Persistent Low Rates of Treatment of Metabolic Risk Factors in People With Psychotic Disorders: A PHAMOUS Study

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ABSTRACT

Objective: People with psychotic disorders have an increased metabolic risk and a shortened life expectancy compared to the general population. Two large studies showed that metabolic disorders were untreated in a majority of the patients. Since then, guidelines have urged monitoring of metabolic health. This study examined the course of metabolic disorders over time in people with psychotic disorders and investigated current treatment rates.

Methods: A total of 1,259 patients with psychotic disorders, as defined by the *DSM-IV*, from 4 Dutch mental health institutions participated in 3 yearly assessments of the Pharmacotherapy Monitoring and Outcome Survey (PHAMOUS) between 2006 and 2014. Patients' metabolic parameters were measured, and the use of pharmacologic treatment for hypertension (systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg), dyslipidemia (5% ≤ Systematic COronary Risk Evaluation [SCORE] risk < 10% and low-density lipoprotein [LDL] cholesterol level ≥ 2.5 mmol/L or SCORE risk ≥ 10% and LDL cholesterol level ≥ 1.8 mmol/L and/or triglycerides ≥ 2.3 mmol/L), and hyperglycemia (hemoglobin A_{1c} concentration > 7% and/or fasting glucose concentration ≥ 7.2 mmol/L) was recorded.

Results: Prevalence of the metabolic syndrome, as defined by the National Cholesterol Education Program criteria, was > 50% at each assessment. On the basis of the European Society of Cardiology guidelines, pharmacotherapy for metabolic disorders was recommended for 52%–59% of the patients at each assessment. Treatment rates with antihypertensive (from 31% to 38%, $P < .001$) pharmacotherapy increased throughout the assessments. However, half of the patients were not treated for their metabolic risk factors while being monitored for 3 years or longer. Older patients were more likely to receive treatment, and patients who received treatment had lower blood pressure and lower cholesterol and triglyceride concentrations than patients not receiving the recommended treatment.

Conclusions: Metabolic risk factors are still seriously undertreated in people with psychotic disorders. Better adherence to and better implementation of guidelines about monitoring and treating metabolic disorders in psychiatry are crucial.

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Compared to the general population, people with psychotic disorders have an increased metabolic risk and a shortened mean life expectancy.[1,2] They are also more likely to suffer from metabolic syndrome (MetS),[3] a constellation of interrelated risk factors for cardiovascular diseases: increased waist circumference, hypertension, decreased high-density lipoprotein (HDL) cholesterol, hypertriglyceridemia, and hyperglycemia.[4]

A recent meta-analysis[5] suggests that lifestyle interventions effectively reduce metabolic disorders in people with severe mental illness. However, when hypertension and dyslipidemia are too severe or when changes in lifestyle and type of antipsychotics are not sufficient, pharmacotherapy with antihypertensive and lipid-lowering drugs is recommended.[6] Treatment with antihyperglycemic drugs may also be recommended when patients are diagnosed with diabetes mellitus.[4]

During the last 10 years, 2 large studies[7,8] investigated treatment rates for metabolic disorders in US patients with psychotic disorders. They showed that only 38%–54% of the patients with hypertension received adequate antihypertensive treatment, 11%–41% of the patients with dyslipidemia received treatment with lipid-lowering drugs, and 55%–60% of the diabetes mellitus patients received antihyperglycemic drug treatment.[7,8] In the meantime, alarming reports[9–15] on the physical health of this population have accumulated.

Aim

In this study, we first investigated the prevalence, incidence, and reversal rates of MetS in a longitudinal cohort of people with psychotic disorders. Second, we examined for how many patients treatment with antihypertensive, lipid-lowering, and antihyperglycemic drugs was recommended according to guidelines and the rates of patients receiving treatment according to these guidelines. Third, we explored which demographic and disease variables predict receipt of treatment for metabolic disorders. Last, we investigated whether patients receiving recommended treatment have less-severe metabolic risk factors than patients not receiving treatment.

METHODS

- High premature cardiovascular mortality rates and the generally increased metabolic risk in people with psychotic disorders emphasize the importance of treating metabolic risk factors in these patients.
- Despite the increased metabolic risk, low rates of treatment for metabolic risk factors are seen even among patients most compliant with follow-up screenings when adequate health monitoring is installed.

Clinical Points

Sample and Procedure

Data for this study were extracted from a large ongoing Dutch observational cohort study, the Pharmacotherapy Monitoring and Outcome Survey (PHAMOUS).[16] Mental and physical health of patients with psychotic disorders from 4 mental health institutions in the northern Netherlands are assessed yearly using Routine Outcome Monitoring (ROM), which is part of the regular clinical practice of the participating organizations. ROM procedures are fully explained to participants, after which they are free to opt out of having their anonymized data used in the research database. The procedures are in accordance with local and international rules, as confirmed by the local ethics committee of the University Medical Center of Groningen. Assessments were carried out between 2006 and 2014. By 2014, 8,372 patients were included in the PHAMOUS cohort, and the following screening rates were recorded throughout the years: 1.2% (2006), 4.7% (2007), 11.9% (2008), 19.2% (2009), 34.8% (2010), 42.8% (2011), 42.2% (2012), 53.1% (2013), and 65.7% (2014).

Participants

Inclusion criteria were (1) diagnosis of a psychotic disorder or mood disorder with psychotic features as defined by the *DSM-IV* and (2) participation in at least 3 assessments with data on all 5 MetS criteria. Consecutive assessments had intervals between 9 and 24 months. An overview of the sample demographics is provided in Table 1.

Measurements

Assessments were performed by a trained nurse and included (*a*) body mass index (BMI, kg/m^2); (*b*) waist circumference (centimeters) measured with a flexible measuring tape between the lower rib and the upper edge of the hip bone; (*c*) systolic and diastolic blood pressure (mm Hg), measured twice with an interval of 15 seconds using a manometer (reported systolic blood pressure and diastolic blood pressure scores are the mean values of the 2 measurements); (*d*) a blood sample to establish total cholesterol (mmol/L), HDL cholesterol (mmol/L), low-density lipoprotein (LDL) cholesterol (mmol/L), triglycerides (mmol/L), glucose (mmol/L), and hemoglobin A_{1c} (HbA_{1c}, % of total hemoglobin) (participants were asked to refrain from caloric intake for 8 hours before the blood sample was collected, but fasting status was not always reported; therefore we evaluated both total glucose [the entire sample] and fasting glucose concentrations [patients with confirmed fasting status]); (*e*) severity of psychotic symptoms, assessed with the Positive and Negative Syndrome Scale (PANSS)[17] remission criteria[18]; (*f*) self-reported smoking (yes/no), alcohol use (units per week), and cannabis use (yes/no); and (*g*) prescribed pharmacotherapy for metabolic disorders (ie, antihypertensive, lipid-lowering, and antihyperglycemic drugs) and antipsychotic drugs used (ie, clozapine, olanzapine, risperidone, quetiapine, aripiprazole, haloperidol, or other) as reported by the patient or as recorded in the patient's files.

Defining Metabolic Syndrome

MetS was diagnosed when 3 or more of the following National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP-III) criteria[4] were fulfilled: waist circumference ≥ 88 or ≥ 102 cm (female or male, respectively); systolic blood pressure ≥ 130 mm Hg and/or diastolic blood pressure ≥ 85 mm Hg or receiving antihypertensive drug treatment; serum HDL cholesterol concentration < 1.3 or < 1.03 mmol/L (female or male, respectively) or receiving lipid-lowering drugs; serum triglycerides concentration ≥ 1.7 mmol/L or receiving lipid-lowering drugs; and fasting serum glucose concentration ≥ 6.1 mmol/L or receiving antihyperglycemic drug treatment, in accordance with World Health Organization guidelines.[19,20]

Treatment Guidelines

International guidelines of the European Society of Cardiology (ESC), the International Diabetes Federation (IDF), and the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus were used to determine whether drug treatment for metabolic risk factors was recommended. The European guidelines concur with the American guidelines for hypertension, dyslipidemia, and diabetes.[21–24] Treatment recommendation rates are based on guidelines valid at the time of assessment, as described in Figure 1. Patients with a prescription for antihypertensive, lipid-lowering, or antihyperglycemic pharmacotherapy were considered both to have needed and to have received treatment.

Hypertension

The European Society of Hypertension (ESH) and ESC guidelines[25–27] recommend antihypertensive drug treatment for systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg.

Dyslipidemia

The ESC and European Atherosclerosis Society (EAS) treatment guidelines, based on risk estimation by the SCORE model,[28] recommend lipid-lowering drugs for patients with SCORE ≥ 5 combined with triglyceride level ≥ 5 mmol/L or LDL cholesterol level ≥ 3 mmol/L (until 2010)[29] and for patients with SCORE ≥ 5 and < 10 and

Table 1. Baseline Characteristics[a]

Variable	Total Sample (N = 1,259)	Treatment Recommended (n = 654)	No Treatment Recommended (n = 605)	*P*
Male	63.6 (801)	66.5 (435)	60.5 (366)	.027*
Age, mean (SD), y	43.7 (11.1)	46.4 (10.7)	40.8 (10.7)	< .001**
Illness duration, mean (SD), y	16.4 (10.3)	18.8 (10.4)	13.9 (9.6)	< .001**
Ethnicity				
White	92.0 (1,158)	92.5 (605)	91.4 (553)	.472
African European	3.3 (42)	3.4 (22)	3.3 (20)	.954
Asian	2.2 (28)	2.4 (16)	2.0 (12)	.578
Other	2.5 (31)	1.7 (11)	3.3 (20)	.004**
Diagnosis				
Schizophrenia	49.3 (621)	50.3 (329)	48.3 (292)	.469
Schizophreniform disorder	1.4 (18)	0.9 (6)	2.0 (12)	.111
Schizoaffective disorder	11.8 (148)	13.8 (90)	9.6 (58)	.022*
Substance-induced psychosis	0.5 (6)	0.6 (4)	0.3 (2)	.469
Delusional disorder	1.6 (20)	1.5 (10)	1.7 (10)	.861
Psychosis NOS	26.8 (338)	23.1 (151)	30.9 (187)	.002**
Depressive disorder	3.9 (49)	5.0 (33)	2.6 (16)	.028*
Bipolar disorder	4.7 (59)	4.7 (31)	4.6 (28)	.925
Antipsychotic drug use				
Overall	85.0 (1,070)	85.6 (560)	84.3 (510)	.509
Clozapine	27.3 (344)	31.0 (203)	23.3 (141)	.002**
Olanzapine	23.7 (298)	22.9 (150)	24.5 (148)	.524
Risperidone	16.2 (204)	12.7 (83)	20.0 (121)	< .001**
Quetiapine	10.7 (135)	11.2 (73)	10.2 (62)	.600
Aripiprazole	9.1 (114)	8.0 (52)	10.2 (62)	.156
Haloperidol	3.8 (48)	4.1 (27)	3.5 (21)	.543
Other	10.2 (129)	12.8 (84)	7.4 (45)	.002*
Antipsychotic dosage chlorpromazine equivalent, mean (SD), mg/d	455.2 (320.3)	482.5 (1,044.5)	500.4 (2,003.3)	.757
Antidepressant use	67.5 (850)	35.6 (233)	29.1 (176)	.013*
Smoking	58.5 (736)	61.6 (403)	55.0 (333)	.018*
Alcohol intake units per week, mean (SD)	9.6 (11.3)	10.0 (11.2)	9.3 (11.4)	.564
Cannabis use	8.0 (101)	7.2 (46)	9.3 (55)	.186
PANSS score (remission criteria), mean (SD)	15.5 (6.0)	15.7 (6.0)	15.2 (6.0)	.185
Diabetes mellitus	10.9 (137)	20.2 (132)	0.8 (5)	< .001**
BMI				
Mean (SD), kg/m^2	28.3 (5.7)	29.9 (5.8)	26.6 (4.9)	< .001**
Underweight (BMI < 18.5)	1.7 (21)	0.8 (5)	2.6 (16)	.009**
Normal weight (BMI 18.5–24.9)	26.1 (328)	16.7 (109)	36.3 (219)	< .001**
Overweight (BMI 25–29.9)	38.3 (482)	37.9 (248)	38.7 (234)	.782
Obese (BMI ≥ 30)	33.3 (419)	43.4 (284)	22.3 (135)	< .001**

[a]Values shown as % (n) unless otherwise noted.
*Significant at α < .05. **Significant at α < .01.
Abbreviations: BMI = body mass index, NOS = not otherwise specified, PANSS = Positive and Negative Syndrome Scale.

LDL cholesterol level ≥ 2.5 mmol/L, SCORE ≥ 10 and LDL cholesterol level ≥ 1.8 mmol/L, or triglyceride level ≥ 2.3 mmol/L (2011 and onward).[30]

Diabetes Mellitus

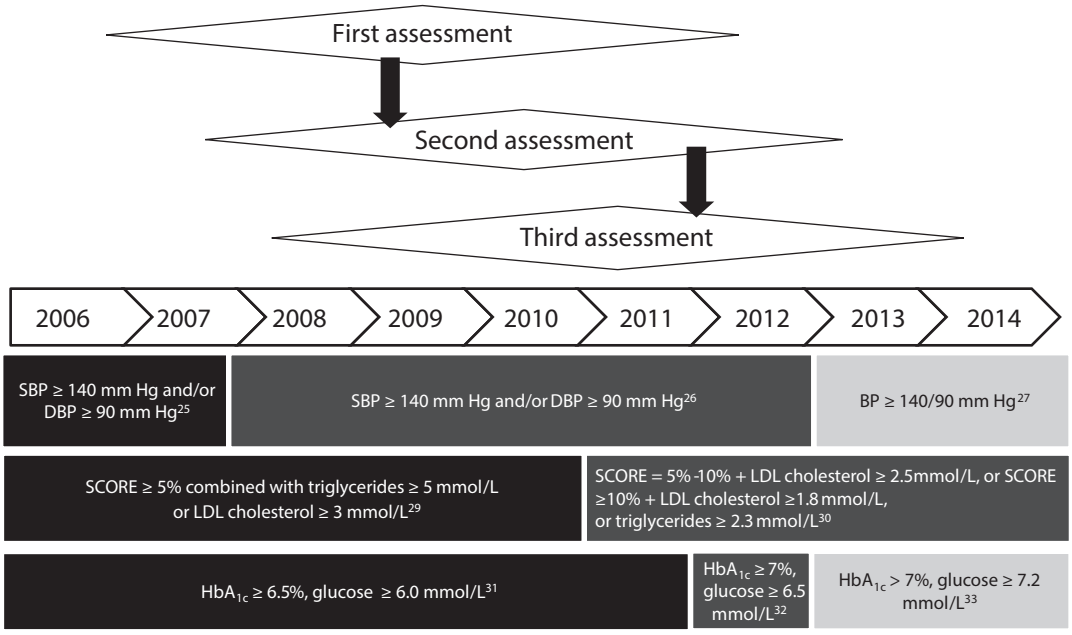
According to guidelines, a diagnosis of diabetes mellitus is required for treatment with antihyperglycemic drugs.[31–33] Patients reported whether they had been diagnosed with diabetes mellitus by their treating physician during the interview as part of the assessments. In addition, patients were considered to have diabetes mellitus at the third study assessment when they had fasting glucose concentrations ≥ 7.0 mmol/L at the first 2 study assessments,[34] regardless of whether or not a diagnosis of diabetes mellitus was self-reported in the third interview.

The IDF, ESC, and European Association for the Study of Diabetes (EASD) guidelines recommend antihyperglycemic drugs for patients diagnosed with diabetes mellitus when HbA_{1c} is ≥ 6.5% and/or fasting glucose concentrations ≥ 6.0 mmol/L or postprandial glucose concentrations ≥ 8.0 mmol/L (2005 to 2011),[31] HbA_{1c} is ≥ 7% and/or fasting glucose concentrations ≥ 6.5 mmol/L or postprandial glucose concentrations ≥ 9.0 mmol/L (2012),[32] or HbA_{1c} is > 7% and/or fasting glucose concentrations ≥ 7.2 mmol/L or postprandial glucose concentrations ≥ 10.0 mmol/L (2013 and onwards)[33] are measured.

Data Analysis

To establish the prevalence of MetS in each assessment, the number of patients with MetS was divided by the total number of patients. Incidence in each assessment was calculated by dividing the new MetS cases by the number of patients who did not meet the MetS criteria in the previous assessment. New cases were patients who met the MetS criteria in 1 assessment, but not in previous assessments. Remission was not meeting the MetS criteria in 1 assessment but meeting the criteria in the previous assessment. Remission rates were calculated by dividing the

Figure 1. Assessments and Guidelines Over Time[a]



[a]Values for triglycerides, cholesterol, and glucose are serum concentrations.
Abbreviations: DBP = diastolic blood pressure, HbA_{1c} = hemoglobin A_{1c}, HDL = high-density lipoprotein, LDL = low-density lipoprotein, SBP = systolic blood pressure, SCORE = Systematic COronary Risk Evaluation.

number of remitted cases by the number of MetS patients in the previous assessment.

Second, with generalized estimating equations (GEE), we examined whether the rates of patients needing drug treatment according to guidelines differed over the 3 assessments. GEE tests were also used to examine whether rates of patients receiving the recommended antihypertensive, lipid-lowering, and antihyperglycemic drugs differed over the 3 assessments to see whether treatment rates increased over time.

Third, to investigate what factors predict treatment, we used a multinomial logistic regression model with a backward elimination approach and Pearson correction. The following potential predictors were included: age and illness duration,[14] sex,[35] total score for the PANSS remission criteria,[36] smoking,[37] alcohol intake,[38] cannabis use,[39] and type and dosage (in chlorpromazine equivalents) of antipsychotic medication.[40,41] For the purpose of this model, all patients for whom treatment was recommended during at least 1 assessment were divided into 3 categories as the dependent variable: (1) never received treatment while treatment was recommended; (2) received treatment at some, but not all assessments while treatment was recommended; and (3) receiving appropriate treatment at all assessments when treatment was indicated. Wald test statistics and odds ratios (ORs) with 95% confidence intervals (CIs) between categories were calculated to determine the significance of the predictors.

Last, the course of different metabolic risk factors over the 3 assessments was examined with mixed modeling. At each assessment, all patients included in the study were divided into 3 treatment categories, separately for antihypertensive medication (systolic blood pressure and diastolic blood pressure), lipid-lowering drugs (total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides), and antihyperglycemic medication (glucose and HbA_{1c}): (1) patients for whom drug treatment was not recommended, (2) patients who did not receive pharmacotherapy when treatment was recommended, and (3) patients who received the recommended drug treatment. The longitudinal structure of the data imposed a correlation between the repeated observations that was addressed by assuming an unstructured covariance matrix: no constraints were imposed on the values and each (co)variance was estimated uniquely from the data. Covariates age, gender, illness duration, type of antipsychotic medication, smoking, alcohol intake, and cannabis use were included in the model as fixed factors. Differences between treatment categories were tested using the Wald test statistic. We included time (assessments 1, 2, and 3) and treatment groups as an interaction term to examine if differences were consistent throughout the 3 assessments.

SPSS 22.0 was used for all statistical analyses.[42]

RESULTS

In total, 1,259 patients fulfilled the inclusion criteria for this study (see Supplementary eFigure 1 at Psychiatrist.com). This subsample was similar to the overall cohort, in which the mean age was 43.3 years, the mean PANSS remission score was 16.0, the male prevalence was 65.2%, and the prevalence of MetS was 55.5%. The total mean (SD)

Table 2. Prevalence, Incidence, and Remission of Metabolic Syndrome and Individual Criteria[a]

Variable	Assessment 1	Assessment 2	Assessment 3	Wald χ^2	*P*
Fasting glucose					
Prevalence	51.5 (452)	52.6 (526)	52.2 (518)	0.52	.773
Incidence		10.0 (98)	8.9 (91)	0.70	.401
Remission		9.7 (95)	10.2 (105)	0.14	.706
Total glucose					
Prevalence	51.2 (644)	52.7 (664)	52.3 (658)	1.58	.453
Incidence		11.4 (144)	11.0 (139)	0.09	.766
Remission		9.8 (124)	11.5 (145)	1.64	.201
Waist circumference ≥ 88/102[b] cm					
Prevalence	66.6 (839)	66.9 (842)	66.6 (838)	0.11	.945
Incidence		6.8 (86)	6.2 (78)	0.39	.532
Remission		6.6 (83)	6.5 (82)	0.01	.938
SBP ≥ 130 and/or DBP ≥ 85 mm Hg					
Prevalence	60.9 (767)	63.1 (794)	61.5 (774)	2.09	.352
Incidence		16.0 (201)	13.8 (174)	1.94	.163
Remission		13.8 (174)	15.4 (194)	1.09	.297
Serum HDL cholesterol level < 1.0/1.03[c] mmol/L					
Prevalence	52.0 (655)	51.6 (650)	49.7 (626)	3.82	.148
Incidence		9.8 (124)	8.4 (106)	1.41	.236
Remission		10.2 (129)	10.3 (130)	0.00	.950
Serum triglycerides level ≥ 1.7 mmol/L					
Prevalence	49.7 (626)	50.3 (633)	48.6 (612)	1.71	.425
Incidence		11.0 (139)	9.5 (120)	1.39	.238
Remission		10.5 (132)	11.2 (141)	0.30	.586
Fasting serum glucose level ≥ 6.1 mmol/L					
Prevalence	27.3 (239)	28.2 (282)	31.4 (312)	8.17	.017*
Incidence		9.9 (75)	11.2 (95)	0.60	.440
Remission		8.5 (64)	8.6 (73)	0.01	.928
Total serum glucose level ≥ 6.1 mmol/L					
Prevalence	25.4 (320)	28.3 (356)	30.8 (388)	18.08	< .001**
Incidence		10.8 (136)	11.1 (140)	0.06	.810
Remission		7.9 (100)	8.6 (108)	0.31	.579

[a]Values at each assessment shown as % (n). N = 1,259 at all 3 assessments except for fasting glucose and fasting serum glucose level ≥ 6.1 mmol/L; for those variables, N = 877 at assessment 1, N = 1,000 at assessment 2, and N = 993 at assessment 3. The threshold values for SDP, DBP, and serum HDL cholesterol are those included in the National Cholesterol Education Program Adult Treatment Panel criteria.
[b]Female/male.
[c]Male/female.
*Significant at α < .05. **Significant at α < .01.
Abbreviations: DBP = diastolic blood pressure, HDL = high-density lipoprotein, SBP = systolic blood pressure.

follow-up time was 27.7 (5.2) months (range, 19–46 months), with a mean (SD) interval of 13.7 (3.6) months between the first 2 assessments and 13.5 (3.4) months between the second and third assessment.

Diagnosis of Diabetes Mellitus

At the first assessment, 10.9% of the patients had a diabetes mellitus diagnosis; the percentage significantly increased to 12.7% at the second and 15.3% at the third assessment (Wald $\chi^2 = 58.17$, $P < .001$). Of the diabetes mellitus patients at the third assessment, 14.7% reported being diagnosed with diabetes mellitus. An additional 8 patients (0.6%) did not report having diabetes mellitus, but had fasting glucose levels ≥ 7.0 mmol/L at the first 2 assessments and were therefore considered to have diabetes mellitus at the third assessment. Fasting blood samples were collected in 69.7% (first assessment), 79.4% (second assessment), and 78.9% (third assessment) of the patients.

MetS and Treatment Rates

Over half of the patients were diagnosed with MetS; prevalence, incidence, and reversal rates did not differ throughout the assessments. An overview of the prevalence rates of MetS and its individual components is presented in Table 2.

The rates of patients for whom antihypertensive and lipid-lowering treatment was recommended according to the guidelines significantly increased over the 3 assessments. The number of patients for whom treatment with antihyperglycemic drugs was recommended did not change significantly based on fasting glucose, but slightly increased when total glucose was examined. An increasing number of patients received treatment with antihypertensive and lipid-lowering drugs during the consecutive assessments, but treatment rates with antihyperglycemic drugs did not change. Of the patients not receiving the recommended treatment, up to one-third had severe risk factors, ie, systolic blood pressure ≥ 155 mm Hg, LDL cholesterol level ≥ 4.0 mmol/L, or fasting glucose level ≥ 8.5 mmol/L. An overview of treatment rates is presented in Table 3.

Receiving Treatment for Other Metabolic Risk Factors

Of the patients remaining untreated for hypertension, 11.8% received drug treatment for at least 1 other metabolic risk factor at the first assessment; the percentage significantly increased to 15.4% at the second and 16.8% at the third

Table 3. Prevalence of Treatment Recommendation and Treatment Prescriptions[a]

Disposition of Treatment	Assessment 1	Assessment 2	Assessment 3	Wald χ^2	*P*
Treatment was recommended					
Overall	51.9 (654)	55.8 (703)	59.3 (746)	25.15	<.001**
Antihypertensive drugs	42.0 (529)	43.9 (553)	45.8 (576)	6.29	.043*
Lipid-lowering drugs	21.0 (264)	27.6 (347)	31.5 (397)	72.3	<.001**
Antihyperglycemic drugs (fasting glucose)	8.0 (70)	8.7 (87)	10.2 (102)	1.53	.464
Antihyperglycemic drugs (total glucose)	7.1 (90)	8.3 (104)	9.2 (116)	10.67	.005**
Patients receiving the recommended treatment					
Overall	43.0 (281)	48.2 (339)	50.4 (376)	41.74	<.001**
Antihypertensive drugs	31.0 (164)	35.3 (195)	37.8 (218)	18.83	<.001**
Lipid-lowering drugs	56.1 (148)	55.0 (191)	55.7 (221)	11.99	.002**
Antihyperglycemic drugs (fasting glucose)	74.3 (52)	77.0 (67)	72.5 (74)	0.49	.784
Antihyperglycemic drugs (total glucose)	76.7 (69)	77.9 (81)	74.1 (86)	0.83	.661
Patients not receiving the recommended treatment					
SBP ≥ 155 mm Hg	14.8 (54)	16.5 (59)	18.7 (67)	…	…
Serum LDL cholesterol level ≥ 4.0 mmol/L	35.3 (41)	32.7 (51)	25.6 (45)	…	…
Fasting serum glucose level ≥ 8.5 mmol/L	16.7 (3)	15.0 (3)	25.0 (7)	…	…
Total serum glucose level ≥ 8.5 mmol/L	23.8 (5)	17.4 (4)	23.3 (7)	…	…

[a]Values at each assessment shown as % (n). N = 1,259 at all 3 assessments.
*Significant at α < .05. **Significant at α < .01.
Abbreviations: LDL = low-density lipoprotein, SBP = systolic blood pressure.
Symbol: … = not applicable.

assessment (Wald $\chi^2 = 14.48$, $P = .001$). Of the patients who remained untreated for dyslipidemia, 20.7% received drug treatment for at least 1 other metabolic risk factor at the first assessment, and the percentage significantly increased to 20.5% at the second and 26.1% at the third assessment (Wald $\chi^2 = 7.04$, $P = .030$). Of the patients who remained untreated for diabetes mellitus, 38.9% (fasting glucose) or 38.1% (total glucose) received pharmacotherapy for at least 1 other metabolic risk factor at the first assessment. This percentage did not significantly increase during the follow-up assessments (Wald $\chi^2 = 1.84$, $P = .398$ and Wald $\chi^2 = 4.11$, $P = .128$ for fasting glucose and total glucose, respectively).

Predicting Treatment

Only age significantly predicted receipt of treatment. When age increased, patients were more likely to be treated as recommended by guidelines than to be treated at some but not all assessments (Wald $\chi^2_1 = 12.96$, $P < .001$, OR = 1.081, 95% CI, 1.04–1.13).

Treatment and Severity of Metabolic Risk Factors

The mean values of metabolic risk factors, separately for patients receiving the recommended pharmacotherapy, patients not receiving the recommended pharmacotherapy, and patients without a treatment indication for metabolic risk factors to demonstrate the severity of metabolic risk in each group, are presented in Table 4. At all 3 assessments, systolic and diastolic blood pressure and total cholesterol, LDL, cholesterol and triglyceride concentrations were lower in patients receiving treatment compared to patients not receiving the recommended pharmacotherapy. HDL cholesterol concentrations did not differ between patients who did and patients who did not receive the recommended pharmacotherapy. Fasting glucose concentrations were lower in patients receiving treatment compared to patients not receiving the recommended treatment at the second and third assessments, but not at the first assessment ($F = 11.07$, $P < .001$). HbA_{1c} level was higher in treated patients compared to patients not receiving the recommended treatment, but the differences became smaller throughout the assessments ($F = 3.32$, $P = .010$).

DISCUSSION

In this study, over half of the patients with psychotic disorders suffered from MetS, and in almost two-thirds, pharmacologic treatment for metabolic risk factors was recommended according to internationally accepted guidelines. Prevalence of MetS in our study (> 50%) was higher than in the general Dutch population aged 40–49 years (22%)[43] and higher than reported in a large meta-analysis of schizophrenia patients (33%),[14] a finding that is probably related to the older age and longer illness duration of the patients in our sample.[14,44] There was a higher prevalence of patients in our sample for whom treatment for hypertension was recommended (42%–46%) compared to the general European population (30%), but twice as many people in the general population received the recommended antihypertensive drug treatment.[45] The prevalence of diabetes mellitus in our study was considerably higher (11%–15%) than in the general European population (6%).[46] Rates of patients receiving antihyperglycemic drugs were lower than treatment rates in the general US adult population with diabetes mellitus (86%).[47] The rates of receiving lipid-lowering drugs (54%) found in the general US population with dyslipidemia were comparable with our results.[48]

Pharmacotherapy for metabolic disorders was recommended for up to 60% of the patients according to the guidelines. Over half of these patients did not receive any treatment at all. Pharmacologic treatment for metabolic disorders seemed effective in lowering systolic and diastolic blood pressure and total cholesterol, LDL cholesterol, and triglycerides concentrations. For glucose concentrations,

Table 4. Course of Treated and Untreated Metabolic Disorders Using Mixed Modeling[a]

	Assessment 1		Assessment 2		Assessment 3		Time × Treatment Interaction	
Disorder and Treatment Group	Mean	95% CI	Mean	95% CI	Mean	95% CI	*F*	*P*
Hypertension								
SBP, mm Hg							0.98	.418
No treatment indicated	123.85	119.55–128.14	124.74	120.46–129.01	125.30	121.04–129.56		
Not receiving recommended treatment	141.24	136.80–145.68	142.08	137.66–146.49	144.25	139.87–148.63		
Receiving recommended treatment	132.50	127.54–137.45	133.42	128.77–138.08	132.78	128.10–137.46		
DBP, mm Hg							1.48	.205
No treatment indicated	79.93	76.94–83.93	80.11	77.13–83.08	79.45	76.48–82.42		
Not receiving recommended treatment	93.99	90.91–97.08	93.32	90.24–96.39	92.35	89.29–95.41		
Receiving recommended treatment	85.94	82.51–89.37	85.76	82.53–88.98	86.99	83.72–90.26		
Dyslipidemia								
Total serum cholesterol level, mmol/L							0.89	.470
No treatment indicated	5.29	4.96–5.62	5.22	4.90–5.55	5.27	4.94–5.59		
Not receiving recommended treatment	5.64	5.25–6.03	5.63	5.28–5.99	5.70	5.35–6.05		
Receiving recommended treatment	4.67	4.26–5.08	4.35	3.98–4.73	4.51	4.12–4.89		
Serum HDL cholesterol level, mmol/L							0.58	.681
No treatment indicated	1.27	1.11–1.43	1.30	1.14–1.45	1.30	1.14–1.46		
Not receiving recommended treatment	1.11	0.93–1.29	1.21	1.03–1.39	1.14	0.97–1.30		
Receiving recommended treatment	1.13	0.94–1.32	1.16	0.97–1.36	1.21	1.03–1.39		
Serum LDL cholesterol level, mmol/L							0.82	.511
No treatment indicated	3.50	3.23–3.77	3.48	3.21–3.74	3.51	3.24–3.77		
Not receiving recommended treatment	3.62	3.29–3.96	3.63	3.34–3.91	3.57	3.28–3.86		
Receiving recommended treatment	2.91	2.57–3.26	2.72	2.41–3.02	2.82	2.50–3.13		
Serum triglycerides level, mmol/L							1.50	.199
No treatment indicated	1.80	1.45–2.14	1.68	1.34–2.01	1.61	1.27–1.95		
Not receiving recommended treatment	3.05	2.65–3.46	2.99	2.62–3.35	3.01	2.64–3.37		
Receiving recommended treatment	2.20	1.78–2.62	1.77	1.38–2.16	1.77	1.37–2.17		
Diabetes mellitus								
Fasting serum glucose level, mmol/L							11.07	<.001**
No treatment indicated	5.74	5.21–6.26	5.65	5.14–6.16	5.67	5.16–6.18		
Not receiving recommended treatment	7.43	6.46–8.47	7.27	6.06–8.48	8.70	7.80–9.60		
Receiving recommended treatment	9.64	8.85–10.42	7.22	6.51–7.93	8.37	7.36–9.38		
Total serum glucose level, mmol/L							2.04	.086
No treatment indicated	5.67	[5.25–6.09	5.67	5.25–6.08	5.67	5.26–6.08		
Not receiving recommended treatment	7.52	6.54–8.50	7.42	6.17–8.68	8.75	7.91–9.58		
Receiving recommended treatment	8.76	8.15–9.38	8.42	7.80–9.03	8.41	7.48–9.33		
HbA_{1c} %							3.32	.010*
No treatment indicated	5.34	4.98–5.70	5.42	5.07–5.77	5.19	4.83–5.54		
Not receiving recommended treatment	5.99	5.14–6.85	6.29	5.47–7.12	6.06	5.33–6.80		
Receiving recommended treatment	7.29	6.74–7.83	6.42	5.94–6.91	6.30	5.21–7.40		

[a]Variables entered in the model are age, sex, illness duration, type antipsychotic drugs, smoking status, alcohol use, cannabis use. Covariates appearing in the model are evaluated at the following values: age = 44.2 years, illness duration = 17.7 years.
*Significant at α < .05. **Significant at α < .01.
Abbreviations: DBP = diastolic blood pressure, HbA_{1c} = hemoglobin A_{1c}, HDL = high-density lipoprotein, LDL = low-density lipoprotein, SBP = systolic blood pressure.

this effect was reversed, although the differences for HbA_{1c} became smaller throughout the assessments. Managing glucose control has been proven difficult in both the general and the psychiatric population, which may explain these inconsistent findings.[49]

Our findings tap a serious health problem that in reality may be even worse. In spite of American Diabetes Association/American Psychiatric Association guidelines that recommend frequent screening of metabolic risk factors in people taking antipsychotic drugs,[50] a recent review demonstrated that metabolic risk factors still remain unscreened in 70% of these patients.[51] However, the current study shows that screening rates have increased throughout the last decade. Furthermore, patients' actual metabolic risk may be underestimated because the current guidelines and risk models are based on the general population. Guidelines for metabolic disturbances might need updating to include metabolic risk models specifically designed for people with psychotic disorders, such as the recently proposed PRIMROSE models.[52] These models include psychiatric diagnosis and the use of antidepressant and antipsychotic drugs as additional predictors on top of the standard risk factors used in most other prediction models (ie, age, sex, systolic blood pressure, cholesterol, smoking).

The data do not reveal why patients are not treated with recommended pharmacotherapy. Maybe patients are referred to general practitioners but do not actually visit them, or physicians might be reluctant to prescribe pharmacotherapy due to the relatively young age of patients and might prefer to suggest lifestyle interventions. Also, when multiple metabolic dysregulations are present, often only one antimetabolic drug is prescribed. Possibly, treating physicians anticipate that treating one risk factor might improve overall metabolic health. Finally, patients themselves can refuse treatment. To what extent these factors contribute to the low treatment rates cannot be extrapolated from the present data.

Limitations

The observational nature of our data does not allow the examination of medication effects, which may be overestimated or underestimated due to confounding by indication. This subsample may be biased in containing only patients with 3 consecutive completed assessments, with having participated in less than 3 assessments being the main reason for exclusion (60% of the original sample). However, patients in this subsample did not differ from the total PHAMOUS cohort on demographical variables, MetS indicators, and psychopathology. No information is available on the number of patients opting out of participation in one or more PHAMOUS screenings.

It is not known whether all patients had refrained from caloric intake for 8 hours before glucose was measured. Although in our sample fasting glucose and total glucose were not considerably different, we cannot rule out that fasting glucose levels have been overestimated. Also, no information was available on patients' compliance with the prescribed pharmacotherapy, which may have led to an underestimation of treatment effects.

Information was available only on pharmacologic treatment and not on whether patients participated in lifestyle interventions. Participating in lifestyle interventions could explain why some patients were not receiving treatment, but not all considering that 15%–35% of the untreated patients had severe metabolic risk factors.

Although it is expected that treatment for metabolic risk factors will ultimately reduce cardiovascular mortality in people with psychotic disorders, data to support this hypothesis were not available.

Clinical Implications

Despite increasing knowledge about metabolic risk in psychotic disorders; well-established effectiveness of antihypertensive, lipid-lowering, and antihyperglycemic drugs; as well as patients' readiness to accept physical health monitoring,[53] treatment rates for metabolic disorders in this cohort were similar to the results of 2 large US trials published during the previous decade.[7,8] Low rates of treatment for metabolic risk factors are seen even among patients most compliant with follow-up screenings when adequate health monitoring is installed. Our findings strongly support the "Don't just screen, intervene!" claim that is receiving growing international attention.[54] Routine outcome monitoring of metabolic health is not a goal in and of itself, and if monitoring does not result in better care, we should urgently examine current monitoring, referral, and treatment practices.

Although psychiatrists seem to be well aware of increased metabolic risk, and most international guidelines acknowledge the importance of monitoring,[55,56] psychiatrists and general practitioners may hold different views as to who is responsible for monitoring and treating metabolic disorders.[57,58] Thus, clear communication between psychiatric services and medical care physicians is highly needed, a fact that might become self-evident when services are more integrated.[59] Ideally, general practitioners, psychiatrists, and patients will together acknowledge the increased risk and set up an adequate (pharmacotherapeutic) treatment plan based on the monitoring results.[54,57,60] To our view, doing so would greatly improve the metabolic care of psychiatric patients.

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Supplementary Material

Article Title: Persistent Low Rates of Treatment of Metabolic Risk Factors in People With Psychotic Disorders: A PHAMOUS Study

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Supplementary eFigure 1.