Antidepressant Use in Children With Cancer


In 2007, cancer was diagnosed in 10,400 children and adolescents under the age of 15 years.1 While cancer remains the second leading cause of death in children, increasing numbers of children with cancer are surviving into adulthood.2 Over the past 30 years, 5-year survival rates for children with cancer have significantly improved, from 59% in 1975 to 1977 to 80% in 1996 to 2004.3 Pediatric cancer, increasingly considered a chronic rather than an acute condition, is an intense emotional and physical experience for patients and their families.4

Comprehensive psychiatric assessment of these children is complicated by symptoms of medical comorbidities that overlap mental health conditions. Few resources exist to guide clinicians in the psychiatric treatment of children with cancer. This article describes the sparse research from small clinical studies on the extent of psychiatric treatment in children with cancer and evidence from outcome studies of medication use in these children. Minimal knowledge on the role of antidepressants in such children motivated us to examine the question in a broad population-based approach.

Psychopathology
One area of interest in caring for children with cancer is the prevalence of psychiatric diagnoses. Assessment of psychiatric disorders in these children from either research or community settings is difficult because of the complex medical and emotional presentation of illness.5,6 DSM-IV criteria for mood disorders, for example, include both somatic and cognitive symptom criteria, and clinicians must decide which symptoms are caused by the illness and treatment and which are related to a separate psychiatric diagnosis.7
In addition, doctors and nurses may overestimate psychosocial distress and symptoms in children and adolescents with cancer. Assessment tools for psychiatric disorders are not often validated in children with medical illnesses, which may lead in part to the varying research prevalence of psychiatric disorders in this population. Reports of psychiatric illness in children with cancer range from a high of 17% to rates that do not differ significantly from those for the general population. Specific cancers and their treatments may also contribute to the variable rates of depression. Without more precise estimates that generalize to large youth populations, it is unclear whether children with cancer are at higher risk for a psychiatric disorder than children who are not medically ill.

**Mood comorbidities**

- In a clinical study of adolescents who had recently received a diagnosis of cancer, 12% had clinically significant symptoms of anxiety and 21% had clinically significant symptoms of depression.
- Adolescent cancer survivors have been shown to be at increased risk for depression, anxiety, and attention-deficit symptoms as well as antisocial behaviors relative to sibling controls. Pediatric cancer survivors may be at increased risk for suicidal ideation and suicide attempts later in life.
- A survey of pediatric oncologists found that half had prescribed an SSRI for a patient, often without consultation from a mental health professional.
- Antidepressant medications may be prescribed more frequently for children and adolescents with cancer than for children in the general population.

Regardless of whether a patient fulfills all criteria for a psychiatric disorder, mood symptoms are commonly reported by children with cancer. In a clinical study of adolescents who had recently received a diagnosis of cancer, 12% had clinically significant symptoms of anxiety and 21% had clinically significant symptoms of depression.

Adolescent cancer survivors have been shown to be at higher risk than sibling controls for depression, anxiety, and attention deficit symptoms as well as antisocial behaviors. Survivors of childhood cancer may be at increased risk for suicidal ideation and suicide attempts later in life. Posttraumatic stress symptoms are another concern in children with cancer: diagnosis and medical treatments can become a traumatic stressor for these patients. As a result, clinicians who treat children with cancer may focus on treating particular symptoms, such as mood, anxiety, or fatigue, rather than on a specific diagnosis.

**Psychological interventions**

Options for symptomatic treatment are limited, and their efficacy has not been established in children with cancer. Psychological interventions have shown promise in decreasing distress, but they have not shown an effect on clinical outcomes. Psychopharmacological efficacy studies have been limited to an open-label trial of fluvoxamine in 15 children and adolescents with cancer, which showed good tolerability and improvement in psychiatric symptoms. There was also an open trial of citalopram in 4 children with cancer, which also showed good tolerability and a decrease in depressive symptoms.

Fluoxetine has been shown to be effective in treating depression in randomized controlled trials of children and adolescents who are not medically ill. This agent is the only SSRI currently approved for treatment of depression in youth. Nevertheless, SSRIs and other antidepressants are often used off-label at the discretion of the clinician; this suggests the need to estimate the frequency with which these agents are used to address specific conditions in children with cancer where the need may be both acute and ongoing.

Many children with cancer are being treated for mood or physical symptoms with psychotropic medications. A survey of pediatric oncologists found that half had prescribed an SSRI for a patient,
often without consultation from a mental health clinician.\(^{18}\) In addition, a review of hospitalized children reported that 10% of children with cancer had received an antidepressant medication within a year of the cancer diagnosis.\(^{19}\) In another study, a psychotropic medication had been prescribed for 14% of children with cancer when they were admitted to an NIH clinical center.\(^{20}\) These sparse study findings are not sufficient to understand the extent of antidepressant use in community-based practice and suggest the need for a large population-based study.

**A pharmacoepidemiological study**

A large pediatric cross-sectional pharmacoepidemiological study was undertaken with administrative claims data for 2000 and 2001 from 2.7 million patients aged 2 through 17 years who had had 3 or more months of Medicaid coverage. There were 1040 patients with at least 2 International Classification of Diseases, 9th revision, Clinical Modification diagnosis claims for cancer treatment. A randomly selected age-, gender-, and race/ethnicity-matched group of 10 controls for each case was developed (\(n = 10,400\)).

After controlling for gender, age, race/ethnicity, and psychiatric comorbidities, the likelihood of antidepressant use was nearly twice as common in youths with cancer as in the control group (1.87; 95% confidence interval, 1.43-2.44). Specifically, antidepressants were prescribed for 8.8% of youths with cancer compared with 5.2% of matched controls.\(^{21}\)

Irrespective of the cancer diagnosis, antidepressant use was 5.4 times more likely in youths who had attention-deficit/hyperactivity disorder (ADHD). Likewise, African American and Hispanic youth were 60% less likely to have received an antidepressant, irrespective of the cancer diagnosis. These demographic and comorbidity treatment findings reemphasize the well-established role of race/ethnicity in explaining disparities in health services and demonstrate possible indications for off-label use of antidepressants in pediatric ADHD.

The estimated prevalence of antidepressant use in the Medicaid-insured youth with cancer was about 9% versus about 5.2% in those aged 2 through 17 years who did not have cancer.\(^{22}\) By comparison, in an HMO youth cohort, the prevalence of antidepressant use was 1.75% among 5- to 17-year-olds in 2000 and 2001.\(^{23}\) Thus, it appears that children with cancer are being treated with psychotropic medications, particularly antidepressants, at a higher rate than matched noncancer controls or community-treated populations. The data suggest that clinicians may be responding to high levels of symptoms and poor functioning.

**Conclusions**

Given the greater prevalence of antidepressant use and the higher prevalence of psychiatric symptoms in children with cancer than in the general pediatric population, further research is imperative. Prioritizing antidepressant research would help ensure a solid evidence base of efficacy, safety, and tolerability in youths undergoing cancer treatment.

To date, only youths with Medicaid insurance have been studied. This population probably includes many chronically ill youths, for whom cancer is a significant condition. The need to expand the research evidence on the role of antidepressants in youths with cancer is further heightened by the current controversy surrounding SSRI use in children. Well-designed studies with adequate assessment and follow-up are essential. Current studies are limited by sample size, few comparison groups, and failure to assess comprehensive treatment interventions. In addition, validated instruments to assess psychiatric symptoms in pediatric oncology populations are needed to best identify those patients in need of treatment.

The increased prevalence of antidepressant use among Medicaid-insured pediatric oncology patients suggests that clinicians may be responding to some form of distress in their patients that is possibly biologically triggered. Further research will elucidate the most effective and safe treatments for these patients.

It is also important to remember that medications are only one aspect of comprehensive psychosocial care of children with cancer. Nonpharmacological interventions such as cognitive-behavioral therapy, guided imagery, and hypnosis may help manage symptoms, and further research is needed to see the effect of these treatments on clinical outcomes. Collaborative efforts by pediatric oncologists, psychiatrists, and other mental health clinicians will no doubt enhance resilience in this population by ensuring that they receive comprehensive psychosocial care to maintain the best possible quality of life in the face of physical challenges.

**References:**
References

Evidence-Based References

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