Sociodemographic Characteristics and Cardiovascular Risk Factors in Patients With Severe Mental Disorders Compared With the General Population

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Objective: To study the prevalence and distribution of cardiovascular risk factors in a group of patients with severe mental disorders compared with the general population and investigate if differences in sociodemographic background variables between groups were associated with differences in risk profile.

Method: We compared data from the ongoing Ulleval 600 Study (205 pharmacologically stable outpatients with DSM-IV psychotic disorders) with data from the 2000–2001 Oslo Health Study (18,770 individuals from the general population of the same area). Subjects were stratified according to age and gender and compared for ethnic background, level of education, marital status, and prevalence of risk factors.

Results: Patients had an overall prevalence of smoking, obesity, hypertension, dyslipidemia, and diabetes mellitus about twice that of the reference group. Patients aged 18 through 50 years had the highest level of risk factors when compared with the general population. There was no major difference in ethnic background or educational level between cohorts.

Conclusion: The increased cardiovascular risk profile in patients is particularly pronounced in young individuals and could not be explained by sociodemographic variables alone.

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The modern lifestyle, with easy access to high-calorie foods and a reduced physical workload, has led to an increase in obesity, disposing for the metabolic syndrome. People with metabolic syndrome are at risk for developing diabetes and cardiovascular disease (CVD) and have an increased mortality from CVD and all causes.[1] Along this line of concern for public health, attention has been drawn to the somatic health situation of patients with severe mental disorders.[2] Individuals with schizophrenia and bipolar disorders have an increased mortality compared with the general population, not only from suicide and accidents but also from natural causes, with CVD being responsible for the largest total number of excess deaths.[3–5] Several studies have pursued this issue and found that both smoking and the various components of the metabolic syndrome (overweight, hyperglycemia, hypertension, and dyslipidemia) are prevalent in patients with severe mental disorders.[6–12]

Under "obesogenic" conditions, a central question is why some people develop metabolic disturbances and

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others do not. We know that genetic factors are important,[13] but sociocultural factors also play a role, the typical example being well-educated people making better lifestyle choices than less-educated ones.[14] When studying metabolic risk profiles in clinical groups and in the general population, sociodemographic factors should therefore be taken into account.

Most previous somatic health studies of people with severe mental disorders have been in the form of epidemiologic surveys[15,16] or have been conducted among hospitalized patients, often as part of randomized, controlled drug trials. Both approaches have weaknesses. Large surveys do not permit thorough clinical examination of separate individuals, and hospitalized patients may not be representative of the clinical population at large. Inpatients may be more severely affected, less physically active, and receiving more medication than outpatients. Furthermore, randomized, controlled drug trials are often sponsored by pharmaceutical companies and limited by strict inclusion criteria.

New information is now being retrieved from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study, initiated by the National Institute of Mental Health. This study has a rigorous design and includes data on a large sample of schizophrenia patients treated under real-life conditions. Baseline data from the CATIE study show that among 686 subjects, metabolic syndrome prevalence was over 50% in females and over 35% in males. When comparing with data from the general population, schizophrenia patients, especially women, were found to have a highly raised risk of developing CVD on the basis of metabolic disturbances.[11]

Several lines of evidence pinpoint pharmacologic treatment as a major cause of such disturbances in the mentally ill, and some atypical antipsychotics seem particularly liable to cause overweight, glucose intolerance, dyslipidemia, and hormonal disturbances.[17–21] However, the etiology and mechanisms behind this relationship remain unknown, the literature is somewhat inconclusive, and the possible confounding of sociodemographic factors has, so far, not been properly addressed.

Cardiovascular risk factors are not equally distributed in the general population over time. Epidemiologic studies have shown that the prevalence of both smoking and overweight-related disorders are highly related to age, gender, ethnicity, level of education, and marital status.[14,22–24] In addition, these studies have found that risk factors can change in the course of a few years with altered lifestyle in a given population. We have therefore compared a patient sample with the general population of the same geographical area for data collected within a time span of 4 years on both demographic and risk variables. The Norwegian health care system is publicly funded and the only provider of psychiatric services. This fact made it possible to study a representative sample of patients under real-life conditions. The data were compared with the data from the Oslo Health Study (HUBRO),[25] a large population-based health survey accomplished in the general population of Oslo in 2000 and 2001.

The aim of the present study was to investigate the prevalence and distribution of cardiovascular risk factors in a sample of pharmacologically stable outpatients with psychotic disorders from the city of Oslo and compare their risk profile to that of the general population. We wanted, furthermore, to examine whether differences in sociodemographic variables could explain differences in risk profiles between the patient and the reference group.

METHOD

The 2002–2005 Ulleval 600 Study (U600)

The thematic research area psychotic disorders (TOP Study), University of Oslo—Ulleval 600 Substudy (U600) started inclusion of patients in 2002 and was carried out by the University of Oslo in collaboration with Ulleval University Hospital on the basis of the specialist psychiatric services in Ulleval health care sector, Oslo County, Norway. The population of the health care sector, with a total of 187,000 inhabitants, lives in urban and suburban parts of Oslo. The treatment system is catchment area–based and publicly funded. Patients are referred from primary care. The core basis of the psychiatric specialist treatment system is subsector catchment area-based outpatient units, with the addition of acute, intermediate, and long treatment units. Eligible patients were all those meeting study criteria and giving informed written consent to participation. Data on all patients included in the study from start-up in October 2002 through May 2005 are summarized in this report. The Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate approved the study.

Subjects. Inclusion criteria consisted of being registered in the Ulleval University Hospital psychiatric services; being aged 18 to 65 years; meeting the DSM-IV criteria for schizophrenia, schizoaffective disorder, or bipolar disorder; understanding and speaking a Scandinavian language; having no history of severe head trauma; having an IQ score over 70; and being willing and able to give informed consent.

Two hundred five subjects met inclusion criteria, 102 men, with mean ± SD age 36.1 ± 10.8 years, and 103 women, with mean ± SD age 37.1 ± 11.8 years. One hundred three patients (61 men, 42 women) had diagnoses of schizophrenia, schizoaffective disorder, or schizophreniform disorder (in this article called *schizophrenia*). Eighty-three patients (35 men, 48 women) had diagnoses of bipolar I or bipolar II disorder (in this article called *bipolar disorder*). Nineteen patients (6 men, 13 women) had diagnoses of psychosis not otherwise specified (NOS), paranoid psychosis, bipolar disorder NOS, or severe de-

pression with psychotic symptoms (in this article called *other psychotic disorders*). There was an inverse proportion between men and women in the number of schizophrenia versus bipolar and other psychotic disorders (61/42 vs. 41/61).

Of the patients, 28 (26 with schizophrenia, 2 with bipolar disorder) were hospitalized at the time of assessment, and 177 were outpatients. Duration of illness was in the range of 0 to 48 years, estimated from first contact with the specialized psychiatric service, mean ± SD value 9.7 ± 9.7 years for all patients, 8.6 ± 8.8 years for the men, and 10.7 ± 10.5 years for the women. Mean ± SD Global Assessment of Functioning Scale (GAF) symptom severity domain score was 49.3 ± 13.7 for the men and 52.4 ± 15.1 for the women, while mean ± SD GAF level of functioning domain score was 49.5 ± 12.6 for the men and 52.2 ± 14.6 for the women, respectively.

Antipsychotic drugs were given to 73% of the patients (N = 149), and 18% (N = 37) received 2 or more different antipsychotics. Lithium was given to 11% (N = 22), and antiepileptic mood stabilizers to 36% (N = 73). Antidepressants were given to 38% of the patients (N = 77). Substantially more men than women received antipsychotic medication (84% vs. 61%), and more women than men received lithium (14% vs. 8%). There was no major difference in the percentage of men and women receiving antiepileptics or antidepressants. As many as 11% of the patients (N = 22) received no antipsychotic or mood-stabilizing medication, significantly more women than men (18% vs. 4%). These figures correspond well with other studies estimating standard drug regimes given to Norwegian patients with major psychoses.

Measures. Patients were invited to participate in the study by the clinician responsible for their treatment. All assessments were made by a group of 6 trained psychiatrists. History of mental illness, actual symptoms, lifestyle, and pharmacologic treatment was obtained from an interview with the patient, with additional information collected from treatment records and clinical staff. The Structured Interview for the DSM-IV Axis I disorders was used for diagnostic purposes. Difficult diagnostic evaluations were discussed in team meetings with a senior professor of psychiatry to arrive at consensus. Psychosocial functioning was measured by the GAF, and the scores were split into GAF symptom severity and GAF level of functioning domains to improve psychometric properties. Interrater reliability for both GAF scores was good, with an intraclass correlation coefficient (1.1) of 0.86.

Physical exams were performed immediately after the interview. Blood pressure (BP) was measured manually in a sitting position after resting and body mass index (BMI: weight in kg/height in m^2) calculated by asking patients about their height and weighing them on calibrated digital weights while wearing light clothing but without shoes. Patients were asked about their smoking habits. Fasting blood samples were taken within 2 weeks of the interview and analyzed for serum glucose and serum lipids (total cholesterol, high-density lipoprotein cholesterol [HDL], and triglycerides). All analyses were performed at Ulleval University Hospital, Department of Clinical Chemistry, on an Integra 800 instrument from Roche Diagnostics (Hoffmann-La Roche Ltd., Diagnostics Division, Basel, Switzerland), using standard methods.

The 2000–2001 Oslo Health Study (HUBRO)

The population-based HUBRO survey was conducted in Oslo from May 2000 to September 2001 by the Norwegian Institute of Public Health in collaboration with the Oslo City Council and the University of Oslo. The Regional Committee for Medical Research Ethics reviewed the study protocol, and the Norwegian Data Inspectorate approved the study. All participants gave their written consent. More details about this study can be obtained from the Norwegian Institute of Public Health.[25]

Subjects. All citizens aged 30, 40, 45, 59 to 60, and 75 to 76 years were invited to attend the screening station located in the city center. Of the 40,888 citizens invited, a total of 18,770 individuals (46%) participated in the survey. In this article, we have excluded the individuals 75 to 76 years old because no patients in the Ulleval 600 Clinical study were close to this age. Thus the reference group includes 6879 men and 8307 women, altogether 15,186 individuals in the age group of 30 to 60 years.

Measures. At screening, a simple clinical examination was conducted. A venous nonfasting blood sample was analyzed for serum total cholesterol, HDL, triglycerides, and glucose. Serum analyses were performed in the same laboratory as for patients (at Ulleval University Hospital), using the same instruments and methods. An automatic device (DINAMAP, GE Healthcare Technologies, Waukesha, Wis.) measured systolic and diastolic blood pressure. Body weight and height were measured with an electronic scale according to a standard protocol.[25] The participants were wearing light clothing without shoes. At the screening station, the main questionnaire was collected from the attendees, and they were given 2 supplementary questionnaires, which they were instructed to fill in at home and return by mail in prestamped envelopes.

In the present article, we have used the following variables: age, gender, country of birth, and marital status (all information from Statistics Norway); BMI, blood pressure, and blood samples (from the clinical examination), and years of education, country of birth of the parents, daily smoking, self-reported diabetes, and use of diabetes medication (information from questionnaires).

Data Analysis

Stratification by age. Men and women were compared separately on all variables. Patients were divided into 3 different age groups (called *young*, *middle-aged*, and *old*)

Table 1. Demographic Variables[a]

Variable	Women		Men	
	U600	HUBRO	U600	HUBRO
All ages	N = 103	N = 8307	N = 102	N = 6879
Age, mean (SD), y	37.1 (11.8)	43.8 (11.2)**	36.1 (10.8)	44.4 (11.4)**
Education, mean (SD), y	13.8 (3.1)	14.1 (4.2)	13.3 (3.1)	14.3 (4.0)
White, % (N)	89.3 (92)	89.7	83.3 (85)	86.8
Not married, % (N)	75.7 (78)	52.0**	83.3 (85)	49.5**
Young (18–35 y)	N = 53	N = 2288	N = 51	N = 1826
Age, mean (SD), y	27.6 (4.4)	30.0 (0.0)**	27.3 (4.5)	30.0 (0.0)**
Education, mean (SD), y	13.4 (2.7)	15.6 (3.7)**	12.6 (2.5)	15.3 (3.4)**
White, % (N)	86.8 (46)	87.0	78.4 (40)	88.3
Not married, % (N)	77.4 (41)	69.6	96.1 (49)	76.3*
Middle-aged (36–50 y)	N = 34	N = 3662	N = 40	N = 2936
Age, mean (SD), y	42.1 (4.1)	42.4 (2.5)	41.6 (4.2)	42.4 (2.5)
Education, mean (SD), y	14.4 (3.1)	14.3 (4.1)	13.7 (3.5)	14.4 (3.8)
White, % (N)	91.2 (31)	87.9	85.0 (34)	81.7
Not married, % (N)	70.6 (24)	46.2*	70.0 (28)	44.2*
Old (51–65 y)	N = 16	N = 2357	N = 11	N = 2117
Age, mean (SD), y	57.6 (4.7)	59.5 (0.5)**	57.0 (4.0)	59.5 (0.5)**
Education, mean (SD), y	13.8 (3.9)	12.3 (4.1)	14.8 (3.1)	13.2 (4.3)
White, % (N)	93.8 (15)	95.6	100.0 (11)	93.2
Not married, % (N)	81.3 (13)	44.0*	72.7 (8)	33.7

[a]Mean values (SD) and prevalences of sociodemographic variables for the patient group (U600) and the reference group (HUBRO), compared for the entire cohorts and for both cohorts split into age-groups. t Tests and Yates corrected χ^2 test have been performed. HUBRO data from Søgaard and Selmer.[25]

*$p < .01$.

**$p < .001$.

Abbreviations: HUBRO = Oslo Health Study, SD = standard deviation, U600 = Ulleval 600 Study.

to match, as closely as possible, the HUBRO data. The total age range for patients was 18 to 65 years, mean ± SD age 36.6 ± 11.3 years, and for the reference group 30 to 60 years, mean ± SD age 44.1 ± 11.3 years. The young group was made up of patients aged 18 to 35 years versus controls aged 30 years. The middle-aged group was made up of patients age 36 to 50 years versus controls aged 40 to 45 years. The old group was made up of patients aged 51 to 65 years versus controls aged 59 to 60 years.

Selected cutoff for continuous variables. In this study, cutoff values for the individual metabolic risk variables were set according to the World Health Organization (WHO) definition of the metabolic syndrome.[26] Fasting plasma glucose ≥ 6.1 mmol/L was chosen as the measure for impaired fasting glucose. BMI ≥ 30 kg/m^2 was used as the measure for obesity. Triglycerides ≥ 1.7 mmol/L and HDL < 0.9 mmol/L (men) and < 1.0 mmol/L (women) were chosen as independent measures of hyperlipidemia. Hypertension was defined as systolic BP ≥ 140 mm Hg and/or diastolic BP ≥ 90 mm Hg. In addition, high total serum cholesterol levels were set at ≥ 6.2 mmol/L.[27]

Statistical procedures. All analyses were done using the SPSS (SPSS, Inc., Chicago, Ill.) 12.01 software package for Windows. Men and women were compared separately, first by comparing values for all patients with all controls, second by stratifying each gender into matching age groups and comparing them separately. In evaluating sociodemographic factors, we used independent sample t tests to compare continuous variables and Yates corrected χ^2 tests to compare categorical variables in the patient and the reference group. To compensate for age differences between groups, metabolic variables have been adjusted to age and compared by using a univariate analysis of covariance.

To avoid type I errors caused by a large N, we used an a priori significance level of $p < .01$. To control for the effects of multiple comparisons, when metabolic risk factors were compared, we also did Bonferroni corrections, i.e., we divided the p value by the number of within-group comparisons. The analyses thus demand group differences with $p < .002$ (.01/5) to establish significance within each metabolic group variable.

RESULTS

Demographic Variables

Table 1 compares sociodemographic variables separately for men and women of different ages in the study and reference population (controls). Mean age was significantly lower for patients than for controls in all age groups, except for the middle-aged group. Patients and controls were very similar in ethnic background, both samples consisting primarily of whites. For both genders, the educational level of patients was significantly lower only in the youngest group. More patients than controls in all age groups were either unmarried or divorced.

Risk Variables, All Ages

Table 2 and Figure 1 show the age-adjusted values of cardiovascular risk variables for the patient group compared with the reference population.

Table 2. Metabolic Risk Variables, Age-Adjusted Values[a]

	Women		Men	
Variable	U600	HUBRO	U600	HUBRO
All ages	N = 103	N = 8307	N = 102	N = 6879
Body mass index, kg/m^2	27.1 (26.2, 28.0)	25.1 (25.0, 25.2)**	27.4 (26.7, 28.2)	26.4 (26.3, 26.5)
Cholesterol, mmol/L	5.6 (5.4, 5.8)	5.4 (5.4, 5.4)[b]	5.8 (5.5, 6.0)	5.6 (5.6, 5.6)[b]
HDL cholesterol, mmol/L	1.6 (1.549, 1.7)	1.6 (1.6, 1.6)[b]	1.2 (1.1, 1.3)	1.3 (1.3, 1.3)[b]
Systolic BP, mm Hg	129 (124, 131)	125 (124, 125)	132 (129, 135)	133 (132, 133)
Diastolic BP, mm Hg	83 (81, 85)	72 (72, 72)**	88 (86, 90)	78 (78, 79)**
Triglycerides, mmol/L	1.6 (1.5, 1.8)	1.3 (1.3, 1.3)[b]	1.8 (1.5, 2.0)	1.9 (1.9, 1.9)[b]
Glucose, mmol/L	5.4 (5.2, 5.7)	5.2 (5.2, 5.2)[b]	5.6 (5,3, 5,9)	5.5 (5,5, 5.5)[b]
Young	N = 53	N = 2288	N = 51	N = 1826
Body mass index, kg/m^2	25.4 (24.1, 26.7)	24.1 (24.0, 24.2)	26.6 (25.4, 27.9)	25.7 (25.6, 25.8)
Cholesterol, mmol/L	5.1 (4.8, 5.5)	4.9 (4.9, 5.0)[b]	5.5 (5.2, 5.9)	5.1 (5.1, 5.1)[b]
HDL cholesterol, mmol/L	1.6 (1.5, 1.8)	1.6 (1.6, 1.6)[b]	1.2 (1.1, 1.3)	1.3 (1.2, 1.3)[b]
Systolic BP, mm Hg	118 (115, 122)	117 (117, 118)	127 (123, 130)	129 (128,129)
Diastolic BP, mm Hg	80 (78, 83)	67 (67, 68)**	83 (80, 86)	72 (71, 72)**
Triglycerides, mmol/L	1.3 (1.1, 1.5)	1.1 (1.1, 1.1)[b]	1.8 (1.4, 2.2)	1.8 (1.7, 1.8)[b]
Glucose, mmol/L	5.2 (5.0, 5.5)	4.9 (4.9, 5.0)[b]	5.1 (4.8, 5.5)	5.1 (5.1, 5.1)[b]
Middle-aged	N = 34	N = 3662	N = 40	N = 2936
Body mass index, kg/m^2	28.2 (26.6, 29.8)	25.2 (25.1, 25.3)**	28.3 (27.1, 29.4)	26.4 (26.3, 26.5)*
Cholesterol, mmol/L	5.6 (5.3, 5.9)	5.3 (5.3, 5.3)[b]	5.9 (5.6, 6.2)	5.7 (5.6, 5.7)[b]
HDL cholesterol, mmol/L	1.5 (1.4, 1.7)	1.6 (1.6, 1.6)[b]	1.2 (1.1, 1.3)	1.3 (1.3, 1.3)[b]
Systolic BP, mm Hg	126 (122, 131)	122 (121, 122)	131 (126, 135)	130 (130, 130)
Diastolic BP, mm Hg	83 (79, 87)	72 (72, 72)**	88 (84, 91)	79 (78, 79)**
Triglycerides, mmol/L	1.6 (1.3, 1.8)	1.2 (1.2, 1.3)[b]	1.9 (1.4, 2.3)	2.0 (2.0, 2.0)[b]
Glucose, mmol/L	5.2 (4.8, 5.6)	5.2 (5.2, 5.2)[b]	5.5 (5.0, 6.0)	5.5 (5.4, 5.5)[b]
Old	N = 16	N = 2357	N = 11	N = 2117
Body mass index, kg/m^2	27.1 (24.6, 29.7)	26.1 (26.0, 26.2)	26.9 (24.6, 29.2)	27.1 (27.0, 27.2)
Cholesterol, mmol/L	6.1 (5.6, 6.7)	6.1 (6.1, 6.1)[b]	5.9 (5.1, 6.8)	5.9 (5.9, 6.0)[b]
HDL cholesterol, mmol/L	1.6 (1.3, 1.8)	1.7 (1.7, 1.7)[b]	1.3 (1.1, 1.6)	1.4 (1.4, 1.4)[b]
Systolic BP, mm Hg	138 (126, 150)	136 (135, 137)	142 (130, 153)	140 (139, 140)
Diastolic BP, mm Hg	85 (78, 92)	76 (76, 77)	89 (82, 96)	84 (84, 84)
Triglycerides, mmol/L	2.4 (1.9, 2.9)	1.5 (1.5, 1.5)[b]	1.6 (0.9, 2.2)	1.9 (1.8, 1.9)[b]
Glucose, mmol/L	6.2 (5.4, 7.0)	5.5 (5.4, 5.5)[b]	5.5 (4.4, 6.6)	5.8 (5.8, 5.9)[b]

[a]Mean (95% CI) values of metabolic risk variables for the patient group (U600) and the reference group (HUBRO), compared for the entire cohorts and for both cohorts split into age groups. Values have been adjusted for age differences between groups. HUBRO data from Søgaard and Selmer.[25]
[b]Nonfasting blood samples. Fasting vs. nonfasting status is of importance only for triglycerides and glucose. These values are therefore not statistically compared with the fasting values of the patient group.
*$p < .002$.
**$p < .001$.
Abbreviations: BP = blood pressure, HDL = high-density lipoprotein, HUBRO = Oslo Health Study, U600 = Ulleval 600 Study.

When comparing individual risk factors, we find smoking, obesity (BMI ≥ 30 kg/m^2), hypertension (BP ≥ 140/90 mm Hg), and dyslipidemia to be much more common in patients of both genders, with prevalences about twice those in the reference population. Hypertension was mainly due to increased diastolic BP in patients. Systolic BP did not differ significantly between the 2 cohorts. Total cholesterol levels were only moderately elevated in patients. However, twice as many individuals in the patient group as in the reference group had a low HDL cholesterol fraction (< 0.9 mmol/L for men and < 1.0 mmol/L) for women).

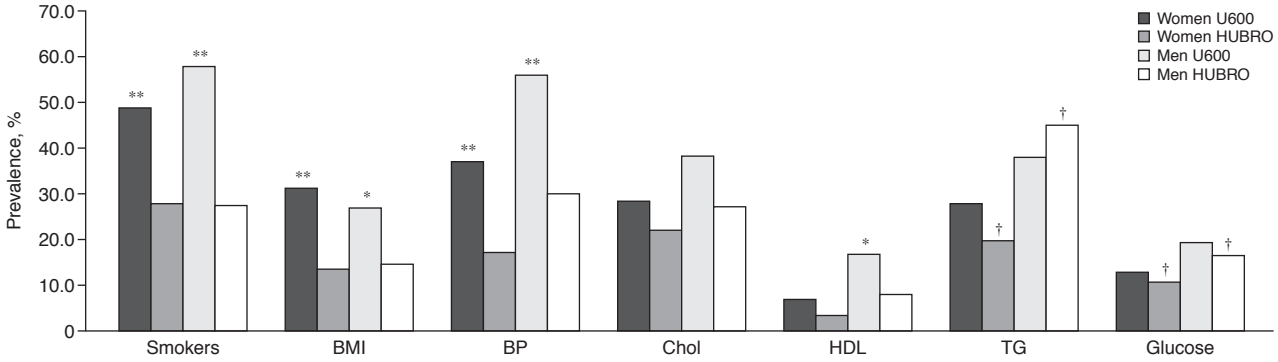
Levels for triglycerides and glucose were difficult to compare between cohorts due to the lack of fasting blood samples in HUBRO. However, fasting levels of triglycerides meeting high-risk criteria (≥ 1.7 mmol/L) were seen in about one third, and fasting levels of glucose ≥ 6.1 mmol/L were seen in 13% to 19% of patients. These prevalences, as well as mean values for triglycerides and glucose, although fasting, were higher than in the nonfasting reference group, with the exception of triglycerides in males. History of diabetes mellitus was recorded in both cohorts, and in the patient group, 3.9% were on antidiabetic medication as compared with 2.2% in the reference group.

Age-Related Risk Factors

Table 2 shows the mean values and Figure 2 shows the prevalence of individual risk factors meeting the chosen high-risk criteria for different age groups of men and women in the 2 samples.

Distribution of risk variables across age groups and genders was different in the patient and in the reference group. In the general population, daily smoking was most frequent in middle-aged individuals, with a prevalence of about 33% in 40- to 45-year-old men and women alike. In patients, daily smoking was most common, with very high prevalence figures in the young group and a steady decline with age until reaching almost the level of the general population in the old group.

Figure 1. Variables Meeting High-Risk Criteria[a]



[a]Prevalence of risk factors for CVD in the patient group (U600) and the reference group (HUBRO), compared by gender, all ages included. Metabolic values have been adjusted for age-differences between groups: HUBRO data from Søgaard and Selmer.[25]
*p < .002.
**p < .001.
†Nonfasting blood samples. Values are not statistically compared with the fasting values of the patient group.
Abbreviations: BMI = body mass index ≥ 30 kg/m^2, BP = blood pressure ≥ 140/90 mm Hg, Chol = cholesterol ≥ 6.2 mmol/L, CVD = cardiovascular disease, Glucose = glucose ≥ 6.1 mmol/L, HDL = high density lipoprotein < 0.9 mmol/L (men), and < 1.0 mmol/L (women), HUBRO = Oslo Health Study, TG = triglycerides ≥ 1.7 mmol/L, U600 = Ulleval 600 Study.

In the general population, BMI and the prevalence of obesity were strongly correlated with age. This was not the case in patients. The young and middle-aged male patients had 2 times, and female patients had 2 to 3 times as much obesity as in the corresponding reference groups. In the old age groups, there was hardly any difference in BMI between the 2 cohorts.

The rate of hypertension was consistently higher in the patients than in controls, compared by gender, but correlated with age, as in the normal population. Elevated diastolic BP made up the bulk of hypertension in all age groups.

Total cholesterol levels were moderately elevated in young and middle-aged patients of both genders as compared with the corresponding reference groups, and the HDL-cholesterol fraction was lower in all age groups of patients. However, for this variable the number of subjects was very small.

Triglyceride and glucose values could not be properly compared between the cohorts, because only nonfasting blood samples were available in the reference group. However, triglyceride and glucose levels did increase with age in both populations, one exception being a small decrease in triglycerides for old men, similar in patients and in controls. Middle-aged female patients, on the other hand, had a slight decrease with age in the prevalence of individuals meeting risk criteria for both triglycerides and glucose.

In the HUBRO population, diabetes was strongly correlated with age, with only 2% of 40- to 45-year-old individuals having previously diagnosed diabetes. In the U600 cohort, 8 individuals had diagnosed diabetes, and of these, 5 were women under 40 years of age.

Metabolic Syndrome Risk

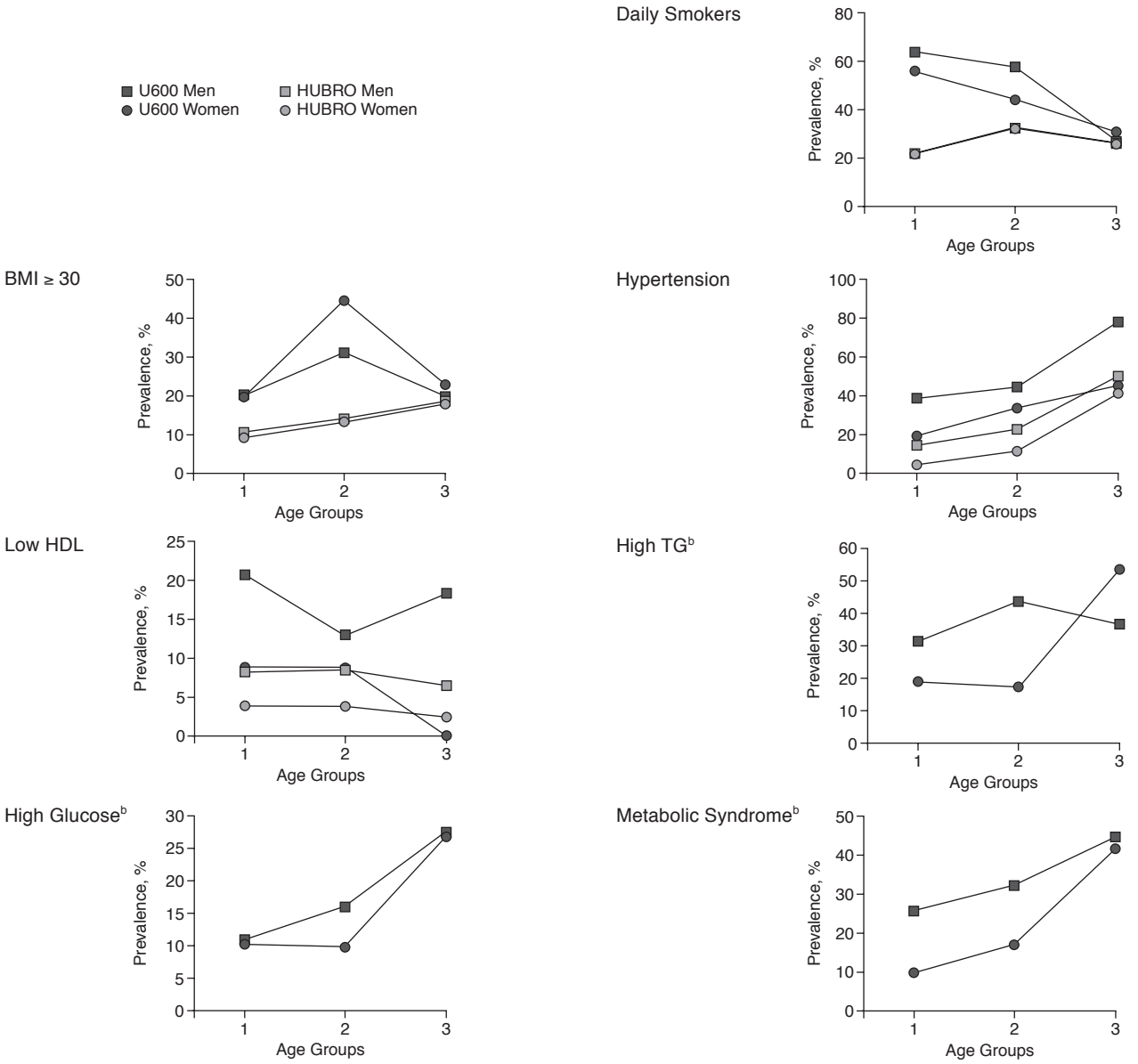
All frequently used definitions of metabolic syndrome are based on fasting blood measures of metabolic variables. In this study, we have thus not been able to compare the prevalence of the full metabolic syndrome between the patient and the normal population. Only individual variables, where fasting versus nonfasting status is of little importance (BMI, total cholesterol, HDL cholesterol, and blood pressure), have been compared.

To estimate the prevalence of metabolic syndrome in our patient population, we used the National Cholesterol Education Program, Adult Treatment Panel III (NCEP ATPIII) criteria,[28] modified by using BMI ≥ 30 kg/m^2 in lieu of waist circumference as the measure for obesity. Neglecting patients with missing values, the rate of metabolic syndrome was 30% (N = 26) in male and 17% (N = 14) in female patients. There was a steep rise with age in the prevalence of metabolic syndrome for both genders. This is known to be the case in all normal populations studied. However, metabolic syndrome was strikingly frequent in young patients, with a 26% (N = 11) prevalence in young males and a 10% (N = 4) prevalence in young females.

DISCUSSION

The major finding of the present study is that patients with psychotic disorders have an increased risk for CVD compared with individuals in the surrounding general population. Patients have more cigarette smoking, overweight, hypertension, dyslipidemia, and glucose intolerance than controls. The differences are clinically significant. The distribution of risk factors in patients is different

Figure 2. Risk Variables, Related to Age[a]



[a]Prevalence of risk factors for CVD related to age and compared by gender in the patient group (U600) vs. the reference group (HUBRO). HUBRO data from Søgaard and Selmer.[25]
[b]Fasting blood samples were not obtained in HUBRO.
Abbreviations: BMI = body mass index, BP = blood pressure, CVD = cardiovascular disease, HDL = high density lipoprotein, HUBRO = Oslo Health Study, TG = triglycerides, U600 = Ulleval 600 Study.
Definitions: age group 1 = young (18–35 years), age group 2 = middle-aged (36–50 years), age group 3 = old (51–65 years), high glucose = glucose ≥ 6.1 mmol/L, high TG = TG ≥ 1.7 mmol/L, hypertension = BP ≥ 140/90 mm Hg, low HDL = HDL < 0.9 mmol/L (men) and HDL < 1.0 mmol/L (women).

from that in the general population, and young to middle-aged patients (18 to 50 years) have the most striking risk profile. Differences in sociodemographic background did not seem to explain the large increase in CVD risk among patients.

The finding of an increased risk for CVD in patients with severe mental disorders is in line with other, recently published studies. Heiskanen et al.,[8] Basu et al.,[9] and Cohn et al.[10] all reported prevalences of the metabolic syndrome in patients with schizophrenia and schizoaffective disorder at least 2 times higher than in the general population, data now supported from the findings of the CATIE study.[11] The large patient number in CATIE has also allowed for good estimates of differences between genders and between race/ethnic groups. However, international lack of agreement on the definition of the

syndrome has made comparative studies of the metabolic syndrome across populations difficult, and representative reference populations are not easily found. Even the CATIE study may have overestimated the metabolic syndrome prevalence in schizophrenia when comparing with the Third National Health and Nutrition Examination Survey, where inclusion was done from 1988 to 1994, more than 10 years prior to the CATIE inclusion period. Smoking was not accounted for in either of the previous studies; neither were CV risk differences due to such important sociodemographic factors as educational level and marital status accounted for. Differences in distribution across age ranges have also not been properly focused, although Cohn and coworkers[10] showed the metabolic syndrome to be equally prevalent in patients under and over 45 years of age, and CATIE showed a large prevalence of overweight in young patients, which is in accordance with our results.

In the present study, data have been collected from a representative cohort of relatively young, ethnically homogenous, and well-characterized individuals with verified psychotic disorders studied under real-life conditions while receiving "treatment as usual." Most individuals of the cohort were outpatients, thus minimizing the confounding effects of hospitalization and making comparison with a community sample more valid. Reference data have been collected from the general population of the same restricted geographical and sociocultural area within a limited time span, thus avoiding falsely enlarged differences between patients and controls because of the temporal trends towards more overweight and metabolic disturbances in the overall population. In the reference population (HUBRO), self-selection according to sociodemographic variables had little impact on prevalence estimates. Unhealthy persons attended the HUBRO screening (in response to a letter of invitation) to a lesser degree than healthy individuals, but social inequality in health by different sociodemographic variables seemed unbiased.[29]

Considering individual risk variables separately, we find that young patients are most prone to smoking, while in the general population of Oslo, smoking is most frequent in the middle-aged group. This could possibly be understood as part of the stress involved in newly onset illness in young patients. However, the low level of education in this group also correlates well with their smoking habits, as has been shown for smoking in the general population.

The HUBRO study[25] has shown that, in the general population of Oslo, triglycerides increase with age up till the age of 45 years, while total cholesterol, glucose, blood pressure, and weight increase up till the age of 60 years. In the U600 cohort, the tendency is largely the same for lipids, glucose, and blood pressure but not for weight. Patients under the age of 50 have the most marked increase in BMI as compared with the general population, and obesity is particularly frequent in middle-aged women. Surprisingly, the same group of women has the lowest level of triglycerides and glucose, variables that are usually well correlated with body weight. We have no explanation for this phenomenon, but the data seem to be in line with other studies suggesting that drugs may cause severe overweight at an early age in women in particular.[23] Since so many more female than male patients have discontinued medication therapy, we can only speculate as to whether overweight may have led to nonadherence with medication, thereby normalizing serum levels of lipids and glucose but not reversing the weight problem.

The HUBRO study[25] shows a clear negative correlation between level of education and obesity in women. This is not the case in the U600 data. The high prevalence of young female patients having diabetes also suggests a particular vulnerability related to female gender, but here the numbers are too small to be conclusive. Further studies are needed to find out whether women are genetically more disposed to pharmacologic side effects than men.

There were no significant differences in sociodemographic background between patients and controls as to ethnicity or educational level. In all age groups, patients were slightly younger than controls. The only real difference was in marital status, with a large number of patients being unmarried or divorced. In Norwegian population-based studies, single status has been shown to be associated with a poorer lifestyle and more CVD risk in men but not in women.[14]

One of the limitations of this study is the relatively modest number of patients included. Another limitation is the use of BMI as the measure of obesity in lieu of the NCEP criterion (waist circumference > 102 cm for men and > 88 cm for women), probably leading to obesity being underestimated in our study as compared with others (like the CATIE trial[11]), particularly for women.[1] Also, the lack of fasting blood samples in the HUBRO[25] material has hindered us from properly comparing values for triglycerides and glucose in the patient and the reference populations. We have not been able to compare prevalences of the metabolic syndrome between patients and the general population, since no such prevalence, to our knowledge, has been estimated in Norwegian population studies. Nor have we been able to find good population-based metabolic syndrome studies for young individuals from other European countries. However, Europeans have been shown to have a generally much lower prevalence of metabolic syndrome than Americans. When using available data from the United States,[30] the prevalence of metabolic syndrome in young U.S. adults, aged 20 through 29 years, has been estimated at 6.7%, while young patients in the U600 sample had a metabolic syndrome prevalence of 10% in women and 26% in men.

The results of the present study further underscore the need for an integrated medical and psychiatric care model for patients with psychotic disorders. Both schizophrenia and bipolar disease may best be conceptualized as

somatic-psychiatric syndromes, with metabolic disturbances constituting an integral part of the disorders. The reason these somatic and psychiatric syndromes occur together may be a linked genetic susceptibility for psychosis and metabolic disturbances, disease-related stress, and poor lifestyle, together with adverse effects of psychopharmacologic treatment. The relative contribution of these factors needs to be further investigated, ideally in first-episode and prospective studies. Meanwhile, efforts should be made to provide users of psychiatric services with adapted and adequate lifestyle intervention programs. Psychiatric staff should be further educated and allocated the necessary resources for screening and supervision of CVD risk factors in their patients, with a particular emphasis on the young and middle-aged groups. Guidelines for pharmacologic treatment should be based upon individual risk profiles, and gender should be taken strongly into consideration when making choices of drugs and dosages.

Drug name: lithium (Eskalith, 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 U.S. Food and Drug Administration–approved labeling has been presented in this article.

Financial disclosure: In the spirit of full disclosure and in compliance with all ACCME Essential Areas and Policies, the faculty for this CME article were asked to complete a statement regarding all relevant financial relationships between themselves or their spouse/partner and any commercial interest (i.e., a proprietary entity producing health care goods or services) occurring within at least 12 months prior to joining this activity. The CME Institute has resolved any conflicts of interest that were identified. The disclosures are as follows: Drs. Birkenaes, Søgaard, Engh, Jonsdottir, Ringen, Vaskinn, Friis, Sundet, Opjordsmoen, and Andreassen have no significant commercial relationships to disclose relative to the presentation.

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