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Prevalence of metabolic syndrome and its associated risk factors in an African–Caribbean population with severe mental illness

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ABSTRACT

This cross-sectional study aims to determine the prevalence of metabolic syndrome (MetS) in patients with severe mental illness (SMI) on a Caribbean island, Curaçao, using the modified National Cholesterol Education Program Adult Treatment Panel III criteria. Among 350 patients (240 men and 110 women) with a mean age of 51.9 years (*S.D.* = 13.5) MetS prevalence was 37.4%, significantly higher in female patients (63.6%) compared to male patients (25.4%). Increased waist circumference was present in 51.1%, low HDL in 50.6%, hypertension in 49.4%, hyperglycemia in 28.6% and 25.7% had hypertriglyceridemia. Except for hypertriglyceridemia, all criteria were more prevalent in female patients. Binary logistic regression analysis indicated that female gender, outpatient treatment setting and the absence of substance use disorder were all significant predictors for MetS. Compared to data from the general population obtained by the 2013 National Health Survey Curaçao, this study showed significantly higher prevalence of diabetes and hypertension in patients with SMI. Moreover, female patients had the highest prevalence of diabetes (28.2%), obesity (50.0%) and increased waist circumference (88.2%). This study demonstrates that African-Caribbean patients with SMI are at high-risk for MetS, especially female patients. Our data suggest to focus on modifiable lifestyle risk factors, as promoting physical activity and healthy dietary habits.

1. Introduction

People with severe mental illness (SMI) have a 2–2.5 times higher risk of premature mortality with a 10–20 years reduced life expectancy compared to the general population (Chesney et al., 2014; Walker et al., 2015). Premature mortality for people with SMI occurs in two-thirds of the cases by natural causes -mainly cardiovascular disease (CVD) and one-third by unnatural causes, including suicide and accidental death (Correll et al., 2017; Liu et al., 2017; Reininghaus et al., 2015; Ringen et al., 2014). The concept of metabolic syndrome (MetS) was introduced to facilitate identification of people with a high-risk of developing CVD. MetS clusters 5 risk factors for CVD: an increased waist circumference, an elevated fasting glycaemia, hypertension, low high-density lipoprotein (HDL) level and hypertriglyceridemia. In the general population MetS is associated with a 2-fold risk for developing CVD within 5–10 years and a 5-fold risk for developing type 2 diabetes mellitus (Alberti et al., 2005; Eckel et al., 2005). Various validated and reliable definitions of MetS have been formulated by different expert groups (Alberti et al., 2006, 2009; Grundy et al., 2005; Stone et al., 2005).

The high burden of CVD morbidity and mortality among people with SMI appears to have a multifactorial etiology (De Hert et al., 2011a; Nousen et al., 2013; Penninx, 2017). To name a few: first, lifestyle risk factors including smoking, substance abuse, lack of physical activity and bad dietary habits are highly prevalent in people with SMI (Carra et al., 2014; Dipasquale et al., 2013; Osborn et al., 2008; Vancampfort et al., 2017). Second, health care avoidance and factors related to a lower socioeconomic status as poor access to health care services frequently occur (De Hert et al., 2011a, b). Third, psychotropic drugs such as antipsychotics, mood stabilizers and certain

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antidepressants can induce weight gain and metabolic dysregulation (Bak et al., 2014; Correll et al., 2015; Mitchell et al., 2013a; Stahl et al., 2009). Also, there is growing evidence for a common pathophysiological ground between MetS and SMI for the development of metabolic abnormalities involving inflammatory processes, hypothalamic-pituitary-adrenal axis dysregulation, shared genetic vulnerabilities and epigenetic interactions (Mori et al., 2015; Peerbooms et al., 2011; Schiavone and Trabace, 2017; van Winkel et al., 2010; Vancampfort et al., 2013). Consequently, early glucose dysregulation has been demonstrated in antipsychotic-naïve patients experiencing a first-episode psychosis (Perry et al., 2016; Pillinger et al., 2017). Moreover, a significantly increased prevalence of diabetes was found in relatives of patients with schizophrenia, supporting for a genetic link between SMI and the glucose homeostasis (Van Welie et al., 2013). In summary, patients with SMI seem to be more susceptible to develop MetS in the course of their mental illness compared to the general population (Mitchell et al., 2013b; Vancampfort et al., 2015).

Indeed, the high prevalence of MetS in patients with SMI is illustrated by a meta-analysis of Vancampfort et al. (2015) reporting a pooled MetS prevalence of 33.6% in people with SMI, corresponding with a 1.6 fold increased risk for MetS compared to the general population. This meta-analysis has shown that MetS prevalence did not significantly differ by gender, but significantly increased with older age and higher BMI. Some heterogeneity was seen in the pooled MetS prevalence rates between different geographical regions: European studies (32.0%), studies performed in the United States (36.4%), Canada (27.4%), South-America (25.8%), Australia (50.2%), Asia (31.0%), and South-Africa (23.0%) (Vancampfort et al., 2015). The prevalence of MetS seems to be lower in African studies e.g. Ghana (14.1%) and South-Africa (23.0%), this may be partly explained by the age differences between study samples (Owusu-Ansah et al., 2018; Saloojee et al., 2016). Unfortunately, meta-analyses did not analyze ethnicity as a mediating variable due to incomplete data on ethnic distribution in most studies (Mitchell et al., 2013b; Vancampfort et al., 2015). In contrast, the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study conducted in 2009 in the USA, is to date one of the largest data sets on MetS in patients with schizophrenia where ethnic distribution was taken into account (McEvoy et al., 2005). The CATIE study found that gender and ethnicity were both significant predictors for MetS, with female patients among all ethnic groups exhibiting a higher risk for developing MetS. Prevalence of MetS was almost twice as common among African–American female patients (43.1%) compared to the African-American male patients (22.7%) (McEvoy et al., 2005). Also, population-based studies demonstrated a varying MetS prevalence among ethnic groups, especially women of African descent appear to be at greater risk for MetS (Agyemang et al., 2012; Ferguson et al., 2010a, b; Khan et al., 2015; Moore et al., 2017; Tillin et al., 2005).

There is paucity of data regarding MetS prevalence in African–Caribbean populations with SMI (Francis et al., 2015). One Jamaican study with a small sample of 38 patients with SMI found a MetS prevalence of 28.9%, compared to 18.4% in the general population (Ferguson et al., 2010a, b; Gossell-Williams et al., 2012). No studies on the prevalence of MetS have so far been undertaken in Curaçao. Despite that, epidemiological studies show that the Caribbean region is currently suffering from an obesity and diabetes epidemic, with a major health challenge of non-communicable diseases (Alleyne, 2018; Ferguson et al., 2010a, b; Pan American Health Organization, 2011; Razzaghi et al., 2019). Caribbean countries also share the same lifestyle risk factors such as a sedentary lifestyle and unhealthy dietary habits. Also in Curaçao, the 2013 National Health Survey showed also a high prevalence of diabetes (9.3%) and obesity (28.3%) in the general population (Verstraeten et al., 2013). As obesity and a sedentary lifestyle are known to be the driving forces of MetS, and taking into account the characteristics of the general population and the pre-existing risk for MetS in people with SMI, we assume that the prevalence of MetS in SMI in Curacao will be among the highest MetS prevalence reported globally, particularly in women (Grundy, 2008). The aim of the study is to investigate the prevalence of MetS in African-Caribbean patients with SMI in Curaçao. In addition, possible risk factors are assessed for their association with MetS

2. Materials and methods

2.1. Study setting

Curaçao had at the time of study approximately 155,000 inhabitants with a male to female ratio of 0.84. Median age of the population is 39.8 years, and life expectance is 81.0 years for women and 75.4 years for men (Central Bureau of Statistics Curaçao, 2015). The majority of the people in Curaçao are African–Caribbean or mixed ethnicity (85%) and there are Dutch, Latin-American, Jewish and Asian minorities (15%) (Pan American Health Organization, 2012). The healthcare system in Curaçao, a former colony of the Netherlands, is based on the Dutch healthcare system i.e. all inhabitants have access to high standard healthcare services and are entitled to medical insurance coverage. Curaçao has a high-income economy, with one of the highest standard of living in the Caribbean region (Pan American Health Organization, 2017). On estimation based, 90% of all people with SMI in Curaçao are receiving care by the only mental health institution in Curaçao, namely “Stichting Geestelijke Gezondheidszorg Curaçao” (GGz Curaçao). The 199-bedded Dr. David Ricardo Capriles (Klinika Capriles), part of GGz Curaçao, is the only psychiatric hospital in Curaçao and has a solid staff of 5 full-time psychiatrists, from them 2 were trained in the Netherlands and 1 in Belgium (Stichting Geestelijke Gezondheidszorg Curaçao, 2015).

2.2. Study participants

Eligible study participants were recruited from the inpatient and outpatient's services of the psychiatric hospital Klinika Capriles and the supportive housing “Fundashon Sonrisa” which are part of GGz Curaçao (PJG). Study enrollment took place between May 2014 and September 2014. All participants were 18 years and older and suffered from a serious mental illness (see Table 1). Psychiatric diagnoses were confirmed by a clinical psychiatrist, based on the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders IV-Text Revision (DSM-IV-TR). The psychiatric diagnoses were noted in the in the electronic patient dossier and were crosschecked by co-author (PJG) for each patient before inclusion in this study. Substance use disorder (SUD) was considered as a comorbid psychiatric diagnosis. The psychiatric diagnoses are shown in Table 1. Information on the duration of illness was extracted from the electronic medical records (PJG) and had to be at least 2 years, causing substantial impairment in one or more major life activities (Ruggeri et al., 2000).There were no exclusion criteria. The study was approved by the Ethical Committee of the Caribbean Medical University (Willemstad, Curaçao) (IRB00011617). One of the authors (PJG) wrote the study statement in Papiamentu and in Dutch. The treating psychiatrists explained the purpose of the study to each patient individually. Thereafter, oral and written informed consents were obtained from all study participants.

2.3. Data collection

Clinical data such as psychiatric diagnosis, relevant medical conditions, use and dose of pharmacological treatment, smoking and demographic data were retrieved from the electronic medical records by the psychiatrist (PJG). All data were crosschecked through patient interview and missing data were asked during the same interview by trained medical students in a uniform way (PJG). The chlorpromazine equivalent dose was calculated for all prescribed antipsychotics, resulting in a summed daily dose for each participant (Gardner et al.,

Table 1
Demographic and clinical characteristics of the study patients differentiated by gender.

	All (n = 350)	Male (n = 240)	Female (n = 110)	P-value
Age (year), mean ± SD	51.9 ± 13.5	50.1 ± 13.9	55.8 ± 11.8	<.001
Age group (year),%(*n*)				<.001
18–24	2.6(9)	3.3(8)	0.9(1)	.183
25–34	9.7(34)	12.1(29)	4.5(5)	.027
35–44	18.0(63)	20.0(48)	13.6(15)	.150
45–54	25.1(88)	26.3(63)	22.7(25)	.481
55–64	18.0(63)	20.0(48)	13.6(15)	.150
65–74	28.0(98)	27.1(65)	30.0(33)	.573
75–84	13.4(47)	7.1(17)	27.3(30)	<.001
Treatment setting,%(n)				.206
Inpatients	47.7(167)	50.0(120)	42.7(47)	
Outpatients	53.3(183)	50.0(120)	57.3(63)	
Psychiatric diagnosis,%(*n*)				<.001
Schizophrenia	69.4(243)	77.5(186)	51.8(57)	
Other psychotic disorder	14.0(49)	12.1(29)	18.2(20)	
Schizoaffective disorder	6.9(24)	3.3(8)	14.5(16)	
Bipolar disorder	5.1(18)	3.3(8)	9.1(10)	
Depressive disorder	2.0(7)	0.8(2)	4.5(5)	
Other diagnosis	2.6(9)	2.9(7)	1.8(2)	
Comorbid substance related disorder	38.0(133)	52.1(125)	7.3(8)	<.001
Smoking, yes/no, %(n) §	38.9(136)/30.6(107)	47.5(114)/19.2(46)	20.0(22)/55.5(61)	<.001b
Anthropometric measurements				
Waist circumference (cm)	99.0 ± 15.1	96.2 ± 13.8	105.1 ± 16.2	<.001
Systolic BP(mmHg)	122.5 ± 15.1	120.9 ± 14.4	126.1 ± 15.9	.002
Diastolic BP(mmHg)	77.7 ± 10.3	77.3 ± 9.9	78.4 ± 11.0	.193
HDL (mg/dL)*	42.0 ± 17.0	41.0 ± 16.0	48.0 ± 19.0	<.001
TG (mg/dL)*	93.0 ± 65.0	97.0 ± 66.0	88.5 ± 66.0	.05
FG (mg/dL)*	88.0 ± 17.0	87.0 ± 15.0	90.5 ± 27.0	.004
BMI (kg/m^2)	27.0 ± 6.2	25.6 ± 5.3	30.5 ± 6.7	<.001
BMI category %(*n*)				<.001
Underweight <18.5	2.9(10)	4.2(10)	0.0(0)	.037
Normal ≥18.5–<25.0	33.4(117)	40.8(98)	17.3(19)	<.001
Overweight ≥25.0–<30.0	30.0(105)	33.8(81)	21.8(24)	.063
Obesity ≥30.0	28.0(98)	17.9(43)	50.0(55)	<.001

All data are described as proportions and number %(n), as mean ± standard deviation or as (*) median ± interquartile.
P-values are described at <.01 meaning statistical significance. (§)30.6% missing data.
Abbreviations: MetS = metabolic syndrome, BP = blood pressure, HDL = high-density lipoprotein, TG = triglycerides, FG = fasting glucose, BMI = Body Mass Index.

2010). Anthropometric measurements were gathered by the general practitioner (SC) from Klinika Capriles at the same time period of the study inclusion, or by medical students trained by the general practitioner (SC), using the same standardized protocol together with a trained nurse. Blood pressure was measured once in sitting position after a 5-minutes rest using a calibrated sphygmomanometer. Weight was measured to the nearest 0.1 kg with a calibrated standard scale and height was measured to the nearest 1 cm without shoes, according to a standardized protocol. Waist circumference was measured using the standardized World health organization (WHO) method, midway at the top of the iliac crest and lower margin of the ribs in a standing position after expiration placing tape in a horizontal plane measured to the nearest 0.5 cm (World Health Organization, 2011). Body Mass Index (BMI) was divided underweight <18.5 kg/m^2, normal ≥18.5–<25.0 kg/m^2, overweight ≥25.0–<30.0 kg/m^2 and obesity ≥30.0 kg/m^2 (World Health Organization, 2018). The following blood laboratory tests: high density lipoprotein (HDL) cholesterol, total triglycerides and fasting blood glucose were obtained by 8 h-overnight fasting venous blood samples. In the case that a laboratory result was available up to a maximum of 9 months prior to the anthropometric measurements, these data were used. In case of older blood results, a new fasting blood sample was collected and analyzed. Blood samples were analyzed using the ARCHITECT ci8200 integrated analyzer (Abbott). Plasma glucose was measured in fluoride-plasma with an Abbott hexokinase method, serum HDL-Cholesterol was measured with an Abbott homogeneous Ultra HDL assay and triglycerides were measured with an Abbott enzymatic method, making use of lipase.

2.4. Definition of metabolic syndrome

To assess MetS, we applied the diagnostic criteria of the National Cholesterol Education Program Adult Treatment Panel III with the adapted value of fasting glucose of 100 mg/dl as suggested by the American Diabetes Association (ATP-III-A) (Stone et al., 2005). The ATP-III-A criteria are feasible to use in clinical settings and are widely applied in research studies, this facilitates comparison of our findings with other studies (Eckel et al., 2005; Vancampfort et al., 2015). To diagnose MetS, the presence of 3 or more of the 5 criteria are required: an increased waist circumference (>102 cm in males, >88 cm in females), high blood pressure (systolic ≥ 130 mmHg or diastolic ≥ 85 mmHg), low HDL (< 40 mg/dL in males, < 50 mg/d in females), hypertriglyceridemia (≥ 150 mg/dL) and elevated fasting glucose (FG ≥ 100 mg/dL). The criteria were also satisfied when treatment was used for hypertension, low HDL, hypertriglyceridemia or diabetes.

2.5. Comparison to the general population

The National Health Survey Curaçao (NHSC) is a large population-based survey performed in 2013, which aimed to gather nationally representative data on important health determinants and health status of the adult population (Verstraeten et al., 2013). The detailed description of the methodology of the NHSC is published on the website of the Institute for Public Health Curaçao. In brief, the survey was based on the international validated and standardized protocol of the European Health Interview Survey and the European Health Examination

Survey (EHES) (Eurostat, 2010; Tolonen, 2013). Self-reported data from 3000 participants were collected through face-to-face interviewing during January 2013 and February 2013. To ensure that the data were representative for the general population, sample weights were applied to correct for differences in gender and age. The following control indicators from the NHSC were used to compare to our data: self-reported diabetes, hypertension and BMI-category. In 401 participants, waist circumference was measured using the same protocol as in our study (Tolonen, 2013). To compare our data with the NHSC data, we used the criteria of the EHES for the diagnosis of diabetes and hypertension in the study patients: fasting glucose ≥126 mg/dl or on treatment with antidiabetics and systolic blood pressure ≥140 mmHg or diastolic ≥90mm Hg or on treatment with antihypertensive medication, respectively (Tolonen, 2013).

2.6. Statistical analysis

All statistical analyses were performed using SPSS Statistics® (version 25). Descriptive statistics were computed for all demographic and clinical data. Continuous variables were presented as mean ± standard deviation for normally distributed data or as median ± interquartile range for non-normally distributed data. Categorical variables were expressed as proportions and frequencies. Differences between normally distributed continuous variables were assessed by means of the independent student's t-test, differences between non-normally distributed variables by the Mann–Whitney U test and differences between categorical data were analyzed using chi-square analysis. To reduce type 1 errors and to correct for multiple testing in the univariate analysis, a p-value of $<.01$ was considered as statistically significant (Perezgonzalez, 2015). Additionally, a binary logistic regression analysis was conducted to assess the relationship of the presence of MetS (yes/no) as the dependent binary variable with possible independent predictor variables. We applied the hierarchical entry method. To control for the effect of gender and age, these variables were entered in the first block. In the second block, the variables that were significantly associated with MetS in the univariate analysis were entered. In the binary logistic regression analysis, a p-value of $<.05$ was regarded as statistically significant. Finally, prevalence rates of the control variables: diabetes, hypertension, waist circumference and BMI-category within the study sample were compared to the prevalence rates in the general population using chi-square analysis for categorical data.

3. Results

3.1. Demographic and clinical characteristics of the study patients

There were 419 patients with SMI (287 men and 132 women) enrolled in the study, only 350 patients (240 men and 110 women) had sufficient data including laboratory and clinical measurements to assess MetS using the ATP-III-A definition. Table 1 shows the demographic and clinical characteristics of the 350 study patients differentiated by gender. There were significantly more male patients (68.6%) than female patients (31.4%) included in this study (χ^2 (1) = 48.29, $p < .001$). Female patients were significantly older ($M = 55.8$ years, $S.D. = 11.8$) than male patients ($M = 50.1$ years, $S.D. = 11.8$, $p < .001$). A significant association between gender and psychiatric diagnosis was found, with male patients more likely to be diagnosed with schizophrenia and related psychotic disorders and female patients more likely to be diagnosed with affective and other disorders ($\chi^2(2) = 6.03$, $p = .01$). There was a high rate of comorbid substance use disorder (SUD) (38.0%), significantly more male patients (52.1%) than female patients (7.3%) were diagnosed with SUD. Cocaine use disorder is the most common SUD (28.9%), followed by cannabis use disorder (28.1%) and alcohol use disorder (24. 9%). For all patients, data on the use and dosage of psychotropic drugs were available. The pharmacological treatment of the patients is displayed in Table 2. Olanzapine was most frequently prescribed (42.9%) followed by haloperidol (24.9%).

3.2. Prevalence of metabolic syndrome and its criteria

Table 3 presents the prevalence of MetS and its 5 criteria differentiated by gender. The overall MetS prevalence according to the ATP-III-A definition was 37.4%. Female patients had a significantly higher MetS prevalence (63.6%,) compared to their male counterparts (25.4%) ($\chi^2(1) = 47.1$, $p < .001$). Patients with MetS were significantly older ($M = 54.7$ years, $S.D. = 11.9$) compared to patients without MetS ($M = 50.2$ years, $S.D. = 14.2$, $p = .003$). The peak prevalence in MetS was in the 55–64 year-age-group in men (31.1%) and in the ≥65 year-age-group in women (31.4%). Patients with MetS had a significantly higher BMI ($M = 30.7\ kg/m^2$, $S.D. = 6.7$) than patients without MetS ($M = 24.9\ kg/m^2$, $S.D. = 4.7$, $p < .001$). The most common criterion in the study patients was an increased waist circumference (51.1%), and the least prevalent criterion was hypertriglyceridemia (25.7%). Patients met on average 2.1 criteria ($S.D. = 1.4$), with female patients meeting significantly more criteria ($M = 2.8$, $S.D. = 1.4$) than male patients ($M = 1.7$, $S.D. = 1.4$, $p < .001$). In the univariate analyses no significant association was found between MetS and type or generation of antipsychotics used. Neither did we find a difference in MetS prevalence between patients using olanzapine or clozapine compared to patients using other or no antipsychotic ($\chi^2(1) = 3.95$, $p = .05$). Yet there was a significant effect for the chlorpromazine equivalent dose; patients with MetS used a lower chlorpromazine equivalent dose ($M = 400.0$ mg, $S.D. = 172.4$) than patients without MetS ($M = 478.0$ mg, $S.D. = 277.4$, $p = .004$). No associations were found between MetS and other psychotropic agents used. There was a significant association between treatment setting (in or outpatient) and MetS ($\chi^2(1) = 7.65$, $p = .006$). Furthermore, no significant associations between MetS and primary DSM-IV-R diagnoses were found. A significant association was found between MetS and comorbid SUD ($\chi^2(1) = 24.56$, $p < .001$). Also, smoking was significantly associated with MetS ($\chi^2(1) = 11.59$; $p = .001$).

3.3. Predictors of metabolic syndrome

Table 4 shows the binary logistic regression analysis. In the first block of the model, gender was the only significant predictor variable for MetS. The model, including age and gender, shows a good fit based on the Hosmer and Lemeshow test ($\chi^2(8) = .99$, $p = .998$), and the included variables contributed significantly to the regression model ($\chi^2(2) = 49.77$, $p < .001$). After the addition of the second block to the model, treatment setting and SUD showed to be significant predictors of MetS. Based on the odds ratio, female patients were almost 4 times more likely to have MetS compared to male patients ($p < .001$). Furthermore, outpatients were twice more likely having MetS compared to inpatients. However, a co-morbid SUD was associated with lower odds of having MetS. The model had a good fit based on the Hosmer and Lemeshow test ($\chi^2(8) = 6.98$, $p = .539$) after inclusion of the second block. Adding the variables of the second block to the regression model resulted in a significant change in the predictive value of the model ($\chi^2(4) = 12.31$, $p = .015$).

3.4. Comparison to the general population

The prevalence of metabolic abnormalities in the general population compared to the study patients, differentiated by gender, is presented in Table 5. Diabetes prevalence is significantly higher in patients with SMI (16.9%) compared to the general population (9.3%) ($\chi^2(1) = 19.96$, $p < .001$). After controlling for gender, this significant difference in diabetes prevalence remained only in the female patients (28.2% vs. 9.7%, χ^2 (1) = 36.48, $p < .001$). Furthermore, hypertension is significantly higher in all patients with SMI (37.4%) than in the general

Table 2
Pharmacological treatment of the study patients differentiated by gender (n = 350).

	All (n = 350)	Male (n = 240)	Female (n = 110)	P-value
Type antipsychotic				.3
None	2.9(10)	2.5(6)	3.6(4)	.6
1st generation	21.7(76)	19.2(46)	27.3(30)	.09
2nd generation	46.9(164)	48.8(117)	42.7(47)	.3
Combination 1st and 2nd	28.6(100)	29.6(71)	26.3(29)	.4
Antipsychotic treatment				
Monotherapy	64.9(227)	65.4(157)	63.6(70)	.8
Polytherapy	32.3(113)	32.1(77)	32.7(36)	
First generation antipsychotic				
Haldoperidol	24.9(87)	26.3(63)	21.8(24)	.4
Zuclopentixol	10.3(36)	9.6(23)	10.9(12)	.7
Flupentixol	8.3(29)	5.0(12)	15.5(17)	.001
Second generation antipsychotic				
Olanzapine	42.9(150)	47.1(113)	33.6(37)	.02
Risperidone	17.1(60)	13.8(33)	24.5(272)	.02
Clozapine	8.3(29)	10(24)	4.5(5)	.09
Anticholinergic	32.6(114)	33.3(80)	30.9(34)	.7
Benzodiazepine	50.3(176)	54.2(130)	30.9(34)	.03
Antidepressant	9.4(33)	6.7(17)	15.5(17)	.01
Mood stabilizer	21.1(74)	17.9(43)	28.2(31)	.03
Total number psychotropic drugs*	2.6 ± 1.2	2.6 ± 1.2	2.6 ± 1.4	
Chlorpromazine equivalency (daily dose in mg)*	448.9 ± 277.3	485.5 ± 271.9	369.2 ± 273.6	<0.001
Antidiabetic medication	13.4(47)	9.2(22)	22.7(25)	.001
Antihypertensive medication	22.6(79)	18.3(44)	31.8(35)	.005
Lipid-lowering medication	19.1(67)	16.3(39)	25.5(28)	.03

All data are described as proportions and number % (n), or as mean ± standard deviation if mentioned by (*).
P-values are described at <.01 meaning statistical significance.

population (19.9%) ($\chi^2(1) = 57.42$, $p < .001$). When controlling for gender, female patients with SMI have a significantly higher prevalence of increased waist circumference (88.2%) than women in the general population (65.3%) ($\chi^2(1) = 20.07$, $p < .001$). Likewise, female patients have the highest obesity rate (50.0%), significantly higher than in women in the general population (32.6%) ($\chi^2(1) = 13.8$, $p < .001$). No significant differences in BMI-categories and waist circumference criterion between the male samples were found.

4. Discussion

The overall MetS prevalence in African–Caribbean patients with SMI in Curaçao is 37.4%. As we hypothesized, the prevalence of MetS in this study is in line with the pooled MetS prevalence measured in the USA (36.4%) (Vancampfort et al., 2015). The most striking finding in this study is the large gender gap in MetS prevalence. African-Caribbean female patients have an alarmingly high MetS prevalence, 2.5 times higher than male patients (63.6% vs. 25.4%, $p < .001$) and were almost 4 times more likely to have MetS. When examining the individual criteria of MetS, these were very prevalent as well. Approximately 50% of patients in this study met the criteria for hypertension, low HDL level and increased waist circumference. All criteria were significantly more common in female patients, except for the hypertriglyceridemia criterion. Triglyceride levels are known to remain low in people of African descent, in spite of the presence of insulin resistance, type 2 diabetes or CVD. This is known as the triglyceride paradox, and is likely moderated by genetic factors (Osei and Gaillard, 2017; Tillin et al., 2013; Yu et al., 2012). Furthermore, in this study, 50% of female patients were obese. BMI is supposed to be highly intercorrelated with waist circumference, explaining the concerningly high proportion of female patients with an increased waist circumference compared to male patients in this study (88.2% vs. 34.1%, $p < .001$) (Alberti et al., 2009; Grol et al., 1997).

Our results are consistent with the findings from the African-American subsample of the CATIE study, South African studies and a Ghanaian study demonstrating a significant gender disparity in the prevalence of MetS (McEvoy et al., 2005; Owusu-Ansah et al., 2018; Saloojee et al., 2017, 2016). Saloojee et al. (2016) found a higher MetS prevalence in South African female patients (38.3%) than in the male patients (15.4%, $p < .001$). Likewise, Ghanaian female patients had almost a fourfold increase in risk for developing MetS compared to the male patients (Owusu-Ansah et al., 2018). Nevertheless, our study and the above-mentioned studies are inconsistent with previous meta-analyses, reporting no gender differences in MetS prevalence (Mitchell et al., 2013b; Vancampfort et al., 2015). The higher MetS prevalence in female patients could be explained by the greater propensity for obesity in African–Caribbean and African women (McEvoy et al., 2005; Saloojee et al., 2016, 2017). Although it is known that obesity is related to poor health outcomes, in African and African-Caribbean populations this notion may interfere with the sociocultural conception of beauty and social acceptance toward overweight in women (Chithambo and Huey, 2013; Grol et al., 1997; Hoek et al., 2005). Women of African descent have reported higher self-rated attractiveness and lower body weight perception in spite of their higher BMI compared to Caucasian women (Chithambo and Huey, 2013). Illustrative of this is the finding of Hoek et al. (2005) of nonexistent cases of anorexia nervosa among the African–Caribbean population in Curaçao.

MetS prevalence increased with older age in the univariate analysis, but not in the binary logistic regression analysis contrary to previous meta-analyses (Mitchell et al., 2013b; Vancampfort et al., 2015). Nonetheless, our study patients were old with a mean age of 51.9 years ($S.D.$ = 13.5) and in keeping with other studies the peak MetS prevalence was in the 55–64-year-old age group (30.5%) (Ventriglio et al., 2015). Considering the older mean age of the female patients (55.8 years, $S.D.$ = 11.8), the higher MetS prevalence in women may partly be explained by low estrogen levels in the postmenopausal period, that are suggested to promote obesity (Pradhan, 2014; Razzouk and Muntner, 2009; Regitz-Zagrosek et al., 2007). Further, increasing age is related with a longer lifespan exposure to unhealthy lifestyle factors such as bad dietary habits and a poor physical activity level (Vancampfort et al., 2015). Especially women seem to have a more sedentary lifestyle, and are less often engaging in physical activity compared to men (Verstraeten et al., 2013). Conversely, there was a decreasing prevalence of MetS in the male patients in the oldest (≥65

Table 3
Prevalence of the metabolic syndrome and its criteria differentiated by gender (n = 350).

	All (n = 350)	Male (n = 240)	Female (n = 110)	P-Value
MetS prevalence as defined by ATP-III-A[a],% (n)	37.4 (131)	25.4 (61)	63.6 (70)	<.001
Prevalence of the individual criteria for MetS, %(n):				
Waist circumference (M > 102 cm, F > 88 cm)[a]	51.1 (179)	34.1 (82)	88 0.2 (97)	<.001
BP (systolic ≥ 130 mmHg or diastolic ≥ 85 mmHg)[b]	49.4 (173)	42.5 (102)	64.5 (71)	<.001
HDL (M < 40 mg/dL F < 50 mg/d)[c]	50.6 (177)	46.7 (112)	59.1 (65)	.009
TG (≥150 mg/dL)[c]	25.7 (90)	25.0 (60)	27.2 (30)	.60
FG (≥100 mg/dL)[d]	28.6(100)	23.3 (56)	40.0 (44)	<.001
Number of criteria for MetS met, %(n):				<.001
0	15.7 (55)	21.7 (52)	2.7 (3)	
1	21.1 (74)	27.1 (65)	8.2 (9)	
2	25.7 (90)	25.8 (62)	25.5 (28)	
3	20.6 (72)	12.5 (30)	38.2 (42)	
4	13.1 (46)	9.2 (22)	21.8 (24)	
5	3.7 (13)	3.8 (9)	3.6 (4)	
Age-specific prevalence of MetS[b] (year), %(n):				.008
18–24	0 (0)	0 (0)	0 (0)	–
25–34	6.1 (8)	9.8 (6)	2.9 (2)	.096
35–44	16.8 (22)	18.0 (11)	15.7 (11)	.723
45–54	23.7 (31)	27.9 (17)	20.0 (14)	.291
55–64	30.5 (40)	31.1 (19)	30.0 (21)	.887
65–84	22.9 (30)	13.1 (8)	31.4 (22)	.013

All data are described as proportions and number, % (n), P-values <.01 meaning statistical significance.

[a] MetS was diagnosed in the minimal presence of 3 criteria.

[b] Or if treatment with antihypertensives.

[c] Or if treatment with lipid lowering medication.

[d] Or if treatment with antidiabetic medication.

Abbreviations: MetS = metabolic syndrome, ATP-III-A = Adult Treatment Panel III guidelines of the National Cholesterol Education Program with adapted value of fasting glucose of 100 mg/dl as suggested by the American Diabetes Association definition for the metabolic syndrome (MetS), M = male, F = female, BP = blood pressure, HDL = high-density lipoprotein, TG = triglycerides, FG = fasting glucose.

Table 4
The binary logistic regression analysis for variables predicting the metabolic syndrome.

Block	Predictor	B	SE	OR	95% CI
0	Constant	−0.51**	0.11	0.60	
1	Age	0.02	0.01	1.02	0.99–1.04
	Gender (male vs. female)	1.56 **	0.25	4.76	2.91–7.78
2	Age	0.02	0.01	1.02	0.99–1.04
	Gender	1.37**	0.29	3.92	2.21–6.96
	Treatment setting (inpatients vs. outpatients)	0.68**	0.27	1.98	1.18–3.34
	Smoking (no vs. yes)	0.18	0.36	1.20	0.66 –2.18
	Substance use disorder (no vs. yes)	−0.65*	0.32	0.52	0.28–0.98
	Chlorpromazine equivalent	−0.00	0.01	0.99	0.98–1.02

Note: N = 350.

* p < .05,.

** p < .01.

Block 1: R^2= 0.12 (Hosmer and Lemeshow), 0.13 (Cox and Snell), 0.18 (Nagelkerke). Model $\chi 2(2) = 49.77$, p < .01

Block 2: R^2= 0.15 (Hosmer and Lemeshow), 0.16 (Cox and Snell), 0.22 (Nagelkerke). Model $\chi 2(6) = 62.07$, p < .01 Abbreviations: OR = adjusted odds ratio; CI = confidence interval.

years) age-group, this could be attributed to the smaller sample size from that age group, but they could as well be a group of survivors, while other patients already deceased due to CVD at a younger age.

The results from this study demonstrate that outpatients were almost twice more likely having MetS compared to inpatients, contradicting the findings of the meta-analysis of Mitchell et al. (2013a, b) and the Canadian study of Cohn et al. (2004). However, it is in agreement with the results of the large multicenter survey of Sugai et al. (2016) indicating a higher prevalence of MetS in Japanese outpatients with schizophrenia compared to inpatients (34.2% vs. 13%). Likewise, Japanese outpatients were significantly more likely to be obese and had a higher prevalence of diabetes mellitus, hypertension and hypertriglyceridemia (Sugai et al., 2016). Possibly this is related to the lower physical activity level in outpatients compared to inpatients as suggested by the meta-analysis of Vancampfort et al. (2017). Of the 165 inpatients included in this study, 25 patients are living in protective housing and 108 patients are admitted in long stay wards for many years. Consequently, we can hypothesize that the inpatients in this study were more frequently monitored and benefitted from the already implemented health program for MetS in GGz Curaçao. Fast-food chains are omnipresent in Curaçao, consuming high-calorie meals and late night eating out at food trucks is common among the general population (Pan American Health Organization, 2011; Verstraeten et al., 2013). Inpatients may have a more balanced diet, and additionally, seeing that there are no fast-food restaurants in the vicinity of the psychiatric center, patients do not have easy access to them (Caspi et al., 2012; Pereira et al., 2005).

MetS prevalence did not differ between the primary psychiatric diagnoses, but our findings support that the presence of comorbid SUD is associated with lower odds of having MetS. Substance use is often associated with treatment noncompliance, self-neglect, malnutrition and underweight (Farabee and Shen, 2004; Mitchell et al., 2009; Vancampfort et al., 2016a, b; Virmani et al., 2006, 2007). The patients in this study mostly abused cocaine, which is generally supposed to reduce appetite (Ersche et al., 2013). Chronic cocaine use may lead to weight loss as a result of a reduction of the intra-abdominal fat mass (Meule, 2014; Sansone and Sansone, 2013). In addition, Vidot et al. (2016) reported lower odds of having MetS in adults with current and past use of cannabis in the USA. Also, cannabis and tobacco smoking are known to precipitate the cytochrome P540 1A2 activity and increases the metabolism in the liver of antipsychotics such as olanzapine and clozapine, which are known for their high risk of weight gain and MetS (Tsuda et al., 2014).

Although the male to female ratio in Curaçao is 0.84, this population with SMI shows a much greater number of male patients as compared to female patients. There are several explanations that should be taken into consideration. First, epidemiological studies suggest a greater ratio of men suffering from schizophrenia (Aleman et al., 2003; Leung and Chue, 2000; Ochoa et al., 2012). This male predominance seems to be associated across different regions with a higher comorbidity of substance abuse in men (Aleman et al., 2003; Lacey et al., 2016; Leung and Chue, 2000; Ochoa et al., 2012). Likewise, in this study comorbid SUD was present in 52.1% of the male patients compared to 7.3% of the female patients. Second, SUD in male patients may trigger violent behavior and precipitate psychotic disorders and is associated with poverty and social isolation (Aleman et al., 2003; Lacey et al., 2016; Marconi et al., 2016; Ochoa et al., 2012; Roncero et al., 2014). Hence, male patients with SUD are more likely to commit socially disruptive behaviors leading to (forced) hospitalizations (Farabee and Shen, 2004; Mitchell et al., 2009; Vancampfort et al., 2016a, b; Virmani et al., 2006, 2007). Third, women in the Caribbean are presumably more socially integrated and therefor may rely on a larger social network that supports them apart from psychiatric services (Lacey et al., 2016).

The MetS prevalence in this study is more than twice the MetS prevalence found in a Jamaican study, which is one of the few population-based studies on MetS conducted in an African-Caribbean population. In a large dataset of 1870 Jamaican participants, the prevalence of MetS was 18.4%, significantly higher in women (23%) than

Table 5
Prevalence of metabolic abnormalities in the general population compared to patients with severe mental illness, differentiated by gender.

	All		p	Male		p	Female		p
	Control	Patients (n = 350)		Control	Patients (n = 240)		Control	Patients (n = 110)	
Diabetes[a,*]	9.3	16.9	<.001	8.6	11.7	.13	9.7	28.2	<.001
Diabetes by age group (year)[a,*]									
18–25	0	0	–	0	0	–	0	0	–
25–34	3.0	0	–	3.9	0	–	2.3	0	–
35–44	4.0	4.8	.97	5.6	4.2	.96	2.7	6.7	.91
45–54	5.8	10.2	.11	5.4	7.9	.44	6.0	16.0	.14
55–64	14.6	27.6	.002	14.3	20.0	.27	14.8	42.4	<.001
65–74	24.0	36.2	.07	19.6	35.3	.14	27.1	36.7	.28
75+	21.0	27.3	.93	18.6	20.0	.72	23.3	100.0	–
Hypertension[b,*]	19.9	37.4	<.001	15.4	32.9	<.001	23.5	47.5	<.001
BMI category[**]									
Underweight	1.9	2.9	.22	1.8	4.2	.02	1.9	0	.26
Normal	33.0	33.4	.87	35.6	40.8	.13	30.8	17.3	.002
Overweight	36.8	30.0	.01	39.3	33.8	.10	34.7	21.8	.006
Obesity	28.3	28.0	.62	23.3	17.9	.07	32.6	50.0	<.001
Waist [c,***]	55.0	51.1	.31	38.8	34.1	.36	65.3	88.2	<.001

All data are described as proportions; *P*-values are described at <.01 meaning statistical significance.
Control data from the 2013 National Health Survey Curaçao.
* Self-reported data from 3000 patients (1081 men, 1919 women).
** Self-reported data in 2405 patients (1102 men, 1303 women).
*** Data from physical measurement in 401 patients (129 men, 284 women).
[a] In patients: diabetes if fasting glucose ≥126 mg/dL or on treatment with antidiabetic medication.
[b] In patients: hypertension if systolic ≥140 mmHg or diastolic ≥90 mmHg or on treatment with antihypertensives.
[c] Increased waist circumference, Male > 102 cm, Female > 88 cm.

in men (11%) (Ferguson et al., 2010a, b). When comparing our data with control indicators from the general Curaçaoan population; patients with SMI appear to have a significantly higher prevalence of hypertension and diabetes (Verstraeten et al., 2013). In both samples, diabetes prevalence was increasing with age. In line with the study of De Hert et al. (2006) the prevalence of diabetes was higher in patients with SMI in almost every age-group, despite that only a significant difference was observed in the 55–64-year-old age group. However, this could be due to the smaller sample size of patients in the younger age groups. After controlling for gender, female patients seem to have the highest burden of metabolic abnormalities; having the highest prevalence of diabetes (28.2%), hypertension (47.5%), obesity (50.0%) and increased waist circumference (88.2%) compared to both the general population and the male patients. Pre-existing metabolic abnormalities in patients with SMI, suggesting a genetic linkage between SMI and metabolic disturbances, may contribute to the high MetS and diabetes prevalence in the study patients (Mitchell et al., 2013a; Pillinger et al., 2017; Van Welie et al., 2013; Vancampfort et al., 2013; 2016b). Also, there is growing evidence for shared pathophysiological processes between metabolic abnormalities and SMI involving increased levels of pro-inflammatory cytokines (Perry et al., 2016, 2019; Vancampfort et al., 2016a). Moreover, obesity is also known to be associated with increased inflammation (Vancampfort et al., 2013). Besides, the higher prevalence of metabolic abnormalities in the study patients might also be due to the use of antipsychotics. Several studies have suggested a greater susceptibility to obesogenic and diabetogenic side effects of antipsychotics in people of African descent with SMI, particularly in women of African descent (Ader et al., 2008; Carliner et al., 2014; Meyer et al., 2009)

A major strength of the study is that it was entirely conducted on an island in the Caribbean, Curaçao, a unique catchment area and very appropriate for epidemiological surveys. Furthermore, almost all psychiatric patients in this catchment area were included, preventing selection bias. However, the generalizability of the results to other countries and populations requires that specific aspects of other countries and populations such as sociocultural aspects, race, age distribution, prevalence of co-morbidity, health care organization and budget, and others, should be taken into account. Despite the above mentioned, the results might not be generalized to all African-Caribbean populations, but only to other middle and high-income Caribbean small island developing states with a majority African-Caribbean population. Our study has some limitations. First, we had no data on MetS prevalence in the general population of Curaçao. Nevertheless, control data on diabetes, hypertension, obesity and waist circumference were available and could be compared to the data of this study. However, the self-reported data from the NHSC could underestimate the population prevalence. Tolonen et al. (2014) found lower prevalence rates of self-reported diabetes and hypertension, only in men, and a lower prevalence of self-reported obesity in both genders. Second, causal relationships cannot be established due to the cross-sectional design of this study, stressing the need of follow-up data. Third, it could be that other contributing factors for MetS that were not measured would have influenced the results such as socioeconomic status, physical activity level and dietary habits. Finally, the direct effect of antipsychotic treatment on MetS cannot be investigated because of the cross-sectional design of the study, the inclusion of older patients with a long duration of illness and long treatment history as weight gain induced by antipsychotics already has reached a ceiling effect (Alvarez-Jiménez et al., 2008; Bak et al., 2014; Correll et al., 2007).

5. Conclusions

To date, this is the largest study conducted in an African-Caribbean population with SMI examining the prevalence of MetS and its associated risk factors. The present study highlights the high prevalence of MetS (37.4%) in patients with SMI in Curaçao, as well as the large gender gap with nearly two out of three female patients suffering from MetS compared to one in four male patients. The higher MetS prevalence in female patients seems to be driven by a very high prevalence of obesity (50.0%). Also, the high prevalence of MetS in this study illustrates the interplay between genetic and environmental risk factors in the specific sociocultural context of a small island developing state in the Caribbean. This study supports that screening and treatment of metabolic abnormalities should be an indispensable part in the standard of care for patients with SMI.

Data statement

The research data are not publicly available to protect patient confidentiality. Requests to access the data should be directed to L. de Caluwé, Laura_deCaluwé@hotmail.com.

CRediT authorship contribution statement

Laura de Caluwé: Data curation, Formal analysis, Writing - original draft. **Nora van Buitenen:** Formal analysis, Data curation, Writing - review & editing. **Petra J. Gelan:** Conceptualization, Methodology, Data curation. **Cleo L. Crunelle:** Writing - original draft, Writing - review & editing. **Roeland Thomas:** Methodology, Data curation. **Sharon Casseres:** Conceptualization, Methodology, Data curation. **Frieda Matthys:** Writing - original draft, Writing - review & editing. **Peter van Harten:** Formal analysis, Writing - review & editing. **Wiepke Cahn:** Formal analysis, Writing - review & editing.

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Supplementary materials

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