularly strong among adolescent females. Further research has discovered that cancer survivors suffer from higher rates of separation anxiety and compulsive disorders (Szentes et al., 2018) and generalized anxiety (Mitchell et

al., 2013). Other studies have found an increased risk for anxiety (Maurice-Stam et al., 2008), somatic concerns (Carpentieri et al., 2003) and post-traumatic stress symptoms (Kazak et al., 1999), although the literature isn't homogeneous on the latter. A recent paper (Howard Sharp et al., 2015) suggested that levels of PTSD in children with cancer aren't higher than those of healthy peers, however, Brown and colleagues (2003), found incidence rates ranging from 20% to 35% among pediatric cancer survivors. Individual differences in mental health outcomes seem extremely vast and understanding how other factors like resilience and emotional regulation affect them is an important goal in pediatric cancer research, as suggested by Katz and colleagues (2015), who found an important correlation between poor emotional regulation and internalizing and somatic symptoms in pediatric cancer patients. Somatic concerns in children with low emotional regulation might be linked to the inability to correctly identify the sensations caused by negative emotions, attributing them to physical symptoms (Katz et al., 2015). Somatic complaints experienced by survivors of childhood cancer include nausea, headaches, dizziness, fatigue, impaired vision, a higher infection rate, and bodily pain (Bhatia et al., 2005). These symptoms tend to decrease over time. Erickson and Steiner (1999) found that cancer survivors can exhibit higher levels of somatic distress even years after treatment concludes. Children treated for brain tumor may exhibit overall deficits in global IQ, especially in the processing speed subscales, which may be caused by a loss of integrity of white matter tracts in the brain (Szentes et al., 2018). The same study examined the correlation between cognitive deficits and psychological symptoms but didn't find any significant relationship between the two variables. It is very likely that mental health problems encountered in brain cancer survivors aren't a consequence of the cognitive impairments caused by the tumor and its treatment; on the contrary, they are mainly related to the traumatic and life-threatening nature of the disease (Szentes et al., 2018).

1.4 The impact of COVID-19 on chronically ill children

The COVID-19 pandemic severely influenced the pediatric population due to the constant need for social isolation (Jiao et al., 2020). Researchers have already described the risk of acute stress disorder, adjustment disorder and grief in children during pandemics (Sprang et al., 2013) and more recent studies have found that the quality of life of children and

adolescents during the COVID-19 epidemic decreased significantly (Raven-Sieberer et al., 2021). This is especially true for children with chronic diseases, who often are at an increased risk of infection or complications because of their illness and report an even larger decrease in quality of life compared to their healthy peers.

1.4.1 Psychological health of diabetic children during the COVID-19 pandemic

A literature search regarding the incidence of COVID-19 found no evidence to prove that diabetic children are more susceptible to the virus than their non-diabetic peers (D'Annunzio et al., 2020), however, this population was affected by the pandemic in more ways than healthy people. Although recent studies have found no evidence that T1D patients are more at risk of infection, diabetic individuals experienced the awareness of being considered a risk group, since any kind of infection can worsen the degree of metabolic control; additionally, as hospital access was limited for a great part of the pandemic, children and adolescents with T1D were unable to adhere to the scheduled outpatient follow-up visits and had to modify the management of their illness (Passanisi et al., 2020). Furthermore, the COVID-19 lockdown limited the opportunities for physical activities, increasing the risk for T1D patients, since sedentary behavior might negatively affect glycemic control (Hall et al., 2021), and, in turn, the worsening of metabolic control may negatively affect the quality of life and resilience levels in diabetic patients (Lukacs et al., 2018). A recent study about the effects of quarantine on pediatric T1D patients found that, although very stressful from a psychological point, children and adolescents were able to adapt to the situation and develop resilience and coping skills (Passanisi et al., 2020). Almost all of the subjects in this research took advantage of this time to learn new skills. More than half of the patients did not change their eating habits and the majority regularly practiced physical activity at home. However, almost half of the sample reported that the quarantine had been an additional heavy burden on their perspective of the disease. Children younger than 12 years old were the most affected by the quarantine period in their approach to their illness and measured their glucose levels more frequently than their older counterparts (Passanisi et al., 2020). Anyhow, the researchers found that most of the study participants adjusted well to quarantine as demonstrated by their management of the disease. Building resilience during this time was

made possible with the help of technology, which not only assisted children and adolescents in managing their illness thanks to medical devices (like insulin pumps or glucose sensors), but it also proved to be fundamental in preserving social interactions and continuing school learning even during lockdown, through the use of smartphones, computers and social media (Passanisi et al., 2020). Moreover, technology was found to help all dimensions of children's wellbeing, from emotional to physical, social to spiritual and intellectual (Goldschmidt et al., 2020). All the time spent at home during the pandemic made diabetes management return mainly to the parents' hands. A recent study to evaluate the effectiveness of exclusive parental care in pre-school and elementary school children suffering from T1D found that parental care was associated with better metabolic performance despite the change in lifestyle (Schiaffini et al., 2020).

1.4.2 Psychological health of children suffering from cancer children during the COVID-19 pandemic

Children suffering from cancer may have a weakened immune system and therefore are at an increased risk of suffering from complications and unique health problems due to a coronavirus infection (Mirlashari et al., 2020). As pediatric cancer patients are at an increased risk of infection, they are considered a high-risk group and have been recommended higher-level measures like "excessive social distancing" (Slone et al., 2020). Moreover, the impact of the pandemic on this population was especially serious because children undergoing chemotherapy require regular outpatient care and intermittent hospital admission, both of which were substantially reduced during quarantine to prevent the spread of the virus. These measures could have critical consequences on children with cancer and pose a major challenge because of the risk of sub-optimal care and lack of support (Alshahrani et al., 2020). In an observational study carried out on pediatric cancer patients in Saudi Arabia, the majority of the subjects reported not feeling safe while visiting the hospital due to fear of contracting the virus, while only a third of them preferred hospital visits due to the perception of a more accurate assessment and care (Alshahrani et al., 2020). The patients of the same study appeared more concerned than the general population about the potential complications resulting from contagion. Almost all of the participants in the study reported being fearful

for their own health or a family member's and experienced a decrease in their quality of life, mainly because of the limitations in social activities, social isolation, anxiety, fear and loneliness. Most parents were concerned about behavioral changes that occurred in their children during the pandemic, which included anxiety, anger, depression, fear, insomnia and nightmares (Alshahrani et al., 2020). Another study carried out to determine the quality of life in children suffering from cancer during the first six months of the pandemic found that, although there was no statistically significant change in the pain that the children experienced, procedural and treatment anxieties of the children increased during this time, most likely due to the stress of the pandemic (Önal et al., 2021). Moreover, their cognitive state, perceived physical appearance and communication skills showed a significant decrease, as well as their overall quality of life (Önal et al., 2021). Their occupational performance (which is the ability to carry out tasks for one's own self-management) and satisfaction scores decreased as well. Additionally, parents reported that their children were in need of physical, psychological and social support. (Önal et al., 2021). This research found that, on top of treatment-related anxiety, pediatric cancer patients experienced increased worry and psychosocial stress. Additionally, Önal and colleagues highlighted the fact that the reduction of hospitalization limited the opportunities for social activities of children, which in turn brought them to increase internet use; this factor correlated to lower scores in physical and emotional well-being, as well as self-esteem in children with cancer (Riiser et al., 2020).

CHAPTER 2: RESEARCH

2.1 Objectives

This study examined the psychological functioning of children with chronic conditions (diabetes mellitus type 1 and cancer) and their mothers, as well as its correlation with anxiety and COVID-19 related concerns. We also compared the results of each clinical group with the other and with the control group. This study's focus is on the groups of children, rather than the mothers or the relationship between the two.

2.2 Hypothesis

Hypothesis 1: we expect that chronically ill children will have higher scores in the COVID-19 related variables "Fear of infection" and "Worry about returning to normal activities", as they are more susceptible to infection and/or complications resulting from COVID-19 (D'Annunzio et al., 2020; Mirlashari et al., 2020).

Hypothesis 2: we expect to find that chronically ill children will score higher values in internalizing problems compared to the healthy control group, in accordance with pre-existing literature that found that youths suffering from a chronic disease are more susceptible to symptoms of anxiety, depression and withdrawal (Bennett, 1994; Grey et al., 1995).

Hypothesis 3: we expect to encounter higher rates of anxiety in the chronically ill groups, especially in the cancer group, as children suffering from cancer have been reported to be at higher risk of generalized anxiety (Mitchell et al., 2013), while the literature regarding anxiety disorders in diabetic children isn't homogeneous. Moreover, we anticipate higher scores in the Separation Anxiety Assessment Scale (SAAS-C) for the cancer group's children, since the previous studies report a higher prevalence of separation anxiety in this population (Szentes et al., 2018).

Hypothesis 4: we expect a correlation between the children's scores on anxiety scales (SAAS-C and STAI-C) and the COVID-19 survey variables, as we anticipate that a higher preoccupation with the pandemic will be associated with greater symptoms of anxiety-related disorders.

2.3 Method

2.3.1 Participants

Our samples were composed of 148 children, of which 65 (43,9 %) were females and 83 (56,1%) were males. 33 of them suffered from cancer, 56 were diagnosed with type 1 diabetes and 59 were part of the control group and weren't affected by any chronic medical condition. The children's ages ranged from 7 to 15 years old. Exclusion criteria for the clinical groups were comorbidity with other chronic illnesses, psychiatric disorders and poor understanding of the Italian language. As for the control group, we excluded children with chronic psychiatric or neurological illnesses and low comprehension of the Italian language. In the diabetic patients' sample, we included 56 children, of which 35 males and 21 females, all with a type 1 diabetes diagnosis. The mean age of the group was 11,64 years old (SD = 2,47). The cancer patients' sample was composed of 33 subjects, of which 16 males and 17 females, suffering from a variety of forms of cancer (both blood and solid tumors). The mean age for this group was 11.13 years old (SD = 3,15). Time passed from diagnosis ranged from 2 to 66 months, with an average of 22,42 months (SD = 12,36). In the children's control group, we included 61 children between the ages of 7 and 15 years old (M = 11,36, SD = 2,523). Moreover, we recruited 56 mothers of children with T1D, whose ages ranged between 29 and 53 years (M = 44,05, SD = 5,741), and 33 mothers of children with oncological illnesses, whose ages ranged between 29 and 54 (M = 41,76, SD = 6,205). The mothers' control group included 61 women between 33 and 61 years of age (M = 44,97, SD = 5,434).

2.3.2 Procedures

The data concerning our diabetic patients' sample were collected from the database of the Regional Center for Pediatric Diabetes of the University Hospital of Verona, a specialized center for pediatric diabetology, between July and August 2021. The patients were recruited during routine visits and consent from both parents, as well as 12 years old and older children, was needed for the child's participation in the study. At this point, the participants filled out a booklet composed of a series of questionnaires and a survey about COVID-19 related concerns, specifically created for this research. The questionnaires could be compiled in person, either on paper or through a tablet, or from the patients' own homes, on their

smartphones or personal computers, through a link to the platform Google Forms. The link, as well as an alphanumeric code, were provided through email. The code was specific for every individual and had to be inserted at the beginning of the online questionnaire, in order to recognize the subject and ensure that only the medical staff knew the identity and personal data of the respondents. Completing the booklet and the survey took about 40 minutes, on average. The project was approved by the Padova ethics committee (CESC VR-RO). As for the cancer patients' sample, the data was collected from the "Nadia Toffa" pediatric ward of the Taranto Central Hospital, between November 2020 and May 2021. The patients were recruited while they were in outpatient care, inpatient care, or day hospital. Participation in the study was proposed at least 3 to 4 weeks after diagnosis, when research shows a better psychological adjustment to the illness in the family. Once both parents and 12 years old or older children consented to participate in the study, the same booklet and survey were administered, either on paper or through Google Forms. Participants filing the questionnaire online received an email with a link to the booklet and a personal alphanumeric code, to ensure their privacy. The project was approved by the Padova ethics committee (observational study n.977/CE). The control group's participants were recruited through snowball sampling.

2.3.3 Measures

2.3.3.1 Online survey

An ad hoc online survey was created to explore the psychological effects of Covid-19 on children with chronic conditions and their parents. The survey is composed of two items employing a 3-point Likert scale and evaluates the child's fear of infection and worry about returning to normal activities. High scores in these items show a lower mental and physical health in both the children and the parents.

2.3.3.2 Standardized scales and questionnaires

Children assigned to clinical and control groups were asked to complete the Strengths and Difficulties Questionnaire (SDQ, Goodman, 2001), the Separation Anxiety Assessment Scale for Children (SAAS–C; Eisen & Schaefer, 2005) and the State Trait Anxiety Inventory for

Children (STAI-C; Spielberger et al., 1973). Mothers were evaluated with the General Health Questionnaire-12 (GHQ-12, Goldberg, 1972)

The Strengths and Difficulties Questionnaire (SDQ; Goodman, 2001) is a self-report questionnaire created to assess psychological functioning in children and adolescents, in order to identify those at high risk of developing behavioral or emotional problems. The Italian version of the questionnaire was validated for children between the ages of 6 and 18 years old (Di Riso et al., 2010). The SDQ comprises 25 items divided into 5 subscales of 5 items each and measured on a 3-point Likert scale. The subscales are the following: "Emotional symptoms (EMO)", "Conduct problems (COND)", "Hyperactivity/inattention (HYPER)", "Peer relationships problems (PEER)" e "Prosocial behavior (PROS)". The first four subscales evaluate dysfunctional aspects of the child and the sum of these scores generates the Total Difficulties Score (TDS) an index of weakness in psychological functioning. On the contrary, the "PROS" subscale measures adaptive behavior. "EMO" and "PEER" subscales can be summed together to evaluate internalizing symptoms (INT), while "COND" and "HYPER" are used to evaluate externalizing symptoms (EXT). The questionnaire has been proven to have satisfactory construct and concurrent validity.

The Separation Anxiety Assessment Scale for Children (SAAS–C; Eisen & Schaefer, 2005) is a 34-item self-report scale developed for the evaluation of separation anxiety in children from 6 to 17 years of age. The SAAS-C employs a 4-point Likert scale and is composed of six subscales that measure different dimensions of separation anxiety: Fear of Abandonment (5 items), Fear of Being Alone (5 items), Fear of Physical Illness (5 items), Worry about Calamitous Events (5 items), Frequency of Calamitous Events (5 items), and Safety Signal Index (9 items). The first and second subscales focus on the avoidance component, the third and fourth address the maintenance component, while the fifth assesses whether there have been actual events in the child's life that could explain their separation anxiety. The Safety Signal Index refers to people, places and objects that can help the child soothe and feel safer during anxiety-inducing situations. The scale has been proven to have good validity and reliability.

The State Trait Anxiety Inventory for Children (STAI-C; Spielberger et al., 1973) was developed to provide separate measures of state and trait anxiety, as well as a total anxiety score, in children from 9 to 12 years of age, although it has been used with subjects as young as 5 years (e.g., Schisler, Lander, & Fowler-Kerry, 1998). The STAI-C uses a 4-point Likert scale. The "State anxiety" subscale measures transitory anxiety states that include feelings of apprehension, tension and worry evoked in response to situations perceived as stressful. The "Trait anxiety" subscale assesses individual differences in the tendency to experience anxiety states in stressful situations. The inventory has been proven to have satisfactory psychometric properties.

The General Health Questionnaire-12 (GHQ-12, Goldberg, 1972; 1993) is a self-report questionnaire used to assess common mental disorders in adults and adolescents. There are versions with different numbers of questions (12, 28, 30 and 60); we employed the twelve-item version, in which six items relate to positive emotions and the other six to negative emotions. Every item is evaluated on a 4-point Likert scale. The final score determines an estimate of the subject's general psychological wellbeing; high scores indicate poor mental health. The Italian version (Piccinelli et al., 1993) has been proven to have good validity and reliability.

CHAPTER 3: RESULTS

3.1 Data analysis

Normal distribution of the variables was verified through the Shapiro-Wilk normality test. Subsequently, if the distribution appears normal, an Anova (analysis of variance) test was utilized; contrariwise, a non-parametrical test (Kruskal-Wallis test) was applied to the data, which verified whether or not the samples came from the same distribution. If the variables were factorial, the Chi-squared test was utilized to determine the homogeneity of the samples. Finally, a Pearson's correlation coefficient was used to detect eventual correlations between different subscales.

3.2 Differences and comparisons between the children's groups

3.2.1 Results associated to Hypothesis 1: children's survey variables

SUBSCALE	**MEDIAN Control (CON)**	**MEDIAN Diabetic (D)**	**MEDIAN Cancer (CAN)**	**STATISTIC SIGNIFIC-ANCE**	**COMPARI-SONS**
Fear of infection	2,00	1,00	2,00	**p < .001**	Con > D Can > D
Worry about returning to normal activities	1,00	1,00	1,00	**0.034**	

Table 1: medians and comparisons of the three clinical groups' scores in the survey about Covid.

The groups weren't normally distributed and were significantly different in the item "Fear of infection"; in particular, the diabetic group reported lower values than the control and cancer groups.

3.2.2 Results associated to Hypothesis 2 & 3: SDQ, SAAS-C, STAI-C scores

SUBSCALE	MEDIAN Control (CON)	MEDIAN Diabetic (D)	MEDIAN Cancer (CAN)	STATISTIC SIGNIFIC-ANCE	COMPARI-SONs
SDQ					
Total Difficulties Scale (TDS)	11,00	7,00	9,50	0.122	
Internalization problems	4,00	2,00	4,00	**0.013**	Con > D
Externalization problems	5,00	4,00	4,00	0.255	
Conduct problems	2,00	2,00	2,00	0.150	
Hyperactivity/inattention	3,00	3,00	2,00	0.300	
Peer problems	2,00	1,00	1,00	0.539	
Prosocial behavior	7,00	8,00	8,00	0.075	
Emotional symptoms	3,00	1,00	3,00	**0.010**	Con > D
SAAS-C					
Fear of being alone	6,00	5,00	8,00	**p < .001**	Can > Con Can > D
Fear of abandonment	5,00	5,00	6,00	**0.003**	Can > D
Fear of physical injuries	6,00	6,00	7,00	0.061	

Worry for calamitous events	10,00	8,00	9,00	**0.008**	Con > D
Frequency of calamitous events	11,00	10,00	9,00	**0.010**	
Safety signal index	13,00	12,00	16,00	**0.020**	Can > D
SAAS total	54,00	47,00	53,00	**0.005**	Con > D Can > D
STAI-C					
Trait anxiety	33,00	30,00	29,00	**0.050**	Con > D
State anxiety	30,00	31,00	30,00	0.441	
Total anxiety	63,00	61,00	58,50	0.095	

Table 2: comparisons of the three clinical groups' scores in the SDQ, SAAS-C and STAI-C

In the SDQ, the sample groups appeared to be homogeneous in the TDS and most of the subscales, except for "Internalization problems" and "Emotional symptoms", where the diabetic patients' group had significantly lower scores than the control group. Children tested with the SDQ, specifically in the Total Difficulties Scale, tended to score in the normal range although the control group appeared to be the one with the highest percentage of clinical symptoms (10.5%).

As for the SAAS total and most of the subscales, the diabetic patients' group appeared to have significantly lower scores than other groups. Moreover, we found a particularly significant difference ($p < .001$) in the "Fear of being alone" subscale, where the cancer group had higher scores than the diabetic group.

Finally, in the STAI-C, we found that the control group had significantly higher scores than the diabetic patients' group in the "Trait Anxiety" subscale. Many children tested with the STAI-C scored in the clinical range: in the "Trait Anxiety" subscale, the control group had

the highest percentage of clinical scores (19,3%), while cancer patients reported higher clinical symptoms in the "State anxiety" (48,4%) and "Total anxiety" subscales (31,0%).

3.3 Results associated to Hypothesis 4: Correlations between survey variables and SDQ, SAAS-C, STAI-C scores

3.3.1 Cancer patients' group

	Fear of infection	**Worry for normal activities**	**SAAS-C**	**SDQ (TDS)**	**STAI-C**	**GHQ (mothers)**
Fear of infection	-					
Worry for normal activities	.343 (p=.059)	-				
SAAS-C	.303 (p = .098)	**.434* (p=.015)**	**-**			
SDQ	**-.366* (p=.047)**	.097 (p=.612)	.308 (p=.097)	-		
STAI-C	**-**.299 (p=.115)	**-**.007 (p=.970)	.280 (p=.141)	**.871* (p<.01)**	-	
GHQ	.121 (p=.515)	.025 (p=.896)	.143 (p=.442)	-.156 (p=.410)	-.201 (p=.295)	-

Table 3: the tables show the correlations and their significance. *Correlation is significant for $p < .05$ (2-code).

The survey variable "Worry for returning to activities" correlated positively with scores on the SAAS-C, while the variable "Fear of infection" correlated negatively with total SDQ scores. A strong positive correlation was found between total STAI-C scores and SDQ scores. Children's psychological well-being didn't seem to correlate with the general mental health of their mothers (measured with the GHQ).

3.3.2 Diabetic patients' group

	Fear of infection	**Worry for normal activities**	**SAAS-C**	**SDQ (TDS)**	**STAI-C**	**GHQ (mothers)**
Fear of infection	-					
Worry for normal activities	.238 (p=.083)	-				
SAAS-C	**.339* (p=.012)**	**.302* (p=.026)**	**-**			
SDQ	.141 (p=.309)	.101 (p=.429)	.193 (p=.163)	-		
STAI-C	.141 (p=.310)	-.009 (p=.950)	.192 (p=.165)	**.777* (p<.01)**	-	
GHQ	-.167 (p=.227)	-.099 (p=.476)	-.032 (p=.819)	.187 (p=.177)	.166 (p=.230)	-

Table 4: the tables show the correlations and their significance. *Correlation is significant for $p < .05$ (2-code).

Significant positive correlations in the diabetic patients' group have been found between SAAS-C scores and both survey variables ("Fear of infection" and "Worry about returning to normal activities"). This means that higher SAAS-C scores were related to higher scores in the COVID-19 survey. Children's psychological well-being didn't seem to correlate with the general mental health of their mothers (measured with the GHQ).

CHAPTER 4: DISCUSSION

This study's goal was to explore the psychological impact of the COVID-19 pandemic on a sample of 148 children, whose ages range between 7 and 15 years. We examined the psychological well-being of 33 children with cancer and 56 with type 1 diabetes and compared it to a control group of 59 children similar in age and gender, focusing mainly on internalizing and externalizing problems, with particular attention to anxiety disorders. Additionally, we measured their fear of infection and worry in relation to the return to normal activities after the end of quarantine and compared them to those of their healthy peers. Lastly, we studied how these variables – worries related to the pandemic and test scores – related to each other.

The results associated with our first hypothesis concerning the survey variables highlighted that our cancer group's patients experienced a greater fear of infection compared to the diabetic group patients. Similarly, our control group reported higher values than the diabetic group. These results do not line up with our expectations, as we hypothesized that the chronically ill groups would score higher levels than control group in the COVID-19 related variables seeing that they are more susceptible to complications resulting from infections. We can conclude that children suffering from cancer don't experience higher rates of fear of infection compared to their healthy peers. We did not anticipate this, as researchers previously found that youths suffering from cancer reported greater concerns in relation to the infection and its resulting complications than the general population (Alshahrani et al., 2020). Alshahrani and colleagues also reported that the majority of parents thought their children suffering from cancer had a reasonable understanding of the virus, and half of them received education material from the hospital. In our case, the education provided by the healthcare system and a consequent understanding of the pandemic, together with a strong family support, might have positively influenced the fear of infection in our group. Children suffering from T1D appeared to be less fearful than the general population and their clinical counterparts. The findings regarding diabetic children, although contradicting our hypothesis, can be explained by the research done by Passanisi and colleagues (2020), who reported that their sample of diabetic children seemed to adapt well to quarantine, developing

various coping skills and resilience. These functional adjustments could explain why diabetic children appeared less worried about the pandemic than the control group and cancer group.

The SDQ (Strength and Difficulties Questionnaire) results contradicted our second hypothesis, reporting that the control group had statistically higher scores than diabetic children in internalizing symptoms and emotional problems. Healthy children also scored higher values than the cancer group in many SDQ subscales, however, in this case, we didn't find any statistical significance. We did not anticipate these results since previous studies agreed on the fact that chronically ill children have more internalizing and externalizing problems than their healthy peers (Eilersten et al., 2011; Thompson et al., 2009). This could be explained by the larger support that chronically ill children potentially received from parents and the healthcare system during the pandemic, although this is just a hypothesis that may need further investigations. Moreover, recent studies have found that even healthy children have been largely and negatively affected by the pandemic, lowering their quality of life (Jiao et al., 2020; Raven-Sieberer et al., 2021). This factor could possibly minimize the differences in mental health that many researchers encountered in the past between chronically ill children and their healthy peers, as both these groups have experienced large amounts of stress and isolation in the past couple of years.

Our third hypothesis was confirmed as cancer patients reported higher levels of anxiety than control and/or diabetic group in both the SAAS-C and the STAI-C. Significantly higher scores of the diabetic group compared to the cancer group were found in many subscales of the SAAS-C like: "fear of being alone", "fear of abandonment", "safety signal index" and "SAAS total". This is coherent with pre-existing literature stating that children with cancer have higher rates of anxiety disorders, especially separation anxiety (Szentes et al., 2018). This might be due to the hospitalization and intrusive procedures they need to undergo which are usually perceived as threatening by the children (Pao & Bosk, 2011). In the SAAS total subscale, the diabetic group had significantly lower scores than both the cancer and control groups and in the STAI-C's subscale "Trait Anxiety", controls have significantly higher scores than diabetic children, reinforcing once more the idea that T1D isn't necessarily associated with anxiety disorders (Grey et al., 1995), and that the pandemic has worsened the

conditions of all types of children and adolescents, both healthy and sick (Jiao et al., 2020; Raven-Sieberer et al., 2021). Anyhow, lower levels of anxiety in diabetic children during the pandemic might be related to the fact that the management of their illness has gone back to the hands of their parents, lifting the burden from the patients while helping them maintain a good metabolic rate (Schiaffini et al., 2020).

Our fourth hypothesis was partially verified as significant positive correlations between the SAAS-C and the survey variables have been found in the diabetic group, as well as a significant correlation between the SAAS-C and the subscale "worry for returning to normal activities" in the cancer group. These findings confirmed our expectations that a higher presence of anxiety symptoms is associated with a greater preoccupation with the pandemic. The longer time spent at home by the children could worsen the separation anxiety they experience, explaining why pandemic-related concerns correlated with the SAAS-C. This factor was taken into consideration by Pelaez and Novak, who suggest that the conditions created by the COVID-19 pandemic served as a catalyst for separation anxiety. Events like the hospitalization or death of a parent or relative, the worrisome news and the preoccupations of adults in response to the latter can increase anxiety in children. Moreover, social distancing and constant isolation have caused families to develop stronger attachments and dependencies at home, which in turn make it harder for both children and parents to adapt to life after the pandemic and can make the return to school particularly difficult (Pelaez & Novak, 2020).

4.1 Limitations

This study presents some noteworthy limitations. First of all, our samples were small, therefore our findings may not be generalized to the whole population, and our cancer group had significantly fewer participants than our diabetic and control groups, which could have influenced our results. Moreover, our data were collected during different periods of time for the different groups; this factor could have affected our findings since the preoccupation with the pandemic changed a lot during the course of the seasons as the number of infected and deaths fluctuated. For example, our diabetic group's data were collected during the summer months of 2021, when the COVID-19 infection curve had flattened compared to the previous

winter and spring, when our cancer group's data were collected. The children were told to file the questionnaires autonomously, however for at-home compiling we cannot be certain that other family members haven't interfered with the patient's answers. Finally, the lack of data before the lockdown represents a significant limitation, since we cannot know the full extent to which the pandemic affected the children' mental health.

4.2 Future developments

The present research explored the psychological functioning and well-being of chronically ill children during the COVID-19 pandemic, focusing specifically on the influence of the pandemic on anxiety disorders. At this point in time, there isn't much literature regarding the effects of the pandemic on children suffering from cancer and type 1 diabetes. Further studies need to be done to establish the extent of the way the pandemic has affected children, especially those with chronic medical conditions. It is important that future research will employ larger samples of similar numerosity, to allow generalization of the results and prevent different sized samples from affecting them. However, since the pandemic seems to be coming to an end, further investigations should involve longitudinal studies exploring the long-term effects of the virus outbreak and lockdown on chronically ill children in order to discover the ways in which COVID-19 has permanently affected the psychological functioning of this population. Moreover, new developments could focus on examining other anxiety-related conditions resulting from the pandemic, such as obsessive-compulsive disorder or social anxiety. Additional studies could be done to determine if and how the COVID-19 outbreak has affected the physical symptoms of chronically ill children. Further research would allow a better understanding of the mental well-being of this population and improve psychological interventions and treatments.

4.3 Conclusions

The current study focused on the psychological well-being of children suffering with cancer and type 1 diabetes during the COVID-19 pandemic. Concerning COVID-19 related worries, both healthy children and children with cancer reported higher preoccupation than diabetic patients. Moreover, our cancer group reported generally higher anxiety levels than

diabetic patients. For the most part, children suffering with T1D seemed to cope better with the COVID-19 outbreak compared to both children suffering with cancer and healthy peers. Unlike what we had anticipated, healthy children often reported psychological symptoms comparable to those of chronically ill children. Lastly, we discovered that higher levels of separation anxiety symptoms were associated to greater COVID-19 related worries in both clinical groups. This research highlights the need for special attention to the consequences of the coronavirus outbreak in both chronically ill children and their healthy peers, whose psychological well-being has decreased significantly as well, despite better physical health. More efforts need to be put into developing specific treatments and interventions for children suffering from the consequences of the pandemic in order to allow a seamless transition to the post-pandemic period.

BIBLIOGRAFIA:

Al Hayek, A. A., Robert, A. A., Braham, R. B., Issa, B. A., & Al Sabaan, F. S. (2015). Predictive risk factors for fear of hypoglycemia and anxiety-related emotional disorders among adolescents with type 1 diabetes. *Medical Principles and Practice*, *24*(3), 222-230.

Atkinson, M. A., Mcgill, D. E., Dassau, E. & Laffel, L. (2020). "Type 1 diabetes mellitus". *Williams Textbook of Endocrinology*. Elsevier. pp. 1403–1437.

Bennett, D. S. (1994). Depression among children with chronic medical problems: a meta-analysis. *Journal of pediatric psychology*, 19(2), 149-169.

Bhatia, S., & Landier, W. (2005). Evaluating survivors of pediatric cancer. *The Cancer Journal*, 11(4), 340-354..

Brown, R. T., Madan-Swain, A., & Lambert, R. (2003). Posttraumatic stress symptoms in adolescent survivors of childhood cancer and their mothers. *Journal of Traumatic Stress*, 16(4), 309– 318.

Calder, P. C., & Grimble, R. F. (2002). Polyunsaturated fatty acids, inflammation and immunity. *European journal of clinical nutrition,* 56(3), S14-S19.

Carpentieri, S. C., Meyer, E. A., Delaney, B. L., Victoria, M. L., Gannon, B. K., Doyle, J. M., & Kieran, M. W. (2003). Psychosocial and behavioral functioning among pediatric brain tumor survivors. *Journal of neuro-oncology*, 63(3), 279-287.

Chavira, D. A., Garland, A. F., Daley, S., & Hough, R. (2008). The impact of medical comorbidity on mental health and functional health outcomes among children with anxiety disorders. *Journal of developmental and behavioral pediatrics*: JDBP, 29(5), 394.

Cruz, I., Marciel, K. K., Quittner, A. L., & Schechter, M. S. (2009, October). Anxiety and depression in cystic fibrosis. In *Seminars in respiratory and critical care medicine* (Vol. 30, No. 05, pp. 569-578). © Thieme Medical Publishers.

d'Annunzio, G., Maffeis, C., Cherubini, V., Rabbone, I., Scaramuzza, A., Schiaffini, R., ... & Maghnie, M. (2020). Caring for children and adolescents with type 1 diabetes mellitus: Italian Society for Pediatric Endocrinology and Diabetology (ISPED) statements during COVID-19 pandemia. *diabetes research and clinical practice*, 168, 108372.

Decker, C. L. (2007). Social support and adolescent cancer survivors: A review of the literature. *Psycho-Oncology: Journal of the Psychological, Social and Behavioral Dimensions of Cancer*, 16(1), 1-11.

Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycemia (PDF). Geneva: World Health Organization. 2006. p. 1.

Delli, A. J., & Lernmark, Å. (2016). Type 1 (Insulin-Dependent) Diabetes Mellitus. *Endocrinology: Adult and Pediatric*, Vol: 1-2, Page: 672-690.

DiMeglio, L. A., Evans-Molina, C., & Oram, R. A. (2018). Type 1 diabetes. *The Lancet*, *391*(10138), 2449-2462.

Eilertsen, M. E. B., Rannestad, T., Indredavik, M. S., & Vik, T. (2011). Psychosocial health in children and adolescents surviving cancer. *Scandinavian Journal of Caring Sciences*, *25*(4), 725-734.

Eiser, C., Hill, J. J., & Vance, Y. H. (2000). Examining the psychological consequences of surviving childhood cancer: Systematic review as a research method in pediatric psychology. *Journal of Pediatric Psychology, 25*(6), 449-460

Goldschmidt, K. (2020). The COVID-19 pandemic: Technology use to support the wellbeing of children. *Journal of pediatric nursing*, *53*, 88

Grey, M., Cameron, M. E., Lipman, T. H., & Thurber, F. W. (1995). Psychosocial status of children with diabetes in the first 2 years after diagnosis. *Diabetes care*, 18(10), 1330-1336.

Guite, J. W., & Kazak, A. E. (2010). Anxiety symptoms and disorders.

Hall, G., Laddu, D. R., Phillips, S. A., Lavie, C. J., & Arena, R. (2021). A tale of two pandemics: How will COVID-19 and global trends in physical inactivity and sedentary behavior affect one another?. *Progress in cardiovascular diseases*, *64*, 108.

Hanson, C. L., Cigrang, J. A., Harris, M. A., Carle, D. L., Relyea, G., & Burghen, G. A. (1989). Coping styles in youths with insulin-dependent diabetes mellitus. *Journal of consulting and clinical psychology*, *57*(5), 644.

Howard Sharp, K. M., Rowe, A. E., Russell, K., Long, A., & Phipps, S. (2015). Predictors of psychological functioning in children with cancer: Disposition and cumulative life stressors. *Psycho-Oncology*, 24(7), 779– 786.

Jiao, W. Y., Wang, L. N., Liu, J., Fang, S. F., Jiao, F. Y., Pettoello-Mantovani, M., & Somekh, E. (2020). Behavioral and emotional disorders in children during the COVID-19 epidemic. *The journal of Pediatrics*, *221*, 264-266.

Julie M. Buser, Kristen Lake, Emily Ginier, "Environmental Risk Factors for Childhood Cancer in an Era of Global Climate Change: A Scoping Review", *Journal of Pediatric Health Care*, Volume 36, Issue 1, 2022, Pages 46-56.

Katsarou, A., Gudbjörnsdottir, S., Rawshani, A., Dabelea, D., Bonifacio, E., Anderson, B. J., ... & Lernmark, Å. (2017). Type 1 diabetes mellitus. *Nature reviews Disease primers*, 3(1), 1-17.

Kaatsch, P. (2010). Epidemiology of childhood cancer. *Cancer treatment reviews*, 36(4), 277-285.

Katz, L. F., Heleniak, C., Kawamura, J., & Jakubiak, J. (2015). Emotion regulation, internalizing symptoms and somatic complaints in pediatric survivors of acute lymphoblastic leukemia. *Psycho-Oncology*, *24*(11), 1536-1544.

Kazak, A. E., Simms, S., Barakat, L., Hobbie, W., Foley, B., Golomb, V., & Best, M. (1999). Surviving Cancer Competently Intervention Program (SCCIP): a cognitive-behavioral and

family therapy intervention for adolescent survivors of childhood cancer and their families. *Family Process*, 38(2), 176-191.

Krischer, J. P., Lynch, K. F., Lernmark, Å., Hagopian, W. A., Rewers, M. J., She, J. X., ... & TEDDY Study Group. (2017). Genetic and environmental interactions modify the risk of diabetes-related autoimmunity by 6 years of age: the TEDDY study. *Diabetes care*, 40(9), 1194-1202.

Lamb, M. M., Miller, M., Seifert, J. A., Frederiksen, B., Kroehl, M., Rewers, M., & Norris, J. M. (2015). The effect of childhood cow's milk intake and HLA-DR genotype on risk of islet autoimmunity and type 1 diabetes: The Diabetes Autoimmunity Study in the Young. *Pediatric diabetes*, 16(1), 31-38.

Lamb, M. M., Yin, X., Barriga, K., Hoffman, M. R., Baron, A. E., Eisenbarth, G. S., ... & Norris, J. M. (2008). Dietary glycemic index, development of islet autoimmunity, and subsequent progression to type 1 diabetes in young children. *The Journal of Clinical Endocrinology & Metabolism*, 93(10), 3936-3942.

Lavigne, J. V., & Faier-Routman, J. (1992). Psychological adjustment to pediatric physical disorders: A meta-analytic review. *Journal of pediatric psychology*, 17(2), 133-157.

Mayo Clinic, "Diabetes – Symptoms and Causes", 2020. https://www.mayoclinic.org/diseases-conditions/diabetes/symptoms-causes/syc-20371444

Maurice-Stam, H., Oort, F. J., Last, B. F., Brons, P. P., Caron, H. N., & Grootenhuis, M. A. (2008). Longitudinal assessment of health-related quality of life in preschool children with non-CNS cancer after the end of successful treatment. *Pediatric blood & cancer*, 50(5), 1047-1051.

Mirlashari, J., Ebrahimpour, F., & Salisu, W. J. (2020). War on two fronts: Experience of children with cancer and their family during COVID-19 pandemic in Iran. *Journal of Pediatric Nursing*, 57, 25–31.

Mitchell, A. J., Ferguson, D. W., Gill, J., Paul, J., & Symonds, P. (2013). Depression and anxiety in long-term cancer survivors compared with spouses and healthy controls: a systematic review and meta-analysis. *The lancet oncology*, 14(8), 721-732.

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), "Causes of Diabetes". August 2014. https://www.niddk.nih.gov/health-information/diabetes/overview/symptoms-causes?dkrd=hiscr0005

National Institute of Health (NIH), National Cancer Institute, "Childhood cancers", April 2021. https://www.cancer.gov/types/childhood-cancers

Norris, J. M., Johnson, R. K., & Stene, L. C. (2020). Type 1 diabetes—early life origins and changing epidemiology. *The lancet Diabetes & endocrinology*, 8(3), 226-238.

Pan-American Health Organization. (2014). Early diagnosis of childhood cancer. Pan-American Health Organization. https://iris.paho.org/handle/10665.2/34850

Pao, M., & Bosk, A. (2011). Anxiety in medically ill children/adolescents. *Depression and Anxiety,* 28(1), 40-49.

Pelaez, M., & Novak, G. (2020). Returning to school: separation problems and anxiety in the age of pandemics. *Behavior analysis in practice*, 13(3), 521-526.

Ravens-Sieberer, U., Kaman, A., Erhart, M., Devine, J., Schlack, R., & Otto, C. (2021). Impact of the COVID-19 pandemic on quality of life and mental health in children and adolescents in Germany. *European Child & Adolescent Psychiatry*.

Richardson, L. P., Lozano, P., Russo, J., McCauley, E., Bush, T., & Katon, W. (2006). Asthma symptom burden: relationship to asthma severity and anxiety and depression symptoms. *Pediatrics*, 118(3), 1042-1051.

Richie, M. A. (2001). Self-esteem and hopefulness in adolescents with cancer. *Journal of Pediatric Nursing*, 16(1), 35-42.

Riiser, K., Helseth, S., Haraldstad, K., Torbjornsen, A., & Richardsen, K. R. (2020). Adolescents' health literacy, health protective measures, and health-related quality of life during the COVID-19 pandemic. *PLoS ONE*, 15(8), e0238161

Slone, J. S., Ozuah, N., & Wasswa, P. (2020). Caring for children with cancer in Africa during the COVID-19 crisis: Implications and opportunities. *Pediatric Hematology and Oncology*, 37(7), 549–553.

Sloper, P. (2000). Predictors of distress in parents of children with cancer: A prospective study. *Journal of Pediatric Psychology*, 25, 79–92.

Snell, C., & DeMaso, D. R. (2010). Adaptation and coping in chronic childhood physical illness.

Sprang, G., & Silman, M. (2013). Posttraumatic stress disorder in parents and youth after health-related disasters. *Disaster medicine and public health preparedness*, *7*(1), 105-110.

Sundaram, P. C., Day, E., & Kirk, J. M. W. (2009). Delayed diagnosis in type 1 diabetes mellitus. *Archives of disease in childhood*, 94(2), 151-152.

Szentes, A., Erős, N., Kekecs, Z., Jakab, Z., Török, S., Schuler, D., ... & Garami, M. (2018). Cognitive deficits and psychopathological symptoms among children with medulloblastoma. *European Journal of Cancer Care*, *27*(6), e12912.

Thompson, A. L., Gerhardt, C. A., Miller, K. S., Vannatta, K., & Noll, R. B. (2009). Survivors of childhood cancer and comparison peers: The influence of peer factors on later externalizing behavior in emerging adulthood. *Journal of Pediatric Psychology, 34*(10)

Tsai, M. H., Hsu, J. F., Chou, W. J., Yang, C. P., Jaing, T. H., Hung, I. J., ... & Huang, Y. S. (2013). Psychosocial and emotional adjustment for children with pediatric cancer and their primary caregivers and the impact on their health-related quality of life during the first 6 months. *Quality of life Research*, *22*(3), 625-634.

Verbeeten, K. C., Elks, C. E., Daneman, D., & Ong, K. K. (2011). Association between childhood obesity and subsequent Type 1 diabetes: a systematic review and meta-analysis. *Diabetic Medicine*, 28(1), 10-18.

Von Essen, L., Enskär, K., Kreuger, A., Larsson, B., & Sjödén, P. O. (2000). Self-esteem, depression and anxiety among Swedish children and adolescents on and off cancer treatment. *Acta Paediatrica, 89*, 229-236.

Waernbaum I, Dahlquist G, Lind T. Perinatal risk factors for type 1 diabetes revisited: a population-based register study. *Diabetologia* 2019; 62: 1173–84.

World Health Organization. (2021). CureAll framework: WHO global initiative for childhood cancer: increasing access, advancing quality, saving lives. World Health Organization. https://apps.who.int/iris/handle/10665/347370

Wysocki, T. (1993). Associations among teen-parent relationships, metabolic control, and adjustment to diabetes in adolescents. *Journal of Pediatric Psychology*, *18*(4), 441-452.