# The challenge of managing bipolar I patients beyond the manic episode

**Chairman:** Roger McIntyre, Canada

Official satellite symposium of the 17th Annual Conference of the International Society of Bipolar Disorders (ISBD) sponsored by H. Lundbeck A/S

The Westin Harbour Castle Hotel, Toronto, Canada

**Date:** Friday 5th June 2015

**Time:** 12:15–13:45

**Room:** Plenary Hall

**Programme**

| | | |
|---|---|---|
| 12:15–12:25 | Film | |
| 12:25–12:30 | Introduction | Chairman |
| 12:30–12:50 | Bipolar I disorder: disease burden and challenges in management | Lakshmi Yatham, Canada |
| 12:50–13:10 | Diagnosing and recognising anxiety, irritability and agitation (AIA) as hallmarks for mania with depressive symptoms | Trisha Suppes, USA |
| 13:10–13:30 | Suicide risk in bipolar I disorder related to mania with depressive symptoms, and implications for treatment | Roger McIntyre, Canada |
| 13:30–13:45 | Panel discussion/debate | Faculty |

## Satellite symposium overview

The symposium will begin with a short educational video, which presents a clinician-led interview of a bipolar I disorder 'mixed state' patient. It is important to identify such patients because they are at increased risk of suicide.

Suicide in bipolar disorder is a major public health problem; it is the leading cause of death among patients with bipolar disorder, and carries personal, societal, and economic consequences.[1,2] The first presentation will provide an overview of the epidemiology of suicide in bipolar disorder (prevalence, risk factors, impact, and burden). This presentation will also review the DSM-5 criteria for bipolar I disorder 'with mixed features', and the utility of the Mini International Neuropsychiatric Interview (MINI) module in identifying at-risk patients (patients presenting with 'mania with depressive symptoms' are at increased risk of suicide).[3-5]

The second presentation highlights that the diagnosis of mania with depressive symptoms is often delayed. Given the increased risk of suicide in patients experiencing mania with depressive symptoms,[5] it is important to recognise and identify such patients early, and to intervene accordingly. Symptoms of anxiety, irritability, and agitation (AIA) are prevalent in mania with depressive symptoms,[5,6] and therefore may be considered as 'gateway symptoms', alerting physicians to patients who may be vulnerable to suicide, allowing appropriate intervention.

Following on from this, the final presentation will discuss the treatment options for mania with depressive symptoms,[7-9] focussing on the efficacy data for asenapine.[7]

The symposium ends with a panel discussion/debate to identify the key challenges in managing mania with depressive symptoms from a hospital, community, and carer perspective.

**References**

1. Latalova K, Kamaradova D, Prasko J. Psychiatr Danub 2014; 26 (2): 108–114.

2. Fajutrao L, Locklear J, Priaulx J, Heyes A. Clin Pract Epidemiol Ment Health 2009; 5: 3.

3. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Copyright © 2013. American Psychiatric Association, Arlington, VA, USA.

4. Hergueta T, Weiller E. Int J Bipolar Disord 2013; 1: 21.

5. Young AH, Eberhard J. Neuropsychiatr Dis Treat 2015; 11: 1137–1143.

6. Vieta E, Grunze H, Azorin JM, Fagiolini A. J Affect Disord 2014; 156: 206–213.

7. McIntyre RS, Tohen M, Berk M, et al. J Affect Disord 2013; 150 (2): 378–383.

8. McIntyre RS, Miguelez M, Vogel Marler S, et al. Poster presented at the American Psychiatric Association Annual Meeting. San Francisco, CA. May 18–22, 2013.

9. Tohen M, McIntyre RS, Kanba S, et al. J Affect Disord 2014; 168: 136–141.

# Bipolar I disorder: disease burden and challenges in management

**Lakshmi Yatham**

Suicide in bipolar disorder is a major public health concern, which, not only, has an emotional impact on friends and family,[1] but also carries an economic burden through lost productivity from premature mortality.[2] The risk for suicide among patients with bipolar disorder can be 20–30 times greater than in the general population.[3] Drivers for suicide risk/attempts in patients with bipolar disorder include prior suicide attempts, family history, female gender, younger age at illness onset, depressive polarity of first illness episode, and substance abuse, among other risk factors.[3,4] The risk of suicide can be monitored through various, non-validated methods such as assessing the number of emergency room admissions, reviewing the length of hospitalisation, or monitoring social media for indications that a patient may be at a high risk of suicide.

With the new DSM-5 criteria for bipolar disorder, there is an increased focus on dimensionality, with a 'mixed features' specifier being applied to episodes where symptoms from the opposing pole – mania/hypomania or depression – are present.[5] In patients with bipolar I disorder, the presence of mania with depressive symptoms is associated with a higher rate of post-episode suicide attempts than if these symptoms were absent.[6] The overall risk of suicide is higher in patients experiencing mania with depressive symptoms, as is the prevalence of suicidality during the current episode.[6,7]

The Mini International Neuropsychiatric Interview (MINI) module is a validated patient self-rating scale, which provides a means of identifying mania with depressive features in hypomanic and manic episodes in bipolar I disorder.[8] Indeed, in one study, the MINI module was used to identify that 34% of patients with bipolar I disorder were experiencing mania with depressive symptoms during their current manic episode.[6] One item of the MINI module captures aspects of suicidal ideation and behaviour, providing a means of assessing suicidality in patients experiencing mania with depressive symptoms.[8]

**References**

1. Latalova K, Kamaradova D, Prasko J. Psychiatr Danub 2014; 26 (2): 108–114.

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# Diagnosing and recognising anxiety, irritability, and agitation (AIA) as hallmarks for mania with depressive symptoms

**Trisha Suppes**

**Abstract**

Bipolar I disorder is a chronic disease characterised by periods of mania or hypomania, depression, or combinations of both ('mixed states').[1] The diagnostic criteria for a mixed episode prior to the DSM-5 criteria were recognised as too restrictive, and not reflecting clinical reality or consistent with new data from large data sets – hence the need for a revised definition of boundaries.[1] The DSM-5 redefines the 'mixed episode' criteria, using instead a 'mixed features' specifier which applies to a full mood episode where syndromal or subsyndromal symptoms from the opposing pole are present and can apply to either manic or depressive episodes.[1]

The DSM-5 'mixed features' specifier is an evidence-based aid to prompt the identification of depressive symptoms in mania. The presence of anxiety and irritability or agitation during a manic episode may be important as a relevant clue that depressive symptoms may also be present during the episode. In one large self-report study, 72% of patients who experienced mania with depressive symptoms suffered from anxiety, irritability and agitation (AIA).[2]

AIA symptoms may be considered as 'gateway symptoms' alerting physicians to patients who may experiencing depressive symptoms during a manic episode,[2] making it possible to consider the most appropriate treatment options. Given the increased risk of suicide in patients with bipolar I disorder experiencing mania with depressive symptoms,[3] it is important to recognise and identify AIA symptoms early, and intervene accordingly.

Presently, the management of mania with depressive symptoms in bipolar I disorder lacks focus on the treatment of symptoms such as AIA. Asenapine,[a] among other atypical antipsychotics, has been evaluated as a potential treatment option for mania with depressive symptoms.[4] Efficacy in treating mania and/or depressive symptoms in these patients might suggest a potential beneficial effect on AIA symptoms.

[a]Asenapine is indicated for the treatment of moderate to severe manic episodes associated with bipolar I disorder in adults.

**References**

1. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Copyright © 2013. American Psychiatric Association, Arlington, VA, USA.

2. Vieta E, Grunze H, Azorin JM, Fagiolini A. J Affect Disord 2014; 156: 206–213.

3. Young AH, Eberhard J. Neuropsychiatr Dis Treat 2015; 11: 1137–1143.

4. McIntyre RS, Tohen M, Berk M, et al. J Affect Disord 2013; 150: 378–383.

# Suicide risk in bipolar I disorder related to mania with depressive symptoms, and implications for treatment

**Roger McIntyre**

**Abstract**

In bipolar I disorder, mania with depressive symptoms is associated with a higher prevalence of suicide attempts.[1] Consequently, it is important to recognise and identify these symptoms at the earliest opportunity. The DSM-5 'with mixed features' specifier,[2] and accompanying patient-rated Mini-International Neuropsychiatric Interview (MINI) module,[3] were designed to aid the diagnosis of mania with depressive symptoms in patients with bipolar disorder. However, the initial focus of intervention is to treat the emerging symptoms of mania, often overlooking a diagnosis of mania with depressive symptoms, and delaying suitable treatment.

The presence of anxiety, irritability, and agitation (AIA) symptoms is gaining recognition as a relevant discriminator for the presence of mania with depressive symptoms.[4] AIA symptoms are predominant, and more severe, in patients experiencing depressive symptoms during an episode of mania.[1,4] Early recognition of AIA symptoms could identify individuals who may have mania with depressive symptoms, and who may be vulnerable to potential suicide, allowing for appropriate intervention.

Published research on the use of atypical antipsychotics in the treatment of mixed episodes is limited; most available data represent sub-group or post hoc analyses of studies that included both manic and mixed states.[5] A meta-analysis of such studies indicates that atypical antipsychotics are effective in treating manic symptoms in patients with mixed episodes experiencing syndromal mania and syndromal depression.[5] Evidence-based treatment options for managing mania with depressive symptoms are limited. Various atypical antipsychotics have been investigated in clinical trials and evaluated as potential treatment options for patients who are exhibiting mania with depressive symptoms.[6-8] Proven efficacy in treating mania with depressive symptoms could, potentially, result in a reduced suicide risk.

**References**

1. Young AH, Eberhard J. Neuropsychiatr Dis Treat 2015; 11: 1137–1143.

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8. Tohen M, McIntyre RS, Kanba S, et al. J Affect Disord 2014; 168: 136–141.