



## Concurrent Disorders: Treatment of Comorbid Alcohol Use Disorder and Major Depressive Disorder

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### Background

Alcohol use disorder (AUD) and major depressive disorder (MDD) frequently co-occur, with prevalence estimates suggesting up to 85% of people with AUD experience significant depressive symptoms during their illness.<sup>1,2</sup> This comorbidity is associated with greater illness severity, poorer treatment response, increased risk of recurrence and substantial socioeconomic burden.<sup>3,4</sup> Given these challenges, many patients often benefit from an integrated treatment approach that concurrently addresses both disorders rather than treating them in isolation.<sup>5</sup>

Despite the high prevalence of AUD–MDD comorbidity, health-care providers may be unfamiliar with evidence-based treatment approaches for this population.<sup>6</sup> Untreated depression in people with AUD is strongly associated with increased recurrence risk, poorer functional outcomes and higher mortality rates.<sup>7</sup> Differentiating between primary MDD, which predates or persists beyond alcohol use, and alcohol-induced depression, which emerges due to chronic alcohol consumption, is critical in guiding treatment decisions.<sup>3,8</sup> Research suggests that while some cases of alcohol-induced depression remit with abstinence, a significant proportion of people initially diagnosed

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with substance-induced depression later meet criteria for independent MDD, highlighting the importance of reassessment following sustained abstinence.<sup>3,4</sup>

The role of antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs), in treating MDD within AUD populations has been debated.<sup>9,10</sup> Some concerns have been raised regarding their potential impact on alcohol consumption, yet meta-analytic evidence largely supports their efficacy in improving depressive symptoms without consistently worsening alcohol-related outcomes.<sup>11,12</sup>

A restrictive approach to antidepressant prescribing in this population may lead to premature discontinuation of effective treatment, which is not recommended. Instead, treatment decisions should be guided by individualized assessment, accounting for the chronicity of depression, family history and prior treatment response.

SSRIs and other antidepressants have demonstrated efficacy and a favourable safety profile in people with comorbid AUD and MDD.<sup>11–13,14–16</sup> The presence of AUD is not a contraindication to antidepressant therapy, and clinicians should consider first-line antidepressant treatment for MDD when indicated. Treatment decisions should be informed by a comprehensive psychiatric and substance use history to help determine whether depressive symptoms are primary or substance-induced. Important factors to assess include the temporal relation between depressive symptoms and alcohol use, family history, and previous treatment responses. Informed consent should be obtained after a discussion of potential benefits and risks. Although antidepressants can be beneficial, it is important to avoid unnecessary polypharmacy and to carefully evaluate the appropriateness of antidepressant therapy, particularly in cases of transient, alcohol-induced depressive symptoms. Existing depression treatment guidelines, including those from the Canadian Network for Mood and Anxiety Treatments (CANMAT), should guide clinical decision-making.<sup>5</sup>

Multiple meta-analyses and real-world effectiveness studies support the use of antidepressant therapy in people with comorbid MDD and AUD, demonstrating improvements in depressive symptoms and, in some cases, reductions in alcohol consumption.<sup>11,15,17–19</sup> Most studies recommend the use of antidepressants in this population, with no evidence suggesting SSRIs consistently increase alcohol consumption. Notably, no major meta-analyses explicitly advise against the use of SSRIs for comorbid AUD and MDD, further supporting their role in an evidence-based treatment approach.

Combining SSRIs with AUD treatment in people with concurrent depression and AUD can lead to substantial

benefits. Pettinati and colleagues found the combination of sertraline and naltrexone led to better outcomes than naltrexone alone.<sup>20</sup> Moak and others found that people treated with sertraline and cognitive-behavioural therapy (CBT) for AUD had fewer drinks per day than those randomized to placebo plus CBT for AUD.<sup>21</sup> The systematic review by Stokes and colleagues also found that pharmacological treatment improved the odds of alcohol abstinence in people with MDD.<sup>22</sup>

Integrated care approaches that combine both substance use disorder and mental health treatment have shown promising results for people with comorbid AUD and depression. For instance, research has demonstrated that integrated care models, which include both pharmacological interventions, like SSRIs, and psychotherapeutic treatments, such as CBT, have yielded favourable outcomes in improving both depressive symptoms and alcohol use measures in this population.<sup>23,24</sup> Cochrane reviews have noted that antidepressants, including SSRIs, may be useful for treating MDD, anxiety disorders, or a combination of these conditions in people with co-occurring AUD. These studies highlight the importance of providing concurrent treatment for both conditions.<sup>11,25</sup>

## Summary

Although concerns about antidepressant use in people with AUD–MDD have been raised, extensive research supports their efficacy when used appropriately. The risks of untreated depression—including increased recurrence rates, worse functional outcomes, greater disease burden and higher mortality—necessitate a balanced, individualized approach to treatment. Treatment decisions should be guided by a comprehensive assessment and serial follow up that considers depression chronicity, active suicide risk, mood improvement with abstinence or significant reduction in alcohol use, and prior response to antidepressants. Earlier initiation of an antidepressant may be warranted if depressive symptoms are severe (especially with melancholic features) and (or) if active suicidal ideation is present. Access to integrated, evidence-based treatment should be prioritized to improve outcomes for a high-risk population already facing multiple barriers to care, including long wait times to treatment, substance use stigma and socioeconomic instability.

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