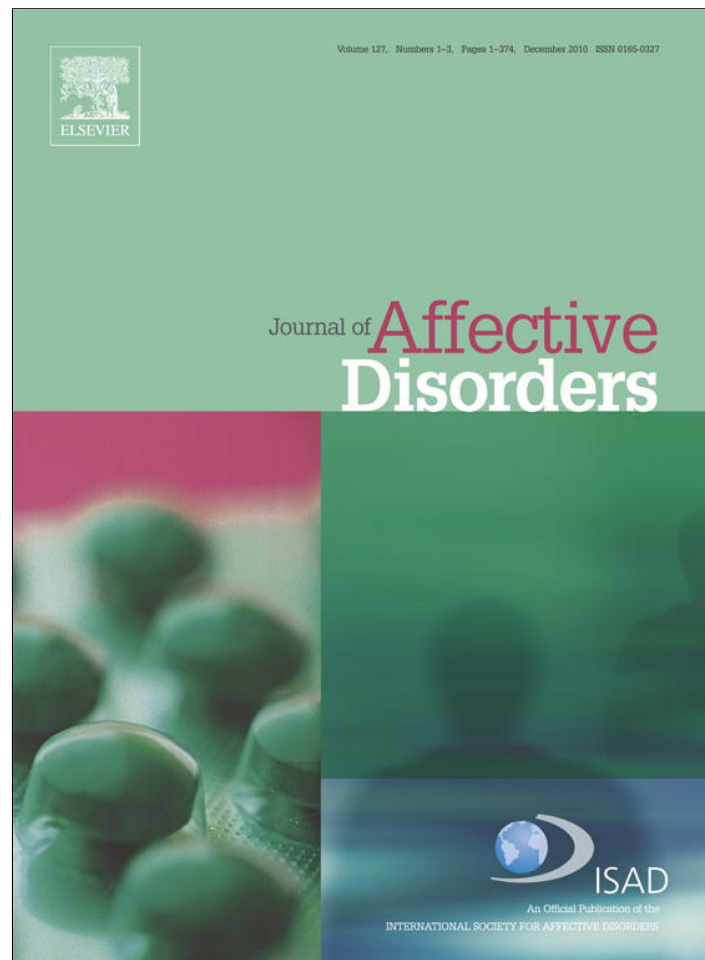


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Preliminary communication

## Explained factors of suicide attempts in major depression

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## ABSTRACT

**Objective:** The aim of this study is to identify risk factors for suicide attempts including bipolarity. **Method:** The paper presents the most recent data on suicide attempts and depression with or without hypomanic features from three French “Bipolact”, studies including 2249 patients with recurrent or resistant depression. Hypomania and BP-II disorder were defined by a score of 10 or more on the Hypomania Checklist-20.

Attempters and non-attempters were compared, and multivariate logistic regression analyses were performed on all the significant variables obtained in univariate tests.

**Results:** Rates of suicide attempts and of a family history of suicide were higher in BP-II disorder. Suicide attempts were best explained by a family history of suicide and mood disorders, recurrence of depression, the “irritable–risk-taking” dimension of hypomania, substance abuse, and need of psychiatric treatment.

**Limitations:** The study does not deal with DSM-IV BP-II disorder.

**Conclusion:** Clinicians need to be familiarized with these risk factors.

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## 1. Introduction: the French Bipolact studies

Bipolar-II (BP-II) disorder is officially recognized as a mental disorder in DSM-IV-TR and defined by the presence of hypomanic episodes alternating with major depression. Despite data supporting the clinical complexity and high morbidity and mortality rates of BP-II, the disorder is often overlooked or misdiagnosed as unipolar major depression or personality disorder (Allilaire et al., 2001; Angst et al., 2005a). Moreover, many clinicians still regard it as a milder form of manic-depressive illness.

These unsolved problems prompted the large-scale, nationwide French investigation of hypomania prevalence rates in resistant and recurrent depressions, by means of three large studies (Bipolact surveys) carried out in both psychiatric and primary care settings (Hantouche et al., 2009). This research is part of a national project for medical education on bipolar disorders established in the 1990s

(EPIDEP study: Allilaire et al., 2001; Hantouche et al., 2006) and continued in September 2004.

The main goal of this paper is to analyze risk factors for suicide attempts in patients with major depressive episodes (MDE), given the great complexity of those factors (Rihmer, 2007). This can often interfere with the successful prevention of suicidality, which implies recognition of factors that can be modified. Especially BP-II disorder and other soft BP conditions are important risk factors and often overlooked (Rihmer, 2005; Akiskal, 2007). Effective hypomania screening appeared therefore to be highly relevant (Angst et al., 2005a).

## 2. Method

The purpose of the French Bipolact studies was to familiarize clinicians with frequently hidden BP-II disorder. Three studies on MDE were carried out:

- in primary care patients with recurrent MDE  $N = 937$
- in psychiatric out-patients with recurrent MDE  $N = 758$
- in psychiatric out-patients with resistant MDE  $N = 554$ .

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For all three studies, each investigator had to recruit 4 consecutive patients suffering from a current MDE (DSM-IV) with no known prior diagnosis of bipolar disorder.

### 2.1. Selection criteria

- Recurrent depression: current MDE plus one prior episode in the last 5 years or 2 or more in lifetime.
- Resistant depression: current MDE not responding to two or more antidepressants (of different classes) prescribed at sufficient dose and for a sufficient duration.
- Patients with a prior diagnosis of mania were excluded.

### 2.2. Populations selected

In all, 623 physicians participated in the Bipolact studies. From the total population (A, B and C = 2249) 306 patients (14%) were eliminated from the final analyses because of missing data. Thus, 1943 were included in the statistical analyses.

### 2.3. Assessment method

- Clinicians' assessment: socio-demographic features, DSM-IV criteria for MDE, dominant clinical picture of current MDE (for example “anxious”, “agitated”, “retarded”, “psychotic”, “somatic”, “atypical”, and “choleric”), and other features related to personal past history (suicide attempts, ups and downs in temperament, interpersonal sensitivity, and eccentric character), family history, and past drug response (for resistant depression only).
- Patients' self-assessment: the Hypomania Checklist (HCL-20 items – with yes/no answers). A score of 10 or more items was used as the cut-off for defining cases of hypomania, a cut-off validated in an earlier French study, EPIDEP (Hantouche et al., 2006). We also used the double dimension of hypomania, “sunny” (hyperactivity plus elated mood) versus “dark” (irritability plus risk-taking), as obtained from exploratory factor analysis on the 20 items of the HCL (Hantouche et al., 2003, 2009).

Hypomania and HCL-BP-II disorder were defined by a score of 10 or more on the Hypomania Checklist-20.

More information on the methodology is available in the paper of Hantouche et al. (2009). Its most important finding was the high rates of hypomania: around 62% in both recurrent depression samples (primary care and psychiatric settings) and 55% in resistant major depression. Hypomania was significantly associated with the presence of “ups and downs” (cyclothymic traits), a family history of bipolarity, and substance abuse (Hantouche et al., 2009).

First, the rates of suicide attempts and of a family history of suicide were compared in the BP-II patients and unipolars in each of the three populations. Then, in the combined populations, suicide attempters were compared with non-attempters. Finally, a logistic multivariate regression with stepwise analysis (Hosmer and Lemeshow Goodness-of-Fit Test) was carried out on all the available significant qualitative and quantitative features obtained from the inter-group comparisons.

## 3. Results

### 3.1. Global rates of suicide attempts

477 (24.5%) of the total population (A + B + C) of 1943 patients with major resistant or recurrent depression were positive for recurrent or serious suicide attempts. The rate varied in the three subsamples, being significantly higher in patients seen in psychiatric settings (B = 26.4%, C = 30.7%) than in primary care patients (A = 19.4%).

When unipolar and HCL-BP-II groups were compared within the three studies (A, B, C), the suicide attempt rates were consistently higher in all three BP-II subgroups (22.9%, 27.4%, and 37.8%) than in the corresponding UP subgroups (13.6%, 24.3%, and 21.9%); the same trend was found for a family history of suicide: BP-II subgroups (17.5%, 16.0%, and 18.9%) versus UP subgroups (11.8%, 9.7%, and 13.8%).

### 3.2. Characteristics of suicidal depressed patients

In Table 1, the three studies were merged for an overall comparison of suicide attempters versus non-attempters. The two groups did not differ in gender or age but did in all illness-related characteristics.

When all significant variables were entered into a multivariate logistic regression, a family history of suicide emerged as the most robust factor explaining suicidal behavior in depression. It was followed by the number of prior depressive episodes, whether the patient was seen in a psychiatric setting, levels of “dark” hypomania (dimension

**Table 1**

Clinical characteristics of major depressive patients with versus without suicide attempts.

Total population	Suicide attempts		p
	Present 544	Absent 1686	
Male gender	178 (32.7%)	574 (34.0%)	0.5699
Mean age (years)	46.63 (±11.08)	46.94 (±12.15)	0.7004
Married	212 (±39.0%)	812 (±48.8%)	<0.0001
Number of depressive symptoms	7.42 (±1.20)	6.85 (±1.23)	<0.0001
Number of depressive episodes	5.02 (±3.80)	4.07 (±2.77)	<0.0001
Onset of first depression <26 years	313 (56.8%)	799 (47.1%)	<0.0001
Post-partum occurrence	64 (17.5%)	252 (22.7%)	0.0362
Substance abuse	213 (38.7%)	481 (28.3%)	<0.0001
Eccentric/irritable character	201 (36.5%)	459 (27.0%)	<0.0001
Ups and downs (cyclothymic trait)	374 (67.9%)	1060 (62.4%)	0.0207
Social/professional instability	281 (51.0%)	723 (42.6%)	0.0006
Family history			
– Bipolar disorder	104 (19.0%)	199 (12.0%)	<0.0001
– Depression	273 (49.8%)	697 (42.0%)	0.0013
– Suicide	129 (23.5%)	204 (12.3%)	<0.0001
Hypomania score (HCL-20)			
– Score 10 or more	380 (69.0%)	986 (58.1%)	<0.0001
– “Sunny” score	7.48 (±3.07)	7.04 (±3.24)	0.0068
– “Dark” score	3.65 (±2.07)	3.18 (±2.09)	<0.0001

“Sunny” hypomania: hyperactivity + elated mood.

“Dark” hypomania: irritability, risk-taking and substance overuse.

**Table 2**

Risk factors for suicide attempts: multivariate logistic regression.

	Summary of stepwise selection		Odds ratio estimates		
	Score Chi-Square	Pr>Chi-Square	Point estimate	95% Wald confidence limits	
Family history of suicide	44.0737	<.0001	2.006	1.526	2.639
Number of depressive episodes	37.9440	<.0001	1.100	1.061	1.140
Psychiatric settings	17.2528	<.0001	1.625	1.298	2.035
Score on "dark" dimension of hypomania	18.4546	<.0001	1.068	1.010	1.130
Marital status other than married	10.1335	0.0015	1.393	1.116	1.738
Substance abuse	6.5411	0.0105	1.374	1.082	1.745
Family history of bipolar disorder	5.2748	0.0216	1.486	1.102	2.004
Family history of depression	5.3408	0.0208	1.294	1.040	1.612

"Dark" hypomania: irritability, risk-taking and substance overuse.

including irritability, risk-taking and substance overuse), substance abuse, and not being married (Table 2).

The explained model showed good specificity (79.1%) and predictive negative value (81.0%), but poor sensitivity (43.0%) and low predictive positive value (40.1%).

#### 4. Discussion

There is evidence that suicide rates among mood disorder patients are more than 20-fold higher than in the general population and that suicidal behavior is much more lethal in bipolar disorder than in the general population (Pompili et al., 2009).

In a review (Rihmer, 2005) of 10 published studies which had analyzed over 3000 unipolar, BP-I, and BP-II patients separately, the pooled data showed the rate of previous suicide attempts to be highest among BP-II patients, followed by BP-I and unipolar cases; bipolar patients, in general, and BP-II patients, in particular, are overrepresented among both committed and attempted suicides.

The Bipolact data showed higher rates of suicide attempts in HCL-BP-II (hypomania defined by a cut-off score of 10 on the self-rated HCL-20) versus unipolar major depressives. However, a large-scale, 40–44-year follow-up study (Angst et al., 2005b) found a higher suicide rate in 186 unipolar (14%) than in 220 bipolar (I + II) patients (8%). The difference could be related to the method of defining hypomania and to the nature of the selected sample.

The particular interest of our data is that they were obtained in various settings (primary care and psychiatric settings) away from university centers and therefore reflect the real world of clinical practice all over France. In addition, the Bipolact studies have used the hypomania self-rating instrument with a dimensional definition, which appeared sensitive and suitable for screening BP-II disorder (Angst et al., 2005a; Hantouche et al., 2006).

The link between suicide risk and bipolar disorder (BPD) was also shown in a recent French study (Guillaume et al., 2010). In a sample of 211 patients suffering from depression and hospitalized after a suicide attempt, serious suicide attempts and a family history of suicide were closely associated with a diagnosis of BPD. Guillaume et al's study did not specify subtypes of BPD. Our study mainly focused on the HCL-BP-II diagnosis. Moreover, it showed that the "dark" side of hypomania (irritability, risk-taking) is significantly associated with suicide attempts. This hypomanic dimension is mostly

present in highly recurrent and instable forms of BPD (Akiskal et al., 2003). Indeed, BPD with cyclothymic temperament, early age of onset, rapid cycling, and highly recurrent depressive episodes seems to be the most suicidal form (Azorin et al., 2010).

Before starting any (especially antidepressant) treatment for depression, clinicians must examine each patient carefully and look systematically for hypomania (Akiskal, 2007; Angst et al., 2005a). Moreover, bipolar patients may exhibit highly perturbed mixed states, which usually increase the suicide risk, especially if treated only with antidepressants and unprotected by mood stabilizers (Pompili et al., 2009).

Besides the association with HCL-BP-II, our study found that a family history of completed suicide and of depressive and bipolar disorders was also linked with suicide attempts. This finding confirms those of other studies (Angst et al., 2005b; Slama et al., 2004; Roy and Janal, 2005; Hawton et al., 2005; Borges et al., 2006). Recently, Torzsa et al. (2009) reported that a family history of suicide was significantly more common among patients with current major depression. Fifty percent of patients with a family history of suicide had current major depression.

Finally, substance abuse emerged in our study as a major factor of suicidal behavior.

Our data and other studies suggest that cumulative factors act on suicide risk: BP diagnosis, early age of onset, cyclothymic traits, large number of depressive episodes, comorbid alcohol abuse, and suicide in the family. For Slama et al. (2004), this clinical configuration could constitute a special BP subgroup at risk of suicidal behavior.

#### 5. Limitations of the study

The original focus of the Bipolact surveys was not primarily on suicide risk, thus assessment was limited to reported lifetime suicide attempts. Secondly, the study does not deal with DSM-IV BP-II disorder; the diagnosis of hypomania relied on the scores obtained from the self-rated Hypomania Checklist; any bipolar patients could therefore be included in the analyses (even though the selection was of depressive patients with no known earlier diagnosis of mania).

#### 6. Conclusions

The national Bipolact studies consistently showed an increased suicide risk in recurrent or resistant depression associated with hypomania (when dimensionally assessed).

The application of self-assessment for hypomania turned out to be useful for the BP-II diagnosis. In addition, the Bipolact data helped identify relevant factors explaining the suicide risk in recurrent or resistant major depression.

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#### Conflict of interest

The authors declare the absence of conflict of interest.

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