Obesity and Associated Complications in Patients With Severe Mental Illnesses: A Cross-Sectional Survey

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Background: This naturalistic cross-sectional survey of patients with severe mental illnesses explores the association between important variables and obesity, extreme obesity, diabetes mellitus type 2, hypertension, and hyperlipidemia in the clinical environment.

Method: Weight and height were obtained from 560 patients with severe mental illnesses (including DSM-IV schizophrenia, schizoaffective disorder, bipolar disorder, and major depressive disorder) at central Kentucky inpatient and outpatient facilities to estimate their body mass index (BMI). Chart diagnoses of diabetes mellitus, hypertension, and hyperlipidemia were obtained.

Results: When comparing the patients with severe mental illnesses with Kentucky adults from the general population, the odds ratio (OR) of obesity (BMI ≥ 30 kg/m^2) was 2.6 (95% confidence interval [CI] = 2.2 to 3.0), and the OR of diabetes mellitus was 2.9 (95% CI = 2.3 to 3.6). Female gender, African American race, early start of psychiatric medication, and long psychiatric medication duration were significantly associated with obesity. Current alcohol and nicotine use exhibited significant ORs of obesity lower than 1, particularly in males. Obesity was closely associated with hypertension, type 2 diabetes mellitus, and hyperlipidemia. These complications were closely associated with each other and may indicate a further progression of obesity after aging.

Conclusions: These results suggest a complex pattern of variables that may influence the development of obesity and its complications in patients with severe mental illnesses, but they need replication. The major factors associated with obesity appear to be a long-term illness or treatment duration and substance use. The former may be more important in females, while the latter may be more important in males. Clinical diagnoses (schizophrenic or mood disorders) or current treatment did not appear to be fundamental factors.

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In the last 2 years, scientific journals[1] and lay media[2] have stressed that there is an obesity epidemic in the United States. In the last few years, psychiatrists began recognizing that the arrival of atypical antipsychotics shifted the focus on side effects from abnormal movements to obesity and its complications. The new concept of metabolic syndrome groups together abdominal obesity with hypertension, hyperglycemia, and hyperlipidemia.[3] Several medical organizations have recently published consensus guidelines[4] for antipsychotics reflecting the complexity of the subject. First, severe mental illnesses such as schizophrenia[5] or bipolar disorder[6] are associated with obesity (typically defined as a body mass index [BMI] ≥ 30 kg/m^2). Second, many antipsychotics may contribute to weight gain, but olanzapine and clozapine appear to pose the greatest risks.[7–16] The individual contributions of the severe mental illnesses versus the antipsychotics (and other medications) are hard to discern; the duration of psychotropic treatment in developing countries is closely related to the duration of the psychiatric diagnosis. Moreover, other factors possibly associated with weight change, such as lower educational levels or substance use, are strongly associated with severe mental illnesses.

The body of knowledge about obesity in patients with severe mental illnesses comes from a variety of study designs. For example, the literature on obesity in these pa-

tients includes studies focused on U.S. army personnel,[17] the U.S. adult population,[18] a U.S. sample of patients with severe mental illnesses versus the U.S. general population,[19] longitudinal studies with small samples comparing atypical antipsychotics,[20] combinations of clinical trials,[21] long-term clinical trial follow-ups,[22] and cross-sectional surveys in a severe mental illness sample.[23] The literature provides few cross-sectional surveys in large samples of patients with severe mental illnesses, although we found 2 large studies with institutionalized patients.[24,25] The current cross-sectional survey includes a large sample (N = 560) of outpatients and inpatients with severe mental illnesses from central Kentucky. Kentucky is among the states with the highest rates of overweight people (2001 Kentucky prevalence was 62%, which was the fourth highest in the country; U.S. mean was 58% and the range for all other states was 51%–64%).[26] Obviously, large naturalistic cross-sectional surveys are affected by the noise of clinical practice, where clinical and demographic variables cannot be closely controlled. Thus, naturalistic cross-sectional surveys may not ideally rule out the possible effect of specific variables; rather, they may identify variables having a possible major importance in the "noisy" clinical environment. This study's objective was to explore the association of a number of clinical and demographic variables with obesity and some of its complications (e.g., hypertension, type 2 diabetes mellitus, and hyperlipidemia).

METHOD

Sample

This study explored a sample of 560 inpatients and outpatients from central Kentucky facilities. The sample was collected in the context of a risperidone pharmacogenetics investigation. Risperidone is the medication that psychiatrists most frequently prescribe at these facilities (it is usually their first choice). Patients with past or current risperidone treatment who were willing to sign a written informed consent (approved by 2 institutional review boards) were included. From July 2000 to March 2003, inpatients were recruited from 2 facilities. Eastern State Hospital (ESH) in Lexington admits approximately 1600 patients per year and is the primary psychiatric hospital for acute admissions in one third of Kentucky. Central State Hospital in Louisville admits approximately 900 patients per year and covers a different catchment area. Outpatients were recruited from the Bluegrass Community Mental Health Centers (providing outpatient services for ESH's catchment area) and from the University of Kentucky Outpatient Clinic. Table 1 provides demographic and clinical characteristics of the total sample.

Weight and height were obtained from the patients' charts or, when unavailable, measured by the research team using the clinical setting's available instruments.

Table 1. Demographic and Clinical Characteristics of Patients With Severe Mental Illnesses (N = 560) Compared With Kentucky General Population

Characteristic	Mean	SD	95% CI	Ky (%)[a]
Age, y	42.6	12.9		
Age at start of psychiatric meds, y	26.8	11.7		
Duration of psychiatric meds, y	15.9	11.5		
BMI, kg/m^2	30.7	8.3		
Education, y	11.3	3.1		
	N	%		
Age ≥ 35 y	413	74		
Gender				
Male	303	54		
Female	257	46		
Race				
White	457	81		
African American	93	17		
Other	10	2		
Inpatients	430	77		
Marital status				
Single	254	45		
Divorced	158	28		
Married	92	17		
Other	56	10		
DSM-IV diagnoses[b]				
Schizophrenia	157	28		
Schizoaffective disorder	108	19		
Bipolar disorder	99	18		
Major depressive disorder	67	12		
Start of psychiatric medication				
Early age (≤ 24 y)	294	53		
Very early age (≤ 18 y)	109	20		
Late age (> 33 y)	139	25		
Duration of psychiatric medication				
≥ 5 y	452	81		
≥ 24 y	150	27		
Antipsychotics				
None	24	4		
Risperidone	341	61		
Olanzapine	91	16		
Daily smoking				
Current	370	66		
Ever	427	76		
Stopped daily nicotine use	55	10		
Current smoking[c]	387	69	65 to 73	31[d,g]
Alcohol abuse/dependence				
Last year	201	36		
Ever	360	64		
Drug abuse/dependence				
Last year	158	28		
Ever	291	52		
Weight				
Overweight (BMI ≥ 25 kg/m^2)	414	74	70 to 78	62[d,f]
Obesity (BMI ≥ 30 kg/m^2)	257	46	42 to 50	25[d,g]
Extreme obesity (BMI ≥ 40 kg/m^2)	73	13	10 to 16	NA
Diabetes mellitus	101	18	15 to 21	7[d,g]
Type 1	19	3		NA
Type 2	82	15		NA
Hypertension	151	27	23 to 31	30[e,g]
Hyperlipidemia	74	13	10 to 16	NA

[a]Prevalence in the Kentucky general adult population.
[b]Main clinical diagnoses; only the most frequent are described.
[c]Total current nicotine use was 70% (392/560). In addition to cigarettes, this includes current use of other forms of tobacco.
[d]One-sided z test for differences between patient and Kentucky prevalences: p value < .001.
[e]One-sided z test for differences between patient and Kentucky prevalences: p value = .1.
[f]Data from Ahluwalia et al.[26]
[g]Data from Leach.[27]
Abbreviations: BMI = body mass index, NA = not available.

Table 2. Association Between Obesity (BMI ≥ 30) and Other Variables in Univariate Analyses in All Subjects (N = 560)

Variable	OR	95% CI	p
Outpatient status	1.5	1.0 to 2.2	.04
Female gender	2.1	1.5 to 2.9	< .001
African American race	1.4	0.88 to 2.1	.12
Mood disorders	1.4	0.97 to 2.0	.07
Schizophrenic disorders	0.78	0.56 to 1.1	.14
Alcohol abuse/dependence			
Last year vs before last year	0.65	0.43 to 0.99	.05
Last year vs never	0.53	0.35 to 0.79	.002
Last year drug abuse/dependence	0.61	0.42 to 0.89	.01
Ever daily smoking	0.53	0.36 to 0.79	.001
Current nicotine use	0.54	0.37 to 0.78	.001
Early start of psychiatric medications (patient age ≤ 24 y)	1.6	1.1 to 2.2	.006
Duration of psychiatric medications ≥ 5 y	2.6	1.7 to 4.2	< .001

Past and present diagnoses of diabetes mellitus, hypertension, and hyperlipidemia, as well as clinical psychiatric diagnoses, were obtained from the charts.

Statistics

The prevalence and 95% confidence interval (CI) of obesity (BMI ≥ 30 kg/m^2) among patients were compared with the corresponding values in the Kentucky general adult population[27] (Table 1) by computing an odds ratio (OR) with a bootstrap CI.[28,29] Similar comparisons and computations were performed for the available prevalences of overweight (BMI ≥ 25 kg/m^2), current smoking, diabetes mellitus, and hypertension.

The association between obesity and clinical and demographic variables was initially explored by means of 2-way cross tabulations for univariate analyses.[29] As a measure of association, ORs were used along with 95% CIs. Variables with a p value < .25[30] are reported in Table 2 and were included as independent variables in a multivariate logistic regression that used obesity as the dependent variable and provided adjusted ORs for the independent variables (Table 3 describes significant variables in the logistic regression). The Hosmer-Lemeshow goodness-of-fit test was used to examine the fitness of the logistic models; all fit well.[29,30] Similar logistic regression models were developed for the most important subsamples: males, females, patients with schizophrenic disorders (defined as those having a DSM-IV clinical diagnosis of schizophrenia or schizoaffective disorder), and patients with mood disorders (DSM-IV bipolar disorder or major depressive disorder) (Table 3).

Additional univariate and logistic regression analyses were conducted using hypertension, diabetes mellitus type 2, hyperlipidemia (Tables 4–6), and extreme obesity (BMI ≥ 40 kg/m^2) as dependent variables. The analysis of extreme obesity used only the obese patients (N = 257), and the analysis of diabetes mellitus type 2 excluded 19 subjects with diabetes mellitus type 1.

Table 3. Variables Associated With Obesity (BMI ≥ 30) in Logistic Regressions

Variable	OR	95% CI	p
All Subjects (N = 560)[a]			
Female gender	1.9	1.3 to 2.7	< .001
African American race	1.6	0.99 to 2.5	.06
Schizophrenic disorders	0.66	0.46 to 0.95	.03
Current nicotine use	0.55	0.37 to 0.81	.003
Early start of psychiatric medications (patient age ≤ 24 y)	1.5	1.1 to 2.2	.02
Duration of psychiatric medications ≥ 5 y	2.9	1.8 to 4.8	.03
Male (N = 303)[b]			
Alcohol abuse/dependence			
Last year vs before last year	0.48	0.24 to 0.91	.02
Last year vs never	0.48	0.27 to 0.83	.009
Early start of psychiatric medications (patient age ≤ 24 y)	1.6	0.97 to 2.6	.06
Current nicotine use	0.53	0.29 to 0.97	.04
Female (N = 257)[c]			
African American race	2.9	1.4 to 6.2	.005
Schizophrenic disorders	0.45	0.26 to 0.77	.004
Early start of psychiatric medications (patient age ≤ 24 y)	1.8	1.1 to 3.0	.03
Duration of psychiatric medications ≥ 5 y	3.0	1.5 to 6.1	.002
Schizophrenic disorders (N = 265)[d]			
African American race	1.8	0.94 to 3.5	.07
Alcohol abuse during last year	0.54	0.31 to 0.96	.04
Duration of psychiatric medications ≥ 5 y	8.2	2.2 to 29.9	.001
Current nicotine use	0.41	0.22 to 0.75	.004
Mood disorders (N = 166)[e]			
Female	2.2	1.1 to 4.4	.02
African American race	9.7	2.1 to 45.9	.004
Ever used nicotine daily	0.42	0.19 to 0.91	.04
Early start of psychiatric medications (patient age ≤ 24 y)	2.3	1.2 to 4.64	.02

[a]Hosmer-Lemeshow goodness-of-fit test: $\chi^2 = 11.6$, df = 8, p = .17.
[b]Hosmer-Lemeshow goodness-of-fit test: $\chi^2 = 2.0$, df = 6, p = .92.
[c]Hosmer-Lemeshow goodness-of-fit test: $\chi^2 = 5.5$, df = 6, p = .49.
[d]Hosmer-Lemeshow goodness-of-fit test: $\chi^2 = 1.6$, df = 4, p = .80.
[e]Hosmer-Lemeshow goodness-of-fit test: $\chi^2 = 3.9$, df = 5, p = .57.

RESULTS

Prevalences of Obesity, Diabetes Mellitus, and Hypertension

The prevalences of overweight, obesity, and diabetes mellitus in patients with severe mental illnesses were significantly higher than those in the Kentucky adult general population (p < .001, Table 1). When comparing patients with adults from the Kentucky general population, we found that the OR for overweight was 1.7 (95% CI = 1.5 to 2.1), the OR for obesity was 2.6 (95% CI = 2.2 to 3.0), the OR for diabetes mellitus was 2.9 (95% CI = 2.3 to 3.6), and the OR for current smoking was 5.0 (95% CI = 4.2 to 6.0). Since Kentucky is one of the states with the highest prevalence of overweight people, it is very worrisome that obesity prevalence among patients with severe mental illnesses was much higher than that among Kentucky's general adult population; however, the prevalence of hypertension in patients was not significantly different (OR = 0.86, 95% CI = 0.71 to 1.03).

Table 4. Variables Associated With Hypertension in Univariate Analyses and Logistic Regression (N = 560)

	Univariate Analyses			Logistic Regression[a]		
Variable	OR	95% CI	p	OR	95% CI	p
Obesity (BMI ≥ 30)	2.7	1.8 to 3.9	< .001	2.1	1.3 to 3.2	.001
Diabetes mellitus	6.2	3.9 to 9.9	< .001	5.4	3.3 to 9.0	< .001
Hyperlipidemia	3.7	2.3 to 6.2	< .001	2.0	1.1 to 3.5	.016
Age ≥ 35 y	4.3	2.4 to 7.7	< .001	2.4	1.2 to 4.5	.009
Bipolar disorder	1.8	1.1 to 2.9	.01			NS
Last year alcohol abuse/dependence	0.44	0.29 to 0.68	< .001			NS
Last year drug abuse/dependence	0.49	0.31 to 0.77	.002			NS
Duration of psychiatric medications ≥ 24 y	3.1	2.1 to 4.7	< .001	2.7	1.7 to 4.3	< .001
Current daily smoking	0.52	0.35 to 0.76	.001			NS
Stopped daily smoking	2.1	1.2 to 3.9	.009	1.8	0.93 to 3.5	.08

[a]Hosmer-Lemeshow goodness-of-fit test: $\chi^2 = 9.4$, df = 6, p = .16.
Abbreviations: BMI = body mass index, NS = not significant.

Table 5. Variables Associated With Type 2 Diabetes Mellitus in Univariate Analyses and Logistic Regression (N = 541)[a]

	Univariate Analyses			Logistic Regression[b]		
Variable	OR	95% CI	p	OR	95% CI	p
Obesity (BMI ≥ 30)	3.1	1.9 to 5.1	< .001	2.4	1.4 to 4.1	.002
Hypertension	5.8	3.5 to 9.5	< .001	3.9	2.3 to 6.6	< .001
Hyperlipidemia	3.3	1.9 to 5.9	< .001	1.9	1.0 to 3.5	.05
Age ≥ 35 y	2.9	1.4 to 5.7	.002			NS
Female gender	1.9	1.2 to 3.0	.009			NS
Last year alcohol abuse/dependence	0.25	0.13 to 0.48	< .001	0.36	0.18 to 0.70	.003
Last year drug abuse/dependence	0.23	0.11 to 0.49	< .001			NS
Current nicotine use	0.64	0.39 to 1.0	.08			NS
Late start of psychiatric medications (patient age > 33 y)	1.5	0.9 to 2.5	.11	2.0	1.1 to 3.7	.03
Duration of psychiatric medications ≥ 5 y	2.9	1.3 to 6.5	.007	2.2	0.87 to 5.6	.09

[a]Excluded 19 subjects with diabetes mellitus type 1.
[b]Hosmer-Lemeshow goodness-of-fit test: $\chi^2 = 7.4$, df = 8, p = .49.
Abbreviations: BMI = body mass index, NS = not significant.

Table 6. Variables Associated With Hyperlipidemia in Univariate Analyses and Logistic Regression (N = 560)

	Univariate Analyses			Logistic Regression[a]		
Variable	OR	95% CI	p	OR	95% CI	p
Obesity (BMI ≥ 30)	2.1	1.3 to 3.5	.003	1.7	0.99 to 2.9	.05
Hypertension	3.7	2.2 to 6.1	< .001	2.2	1.3 to 3.9	.005
Diabetes mellitus	3.4	2.0 to 5.9	< .001	2.1	1.2 to 3.9	.01
Age ≥ 35 y	5.7	2.2 to 14.4	< .001	4.3	1.7 to 11.2	.003
White race	2.8	1.2 to 6.7	.01	3.2	1.3 to 7.8	.01
Last year alcohol abuse/dependence	0.53	0.30 to 0.93	.03			NS
Last year drug abuse/dependence	0.61	0.33 to 1.1	.1			NS
Stopped daily smoking	2.2	1.1 to 4.3	.03			NS
Very early start of psychiatric medications (patient age ≤ 18 y)	2.5	1.1 to 5.7	.02			NS
Duration of psychiatric medications ≥ 14 y	2.0	1.2 to 3.4	.006			NS

[a]Hosmer-Lemeshow goodness-of-fit test: $\chi^2 = 4.3$, df = 6, p = .63.
Abbreviations: BMI = body mass index, NS = not significant.

Variables Associated With Obesity

Univariate analyses suggested that female gender was significantly associated with obesity (Table 2). Although mood disorders may be associated with obesity, it appears that schizophrenic disorders may not (moreover, the OR for schizophrenic disorders was less than 1). Interestingly, current presence of substance use was associated with an absence of obesity (all ORs for active substance use were lower than 1). Early start of psychiatric medications (patient age ≤ 24 years) and taking psychiatric medications for at least 5 years were associated with obesity. Current treatments with the most frequently taken antipsychotics, risperidone and olanzapine, were very far from being significantly associated with a BMI ≥ 30 kg/m^2 (risperidone, OR = 0.96, 95% CI = 0.68 to 1.4; olanzapine, OR = 0.82, 95% CI = 0.52 to 1.3).

When using all subjects, the logistic regression model of obesity indicated that female gender, taking psychiatric medications for at least 5 years, and early start of psychiatric medications had adjusted ORs significantly greater than 1, whereas schizophrenic disorders and current nicotine use had significant adjusted ORs lower than 1 (Table 3). African American patients had a borderline significant OR greater than 1 when compared with patients of other races (Table 3).

The logistic regression model of obesity in males indicated that early start of psychiatric medications had a borderline significant adjusted OR greater than 1, whereas current nicotine use and alcohol disorders had significant adjusted ORs lower than 1 (Table 3). In females, African American race, early start of psychiatric medications, and taking psychiatric medications for at least 5 years had adjusted ORs that were significantly greater than 1, whereas the adjusted OR of schizophrenic disorders was significantly lower than 1 (Table 3). Thus, in females, illness and treatment variables were significant. No substance use variable was significantly associated with obesity in females.

In patients with schizophrenic disorders, taking medication for at least 5 years had a very high adjusted OR (8.2, 95% CI = 2.2 to 29.9); other significant variables were current nicotine and alcohol use during the last year. African American race was borderline significant. In patients with mood disorders, African American race had a very high OR (9.7, 95% CI = 2.1 to 45.9); other significant variables were female gender, ever using nicotine daily, and early start of psychiatric medications (Table 3).

Variables Associated With Extreme Obesity Among 257 Patients With Obesity

Surprisingly, nicotine use was the only significant variable associated with extreme obesity in univariate analyses. Current nicotine users had a lower prevalence of extreme obesity than noncurrent users. The OR that compared current nicotine use with never used nicotine was 0.5 (95% CI = 0.28 to 0.91), and the OR that compared current nicotine use with stopping nicotine use was 0.23 (95% CI = 0.10 to 0.56). When variables with $p < .25$ and nicotine use were combined as independent variables in a logistic regression model of extreme obesity, no other variable besides current nicotine use was significant.

Variables Associated With Hypertension

Obesity, diabetes mellitus, hyperlipidemia, age ≥ 35 years, and taking psychiatric medications for at least 24 years were significantly associated with hypertension in a logistic regression model (Table 4). Stopping daily smoking almost reached significance.

Variables Associated With Type 2 Diabetes Mellitus (after excluding type 1 patients)

Obesity, hypertension, hyperlipidemia, and late start of psychiatric medications were significantly associated with type 2 diabetes in a logistic regression (Table 5). Alcohol abuse in the last year was significantly associated with the absence of type 2 diabetes, exhibiting an adjusted OR lower than 1. Taking psychiatric medications for at least 5 years almost reached a significant association with type 2 diabetes (Table 5).

Variables Associated With Hyperlipidemia

Obesity, hypertension, diabetes mellitus, age ≥ 35 years, and white race were significantly associated with hyperlipidemia in a logistic regression (Table 6).

DISCUSSION

Limitations

This study was originally designed to investigate risperidone pharmacogenetics, not to investigate obesity. It probably represents patients with severe mental illnesses taking antipsychotics in central Kentucky relatively well, since risperidone is the most frequently used antipsychotic. In fact, finding patients taking other antipsychotics who have never taken risperidone is rare. This sample may not represent patients with severe mental illnesses in the United States accurately, because poor and rural people are overrepresented in Kentucky. However, it probably represents patients with severe mental illnesses in Kentucky relatively accurately, since state hospitals and community mental health centers are the main psychiatric treatment providers in this state.

This cross-sectional survey only reflects a moment in time; many of these patients may develop obesity and its complications after this survey. However, this study provides a good idea of crucial variables connected with obesity that clinicians need to consider when seeing patients with severe mental illnesses. This study is also limited in that the research team did not directly measure hyperglycemia, hyperlipidemia, and blood pressure; thus, false negatives may contaminate these variables. As lipid profiles are not routinely measured in our psychiatric settings, the investigators suspect that hyperlipidemia may be the most underdiagnosed variable.

Patients tend to underreport the abuse of alcohol and illegal substances, a factor that may hinder our substance abuse data. Underreporting is probably not a major issue in this study, since 2 experienced research nurses assessed current and prior substance abuse history by interviewing the patients and reviewing their charts for toxicology screens and substance use diagnosis or patients' reports to treating clinicians. More than 3 quarters of the patients had been under psychiatric treatment for over 5 years; it is unlikely that treating clinicians missed many ongoing substance use problems.

The comparisons of prevalences of current smoking, overweight, obesity, diabetes mellitus, and hypertension in this sample and the Kentucky general adult population provide only gross information; the Kentucky general adult population prevalences are not adjusted by demographic factors such as gender and race.

Specific clinical diagnoses of severe mental illnesses such as schizophrenia, bipolar disorder, or major depressive disorder did not appear to have major associations with obesity and obesity complications after adjusting for other variables. We cannot rule out that research diagnoses made through structured interviews may have provided a different outcome. However, we do not think that research diagnoses would change the results very much. Even the significant unadjusted ORs for the specific diagnoses were relatively close to 1; it is unlikely that moving some subjects among diagnostic categories would provide noticeable OR changes to reach high ORs similar to those of substance use and duration of psychiatric medications and illness. Moreover, a changed patient diagnosis would not change his or her prior longstanding psychiatric treatment, and there is substantial overlap in the pharmacologic treatment of schizophrenia and severe mood disorders in this sample. It must be remembered that all patients have been treated with antipsychotics.

Variables Associated With Obesity and Extreme Obesity

It was interesting that the observed associations with obesity were inconsistent across subsamples (Table 3), which suggests the presence of strong interactions

among the variables investigated. In general, if other studies verify our results, female and African American patients with severe mental illnesses appear to be prone to obesity. Similarly, early start of psychiatric medications and taking medications for at least 5 years may be associated with obesity in patients with severe mental illnesses. Current alcohol and nicotine use may be particularly associated with ORs of obesity lower than 1 in males with severe mental illnesses. Among obese patients with severe mental illnesses, current nicotine users may have ORs of extreme obesity lower than 1 when compared with never using nicotine or past nicotine users.

Variables Associated With Hypertension, Type 2 Diabetes Mellitus, and Hyperlipidemia

Obesity, hypertension, type 2 diabetes mellitus, and hyperlipidemia appear to be closely associated with each other in patients with severe mental illnesses. Future studies should consider using the new metabolic syndrome concept[3] to help clarify this picture. Hypertension appears to be associated with greater age (≥ 35 years) and long treatment duration (≥ 24 years), suggesting a long evolution period. The data on type 2 diabetes mellitus appears to be more difficult to interpret; starting psychiatric medications later in life (> 33 years) appears to be associated with type 2 diabetes mellitus. Our limited data suggested that hyperlipidemia might be associated with greater age and white race.

Demographic Variables

Although African American race appears to consistently predict obesity, this variable did not appear to have a consistent effect on obesity complications. For instance, white race appears to be associated with hyperlipidemia. Female gender also appears to be associated with obesity in patients with severe mental illnesses. Greater age (≥ 35 years) appears to be associated with obesity complications, suggesting that obesity may precede more complications as vulnerable subjects age.

Treatment and Illness Variables

Surprisingly, current treatment may not be a major factor associated with obesity; e.g., current olanzapine treatment was not associated with obesity (OR = 0.82, 95% CI = 0.52 to 1.3) or diabetes mellitus (OR = 0.84, 95% CI = 0.43 to 1.6). The lack of a longitudinal patient follow-up may explain this lack of association. Another explanation is that current medication effects may not be as important as the long-term accumulation of risk variables associated with obesity and its complications.

A long duration of psychiatric medications cannot be separated from long illness duration, because this is a retrospective study with chronically ill patients. Similarly, early start of psychiatric medications cannot be separated from early illness onset; thus, these aspects of severe mental illnesses and/or their pharmacologic treatments may be associated with obesity after many years.

Clinical diagnoses did not appear to predict obesity well. If schizophrenic disorders have any effect at all, they appear to protect against obesity, particularly in females. Mood disorders were close to being significantly associated with obesity in a univariate analysis (OR = 1.4, 95% CI = 0.97 to 2.0, p = .07; Table 2). This borderline significance disappeared when controlling for gender through a logistic regression on all subjects (OR = 1.2, 95% CI = 0.86 to 21.8, p = .25), suggesting that the association between mood disorders and female gender may partly explain the borderline significant association between mood disorders and obesity.

Substance Use Variables

Surprisingly, current substance use appeared to be associated with ORs of obesity and suffering from some of its complications that were lower than 1. The complications pattern appears to suggest that the development of obesity complications may finally motivate patients with severe mental illnesses to quit smoking and alcohol abuse. The pattern seen in obesity seems much more complicated. Some analyses suggested that current alcohol and nicotine use might have ORs of obesity lower than 1 when compared with never using these substances. Within obese patients, current nicotine use had ORs of extreme obesity lower than 1 when compared with never using nicotine and stopping nicotine use. If other studies of obese samples replicate our finding that extreme obesity is associated with quitting daily nicotine use and never using daily nicotine, this replication would suggest that some obese patients with severe mental illness very likely have major appetite problems. Although tobacco use has major detrimental effects, nicotine may help control appetite in an obese patient subgroup. We believe that the lower risk of obesity among substance users is probably related to the substance's biological effects on brain appetite systems and other brain systems, but we cannot rule out the part that economical issues may play. If patients with severe mental illnesses spend their limited economical resources buying alcohol or tobacco, they may have less money for food. Regarding the effects of drugs on appetite, nicotine may influence the expression levels of several brain peptides (including leptin, neuropeptide Y, orexin, and uncoupling proteins) and peptide receptors (for neuropeptide Y and orexin).[31] Alcohol's effects on food intake appear quite complex and may depend on alcohol dose and consumption time.[32]

Future Directions

Obviously, these results are limited by the cross-sectional nature of this study and need replication. However, they point to a very complex pattern of variables that may influence the development of obesity and its compli-

cations in patients with severe mental illness. The major players in obesity appear to be a long-term illness or treatment duration and substance use; the former may be more important in females, while the latter may be more important in males. If other studies replicate that these variables are differentially associated with obesity in the different subsamples, it may be important to develop specific nutritional and healthy lifestyle programs for specific subgroups of patients with severe mental illnesses such as females, African Americans, and those who have quit smoking or drinking alcohol. Specific clinical diagnoses (schizophrenic vs. mood disorders) did not appear to be a fundamental factor. Nicotine's possible protective effect on preventing obesity's progression to extreme obesity suggests new opportunities for biological interventions by using appetite-suppressant medications. Identifying genetic markers of the risk of extreme obesity in patients with severe mental illnesses may be important in identifying at-risk subjects and establishing preventive interventions.

Drug names: clozapine (Clozaril, Fazaclo, and others), olanzapine (Zyprexa), risperidone (Risperdal).

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