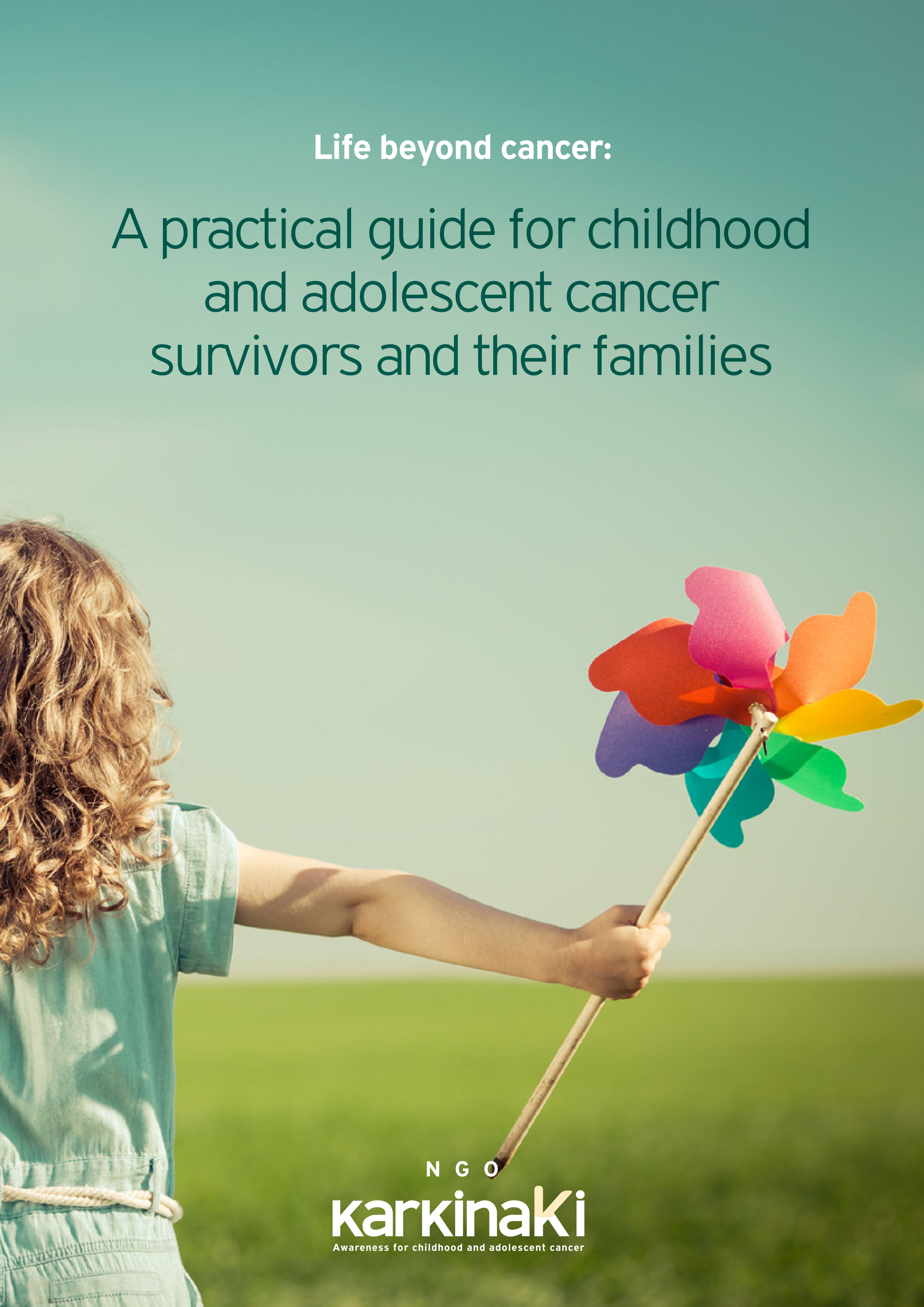
Life beyond cancer:

A practical guide for childhood and adolescent cancer survivors and their families



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Awareness for childhood and adolescent cancer

Introductory note

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Childhood and adolescent cancer can indeed be overcome, and most children diagnosed with cancer emerge victorious in their battle.

As treatment concludes, children and their families enter a period of transition, where they begin to heal and return to everyday life. This phase often presents an opportunity to address and work through physical, psychological, and social trauma, as well as concerns about long-term effects of treatment and survivorship. This transition can be challenging for all involved. We believe that successful outcomes are closely linked to diligent monitoring and effective information sharing between healthcare professionals and affected families.

At the University Hematologic Oncology Unit (POHemU) of the 1st Pediatric Clinic at the National and Kapodistrian University of Athens, we have taken a leading role in the research and treatment of childhood and adolescent cancer. POHemU is a Centre of Excellence and a full member of the European Reference Network on Paediatric Cancer (ERN PaedCan). Our long-term follow-up clinic, led by pediatric consultant Katerina Katsibardi, provides a cross-disciplinary approach to post-treatment care for children and adolescent cancer survivors. In alignment with this approach, we have partnered with the Non-Profit Organization 'KARKINAKI' to offer informational seminars aimed at educating patients and their families about the issues that may arise after the end of treatment.

This guide summarizes key topics discussed in these informational seminars and reflects our conversations with patients and their families. It serves as a testament to the benefits achieved when healthcare professionals collaborate with patient organizations, such as KARKINAKI, to support children and adolescents with cancer.

Childhood cancer, while rare and tragic, presents an opportunity to not only treat young patients effectively but also to minimize the long-term effects of cancer treatment.•••

Late effects of childhood and adolescent cancer survivors

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«Being cancer free is not the same as being free of cancer»

Childhood and adolescent cancer, though rare, affects approximately 150 out of every 1 million children and teenagers. It is the second leading cause of mortality among children aged 16 and below, following accidents. In Europe, around 15,000 children and teenagers are diagnosed with cancer annually, with 330 to 350 cases occurring in Greece. The most common pediatric cancer is acute lymphoblastic leukemia (ALL), following intracranial and central nervous system (CNS) tumors.

Recent advancements have significantly improved survival rates for childhood cancer. In the 1970s, the five-year survival rate for childhood cancer was 60%. However, by 2010, this rate had increased to 80-90% for several types of cancer, including ALL, nephroblastoma (Wilms' tumor), and Hodgkin lymphoma. Progress has also been made in treating more aggressive cancers.

As a result, childhood cancer treatment is now considered a success story in pediatric oncology. Currently, there are over 500,000 childhood cancer survivors in Europe and 400,000 in the United States. In 2020, one in 350 adults had a history of childhood cancer, and this number is expected to rise.

Despite these successes, childhood and adolescent cancer survivors often face long-term health issues due to the disease and its treatments, such as chemotherapy, radiotherapy, and surgery. Long-term follow-up care is crucial. Initially, follow-up appointments are more frequent, every 3-6 months for the first three years, and then every 6 months until the end of the fifth year post-treatment. Annual follow-up care continues even at the phase of survivors' transition into adulthood with regular routine screenings.

Long-term effects of cancer treatment may manifest immediately, within two to five years, or even up to ten years after treatment. Approximately 75% of survivors experience at least one complication, with 25% facing severe or life-threatening side effects. Survivors may also encounter health issues earlier in life, often between ages 35 and 50, compared to the general population.

Common late effects include endocrine disorders (such as hypothyroidism, growth hormone deficiency, and puberty issues), cardiovascular disease, and metabolic syndrome or obesity. For instance, obesity rates among young survivors are around 14%, double than that of healthy children. Survivors also face a sevenfold increased risk of cardiovascular disease and a tenfold higher incidence of early ovarian insufficiency compared to their healthy peers. Bone disorders, hearing impairment, and neurocognitive issues (like learning difficulties) are also prevalent.

Reproductive health is significantly affected, as chemotherapy and radiation therapy can lead to severe fertility problems. Women who survived childhood cancer may experience early menopause before age 40, or even earlier. Girls who received high-dose pelvic radiation are at high risk for early ovarian insufficiency and fertility issues, with more than 50% likelihood of primordial follicle loss.

The late effects of treatment can impact the quality of life for survivors, affecting their reintegration into school and social activities as well as their adjustment to adulthood, with implications for their psychological, social, physical, and professional well-being.

To address these challenges, it is essential for survivors to understand the importance of regular screenings. These evaluations help detect potential recurrences or metastases and identify late effects of treatment early. Early detection and intervention can significantly improve long-term survivorship, reduce morbidity, and enhance overall quality of life.

Specialized clinics for follow-up care, including monitoring late effects, operate within pediatric oncology departments across Greece. These clinics, staffed by multidisciplinary teams, collaborate with adult units to support survivors as they transition into adult care. This integrated approach helps manage late effects and improves long-term outcomes.

While anti-neoplastic treatments have effectively cured many pediatric cancer patients, comprehensive post-treatment monitoring and information sharing are crucial to ensuring long-term survival and minimizing complications. •••

Fertility in childhood and adolescent cancer survivors

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Over the past 40 years, there have been significant advancements in paediatric oncology, resulting in successful treatment for over 80% of children diagnosed with cancer. As these survivors reach adulthood, reproductive challenges often become a prominent concern.

Reproductive challenges mean that girls are at an increased risk of developing ovarian insufficiency caused by chemotherapy and radiation. Boys on the other hand may experience low or zero sperm count when they reach adulthood, and therefore be forced to resort to assisted reproductive methods or sperm donation to be able to have biological children. Currently, several options are available to paediatric and adolescent cancer survivors for fertility preservation. This article briefly presents both the effects of cytotoxic therapy on the function of the ovaries and testicles, as well as ways of preserving ovarian function and sperm freezing. We also discuss methods that are available in cases where fertility preservation was not possible before the start of cancer treatment.

Gonadal toxicity after Chemotherapy and Radiotherapy

Male paediatric and adolescent cancer patients generally face similar risks (high or low) of infertility after anti-neoplastic therapy, regardless of their age. In girls, the risk varies depending on age, type of cancer, and treatment-related factors. It is estimated that girls have approximately 1-2 million primordial follicles at birth. The ovarian reserve decreases to 300,000 - 500,000 follicles during adolescence. However, cytotoxicity caused by chemotherapy, which is used to treat cancer, does not affect all patients in the same way. It appears to be more pronounced in patients receiving chemotherapy with alkylating agents such as cyclophosphamide, busulfan, or melphalan. Radiation therapy also increases the risk of infertility. For example, a radiation dose of 6 Gy in boys would lead to complete azoospermia, while in girls, the equivalent dose leading to amenorrhea is approximately 15 Gy. These numbers are particularly significant for boys and girls who receive a stem cell transplant due to being treated with high doses of alkylating agents and/ or not radiotherapy.

Effective practices in fertility preservation of paediatric and adolescent cancer patients

Discussions about potential long-term fertility risks should begin at the point of diagnosis, even though initiating cancer treatment remains the immediate priority. It is crucial for young patients and their families to receive comprehensive information about fertility risks and preservation options from a dedicated interdisciplinary team. This team should include pediatricians, hematologists, radiation therapists, gynecologists, endocrinologists, surgeons, urologists, and psychologists.

Incorporating fertility consultations into cancer care ensures that patients are well-informed about fertility risks and preservation methods that may become significant when considering parenthood in the future. It is essential for patients and their families to understand the available fertility preservation options, so they can make timely decisions that improve their chances of having biological children. In this regard, cryopreservation of genetic material is particularly important, where feasible.

Premature Ovarian Insufficiency in Girls

Girls who receive chemotherapy and radiation therapy are at an increased risk of developing premature ovarian insufficiency (POI). A primary symptom of POI is amenorrhea, or the absence of menstrual periods, in girls who are at the age when puberty should typically begin. In adulthood, this can manifest as early menopausal symptoms such as hot flashes, sweating, dizziness, and headaches. Additional symptoms associated with POI and low estrogen levels include osteoporosis, cardiovascular disease, atrophy of the genitourinary system, and dyspareunia (painful intercourse). Psychological effects are often difficult to detect and may be underestimated, but can include lowered sex drive, mood changes, trouble sleeping, anxiety, irritability, and difficulty concentrating. Hormonal replacement therapy, in the form of pills or patches, can provide significant benefits for the health of female pediatric and teenage cancer survivors, provided it does not interfere with their treatment protocol.

Fertility preservation options for girls

Certain methods may help preserve fertility in girls and should be discussed early on, as creating a treatment plan can take time. The available options depend on the patient’s age, whether they have reached puberty, and their cancer diagnosis. These methods include ovarian tissue freezing, where part of the ovarian tissue is removed and frozen for future use, which is suitable for girls who have not yet gone through puberty. Another option is ovarian transposition, which involves moving one or both ovaries out of the radiation field to reduce exposure during treatment. For girls who have reached puberty, egg freezing is a viable method, involving stimulating the ovaries to retrieve and freeze eggs.

Additionally, the use of GnRH analogs to suppress ovarian function in post-pubertal girls undergoing treatment offers a new alternative to mitigate the risk of ovarian failure. However, further clinical evidence is needed to confirm the long-term effectiveness of GnRH analogs in preserving ovarian function. Involving young patients in discussions about the risks of fertility and the available fertility preservation options is crucial. This approach not only ensures they are well-informed but also considers the positive psychological impact of having fertility-preserving techniques available for female pediatric cancer survivors

Ovarian Tissue Freezing followed by transplantation

Freezing eggs is not an option for girls who have not gone through puberty. However, ovarian tissue freezing has emerged as a promising solution for these younger girls. Once considered experimental, this method is now becoming a standard practice and has resulted in the birth of over 180 children worldwide. The process begins with a consultation with the healthcare team to determine eligibility. A portion of ovarian tissue is then removed laparoscopically from one of the ovaries. This tissue, rich in primordial follicles, is cryopreserved using a slow freezing protocol. To prevent the reintroduction of malignant cells, the tissue undergoes additional testing. After cancer treatment is complete and when the woman decides to have children, the ovarian tissue can be transplanted either to the pelvis or under the skin, allowing for potential future fertility.

Ovarian transposition

Ovarian transposition involves surgically repositioning the ovaries outside the pelvic radiation field to minimize their exposure to radiation. This procedure is considered for girls undergoing cancer treatments that carry a high risk of infertility due to radiation. During the procedure, the ovaries are moved laparoscopically to a location outside the radiation field. They are then secured with metal staples to help treatment providers avoid including them in the radiation treatment area. Later, when these young women decide to have children, egg retrieval can be performed either laparoscopically or via a transvaginal procedure.

Egg Freezing

A girl who is already going through puberty can freeze her eggs as an effective and well-established method for preserving fertility. This procedure involves a two-week course of fertility drug treatment, which includes hormonal injections administered with a small needle under the skin to help the eggs mature in the ovaries. During this period, doctors regularly conduct ultrasounds and take blood samples to monitor hormone levels. Once the eggs have matured, they are retrieved from the ovaries through a minimally invasive transvaginal procedure performed under anesthesia. This process, known as oocyte retrieval, is quick and the retrieved eggs are cryopreserved using oocyte vitrification. This technique ensures that the eggs can be stored for many years without compromising their quality. When the female survivors decide to have children, the eggs are thawed and prepared for fertilization with their partner's sperm in the lab. The resulting embryos are then transferred into the uterus using a small catheter, usually two to five days later.

Advances in assisted reproduction have significantly improved outcomes, with egg survival rates after thawing exceeding 90%. The embryo implantation rate for women using thawed eggs has a live birth rate of over 50%. It is crucial to consider egg freezing for young women at risk of infertility due to childhood oncological treatments. Even if their menstrual cycle appears normal, there is a significant risk of compromised ovarian function and premature menopause compared to peers without a cancer history. Measuring anti-Müllerian hormone (AMH) levels is a useful indicator of ovarian function and can help determine the need and urgency for egg freezing to preserve fertility.

Fertility preservation options for boys

Methods for reducing the risk of infertility in boys depend on their age and treatment plan. Sperm banking, or cryopreservation, is a common and non-invasive option available to boys who have reached puberty and can ejaculate. For younger boys, who may not yet be able to provide sperm samples, testicular tissue freezing offers a potential solution. This involves conducting a unilateral open testicular biopsy to obtain tissue that may contain stem cells capable of producing mature sperm in the future. However, this approach is still considered experimental, and as of now, no children have been conceived using testicular tissue transplantation

How to monitor reproductive health in adulthood

For girls, monitoring reproductive health may involve tracking menstrual cycles, including their frequency and duration. Young women are encouraged to consult with a gynecologist and undergo diagnostic tests such as ultrasound scans and measurements of the anti-Müllerian hormone. These tests help predict normal menopause or potential loss of ovarian function. If hormonal replacement therapy is deemed necessary, pills or patches can improve sexual health and overall well-being. However, it is important to note that this therapy often does not restore ovarian function, as the damage may be permanent.

For boys, a comprehensive assessment of fertility requires both endocrine evaluations and semen analysis in specialized laboratories. When conception is desired, semen analyses, including assessments of semen volume, sperm concentration, motility, and morphology, provide valuable information about fertility. This data helps young men and their healthcare providers determine the appropriate next steps for diagnosis and treatment.

Egg and sperm donation options

While fertility preservation is a crucial objective for childhood and teenage cancer patients, it is not always feasible. For young survivors with compromised reproductive function, assisted reproductive technologies offer alternative pathways to parenthood. Options such as egg and sperm donation can be explored. Additionally, for young women who have received uterine radiation during childhood treatment -whether pelvic, spinal, or total-body irradiation- surrogacy may be a viable alternative

Conclusion

The ability to have children is a fundamental right for everyone, particularly for those who have experienced cancer in childhood. It is crucial for young patients and their families to receive timely information from a multidisciplinary team about fertility preservation options and assisted reproductive technologies available to them. Addressing these issues promptly at the time of diagnosis helps ensure that young patients and their families can make informed decisions about their fertility and future treatment options.•••

Female health related challenges in girls who are cancer survivors

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In recent years, most girls experience a normal life after cancer.

In some cases, cancer and its treatment can adversely impact the female reproductive function as a result of:

- Surgery
- Chemotherapy
- Radiation therapy
- Solid tumors

This chapter aims to answer questions regarding hormonal and ovarian issues, premature ovarian insufficiency, fertility and sexual relationships of girls who are cancer survivors

What is the typical function of the ovaries?

Ovaries are one of a pair of female glands in which the eggs form and where female hormones are produced. Hormones are chemical messengers in the body that are needed for healthy development in girls. Estrogen and progesterone are two important hormones made in the ovaries. These hormones are involved in the menstrual cycle, fertility, breast development and are also important for maintaining healthy bones.

What is a typical menstrual cycle?

Menstruation, or menstrual periods, typically occur once a month in most teenage girls. A typical menstrual cycle lasts approximately 32 days, from the beginning of one period to the beginning of the next. While 32 days is considered an average cycle, this can vary from person to person. Any menstrual cycle between 21 and 45 days is considered normal. The period itself usually lasts between 2 and 7 days. During the first year of menstruation, irregular periods are quite common. Factors such as stress, intense physical activity, unhealthy eating habits, pregnancy, and cancer treatments can all disrupt the menstrual cycle.

What is the impact of chemotherapy on the ovaries?

The type and amount of chemotherapy can influence ovarian function, with many chemotherapy agents having little or no effect on the ovaries. However, during chemotherapy and for up to a year afterward, the ovaries may temporarily stop working and then resume normal function. Some types of chemotherapy can cause early menopause, leading to premature ovarian failure. This means that instead of menopause occurring around the age of 52 for women, it is likely to start early (early ovarian failure) in their 20s, 30s or 40s.

What is the impact of radiation on the ovaries?

The impact of radiation on ovarian function depends on the treatment area and the dose administered. Radiation targeted at parts of the body outside the pelvis (the lower abdomen below the navel) is unlikely to have a significant effect on the ovaries. However, if the ovaries were exposed to radiation as part of cancer treatment, they may have been damaged. The extent of this damage varies based on the specific area treated and the radiation dose.

How are health problems in the ovaries diagnosed after chemotherapy or radiation?

A doctor can determine if the ovaries have been affected by cancer treatment. Typically, if chemotherapy and/or radiation have significantly impacted the ovaries, they will cease hormone and egg production, and menstruation will stop. It may take up to a year after completing cancer treatment to assess whether the ovaries have partially recovered and if menstrual periods will resume. In some cases, the ovaries may continue to function partially, leading to occasional ovulation and light or infrequent periods due to the release of small amounts of hormones and a limited number of eggs. In such situations, early menopause, also known as early ovarian failure, may occur.

What are the symptoms of early ovarian failure?

Symptoms of early ovarian failure can include:

- Sex traits not developing at puberty
- Amenorrhea (absence of menstrual periods)
- Vaginal dryness
- Mood changes
- Hot flashes
- Lowered sex drive
- Insomnia
- Breast size changes (decrease in breast volume)

Among these symptoms, young girls most frequently report the absence of a menstrual cycle and changes in breast size. Before diagnosing early ovarian failure, doctors should rule out other medical conditions that can cause similar symptoms.

How is early ovarian failure diagnosed?

Early ovarian failure can be diagnosed through a blood test that measures two key hormones: FSH (follicle stimulating hormone) and estradiol. Sometimes, a repeat blood test is needed to obtain an accurate average value of these hormones in the body. Elevated levels of FSH and low estradiol levels may indicate partial ovarian failure. Additionally, an AMH (anti-Müllerian hormone) test may be performed to assess the size of the patient’s egg reserve.

Why are FSH hormones and estrogen important?

In young girls, the pituitary gland in the brain monitors the production of estradiol by the ovaries. If a teenage girl is not menstruating and estradiol production is low, the pituitary gland will release the FSH (follicle-stimulating hormone). This hormone signals the ovaries to start producing estradiol. Normally, the ovaries would respond to this signal by increasing estradiol production, leading to a decrease in FSH levels as the pituitary gland stops releasing it. However, in cases of early ovarian failure, the ovaries do not produce estradiol, resulting in persistently high levels of FSH in the blood.

Is early ovarian failure permanent?

Early ovarian failure can be unpredictable. Following cancer treatment, regular menstrual cycles and ovarian function may or may not resume. While early ovarian failure might occur after treatment, there is a possibility that ovarian function could return, with the ovaries resuming hormone production and potentially egg production. Unfortunately, there is currently no test available to determine whether early ovarian failure will be permanent.

How is early ovarian failure treated?

There is currently no cure for early ovarian failure. However, it is crucial to replace the hormones that the body is no longer producing. This treatment is known as hormone replacement therapy. The hormones that need to be replaced include estradiol, progesterone, or both. These hormones are essential for breast development, menstruation, and maintaining healthy bones.

How is hormone replacement administered?

There are several types of hormone replacement therapy (HRT) available. HRT can be administered as a pill, transdermal patch, vaginal cream or tablet, or vaginal hormone ring. Pills are often the most convenient option for young women. Alternatively, a hormonal patch containing estradiol, which is applied to the skin once or twice a week, may be recommended as it provides hormone levels similar to those produced by the ovaries. The vaginal hormonal ring is another option. Birth control pills, which contain both estrogen and progestogens, can also be used for hormone replacement therapy. While hormone replacement therapy can help replace the hormones that the ovaries no longer produce, it cannot restore egg production if they are no longer available due to cancer treatment

What are some of the outcomes of hormone replacement therapy?

If breast development has not been fully completed, hormone replacement therapy may lead to an increase in breast size. Menstruation may also commence if the uterus is healthy. Symptoms such as premenstrual syndrome, menstrual cramps, irregular periods, or mood swings can also occur, similar to the effects of natural progesterone and estrogen production.

However, it is important to inform your doctor. If side effects from hormone replacement therapy arise - such as breast tenderness, headaches, or mood swings. This allows for the adjustment of treatment to the most suitable type of hormone replacement therapy.

Can girls have a normal sexual life after cancer treatment?

Yes, many girls can lead a normal sexual life after cancer treatment. However, some may feel anxious about how their partner will perceive them if they learn about their cancer experience. Cancer and its treatment can result in physical changes such as surgical scars, hair loss, or weight fluctuations, which may contribute to body image issues and concerns about intimacy. Nonetheless, physical contact alone does not reveal details about one's cancer treatment. Effective communication with partners is crucial for maintaining a healthy sexual relationship, although discussing these matters remains a deeply personal choice for each individual.

Are there any physical changes that affect intercourse?

The impact of cancer and its treatment on sexual health can vary depending on factors such as the type of cancer, treatment methods, and individual health circumstances. Surgery that changes the size or shape of the vagina can lead to difficulties with sexual intercourse. Additionally, early ovarian failure may result in vaginal dryness and reduced sexual interest due to lower hormone levels. Vaginal dryness can cause pain during intercourse, but this issue is often managed with the use of vaginal lubricants. Hormone replacement therapy may help resolve most of these symptoms, potentially restoring normal sexual function and comfort.•••

Cognitive late effects in childhood cancer survivors

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Cognitive learning is crucial, especially for children and adolescents. Currently, 5.5% of children and adolescents aged 5-17 suffer from chronic diseases or conditions that make regular school attendance challenging, often resulting in extended absences. As a result, including these children in special education programmes is considered essential.

The concept of learning involves acquiring new knowledge or transforming existing knowledge, experiences, skills, and behaviors. Learning is profoundly influenced by the social environment and is governed by complex cognitive and mental mechanisms. Disruptions in these mechanisms can significantly impact an individual's ability to learn.

The global health agenda has increasingly focused on improving the treatment and management of childhood cancer. Recently, there has been a growing emphasis on understanding the long-term effects of childhood cancer and its treatments, particularly concerning cognitive development. Evidence indicates that some cancers and their treatments can affect learning and academic performance. Children and teenagers diagnosed with acute lymphoblastic leukemia (ALL) or brain and central nervous system tumors are especially at risk for impaired cognitive function due to treatments such as chemotherapy and radiotherapy. Given that these cancers account for about 40% of childhood cancer cases, understanding the connection between these treatments and cognitive outcomes is crucial. Both the disease and its treatments can potentially lead to long-term physical, neurocognitive, and psychological challenges for childhood and teenage cancer survivors. The terms "chemo brain" and "chemo fog" are commonly used to describe issues with thinking and memory, experienced by children and teenagers during and after cancer treatment.

Our team's meta-analysis found that childhood cancer survivors exhibited a significantly lower overall IQ compared to their healthy peers. This analysis included 16 studies with a total of 1,676 participants, including 991 survivors of acute lymphoblastic leukemia (ALL) and 685 healthy controls, all aged between 6 and 16 years. The participants' IQ levels were assessed using the Wechsler Intelligence Scale for Children. The results highlighted significant differences in cognitive function, showing lower scores in overall intelligence, verbal reasoning, and practical intelligence among the survivors compared to their healthy counterparts.

Verbal reasoning specifically refers to a person's ability to effectively use and understand language, solve problems, and reason logically. In children, it manifests as the capacity to speak their native language fluently and articulate their thoughts clearly, both verbally and in writing. Children with well-developed verbal reasoning skills do well in tasks such as reading, writing, memorizing words and dates, storytelling, and learning foreign languages. Additionally, practical intelligence involves the ability to navigate and organize visual stimuli within time constraints. It encompasses applying knowledge and using resources flexibly to solve problems. This type of intelligence also includes being adaptable and adjusting effectively to changing circumstances and environments.

Young cancer patients and survivors face both social and cognitive challenges. Learning difficulties are often linked to struggles with integrating into the school environment and experiencing bullying. Prolonged absences from school due to treatment and medical interventions can negatively impact children's social connections, leading to social isolation. This isolation can exacerbate the physical and psychological effects of their condition and hinder their efforts to return to a sense of normalcy. As a result, some childhood and teenage cancer survivors may exhibit low motivation to overcome these challenges and resume their everyday lives.

Children in early childhood, particularly those aged 1 to 4 years, are especially vulnerable to the effects of toxic agents such as chemotherapy and radiotherapy. This critical period of intense brain development means that any injury to the developing neural networks can result in cognitive impairments and alterations in the structure and function of the central nervous system. However, the brain's plasticity during these early years offers a significant opportunity to mitigate these toxic effects.

Early and tailored interventions are crucial for children experiencing the effects of chemotherapy and radiotherapy to achieve the best possible outcomes. The school environment provides an ideal setting for implementing these interventions. Designing tailor-made programmes and classrooms is essential to support childhood and teenage cancer survivors. Flexible and specialised education settings allow teachers to assist survivors in completing their education, enhancing both their academic performance and overall quality of life.

Some pediatric oncology centres offer school reintegration programmes to facilitate the return of survivors to school. Accessible educational services and interventions are crucial in addressing the cognitive and psychosocial needs of survivors as part of a holistic care model.

Teachers and psychologists trained in special education play a vital role in monitoring the academic performance and behavioural development of survivors. This helps identify challenges in school performance and social adjustment. Additionally, tracking neurocognitive changes during treatment enables health professionals to make more informed decisions about clinical, educational, and psychological interventions in follow-up treatment of survivors. Programmes specialising in cognitive remediation, such as "Attention Process Training" and "Pay Attention!", have shown relative success in addressing attention deficits and help young patients and survivors to manage distractions. Furthermore, specialized computational programs have been developed to manage working memory deficits in survivors and symptoms of attention deficit hyperactivity disorder (ADHD).

Encouraging childhood and teenage cancer survivors to engage in social networks and group activities can significantly reduce social isolation. One initiative designed to support this is the development of the interactive website LEAP3 AHEAD (Late Effects Awareness for the Physicians, Patients, specifically survivors with acute lymphocytic leukemia, and the Public: Advancing Health and Eliminating All Disparities). This platform aims to educate both the public and professionals involved in the care of young patients about the late effects of cancer treatment. It also offers guidance on facilitating the reintegration of children and teenagers into school and social life.

As survival rates for children and teenagers treated for cancer continue to rise, it is crucial to implement regular, lifelong monitoring of their neurocognitive complications. This ongoing oversight is essential to enhance their educational outcomes, job prospects, and overall quality of life.•••

The role of nutrition in childhood cancer survivors

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The survival rate for childhood cancer survivors has increased to over 80%, with most children living for five years or more, thanks to advances in treatment.

Over 62% of child and adolescent cancer survivors experience long-term effects and suffer from at least one chronic condition, such as obesity, metabolic syndrome, cardiovascular disease, and osteoporosis. For example, the average body mass index (BMI) for survivors of acute lymphoblastic leukaemia (ALL) is approximately 80%, which is higher than that of the general population in similar age groups. Additionally, one in two survivors exhibits increased body fat, low muscle mass, and reduced muscle strength (sarcopenia). These factors negatively impact the quality of life for young cancer survivors.

Childhood cancer survivors are at increased risk of obesity and metabolic syndrome, conditions that, in turn, elevate the risk of cardiovascular disease. This risk is partly due to the cardiotoxic effects of chemotherapy and radiotherapy. While the development of chronic conditions can be significantly attributed to the late effects of cancer treatment, lifestyle factors such as diet and exercise also play a crucial role in influencing the progression of these conditions.

Often, the adverse effects of cancer treatment will manifest either during or immediately after treatment and typically subside over time. However, some survivors may experience long-term or late effects that continue to impact their overall health. Long-term monitoring and early intervention by a multidisciplinary medical team can significantly enhance the quality of life for these childhood cancer survivors.

It is important to note that these adverse effects depend on several factors, including the type of cancer, the specific treatment methods, the type of chemotherapy used, and the area of the body exposed to radiation. Some children treated with corticosteroids, such as prednisone or dexamethasone, may experience weight gain, fluid retention in the face and abdomen, and a decrease in muscle mass. Corticosteroids can also impact how the body utilizes nutrients from food, and may lead to joint pain and osteoporosis (weakened or thinning bones that are more prone to fractures). These effects can also occur in children receiving hormone therapy.

In addition, specific hormones involved in regulating appetite, metabolism, and body weight, such as ghrelin and leptin, are also affected in childhood cancer patients. Disruptions and imbalances in these hormones are known to contribute to obesity and metabolic syndrome in both healthy children and adults. For children undergoing cancer treatment, elevated levels of ghrelin and decreased levels of leptin are often reported. These imbalances result from the long-term effects of chemotherapeutic agents used in treatment, influencing appetite regulation and metabolic health.

High-dose abdominal radiation can disrupt hormone levels produced in the gastrointestinal (GI) system, leading to changes in appetite, taste preferences, and eating behaviour. This type of radiation has been linked to an increased risk of insulin resistance in childhood cancer survivors, which can alter how the body absorbs nutrients. Additionally, abdominal radiation may cause inflammation of the gut and chronic enteritis, resulting in symptoms such as pain, bloating, nausea, and diarrhoea, which complicate nutrient absorption. The radiation can also affect the gut by disrupting the balance of microbes and damaging the integrity of the gut barrier, allowing harmful agents to enter the body and trigger inflammation. These disruptions make it challenging for children and teenage cancer survivors to maintain a healthy and balanced diet after treatment.

Currently, children and teenage cancer survivors often exhibit low adherence to recommended dietary guidelines compared to the general paediatric population, leading to poor diet quality. These survivors typically consume lower amounts of fruits, green vegetables, and pulses, resulting in insufficient intake of fibre, vitamin D, and calcium. Conversely, their diets tend to be high in saturated fats and salt.

Dietary guidelines for cancer survivors have been established by various scientific organizations, including the American Cancer Society, the American Institute for Cancer Research, and the World Cancer Research Fund. However, these recommendations are not always specifically tailored for children and teenagers. The dietary guidelines published by the American Oncology Group for Children, Adolescents, and Young Adult Cancer Survivors advocate for a healthy eating pattern but provide no additional guidance for this age group.

According to the National Dietary Guidelines for Infants, Children, and Adolescents published in 2014, a healthy diet should include the following:

- Daily servings of milk, yogurt, or cheese.
- A variety of fruits and vegetables every day.
- A range of cereals daily, with an emphasis on whole grains.
- Red meat (such as beef, pork, lamb, or goat) and/or white lean meat (such as chicken, turkey, or game) 2-3 times a week, while avoiding processed meats (like ham and sausages).
- Fish and seafood 2-3 times a week, including at least one serving of oily fish (such as sea bream or sardines) per week.
- Legumes at least once a week.
- 4-7 eggs per week.

Olive oil should be the primary fat used, with other sources of fat (like butter) being limited. Sugar and salt intake should also be restricted. Regular physical activity is essential and should be incorporated into daily routines.

Young cancer survivors can also benefit from the principles associated with a Mediterranean diet that alongside dietary suggestions also focus on other aspects of lifestyles such as the importance of rest, social relationships and regular activity. Cooking can also act a social activity with friends and family that is based on biodiversity and the seasonality of cooking with an emphasis on traditional, local and environmentally friendly ingredients

Encouraging childhood cancer survivors to adopt a healthy lifestyle should be tailored to their individual experiences and characteristics. Some children and teenagers may require personalized dietary recommendations. For instance, if a survivor experiences sarcopenia, the multidisciplinary medical team might suggest a diet rich in protein sources such as meat, fish, eggs, dairy products, and pulses, while also limiting fat and sugar intake if there are concerns about an affected blood lipid profile. Additionally, for survivors who develop metabolic syndrome, it may be important to restrict sugar intake (including sugar, jam, and honey) and increase fibre consumption

Undoubtedly, altering dietary habits for childhood cancer survivors can be challenging. It is essential to approach these changes gradually, considering both the specific needs of the survivor and the overall circumstances of the family.•••

The benefits of exercise during and after treatment

Alexandra Mila, Aristotle University of Thessaloniki, Department of Physical Education and Sports Science University of West Attica, Department of Physiotherapy National and Kapodistrian University of Athens Medical School Master's Degree in Molecular and Applied Physiology

We are observing positive improvements in the quality of life for children and teenagers with leukaemia and lymphoma, as well as survivors, through the implementation of movement therapy rehabilitation programmes.

Studies indicate that incorporating exercise alongside medical treatments can positively impact disease progression in childhood cancer care. Evidence shows that physical exercise is a safe complementary therapy, with no reported adverse effects. Specifically, for children and teenagers undergoing treatment for haematological cancers or lymphoma, physical exercise during treatment has not been associated with increased risks of mortality, relapse, or other negative outcomes across various medical protocols.

Physical exercise and an active lifestyle are universally recommended for all age groups. However, as children increasingly spend time indoors engaged in activities like watching TV, playing on screens, and using computers, while also consuming calorie-rich snacks, their levels of physical activity often decrease. This sedentary behaviour, combined with poor dietary habits, can significantly contribute to childhood obesity.

Benefits of active play

Active play is increasingly utilized in clinical practice to enhance social interactions and alleviate anxiety and depressive symptoms in children undergoing cancer treatment. Engaging in active play can help counteract the psychopathology and subsequent fatigue often reported by these children. Play is a crucial activity for achieving developmental milestones, and its absence is associated with poor motor skills, challenges in coping with stressful or traumatic events, and limited social skills. These deficiencies can further impact children's ability to navigate their social environment effectively.

Incorporating structured physical activity, such as active play, can greatly assist children and teenagers in coping with cancer, its treatments, and prolonged hospital stays. Since cancer treatment often disrupts daily routines due to hospitalization, integrating active play and movement therapy early in the treatment process and continuing throughout (when feasible) can support young patients in transitioning back to their daily lives and resuming normal activities post-treatment. This approach not only helps manage the physical and emotional challenges of cancer treatment but also facilitates a smoother return to everyday life.

Building physical strength

Reducing the risk of premature cardiovascular morbidity and mortality in childhood cancer survivors is achievable through physical activity and improvements in insulin sensitivity. Certain chemotherapy agents can damage endothelial cells, which line the blood vessels, leading to long-term cardiovascular issues in young survivors. Aerobic exercise is being investigated as a preventive measure that could mitigate the cardiotoxic effects of chemotherapy, both during and after cancer treatment.

Additionally, non-aerobic exercise can enhance the expression of heat shock proteins (HSPs), which help mitigate the neurotoxic effects of chemotherapy that could lead to cognitive and neurological impairments. The cytoprotective functions of HSPs are significantly boosted following physical activity. Moreover, exercise positively impacts levels of brain-derived neurotrophic factor (BDNF), a neurotrophic factor associated with memory and learning. Reduced levels of BDNF are linked to active disease and subsequent depression, highlighting the beneficial role of exercise in supporting cognitive health and emotional well-being in children undergoing cancer treatment.

Unfortunately, muscle weakness and reduced bone density in childhood and teenage cancer patients often persist throughout treatment and beyond. This highlights the need to implement exercise plans early after diagnosis. Severe joint degeneration and general bone weakening are commonly observed across various cancer types, with muscle loss being more pronounced in the lower body. Strength training is effective in increasing muscle mass and can help counteract sarcopenia resulting from both the disease and the immobility associated with hospitalization. Additionally, muscle strengthening and hypertrophy can help regulate growth hormone levels, which may be adversely affected by cancer and its treatments. Finally, physical activity contributes to improved mood and pain reduction.

For children and teenagers undergoing cancer treatment, getting sufficient sleep can be challenging. Physical activity plays a crucial role in regulating hormones and restoring the circadian rhythm, which is essential for healthy weight management and overall well-being.

Pilot Physical Exercise Programme

Considering the above, an exercise programme is being piloted between the Oncology Department of Hematology, the 1st Pediatric Clinic of the Children's Hospital "Aghia Sophia", the Special Center for Adolescent Medicine (E.K.E.I.) and the Laboratory of Physiology of the Medical School of the University of Athens.

The program's framework includes a supervised physical activity plan tailored for small groups of children, organized by age, to meet individual needs effectively. While young patients undergoing treatment may have compromised immune systems, they frequently experience similar post-exercise symptoms as their healthy peers, such as temporary muscle and joint pain.

However, participating in this exercise programme offers significant benefits, including reduced side effects from treatment, alleviation of cancer-related symptoms, and an overall improvement in long-term quality of life.•••

The Importance of Psychological Support

Christina Faitaki, Person-Centered Psychotherapist, Member of the European Association for Psychotherapy (EAP)

The journey of childhood cancer represents a significant transition for the entire family. This experience profoundly impacts not only the emotional well-being of each family member but also the dynamics and relationships within the family unit.

Emotions

When the fear of cancer recedes and a sense of normalcy returns, both children and parents are left with a complex mix of emotions. It's common to experience a range of intense and sometimes conflicting feelings, such as anxiety about the future, concerns about relapse, alongside gratitude, relief, and joy.

In therapeutic settings, some parents have expressed their emotions with statements like, "I feel as if I've experienced an earthquake I am now dealing with the aftermath—the internal wounds and the losses endured by both my child and the entire family."

It is not uncommon for young survivors and their parents to grapple with positive emotions such as joy and gratitude. Even when reassurances from the medical team and favourable test results are provided, they may not always alleviate fear or remove discomfort.

Using logical argument alone may not necessarily restore mental balance to families. Research shows that parents often encounter various internal and external triggers after treatment ends—such as a child catching a common cold or developing a fever—that are deeply associated with the child's illness. These triggers can make it challenging for parents to escape feelings of overwhelming fear and anxiety.

Here's how parents describe their experiences in therapeutic settings:

- *"The memory of this nightmare lingers... I still grapple with fear and uncertainty."*
- *"I worry that the memories of our time in the hospital and the treatments will never fade. They replay in my mind like a horror movie, leaving me paralyzed with fear."*
- *"It feels like I have an open wound that starts bleeding at the slightest opportunity."*
- *"I keep having nightmares."*

Childhood and teenage cancer survivors, along with their parents and siblings, often face the following challenges:

- **Fear of relapse:** Persistent anxiety about the cancer returning.
- **Concern about long-term effects:** Worries about the impact of treatment on physical health and psychosocial well-being.
- **Parental guilt:** Feelings of guilt over not recognizing signs of the disease sooner or not doing enough to prevent it.
- **Loss of control:** Struggles with feeling unable to ensure the child's continued health.
- **Anxiety about significant dates:** Stress related to anniversaries of diagnosis or upcoming medical check-ups.
- **Difficulty coping:** Challenges in managing the aftermath of the illness or being overly protective.
- **Inadequacy in parenting:** Feelings of inadequacy in parenting roles, particularly concerning siblings.
- **Neglect of personal needs:** Overlooking personal well-being in favor of focusing on the child's needs.
- **Panic attacks and avoidance:** Experiencing panic attacks and developing avoidance behaviors related to trauma.
- **Sleep disturbances:** Trouble sleeping and frequent nightmares.
- **Reintegration issues:** Difficulty returning to social settings, such as school and work.
- **Isolation and loneliness:** Feelings of isolation, uncertainty, and loneliness

Unfortunately, some of these emotions persist over time, and survivors, parents, and siblings may continue to experience prolonged psychological distress long after treatment has ended.

Personal Relationships

The effects of childhood and teenage cancer treatment on relationships are well documented. Family dynamics, as well as personal relationships with friends and extended family members, are significantly impacted. Young cancer survivors often reflect on relationships that were lost, those that endured, and new ones that emerged during and after their treatment.

Relationships with parents

Families experience a profound crisis when a child is diagnosed with cancer. The family's priorities shift dramatically to focus on the care of the sick child, while parents struggle to balance their responsibilities and support other family members. This upheaval inevitably shakes family relationships to their core.

As one survivor shared, "*Cancer brought me closer to my mum. When I was diagnosed, my mum quit her job to stay with me during my treatment and hospital stays. I never had the chance to spend so much time and bond with her before. We are now very close.*"

Relationships with siblings

Healthy siblings are also significantly affected by a cancer diagnosis in the family. They often face a range of conflicted emotions: they may feel anxious and worried about their sick sibling while simultaneously resenting the impact of the disease on family life. It is common for them to feel envious of the attention and focus that parents give to the child undergoing treatment, and they may also experience guilt over these feelings. Despite these challenges, some siblings develop a stronger and deeper bond with the sick child.

As one parent described, "*During my daughter's treatment, my son began having panic attacks at school. We thought we were doing our best to support him, with lots of love and attention from his dad and grandparents, but it seems he suffered in silence. Even now, six years later, he still struggles with panic attacks.*"

Lessons learned by siblings through the cancer experience include:

- **Increased Trust in Parental Support:** Siblings often come to understand that their parents will provide support and care if they face illness or difficulties in the future. This can be comforting and help alleviate feelings of neglect or jealousy.
- **Enhanced Empathy and Compassion:** The experience often fosters greater empathy and compassion towards others who are sick or in need.
- **Improved Health Awareness:** Siblings become more educated about health and cancer, helping to demystify the disease and promote better understanding.
- **Development of Responsibility:** The experience can instill a sense of responsibility, as siblings may take on more roles within the family
- **Strengthened Self-Esteem:** Navigating the challenges of a family illness can bolster self-esteem and personal growth.
- **Increased Maturity:** Siblings often mature more quickly and become better equipped to handle challenging situations.
- **Appreciation of Family Bonds:** The experience underscores the importance of family connections, reinforcing the value of a supportive family unit.

Additionally, many childhood and teenage cancer survivors, along with their siblings, develop a strong interest in helping professions such as medicine, psychology, and social care

Relationships with friends

In the words of a 15-year-old cancer survivor: "*Cancer feels like a tornado tearing through your friendships. When treatment ends, you look around to assess the damage and hope that some of those friendships have managed to survive.*"

It has been observed that some friendships may endure after a child or teenager is diagnosed with cancer, while others might fizzle out. This is not uncommon, as friendships at this stage of life are influenced by various factors such as age, school, neighbourhood, religious beliefs, or involvement in sports. Survivors might try to rekindle old friendships, renegotiate their interactions, or even make new friends altogether. However, physical changes resulting from treatment—such as skin rashes, hair loss, hearing loss, or limb amputation—can make it challenging for some young patients to relate to their old friends. In such cases, peer support can be particularly valuable in the following ways:

- By offering a safe space to make new friends
- By allowing survivors to share their lived experiences with peers who have also had cancer
- By providing emotional understanding and validation about their cancer experience
- By boosting their self-esteem and helping them forge a new path forward

Such shared experiences can form the foundation for deep and enduring friendships

Why is it important to express and accept our emotions?

As Freud noted, suppressed emotions do not disappear; instead, they are buried deeper until they resurface later. To truly accept our emotions, we must first recognize and name them. This process often involves revisiting past experiences in a safe and accepting environment, where we can reframe them from a different perspective. The idea is that each time we retrieve a painful memory, our mind reprocesses it, integrating it with our current perceptions and emotional state. This helps to soothe our emotional reactions and allows us to address and manage these feelings more effectively.

It is crucial for parents to receive information and psychological support early in the process. Evidence from studies, along with our experience in supporting families, demonstrates that timely interventions positively impact both young patients and their parents. Providing psychological support helps childhood and teenage cancer patients, as well as their families, to remain resilient, open, and connected throughout and after their cancer journey

How can parents and teenage cancer patients decide on a mental health professional and therapeutic approach?

There are several therapeutic approaches and professionals that families can choose from when seeking help for the psychosocial effects of pediatric cancer. Some may prefer individual therapy, where sessions focus on personal issues, while others might opt for group therapy, which provides the opportunity to share experiences with others in similar situations.

What is most important is finding a good fit between the patient and the mental health professional. It is crucial that the environment feels safe, comfortable, and respectful, allowing teenagers or parents to openly discuss their feelings and experiences.

What are the benefits of individual therapy?

- They have dedicated therapeutic time solely for themselves.
- The therapist supports them in their journey in a one-on-one relationship.
- They can discuss sensitive issues they might not want to share with others.
- Sessions are scheduled directly with the therapist, accommodating practical needs.
- Each session typically lasts about 50-60 minutes

What are the benefits of group therapy?

- Participants discover they are not alone in their concerns, difficulties, and negative feelings.
- They find relief in realizing that others with shared experiences and similar life paths can understand them deeply.
- They feel liberated and accepted from others in the group.
- Mutual interest and care develop between group members.
- Sessions typically last approximately 1:30 to 2:00 hours.

The gifts of psychotherapy

Psychotherapy is a valuable journey that offers a gift to oneself. It provides an opportunity to reexamine thoughts and feelings, negotiate and redefine goals, values, and priorities in life. Those embarking on this journey seek to enhance their relationship with themselves and with others, aiming to experience a more fulfilling and meaningful life. •••

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