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Research paper

High persistence and low treatment rates of metabolic syndrome in patients with mood and anxiety disorders: A naturalistic follow-up study

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ABSTRACT

Background: Patients with affective and anxiety disorders are at risk of metabolic syndrome (MetS) and, consequently, cardiovascular disease and premature death. In this study, the course and treatment of MetS was investigated using longitudinal data from a naturalistic sample of affective- and anxiety-disordered outpatients (Monitoring Outcome of psychiatric PHARmacotherapy [MOPHAR]).
Methods: Demographics, clinical characteristics, medication use, and MetS components were obtained for n = 2098 patients at baseline and, in a FU-subsample of n = 507 patients, after a median follow-up (FU) of 11 months. Furthermore, pharmacological treatment rates of MetS were investigated at baseline and FU. Finally, demographic and clinical determinants of change in MetS (component) scores were investigated.
Results: At baseline, 34.6 % of n = 2098 patients had MetS, 41.4 % of whom received treatment. Of patients with persisting MetS, 46.1 % received treatment for one (or more) MetS component(s) at baseline, and 56.6 % received treatment at FU. Treatment rates of solely elevated blood pressure and reduced HDL-cholesterol did significantly, but modestly, improve. Higher age, male sex, smoking behavior, low education, diabetes, and depressive versus anxiety disorder were predictors of worse outcome at FU on at least one MetS component.
Limitations: We did not have data on lifestyle interventions as a form of treatment, which might partly have explained the observed low pharmacotherapeutic treatment rates.
Conclusion: MetS (components) show high persistence rates in affective- and anxiety-disordered patients, and are, despite adequate monitoring, undertreated over time. This indicates that adherence and implementation of monitoring protocols should be crucially improved in psychiatric outpatients in secondary care.

1. Introduction

Individuals with MetS have a five- to six-fold increased risk for developing diabetes mellitus type 2 (DM2) and a three- to six-fold increased risk of mortality from cardiovascular diseases (CVD) (Correll et al., 2015; De Hert et al., 2011b, 2011a). Metabolic syndrome (MetS) entails a cluster of five co-occurring metabolic abnormalities that increase the risk of diabetes, stroke, and cardiovascular disease (Correll et al., 2015; De Hert et al., 2011b, 2011a). To fulfill the criteria of MetS, individuals have three or more of the following metabolic abnormalities: elevated waist circumference, elevated blood glucose, elevated triglycerides, reduced high-density lipoprotein (HDL) cholesterol, and/or elevated blood pressure (Grundy et al., 2005). An increased prevalence rate of metabolic syndrome is found not only in patients with serious mental illness (Bruins et al., 2017), but also in patients with mood and anxiety disorders (Noubiap et al., 2022). With MetS prevalence rates of 31.7–37.3 % at a mean age of 42.8 years (Vancampfort et al., 2015, 2013) and 30.5–31.3 % at a mean age of 45.5 years in bipolar disorder

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and in depression (Vancampfort et al., 2015, 2014), relative risks of MetS in these groups are 1.57-1.58 times higher than in age- and gender-matched control groups (Vancampfort et al., 2014, 2013). In patients with anxiety disorders the risk of MetS has been found to be smaller, but still significant (odds ratio = 1.07; 95 % CI 1.01-1.12) (Tang et al., 2017).

The increased prevalence rate of MetS among psychiatric patients may be explained by several risk-factors being more common in this population, including unhealthy lifestyle such as physical inactivity, excessive alcohol intake, smoking (Firth et al., 2020; Salvi et al., 2012), the use of psychotropic drugs (Firth et al., 2020; Mazereel et al., 2020; Salvi et al., 2012; Vancampfort et al., 2013), and symptom severity and poorer functioning (Bai et al., 2016; Ghanei Gheshlagh et al., 2016; Giménez-Palomo et al., 2022; Gramaglia et al., 2018; Hiles et al., 2016; Kocakaya et al., 2020; Malhotra et al., 2016; Mazereel et al., 2020; Nebhinani et al., 2020; Pan et al., 2012; Penninx and Lange, 2018; Räikkönen et al., 2002; Van Reedt Dortland et al., 2010; Vancampfort et al., 2014).

In light of this, clinical practice guidelines (CPGs) recommend frequent monitoring, and treatment of metabolic abnormalities in psychiatric populations (Gelenberg et al., 2010; Hirschfeld et al., 2010; Lehman et al., 2004; Meeuwissen et al., 2015; "National Institute for Health and Care Excellence: Bipolar disorder: Assessment and Management Clinical Guideline", 2014; "National Institute for Health and Care Excellence; Depression in Adults: Recognition and Management Clinical Guideline", 2009; Spijker et al., 2013; Van Alphen et al., 2012; Van Bendegem et al., 2015). However, monitoring (Mitchell et al., 2012; Simoons et al., 2019a, 2018) and treatment practices are still limited (Bruins et al., 2017; Correll et al., 2010; de Jong et al., 2018; Godin et al., 2019, 2014; Schuster et al., 2021). As a result, MetS is often not recognized, leading to undertreatment. For example, Correll et al. (2010) found that patients with bipolar disorder often did not receive treatment for high cholesterol (60 %), diabetes (40 %), hypertension (48 %), or any MetS component (62 %) (Correll et al., 2010). Other studies have found similar or even higher percentages of mood-disorder patients that did not receive treatment for dyslipidemia, hyperglycemia, and/or hypertension (de Jong et al., 2018; Godin et al., 2019, 2014; Schuster et al., 2021). To our knowledge, studies investigating somatic treatment rates in patients with anxiety disorders are currently lacking.

Most studies that investigated prevalence rates of MetS, its determinants, and treatment of its components have been cross-sectional. For screening, diagnostic, and treatment purposes it is important to know how MetS and its treatment change over time and which factors are associated with these changes. Longitudinal studies showed that older age (Vishram et al., 2014), male gender (Vishram et al., 2014), lower education level (Kim et al., 2018), substance use (Sun et al., 2014, 2012), and low levels of physical activity (Cleven et al., 2022) were associated with relatively higher prevalence and/or incidence rates of MetS. Furthermore, elevated depressive symptoms at baseline were prospectively associated with increased waist circumference, mean arterial pressure (MAP), and blood glucose at follow-up (FU) (range: 2-7 years) (Goldbacher et al., 2009; Hiles et al., 2016; Lamers et al., 2016; Lasserre et al., 2017, 2014; Wu et al., 2021; Zhang et al., 2021). Elevated anxiety symptoms at baseline were prospectively associated with increased waist circumference and decreased HDL-cholesterol at 2-year FU (Hiles et al., 2016). Patients with bipolar disorders were at increased risk of developing MetS and/or diabetes, hyperlipidemia, and/or obesity over a FU period of 6 months to 10 years (Malhotra et al., 2013; Pérez-Piñar et al., 2016). Antidepressant drug use at baseline was prospectively associated with increased waist circumference, triglycerides, and blood glucose at a 2-year FU (Hiles et al., 2016). However, to our knowledge, the majority of these longitudinal studies have been performed in patients with depressive disorders (Goldbacher et al., 2009; Hiles et al., 2016; Lamers et al., 2016; Lasserre et al., 2017, 2014; Wu et al., 2021; Zhang et al., 2021), with only few studies in anxiety and/or bipolar disordered patients (Hiles et al., 2016; Malhotra et al., 2013; Pérez-Piñar et al., 2016), and with only one study in patients with depressive and/or anxiety disorders, assessed antidepressant drug use (Hiles et al., 2016).

Considering the lack of studies in anxiety and/or bipolar disordered patients investigating treatment rates of MetS and determinants prospectively associated with change of MetS at follow-up, we aimed to extend previous findings by investigating the prevalence rate of MetS and its individual components, and subsequent treatment of MetS abnormalities in a large naturalistic sample of mood (both major depressive disorder [MDD] and bipolar)- and anxiety-disordered outpatients at 3 outpatient clinics in the Netherlands. We investigated 1) longitudinal patterns of onset, remission, and persistence of MetS and its individual components' abnormalities over a period of at least six months, 2) the proportion of patients who received treatment for any of the parameters that constitute MetS (Grundy et al., 2005), 3) whether somatic treatments were conducted according to CPGs with respect to hypertension, dyslipidemia, and hyperglycemia (Piepoli et al., 2016; Rydén et al., 2013; Williams et al., 2018), and 4) whether baseline demographic and clinical factors were associated with change in continuous MetS and individual MetS component scores.

2. Methods

2.1. Study population

The study sample consisted of patients who presented at the outpatient clinics of Mental Health Service Drenthe between 2016 and July 2020. These patients were consecutively invited for the program Monitoring Outcome of psychiatric PHARmacotherapy (MOPHAR). MOPHAR entails a routine outcome monitoring (ROM) program, combined with medication reconciliation and somatic screening at baseline and at 9-12 months intervals. The objectives of MOPHAR are extensively described elsewhere (Simoons et al., 2019b). Patients who were older than 18 years of age and visited an outpatient department of MHS Drenthe were eligible for inclusion. Patients who were unable to read/write in Dutch were excluded. MOPHAR is registered in the Nederlands Trial Register (NL4779; NTR (trialregister.nl)). Patients provided written informed consent to participate in the study. All procedures were conducted according to the declaration of Helsinki. The independent medical ethics committee in Leeuwarden reviewed and approved the MOPHAR study protocol (RTPO protocol number 928).

2.2. Procedure

As part of MOPHAR, patients underwent a basic physical examination and a medication reconciliation procedure at baseline and at FU. In addition, patients were asked to fill in questionnaires and to visit the laboratory for a blood draw to determine several relevant laboratory parameters. Baseline measurements were completed by 2098 patients, and at least one consecutive MOPHAR screening appointment scheduled at least six months after the baseline measurement (median FU time: 11 months; interquartile range [IQR]: 9–13 months) was used as the FU measurement. In total, 507 patients completed both a baseline and FU measurement.

2.3. Measurements

2.3.1. MetS and its individual components

Metabolic measurements were collected during physical examination (waist circumference, blood pressure in sitting position) and using blood-sample laboratory measurements (HDL-cholesterol, triglycerides, and blood glucose). The presence of MetS was determined according to ATP III criteria (Grundy et al., 2005). According to these criteria, MetS is present if at least 3 of the following 5 criteria are met: 1) elevated systolic blood pressure [SBP] ≥130 mmHg and/or diastolic blood pressure [DBP] ≥85 mmHg, or use of antihypertensive drugs, 2) elevated waist

circumference (≥102 cm in men, ≥88 cm in women), 3) reduced HDL-cholesterol (<1.03 mmol/L in men, <1.3 mmol/L in women), or use of drugs for reduced HDL-cholesterol, 4) elevated triglycerides (≥1.7 mmol/L), or use of drugs for elevated triglycerides, and 5) elevated blood glucose (fasting: ≥6.1 mmol/L, non-fasting: ≥7.8 mmol/L), or use of drugs for elevated blood glucose (Forouhi et al., 2006). Cut-off values for both fasting and non-fasting blood glucose were based on the Dutch general practitioners guideline (Rutten et al., 2013). Whenever data on fasting status were missing, blood glucose values were assumed to be non-fasted. Variables were created for the presence of MetS and its individual components' abnormalities (0 = absent; 1 = present), both for baseline and FU. A detailed overview of the numbers of cases that met, did not meet, or missed data on MetS criteria at baseline and/or at FU is given in Supplementary Tables 1A-F and 2A-F.

The dichotomous MetS variables at baseline and FU were used to determine the pattern of change in MetS status. Of patients with MetS at baseline, those who also had MetS at FU were labeled as having *persistent presence* (0 = absent; 1 = present), whereas those who no longer had MetS at FU were labeled as having *remission* (0 = absent; 1 = present). Of the patients without MetS at baseline, those without MetS at FU were labeled as having *persistent absence* (0 = absent; 1 = present), whereas those with MetS at FU were labeled as having *new onset* (0 = absent; 1 = present).

In addition, individual component scores were used. A continuous total MetS variable (clustered MetS *Z*-score) was constructed to capture changes in the overall severity of MetS. Although this score has not been used often in psychiatric populations (Bruins et al., 2017), it has been shown to demonstrate high sensitivity and specificity and a high accuracy to predict the risk of MetS (Khazdouz et al., 2021). This score was created by standardizing the individual MetS components' continuous scores (z-scores) and dividing the sum of all standardized components by five. In this calculation, the value of standardized HDL-cholesterol was reversed to make sure that higher values on all components were indicative of increased metabolic risk. In addition, the mean arterial pressure (MAP) was used for standardizing blood pressure (Eisenmann, 2008).

2.3.2. Medication use

Both at baseline and FU, medication reconciliation, based on pharmacy records (including over-the-counter drug use), was performed to assess each patient's currently prescribed psychotropic and somatic drugs. In the current study, medication data were used to (1) assess percentages of somatic treatment of metabolic abnormalities, (2) assess whether treatment for hypertension, dyslipidemia, and hyperglycemia as recommended by CPGs (Piepoli et al., 2016; Rydén et al., 2013; Williams et al., 2018) was actually received, and (3) to evaluate the role of medication-use as determinants of changes in continuous MetS (component) scores.

All assessed drugs were classified by using the World Health Organization Anatomical Therapeutic Chemical (ATC) system, see Table 1. For each of the four types of somatic medication, a variable was created indicating whether it was used (0 = no; 1 = yes), both at baseline and FU. In addition, a general variable was created that indicated whether patients used any of the four types of medication to treat MetS (0 = no; 1 = yes). For each psychotropic medication type, a variable was created indicating whether it was used at baseline (0 = no; 1 = yes).

2.3.3. Recommended treatment for hypertension, dyslipidemia, and hyperglycemia

At both baseline and FU, each patient's actual need was determined for three types of treatment (hypertension, dyslipidemia, and hyperglycemia treatment) by applying CPG criteria (Piepoli et al., 2016; Rydén et al., 2013; Williams et al., 2018) to their collected MetS measurements. Details on the applied CPGs and cut-off values used in these guidelines are described in Supplementary Material 1. Based on the described cut-off values, separate variables were created indicating whether hypertension, dyslipidemia, and/or hyperglycemia treatment was recommended (0 = no; 1 = yes). These variables were created both for baseline and FU.

Table 1
Classification of somatic and psychotropic drugs.

	Classification anatomical therapeutic chemical (ATC)
Somatic drugs	
Antihypertensive drugs	C02, C03, C07, C08, and C09
Antidiabetic drugs	A10
Drugs for reduced HDL-cholesterol	C10AA, C10AX, C10BA01 through C10BA09, C10BA11, C10BA12, and C10BX
Drugs for elevated triglycerides	C10AB, C10AD, C10BA03, C10BA04, C10BA09, and C10BA12
Psychotropic drugs	
Non-selective monoamine reuptake inhibitors	N06AA
Selective serotonin reuptake inhibitors	N06AB
Monoamine oxidase inhibitors	N06AF, N06AG
Other antidepressant drugs	N06AX
Atypical antipsychotics	N05AL05, N05AX12, N05AX16. N05AX15, N05AH02, N05AE05, N05AH03, N05AX13, N05AH04, N05AX08, N05AE03, and N05AL01
Typical antipsychotics	N05AD06, N05AF03, N05AF01, N05AG01, N05AD01, N05AG03, N05AG02, N05AD05, and N05AF05
Anxiolytic drugs	N05B
Hypnotic drugs and sedatives	N05C
Mood stabilizers	N05AN01, N03AF01, N03AF02, N03AG01, and N03AX09

2.3.4. Baseline determinants of MetS at follow-up

Information on determinants, as described in the *Introduction*, that are associated with change in MetS parameter values, was collected. These determinants entailed: demographics (Vishram et al., 2014), education (low [0 = no; 1 = yes], middle [0 = no; 1 = yes], high [0 = no; 1 = yes]; reference: high) (Kim et al., 2018), psychiatric disease (depressive disorders [0 = no; 1 = yes], anxiety disorders [0 = no; 1 = yes], bipolar disorders [0 = no; 1 = yes], personality disorders [0 = no; 1 = yes], developmental disorders [0 = no; 1 = yes], miscellaneous disorders [0 = no; 1 = yes]; reference: depressive disorders) (Ji et al., 2023; Pan et al., 2012; Tang et al., 2017; Vancampfort et al., 2015, 2014, 2013), smoking (never smoked [0 = no; 1 = yes], former smoker [0 = no; 1 = yes], current smoker [0 = no; 1 = yes]; reference: never smoked) (Garcia-Portilla et al., 2010; Slagter et al., 2014; Sun et al., 2012), alcohol units per week (Slagter et al., 2014; Sun et al., 2014) and cannabis use (0 = no; 1 = yes) (Bruins et al., 2016), previous (pharmacotherapeutic) treatments (Correll et al., 2015; De Hert et al., 2011b; Mazereel et al., 2020), symptom severity (Pan et al., 2012), and health-related disability levels (Malhotra et al., 2016). To assess symptom severity, the Dutch version of the Outcome Questionnaire (OQ)-45 was administered, a 45 item self-report questionnaire (De Jong et al., 2007). The OQ-45 total score was used in the analyses. To assess health-related disability levels over the past 30 days, the 12-item Disability Assessment Schedule II (WHO-DAS) was administered ("Handbook of psychiatric measures, 2nd ed. - PsycNET", n.d.). The above-described baseline medication-use variables were also used as determinants.

2.4. Statistical analyses

Cross-sectional analyses were conducted both in the complete baseline sample ($n = 2098$) and the subsample with both a baseline and FU measurement (the 'follow-up' sample; $n = 507$). All longitudinal analyses were performed in the 'follow-up' sample. To evaluate the degree at which the follow-up sample (n = 507) was representative of the rest of the complete study sample ($n = 1591$), we compared patients

with and without a FU measurement on age and OQ-45 scores using an independent samples *t*-test, on WHO-DAS scores using a Mann-Whitney *U* test, and on gender and psychiatric diagnoses using a Chi-Square test. The results are described in Supplementary Material 2.

2.4.1. Cross-sectional analyses

Patient characteristics were described as means and standard deviations for normally-distributed continuous variables, medians and IQR for continuous variables that were not normally-distributed, and as frequencies and percentages for categorical variables. Next, the proportions of MetS and its individual components' abnormalities (0 = no; 1 = yes) and received treatment for MetS and its individual components' abnormalities (0 = no; 1 = yes) were calculated. Furthermore, it was evaluated how often patients received treatment for hypertension, dyslipidemia, and hyperglycemia in line with CPGs. These analyses were done using cross-tabulation in complete-case subsamples.

2.4.2. Longitudinal analyses

Proportions of persistent presence, new onset, remission, and persistent absence of MetS and of each of its individual components' abnormalities at FU were calculated by cross-tabulating the presence of MetS (or one of its components' abnormalities) at baseline with its presence at FU. Next, paired comparisons using (asymptotic) McNemar tests were used to test if proportions of MetS and its individual components' abnormalities differed significantly between baseline and FU. Paired comparisons using McNemar tests were also used to test if proportions of received treatment for MetS and each of its individual components' abnormalities differed between baseline and FU. The latter

Table 2
Characteristics of the complete study sample at baseline (n = 2098) and the follow-up sample at both baseline and follow-up (n = 507).

	Complete study sample (*n* = 2098)		Follow-up sample (*n* = 507)‡			
	Baseline		Baseline		Follow-up	
	Sample descriptive	Available measurements (n)	Sample descriptive	Available measurements (n)	Sample descriptive	Available measurements (n)
Sex						
Female sex, n (%)	1203 (58.6 %)	2098	306 (60.4 %)	507	306 (60.4 %)	507
Age (years) (mean | SD)	46 | 16	2098	47 | 14	507	48 | 14	507
Follow-up time (months) (median | IQR)	N/A	N/A	N/A	N/A	11 | 9–13	507
Diagnosis baseline measurement, n (%)						
Depressive disorders	559 (26.6 %)	2098	98 (19.3 %)	507	85 (16.8 %)	507
Anxiety disorders	458 (21.8 %)	2098	59 (11.6 %)	507	60 (11.8 %)	507
Personality disorders	303 (14.4 %)	2098	73 (14.4 %)	507	76 (15.0 %)	507
Bipolar disorders	299 (14.3 %)	2098	191 (37.7 %)	507	217 (42.8 %)	507
Developmental disorders	201 (9.6 %)	2098	25 (4.9 %)	507	28 (5.5 %)	507
Miscellaneous	129 (6.1 %)	2098	36 (7.1 %)	507	28 (5.5 %)	507
Unspecified	149 (7.1 %)	2098	25 (4.9 %)	507	13 (2.6 %)	507
Somatic problems, n (%)						
Diabetes	171 (8.4 %)	2026	46 (9.3 %)	497	52 (10.5 %)	494
Dyslipidemia	377 (19.2 %)	1968	112 (22.9 %)	490	110 (23.2 %)	474
Cardiovascular disease	219 (15.9 %)	2007	92 (18.5 %)	497	85 (17.5 %)	486
Obesity	438 (21.6 %)	2026	129 (26.0 %)	497	142 (29.0 %)	489
SCORE (median | IQR)	0.002 | 0.0002–0.0125	915	0.005 | 0.0030–0.0145	290	0.012 | 0.0022–0.0315	82
Substance use						
Smoking (current), n (%)	644 (38.7 %)	1678	174 (34.3 %)	442	32 (31.4 %)	102
Cannabis, n (%)	186 (11.2 %)	1662	40 (7.9 %)	426	4 (3.9 %)	102
Min. alcohol units per week (median | IQR)	0.5 | 0–2	1645	0.50 | 0–2.0	422	0.25 | 0–0.56	102
WHO-DAS II score (median | IQR)	25 | 18–32	1719	24 | 17–32	463	22 | 16–29	413
OQ-45 score (mean | SD)	77 | 26	967	73 | 28	203	70 | 27	75
Somatic medication, n (%)						
Use of somatic medication	537 (25.6 %)	2098	125 (24.7 %)	507	173 (34.1 %)	507
Antihypertensive drug	423 (20.2 %)	2098	96 (18.9 %)	507	135 (26.6 %)	507
Antidiabetic drug	162 (7.7 %)	2098	43 (8.5 %)	507	49 (9.7 %)	507
Statines	192 (9.2 %)	2098	46 (9.1 %)	507	65 (12.8 %)	507
Fibrates	1 (0.0 %)	2098	1 (0.2 %)	507	1 (0.2 %)	507
Psychiatric medication						
Use of psychiatric medication, n (%)	1164 (55.5 %)	2098	343 (67.7 %)	507	408 (80.5 %)	507
Tricyclic antidepressants (TCA's), n (%)	140 (6.7 %)	2098	42 (8.3 %)	507	41 (8.1 %)	507
Selective Serotonin Reuptake Inhibitors (SSRI's), n (%)	411 (19.6 %)	2098	97 (19.1 %)	507	120 (23.7 %)	507
Monoamine Oxidase inhibitors (MAOi's), n (%)	12 (0.6 %)	2098	8 (1.6 %)	507	11 (2.2 %)	507
Other antidepressants, n (%)	226 (10.8 %)	2098	50 (9.9 %)	507	66 (13.0 %)	507
Typical antipsychotics, n (%)	37 (1.8 %)	2098	9 (1.8 %)	507	19 (3.7 %)	507
Atypical antipsychotics, n (%)	408 (19.4 %)	2098	139 (27.4 %)	507	181 (35.7 %)	507
Anxiolytics, n (%)	379 (18.1 %)	2098	95 (18.7 %)	507	106 (20.9 %)	507
Hypnotics/sedatives, n (%)	225 (10.7 %)	2098	56 (11.0 %)	507	94 (18.5 %)	507
Mood stabilizers, n (%)	262 (12.5 %)	2098	170 (33.5 %)	507	218 (43.0 %)	507

‡ Study sample with both a baseline and follow-up measurement; IQR: Interquartile Range; OQ: Outcome Questionnaire; SCORE: Systematic COronary Risk Evaluation; SD: standard deviation; WHO-DAS II: WHO-Disability Assessment Schedule II; "miscellaneous" includes psychotic, substance-related, and somatoform disorders.

analyses were conducted only in patients with persistent presence, because treatment for MetS at both baseline and FU is specifically indicated in these patients.

2.4.3. Regression analyses

Regression analyses (Twisk, 2013) were performed to investigate associations of baseline determinants with changes in continuous severity of MetS and its individual components at FU. In each analysis, the FU value of the continuous MetS variable was the dependent variable and its baseline value was included as an independent variable next to the baseline determinants of interest. First, analyses were run for each combination of determinant and outcome, starting with a crude model that only contained the baseline value of the outcome, followed by models that added one by one determinants of interest. Second, multivariable analyses were run for each outcome, including only the baseline value and the determinants that showed a significant association ($p < 0.05$) in the first step. All analyses were conducted with complete cases. Model assumptions (conditional normality; homoscedasticity) were checked by inspection of residual plots and Q-Q plots. Dependent variables were natural log-transformed and analyses rerun when assumptions were not met. All analyses were conducted with IBM SPSS Statistics version 28.0 for Windows (Armonk, New York, USA). A p-value < 0.05 was considered to indicate statistical significance.

3. Results

3.1. Cross-sectional analyses

3.1.1. Sample characteristics

Table 2 presents the characteristics of the study groups. In the complete baseline study sample ($n = 2098$), 58.6 % was female and the mean age was 46 years (SD = 16). The most frequent psychiatric diagnosis was a depressive disorder (26.6 %), followed by anxiety disorder (21.8 %), personality disorder (14.4 %), and bipolar disorder (14.3 %). In the follow-up subsample ($n = 507$), 60.4 % was female and the mean age was 47 years (SD = 14) at baseline. In this subsample, the most frequent psychiatric diagnosis at baseline was a bipolar disorder (37.7 %), followed by depressive disorder (19.9 %), personality disorder (14.4 %), and anxiety disorder (11.6 %).

3.1.2. The complete study sample: prevalence rates and proportions of treatment of MetS

Of the complete study sample at baseline ($n = 2098$), 34.6 % met the criteria of MetS. More specifically, 62.8 % had elevated blood pressure, 36.3 % had reduced HDL-cholesterol, 29.2 % had elevated triglycerides, 13.9 % had elevated blood glucose, and 61.4 % had elevated waist circumference (Table 3). Of those with MetS, 41.4 % received any MetS treatment; 31.3 % received treatment for elevated blood pressure, 20.5 % for reduced HDL-cholesterol, and 52.0 % for elevated blood glucose. No patients received treatment for elevated triglycerides (Table 3).

3.1.3. The follow-up subsample: prevalence rates and proportions of treatment of MetS

In the follow-up subsample ($n = 507$), 36.7 % met the criteria for MetS at baseline and 41.2 % at FU. More specifically, at baseline, 63.8 % had elevated blood pressure, 38.5 % had reduced HDL-cholesterol, 30.7 % had elevated triglycerides, 12.1 % had elevated blood glucose, and 69.5 % had elevated waist circumference. At FU, this was 65.4 % for elevated blood pressure, 40.2 % for reduced HDL-cholesterol, 33.4 % for elevated triglycerides, 13.5 % for elevated blood glucose, and 68.7 % for elevated waist circumference (Table 4).

In the patients with persistent presence of MetS and/or its individual components' abnormalities, any form of somatic pharmacotherapy was received in 46.1 % of patients with MetS at baseline, while this was 56.6 % at FU. For elevated blood pressure, 33.7 % received treatment at baseline, while this was 44.3 % at FU. For reduced HDL-cholesterol, 27.2 % received treatment at baseline, while this was 37.0 % at FU. For elevated blood glucose, 70.8 % received treatment at baseline, while this was 79.2 % at FU. None of the patients with persistent presence of elevated triglycerides received treatment, neither at baseline nor at FU (Table 4).

Table 3
Prevalence rates and treatment proportions of MetS and its metabolic components' abnormalities in the complete study sample at baseline.

	Complete study sample (n = 2098)[†]	
	Baseline	
	n (%)	Cases with available measurements (n)
Metabolic syndrome (MetS)		
Prevalence rate	348 (34.6 %)	1005
Treatment present	144/348 (41.4 %)	–
Elevated blood pressure		
Prevalence rate	1251 (62.8 %)	1992
Treatment present	391/1251 (31.3 %)	–
Reduced HDL-cholesterol		
Prevalence rate	390 (36.3 %)	1074
Treatment present	80/390 (20.5 %)	–
Elevated triglycerides		
Prevalence rate	314 (29.2 %)	1077
Treatment present	0/314 (0 %)	–
Elevated blood glucose		
Prevalence rate	148 (13.9 %)	1062
Treatment present	77/148 (52.0 %)	–
Elevated waist circumference		
Prevalence rate	1146 (61.4 %)	1866
Treatment present	n/a	–

[†] Numbers (n) and proportions (%) are based on baseline data, see Supplementary Table 1A-F; HDL: high-density lipoprotein; n/a: not applicable.

3.2. Longitudinal analyses

3.2.1. Persistence, new onset, remission of MetS

Table 4 presents the proportions of persistent presence, new onset, remission, and persistent absence of MetS and its individual components' abnormalities in the follow-up subsample. In 77.6 % (76/98) of the subsample, MetS at baseline had persisted at FU, while 22.4 % (22/98) showed remission at FU. Proportions of persistent presence of individual MetS components' abnormalities at FU, were 70.6 % (24/34) for elevated blood glucose, 71.1 % (64/90) for elevated triglycerides, 82.1 % (92/112) for reduced HDL-cholesterol, 82.3 % (225/310) for elevated blood pressure, and 90.1 % (300/333) for elevated waist circumference. This indicated that elevated blood glucose had the highest proportion of remission at FU (29.4 % [10/34]). Furthermore, elevated blood glucose had the lowest proportion of new onset at FU (5.7 % [14/247]).

3.2.2. Paired comparisons between baseline and follow-up measurements

McNemar analyses showed no significant differences between baseline and FU in proportions of MetS and its individual components' abnormalities (Table 4). In the patients with persistent presence of MetS and/or its individual components' abnormalities, a significant but small increase was found between baseline and FU in the treatment of elevated blood pressure ($\chi^2 = 16.5$; $p \leq 0.001$) and in the treatment of reduced HDL-cholesterol ($\chi^2 = 5.8$; $p \leq 0.01$), but not in the treatment of elevated blood glucose or elevated triglycerides (Table 4).

3.2.3. Baseline determinants of change in MetS at follow-up

Table 5 presents results of multivariate regression analyses between baseline determinants and MetS and its individual components at FU,

Table 4
Prevalence rates, persistence, remission, new onset, and treatment proportions of MetS and its metabolic components' abnormalities in the follow-up sample.

	Follow-up sample (n = 507)‡					
	Baseline		Follow-up		McNemar	
	n (%)	Cases with available measurements (n)	n (%)	Cases with available measurements (n)	X^2	*p*
Metabolic syndrome (MetS)						
Prevalence rate	98 (36.7 %)	267	110 (41.2 %)	267	2.16	0.14
Persistent presence	–	–	76/98 (77.6 %)	–		
Treatment present	35/76 (46.1 %)	76	43/76 (56.6 %)	76	3.50	0.57
Remission	–	–	22/98 (22.4 %)	–		
New onset	–	–	34/169 (20.1 %)	–		
Persistent absence	–	–	135/169 (79.9 %)	–		
Elevated blood pressure						
Prevalence rate	310 (63.8 %)	486	318 (65.4 %)	486	0.42	0.52
Persistent presence	–	–	255/310 (82.3 %)	–		
Treatment present	86/255 (33.7 %)	255	113/255 (44.3 %)	255	16.49	<0.001
Remission	–	–	55/310 (17.7 %)	–		
New onset	–	–	63/176 (35.8 %)	–		
Persistent absence	–	–	113/176 (64.2 %)	–		
Reduced HDL-cholesterol						
Prevalence rate	112 (38.5 %)	291	117 (40.2 %)	291	0.36	0.55
Persistent presence	–	–	92/112 (82.1 %)	–		
Treatment present	25/92 (27.2 %)	92	34/92 (37.0 %)	92	5.82	<0.01
Remission	–	–	20/112 (17.9 %)	–		
New onset	–	–	25/179 (14.0 %)	–		
Persistent absence	–	–	154/179 (86.0 %)	–		
Elevated triglycerides						
Prevalence rate	90 (30.7 %)	293	98 (33.4 %)	293	0.82	0.37
Persistent presence	–	–	64/90 (71.1 %)	–		
Treatment present	0/64 (0 %)	64	0/64 (0 %)	64	n/a	n/a
Remission	–	–	26/90 (28.9 %)	–		
New onset	–	–	34/203 (16.7 %)	–		
Persistent absence	–	–	169/203 (83.3 %)	–		
Elevated blood glucose						
Prevalence rate	34 (12.1 %)	281	38 (13.5 %)	281	n/a	0.54
Persistent presence	–	–	24/34 (70.6 %)	–		
Treatment present	17/24 (70.8 %)	24	19/24 (79.2 %)	24	0.25	0.63
Remission	–	–	10/34 (29.4 %)	–		
New onset	–	–	14/247 (5.7 %)	–		
Persistent absence	–	–	233/247 (94.3 %)	–		
Elevated waist circumference						
Prevalence rate	333 (69.5 %)	479	329 (68.7 %)	479	0.15	0.70
Persistent presence	–	–	300/333 (90.1 %)	–		
Treatment present	n/a	n/a	n/a	n/a	n/a	n/a
Remission	–	–	33/333 (9.9 %)	–		
New onset	–	–	29/146 (19.9 %)	–		
Persistent absence	–	–	117/146 (80.1 %)	–		

‡ Study sample with both a baseline and follow-up measurement; numbers (n) and proportions (%) are based on complete cases data, see Supplementary Table 2A-F; HDL: high-density lipoprotein; n/a: not applicable.

adjusted for their baseline values. Results of univariate analyses are presented in Supplementary Table 3. Table 5 showed that, compared to males, females had higher HDL-cholesterol (0.09; 95 % CI [0.05, 0.13]) and lower MAP (-2.06; 95 % [-3.77, -0.35]), when adjusted for these outcomes' baseline values. In addition, older age was associated with a higher baseline-adjusted MAP (0.08; 95 % [0.02, 0.15]) at FU. Furthermore, compared to a high education level, patients with a lower education level had higher baseline-adjusted blood glucose (0.05; 95 % [0.01, 0.09]) at FU. Patients who smoked had lower baseline-adjusted HDL-cholesterol (-0.07; 95 % [-0.12, -0.03]) at FU, compared to patients who never smoked. Compared to patients without diabetes, patients with diabetes had higher baseline-adjusted blood glucose (0.09; 95 % [0.01, 0.18]) at FU. Finally, compared to depressive-disordered patients, anxiety-disordered patients had lower baseline-adjusted triglyceride (-0.26; 95 % [-0.46, -0.05]) and MAP (-2.95; 95 % [-5.85, -0.05]) values at FU.

4. Discussion

In this large transdiagnostic patient group (mean age: 46 years) with common mental disorders visiting outpatient clinics in specialized mental healthcare, we found a prevalence rate of MetS at baseline of 36.7 % and at FU of 41.2 %. Abnormalities in its individual components persisted (range: 70.6 %–90.1 %) over a median FU time of 11 months. In those patients who persisted in individual metabolic components' abnormalities, treatment proportions ranged from 27.2 % (reduced HDL-cholesterol) to 70.8 % (elevated blood glucose) at baseline, while this ranged from 37.0 % (reduced HDL-cholesterol) to 79.2 % (elevated blood glucose) at FU. None of the patients with persistent elevated triglycerides received treatment, neither at baseline nor at FU. In multivariate analyses, female sex was associated with higher HDL-cholesterol levels and lower MAP at FU. Older age was associated with higher MAP at FU. Low educational level was associated with higher blood glucose levels at FU, compared to high educational level. Furthermore, current smoking behavior was associated with lower HDL-cholesterol levels at FU, compared to patients who never smoked. Having diabetes was associated with higher blood glucose levels at FU, compared to patients without diabetes. Finally, patients with anxiety disorders showed lower triglycerides levels and MAP at FU, compared to patients with a depressive disorder. No determinants of waist circumference and *Z*-score MetS severity were found in multivariable analyses.

Table 5
Overview of multivariate analyses results between baseline covariates and changes in MetS severity and its individual components at follow-up[‡].

	Triglycerides ($n = 293$)[b†]			HDL-cholesterol ($n = 291$)[b†]			Blood glucose ($n = 281$)[b†]			Mean Arterial Pressure ($n = 486$)[b]		
Baseline covariates[a]	Estimates	CI 95 %		Estimates	CI 95 %		Estimates	CI 95 %		Estimates	CI 95 %	
Reference	0,40***	0,34	0,47	0,48***	0,43	0,53	0,11***	0,09	0,13	0,62***	0,56	0,69
Sex (reference: Male)												
Female	−0,09	−0,21	0,02	0,09***	0,05	0,13	–	–	–	−2,06*	−3,77	−0,35
Age	–	–	–	–	–	–	–	–	–	0,08*	0,02	0,15
Education level (reference: high education level)												
Low education level	–	–	–	–	–	–	0,05*	0,01	0,09	–	–	–
Medium education level	–	–	–	–	–	–	0,02	−0,01	0,06	–	–	–
Smoking (reference: never smoked)												
Current smoker	–	–	–	−0,07**	−0,12	−0,03	–	–	–	–	–	–
Former smoker	–	–	–	−0,04	−0,09	0,02	–	–	–	–	–	–
Somatic comorbidity												
Diabetes	–	–	–	–	–	–	0,09*	0,01	0,18	–	–	–
Hypercholesterolemia	–	–	–	–	–	–	0,02	−0,02	0,06	–	–	–
Cardiovascular disease	–	–	–	–	–	–	–	–	–	–	–	–
Obesity	–	–	–	–	–	–	–	–	–	–	–	–
Psychiatric diagnosis (reference: depressive disorders)												
Anxiety disorders	−0,26*	−0,46	−0,05	–	–	–	0,00	−0,06	0,06	−2,95*	−5,85	−0,05
Personality disorders	−0,17	−0,34	0,01	–	–	–	−0,02	−0,07	0,03	−2,14	−4,93	0,64
Bipolar disorders	−0,02	−0,17	0,14	–	–	–	0,01	−0,03	0,05	−1,72	−3,86	0,41
Developmental disorders	0,24	−0,02	0,49	–	–	–	0,02	−0,05	0,09	0,35	−3,64	4,35
Miscellaneous	−0,08	−0,31	0,15	–	–	–	0,06	−0,01	0,12	−1,37	−4,93	2,18
Psychotropic drugs												
Use of psychotropic drugs	–	–	–	–	–	–	–	–	–	–	–	–
TCA	–	–	–	–	–	–	–	–	–	–	–	–
SSRI	–	–	–	–	–	–	–	–	–	–	–	–
MAO-inhibitors	–	–	–	–	–	–	–	–	–	–	–	–
Other antidepressants	–	–	–	–	–	–	–	–	–	–	–	–
Typical antipsychotics	–	–	–	–	–	–	–	–	–	–	–	–
Atypical antipsychotics	–	–	–	–	–	–	–	–	–	–	–	–
Anxiolytics	−0,12	−0,26	0,01	–	–	–	–	–	–	–	–	–
Hypnotics/sedatives	–	–	–	–	–	–	–	–	–	–	–	–
Mood stabilizers	–	–	–	–	–	–	–	–	–	–	–	–

[a] Based on baseline measurement.
[b] Based on complete cases data; CI: confidence interval; HDL: high-density lipoprotein; MAO: monoamine oxidase; SSRI: selective serotonin reuptake inhibitor; TCA: tricyclic antidepressant.
[†] Natural log transformed.
[‡] No significant associations were found in univariate analyses of waist circumference and *Z*-score MetS.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

4.1. Proportions of MetS and its individual components' abnormalities

The prevalence rates of MetS in the current study were similar to those previously reported in patients with depressive, bipolar, or anxiety disorders (30.5–37.3 %) (Moreira et al., 2019; Skogberg et al., 2022; Vancampfort et al., 2015, 2014, 2013). In addition, the prevalence rates for reduced HDL-cholesterol, elevated triglycerides, and elevated blood glucose in the current study were similar to those previously reported in patients with mood and anxiety disorders (reduced HDL-cholesterol [27.8 %–52.0 %]; elevated triglycerides [30.1 %–49.7 %]; elevated blood glucose [11.4 %–25.4 %]) (Bruins et al., 2017; Hung et al., 2014; Vancampfort et al., 2014, 2013). However, in the current study, the prevalence rate of elevated blood pressure (63.8 %–65.4 %) and elevated waist circumference (68.7 %–69.5 %) were higher compared to previous work (elevated blood pressure [36.7 %–47.1 %]; elevated waist circumference [38.0 %–50.3 %]) (Vancampfort et al., 2015, 2014, 2013). A possible explanation for these differences might be that the mean age of the current study population (46.9 years) was higher than in previous studies (41.3–45.5 years) (Vancampfort et al., 2015, 2014, 2013). Both waist circumference and blood pressure are known to increase with age (Chow et al., 2013; Stevens et al., 2010).

Longitudinal analyses showed that the prevalence rate of MetS and its individual components did increase slightly, while the rates of elevated waist circumference decreased, although these changes were not significant. In addition, persistence rates ranged from 70.6 % for elevated blood glucose to 90.1 % for elevated waist circumference. There are at least four possible explanations for these high persistence rates. First, age of the follow-up subsample increased. It is well-known that the prevalence rate of MetS increases with age (Hildrum et al., 2007). Second, we observed an increase in somatic-drug use. Cases meet the ATP III criteria for an individual metabolic abnormality when the individual receives a somatic prescription for that abnormality (Grundy et al., 2005). Therefore, an increase in somatic drug prescription may have led to more cases meeting ATP criteria for individual metabolic components. Third, there was an increase in psychotropic drug use between baseline and FU (Table 2). Previous literature has indicated that antipsychotic and antidepressant drugs, and mood stabilizers may negatively impact on metabolic abnormalities in patients with mental disorders (Mazereel et al., 2020). Although we did not formally test whether psychotropic drug use persisted or increased between baseline and FU, the presence of psychotropic drugs may have still impaired recovery of metabolic abnormalities and contributed to their persistence in the long-term. Fourth, although we did not formally test the lifestyle behaviors of our study sample, it is well known that, associated with their psychiatric condition, unhealthy lifestyle patterns can substantially contribute to persistence of metabolic syndrome components in patients

with common mental disorders (Firth et al., 2020). Although there is an increased awareness among healthcare professionals of the negative impact of somatic outcomes on mental health outcomes, still regrettably, very few lifestyle programs are implemented in psychiatric treatment programs.

4.2. Low somatic treatment rates: potential explanations and solutions

The low treatment rates for individual components' abnormalities aligns with previous findings. A cross-sectional study by Godin et al. (2019) in 205 patients with treatment-resistant depression showed that 29.4 % received treatment for hypertension. Furthermore, 15.0 % received treatment for lipid disorders (reduced HDL-cholesterol and/or elevated triglycerides (Godin et al., 2019)), the latter being substantially lower than in our study. In the current study, 27.2 % of the patients who persisted in reduced HDL-cholesterol were treated for this at baseline, while this was 37.0 % at FU. Interestingly, no patients were treated for persistent elevated triglycerides at either time point. A possible explanation for the latter may be that the Dutch cardiovascular risk assessment guideline does provide specific recommendations on statin use to control lipid levels, considering the relatively stronger effect of statins compared to fibrates ("Behandeling lipiden CVRM - Richtlijn - Richtlijnendatabase", n.d.). When we combined treatment rates in cases with persistent reduced HDL-cholesterol and/or elevated triglycerides, treatment rates for at least one of the two metabolic abnormalities (baseline: 20.8 %; FU: 30.0 %) were more in line with Godin et al. (2019) (Godin et al., 2019). Other previous studies among patients with bipolar disorders showed similar or even lower percentages of treatment for hyperglycemia (18.0 %–24.0 %), lipid disorders (16.0 %–36.7 %), and hypertension (22.0 %–79.2 %), compared the those in the current study (de Jong et al., 2018; Kreyenbuhl et al., 2006; Schuster et al., 2021; Smith et al., 2013). Furthermore, Bruins et al. (2017) found that in the PHAMOUS program, which is a parallel program to MOPHAR and designed for patients with psychotic disorders or mood disorders with psychotic features, only half of the patients with metabolic abnormalities actually received somatic treatment, despite being recommended pharmacotherapy for hypertension, dyslipidemia, and hyperglycemia by the CPGs and being monitored for at least 3 years (Bruins et al., 2017). This indicates that while regular monitoring is present through monitoring programs including MOPHAR and PHAMOUS, this does not necessarily lead to the recommended interventions. In fact, a recent study in $n = 1283602$ patients with mental disorders found that they are 20-25 % less likely to be treated for cardiovascular diseases compared to comparable individuals without mental disorders (Solmi et al., 2021).

There are several explanations for the low somatic treatment rates observed in the current study. First, mental healthcare professionals may lack the necessary training and experience to appropriately recognize and address the somatic-care needs of their patients (Kohn et al., 2022). This situation may be maintained by insufficient communication and differing views between psychiatric and general practice healthcare professionals in the Netherlands about who is responsible for screening and treatment of somatic abnormalities in psychiatric outpatients (van Hasselt et al., 2015). Generally, in daily practice the treating psychiatrists are responsible for somatic monitoring of their patients, but when faced with abnormalities, they refer to general practitioners for treatment of these abnormalities (Brouwer et al., 2021; Nederlof et al., 2018). Subsequently, whereas in psychiatric practice MetS criteria are used as the gold standard, in general practice different standards, criteria, and cut-off values are used to assess cardiovascular risk (Quadackers et al., 2023). Cardiovascular risk in somatic primary care is expressed in mortality risk (SCORE (Conroy et al., 2003)), whereas in psychiatric care, this is expressed in the presence or absence of MetS. Quadackers et al. (2023) observed that the cardiovascular risk in psychiatric patients may be underpredicted when using the SCORE model, potentially leading to undertreatment (Quadackers et al., 2023). In view of the increased somatic morbidity and mortality risk of psychiatric conditions, this means that mood- and anxiety-disordered patients are not receiving the necessary somatic treatment, not even when they are actually screened (Quadackers et al., 2021). Finally, CPGs on somatic monitoring in psychiatric conditions lack clear and well-defined instructions on how to respond to aberrant monitoring parameters in this group (Brouwer et al., 2021; Nederlof et al., 2018). Hence, there is a need to bridge the gap between standards in somatic and psychiatric care. An example of a suggested solution is to multiply the SCORE value by 1.5 for mood- and anxiety-disorder patients, to correct for a potential underestimation of mortality risk (Quadackers et al., 2023, 2021).

4.3. Baseline determinants of change at follow-up in MetS and its individual components

Female sex was a determinant of higher HDL-cholesterol and lower MAP at FU, which can be partly explained by a protective estrogen effect in pre-menopausal women as compared to men (Maranon and Reckelhoff, 2013; Wang et al., 2011). In addition, increasing age was associated with higher baseline-adjusted MAP at FU, which has been widely acknowledged in previous literature (Mills et al., 2020; Mutz et al., 2022). The association between education level and elevated blood glucose levels is corroborated by previous literature indicating that low educational level is associated with an overall increased risk of type 2 diabetes mellitus (Agardh et al., 2011; Sacerdote et al., 2012), and low levels of physical activity and unhealthier lifestyle (Kari et al., 2020; Teo et al., 2013). With regard to smoking, our finding is supported by previous literature indicating that smokers have significantly lower HDL-cholesterol levels compared to non-smokers (Craig et al., 1989; Nakamura et al., 2009) and smoking cessation is associated with an increase in HDL-cholesterol (Forey et al., 2013). Furthermore, having diabetes is associated with higher baseline-adjusted blood glucose levels at FU. In fact, hyperglycemia is common in patients with diabetes mellitus type 1 or 2, due to the lack of insulin production or insulin resistance (World Health Organization, 2023). Finally, anxiety disorders were associated with a baseline-adjusted decrease in triglycerides and MAP at FU, compared to depressive disorders. For triglycerides, this finding aligns with a study by De Kluiver et al. (2021), who found that patients with depression have significantly higher levels of, for example triglycerides, whereas these levels are significantly lower in patients with an anxiety disorder, both compared to healthy controls (de Kluiver et al., 2021). This may indicate that factors including overweight and unhealthy lifestyle may be more strongly associated with depressive than with anxiety disorders (de Kluiver et al., 2021). With regard to MAP, previous literature has suggested that both depressive and anxiety disorders are associated with low blood pressure (Hildrum et al., 2011, 2008) rather than high blood pressure, compared to healthy controls (Shinn et al., 2001). A possible explanation may be that anhedonia and lack of motivation and, consequently, less physical activity may be less urgent in anxiety disordered-patients than in depressive disordered-patients, as physical activity is associated with lower blood pressure (Borjesson et al., 2016). Indeed, it has previously been found that depressed patients are less active than those with anxiety disorders (Helgadóttir et al., 2015).

4.4. Strengths and limitations

Strengths of the current study are the relatively large and diverse naturalistic population of patients with affective, anxiety, personality, and developmental disorders and the prospective study design with systematically gathered determinant variables, psychological and somatic outcome variables, and medication data. However, some limitations need to be mentioned when interpreting the results. First, our study population did not include a comparison group of mentally healthy individuals from the general population to study the time course of MetS. Second, the current naturalistic setup only allows monitoring patients who are still being treated at our outpatient services. As a result

of selection bias, this may lead to over-representation of i.e., bipolar disordered-patients, who tend to have longer treatment trajectories and use more psychotropic medication, which are both associated with MetS and/or metabolic abnormalities (Chakrabarti et al., 2012; Vancampfort et al., 2013). Third, we did not have data on lifestyle interventions as a form of somatic treatment, which might partly have explained the observed low pharmacotherapeutic treatment rates. The observed treatment rates may therefore underestimate the total treatment rates in the studied sample. Fourth, we were unable to reliably test whether patients were treated according to guideline recommendations, considering low number of patients, because of missing necessary information (see Supplementary Material 3A and 3B for complete results). Fifth, the proportion of missing data and choice to run complete-case analyses may have influenced the current findings of the regression analyses (e.g., reduction of generalizability and statistical power). We decided to conduct our analyses in complete cases only, because we found that after multiple imputation, a number of assumption violations (not normally distributed residuals and heteroscedasticity) occurred, which were not present prior to multiple imputation. However, as this study was more exploratory in nature, the current findings can be informative for future research's feature selection of determinants to establish a model for predicting change in metabolic parameters over multiple time points in patients with mood- and anxiety disorders. Finally, in our opinion, a limitation of the MetS concept is that cases meet the ATP III criteria for an individual metabolic abnormality when the individual receives a somatic prescription for that abnormality (Grundy et al., 2005), regardless of any normalization in metabolic components due to somatic prescription. Therefore, to assess whether somatic treatment leads to improved prevalence rates of MetS and its individual components' abnormalities, we would recommend to exclude somatic treatment from the ATP III criteria in future research.

In conclusion, the prevalence rate of MetS and its individual components' abnormalities were high and did not significantly change over time in patients with mood and anxiety disorders. In addition, treatment rates were low and, with the exception of treatment for elevated blood pressure and reduced HDL-cholesterol, did not significantly improve over time, even when metabolic abnormalities persisted. This indicates that metabolic abnormalities are treated insufficiently, even in a setting where metabolic abnormalities are monitored. A solution to increase treatment rates of MetS and its individual components' abnormalities could be to better integrate somatic and psychiatric care.

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CRediT authorship contribution statement

Jurriaan M.J.L. Brouwer: Conceptualization, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Klaas J. Wardenaar:** Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Edith J. Liemburg:** Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Bennard Doornbos:** Investigation, Writing – original draft, Writing – review & editing. **Hans Mulder:** Conceptualization, Investigation, Supervision, Writing – original draft, Writing – review & editing. **Danielle C. Cath:** Conceptualization, Investigation, Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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