

Suicide risk in mood disorders

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Purpose of review

The aim of this review is to highlight the traditional and newly recognized suicide risk factors in patients with mood disorders.

Recent findings

Current research findings clearly suggest that suicidal behaviour in patients with mood disorder is a 'state-dependent' phenomenon. Recently, there is, however, a growing body of evidence that besides the well accepted clinically explorable suicide risk factors in mood disorders (e.g., severe depression, prior suicide attempt, comorbid anxiety, substance use, personality disorders and so on), mixed state of depression could also be an important precursor of suicidal behaviour. This might be particularly true in unrecognized cases of bipolar depressives, when antidepressant monotherapy (unprotected by mood stabilizers or atypical antipsychotics) can worsen the clinical picture and rarely induce an aggressive or self-destructive behaviour.

Summary

In the majority of patients with mood disorders, suicidal behaviour is predictable and preventable, with a good chance. A careful and systematic exploration of suicide risk factors in patients with mood disorder helps clinicians to identify patients at high suicide risk. A successful, acute and long-term treatment of these patients substantially reduces the suicidal behaviour even in this high-risk population.

Keywords

attempted suicide, committed suicide, mood disorders, suicidal ideation, suicide risk factors

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Abbreviation

MDE major depressive episode

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Introduction

In spite of the great decline in suicide mortality in most countries with traditionally high baseline suicide rates during the last two decades [1*], completed and attempted suicides still remain a major public health problem. Suicidal behaviour is neither a 'normal' response to the levels of stress experienced by most people nor a linear consequence of major mental disorders. Suicide is a very complex, multicausal human behaviour with many 'causes' and several biological as well as psychosocial and cultural components. In our previous studies [2,3], we had proposed the hierarchical classification of suicide risk factors demonstrating that suicidal behaviour is associated with a number of (a) psychiatric (e.g., major mental disorders), (b) psychosocial (e.g., adverse life situations) and (c) demographic (e.g., male gender) risk factors with varying prognostic utility. Although the statistical relationship between the different demographic and psychosocial risk factors and suicidal behaviour is well demonstrated, it has a very limited value in predicting suicide in individual cases, particularly at the level of general population. As suicides and attempted suicides are very rare in the absence of current major mental disorders [2–7], psychiatric suicide risk factors (current major depression, substance use disorder and schizophrenia particularly with prior suicide attempt), however, are the most powerful and clinically useful predictors of suicide, especially if secondary (psychosocial) and tertiary (demographic) risk factors are also present [2,3] (Table 1). More than 90% of suicide victims and attempters have at least one current axis I (mainly untreated) major mental disorder, most frequently major depressive episode (MDE) (56–87%), substance use disorders (26–55%) and schizophrenia (6–13%). Comorbid anxiety and personality disorders as well as concomitant serious medical disorders are also frequently present, but they are quite rare as principal (or only) diagnoses [3–7].

Prospective and retrospective studies [8–10,11**] clearly support the evident clinical observation that if patients with major mood disorder commit or attempt suicide, they do it mostly during their MDE (78–89%) and less frequently in dysphoric mania (11–20%) but very rarely during euphoric mania and euthymia (0–7%), indicating that suicidal behaviour in patients with mood disorder is a 'state-dependent' phenomenon. Therefore, to treat acute mood episodes effectively and to stabilize the period of euthymia is essential for suicide prevention. As the vast majority of patients with mood disorder never commit

Table 1 Hierarchical classification of suicide risk factors and their prognostic utility

	Person at risk			
	1	2	3	4
Suicide risk factors				
(1) Primary (psychiatric/medical)				
Current axis I major mental disorders	–	–	+	+
Prior suicide attempt/current suicidal ideation	–	–	+	+
Comorbid axis II (personality) disorder	–	–	+	+
Family history of suicide	–	–	+	+
(2) Secondary (psychosocial)				
Adverse childhood experiences	–	+	–	+
Permanent adverse life situations	–	+	–	+
Acute psychosocial stressors	–	+	–	+
(3) Tertiary (demographic)				
Male gender	+	+	–	+
Adolescence (men) old age (both sexes)	+	+	–	+
Minority groups ^a	+	+	–	+
Suicide risk ^b	0	1	2	3

^a Relatives of suicide victims, victims of disasters, bisexuality, same sex orientation.

^b Suicide risk: 0 = negligible, 1 = low, 2 = high, 3 = very high.

suicide and about half of them never attempt suicide [5,6,11^{**},12^{*}], special clinical characteristics of mood disorder as well as some familial and psychosocial factors, however, should also play a contributory role in self-destructive behaviour.

The purpose of this review is to summarize the well known and most recent research findings on the clinically explorable suicide risk factors in patients with mood disorders, particularly in the light of currently emerging debate on the relationship between suicidal behaviour and antidepressant medication [1^{*}]. As the risk factors for attempted and completed suicide show only a few differences [4–7,12^{*}] and suicide attempt is the most powerful predictor of committed suicide, particularly in patients with mood disorder [12^{*},13–15,16^{**},17^{*}], the risk factors for attempted and completed suicide are not discussed separately in this review. Similarly, as repeated suicide attempters frequently change their method from non-violent/nonlethal to violent/lethal (but the opposite is quite rare) [18,19], this is also the case for violent/lethal and nonviolent/nonlethal suicide attempts.

Suicide risk factors in patients with mood disorders

As suicidal behaviour manifests in patients with mood disorder in a state-dependent fashion [8–10,11^{**}], a majority (but not all) of suicide risk factors are timely related to the given mood episodes.

Risk factors related to current or past mood episodes

The most powerful clinically explorable suicide risk factors in mood disorders are mainly related to the major mood episodes. They are also called ‘proximal’ risk factors and are listed in Table 2. Suicidal ideation, a

Table 2 Suicide risk factors in mood disorders, related to current or past mood episodes

(1) Major depressive episode
Current suicidal ideation, plan, wish to die
Prior suicide attempt (ideation, plan)
Severe depression (hopelessness, guilt)
Inpatient status, recent discharge
Bipolar II > bipolar I > unipolar
Depressive mixed state/agitation
Cyclothymic premonitory personality
Psychotic features (bipolar disorder)
Comorbid anxiety, substance use and serious medical disorders
(2) Mania
Dysphoric (mixed) mania
Comorbid anxiety, substance use disorders
(3) Mixed major affective episode [see (1) and (2)]

major precursor of attempted and completed suicide [11^{**},14,17^{*},20,21^{*}] that shows high consistency across MDEs [22^{**}] and, of course, recent suicide attempt are the most alarming signs of the short-term suicide risk.

Patients with minor depression and pure dysthymic disorder (dysthymia without ‘comorbid’ major depression) are relatively underrepresented among suicide victims and attempters [4,7,23,24], which is consistent with the universal finding that severity of symptoms of depression (particularly in the presence of hopelessness and guilt) is a significant suicide risk factor in patients with depression [11^{**},12^{*},14,17^{*},25,26^{**},27^{*}]. The suicide risk in hospitalized patients with mood disorder is very high [16^{**},17^{*}] and peaks immediately after hospital admission and discharge, particularly in the case of short hospital treatment [28^{*}].

With regard to the role of the unipolar–bipolar nature of mood disorders in suicide prediction, a recent review [29] of 10 published studies including more than 3000 patients has concluded that bipolar patients, in general, and bipolar II patients, in particular, are overrepresented among both committed and attempted suicides. Another recent study [11^{**}] investigating 90 bipolar I and 101 bipolar II patients also found a (nonsignificant) trend for higher rate of prior suicide attempts at index episode in bipolar II (25%) than in bipolar I patients (16%). On the contrary, however, another large-scale, 40–44-year follow-up study [16^{**}] has found that a higher rate of 186 unipolar (14%) than the 220 bipolar (I + II) patients (8%) committed suicide.

A relatively newly recognized important proximate suicide risk factor in MDE might be the mixed state of depression (three or more simultaneously cooccurring intradepressive hypomanic symptoms) [30^{**},31,32^{**}], as the frequency of past suicide attempts and suicidal ideation has been reported to be much higher among mixed than nonmixed unipolar and bipolar patients with

major depression [31,33–35]. In our most recent study [36**], we used the opposite strategy, and we analysed the frequency and clinical characteristics of mixed states of depression among the consecutively investigated 100 nonviolent suicide attempters. Current mixed depression was present in 63% of the total sample and in 71% among the 89 suicide attempters with depression. Irritability, distractibility and psychomotor agitation were present in more than 90% of patients with mixed depression. The rate of mixed depression was significantly higher among the 29 patients with bipolar (I + II) depression than in 60 suicide attempters with nonbipolar depression (90 and 62%, respectively). These figures are almost two times higher than the same rates (59 and 27%, respectively) that were previously reported among 241 bipolar II and 164 nonsuicidal outpatients with unipolar major depression [37]. These findings indicate that suicide attempters with depression come primarily from mixed bipolar and unipolar depressions and support the role of mixed depression in suicidal behaviour. These results can also explain, at least in part, why bipolar II depression (which is most often mixed in nature) carries the highest suicide risk among all subtypes of major mood disorders [29].

Investigating 247 adolescent outpatients with current MDE (100 of them have had bipolar I or bipolar II disorder), a close link between suicidality and bipolar mixed depression has also been observed but only for girls: out of the 82 patients with mixed depression, girls had nearly four times the risk of having made a past suicide attempt compared with patients having non-mixed depression [38].

Another recent study [30**] of ours has demonstrated that outpatient ‘unipolar’ mixed major depression and agitated depression are greatly overlapping conditions (90% of patients with agitated depression also met the criteria for mixed state of depression), and a significantly higher rate of patients with agitated than nonagitated depression (62 versus 43%) showed current suicidal ideation and positive family history of bipolar II disorder (24 versus 12%). Of symptoms of mixed depression, we found a significant association between suicidal ideation, psychomotor activation and racing thought. The results support the view that agitated unipolar depression should also be classified as a bipolar mixed state of depression and are in good agreement with prior studies [5,34,39], showing that agitation is a suicide risk factor in patients with depression.

The role of ‘mood instability’ (i.e., ‘bipolarity’) in the suicidal behaviour was also supported by two other recent studies [40**,41], showing that a history of rapid mood switching and panic attacks was associated with an increased likelihood of history of self-reported suicidal thought or action [40**], and variability in suicidal ideation was a significantly better predictor of previous

suicide attempts than duration and intensity of ideation [41]. The persistent, frequent and marked instabilities of mood, thinking and behaviour are the most characteristic features of cyclothymia, which is the attenuated manifestation of major bipolar mood disorders. Cyclothymia might be a predisposing factor for suicidal behaviour, as two recently published studies [42,43**] found that in patients with MDE, cyclothymic personality was significantly related to lifetime and current suicidal behaviour (ideation and attempts) both in an adult sample [42] and in a paediatric sample [43**].

The recognition of the important role of ‘pseudo-unipolar’ mixed states of depression in suicidal behaviour [1*,30**,31,36**] has clear implications for suicide prevention. The correct identification of the ‘covert’ bipolar nature of the given episode of depression, as reflected in mixed/agitated clinical picture, is crucial for selecting the most appropriate treatment. A growing body of evidence exists that antidepressant monotherapy, unprotected by mood stabilizers or atypical antipsychotics in patients with bipolar and bipolar spectrum (including ‘unipolar’ mixed states of depression and unipolar depression with cyclothymic personality and with bipolar family history) can not only produce (hypo)manic switches and rapid cycling but also worsen the preexisting mixed state of depression or generate mixed conditions *de novo*, resulting in treatment resistance, destabilization of the mood disorder, worsening of the depression and, ultimately, suicidal behaviour in few patients [1*,30**,31]. In other words, the rarely observed suicidality–antidepressant link appears mediated by agitated, excited mixed states of depression, and recent data suggest that concomitant use of mood stabilizers, atypical antipsychotics or benzodiazepines in such cases could prevent the newly developing suicidality in this high-risk population [1*,30**,31].

The psychotic/nonpsychotic nature of major mood episodes does not seem fundamental regarding suicidal behaviour in unipolar depression [44]. Psychotic symptoms, however, were significantly associated with completed suicide in adults [16**] and with suicidal ideation and plans in paediatric [45] bipolar I and bipolar II patients.

In agreement with the previous findings, recent studies [6,12*,14,21*,27,39,46–48] also show that comorbid anxiety/anxiety disorders and comorbid substance use disorders as well as concomitant serious medical illnesses increase the risk of all forms of suicidal behaviour in unipolar depression and bipolar disorder.

As untreated MDE is the most frequent diagnosis in suicide victims and attempters [1*,3,4,16**,23,29], suicidal behaviour in bipolar patients is not exclusively restricted to episodes of depression as mixed (major) affective episode (meeting the full syndromal criteria for mania and major

depression at the same time) also increases the risk of attempted and completed suicide [9,11^{**},12^{*}]. In addition, a recent study [49] demonstrated that the distinction between mixed (dysphoric or depressive) mania and pure (euphoric) mania is also crucial for predicting suicide risk: more than 40% of patients with dysphoric mania had current suicidal ideation or attempt, whereas for patients with pure mania it was less than 10%.

Risk factors unrelated to current or past mood episodes

The fact that adverse childhood experiences and current psychosocial stressors have a predisposing and triggering role in suicidal behaviour is well known. Although clinicians cannot influence what has happened in the past history of their patients, collecting information about family history and early development as well as current psychosocial circumstances is also important in predicting suicide risk. The well recognized (familial and psychosocial) suicide risk factors in patients with mood disorder that are not directly related to current or past mood episodes (e.g., distal suicide risk factors) are listed in Table 3.

The voluminous literature on this subject consistently shows that family history of committed suicide (and mood disorder) in first-degree relatives [12^{*},27,47,50], adverse childhood experiences (parental loss and emotional, physical and sexual abuse) [12^{*},21^{*},47,50,51^{*},52], early onset of mood disorder [12^{*},16^{**},27,47,48], comorbid (mostly cluster B) personality disorder and aggressive/impulsive personality features, as well as cigarette smoking [11^{**},14,23,24,26^{**},51^{*},53,54^{*},55^{*}], adverse life situations (unemployment, isolation and acute psychosocial stressors) [3,6,21^{*},26^{**},55^{*}] and lack of emotional, social and medical/psychiatric support [3,9,16^{**},24,29] are significantly associated with completed and attempted suicides, both in the general population and in patients with mood disorders.

In contrast to the fact that men are markedly overrepresented among unselected suicide victims compared with women among suicide attempters [3,5,19,21^{*},23,28^{*}], gender is not a significant predictor of committed [16^{**},17^{*}] and attempted [14,26^{**},27,47,52,53] suicides in patients with unipolar or bipolar mood disorder.

Table 3 Suicide risk factors in mood disorders unrelated to current or past mood episodes

Family history of committed (attempted) suicide in first-degree relatives
Adverse childhood experiences (parental loss, emotional, physical and sexual abuse)
Early onset of mood disorder
Comorbid (cluster B) personality disorder
Aggressive/impulsive personality features
Cigarette smoking
Permanent adverse life situations (isolation, unemployment)
Acute psychosocial stressors
Lack of emotional, social, psychiatric/medical support

Depression, suicide and antidepressants

Undoubtedly, the successful acute and long-term pharmacotherapy of depression (including antidepressants, mood stabilizers, anxiolytics and antipsychotics) significantly reduces the risk of suicidal behaviour in the vast majority of patients and the widespread use of antidepressants in the new selective serotonin reuptake inhibitor ‘(SSRI)-era’ appears to have actually led to a highly significant decrease in suicide rates in most countries with traditionally high baseline suicide rates [1^{*},3,16^{**},29,56]. On the contrary, antidepressants (particularly as monotherapy), however, can worsen depression and therefore indirectly increase the risk of suicidal behaviour in a very small, vulnerable subpopulation [1^{*},30^{**},31,57]. This low risk of ‘suicide-inducing potential’ of antidepressants is relatively higher for non-SSRI compounds that show marked noradrenergic (maprotiline, mianserine) or serotonergic and noradrenergic activity [moclobemide, venlafaxine, mirtazapine and some tricyclic antidepressants (TCAs)] than the SSRI compounds [1^{*},56,58,59]. Recent findings strongly suggest that when antidepressants worsen depression in a few patients, its psychopathological substrate might well reside in an agitated, excited, mentally overstimulated, anxious mixed state of depression [1^{*},30^{**},31,36^{**},38]. Consequently, the recognition of the bipolar nature of depression (including the soft bipolarity) and the introduction of concomitant mood stabilizers or atypical antipsychotics as well as anxiolytics, if needed, are recommended in such cases to minimize the development of the heteroaggressive and autoaggressive outcome.

An important note to be made, however, is that in a recently published clinical psychotherapy trial, which enrolled adolescent outpatients with major depression similar to those enrolled in pharmacotherapy clinical trial, rates of newly emergent suicidality in patients receiving only psychotherapy were comparable with those observed in antidepressant trials [60^{**}]. Considering all the above factors, psychiatrists must always be vigilant of the risk of suicidal behaviour when prescribing antidepressants or implementing psychotherapy for patients with depressive disorders where the risk of suicidality is inherently extremely high. A detailed discussion of the relationship between depression, suicidal behaviour and antidepressants is outside the frame of this study, and this topic has been reviewed recently elsewhere [1^{*}].

Conclusion

Suicide is a rare event in the general population, but it is quite common among patients with mood disorder who are in contact with different levels of the healthcare system [2,3,5,6,61]. Of course, we are unable to prevent all suicides. It has, however, been demonstrated that successful acute and long-term treatment of unipolar depression and bipolar disorders markedly reduces suicide morbidity and mortality, even in this high-risk

population [1*,3,16**,29,30**]. As more than two thirds of suicide victims die in their first attempt [1*,5,8,19] and as the same rate of them have (mostly untreated) current MDE [2,5,6,23,29], it is very important to detect suicide risk factors, particularly in patients with mood disorder, as early as possible and intervene prior to the person making the first suicide act. More early, widespread and effective treatment of major mood disorders should result in the decline of suicide mortality of these patients, which, after a given point of time, will appear on the level of the general population [1*,30**]. It is well accepted that remarkable progress has been made in the management of depression and several other disorders, including, for example, hypertension since the 1950s. As hypertension is present in 75% of patients with stroke and with coronary heart disease [62] (like depression among suicide victims and attempters), cardiologists should be right if they declare that better treatment of hypertension was a significant (but not the only) contributory factor in a markedly reduced morbidity and mortality from stroke and coronary heart disease in the USA between 1970 and 2000 [62]. The careful and systematic exploration of traditional and newly recognized suicide risk factors in mood disorders helps clinicians to identify the patients with suicidal behaviour who frequently contact mental health and primary care services in the last weeks or months of their life [61].

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 73–76).

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- 11 Valtonen H, Suominen K, Mantere O, *et al.* Suicidal ideation and attempts •• in bipolar I and bipolar II disorders. *J Clin Psychiatry* 2005; 66:1456–1462.
- Data presented here are a part of Jorvi Bipolar study involving a large and representative sample of both inpatients and outpatients with bipolar I and II disorder from three different Finnish cities. The finding that 80% of all the 191 patients had serious suicide ideation or ideation plus attempts over lifetime underlines the importance of bipolar disorder in suicidal behaviour.
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