The Level of Cardiovascular Risk Factors in Bipolar Disorder Equals That of Schizophrenia: A Comparative Study

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Objective: In schizophrenia, increased rates of somatic mortality have been shown to correspond with a high prevalence of cardiovascular risk factors, including smoking and the metabolic syndrome. In bipolar disorder, the amount of cardiovascular risk is still largely unknown. This study compares the prevalence of smoking and metabolic disturbances in bipolar disorder and schizophrenia in a representative sample of patients under naturalistic conditions. It also compares the prevalence of risk factors in each diagnostic group with the general population.

Method: Longitudinal data on clinical groups from October 2002 through December 2005 were from the Oslo TOP Study (DSM-IV bipolar disorder [N = 110] and schizophrenia [N = 163]). Reference data were from the 2000 to 2001 Oslo Health Study (18,770 individuals of the same area). Background variables, prevalence of smoking, and age-adjusted levels of metabolic risk factors were compared between diagnostic groups. Risk factors in both groups were then compared with the general population.

Results: Patients with bipolar disorder had higher levels of education, better social functioning, fewer psychiatric symptoms, and less use of medication than patients with schizophrenia. There was no significant difference between diagnostic groups in the prevalence of smoking, obesity, metabolic syndrome, or diabetes. The mean level of high density lipoprotein cholesterol was lower in schizophrenia ($p < .001$), and systolic blood pressure was higher in bipolar disorder ($p < .05$). Both diagnostic groups had a prevalence of cardiovascular risk factors about twice that of the general population.

Conclusion: The prevalence of cardiovascular risk factors was alarmingly high for bipolar disorder and schizophrenia patients compared with the general population, and the prevalence was approximately the same in both diagnostic groups.

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Patients with severe mental disorders have a mortality rate from somatic causes approximately twice that of the general population, with cardiovascular disease (CVD) being responsible for the largest total number of excess deaths in both schizophrenia and bipolar disorder.[1–4] In correspondence with these figures, recent studies[5–8] have found a substantially higher prevalence of metabolic disturbances in schizophrenia patients compared with the general population. The reason for this disparity is unknown, but it may be related to genetic predisposition, as well as to disease-specific stress, lifestyle factors, and adverse effects of psychopharmacologic treatment.[9–11]

Much less attention has been paid to the existence of CVD risk factors in bipolar disorder, and new advances in this field have been called for.[12] Only a few studies have been published on the prevalence of separate risk variables, such as obesity,[13–15] diabetes mellitus,[16] hypertension,[17] and the metabolic syndrome,[18,19] in this population. In several of these studies, samples were selected from specialized clinics, including mainly treatment-compliant patients, and often excluding those with psychiatric or somatic comorbidity. Only 2 studies made use

of a proper reference group,[13,17] and we have been unable to identify previous clinical studies comparing the CVD risk prevalence in bipolar disorder with other psychiatric conditions.

There is considerable debate among experts regarding the etiology, definition, and overall utility of the metabolic syndrome (MetS) in predicting CVD.[20–22] However, the concept has been widely applied in clinical practice, as it is simple and low cost and helps identify high risk individuals at an early stage, when prevention may still be possible. In the present study, we have chosen to base our investigation on the existence of MetS components (including obesity, hypertension, hyperglycemia, and dyslipidemia), all of which are well-established risk factors in themselves. The aim of the present study was to compare the levels of such risk factors, as well as smoking, in bipolar versus schizophrenia subjects from the same cohort of pharmacologically stable outpatients under real-life conditions. Furthermore, we wanted to compare the prevalence of risk factors in the 2 diagnostic groups with the general population of Oslo.

The Norwegian health care system is catchment area–based, publicly funded, and the only provider of psychiatric services. Patients are referred from primary care. Thus, in the present study, we had access to a representative sample of patients within different diagnostic categories. This report presents data on 273 patients with diagnoses of schizophrenia and bipolar disorder included in the Oslo TOP (Thematic Organized Psychoses Research) Study from 2002 through 2005.[23] We have used reference data from the general population of the same geographic and sociocultural area, collected through the 2000/2001 Oslo Health Study.[24]

Patients with bipolar disorder are generally less impaired, clinically, cognitively, and socially, than patients with schizophrenia and would therefore be considered more capable of taking care of their physical health. Furthermore, antipsychotics known to induce weight gain are less widely used in bipolar disorder than in schizophrenia. These circumstances should favor a more beneficial CVD risk profile in people with bipolar disorder. Thus, our hypothesis is as follows: Patients with schizophrenia will have the largest increase in CVD risk, and patients with bipolar disorder a more moderate increase in risk compared with the general population.

METHOD

The Oslo TOP Study

The TOP Study is an ongoing study that is being carried out by the University and University Hospitals of Oslo, Norway. Patients with severe mental disorders from all health care sectors of Oslo are included. Inclusion criteria are broad, consisting of (1) being registered in the psychiatric services of any 1 of the 4 University Hospitals in Oslo, (2) being 18 to 65 years, (3) meeting DSM-IV criteria for schizophrenia or bipolar disorder, and (4) being willing and able to give written, informed consent of participation.

From the onset of the study in October 2002 through December 2005, a total of 273 patients with diagnoses of bipolar disorder (N = 110) or schizophrenia (N = 163) were included. The bipolar disorder group consisted of patients with bipolar disorder I (N = 62), bipolar disorder II (N = 43), and bipolar disorder not otherwise specified (N = 5). The schizophrenia group consisted of patients with schizophrenia (N = 123), schizophreniform (N = 8), and schizoaffective disorder (N = 32).

All patients were assessed by a group of trained psychiatrists and clinical psychologists. Clinical interviews were performed, with additional information collected from treatment records to determine demographic factors, psychiatric history, medical history, and current use of psychotropic medication, tobacco, alcohol, and illicit drugs. The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)[25] was used, and psychosocial functioning was measured by the Global Assessment of Functioning Scale (GAF, split version).[26] Psychiatric symptom ratings were done using the Positive and Negative Syndrome Scale (PANSS)[27] and the Inventory of Depressive Symptomatology (IDS).[28] Interrater reliability was good, with overall $\kappa = 0.77$ (95% CI = 0.60 to 0.94) for diagnoses and intraclass correlation coefficient = 0.86, df = 1.1, for both symptom and function GAF scores.

Physical examinations were performed immediately after the clinical interview. Blood pressure was measured manually with the patient in a sitting position after resting. Body mass index (BMI: weight in kg/height in m^2) was calculated by asking patients about their height and weighing them on electronic scales with the patients wearing light clothing and no shoes. Waist circumference was measured midway between the lower rib and the iliac crest in the upright position using a nonelastic tape. Blood samples were drawn after an overnight fast of at least 8 hours and analyzed for levels of plasma glucose, high density lipoprotein cholesterol (HDL-C), and triglycerides. All serum analyses were performed at the Department of Clinical Chemistry, Ulleval University Hospital, Oslo, Norway, on an Integra 800 (Roche Diagnostics, Basel, Switzerland), using standard methods.

The 2000 to 2001 Oslo Health Study

The population-based Oslo Health Study was conducted in Oslo from May 2000 to September 2001 by the Norwegian Institute of Public Health in joint collaboration with the Oslo City Council and the University of Oslo. More details about this study can be obtained from the Norwegian Institute of Public Health.[29]

All citizens aged 30, 40, 45, 59 to 60, and 75 to 76 years were invited to attend the screening station located

Table 1. Demographic and Clinical Characteristics of Oslo TOP Study Sample

Characteristics	All Patients		Male		Female	
	Schizophrenia (N = 163)	Bipolar Disorder (N = 110)	Schizophrenia (N = 94)	Bipolar Disorder (N = 43)	Schizophrenia (N = 69)	Bipolar Disorder (N = 67)
Male, % (N)	57.7 (94)	39.1 (43)				
White, % (N)	77.3 (126)	92.7 (102)**	73.4 (69)	95.3 (41)**	82.6 (57)	91.0 (61)
Outpatients, % (N)[a]	76.3 (122)	96.3 (105)***	77.2 (71)	95.3 (41)**	75.0 (51)	97.0 (64)***
Employed, % (N)	19.6 (32)	55.5 (61)***	19.1 (18)	58.1 (25)***	20.3 (14)	53.7 (36)***
Married or cohabiting, % (N)	16.6 (27)	32.7 (36)**	12.8 (12)	32.6 (14)**	21.7 (15)	32.8 (22)
Substance abuse, % (N)	16.0 (26)	19.1 (21)	14.9 (14)	25.6 (11)	17.4 (12)	14.9 (10)
Age, mean (SD), y	33.6 (10.3)	38.7 (11.9)***	33.2 (9.4)	39.4 (12.2)**	34.1 (11.5)	38.3 (11.9)*
Education, mean (SD), y	12.5 (2.6)	14.9 (3.0)***	12.6 (2.7)	14.9 (3.0)***	12.5 (2.5)	14.9 (3.1)***
In treatment, mean (SD), y	7.1 (8.8)	8.8 (10.0)	6.2 (7.8)	8.7 (9.8)	8.3 (9.8)	8.8 (10.2)
GAF symptom, mean (SD)	41.3 (11.4)	59.8 (10.3)***	41.7 (11.5)	59.0 (9.4)***	40.7 (11.2)	60.3 (10.8)***
GAF function, mean (SD)	42.7 (10.9)	57.7 (11.4)***	42.8 (10.4)	56.9 (10.8)***	42.5 (11.6)	58.2 (11.8)***
IDS, total mean (SD)	18.7 (12.9)	15.7 (11.3)	18.1 (12.8)	13.6 (9.3)	19.7 (13.0)	17.0 (12.3)
PANSS, total mean (SD)	64.2 (17.6)	45.7 (9.8)***	64.0 (17.4)	45.7 (8.5)***	64.4 (17.9)	45.6 (10.6)***

[a]Four missing values in this variable (total N = 269).
*p Value < .05.
**p Value < .01.
***p Value < .001.
Abbreviations: GAF = Global Assessment of Functioning, IDS = Inventory of Depressive Symptomatology, PANSS = Positive and Negative Syndrome Scale, TOP = Thematic Organized Psychoses Research.

in the city center. A total of 18,770 individuals participated in the survey. To match the age span of the TOP Study, only individuals in the age group of 30 to 60 years were included as reference group in the present study, 6879 men and 8307 women.

Information on age, gender, country of birth, and marital status was recorded from Statistics Norway (Oslo, Norway). All other information on demographic and health issue data was collected from questionnaires filled out by the participants. At the time of screening, a clinical examination was conducted according to a standard protocol. All participants were measured and weighed on electronic scales. Blood pressure was taken using an automatic device (DINAMAP, Critikon, Tampa, Fla.). Nonfasting venous blood samples were analyzed for HDL-C by the same method and in the same laboratory as in the TOP Study. We have previously shown that there were no major differences in sociodemographic variables between the Oslo Health Study population and the first 205 patients included in the TOP study sample, except for marital status.[23] For the purpose of this study, only data on age, gender, and somatic variables were considered. Both the Oslo Health Study and the TOP Study were approved by the Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate. In both studies, all subjects gave informed, written consent of participation after complete description of the study was given to them.

Metabolic Syndrome: Definition

Several working definitions of the MetS are currently being employed. In this report we based our analyses on the definition proposed by the National Cholesterol Education Program, Adult Treatment Panel III in 2003.[30] For establishing the diagnosis of MetS, at least 3 out of 5 criteria must be present. Cutoff values for the individual variables are (1) fasting plasma glucose ≥ 5.6 mmol/L (100 mg/dL) or taking hypoglycemic medication, (2) triglycerides ≥ 1.7 mmol/L (150 mg/dL), (3) HDL-C < 1.0 mmol/L (40 mg/dL) (men) and < 1.3 mmol/L (50 mg/dL) (women), (4) systolic blood pressure ≥ 130 mm Hg and/or diastolic blood pressure ≥ 85 mm Hg or taking antihypertensive medication, and (5) central obesity with waist > 102 cm (40 in) (men) and > 88 cm (35 in) (women). The present study had waist measurements for a limited number of patients, and we therefore used a slightly modified version of the ATP III definition, based upon BMI ≥ 30 as an alternative measure of central obesity.

Statistical Procedures

All statistical analyses were performed using the SPSS software package for Windows, version 12.01 (SPSS, Inc., Chicago, Ill.). Demographic, clinical, and risk variables are presented as mean (SD) values or proportions. In the comparisons between patients with schizophrenia and bipolar disorder, we used Student t tests for continuous variables and χ^2 tests for dichotomous variables. Univariate analysis of covariance was used to adjust for age differences between diagnostic groups within the TOP Study sample and between the TOP and the Oslo Health Study cohorts. Two-sided tests were used, and the significance level was set to p = .05.

RESULTS

Background Variables in the Oslo TOP Study Sample

Demographic and clinical characteristics of patients within the TOP Study are summarized in Table 1. There

Table 2. Psychotropic Drug Use of Oslo TOP Study Sample, % (N)

	All Patients		Male		Female	
Medication	Schizophrenia (N = 163)	Bipolar Disorder (N = 110)	Schizophrenia (N = 94)	Bipolar Disorder (N = 43)	Schizophrenia (N = 69)	Bipolar Disorder (N = 67)
Minimum 1 antipsychotic	92.0 (150)	45.5 (50)	91.5 (86)	53.5 (23)	92.8 (64)	40.3 (27)
Minimum 2 antipsychotic	29.4 (48)	6.4 (7)	26.6 (25)	9.3 (4)	33.3 (23)	4.5 (3)
Weight-inducing antipsychotic	50.3 (82)	26.4 (29)	51.1 (48)	37.2 (16)	49.3 (34)	19.4 (13)
Lithium	1.2 (2)	20.0 (22)	1.1 (1)	16.3 (7)	1.4 (1)	22.4 (15)
Minimum 1 antiepileptic	23.9 (39)	46.4 (51)	25.5 (24)	51.2 (22)	21.7 (15)	43.3 (29)
Weight-inducing antiepileptic	5.5 (9)	14.5 (16)	5.3 (5)	27.9 (12)	5.8 (4)	6.0 (4)
Minimum 1 antidepressant	35.0 (57)	42.7 (47)	35.1 (33)	37.2 (16)	34.8 (24)	46.3 (31)
Weight-inducing antidepressant	9.3 (15)	20.9 (23)	11.8 (11)	18.6 (8)	5.8 (4)	22.4 (15)
No weight-inducing drug	7.4 (12)	30.9 (34)	7.4 (7)	20.9 (9)	7.2 (5)	37.3 (25)

Abbreviation: TOP = Thematic Organized Psychoses Research.

were more men (58%) in the schizophrenia group and more women (61%) in the bipolar disorder group. Schizophrenia patients were significantly younger than bipolar patients, with a mean (SD) age of 33.6 (10.3) years versus 38.7 (11.9) years ($p < .001$). Patients with bipolar disorder were more often whites of Norwegian origin. They had higher levels of education and were more likely to be outpatients, to be full- or part-time employed, and to be living in stable relationships. GAF scores were considerably higher and PANSS scores were lower in the bipolar than in the schizophrenia group, indicating a higher level of psychosocial functioning and a lower level of psychotic as well as general psychiatric symptoms. There were no significant intergroup differences in duration of treatment, level of depressive symptoms, or prevalence of substance-abuse disorders.

Table 2 shows the current use of psychotropic medication in the 2 clinical groups. Patients with schizophrenia were more often taking antipsychotic medication and on combination therapy with more than 1 antipsychotic. In particular, they were more often taking either olanzapine or clozapine, both of which are known to induce weight gain and other metabolic disturbances.[11] Patients with bipolar disorder were more often taking lithium and taking antiepileptic mood stabilizers. In particular, they were more often taking either valproic acid or carbamazepine, also known to induce weight gain but to a lesser degree than olanzapine and clozapine.[19,31] In addition, bipolar patients were more often taking weight gain–inducing antidepressants such as venlafaxine, mirtazapine, and mianserine. On the other hand, far more patients with bipolar disorder than with schizophrenia were either drug free or received no medication known to be obesogenic.

CVD Risk Factors in the Oslo TOP Study Sample

Table 3 shows CVD risk parameters measured in patients with schizophrenia and bipolar disorder. All metabolic variables are known to be age dependent and were adjusted for age. In general, risk factor levels were similar in the 2 groups of patients. The only significant differences found between diagnostic groups were lower levels of HDL-C in women with schizophrenia, and higher systolic blood pressure in patients with bipolar disorder.

CVD Risk Factors as Compared With the General Population

Table 4 shows prevalence of CVD risk factors in schizophrenia and bipolar patients compared with the general population. The mean (SD) age of the Oslo Health Study sample, 44.1 (11.3) years, was considerably higher than of the TOP sample, 35.7 (11.2) years ($p < .001$). Thus, all metabolic variables were adjusted for age. Daily smoking was significantly more frequent in both schizophrenia and bipolar patients than in the general population. In addition, both clinical groups had significantly more patients that were overweight (BMI ≥ 25), obese (BMI ≥ 30), centrally obese, and hypertensive than the reference population.

Only 2 variables showed a marked difference in prevalence between the bipolar and the schizophrenia group in the TOP Study as compared with the Oslo Health Study sample. Low HDL-C was statistically more prevalent only in schizophrenia patients, and diabetes was more prevalent only in bipolar patients. However, for diabetes the total numbers were small, with only 5/103 bipolar patients having diabetes, all of whom were women.

DISCUSSION

The main finding of the present study was nearly identical levels of CVD risk factors in people with schizophrenia and those with bipolar disorder. Risk factors in both clinical groups were nearly twice as prevalent as in the general population. The only exception was HDL-C, being significantly lower in schizophrenia subjects than in both bipolar subjects and in the control group. This may be an effect of antipsychotic use, but further investigation on the topic is clearly needed.

Several studies[5–8] have documented a largely increased cardiovascular risk in patients with schizophrenia, which is consistent with our results. In addition, our findings are in line with previous studies concerning high rates of

Table 3. Cardiovascular Risk Factors of Oslo TOP Study Sample[a]

	All Patients		Male		Female	
Variable	Schizophrenia (N = 163)	Bipolar Disorder (N = 110)	Schizophrenia (N = 94)	Bipolar Disorder (N = 43)	Schizophrenia (N = 69)	Bipolar Disorder (N = 67)
Daily smoking, % (N)	54.9 (89/162)	50.0 (55/110)	57.0 (53/93)	60.5 (26/43)	52.2 (36/69)	43.3 (29/67)
Obesity (BMI ≥ 30),[b] % (N)	21.7 (32/151)	22.6 (25/107)	22.1 (19/89)	15.0 (7/42)	21.3 (13/62)	27.4 (18/65)
Metabolic syndrome, % (N)	29.7 (41/147)	21.5 (25/104)	35.6 (29/86)	24.1 (12/43)	21.3 (12/61)	19.7 (13/61)
Diabetes mellitus, % (N)	1.7 (3/153)	5.2 (5/103)	1.1 (1/88)	0	2.8 (2/65)	8.6 (5/61)
BMI,[b] mean (SD)	26.4 (4.8)	26.3 (5.0)	27.0 (4.4)	26.2 (3.6)	25.7 (5.1)	26.3 (5.8)
Waist, mean (SD), cm	92.6 (12.4)	93.4 (19.0)	96.2 (10.6)	101.5 (5.0)	85.0 (12.7)	93.0 (20.5)
Systolic blood pressure, mean (SD), mm Hg	122.6 (14.6)	126.9 (18.7)*	124.4 (13.8)	133.4 (18.9)*	116.3 (14.6)	126.0 (18.2)*
Diastolic blood pressure, mean (SD), mm Hg	80.7 (11.2)	81.7 (10.9)	81.8 (10.9)	86.1 (11.5)	76.9 (11.1)	80.9 (10.0)
Trigycerides, mean (SD), mmol/L	1.78 (1.28)	1.49 (1.4)	1.97 (1.41)	1.67 (0.97)	1.51 (1.02)	1.37 (1.62)
HDL-C, mean (SD), mmol/L	1.27 (0.38)	1.47 (0.45)***	1.14 (0.31)	1.20 (0.28)	1.45 (0.39)	1.66 (0.46)**
Fasting glucose, mean (SD), mmol/L	5.3 (1.2)	5.3 (1.3)	5.3 (1.3)	5.3 (0.7)	5.1 (1.1)	5.3 (1.6)

[a]Except for smoking, data are adjusted for age differences between groups. Percents are adjusted for age and may therefore not correspond to total numbers given in parentheses.
[b]Weight in kg/height in m^2.
*p Value < .05.
**p Value < .01.
***p Value < .001.
Abbreviations: BMI = body mass index, HDL-C = high density lipoprotein cholesterol, TOP = Thematic Organized Psychoses Research.

Table 4. Cardiovascular Risk Factors of Oslo Health Study Sample Versus Oslo TOP Study Sample, % (N)[a]

	Oslo Health Study	TOP Schizophrenia			TOP Bipolar Disorder		
Variable	(N = 15,186)	N = 163	Statistic	p Value	N = 110	Statistic	p Value
Daily smoking	27.7 (4157)	54.9 (89/162)	$\chi^2 = 58.731$	< .001	50.0 (55/110)	$\chi^2 = 26.877$	< .001
Overweight (BMI ≥ 25)[b]	52.0 (7866)	67.0 (90/151)	F = 13.713	< .001	62.6 (63/107)	F = 4.875	.027
Obesity (BMI ≥ 30)[b]	14.1 (2085)	24.3 (32/151)	F = 12.735	< .001	24.9 (25/107)	F = 10.297	.001
Central obesity[c]	16.0 (2354)	39.9 (11/31)	F = 13.180	< .001	54.2 (7/13)	F = 14.227	< .001
Hypertension (blood pressure)[d]	43.0 (6356)	60.6 (62/140)	F = 19.602	< .001	60.8 (57/107)	F = 15.183	< .001
Low HDL-C[e]	21.4 (3158)	41.3 (67/156)	F = 35.959	< .001	23.2 (25/104)	F = 0.199	.655
Diabetes mellitus[f]	2.2 (332)	3.3 (3/153)	F = 0.737	.391	5.5 (5/103)	F = 4.925	.026

[a]All data except smoking are adjusted for age-differences between the Oslo Health Study and TOP study sample. Percents are adjusted for age and may therefore not correspond to total numbers given in parentheses.
[b]Weight in kg/height in m^2.
[c]Waist > 102 cm (males), > 88 cm (females).
[d]Systolic blood pressure ≥ 130 mm Hg and/or diastolic blood pressure ≥ 85 mm Hg or taking antihypertensive.
[e]< 1.0 mmol/L (males), < 1.3 mmol/L (females).
[f]Taking antidiabetic medication.
Abbreviations: BMI = body mass index, HDL-C = high density lipoprotein cholesterol, TOP = Thematic Organized Psychoses Research.

obesity,[13–15] diabetes,[16] hypertension,[17] and the MetS[18,19] in bipolar patients. However, to our knowledge, the present study is the first to report on a direct comparison of CVD risk in the 2 diagnostic groups and the first to report on the accumulation of CVD risk factors in bipolar disorder as compared with the general population.

Population studies[32,33] have shown that white ethnicity as well as higher educational and socioeconomic levels are positive indications of a healthy lifestyle and a low prevalence of CVD risk. However, in our sample, the high levels of CVD risk parameters in bipolar individuals could not be explained by racial or sociocultural factors, as a larger proportion of the bipolar than of the schizophrenia group were white, Norwegian-born citizens and had higher levels of education and psychosocial functioning.

Moreover, the findings seem not to be explained by the load of actual psychotropic medication in the 2 clinical groups, one exception being low HDL-C in schizophrenia. Substantially more bipolar patients in our sample received no drugs known to induce metabolic disturbances. At the same time, more schizophrenia patients were prescribed antipsychotics, in particular olanzapine or clozapine, which are known to cause weight gain, diabetes, and dyslipidemia.[11] This incongruity indicates that other factors besides medication should be sought to explain the clustering of CVD risk in bipolar disorder. Interestingly, the co-occurrence of bipolar disorder with metabolic dis-

turbances was observed long before the advent of current medication.[34]

Population studies have shown obesity to be associated with depression, anxiety disorders, and binge eating and negatively associated with substance abuse.[35] In our sample, we had no information on anxiety or eating disorders. However, prevalence of substance abuse was virtually the same in the diagnostic groups, and schizophrenia patients had higher levels of current depressive symptoms. In addition, no correlation was found between BMI and number of previous depressive, manic, or psychotic episodes in either group. Thus, it seems that higher levels of comorbid disorders in bipolar individuals could not explain the surprising number of obesity-related risk factors among them. However, a positive correlation between BMI and duration of treatment was found in both schizophrenia and bipolar disorder.

The etiology of the clustering of CVD risk factors found in patients with bipolar disorder is probably multifactorial and might be explained at different levels.[36] There may be some underlying genetic vulnerability linking metabolic and emotional disturbances in bipolar disorder. However, we were unable to identify previous studies on unmedicated, first-episode patients. In our sample, many of the patients with current overweight or obesity told the raters they were slim until their first mood disorder episode, when, "all of a sudden," they gained a lot of weight. One possible mechanism could be that the large amount of disease-specific stress, through elevated levels of cortisol, would alter metabolism. In addition, psychological factors could have influenced behavior, leading to overeating and physical inactivity. As in other psychiatric conditions, the load of psychotropic drugs received by the patients prior to our investigation would then probably have contributed to this negative development. There is, however, accumulating evidence that feeding is not just a matter of metabolic homeostasis but of emotional regulation.[37] One could speculate that the emotional dysregulation in bipolar disorder would specifically interfere with hunger and feeding mechanisms, leading to obesity and metabolic disturbances in these patients.

The present study had some limitations, one being the lack of data on patients' previous psychotropic medication. Another weakness was the lack of available waist measurements for the majority of the patients, which left us with BMI ≥ 30 as the sole measure of obesity. When calculating the prevalence of MetS in our clinical groups, we thereby probably underestimated this prevalence compared with other studies,[5–8,18,19] particularly in women.[38] Furthermore, we did not have sufficient data in the reference group to make any direct comparison of the prevalence of MetS between the general population and patients. However, this was not the principal aim of the study.

In conclusion, the major finding in our study was that the level of CVD risk factors in bipolar disorder equals that of schizophrenia and that both clinical groups have estimated risks considerably higher than the general population. There is clearly a need for further research on the association between mood disorders and metabolic disturbances, preferably prospective studies with CVD end points in first-episode patients. Until these data are available, we suggest that clinicians should be more aware of somatic health issues in bipolar disorder. Patients with bipolar disorder, as well as patients with schizophrenia, must be regarded as at high risk for type 2 diabetes and CVD.

Drug names: carbamazepine (Carbatrol, Equetro, and others), clozapine (FazaClo, Clozaril, and others), lithium (Eskalith, Lithobid, and others), mirtazapine (Remeron and others), olanzapine (Zyprexa), valproic acid (Depakene, Myproic Acid, and others), venlafaxine (Effexor and others).

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