

Antidepressant Treatment Duration in Pediatric Depressive and Anxiety Disorders: How Long is Long Enough?

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Anxiety and depressive disorders are common in the pediatric primary care setting, and respond to both psychotherapeutic and psychopharmacologic treatment. However, there are limited data regarding the optimal treatment duration. This article systematically reviews guidelines and clinical trial data related to antidepressant treatment duration in pediatric patients with depressive and anxiety disorders. The extant literature suggests 9–12 months of antidepressant treatment for youth with major depressive disorder. For generalized, separation and social anxiety disorders, 6–9 months of antidepressant treatment may be sufficient, though many clinicians extend

treatment to 12 months based on extrapolation of data from adults with anxiety disorders. Such extended treatment periods may decrease the risk of long-term morbidity and recurrence; however, the goal of treatment is ultimately remission, rather than duration of antidepressant pharmacotherapy. Moreover, while evidence-based guidelines represent a starting point, appropriate treatment duration varies and patient-specific response, psychological factors, and timing of discontinuation must be considered for individual pediatric patients.

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Introduction

Anxiety and depressive disorders are common in the pediatric primary care setting and affect 10% of children and adolescents.¹ Successful treatment of depressive and anxiety disorders in youth—whether psychotherapeutic or psychopharmacologic—should restore function, establish remission and decrease the likelihood of relapse and recurrence. With successful treatment, however, the following questions frequently arise in clinical care:

- How long should this patient be treated with an antidepressant? When can the antidepressant that I've started be discontinued? Will the treatment gains be sustained upon discontinuation of the patient's antidepressant medication? If the patient cannot come off medication what is the next best solution?

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To inform best practices for determining duration of antidepressant treatment, we systematically reviewed: (1) current practice guidelines for antidepressant treatment duration, (2) evidence for optimal duration of antidepressant treatment, and (3) specific psychotherapeutic and psychopharmacologic strategies for preventing relapse.

Background

Anxiety and depression are associated with substantial morbidity, including impaired social and academic functioning and increase the risk of suicide and suicide attempts.² Anxiety and depression both respond to psychotherapeutic and psychopharmacologic interventions. However, in some pediatric primary care settings, these disorders may be under-recognized and untreated.³ Data have accumulated during the last several decades that support symptomatic and functional improvement with the use of psychotherapy^{4,5} and selective serotonin reuptake inhibitors (SSRIs),^{6–8} particularly fluoxetine^{9–11} for the treatment of depressive and anxiety disorders in youth.^{4,12–14} However, despite the efficacy of these interventions in short-term treatment studies, the risk of relapse and recurrence remains high, with 5-year recurrence rates of up to 70% and 50% in children and adolescents with

major depressive disorder or anxiety disorders, respectively.^{15,16}

In adults with affective and anxiety disorders, common strategies to prevent recurrence include (1) continuation of acute treatment, (2) utilization of psychotherapy booster sessions to prolong response, and (3) implementation of uniquely tailored recurrence prevention interventions.¹⁷ However, the evidence for these interventions is limited in the pediatric population and these limitations are compounded by the short duration of many acute psychopharmacologic treatment studies, that often describe acute response over ≤ 12 weeks.^{4,9,13,14,18,19} These studies were primarily aimed at establishing the efficacy and determining the safety profile of antidepressants in the short-term; but, data regarding the impact on longer-term outcomes associated with these interventions are limited.

Major depressive disorder (MDD): current guidelines

Acute treatment guidelines for pediatric MDD

Current treatment guidelines focus on the acute treatment of MDD in pediatric patients. Generally, for moderate-to-severe illness, these guidelines recommend treatment with a combination of an evidence-based psychotherapy and an SSRI.^{20–22} SSRIs have the most favorable risk-benefit profile as a first-line medication, with assessment of response every 4 weeks and dose titration when partial response is encountered. While symptomatic remission should occur in many studies by 12 weeks of psychopharmacologic treatment, there are conflicting recommendations for the duration of treatment following depression in pediatric patients. The GLAD-PC guidelines²³ recommend “medications should be maintained for 6–12 months after the full resolution of depressive symptoms.” Similarly, the American Academy of Child & Adolescent Psychiatry (AACAP) Practice Parameters recommend continuation of treatment for 6–12 months “for all patients who have responded to the acute treatment.”²⁴ Further, these parameters suggest that summer may be a preferred period for antidepressant discontinuation and suggest that longer treatment may be recommended for some individuals, particularly for those with risk factors such as multiple past episodes, comorbid disorders, or socio-environmental concerns.²⁴

The Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Guidelines for MDD recommend that maintenance treatment for 6–12

months in youth without a history of MDD prior to the index episode and recommend >1 year of treatment for youth with a prior history of >2 depressive episodes or 1 “severe or chronic episode.”²⁵ These guidelines note that the evidence for these recommendations is limited. Additionally, multiple studies have evaluated longer-term treatment since the publication of GLAD-PC²³ and AACAP Practice Parameters.

Relapse and remission in youth with MDD

While the medical vernacular is replete with references to “relapse” and “remission,” there is considerable variability in the application of these terms to depression. *Relapse* is defined as a *Diagnostic and Statistical Manual of Mental Disorders*—defined depressive episode during a remission period, with remission being a period of no or few depressive symptoms for ≥ 2 weeks but < 2 months.²⁶ Recurrence represents the onset of a new depressive episode during a recovery period, with recovery being the absence of significant depressive symptoms for at least 2 months²⁶ (Fig). Defining relapse and recurrence in adolescents is complicated by fluctuations in affective symptoms whether related to developmental factors or the underlying internalizing disorder.^{17,27}

Controlled medication trials in youth with MDD: duration of treatment effects

Long-term outcomes in the treatment for adolescents with depression study (TADS)

The *treatment for adolescents with depression study* (TADS) evaluated the acute efficacy of (1) fluoxetine (monotherapy), (2) CBT (monotherapy), (3) fluoxetine + CBT, and (4) placebo in adolescents with MDD.¹¹ During the initial 12-week treatment phase, both fluoxetine monotherapy and fluoxetine + CBT resulted in higher response rates compared to CBT alone.²⁸ During the extension phase, by week 18, response rates to CBT (65%) were comparable to fluoxetine (69%), but fluoxetine + CBT resulted in a response rate of 85%.¹¹ In addition, combined treatment resulted in a more rapid effect, but by week 36 comparable response rates (81–86%) were observed.²⁹ Taken together, the results of this study suggest a benefit to longer treatment duration, with remission rates for treated patients increasing from 23% at week 12–60% at week 36.²⁹ The proportion of patients who experienced a sustained response (not necessarily remission) improved similarly, across treatment conditions

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