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Prevalence of diabetes and the metabolic syndrome in a sample of patients with bipolar disorder*

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Abstract

Objectives: The presence of metabolic abnormalities is an important risk factor for cardiovascular disease and diabetes. There are limited data on the prevalence of the metabolic abnormalities in disorders other than schizophrenia in which antipsychotic medication is part of routine treatment.

Methods: Sixty consecutive patients with bipolar disorder (BD) at our university psychiatric hospital and affiliate services were entered in an extensive prospective metabolic study including an oral glucose tolerance test. The prevalence of the metabolic syndrome was assessed based on the National Cholesterol Education Program Adult Treatment Protocol (ATP-III) criteria, the adapted ATP-III criteria using a fasting glucose threshold of 100 mg/dL, and the recently proposed criteria from the International Diabetes Federation (IDF).

Results: The analysis of 60 patients showed a prevalence of the metabolic syndrome of 16.7% (ATP-III), 18.3% (adapted ATP-III) and 30.0%) (IDF), respectively. A total of 6.7% of the patients met criteria for diabetes and 23.3% for pre-diabetic abnormalities.

Conclusions: The metabolic syndrome and glucose abnormalities are highly prevalent among patients with BD. They represent an important risk for cardiovascular and metabolic disorders. Assessment of the presence and monitoring of metabolic abnormalities and its associated risks should be part of the clinical management of patients with BD.

Key words: bipolar disorder - diabetes -metabolic syndrome - physical health

Since the introduction of second-generation antipsychotics and their association with metabolic abnormalities, there has been a rise of interest in the occurrence of metabolic abnormalities in patients treated with these drugs, although the main focus of research was on patients diagnosed with schizophrenia (1-3). The issue of abnormalities in glucose metabolism has received most attention (1, 4-9).

Next to diabetes, there has been a surge of interest into other medical conditions such as cardiovascular morbidity, abnormal lipid metabolism and obesity that also have a serious impact on the physical health. In patients with schizophrenia, recent research has demonstrated a prevalence of 40-50% of the metabolic syndrome, which comprises abnormalities in glucose metabolism, lipid metabolism, obesity and blood pressure (10-12).

In contrast to patients diagnosed with schizophrenia, research on metabolic abnormalities in patients with bipolar disorder (BD) has been relatively scarce. Three retrospective chart reviews of patients with BD (13-15), one of which also investigated diabetes prevalence in patients with schizoaffective disorder and schizophrenia (15),

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found evidence for an increased prevalence of diabetes in these patients when compared to the general population. It has been previously shown, however, that a large proportion of diabetes cases remain undetected when patients are not actively screened for these abnormalities (16-19), which implies that the actual prevalence of diabetes in patients with BD could even be higher than the rates reported in these studies.

With respect to the metabolic syndrome, a study by Fagiolini et al. (20) evaluated the prevalence of the metabolic syndrome in 171 patients with BD, and found a prevalence of 30%, using National Cholesterol Education Program Adult Treatment Protocol (ATP-III) criteria. Furthermore, there is convincing evidence for an increased prevalence of obesity in bipolar patients (21-24), and possibly also for different dietary habits, with bipolar patients consuming more sugars and carbohydrates than controls (25). These data clearly show the relevance of investigating metabolic abnormalities in patients with BD.

To our knowledge, no study has specifically addressed the prevalence of metabolic abnormalities in bipolar patients with a comprehensive metabolic screening using an oral glucose tolerance test. The aim of the current study was to investigate the prevalence of metabolic abnormalities and the metabolic syndrome in a sample of 60 patients with BD.

Methods

At the University Psychiatric Center Katholieke Universiteit Leuven in Kortenberg (Belgium) and its affiliate services, according to international guidelines, patients treated with antipsychotic medication are being asked to participate in an extensive screening and prospective follow-up study of metabolic parameters. The vast majority of patients treated with antipsychotic medication and in follow up in our hospital or its affiliate services are part of this extensive metabolic study, which was started in November 2003. This screening program was described extensively elsewhere (12, 18, 26-28). In short, the study population is a dynamic, naturalistic cohort. Referral by the treating psychiatrist for metabolic screening and monitoring is a clinical routine in our hospital and its affiliate services, certainly for hospitalized patients and to a lesser extent for ambulatory patients. Although no systematic data are being recorded on patients who refuse this monitoring, the clinical experience learns that very few patients do so. Decisions regarding medication, including dose reduction, dose augmentation, and switch strategies, are made by the treating psychiatrist together with the patient. These changes are recorded and patients are monitored by means of laboratory tests, oral glucose tolerance tests (OGTT) and clinical examinations. The baseline characteristics of the first 430 patients with schizophrenia or schizoaffective disorder of this cohort were previously reported (12). The current study describes the baseline characteristics of the first 60 patients with BD. As the diagnosis is a clinical diagnosis recorded by the treating psychiatrist, and no structured diagnostic interview was done, it was not possible to distinguish bipolar I and bipolar II patients.

At baseline, patients received a full fasting laboratory screening, clinical measurements and an electrocardiogram. A 75-g glucose load OGTT was performed on all patients. Patients were initiated on an overnight fast and were monitored during the OGTT. All laboratory analyses were performed in the same laboratory.

The presence of the metabolic syndrome was assessed using ATP-III criteria, the adapted ATP-III criteria (fasting glucose criterion of $\geq$ 100 instead of $\geq$ 110 mg/dL, plus including treatment for hypertension, -lipidemia and -glycemia as criteria) and the recently proposed International Diabetes Federation (IDF) criteria (for overview, see Table 1) (29-31). For the diagnosis of diabetes and pre-diabetic abnormalities, we used the criteria of the American Diabetes Association (ADA) [impaired fasting glucose (IFG): fasting glucose 100-125 mg/dL and impaired glucose tolerance (IGT), glucose 140-199 mg/dL at 2h in the OGTT] (32). Patients did not have a diagnosis of diabetes prior to the baseline metabolic screening.

Descriptive statistics were computed for the basic demographic and clinical variables as well as for the variables relevant for the evaluation of metabolic abnormalities. The influence of the presence/absence of the metabolic syndrome and the presence/absence of glucose abnormalities on continuous variables was assessed by means of an independent samples *t*-est. The association between categorical variables was evaluated by a chi-square test. The study was approved by an ethical committee and all patients gave written informed consent.

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Table 1*. The prevalence of glucose abnormalities depending on the absence ('No') or presence ('Yes') of the metabolic syndrome according to the different definitions*

	Normal values % (n)	**Prediabetes % (n)**	**Diabetes % (n)**	**Total % (n)**	**p[a]**
ATP-III					< 0.001
No	78 (39)	20 (10)	2(1)	83.3 (50)	
Yes	30 (3)	40 (4)	30 (3)	16.7 (10)	
Adapted ATP-III					< 0.001
No	79.6 (39)	18.4 (9)	2(1)	81.7 (49)	
Yes	27.3 (3)	45.4 (5)	27.3 (3)	18.3 (11)	
IDF					< 0.001
No	83.3 (35)	16.7(7)	0(0)	70 (42)	
Yes	38.9 (7)	38.9 (7)	22.2 (4)	30 (18)	
Total	70 (42)	23.3 (14)	6.7 (4)		

ATP-III = National Cholesterol Education Program Adult Treatment Protocol; IDF = International Diabetes Federation. [a]Analysis of variance.

Table 2. *Clinical and demographic data*

	All
Age, mean (SD)	45.3 (13.0)
Sex, % (n)	
Female	56.7 (34)
Male	43.3 (26)
Global Assessment of Functioning, mean (SD)	58.7 (8.7)
Age first admission, mean (SD)	35.9 (12.3)
Number of admissions, mean (SD)	3.3 (2.5)
Duration of illness, mean (SD)	9.4 (10.9)
Number of different drugs, mean (SD)	3.2 (1.5)
BMI (kg/m^2), mean (SD)	24.4 (4.2)
BMI segmentation, mean (SD)	
Normal (20-25 kg/m^2)	70 (42)
Overweight (25-30 kg/m^2)	21.7 (13)
Obese (> 30 kg/m^2)	8.3 (5)
Living situation, % (n)	
Sheltered housing	3.3 (2)
With family	20 (12)
Partner	35 (21)
Alone	36.7 (22)
Residential facility	5 (3)
Occupation, % (n)	
Work	28.3 (17)
Sheltered work	0 (0)
Study/training	3.3 (2)
None	68.3 (41)
Family history of cardiovascular disease, % (n)	40 (24)
Family history of diabetes, % (n)	30 (18)
Family history of lipid disorder, % (n)	30 (18)

BMI = Body mass index.

Results

Subjects

The mean (SD) age of the patients was 45.3 (13.0) years and the mean (SD) duration of illness was 9.4 (10.9) years. Of these patients, 26 were male (43.3%), and all patients were Caucasian. All subjects completed the assessments. The majority of patients were able to live independently in the community (n = 55, or 91.7%) and 17 patients also were employed (28.3%). There was a high prevalence of family history for cardiovascular and metabolic disorders (Table 2). The majority of patients had a normal weight, and obesity was only present in 5 patients (8.3%). Except for 7 patients, all patients were treated with antipsychotic medication. The most frequently used antipsychotics were olanzapine and quetiapine (Table 3). Patients received a mean (SD) of 3.2 (1.5) different medications. Next to antipsychotic medication, patients were treated with anticholinergics (5%), antidepressants (46.5%) and benzodiazepines (35.0%). Thirty patients received mood stabilizers: 20 patients received valproic acid, 10 received lithium, 3 received lamotrigine and 1 received carbamazapine (4 patients took 2 mood stabilizers). Twenty patients took non-psychoactive medication, which was relevant for metabolic disturbances in 9 patients, who all took antihypertensive medication. Except for these 9 patients, no other patients were known with hypertension prior to the baseline screening; similarly, no patients were known with diabetes or lipid disorders prior to the baseline screening.

Table 3. *Medication characteristics*

	% (n)
Anticholinergic	5.0 (3)
Benzodiazepine	35.0 (21)
Antidepressant	46.6 (28)
Mood stabilizer[a]	50 (30)
Valproate	66.7 (20)
Lithium	33.3 (10)
Lamotrigine	10.0 (3)
Carbamazepine	3.3(1)
No antipsychotic	11.7(7)
Only first-generation	0(0)
Only second-generation	78.3 (47)
Combination	10(6)
Second-generation antipsychotic	88.3 (53)
Second-generation	
Aripiprazole	1.9(1)
Clozapine	3.7 (2)
Risperidone	20.4 (11)
Quetiapine	31.5 (17)
Amisulpride	1.8(1)
Olanzapine	40.7 (22)
No medication	0(0)

[a]Four patients combine two mood stabilizers.

Metabolic abnormalities

The prevalence of the metabolic syndrome according to the different definitions is shown in Table 4. There was no significant difference in the prevalence of the metabolic syndrome according to sex, although female patients were significantly more likely to meet the increased waist criterion according either to ATP-III ($\chi^2 = 4.67$, $p < 0.0307$) or IDF criteria ($\chi^2 = 5.98$, $p < 0.0144$). Abnormal lipid values were frequently observed: 35 patients (58.3%) had elevated cholesterol, 31 patients (51.7%) had elevated low-density lipoprotein cholesterol, 16 (26.7%) had elevated triglycerides and 13 (21.7%) had low high-density lipoprotein cholesterol, with all of these elevated measures being uncovered for the first time. Patients meeting criteria for the metabolic syndrome were significantly more likely to take a second-generation antipsychotic, except for patients meeting criteria for the metabolic syndrome according to the IDF definition (ATP-III: 7 of 10 patients, $\chi^2 = 9.4$, $p < 0.01$; adapted ATP-III: 8 of 11 patients, $\chi^2 = 8.1$, $p < 0.0175$; IDF: 16 of 18 patients, $\chi^2 = 2.4$, $p < 0.31$). Patients with the metabolic

syndrome were significantly more likely to be overweight or obese than patients that did not meet criteria for the metabolic syndrome (ATP-III: 8 of 10 patients, $\chi^2 = 17.3$, $p < 0.001$; adapted ATP-III: 9 of 11 patients, $\chi^2 = 21.4$, $p < 0.0001$; IDF: 10 of 18 patients, $\chi^2 = 12.2$, $p < 0.01$).

According to ADA criteria, 4 patients (6.7%) met criteria for diabetes and another 14 (23.3%) met criteria for pre-diabetes (14 IFG, of whom 9 also had IGT). Of the patients with diabetes, 3 were treated with quetiapine and 1 with quetiapine combined with olanzapine. Two of the patients who met criteria for diabetes were not treated with a mood stabilizer; the other 2 were treated with lithium. Patients with diabetes were significantly older than patients without diabetes [$F(1,58) = 4.9$, $p < 0.0314$]. Similarly, patients that met criteria for the metabolic syndrome, regardless of the definition applied, were significantly older than patients not meeting criteria for the metabolic syndrome [ATP-III: $F(1,58) = 14.5$, $p < 0.001$; adapted ATP-III: $F(1,58) = 10.8$, $p < 0.01$; IDF: $F(1,58) = 4.3$, $p < 0.0422$]. Of the patients with pre-diabetic abnormalities, 3 were treated with risperidone, 2 with clozapine, 3 with quetiapine, 5 with olanzapine and 1 without antipsychotic medication (who took two mood stabilizers and an antidepressant). Patients with the metabolic syndrome were more likely to meet criteria for diabetes or pre-diabetic abnormalities in all definitions applied (Table 1). Patients with the metabolic syndrome according to the IDF criteria were more likely to have a family history of diabetes ($\chi^2 = 4.9$, $p < 0.0269$), but this was not found for patients meeting criteria for the metabolic syndrome according to the ATP-III or adapted ATP-III criteria, or for patients who met criteria for diabetes. Likewise, the presence of a family history of lipid disorders or cardiovascular disease was not significantly different in patients with or without diabetes, or in patients with or without the metabolic syndrome for all definitions applied.

Table 4*. Metabolic syndrome criteria prevalence*

	All (n = 60) % (n)	**Male (n = 26) % (n)**	**Female (n = 34) % (n)**	**p[a]**
ATP-III[b]	16.7 (10)	19.2 (5)	17.6 (5)	NS
Criteria				
Waist (male > 102 cm, female > 88 cm)	30.0 (18)	15.4 (4)	41.4 (14)	0.03
Blood pressure (≥ 130/85 mmHg)	48.3 (29)	61.5 (16)	38.2 (13)	NS
HDL (male < 40 mg/dL, female < 50 mg/dL)	21.7 (13)	19.2 (5)	23.5 (8)	NS
Triglycerides (≥ 150 mg/dL)	26.7 (16)	38.4 (10)	17.6 (6)	NS
Glucose (≥ 110 mg/dL)	13.3 (8)	15.1 (4)	11.8 (4)	NS
Adapted ATP-lll[b]	18.3 (11)	19.2 (5)	17.6 (6)	NS
Criteria				
Waist (male > 102 cm, female > 88 cm)	30.0 (18)	15.4 (4)	41.4 (14)	0.03
Blood pressure (≥ 130/85 mmHg)[c]	48.3 (29)	61.5 (16)	38.2 (13)	NS
HDL (male < 40 mg/dL, female < 50 mg/dL)	21.7 (13)	19.2 (5)	23.5 (8)	NS
Triglycerides (≥ 150 mg/dL)	26.7 (16)	38.4 (10)	17.6 (6)	NS
Glucose (> 100 mg/dL)[d]	28.3 (17)	23.1 (6)	32.4 (11)	NS
IDF[e]	30.0 (18)	34.6 (9)	26.5 (9)	NS
Criteria				
Waist (male ≥ 94 cm, female ≥ 80 cm)	60.0 (36)	30.6 (11)	69.4 (25)	0.01
Blood pressure (≥ 130/85 mmHg)	48.3 (29)	61.5 (16)	38.2 (13)	Ns
HDL (male < 40 mg/dL, female < 50 mg/dL)	21.7 (13)	19.2 (5)	23.5 (8)	NS
Triglycerides (≥ 150 mg/dL)	26.7 (16)	38.4 (10)	17.6 (6)	NS
Glucose (≥ 100 mg/dL)	28.3 (17)	23.1 (6)	32.4 (11)	NS

ATP-III = National Cholesterol Education Program Adult Treatment Protocol; IDF = International Diabetes Federation; HDL = high-density lipoprotein; NS = not significant. [a]Analysis of variance.
[b]Metabolic syndrome if 3 of 5 criteria are met. [c]Or if treated with antihypertensive medication. [d]Or if treated with insulin or glucose-lowering medication. [e]Metabolic syndrome if 2 criteria AND the waist criterion are met (waist is obligatory).

Discussion

To our knowledge, this is the first non-retrospective study to directly assess the prevalence of diabetes in patients with BD, by the use of an OGTT. Furthermore, the metabolic syndrome and other metabolic abnormalities were assessed. High rates of diabetes, the metabolic syndrome and metabolic abnormalities were found. These results confirm the high prevalence of the metabolic syndrome in patients with BD, reaching as much as twice the

prevalence of the general Belgian population matched for age (33). The prevalence of diabetes in the current sample was three times higher than the rate of drug-treated diabetes in the general population (34). Therefore, these data clearly demonstrate the need for screening for the metabolic syndrome and diabetes not only in patients diagnosed with schizophrenia, as suggested in the literature (8, 9, 18, 35), but also in patients with BD, or at least those who are being treated with second-generation antipsychotics. The importance of such screening is underlined by the rates of newly detected and previously untreated hypertension in 33% of patients and hypercholesterolemia in 58% of patients, which is in line with high rates of non-treatment in patients with schizophrenia (36).

Despite these increased prevalence rates when compared to the general population, the prevalence of the metabolic syndrome in the current sample of bipolar patients was considerably lower than the prevalence reported by Fagiolini et al. (20). These differences in prevalence rates are likely to be due to lifestyle differences in the European versus the American population but, to our knowledge, no study has specifically handled this issue. Nevertheless, estimates of the metabolic syndrome in the general population have consistently been lower for European than for US populations (37-41).

When compared to patients with schizophrenia or schizoaffective disorder (12), the prevalence of the metabolic syndrome appears lower in the bipolar patient group. Interestingly, rates of glucose abnormalities were as high in bipolar patients as in schizophrenia patients (18), as was the presence of a family history of cardiovascular complications, diabetes and lipid disorders (42). The current results suggest that patients with BD are also at high risk to develop metabolic abnormalities, and thus, that the increased risk for the development of these abnormalities is not limited to patients with schizophrenia. Interestingly, the current results suggest that the development of metabolic abnormalities is only moderately associated with weight, since of the current sample, 43 of the 60 patients had a normal weight (body mass index between 20 and 25 kg/m^2) and only 5 patients met criteria for obesity (body mass index above 30 kg/m^2). Another interesting finding is that female patients were more likely to have increased waist circumference in the current study, which is in line with studies of patients with schizophrenia (12, 43). Unfortunately, the sample size did not permit investigating the liability to develop metabolic abnormalities according to the individual antipsychotic drugs.

The current study also has some limitations. First, and most importantly, the current sample of patients with BD is relatively small. Furthermore, it consisted mainly of patients who were treated with a second-generation antipsychotic (almost 90%), and may thus not be representative for bipolar patients in general. Second, it is a cross-sectional study. We intend to follow up this cohort prospectively, in order to assess metabolic changes during the course of the illness and the function of antipsychotic regimes. Third, we failed to include other parameters, such as dietary habits, physical activity level and psychopathological profile. Fourth, patient recruitment was restricted to one site, which could have influenced our results, since large regional differences in the prevalence of metabolic abnormalities have been reported, at least in the USA (44). Future research should address these issues more specifically, in large, multi-site samples and with prospective study designs.

In conclusion, our data confirm the high prevalence of metabolic abnormalities, and especially glucose metabolism disturbances, for a European population of patients with BD. Caregivers should carefully monitor and treat metabolic abnormalities in these patients.

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References

1. Jin H, Meyer JM, Jeste DV. Atypical antipsychotics and glucose dysregulation: a systematic review. Schizophr Res 2004; 71: 195-212.

2. Allison DB, Casey DE. Antipsychotic-induced weight gain: a review of the literature. J Clin Psychiatry 2001; 62(Suppl. 7): 22-31.

3. Meyer JM, Koro CE. The effects of antipsychotic therapy on serum lipids: a comprehensive review. Schizophr Res 2004; 70: 1-17.

4. Jin H, Meyer JM, Jeste DV. Phenomenology of and risk factors for new-onset diabetes mellitus and diabetic ketoacidosis associated with atypical antipsychotics: an analysis of 45 published cases. Ann Clin Psychiatry 2002; 14: 59-64.

5. Haupt DW, Newcomer JW. Hyperglycemia and antipsychotic medications. J Clin Psychiatry 2001; 62(Suppl. 27): 15-26; discussion 40-41.

6. Scheen AJ, De Hert M. Drug-induced diabetes mellitus: the example of atypical antipsychotics. Rev Med Liege 2005; 60: 455-60.

7. Newcomer JW. Second-generation (atypical) antipsychotics and metabolic effects: a comprehensive literature review. CNS Drugs 2005; 19(Suppl. 1): 1-93.

8. De Nayer A, De Hert M, Scheen A, Van Gaal L, Peuskens J. Conference report: Belgian consensus on metabolic problems associated with second-generation antipsychotics. Int J Psychiat Clin 2005; 9: 130-137.

9. De Hert M, van Eyck D, De Nayer A. Metabolic abnormalities associated with second generation antipsychotics: fact or fiction? Development of guidelines for screening and monitoring. Int Clin Psychopharmacol 2006; 21(Suppl. 2): S11-S15.

10. Heiskanen T, Niskanen L, Lyytikainen R, Saarinen PI, Hintikka J. Metabolic syndrome in patients with schizophrenia. J Clin Psychiatry 2003; 64: 575-579.

11. Basu R, Brar JS, Chengappa KN et al. The prevalence of the metabolic syndrome in patients with schizoaffective disorder-bipolar subtype. Bipolar Disord 2004; 6: 314-318.

12. De Hert M, van Winkel R, Van Eyck D et al. Prevalence of the metabolic syndrome in patients with schizophrenia treated with antipsychotic medication. Schizophr Res 2006; 83: 87-93.

13. Lilliker SL. Prevalence of diabetes in a manic-depressive population. Compr Psychiatry 1980; 21: 270-275.

14. Cassidy F, Ahearn E, Carroll BJ. Elevated frequency of diabetes mellitus in hospitalized manic-depressive patients. Am J Psychiatry 1999; 156: 1417-1420.

15. Regenold WT, Thapar RK, Marano C, Gavirneni S, Kondapavuluru PV. Increased prevalence of type 2 diabetes mellitus among psychiatric inpatients with bipolar I affective and schizoaffective disorders independent of psychotropic drug use. J Affect Disord 2002; 70: 19-26.

16. Taylor D, Young C, Mohamed R, Paton C, Walwyn R. Undiagnosed impaired fasting glucose and diabetes mellitus amongst inpatients receiving antipsychotic drugs. J Psychopharmacol 2005; 19: 182-186.

17. Sernyak MJ, Gulanski B, Rosenheck R. Undiagnosed hyperglycemia in patients treated with atypical antipsychotics. J Clin Psychiatry 2005; 66: 1463-1467.

18. van Winkel R, De Hert M, Van Eyck D et al. Screening for diabetes and other metabolic abnormalities in patients with schizophrenia and schizoaffective disorder: evaluation of incidence and screening methods. J Clin Psychiatry 2006; 10: 1493-1500.

19. De Hert M, Van Eyck D, Hanssens L et al. Oral glucose tolerance tests in treated patients with schizophrenia. Data to support an adaptation of the proposed guidelines for monitoring of patients on second generation antipsychotics? Eur Psychiatry 2006; 21: 224-226.

20. Fagiolini A, Frank E, Scott JA, Turkin S, Kupfer DJ. Metabolic syndrome in bipolar disorder: findings from the Bipolar Disorder Center for Pennsylvanians. Bipolar Disord 2005; 7: 424-430.

21. Elmslie JL, Silverstone JT, Mann JI, Williams SM, Romans SE. Prevalence of overweight and obesity in bipolar patients. J Clin Psychiatry 2000; 61: 179-184.

22. McElroy SL, Frye MA, Suppes T et al. Correlates of overweight and obesity in 644 patients with bipolar disorder. J Clin Psychiatry 2002; 63: 207-213.

23. Fagiolini A, Frank E, Houck PR et al. Prevalence of obesity and weight change during treatment in patients with bipolar I disorder. J Clin Psychiatry 2002; 63: 528-533.

24. Fagiolini A, Kupfer DJ, Houck PR, Novick DM, Frank E. Obesity as a correlate of outcome in patients with bipolar I disorder. Am J Psychiatry 2003; 160: 112-117.

25. Elmslie JL, Mann JI, Silverstone JT, Williams SM, Romans SE. Determinants of overweight and obesity in patients with bipolar disorder. J Clin Psychiatry 2001; 62: 486-491; quiz 492-4193.

26. De Hert M, Peuskens B, van Winkel R et al. Body weight and self-esteem in patients with schizophrenia evaluated with B-WISE(R). Schizophr Res 2006; 88: 222-226.

27. De Hert M, Hanssens L, van Winkel R et al. A case series: evaluation of the metabolic safety of aripiprazole. Schizophr Bull 2007; 33: 823-830.

28. De Hert M, Hanssens L, van Winkel R et al. Reversibility of antipsychotic treatment-related diabetes in patients with schizophrenia: a case series of switching to aripiprazole. Diabetes Care 2006; 29: 2329-2330.

29. Expert Panel on Detection and Evaluation of Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA 2001; 285: 2486-2497.

30. Grundy SM, Cleeman JI, Daniels SR et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation 2005; 112: 2735-2752.

31. International Diabetes Federation. The IDF Consensus Worldwide Definition of the Metabolic Syndrome. Brussels: IDF, 2005.

32. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2006; 29: S43-S48.

33. Rietzschel E, De Buyzere M, De Bacquer D et al. Metabolic syndrome, a map of the cardiovascular damage. Results from the asklepios study in 2528 apparently healthy 35-55 year old subjects. Abstracts from the Conference of the European Society of Cardiology. Eur Heart J 2005; 26: 110-111.

34. Walckiers D, Van der Veken J, Papoz L, Stroobant A. Prevalence of drug-treated diabetes mellitus in Belgium.

Results of a study with the collaboration of a network of pharmacies. Eur J Clin Pharmacol 1992; 43: 613-619.

35. Marder SR, Essock SM, Miller AL et al. Physical health monitoring of patients with schizophrenia. Am J Psychiatry 2004; 161: 1334-1349.

36. Nasrallah HA. Metabolic findings from the CATIE trial and their relation to tolerability. CNS Spectr 2006; 11: 32-39.

37. Ferreira I, Twisk JW, van Mechelen W, Kemper HC, Stehouwer CD. Development of fatness, fitness, and lifestyle from adolescence to the age of 36 years: determinants of the metabolic syndrome in young adults: the Amsterdam growth and health longitudinal study. Arch Intern Med 2005; 165: 42-48.

38. Boulogne A, Vantyghem M. Epidemiological data and screening criteria of the metabolic syndrome. Presse Med 2004; 5: 662-665.

39. Hu G, Qiao Q, Tuomilehto J, Balkau B, Borch-Johnsen K, Pyorala K. Prevalence of the metabolic syndrome and its relation to all-cause and cardiovascular mortality in nondiabetic European men and women. Arch Intern Med 2004; 164: 1066-1076.

40. Ford ES, Giles WH, Mokdad AH. Increasing prevalence of the metabolic syndrome among U.S. adults. Diabetes Care 2004; 27: 2444-2449.

41. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 2002; 287: 356-359.

42. De Hert M, van Winkel R, Van Eyck D et al. Prevalence of diabetes, metabolic syndrome and metabolic abnormalities in schizophrenia over the course of the illness: a cross-sectional study. Clin Pract Epidemol Ment Health 2006; 2: 14.

43. McEvoy JP, Meyer JM, Goff DC et al. Prevalence of the metabolic syndrome in patients with schizophrenia: Baseline results from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia trial and comparison with national estimates from NHANES III. Schizophr Res 2005; 80: 19-32.

44. Ford ES, Mokdad AH, Giles WH, Galuska DA, Serdula MK. Geographic variation in the prevalence of obesity, diabetes, and obesity-related behaviors. Obes Res 2005; 13: 118-122.