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After studying this article, you should be able to:

• Systematically assess patients with bipolar disorder for abnormalities associated with metabolic syndrome

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# **Financial Disclosure**

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# Metabolic Syndrome in a French Cohort of Patients With Bipolar Disorder: Results From the FACE-BD Cohort

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#### **ABSTRACT**

**Objective:** The aim of this study was to estimate the prevalence of metabolic syndrome (MetS) and its components in a cohort of French patients with bipolar disorder; determine correlations with sociodemographic, clinical, and treatment-related factors; and investigate the gap between optimal care and effective care of the treated patients.

**Method:** 654 bipolar disorder patients from the FACE-BD cohort were included from 2009 to 2012. Sociodemographic and clinical characteristics, lifestyle information, and data on antipsychotic treatment and comorbidities were collected, and a blood sample was drawn. The Structured Clinical Interview for *DSM-IV* Axis I Disorders was used to confirm the diagnosis of bipolar disorder. Metabolic syndrome was defined according to the National Cholesterol Education Program Adult Treatment Panel III criteria.

**Results:** 18.5% of individuals with bipolar disorder met criteria for MetS. Two-thirds of bipolar disorder patients did not receive adequate treatment for MetS components. Multivariate analysis showed that risk of MetS in men was nearly twice that in women (OR=1.9; 95% CI, 1.0–3.8), and older patients had a 3.5 times higher risk (95% CI, 1.5–7.8) of developing MetS than patients under the age of 35 years. Moreover, patients receiving antipsychotic treatment had a 2.3 times increased risk (95% CI, 1.2–3.5) of having MetS, independent of other potential confounders.

**Conclusions:** The prevalence of MetS is high in bipolar disorder patients, and there was considerable undertreatment of the components of MetS in this population. The prevention and treatment of cardiovascular diseases in these patients should be assessed systematically. The findings highlight the need for integrated care, with more interaction and coordination between psychiatrists and primary care providers.

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- Because metabolic syndrome is highly frequent in bipolar patients (20% in this cohort), it should be screened for systematically, particularly in men, older patients, and those on atypical antipsychotic treatment.
- Integrated care between psychiatrists and primary care providers and early intervention are crucial in order to reduce cardiovascular diseases, which are known to be one of the most frequent causes of mortality in bipolar patients.

etabolic syndrome (MetS) is a collection of clinical and biological abnormalities resulting in a predisposition to diabetes, cardiovascular disease (CVD), and stroke and recognized as a leading cause of CVD-related mortality in the general population. In patients with bipolar disorder, comorbid CVDs are known to be one of the most frequent causes of mortality, with a frequency well above that of suicide, In and II years shorter for male and female bipolar disorder patients, respectively, than for individuals in the general population without mental illness. For this reason, several studies have evaluated the prevalence of MetS in patients with bipolar disorder, reporting estimates about twice those for the general population. Tes

A recent meta-analysis by Vancampfort et al<sup>8</sup> showed the overall rate of MetS to be 37.3% (95% confidence interval [CI], 36.1–39.0) in individuals with bipolar disorder. Most of the studies analyzed were carried out in North America (10/37) and Europe (11/37), but none included patients from France, and several limitations were noted, such as a small sample size or the enrollment of subgroups of patients. It was therefore difficult to generalize the findings, and studies of larger samples from other countries are required to explore the differences between countries more thoroughly.

Moreover, only a small number of studies have investigated the relationship between MetS in individuals with bipolar disorder and the characteristics, comorbid medical conditions, combinations of drugs taken, and bipolar disorder severity of the patients. Some associations were found between MetS and higher age, a longer duration of the disease, and use of second-generation antipsychotics; however, although some studies focused on demographic factors, and others focused on medication or on clinical characteristics, none have taken an integrative approach. More detailed knowledge of these risk factors would be highly relevant for the development of preventive strategies and to improve our understanding of the mechanisms underlying these associations, but large cohorts would be required.

In addition, the care of patients with multiple comorbidities is often complicated, and although patients often see various health care professionals, there is a lack of coordination between specialties. In this context, it would be useful to evaluate the management of the various components of MetS, but the data required for such an analysis are currently lacking.

Within FACE-BD, the database of individuals with bipolar disorder established by the FondaMental bipolar disorder expert center network, 11 we studied (1) the prevalence of MetS and its components in a large multicenter cohort of French patients with bipolar disorder; (2) its correlation with sociodemographic, clinical, and treatment-related factors; and (3) the gap between optimal care and effective care of the treated patients.

#### **METHOD**

# **Study Population**

The study sample was drawn from patients who were evaluated in hospitals belonging to a network of French bipolar disorder expert centers. The network, supported by the French Ministry of Health, was developed under the aegis of the FondaMental Foundation. This scientific cooperation foundation was created in 2007 and funded by the French Ministry of Research to provide support to general practitioners and psychiatrists requiring assistance in the diagnosis and management of patients with bipolar disorder. All outpatients 16 years or older evaluated at the expert centers and diagnosed with bipolar disorder according to *DSM-IV* criteria (all bipolar subtypes [I, II, and not otherwise specified]) were enrolled in the FondaMental Advanced Centers of Expertise in Bipolar Disorders (FACE-BD) cohort.

Patients were evaluated with a thorough, standardized assessment when they were not in an acute episode and were followed up every 6 months for 3 years. We report here the characteristics of the patients at inclusion. The tools used for assessment have been described elsewhere. The assessment protocol was approved by the institutional review board (Comité de Protection des Personnes Ile de France IX; January 18, 2010), in accordance with the French laws for noninterventional studies. The institutional review board asked us to provide all patients with an informational letter. Written formal consent was not required, but we sought the agreement of the patient in each case before analyzing the clinical data.

# **Data Collected**

On entry into this study, the patients were interviewed by a senior psychiatrist specializing in bipolar disorders, who systematically recorded information relating to the patient's education, marital status, economic status, onset and course of illness, and family history. History of somatic diseases and treatment for these conditions were recorded with a checklist questionnaire. Current psychotropic treatments (first-generation antipsychotic, second-generation atypical antipsychotic, mood stabilizer, lithium, and antidepressants) were detailed. The trade names of all drugs were recorded and coded according to the World Health Organization Anatomical Therapeutic Chemical classification.

The Structured Clinical Interview for *DSM-IV* Axis I Disorders was used to confirm the diagnosis of bipolar disorder and of comorbid psychiatric disorders and to check for a history of mood disorder.<sup>12</sup> Current mood state and residual symptoms were assessed with the Montgomery-

Table 1. Demographic Characteristics of Patients With Bipolar Disorder in the FACE-BD Sample (N = 654)

Characteristic	Value		
Sex, n (%)			
Female	285 (56.3)		
Male	369 (43.6)		
Age tertile, n (%)			
<35 y	208 (31.9)		
35-48 y	213 (32.7)		
>48 y	231 (35.5)		
Education level, n (%)			
< High school graduation	105 (18.0)		
≥ High school graduation	482 (82.0)		
Bipolar subtype, n (%)			
Bipolar I	306 (46.8)		
Bipolar II	254 (38.8)		
Bipolar NOS	94 (14.4)		
Age at onset of bipolar disorder, mean (SD), y	25.1 (10.5)		
Early onset (before 21 y), n (%)	226 (36.2)		
Duration of the disease, mean (SD), y	17.0 (11.2)		
Predominant polarity, n (%) <sup>a</sup>			
Major depressive episode	465 (74.2)		
Manic episode	78 (12.5)		
Mixed	17 (2.7)		
Hypomanic	67 (10.7)		
Lifetime psychiatric comorbidities, n (%)			
Anxiety disorders	264 (43.8)		
Substance abuse	193 (32.1)		
History of suicide attempts	266 (41.7)		
Current medication, n (%)			
Antidepressant	218 (43.8)		
Antipsychotic	161 (39.0)		
Mood stabilizers	287 (57.6)		
Lithium	151 (30.3)		

<sup>a</sup>Or first episode if the patient had had only 1 episode. Abbreviations: FACE-BD = FondaMental Advanced Centers of Expertise in Bipolar Disorders, NOS = not otherwise specified.

Asberg Depression Rating Scale<sup>13</sup> and the Young Mania Rating Scale<sup>14</sup> for manic symptoms. A physical examination was carried out, and a blood sample was collected.

#### **Metabolic Syndrome Definition**

Measures of systolic and diastolic blood pressure were performed after the patient had rested for at least 5 minutes. Weight, height, and waist circumference were also measured in the expert centers. A blood draw for routine blood testing was performed, and triglycerides, low-density lipoprotein, high-density lipoprotein, and total cholesterol, as well as glucose if patients confirmed fasting for at least 10 hours, were collected. All measures of MetS components were based on laboratory blood testing performed in the expert center.

We used the modified National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria to define MetS. Patients were considered as having MetS if they met at least 3 of the following criteria: abdominal obesity (waist circumference > 102 cm for men and > 88 cm for women), hypertriglyceridemia ( $\geq$  1.7 mmol/L or on lipid-lowering medication), low level of high-density lipoprotein (HDL) cholesterol (<1.03 mmol/L in men and <1.29 mmol/L in women), high blood pressure ( $\geq$  130/85 mm Hg or on antihypertensive medication), and high fasting glucose concentration ( $\geq$  5.6 mmol/L or taking glucose-lowering medication).

# **Statistical Analysis**

Categorical variables are expressed as numbers and percentages, and continuous variables, as mean  $\pm$  SD values. We investigated the association of MetS with demographic factors, clinical factors, and antipsychotic medication by carrying out  $\chi^2$  tests for categorical variables and t tests for continuous variables. We estimated crude odds ratios (ORs) with 95% CIs.

For continuous variables, the decision as to whether to treat the variable as a continuous or categorical variable was based on the lowest value of the Akaike information criterion for the corresponding univariate logistic regression model. Variables with P values < .20 in univariate analysis were included in the multivariate logistic regression model to estimate the likelihood that MetS was associated with each factor. Analyses were conducted with SAS (release 9.3; SAS Institute, Cary, North Carolina).

#### **RESULTS**

Between 2009 and 2012, 654 patients were enrolled in the FACE-BD cohort and provided with information about MetS. The characteristics of these patients are displayed in Table 1; 46.8% had bipolar I disorder, and 38.8% had bipolar II disorder. The mean age at bipolar disorder onset was 25.1 years (SD = 10.5), and time since diagnosis ranged from 0 (first episode) to 65 years (median = 15 years).

# **Prevalence of Metabolic Syndrome and Its Components**

The prevalence of MetS in the FACE-BD cohort was estimated at 18.5%. MetS was present in 22.8% of the men and 15.5% of the women. The prevalence of MetS increased with age (Figure 1). After stratification of the sample by age group and sex, we found that the frequency of MetS was significantly higher in men than in women for patients over the age of 40 years (33.5% vs 20.8%, P=.006). In younger patients, the prevalence of MetS was similar in men and women.

Prevalence values for the various conditions constituting MetS in patients with bipolar disorder are presented in Table 2. We found that 34.6% of the patients with bipolar disorder had high blood pressure, 32.8% had low HDL cholesterol levels, 28.9% had hypertriglyceridemia, 35.5% had abdominal obesity, and 16.0% had high fasting glucose concentrations. We also observed that 53.0% of the patients with bipolar disorder were overweight (38.2% had body mass index [BMI] > 25, and 14.8% were obese). In patients with MetS, all of the individual components of the syndrome were highly frequent (>70%), with the exception of high fasting glucose, which was present in 48% of patients. Analyses by sex indicated that men were significantly more likely to have hypertriglyceridemia and to be overweight than women, whereas women were more likely to display abdominal obesity than men.

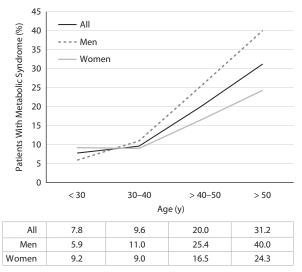
# **Risk Factors for Metabolic Syndrome**

The factors associated with MetS are shown in Table 3. Independent of other potential confounders, the risk of MetS in men was nearly twice that in women, and older patients

(over the age of 48 years) had a risk of developing MetS almost 4 times that of patients under the age of 35 years. As expected, BMI was significantly associated with the frequency of MetS; each 1-point increase in BMI elevated the risk of having MetS by 30%. By contrast, no significant association was found between tobacco use and MetS.

Univariate analysis showed that patients with a long duration of bipolar illness had a higher risk of having MetS; however, this relationship was no longer significant when all potential confounders were taken into account in the multivariate analysis. No association between MetS and bipolar subtype or number or type of episode was observed. The risk of having MetS was associated with the

Figure 1. Age-Specific Prevalence of Metabolic Syndrome<sup>a</sup> in Patients With Bipolar Disorder



<sup>a</sup>National Cholesterol Education Program Adult Treatment Panel III definition.

Table 2. Prevalence of Metabolic Syndrome Components in Patients With Bipolar Disorder, n (%)

	· · · /				
		Patients With			
	Total	Metabolic Syndrome	Men	Women	P
Component	(N = 654)	(n=122)	(n = 65)	(n = 57)	Value <sup>a</sup>
Hypertension <sup>b</sup>	209 (34.6)	87 (73.1)	48 (75.0)	39 (70.9)	.6158
Low HDL cholesterol <sup>c</sup> or treatment	197 (32.8)	87 (73.7)	50 (79.4)	37 (67.3)	.1365
Hypertriglyceridemia <sup>d</sup> or treatment	183 (28.9)	97 (80.2)	57 (89.1)	40 (70.2)	.0093
High fasting glucose <sup>e</sup> or treatment	95 (16.0)	54 (47.8)	28 (45.9)	26 (50.0)	.6628
Abdominal obesity	201 (35.5)	95 (81.2)	41 (67.2)	54 (96.4)	<.0001
Body mass index					
<21	87 (13.3)	0	0	0	.0475
21-25	220 (33.6)	17 (13.9)	8 (12.3)	9 (15.8)	
>25-30	250 (38.2)	55 (45.1)	36 (55.4)	19 (33.3)	
> 30	97 (14.8)	50 (41.0)	21 (32.3)	29 (50.9)	

<sup>&</sup>lt;sup>a</sup>Comparing the prevalence of metabolic component between men and women.

use of atypical antipsychotic medication (OR = 2.3; 95% CI, 1.2–3.5). By contrast, no significant associations were found between MetS and the use of first-generation antipsychotics, antidepressants, lithium, or mood stabilizers.

#### **Effective Treatment**

The percentages of patients with lipid disorders, hypertension, and diabetes receiving treatment for these conditions are presented in Figure 2.

We found that 21.6% of the patients with high blood pressure were on antihypertensive treatment. Similarly, only 27.9% and 10.6% of bipolar disorder patients with dyslipidemia and glycemia disorders, respectively, were treated for these conditions. The percentages of patients with MetS receiving treatment were only slightly higher. Older age was the only factor significantly (P=.03) associated with the likelihood of receiving treatment for these medical conditions. No influence of sex or type of referring doctor (general practitioner, or psychiatrist in private practice or working at a hospital) was found.

## **DISCUSSION**

This study is the first to show that MetS is common in French individuals with bipolar disorder, with a prevalence of 18.5%. The likelihood of MetS was independently related to age, sex, BMI, and atypical antipsychotic medication use. There was considerable undertreatment of the components of MetS in patients with bipolar disorder, with more than two-thirds of the affected patients not receiving effective treatment for these conditions at the time of inclusion.

The prevalence of MetS in French patients with bipolar disorder was slightly lower than that reported in other European countries but was nevertheless consistent with the rates generally reported in Europe.<sup>7,8</sup> Indeed, one recent meta-analysis showed the prevalence of MetS to be 32.4% in European studies of bipolar patients, based on published

values ranging from 19.2% to 40.0%.8 In the same meta-analysis, the prevalence of MetS in North American bipolar patients was estimated at 49.3%. These findings suggest that the prevalence of MetS in bipolar patients may differ considerably between countries, particularly between Europe and North America, with a possible influence of the baseline risk in the corresponding populations: lifestyle, physical exercise, diet, tobacco use, differences in medication regimens, differences in atypical antipsychotic use, differences in access to care and care organization, or environmental and genetic risk factors. The variation in findings may also reflect differences in study methodology or sample characteristics (notably age and diagnostic subgroup), place of recruitment, and sample size.

Studies usually report a prevalence of MetS 2 times higher in bipolar patients compared to the general population. We did not include a control group matched for sex and age, but we were

bDefined as systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 85 mm Hg or antihypertensive medication.

<sup>&</sup>lt;sup>c</sup>Defined as HDL cholesterol < 1.03 mmol/L in men and < 1.29 mmol/L in women.

<sup>&</sup>lt;sup>d</sup>Defined as  $\ge 1.7$  mmol/L.

eDefined as  $\geq$  5.6 mmol/L.

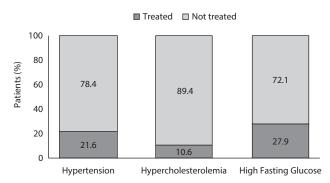
Abbreviation: HDL = high-density lipoprotein.

Table 3. Factors Associated With Metabolic Syndrome in a Cohort of Patients With Bipolar Disorder

	Metabolic	Syndrome <sup>a</sup>		OR (9	5% CI)
	No, n = 532 (81.3%)	Yes, n = 122 (18.7%)	$P^{\mathrm{b}}$	Univariate Analysis	Multivariate Analysis
Demographic factors, n (%)				•	·
Sex					
Male	220 (77.2)	65 (22.8)	.0116	1.6 (1.1-2.4)	1.9 (1.0-3.8)
Female	312 (84.6)	57 (15.5)		1 (ref)	1 (ref)
Age tertile					
<35 y	189 (35.7)	19 (15.6)	<.0001	1 (ref)	1 (ref)
35-48 y	178 (33.6)	35 (28.7)		2.0 (1.1-3.6)	1.6(0.7-3.6)
>48 y	163 (30.8)	68 (55.7)		4.2(2.9-7.2)	3.5 (1.5–7.8)
High school diploma or higher degree of education	395 (83.5)	87 (76.3)	.0720	0.6 (0.4–1.1)	0.8 (0.4–1.4)
Comorbidity					
Smoker (former or current), n (%)	300 (58.8)	77 (64.2)	.2827	1.2 (0.8-1.9)	1.1 (0.6-1.9)
Body mass index, mean (SD)	24.7 (4.2)	30.3 (5.4)	.0003	1.3 (1.2–1.3)	(****
Illness characteristics	. ,				
Bipolar subtype, n (%)					
Bipolar I	248 (80.1)	61 (19.9)	.5460	1 (ref)	
Bipolar II	207 (81.5)	47 (18.5)		0.9 (0.6–1.4)	
Bipolar NOS	80 (85.1)	14 (14.9)		0.7 (0.3–1.3)	
First mood episode, n (%)	· í	` '		, ,	
Depression	382 (82.2)	83 (17.9)	.7197	1 (ref)	
Manic	63(80.8)	15 (19.2)		1.1 (0.6-2.0)	
Mixed	15 (88.2)	2 (11.8)		0.6(0.1-2.7)	
Hypomanic	52 (77.6)	15 (22.4)		1.3 (0.7-2.5)	
Duration of illness tertile, n (%)					
<10 y	162 (32.0)	21 (18.1)	.0003	1 (ref)	1 (ref)
10-21 y	189 (37.3)	38 (32.8)		1.6 (0.9–2.8)	1.3 (0.6–2.8)
>21 y	156 (30.8)	57 (49.1)		2.8 (1.6–4.9)	2.0 (0.9-4.2)
No. of episodes, mean (SD)	7.2 (6.1)	7.6 (6.3)	.5351	1.0 (0.9-1.0)	
MADRS score, mean (SD)	8.5 (7.6)	9.7 (8.9)	.1779	1.0 (0.9–1.0)	1.0 (0.9–1.1)
YMRS score, mean (SD)	2.4 (3.6)	2.6 (3.7)	.6134	1.0(0.9-1.1)	
Rapid cycling, n (%)	63 (13.7)	19 (18.1)	.2445	1.4 (0.8–2.5)	
Medication, n (%)					
First-generation antipsychotic	90 (23.9)	22 (26.5)	.6218		
Atypical antipsychotic	113 (30.0)	34 (41.0)	.0538	1.6 (1.0-2.6)	2.3 (1.2-3.5)
Antidepressant medication	177 (43.3)	41 (46.1)	.6305	1.1 (0.7-1.8)	
Mood stabilizer	235 (57.5)	52 (58.4)	.8668	1.1(0.7-1.8)	
Lithium	123 (30.1)	28 (31.5)	.7964	1.1 (0.6-1.8)	
No. of antipsychotic treatments					
1	120 (83.9)	23 (16.1)	.0034	1 (ref)	
2–3	230 (85.2)	40 (14.8)		1.1 (0.6–1.9)	
≥4	59 (69.4)	26 (30.6)		2.5 (1.2–4.9)	

<sup>&</sup>lt;sup>a</sup>National Cholesterol Education Program Adult Treatment Panel III definition.

Figure 2. Prevalence of Treatment for Lipid Disorders, Hypertension, and Diabetes in Patients With These Conditions



able to compare the prevalence of MetS in bipolar patients with that reported in epidemiologic studies of the general population in France. Two large French population-based samples reported a prevalence of MetS of 7%–8.8% on the basis of the NCEP ATP III criteria, with values ranging from 6.1% to 6.6% in women and 9.7% to 10.2% in men, <sup>16,17</sup> and so our sample has an increased prevalence of MetS of at least the same magnitude reported to date.

The prevalence of MetS in our study was higher in men than in women. This result is consistent with published findings for a sample of Italian individuals with bipolar disorder<sup>18</sup> and a general population sample from several European countries.<sup>19</sup> However, differences between the sexes in terms of the prevalence of MetS in bipolar disorder patients remain a matter of debate, because a meta-analysis and a

 $<sup>^{\</sup>rm b}\chi^2$  test.

Abbreviations: MADRS = Montgomery-Asberg Depression Rating Scale, NOS = not otherwise specified, YMRS = Young Mania Rating Scale.

review of literature revealed no such pattern (although these studies did not control for age). To Pour results are consistent with the many studies reporting a linear increase in MetS prevalence with age. We found that, following stratification by sex, the risk of developing MetS after the age of 40 years was significantly higher in men than in women, whereas the risk seemed to be similar for the 2 sexes before this age. Our investigation of MetS components also showed a difference between men (higher frequency of dyslipidemia) and women (higher frequency of abdominal obesity). Such heterogeneity in the distribution of the various components of MetS has already been reported. In particular, the higher frequency of abdominal obesity in women than in men has been documented by a few clinical studies on bipolar disorder 20,21 and in a general population sample. 16,17

Some studies have shown that the monitoring of MetS components in patients with mental disorders remains inadequate,7,22 but most of these studies focused on schizophrenia patients,<sup>23</sup> and only a limited number of studies have highlighted the extent of undertreatment for cardiometabolic risk factors in patients with bipolar disorder. We found a considerable gap between optimal and effective treatment for patients with MetS components: 78.4% of individuals with hypertension, 89.4% of those with hypercholesterolemia, and 72.1% of those with hyperglycemia were not being treated at the time of entry into the study. Undertreatment of hypertension and diabetes in patients with bipolar disorder are the areas of greatest concern, because of the high rates of CVD-related mortality and morbidity in this population. These results highlight the need for vigorous efforts to manage cardiovascular risk factors in patients with psychiatric diseases.

Relationships between age, BMI, and MetS have repeatedly been reported in published studies.<sup>8,20</sup> We found no association between the presence of MetS and the use of mood stabilizers or antidepressants. However, we found that the use of atypical antipsychotic medication was associated with a higher risk of developing MetS. This finding is consistent with those of most other studies, 24,25 although some previous studies found no association, probably due to small sample size.20 Antipsychotic treatments, particularly those involving atypical antipsychotics, induce substantial weight gain and other metabolic side effects. <sup>26,27</sup> However, one study<sup>28</sup> of young individuals showed that medical disorders, such as obesity and cardiovascular risk factors, generally precede the diagnosis of bipolar disorder, suggesting that this process may be intrinsic to the disease, with antipsychotic treatment not entirely accounting for predisposition to MetS but instead conferring an additive risk for the development of MetS. Due to the nature of our study design (cross-sectional), power issues, and the impossibility of fully controlling for confounders, we decided not to investigate possible associations with individual antipsychotic drugs. However, we are aware that not all atypical antipsychotic drugs have the same impact on weight gain, and more detailed analyses will be performed when we have enough follow-up data.

Two other non–mutually exclusive hypotheses have been raised to explain the association between MetS and bipolar disorder. The first relates to lifestyle: individuals with bipolar disorder have been found to be more likely to consume an unhealthy diet, smoke, and have poor exercise habits than the general population, and this may contribute to the development of MetS.<sup>29</sup> The second hypothesis concerns the existence of common physiologic pathways. Bipolar disorders and MetS have a number of physiologic mechanisms in common, including endocrine disturbances, abnormalities of hypothalamic-pituitary-adrenal function, alterations to endothelium inflammatory reactions, and dysregulation of the sympathetic nervous system.<sup>30,31</sup>

This study had several limitations. Due to the cross-sectional nature of the study, we were unable to draw any firm conclusions concerning the causal nature of the associations observed. Longitudinal studies would be required for this purpose. Furthermore, our sample is probably not representative of all patients with bipolar disorder, particularly because institutionalized, hospitalized patients or outpatients with such severe symptoms that they would be unable to participate were not referred to the participating expert centers. However, we can assume that this would have led to an underestimate, rather than an overestimate, of the prevalence of MetS.

This study also has a number of strengths: the large number of patients with bipolar disorder included, use of reliable diagnostic criteria, and the inclusion of a large number of potential confounding factors in the multivariate analysis. This is, to our knowledge, the first study examining the prevalence and risk factors of MetS in a large French cohort of bipolar patients.

In conclusion, we found that the prevalence of MetS in French bipolar disorder patients was high, as in other countries, although the overall prevalence was lower than in other European countries, as already reported for the general population. 16,17 The high prevalence of cardiovascular risk factors and disease in patients with bipolar disorder is well known and documented, but risk factors often remain untreated in bipolar disorder patients. Regular monitoring of all of the features of MetS is the cornerstone of the early detection and management of this syndrome. The prevention and treatment of cardiovascular diseases in patients with bipolar disorder should help decrease mortality in this population and might also improve quality of life and the course of bipolar disorder. In everyday practice, the modern notion of personalized psychiatry is becoming more widespread. In this approach, the various components of MetS should be assessed systematically, and attempts to improve the patient's lifestyle should be made, through diet, physical exercise, or decreased tobacco consumption. In addition, the psychotropic drug used to treat bipolar disorder should be chosen with care, taking into account the impact of the various drugs on weight gain. These findings also highlight the need for integrated care, with more interaction and coordination between psychiatrists and primary care providers.10

Furthermore, longitudinal studies are also required to determine the causality of the association between risk factors and MetS, particularly for antipsychotic treatment; the course of MetS in bipolar patients; and its impact on the course of the disease.

Drug names: lithium (Lithobid and others).

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside US Food and Drug Administration—approved labeling has been presented in this article.

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# **POSTTEST**

To obtain credit, go to PSYCHIATRIST.COM (Keyword: October) to take this Posttest and complete the Evaluation.

- In this sample of patients with bipolar disorder, each of the following components of metabolic syndrome was found in one-third or more of the total group of patients except:
  - a. Hypertension
  - b. Low high-density lipoprotein (HDL) cholesterol (or treatment for it)
  - c. High fasting glucose (or treatment for it)
  - d. Abdominal obesity
- 2. The prevalence of metabolic syndrome in this sample of patients with bipolar disorder \_\_\_\_\_.
  - a. Was constant across age groups for both sexes
  - b. Increased in men with age but was constant across age groups in women
  - c. Was lower in men than in women after age 50 years
  - d. Was higher in both sexes after age 40 years

- 3. Ms A, who is 35 years old, and Mr B, who is 55 years old, both have bipolar disorder and are being treated with atypical antipsychotics. Which one has greater risk for metabolic syndrome?
  - a. Ms A
  - b. Mr B
  - c. Their risk is the same
- 4. Which of the above patients should be regularly monitored for the components of metabolic syndrome, with coordinated primary care and mental health care provided if abnormalities are found?
  - a. Ms A only
  - b. Mr B only
  - c. Both Ms A and Mr B
  - d. Neither patient needs monitoring