

# Why are there no treatment guidelines for mood disorders and comorbidities?

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Mood disorders, including major depressive disorder (MDD) and bipolar disorder (BD), are among the most prevalent and burdensome medical conditions. In a World Mental Health Survey sponsored by the World Health Organization, the lifetime and 12-month prevalence rates for these 2 disorders in 17 developed and developing countries<sup>1</sup> were 12.5% and 5.6% for major depressive episodes, respectively, and 1% and 0.7% for BD, respectively.<sup>2</sup> A recent commentary on challenges in global mental health identified depression as the third leading contributor to the global disease burden; unipolar depressive disorders and BD, respectively, were ranked first and fourth in an evaluation of the global burden across all mental, neurological, and substance use disorders.<sup>3</sup> Previous studies have highlighted the enormous unmet need for treatment among persons with mood disorders.<sup>4</sup>

Comorbidity has been defined as “any distinct additional clinical entity that has coexisted or may occur during the clinical course of a patient who has the index disease under study.”<sup>5</sup> This may apply equally to  $\geq 2$  physical diseases,  $\geq 2$  mental disorders, or the co-occurrence of mental and physical disorders. Comorbidity is prevalent among persons with mood disorders. In developed countries, 62% of persons identified with major depressive episodes also had a comorbid DSM-IV disorder (50% anxiety disorders and 9% substance use disorders) and 72% had a comorbid chronic physical condition (41% musculoskeletal, 33% respiratory, 20% cardiovascular, and 13% pain conditions).<sup>6</sup> Similarly, for persons with a lifetime prevalence of BD I, 88% had a comorbid DSM-IV disorder (77% anxiety disorders, 54% behavior disorders, and 52% substance use disorders),<sup>2</sup> while in the Systematic Treatment Enhancement Program for Bipolar Disorder study, medical comorbidity was found in 59% of the BD sample.<sup>7</sup> The prevalence of multiple comorbidities appears to be even more striking in BD; in the World Mental Health Survey, the percentage of persons with  $\geq 3$  comorbid DSM-IV disorders was 19% in those with a major depressive episode<sup>6</sup> and in an astonishing 62% of those with BD I.<sup>2</sup>

It seems clear that psychiatric and physical comorbidity is the rule rather than the exception for persons with mood disorders.

Comorbidity also substantially contributes to the disease burden and economic costs of mood disorders. Numerous studies have shown that comorbidity is associated with greater functional and psychosocial impairment, poor adherence and treatment response, prolonged recovery time, increased risk of suicide attempts and completed suicides, increased utilization of health services, and higher morbidity and mortality.<sup>8-11</sup>

Since its inception in 1995, the Canadian Network for Mood and Anxiety Treatments (CANMAT) has published evidence-based and consensus-based treatment guidelines to inform clinical decisions in the management of both MDD<sup>12</sup> and BD.<sup>13</sup> These guidelines have been adopted by practitioners, policy makers, regulatory bodies, and payers across Canada, the United States, and several countries worldwide. Along with the CANMAT guidelines, treatment guidelines for mood disorders also have been created by many esteemed groups including, the American Psychiatric Association, the British Association for Psychopharmacology, and the World Federation of Societies of Biological Psychiatry.<sup>14,15</sup>

A frequent challenge voiced by clinicians treating patients with complex mood disorders is that the evidence base to support guidelines is derived from clinical studies involving highly selected patients who are not representa-

tive of “real world” practices. In 1 study, <10% of individuals encountered in busy clinical settings were considered eligible for enrollment in a standard, pharmacological efficacy trial.<sup>16</sup> More specifically, clinical practice guidelines—for both physical diseases and psychiatric disorders—have been criticized as not being applicable to patients with comorbid conditions.<sup>17</sup> However, it also has been recognized that there is insufficient evidence to produce clinical guidelines for the many different combinations of comorbidities.

Although there are few high quality clinical trials to create evidence-based guidelines for treatment of comorbidities, clinicians frequently ask about treatment options for their patients with mood disorders and comorbid conditions. In response to this, CANMAT decided to formulate treatment recommendations that incorporate both available evidence and expert opinion. A task force was formed and a team of authors, led by Drs. Roger McIntyre, Ayal Schaffer, and Serge Beaulieu, has systematically sifted through the dense literature to derive treatment recommendations for a number of psychiatric and physical comorbidities. They have identified the strength of current evidence and highlighted areas where lack of evidence necessitates recommendations based on expert opinion. We believe that their thoughtful work will prove helpful for clinicians and patients and that it will spur more research and clinical trials on comorbidity in order to build the evidence base for future guidelines.

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